

**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. SELECTED FINANCIAL DATA**

Not applicable.

**B. CAPITALIZATION AND INDEBTEDNESS**

Not applicable.

**C. REASONS FOR THE OFFER AND USE OF PROCEEDS**

Not applicable.

**D. RISK FACTORS**

*Our business faces significant risks. You should carefully consider all of the information set forth in this annual report and in our other filings with the U.S. Securities and Exchange Commission, or the SEC, including the following risk factors which we face and which are faced by our industry. Our business, financial condition or results of operations could be materially and adversely affected if any of these risks occurs. This report also contains forward-looking statements that involve risks and uncertainties. See "Special Note Regarding Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors including the risks described below and elsewhere in this annual report and our other SEC filings. See "Special Note Regarding Forward-Looking Statements" above.*

**Risks Related to the Development and Commercialization of Our Product Candidates**

***We are substantially dependent on the success of our lead product candidate, Nefecon and our recently acquired product candidate, setanaxib. If we are unable to successfully complete clinical development of, obtain regulatory approval for and commercialize Nefecon and setanaxib or experience significant delays in doing so, our business will be materially harmed.***

We currently have no product candidates approved for commercial sale. We have not completed the clinical development of any product candidates and we cannot guarantee that we will ever have marketable drug products. To date, we have invested substantially all of our efforts and financial resources in the research and development of Nefecon, which is currently in an ongoing Phase 3 clinical trial. We reported positive topline results from Part A of NefIgArd in the fourth quarter of 2020, where the trial met the primary and key secondary endpoint. Additionally, as a result of our acquisition of Genkyotex, we are developing Genkyotex's lead product candidate, setanaxib, or GKT831. Setanaxib has shown clinically relevant anti-fibrotic activity in a Phase 2 clinical trial in PBC, a fibrotic orphan disease, despite not achieving its primary endpoint. Based on its Phase 2 results, Genkyotex had interactions with the FDA during 2020 regarding the clinical development pathway for setanaxib in PBC. In January 2021, Genkyotex reported positive data from its Phase 1 clinical trial to evaluate the safety and pharmacokinetics of setanaxib at dosages up to 1,600 mg/day. Based on this data, Genkyotex plans to launch a pivotal and potentially registrational Phase 2/3 trial in setanaxib in PBC in the second half of 2021. In addition, Genkyotex plans to initiate a Phase 2 proof-of-concept study in head and neck cancer in 2021. Our near-term prospects, including our ability to finance our operations and generate revenue, will depend substantially on the successful development and commercialization of Nefecon and, to a lesser degree, setanaxib. The clinical and commercial success of our product candidates will depend on a number of factors, including:

- the timely completion of our planned and ongoing clinical trials;

- our ability to implement strategies to minimize the impact of the COVID-19 pandemic to our business, including with respect to initiating, enrolling, conducting or completing our planned and ongoing clinical trials and addressing any potential disruption or delays to the supply of our product candidates;
- our ability to demonstrate our product candidates' safety and efficacy to the satisfaction of the FDA, EMA, or comparable foreign regulatory authorities based on the endpoints that we are evaluating in our planned and ongoing clinical trials;
- our ability to comply with any requirements imposed by the FDA, EMA or comparable foreign regulatory authorities to conduct additional clinical trials in connection with approval to market our product candidates, including any additional testing following any accelerated or conditional approval by such regulatory authorities;
- our ability to obtain marketing approvals in the United States under the FDA's accelerated approval program and in Europe under the EMA's conditional approval program;
- the FDA's continued position that the 505(b)(2) regulatory pathway is available for Nefecon;
- our ability to confirm long-term renal benefit in Part B of NefIgArd, and anti-fibrotic activity in our pivotal and potentially registrational Phase 2/3 trial in setanaxib in PBC;
- our ability to maintain any regulatory approvals to market our product candidates that we may receive;
- the prevalence and severity of adverse side effects of our product candidates;
- our ability to successfully commercialize our product candidates, if approved for marketing and sale by the FDA, EMA or comparable foreign regulatory authorities, whether alone or in collaboration with others;
- the ability of our third-party manufacturers to manufacture quantities of our product candidates using commercially sufficient processes and at a scale sufficient to meet anticipated demand and to develop, validate and maintain a commercially viable manufacturing process that is compliant with current good manufacturing practices, or cGMP;
- our success in educating physicians and patients about the benefits, risks, administration and use of our product candidates;
- achieving and maintaining compliance with all regulatory requirements applicable to our product candidates;
- acceptance of our product candidates as safe and effective by patients and the medical community;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments;

- our ability to obtain and sustain an adequate level of coverage and reimbursement for our product candidates by third-party payors and patients' willingness to pay out-of-pocket in the absence of such coverage and adequate reimbursement;
- our ability to obtain and sustain an adequate level of reimbursement for our product candidates by third-party payors;
- the effectiveness of our own or any future strategic collaborators' marketing, sales and distribution strategy and operations;
- our ability to obtain, maintain, protect and enforce our intellectual property rights in and to our product candidates;
- our ability to avoid and defend against third-party patent interference or patent infringement claims or other intellectual property related claims;
- a continued acceptable safety profile of our product candidates following approval; and
- if approved, our ability to raise sufficient capital resources to fund the commercialization of our product candidates.

Many of these factors are beyond our control. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. In addition, even if we were to obtain approval, regulatory authorities may approve our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for Nefecon and setanaxib. If we are not successful in commercializing Nefecon and setanaxib, or are significantly delayed in doing so, our business will be materially harmed.

***The regulatory approval processes of the FDA, the EMA and comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain acceptance for filing and regulatory approval for Nefecon, setanaxib or future product candidates, our business will be substantially harmed.***

The time required to obtain approval by the FDA, the EMA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, laws or regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that Nefecon, setanaxib or any product candidates we may seek to develop in the future will never obtain regulatory approval. In March 2021, we announced the submission of an NDA to the FDA for Nefecon for IgAN, but there can be no assurance that the agency will accept such NDA for filing, nor can there be any assurance that Nefecon will receive any marketing approvals.

Any of our product candidates, including Nefecon and setanaxib, could fail to receive regulatory approval for many reasons, including the following:

- to the extent that we seek approval for any additional product candidates based on evaluation of a surrogate marker, including Nefecon, we may be unable to utilize the accelerated approval pathway under Subpart H of the FDA's New Drug Application, or NDA, regulations and comparable regulations promulgated by the EMA if such regulatory authorities do not accept our proteinuria data as a surrogate marker;

- the data collected from clinical trials of our product candidate may not be sufficient to support the submission of an NDA, to the FDA or other submission or to obtain regulatory approval in the United States, the European Union or elsewhere;
- the scientific advice and regulatory feedback provided by the FDA and EMA, as applicable, during the drug development phase is not legally binding, and the FDA or EMA may depart from such advice and feedback on the basis of justified grounds during assessment of future marketing authorization applications.
- we may be unable to demonstrate to the satisfaction of the FDA, the EMA or comparable foreign regulatory authorities that a product candidate is safe or effective for its proposed indication;
- the results of clinical trials may not be sufficiently statistically significant or clinically meaningful as required by the FDA, the EMA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that the product candidate's clinical and other benefits outweigh its safety risks;
- the FDA, the EMA or comparable foreign regulatory authorities may disagree with our interpretation of data from clinical trials;
- the FDA, the EMA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, the EMA or comparable foreign regulatory authorities or the laws they enforce may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy process towards approval as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, financial condition and results of operations. The FDA, the EMA and other comparable foreign regulatory authorities have substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for any of our product candidates. Even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA, the EMA or other comparable foreign regulatory authorities.

Additionally, disruptions at the FDA and other agencies may also lengthen the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which could adversely affect our business. For example, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. Separately, foreign and domestic inspections by the FDA have largely been on hold since March 2020 due to the COVID-19 pandemic, with FDA announcing plans in July 2020 to resume prioritized domestic inspections. Should FDA determine that an inspection is necessary for approval of a marketing application and an inspection cannot be completed during the review cycle due to restrictions on travel, the FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, the FDA may defer action on the application until an inspection can be completed. Additionally, as of June 23, 2020, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals; however, the FDA may not be able to continue its current pace and approval timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the COVID-19 pandemic and travel restrictions the FDA is unable to complete such required inspections during the review period. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs in the future, or if the COVID-19 pandemic continues to affect the operations of regulatory authorities, our ability to obtain approval of our product candidates may be adversely impacted.

***Accelerated approval by the FDA, and conditional approval by EMA, even if pursued for Nefecon or any other future product candidates, may not lead to a faster development process or regulatory review and does not increase the likelihood that our product candidates will receive marketing approval. If we are not successful with this process, the development or commercialization of Nefecon and such other product candidates could be delayed, abandoned or become significantly more costly.***

Based on feedback from the FDA and EMA, we plan to seek approval of Nefecon, and, if considered appropriate by the regulatory authorities, may seek approval of future product candidates using the FDA's accelerated approval and the EMA's conditional approval pathways. For Nefecon, our strategy is to use the accelerated approval pathway that would allow our Phase 3 clinical endpoint for FDA approval to be based on biomarker data from the 200 patients in Part A of the NefIgArd trial. For chronic kidney disease, clinical trials have generally relied on clinical endpoints based on outcomes, which have led to few new therapeutic drug candidates. In certain circumstances, the FDA selectively allows the use of surrogate endpoints to permit a faster development and an accelerated approval path. At our End-of Phase 2 meeting with the FDA, the agency indicated its acceptance of proteinuria as a surrogate marker in IgAN; however, our marketing application for Nefecon will be the first time that the FDA has been asked to issue an approval on the basis of proteinuria as a surrogate endpoint for accelerated approval in IgA nephropathy. Although this trial is designed to support accelerated approval if the data are positive, Nefecon may not have faster development or regulatory review timelines.

As a condition of approval, regulatory agencies may impose specific obligations, including to perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence. For Nefecon, Part B of NefIgArd is intended to serve as such a post-approval confirmatory trial to measure long-term renal benefit and to verify the clinical benefit of Nefecon. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. If the FDA or the EMA do not approve Nefecon on the basis of data presented after Part A of NefIgArd, but instead require the completion of the full Phase 3 clinical trial prior to the filing of marketing applications, the development and commercialization timeline of Nefecon will be delayed. Even if we do receive accelerated approval or conditional approval, we may not ultimately receive full approval from the regulatory agencies. The additional data generated through post-marketing clinical trials may not confirm that the benefit-risk balance of Nefecon or any other future product candidate is positive or the burden to further complete the obligations may become too high.

In the European Union, the conditional marketing authorization is subject to an annual renewal procedure that assesses the marketing authorization holder's compliance with the specific obligations of the authorization. If conditions are not being complied with, the EMA may decide to extend the timeline for the existing obligations, change the scope of such obligations or add new obligations, which may require additional financial resources and time. We may not be able to comply with such changed or additional obligations and may need to withdraw the marketing authorization. The EMA may also decide not to renew the conditional marketing authorization, although such measure is rarely applied in practice. An analysis of reimbursement decisions for conditionally authorized medicines in the European Union has shown some delays in the timeline for reaching a positive health technology recommendation. If this happens for Nefecon or any other future product candidate, it may delay the timing and success of the commercialization of such product.

***The use of proteinuria as a surrogate endpoint with an accelerated approval pathway to enable the advancement of Nefecon is a novel approach in nephrology.***

Part A of our Phase 3 clinical trial of Nefecon was designed with reduction of proteinuria, a surrogate biomarker, rather than an outcomes-based clinical endpoint, as the primary endpoint of the trial intended to support marketing applications with the FDA, EMA and comparable foreign regulatory authorities. The reduction in proteinuria is a novel surrogate biomarker that is designed to facilitate the advancements of new IgAN drugs such as Nefecon through the clinical trial process towards potential regulatory approval. However, we may not succeed in demonstrating the efficacy of Nefecon using this novel biomarker to the satisfaction of the regulatory agencies, notwithstanding positive results in earlier trials. In addition, the FDA, EMA or comparable regulatory authorities have not determined the required level of reduction of proteinuria that we would need to demonstrate in NefIgArd to obtain marketing approvals for Nefecon based on this surrogate biomarker.

Additionally, although we believe we have properly worked with FDA and EMA to facilitate the advancement of proteinuria as a surrogate endpoint, there can be no assurances that FDA and EMA will ultimately accept proteinuria data as a surrogate endpoint for the approval of Nefecon. The FDA and/or EMA may require us to provide additional data to support our regulatory applications, which may increase the complexity, uncertainty and length of the regulatory approval process for Nefecon. The FDA or EMA may also withdraw any approval granted based on a surrogate endpoint of Nefecon if Part B, the post-approval confirmatory phase of NefIgArd, does not validate proteinuria as a surrogate marker endpoint and validate the clinical benefit of Nefecon.

***Clinical trials are difficult to design and implement, and they involve a lengthy and expensive process with uncertain outcomes. We may experience delays in completing, or ultimately be unable to complete, the development and commercialization of our current and future product candidates.***

To obtain the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through extensive clinical trials that our product candidates are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Successful completion of clinical trials is a prerequisite to submitting an NDA to the FDA, a Marketing Authorization Application, or MAA, to the EMA and similar marketing applications to comparable foreign regulatory authorities for each product candidate and, consequently, the ultimate approval and commercial marketing of any product candidates. Failure can occur at any time during the clinical trial process and our future clinical trial results may not be successful.

Differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products. Where a randomized, placebo-controlled clinical trial is designed to allow enrolled subjects to cross-over from the placebo cohort to the treatment cohort, there may be a risk of inadvertent unblinding of subjects prior to cross-over, which may limit the clinical meaningfulness of those data and may require the conduct of additional clinical trials.

In addition, we may experience delays in completing clinical trials and initiating or completing additional clinical trials. We may also experience numerous unforeseen events during our clinical trials that could delay or prevent our ability to receive marketing approval or commercialize the product candidates we develop, including:

- delays in or failure to obtain institutional review board, or IRB, or ethics committee approval for each site;
- delays in or failure to recruit a sufficient number of suitable patients to participate in a trial;
- failure to have patients complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- failure to manufacture sufficient quantities of product candidate for use in clinical trials in a timely manner or shipping delays and interruptions;
- safety or tolerability concerns that could cause us or our collaborators, as applicable, to suspend or terminate a trial if we or our collaborators find that the participants are being exposed to unacceptable health risks;
- changes in regulatory requirements, policies and guidelines;
- failure of our third-party research contractors to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- delays in establishing the appropriate dosage levels in clinical trials; and
- the quality or stability of the product candidate falling below acceptable standards.

Disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, supplying, conducting or completing our planned and ongoing clinical trials. We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted or ethics committees, or by the FDA or other comparable foreign regulatory authorities, or recommended for suspension or termination by the Data Review Committee, or DRC, or Data Safety Monitoring Board, or DSMB, for such trial. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, the EMA or other comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, including those relating to the class to which our product candidates belong, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

If we experience delays in the completion of, or if we terminate, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. From time to time, we may interact with regulatory agencies with the aim of facilitating the development of our product candidates by achieving alignment on an efficient trial design, a modest number of enrolled patients or a relatively expedient timeline. However, there can be no assurances that such alignment will be reached and, even if achieved, that we will realize the intended benefits from these interactions. For example, while the FDA accepted a protocol design modification for NefIgArd that reduced the total trial size from 450 to 360 patients and shortened the follow-up period, there can be no assurance that NefIgArd will proceed in an expedient or capital-efficient manner.

Moreover, if we make changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions, which could delay our clinical development plan or marketing approval for our product candidates. Significant clinical trial delays could also allow our competitors to bring products to market before we do or shorten any periods during which we have the exclusive right to commercialize our product candidates and impair our ability to commercialize our product candidates.

Any of these occurrences may harm our business, financial condition and results of operations significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates or result in the cessation of development of our product candidates.

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

Before obtaining regulatory approvals for the commercial sale of Nefecon, setanaxib or any other product candidates we may develop, we must demonstrate through lengthy, complex and expensive clinical trials that our product candidates are both safe and effective for use in each target indication. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process, and there is a high risk of failure and we may never succeed in developing marketable products.

Clinical trials that we conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. If the results of current or future clinical trials are inconclusive with respect to the efficacy of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance, or if there are safety concerns associated with our product candidates, we may be delayed in obtaining marketing approval, if at all.

Even if the trials are successfully completed, clinical data such as the positive data we reported from Part A of NefIgArd in November 2020 are often susceptible to varying interpretations and analyses, and we cannot guarantee that the FDA, the EMA or other comparable foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. We cannot guarantee that the FDA, the EMA or other comparable foreign regulatory authorities will view our product candidates as having efficacy even if positive results are observed in clinical trials. For example, even if reductions in proteinuria are observed in Part A of NefIgArd, regulatory authorities may determine that such levels of reduction are not sufficient to warrant accelerated or conditional approval. To the extent that the results of the trials are not satisfactory to the FDA, the EMA or other comparable foreign regulatory authorities for support of a marketing application, approval of our product candidates may be significantly delayed, or we may be required to expend significant additional resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates.

Additionally, some of the clinical trials of Nefecon performed to date, including our Phase 2a clinical trial, were open-label trials. An “open-label” clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a “patient bias” where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Moreover, patients selected for early clinical studies often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

***Some of our clinical trials for our product candidates have been conducted outside the United States, and we may in the future conduct clinical trials for our product candidates, outside the United States, and the FDA, EMA or comparable foreign regulatory authorities may not accept data from such trials.***

Some of our clinical trials for our product candidates have been, and we may in the future choose to conduct one or more clinical trials, outside the United States, including in Europe. The acceptance of trial data from clinical trials conducted outside the United States or another jurisdiction by the FDA, EMA or comparable foreign regulatory authorities may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to Good Clinical Practice, or GCP, regulations. Additionally, the FDA’s clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, EMA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.



***The results of early-stage clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Initial success in a clinical trial may not be indicative of results obtained when these trials are completed or in later-stage trials.***

Product candidates in later stages of clinical trials, including those with larger numbers of enrolled patients, may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. For example, while our ongoing NefIgArd trial of Nefecon has a similar trial design as the Phase 2b clinical trial in terms of the endpoints evaluated, and we reported positive data from Part A of the NefIgArd trial, the results from the earlier trial and Part A of the NefIgArd trial may not necessarily be predictive of results that we may observe in Part B of the NefIgArd trial or other trials we may be required to conduct. Furthermore, there can be no assurance that any of our clinical trials will ultimately be successful or support further clinical development of any of our product candidates. There is a high failure rate for drugs proceeding through clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in clinical development even after achieving promising results in earlier preclinical studies and clinical trials, and any such setbacks in our clinical development could have a material adverse effect on our business, financial condition and results of operations.

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

From time to time, we may publish interim, topline or preliminary data from our clinical trials. For example, in November 2020, we announced positive topline results from Part A of NefIgArd, which investigated the effect of Nefecon versus placebo in adult patients with IgAN. Preliminary and interim data from our clinical trials may change as more patient data become available. Preliminary or interim data from our clinical trials are not necessarily predictive of final results. Preliminary and interim data are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues, more patient data become available and we issue our final clinical trial report. Interim, topline and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, preliminary, topline and interim data should be viewed with caution until the final data are available. Material adverse changes in the final data compared to the interim data could significantly harm our business prospects.

***We are pursuing the Section 505(b)(2) and hybrid application pathways for the regulatory approval of Nefecon and our other product candidates. If the FDA or EMA do not conclude that our other product candidates meet the requirements of Section 505(b)(2) or hybrid application, as applicable, or determine that Nefecon no longer qualifies for the Section 505(b)(2) regulatory pathway or hybrid application, as applicable, approval of such product candidates may be delayed, limited or denied, any of which would adversely affect our ability to generate operating revenues.***

We are pursuing a regulatory pathway pursuant to Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FDCA, and the hybrid application of the EU Centralized Procedure pursuant to article 10(3) of Directive 2001/83/EC for the approval of Nefecon. Section 505(b)(2) of the FDCA was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments, and permits the submission of an NDA where at least some of the information required for approval comes from preclinical studies or clinical trials not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The FDA interprets Section 505(b)(2) of the FDCA to permit the applicant to rely upon the FDA's previous findings of safety and efficacy for an approved product. The FDA requires submission of information needed to support any changes to a previously approved drug, such as published data or new studies conducted by the applicant or clinical trials demonstrating safety and efficacy. The FDA could require additional information to sufficiently demonstrate safety and efficacy to support approval.

If the FDA determines that our other product candidates do not meet the requirements of Section 505(b)(2), we may need to conduct additional clinical trials, provide additional data and information and meet additional standards for regulatory approval. If our product candidates do not meet the requirements of Section 505(b)(2) of the FDCA or are otherwise ineligible for approval via the Section 505(b)(2) regulatory pathway, the time and financial resources required to obtain FDA approval for these product candidates, and the complications and risks associated with these product candidates, would likely substantially increase. Moreover, a 505(b)(2) application will not be approved until any non-patent exclusivity listed in the FDA publication Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book, for the listed drug, or for any other drug with the same protected conditions of approval as our product, has expired. An inability to pursue the Section 505(b)(2) regulatory pathway would likely result in new competitive products reaching the market more quickly than our product candidates, which would likely materially adversely impact our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, we cannot assure you that our product candidates will receive the requisite approvals for commercialization.

Some pharmaceutical companies and other actors have objected to the FDA's interpretation of Section 505(b)(2) of the FDCA to allow reliance on the FDA's prior findings of safety and effectiveness. If the FDA changes its interpretation of Section 505(b)(2), or if the FDA's interpretation is successfully challenged in court, this could delay or even prevent the FDA from approving any Section 505(b)(2) application that we submit. Moreover, the FDA has adopted an interpretation of the three-year exclusivity provisions whereby a 505(b)(2) application can be blocked by exclusivity even if it does not rely on the previously-approved drug that has exclusivity (or any safety or effectiveness information regarding that drug). Under the FDA's interpretation, the approval of one or more of our product candidates may be blocked by exclusivity awarded to a previously-approved drug product that shares certain innovative features with our product candidates, even if our 505(b)(2) application does not identify the previously-approved drug product as a listed drug or rely upon any of its safety or efficacy data. Any failure to obtain regulatory approval of our product candidates would significantly limit our ability to generate revenues, and any failure to obtain such approval for all of the indications and labeling claims we deem desirable could reduce our potential revenues.

Moreover, even if these product candidates are approved under the Section 505(b)(2) regulatory pathway the approval may be subject to limitations on the indicated uses for which the products may be marketed or to other conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

***Our product candidates may have serious adverse, undesirable or unacceptable side effects which may delay or prevent marketing approval. If such side effects are identified during the development of our product candidate or following approval we may need to abandon our development of such product candidate, the commercial profile of any approved label may be limited, or we may be subject to other significant negative consequences following marketing approval.***

Undesirable side effects that may be caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, the EMA or other comparable foreign regulatory authorities. Budesonide is a corticosteroid, a class of drugs that is associated with high blood pressure, weight gain, diabetes, serious infections and osteoporosis.

While budesonide has limited systemic availability due to high first pass metabolism and Nefecon is designed to leverage this inherent characteristic for local, rather than systemic effect, there can be no assurance we will avoid any or all of the side effects that may arise with corticosteroid treatment, whether local or systemic.

Although Nefecon has been generally well tolerated in previous clinical trials, the results from our ongoing or future trials may not replicate these observations. In our Phase 2b clinical trial of Nefecon, there were two drug-related serious adverse events, the first in a patient in the 16 mg treatment cohort who developed a deep venous thrombosis, which was classified by the investigator as possibly being treatment-related, and the second in a patient in the 8 mg treatment cohort who experienced aggravation of renal condition, which was classified by the investigator as possibly being treatment-related. In the placebo cohorts, three patients reported four serious adverse events (two events of proteinuria, sciatica and aggravated condition). Of these, two (proteinuria and aggravated condition) were classified by the investigator as possibly being treatment-related at the time when the safety results were blinded. We also observed adverse events that were generally consistent with those known to be associated with systemic corticosteroids like budesonide and a number of patient discontinuations due to mild to moderate adverse events, most frequently, acne and other transitory cosmetic side effects.

The results of our Phase 3 clinical trial for Nefecon or any future clinical trials we conduct may show that our product candidates cause undesirable or unacceptable side effects. In such an event, our trials could be suspended or terminated and the FDA, the EMA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and results of operations significantly.

Additionally, if Nefecon, setanaxib or any of our future product candidates receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by Nefecon, setanaxib or such other products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product and require us to take our approved product off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
- regulatory authorities may require a medication guide outlining the risks of such side effects for distribution to patients, or that we implement a risk evaluation and mitigation strategy plan to ensure that the benefits of the product outweigh its risks;
- we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we may be subject to limitations on how we may promote the product;
- sales of the product may decrease significantly;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us, our collaborators or our potential future partners from achieving or maintaining market acceptance of the affected product or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenue from the sale of our products.

***We may find it difficult to enroll patients in our clinical trials given the relatively smaller patient population who have the diseases for which our product candidates are being developed. If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary marketing approvals could be delayed or prevented.***

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, EMA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. While we recently announced in January 2021 that we completed full enrollment in the ongoing NefIgArd trial, there can be no assurance that we will not experience enrollment challenges in future trials, particularly those for indications with relatively small patient populations. In addition, because we are initially focused on developing product candidates for orphan indications, we may encounter similar challenges for patient enrollment if and when we commence clinical programs for additional product candidates in the future.

Patient enrollment may be affected if our competitors have ongoing clinical trials for product candidates that are under development for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trial instead enroll in clinical trials of our competitors' product candidates. Patient enrollment may also be affected by other factors, including:

- size and nature of the patient population;

- severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;
- patient eligibility and exclusion criteria for the trial in question;
- patients' and clinicians' perceived risks and benefits of the product candidate under study;
- competing clinical trials;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients;
- continued enrollment of prospective patients by clinical trial sites; and
- potential disruptions caused by the COVID-19 pandemic, including difficulties in initiating clinical sites access policies, or enrolling and retaining participants, diversion of healthcare resources away from clinical trials, travel or quarantine policies that may be implemented and other factors.

Our inability to enroll a sufficient number of patients for our clinical trials may result in significant delays or may require us to abandon such trial altogether. Even though we were able to enroll the planned number of patients in the NefIgArd clinical trial, there can be no assurance that we will successfully enroll the necessary number of patients in any additional clinical trials we may conduct. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

***As an organization, we have never completed pivotal clinical trials, and we may be unable to do so for any product candidates we may develop.***

We will need to successfully complete pivotal clinical trials in order to obtain the approval of the FDA, EMA or comparable foreign regulatory authority to market Nefecon or any future product candidate. Carrying out later-stage clinical trials is a complicated process. As an organization, we have completed the first part of our Phase 3 NefIgArd trial, but Part B remains ongoing. Accordingly, we have not yet completed any later stage or pivotal clinical trials. In order to do so, we will need to expand our clinical development and regulatory capabilities, and we may be unable to recruit and train qualified personnel. We also expect to continue to rely on third parties to conduct our pivotal clinical trials. See "Item 3.D.—Risk Factors—Risks Related to our Dependence on Third Parties." Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to filings for market approval for Nefecon or future product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates.

***Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.***

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing or notification to or approval by the FDA, EMA or comparable regulatory authorities. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

**We have been granted orphan drug designation for IgAN, PBC and AIH and may seek orphan drug designation in other indications for future product candidates we develop. We may be unsuccessful or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.**

In May 2010, the FDA granted orphan drug designation to Nefecon to slow the progression of IgAN and delay kidney failure in patients affected by the disease. In November 2016 the European Commission granted Nefecon orphan designation for the treatment of primary IgAN. We have also received orphan drug designation for PBC and AIH. In addition, we acquired a controlling interest in Genkyotex, which owns setanaxib and has received orphan drug designation from the FDA and orphan designation from the European Commission for PBC. We may seek orphan drug designations for other future product candidates. There can be no assurances that we will be able to obtain such designations.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers.

Similarly, in the European Union, the European Commission grants orphan designation after receiving the opinion of the EMA Committee for Orphan Medicinal Products on an orphan designation application. Orphan designation is intended to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions and either (i) such disease affects not more than 5 in 10,000 persons in the European Union or (ii) it is unlikely that the marketing of the medicine in the European Union would generate sufficient return to justify the necessary investment in its development. In each case, orphan designation will only be granted if no satisfactory method of diagnosis, prevention, or treatment for the relevant condition has been authorized, or where such method exists, the product in question would be of significant benefit to those affected. In the European Union, orphan designation entitles a party to a number of incentives, such as protocol assistance and scientific advice specifically for designated orphan medicines, and potential fee reductions depending on the status of the sponsor.

Generally in the United States and the European Union, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA, as applicable, from approving another marketing application for the same drug and indication in the United States or a similar drug for the same indication in the European Union for that time period, except in limited circumstances. The applicable period is seven years in the United States and ten years in the European Union. The European Union exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan designation *inter alia* if the drug is sufficiently profitable such that market exclusivity is no longer justified. Where the European Union marketing authorization application for an orphan drug includes the results of all studies conducted in compliance with an agreed pediatric investigation plan, the ten-year market exclusivity period is extended to twelve years. We obtained a positive opinion from the EMA Pediatrics Committee on our Pediatric Investigation Plan for Nefecon for the treatment of IgAN in December 2019. The European Commission is evaluating the experience gathered with the orphan regulation and may propose changes to the market exclusivity incentive as it exists today.

Orphan drug exclusivity may not effectively protect the product candidate from competition because different therapies can be approved for the same condition and the same therapies can be approved for different conditions but used off-label. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. While we may seek orphan drug designation for other indications for our current and any future product candidates, we may never receive such designations. Further, even with respect to the indications for which we have received orphan designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products, and thus, for example, approval of our product candidates could be blocked for seven years if another company previously obtained approval and orphan drug exclusivity in the United States for the same drug and same condition.

***The target patient population of Nefecon for the treatment of IgAN is small and has not been definitively determined, and if our estimates of the number of treatable patients is lower than expected, our potential revenues from sales of our product candidates, if approved, and our ability to achieve profitability would be compromised.***

Our estimates of both the number of patients who have IgAN, as well as the subset of patients with these diseases in a position to receive Nefecon, if approved, are based on our beliefs and estimates, and these estimates may prove to be incorrect. These estimates have been derived from a variety of sources, including scientific literature, input from physicians that treat patients with the diseases we are targeting, patient foundations and secondary market research databases. For example, our estimates of the prevalence of IgAN in certain geographies are based in part on the published prevalence of IgAN among patient populations in the United States split across ethnicities, and in part on our own analyses of prevalence in Europe, and on published disease incidence rates for certain geographies and estimated for the populations of such geographies. Further, new studies may change the estimated incidence or prevalence of IgAN, and any regulatory approvals that we may receive for Nefecon may include limitations for use or contraindications that decrease the addressable patient population. Accordingly, our target patient populations may turn out to be lower than expected, in which case the potential revenues from sales of our product candidates, if approved, would be lower than expected.

***We were not involved in the early development of setanaxib; therefore, we are dependent on third parties having properly conducted setanaxib's preclinical research, manufacturing control and clinical development.***

We had no involvement in or control over the preclinical and clinical development or manufacturing of setanaxib, which we acquired upon completion of the Acquisition (as defined below). We are dependent on third parties having conducted setanaxib research and development in accordance with legal, regulatory and scientific standards and the applicable protocols; having accurately reported the results of all setanaxib preclinical studies and clinical trials; and having correctly collected and interpreted the data from these studies and trials. If these activities were not compliant, accurate or correct, the clinical development, regulatory approval or commercialization of setanaxib products, if pursued, could be adversely affected.

***We face significant competition for our drug discovery and development efforts, and if we do not compete effectively, our commercial opportunities will be reduced or eliminated.***

The market for biopharmaceutical products is highly competitive. Our competitors include many established pharmaceutical companies, biotechnology companies, universities and other research or commercial institutions, many of which have substantially greater financial, research and development resources than us. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing pharmaceutical products. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, the development of our product candidates. The fields in which we operate are characterized by rapid technological change and innovation. See "Item 4.D.—Business Overview—Competition."

We anticipate that we will continue to face intense and increasing competition as new treatments enter the market and advanced technologies become available. There can be no assurance that our competitors are not currently developing, or will not in the future develop, products that are equally or more effective or are more economically attractive than any of our current or future product candidates. Competing products may gain faster or greater market acceptance than our products and medical advances or rapid technological development by competitors may result in our product candidates becoming non-competitive or obsolete before we are able to recover our development and commercialization expenses. If we, our product candidates do not compete effectively, it may have a material adverse effect on our business, financial condition and results of operations.

***If we fail to develop and commercialize other product candidates in addition to Nefecon, including setanaxib, we may be unable to grow our business and our ability to achieve our strategic objectives would be impaired.***

Although the development and commercialization of Nefecon for the treatment of IgAN is our primary focus, as part of our longer-term growth strategy we plan to evaluate Nefecon or its active ingredient budesonide in other potential indications, including PBC and AIH, and setanaxib for the treatment of PBC and head and neck cancer. We also intend to evaluate additional potential indications for setanaxib, and we may choose to in-license or acquire other product candidates as well as commercial products to treat patients suffering from other orphan diseases with significant unmet medical needs and limited treatment options. These other potential product candidates will require additional, time-consuming development efforts prior to commercial sale, including clinical trials and approval by the FDA, EMA and/or applicable comparable foreign regulatory authorities. All future potential product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives. Our current strategy is to in-license or otherwise acquire product candidates for clinical development rather than discovering such candidates ourselves, and therefore our growth objectives are dependent on our ability to enter into in-licensing arrangements or acquisitions. For any such candidates that we do not intend to conduct preclinical or early-stage clinical research, we may also become reliant on the research efforts of third parties. If we are unsuccessful in identifying and developing additional product candidates, our potential for growth and achieving our strategic objectives may be impaired.

***We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial and management resources, we focus on development programs and product candidates that we identify for specific indications. As such, we are currently primarily focused on the development of Nefecon and setanaxib, and we may forego or delay pursuit of opportunities with other product candidates or for other indications for Nefecon or setanaxib that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future development programs and product candidates for specific indications may not yield any commercially viable products. 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 royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

***Even if Nefecon, setanaxib or any future product candidate of ours receives regulatory approval, it may fail to achieve the degree of market acceptance among physicians, patients, third-party payors and the medical community necessary for commercial success.***

To date, we have no products authorized for marketing, and even if Nefecon, setanaxib or one or more of our future product candidates are approved for commercialization, they may not achieve an adequate level of acceptance by physicians, patients third-party payors and the medical community for commercial success. Despite the studies we have done on the IgAN commercial market opportunity and other pre-commercial activities that we have undertaken, there can be no assurance that we will be successful in marketing Nefecon, if approved. In addition, efforts to educate the medical community and third-party payors on the benefits of Nefecon or our other product candidates may require significant resources and may never be successful which would prevent us from generating significant revenues or becoming profitable. While we believe that the U.S. IgAN market could be adequately covered by a specialized salesforce of approximately 40 representatives, we may underestimate the number of representatives that we will actually require. In addition, we are currently focused on developing drug products that can be approved under abbreviated regulatory pathways in the United States, such as the 505(b)(2) regulatory pathway, and in the European Union such as article 10 (3) Directive 2001/83/EC legal basis, which allows us to rely on existing knowledge of the safety and efficacy of the relevant reference listed drugs to support our applications for approval in the United States and in the European Union. While we believe physicians, patients and other members of the medical community may more readily accept and use our product candidates, if approved, as compared to entirely new chemical entities, our product candidates may nonetheless fail to gain sufficient market acceptance by physicians, patients, other healthcare providers and third-party payors. Market acceptance of our future products by physicians, patients and third-party payors will depend on a number of factors, many of which are beyond our control, including, but not limited to:

- the clinical indications for which our existing or future product candidates are approved;
- physicians, hospitals, treatment centers, and patients considering our existing or future product candidates as a safe and effective treatment;
- the potential and perceived advantages of our product candidates over alternative treatments;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA, the EMA or comparable foreign regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA, the EMA or comparable foreign regulatory authorities;
- the timing of market introduction of our product candidates in relation to other potentially competitive products;
- the cost of our product candidates in relation to alternative treatments;
- the amount of upfront costs or training required for physicians to administer our product candidates;
- the availability of coverage and adequate reimbursement from third-party payors and government; authorities;
- the willingness of patients to pay out-of-pocket in the absence of comprehensive coverage and reimbursement by third-party payors and government authorities;
- the relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies;
- the effectiveness of our sales and marketing efforts and distribution support; and
- the presence or perceived risk of potential product liability claims.



Our efforts to educate physicians, patients, third-party payors and others in the medical community on the benefits and risks of our products, if approved, may require significant resources and may never be successful.

If our product candidates fail to gain market acceptance, this will have a material adverse impact on our ability to generate revenues to provide a satisfactory, or any, return on our investments. Even if some products achieve market acceptance, the market may prove not to be large enough to allow us to generate significant revenues.

***The successful commercialization of Nefecon or any future product candidates we develop will depend in part on the extent to which governmental authorities and health insurers establish coverage and adequate reimbursement levels, as well as pricing policies. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.***

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford Nefecon or any of our future product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for our other products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize, and attract additional collaboration partners to invest in the development of, our product candidates. 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 patient out-of-pocket costs that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the European Union or elsewhere will be available for any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidate and other therapies as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidate, pricing of existing drugs may limit the amount we will be able to charge for our product candidate. These payors may deny or revoke the reimbursement status of a given drug product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on products that we may develop.

Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

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

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs will be covered. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs. Some third-party payors may require pre-approval of coverage for new or innovative drug therapies before they will reimburse health care providers who use such therapies. Increasingly, the third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are seeking greater upfront discounts, additional rebates and other concessions to reduce the prices for therapeutics. If the price we are able to charge for any therapeutics we develop, or the reimbursement provided for such therapeutics, is inadequate in light of our development and other costs, our return on investment could be adversely affected. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Obtaining and maintaining reimbursement status is time-consuming and costly. No uniform policy for coverage and reimbursement for drug products exist among third-party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. 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. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely. Further, due to the COVID-19 pandemic, millions of individuals have lost or will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize our products. It is unclear what effect the Special Enrollment Period may have.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most European Union member states, or Member States, have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Governments may support small scale pharmacy compounding (preparation of a drug in a pharmacy by a qualified pharmacist for an individual patient) of patented drugs as an alternative for expensive innovative drugs (forming a specific risk for orphan drugs with a small population) and may increasingly consider compulsory licensing of patented drugs to provide alternative options and control pharmaceutical prices. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize any products for which we obtain marketing approval.

Moreover, increasing efforts by governmental and third-party payors in the European Union, the United States and other jurisdictions to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products, and government policies and efforts to contain costs could decrease the price we may receive for our products, if approved.

**Recent federal legislation and actions by federal, state and local governments may permit reimportation of drugs from foreign countries into the United States, including foreign countries where the drugs are sold at lower prices than in the United States, which could materially adversely affect our operating results.**

We may face competition in the United States for our development candidates and investigational medicines, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products.

In the United States, the Medicare Modernization Act, or MMA, contains provisions that call for the promulgation of regulations that expand pharmacists' and wholesalers' ability to import cheaper versions of an approved drug and competing products from Canada, where there are government price controls. Further, the MMA provides that these changes to U.S. importation laws will not take effect, unless and until the Secretary of the HHS certifies that the changes will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of products to consumers. On September 23, 2020, the Secretary of the HHS made such certification to Congress, and on October 1, 2020, the FDA published a final rule that allows for the importation of certain prescription drugs from Canada. Under the final rule, States and Indian Tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the FDA for review and authorization. Since the issuance of the final rule, several industry groups have filed federal lawsuits challenging multiple aspects of the final rule, and authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. On September 25, 2020, CMS stated drugs imported by States under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. Separately, the FDA also issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The regulatory and market implications of the final rulemaking and guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances, but legislation, or regulation allowing the reimportation of drugs, if enacted, could decrease the price we receive for our products and adversely affect our future revenues and prospects for profitability.

**We have never commercialized a product candidate before and may lack the necessary expertise, personnel and resources to successfully commercialize our products on our own or together with suitable partners.**

While we are working to build out a sales and marketing infrastructure to support any approvals we may receive for Nefecon and setanaxib, we do not have an existing sales and marketing infrastructure and have no experience in the sale or marketing of biopharmaceutical products. To achieve commercial success for any approved product, we must develop or acquire a sales and marketing organization, outsource these functions to third parties or enter into partnerships.

There are risks involved in both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. If approved by the FDA, we intend to commercialize Nefecon for primary IgAN in the United States independently. In other key territories such as Europe, we intend to commercialize Nefecon through either a broad regional partnership or on a country-by-country basis. Even if we establish sales and marketing capabilities, we may fail to launch or market our products effectively because we have no experience in the sales and marketing of biopharmaceutical products. In addition, recruiting and training a sales force is expensive and time consuming and could delay any product launch. In the event that any such launch is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses, 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 our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;

- the inability of sales personnel to obtain access to or effectively educate adequate numbers of physicians to prescribe our products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- costs of marketing and promotion above those anticipated by us.

If we enter into arrangements with third parties to perform sales and marketing services, our product revenues or the profitability of these product revenues to us could be lower than if we were to market and sell any products that we develop ourselves. Such collaborative arrangements with partners may place the commercialization of our products outside of our control and would make us subject to a number of risks including that we may not be able to control the amount or timing of resources that our collaborative partner devotes to our products or that our collaborator's willingness or ability to complete its obligations, and our obligations under our arrangements may be adversely affected by business combinations or significant changes in our collaborator's business strategy. In addition, we may not be successful in entering into arrangements with third parties to sell and market our products or may be unable to do so on terms that are favorable to us. Acceptable third parties may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we may not be successful in commercializing our products, which in turn would have a material adverse effect on our business, financial condition and results of operations.

***Healthcare legislative reform measures may have a negative impact on our business and results of operations.***

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements, (ii) additions or modifications to product labeling, (iii) the recall or discontinuation of our products or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect our business, financial condition and results of operations.

Among policy makers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% as of January 1, 2019 pursuant to the Bipartisan Budget Act of 2018) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the United States Supreme Court and members of Congress have introduced several pieces of legislation aimed at significantly revising or repealing the ACA. The United States Supreme Court is expected to rule on a legal challenge to the constitutionality of the ACA in early 2021. The implementation of the ACA is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Litigation and legislation related to the ACA are likely to continue, with unpredictable and uncertain results.

Beginning in January 2017, former President Trump signed Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. The former Trump administration had concluded that cost-sharing reduction, or CSR, payments to insurance companies required under the ACA had not received necessary appropriations from Congress and announced that it will discontinue these payments immediately until those appropriations are made. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. On August 14, 2020, the U.S. Court of Appeals for the Federal Circuit ruled in two separate cases that the federal government is liable for the full amount of unpaid CSRs for the years preceding and including 2017. For CSR claims made by health insurance companies for years 2018 and later, further litigation will be required to determine the amounts due, if any. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. On April 27, 2020, the United States Supreme Court reversed the Federal Circuit decision that previously upheld Congress' denial of \$12 billion in risk corridor funding, concluding the government has an obligation to pay these risk corridor payments under the relevant formula. Separately, in December 2018, the CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of the federal district court litigation regarding the method CMS uses to determine this risk adjustment. Since then, the ACA risk adjustment program payment parameters have been updated annually.

Moreover, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to increase the point-of-sale discount (from 50% under the ACA to 70%) that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closed the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Since then, the ACA risk adjustment program payment parameters have been updated annually. In addition, CMS published a final rule that gave states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2030 unless additional Congressional action is taken. The Coronavirus Aid, Relief and Economic Security Act, or CARES Act, which was signed into law in March 2020 and is designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, and subsequent legislation, suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2021. Proposed legislation, if enacted, would extend this suspension for the duration of the pandemic. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws and regulations may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the former Trump administration's budget proposal for fiscal year 2021 includes a \$135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the former Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Additionally, the former Trump administration previously released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contained proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services, or HHS, solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. However, it is unclear whether the Biden administration will challenge, reverse, revoke or otherwise modify these executive and administrative actions after January 20, 2021.

In addition, there have been several changes to the 340B drug pricing program, which imposes ceilings on prices that drug manufacturers can charge for medications sold to certain health care facilities. On December 27, 2018, the District Court for the District of Columbia invalidated a reimbursement formula change under the 340B drug pricing program, and CMS subsequently altered the FYs 2019 and 2018 reimbursement formula on specified covered outpatient drugs, or SCODs. The court ruled this change was not an “adjustment” which was within the Secretary’s discretion to make but was instead a fundamental change in the reimbursement calculation. However, most recently, on July 31, 2020, the U.S. Court of Appeals for the District of Columbia Circuit overturned the district court’s decision and found that the changes were within the Secretary’s authority. On September 14, 2020, the plaintiffs-appellees filed a Petition for Rehearing En Banc (i.e., before the full court), but was denied on October 16, 2020. Plaintiffs-appellees filed a petition for a writ of certiorari at the Supreme Court on February 10, 2021. It is unclear how these developments could affect covered hospitals who might purchase our future products and affect the rates we may charge such facilities for our approved products in the future, if any.

In 2020, former President Trump announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. In response, the FDA released a final rule on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and would have applied to all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. However, in response to a lawsuit filed by several industry groups, on December 28, the U.S. District Court for the Northern District of California issued a nationwide preliminary injunction enjoining government defendants from implementing the MFN Rule pending completion of notice-and-comment procedures under the Administrative Procedure Act. On January 13, 2021, in a separate lawsuit brought by industry groups in the U.S. District of Maryland, the government defendants entered a joint motion to stay litigation on the condition that the government would not appeal the preliminary injunction granted in the U.S. District Court for the Northern District of California and that performance for any final regulation stemming from the MFN Interim Final Rule shall not commence earlier than 60 days after publication of that regulation in the Federal Register. Further, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada and the MFN Model may materially and adversely affect the price we receive for any of our product candidates. Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to an order entered by the U.S. District Court for the District of Columbia, the portion of the rule eliminating safe harbor protection for certain rebates related to the sale or purchase of a pharmaceutical product from a manufacturer to a plan sponsor under Medicare Part D has been delayed to January 1, 2023. Further, implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed. Although a number of these and other measures may require additional authorization to become effective, and the Biden administration may reverse or otherwise change these measures, Congress has indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Further, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act. Under the Cures Act, the manufacturer must develop a policy on evaluating and responding to patient requests for expanded access. The manufacturer must make the policy public and readily available, and must respond to patient requests according to that policy.

We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug, which could have an adverse effect on customers for our product candidates. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

In the European Union, the policy debate is focused on the impact of intellectual property protection and regulatory incentives on innovation and patient access. Specifically, the European Commission has gathered information on the experience with the orphan drug regulation and paediatric regulation and may consider changes to incentives such as market exclusivity for orphan drugs, small scale pharmacy compounding and compulsory licensing of patented drugs.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction, particularly in light of the recent presidential election. In addition, it is possible that additional governmental action is taken to address the COVID-19 pandemic. There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

***Even if we, or any future collaborators, obtain regulatory approvals for Nefecon, setanaxib or any other future product candidate, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products, which could impair our ability to generate revenue.***

Once regulatory approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain regulatory approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we and any future collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA or EMA requirements, including ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practices, or cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA, EMA or other regulatory authorities, to monitor and ensure compliance with cGMPs. Despite our efforts to audit and verify regulatory compliance, one or more of our third-party manufacturing vendors may be found on regulatory inspection by the FDA or other authorities to be not in compliance with cGMP regulations, which may result in shutdown of the third-party vendor or invalidation of drug product lots or processes. In some cases, a product recall may be warranted or required, which would materially affect our ability to supply and market our drug products.

The marketing authorization holder is subject to extensive regulations in relation to the safety monitoring of its marketed products including good vigilance practices, or GVP, and will be subject to monitoring by the FDA, EMA and other regulatory authorities involving inspections of pharmacovigilance systems. Non-compliance with GVP can result in inspection follow-up, actions on the marketing authorization (such as suspensions or restrictions), as well as administrative penalties and civil or criminal liabilities.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction, particularly in light of the recent presidential election. In addition, it is possible that additional governmental action is taken to address the COVID-19 pandemic.

Accordingly, assuming we, or any future collaborators, receive regulatory approval for one or more of our product candidates, we, and any future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any future collaborators, are not able to comply with post-approval regulatory requirements, we, and any future collaborators, could have the regulatory approvals for our products withdrawn by regulatory authorities and our, or any future collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

***Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not mean that we will be successful in obtaining marketing approval of our current and future product candidates in other jurisdictions.***

Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain marketing approval in any other jurisdiction, while a failure or delay in obtaining marketing approval in one jurisdiction may have a negative effect on the marketing approval process in others. For example, even if the FDA grants marketing approval of Nefecon, setanaxib or any other future product candidate, the EMA and comparable foreign regulatory authorities must also approve the manufacturing, marketing and promotion of the product candidate in those jurisdictions. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.



***We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or at the commercial stage; and our product liability insurance may not cover all damages from such claims.***

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of biopharmaceutical products. Currently, we have no products that have been approved for commercial sale; however, the current and future use of our existing or future product candidates by us and our collaborators in clinical trials, and the potential sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients who use the product, healthcare providers, pharmaceutical companies, our collaborators or others selling such products. Any claims against us, regardless of their merit, could be difficult and costly to defend and could materially adversely affect the market for our product candidates or any prospects for commercialization of our product candidates. Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a product, even after regulatory approval, may exhibit unforeseen side effects. If any of our product candidates were to cause adverse side effects during clinical trials or after approval of the product candidate, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products due to negative public perception;
- injury to our reputation;
- withdrawal of clinical trial participants or difficulties in recruiting new trial participants;
- initiation of investigations by regulators;
- costs to defend or settle the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenues from product sales; and
- the inability to commercialize any of our product candidates, if approved.

Although we believe we maintain adequate product liability insurance for our product candidates, it is possible that our liabilities could exceed our insurance coverage. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for any of our product candidates. However, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Should any of the events described above occur, this could have a material adverse effect on our business, financial condition and results of operations.

***Off-label use or misuse of our products may harm our reputation in the marketplace or result in injuries that lead to costly product liability suits.***

We are developing Nefecon initially for the treatment of IgAN. If Nefecon is approved by the FDA, EMA or comparable foreign regulatory authorities, we may only promote or market it for its specifically approved indications. We will train our marketing and sales force against promoting Nefecon or any future product candidates for uses outside of the approved indications for use, known as "off-label uses." We cannot, however, prevent a physician from using our products off-label, when in the physician's independent professional medical judgment he or she deems it appropriate. Furthermore, the use of our products for indications other than those approved by the FDA, EMA or comparable foreign regulatory authorities may not effectively treat such conditions, and may increase the adverse events when compared to use for its approved indication. Any such off-label use of Nefecon or future product candidates could harm our reputation in the marketplace among physicians and patients. There may also be increased risk of injury to patients if physicians attempt to use our products for these uses for which they are not approved, which could lead to product liability suits that that might require significant financial and management resources and that could harm our reputation.

***EU drug marketing and reimbursement regulations may materially affect our ability to market and receive coverage for our products in the European Union member states.***

We intend to seek approval to market our product candidates in the United States, the European Union and selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the European Union, the pricing of drugs is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future healthcare reform measures.

Much like the federal Anti-Kickback Statute prohibition in the United States, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to induce or reward improper performance generally is governed by the national anti-bribery laws of EU Member States, and the Bribery Act 2010 in the United Kingdom. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the United Kingdom despite its departure from the European Union.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

In addition, in most foreign countries, including the European Economic Area, or EEA, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU Member States and parallel distribution, or arbitrage between low-priced and high-priced Member States, can further reduce prices. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be required to conduct a clinical trial or other trials that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales and the potential profitability of any of our product candidates in those countries would be negatively affected.

## Risks Related to Our Financial Position and Need for Additional Capital

***We have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.***

We are a clinical-stage biopharmaceutical company with a limited operating history. Since our inception, we have incurred significant operating losses. We incurred total comprehensive losses of SEK 32.6 million and SEK 444.6 million for the year ended December 31, 2019 and December 31, 2020, respectively. As of December 31, 2019 and December 31, 2020, we had an accumulated loss of SEK 488.1 million and SEK 918.6 million, respectively. Our losses resulted principally from costs incurred in clinical development of Nefecon and setanaxib and from administrative costs associated with our operations. We expect to continue to incur significant and increasing operating losses for the foreseeable future, and we do not know whether or when we will become profitable. Our losses, among other things, will continue to cause our working capital and shareholders' equity to decrease. We anticipate that our expenses will increase substantially if and as we:

- continue to develop and advance Nefecon, setanaxib, and any other product candidates;
- initiate and continue clinical development for Nefecon or its active ingredient budesonide in other potential indications, such as primary biliary cholangitis, or PBC, autoimmune hepatitis, or AIH, and setanaxib for PBC head and neck cancer;
- seek regulatory approval for Nefecon, setanaxib and/or any product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure and scale-up external manufacturing to commercialize Nefecon and setanaxib, if approved;
- maintain, expand and protect our intellectual property portfolio, including litigation costs associated with defending against alleged patent infringement claims;
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts;
- expand our operations in the United States and Europe;
- incur additional legal, accounting and other expenses associated with operating as a public company in the United States; and
- experience any delays or encounter any issues with regards to any of the above, including, but not limited to, failed studies, ambiguous trial results, safety issues or other regulatory challenges, including any unforeseen costs we may incur as a result of clinical trial or supply chain delays or other business interruptions due to the COVID-19 pandemic.

To date, we have funded our operations through public and private placements of equity securities, upfront payments, and interest income from the investment of our cash and financial assets.

We do not currently have any approved products and have never generated any revenue from product sales. To become and remain profitable, we must succeed in developing and eventually commercializing Nefecon, setanaxib and/or other approved products that generate significant revenue. This will require us to be successful in a range of challenging activities, including successfully completing our ongoing Phase 3 clinical trial of Nefecon, in-licensing and developing additional product candidates or indications for Nefecon, budesonide or setanaxib, obtaining regulatory approval for any product candidates that successfully complete clinical trials, establishing marketing capabilities and ultimately selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of many of these activities. We may never succeed in these activities and, even if we do, may never generate revenue that is significant enough to achieve or maintain profitability. Even if Nefecon, setanaxib or another product candidate that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond our current expectations if we are required by the FDA, the EMA or comparable foreign regulatory authorities to perform clinical trials or studies in addition to those that we currently anticipate, including any post-approval commitments or trial requirements. Even if we are able to generate revenue from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our common shares and ADSs and could impair our ability to raise capital, expand our business, maintain our research and development efforts or continue our operations. A decline in the value of our common shares or ADSs could also cause you to lose all or part of your investment.

***We will need substantial additional funding in order to fund our operations. Failure to obtain this necessary capital at acceptable terms and when needed may force us to delay, limit or terminate certain or all of our operations and pursuit of our growth strategy.***

Our operations have consumed substantial amounts of cash since inception. We expect to require substantial additional funding in the future to sufficiently finance our operations and advance the clinical development, seek regulatory approval and potentially commercialize Nefecon or any other product candidates we may develop.

As of December 31, 2020, we had SEK 996.3 million in cash. Based on our current operating plan, we expect that our existing cash, will enable us to fund our operating expenses and capital expenditure requirements into the third quarter of 2022. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the initiation, progress, timing, costs and results of clinical trials for Nefecon or clinical trials for any future product candidates;
- the number of potential new product candidates we identify and decide to develop, if any;
- the time and costs involved in obtaining regulatory approval for Nefecon and other product candidates we may choose to develop, and any delays we may encounter as a result of evolving regulatory requirements or adverse clinical trial results with respect to any of our product candidates;
- the extent to which we develop, in-license or acquire other product candidates and technologies;
- the costs involved in growing our organization to the size needed to allow for the development and potential commercialization of Nefecon or future product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending against any intellectual property claims or infringements raised by third parties;
- the costs related to our obligations under our existing collaboration agreements and the entry into new collaboration agreements;

- the cost and timing of future pre-commercialization activities and, with respect to any product candidates that receive regulatory approval, post-commercialization activities, and costs involved in the creation of an effective sales and marketing organization;
- the revenue, if any, we may receive either directly from commercial sales or in the form of royalty or milestone payments from future sales of Nefecon or future product candidates, if approved;
- the cost and timing of completion of commercial-scale manufacturing activities;
- the effect of competing technological and market developments; and
- the costs of operating as a public company in both the United States and Sweden.

Until we can generate sufficient product revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements.

Our ability to raise additional funds will depend on financial, economic and market conditions and other factors, over which we may have no or limited control. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as necessary. If adequate funds are not available on commercially acceptable terms when needed, we may be forced to delay, reduce or terminate the development or commercialization of all or some of our product candidates or research programs or we may be unable to take advantage of future business opportunities.

***Raising additional capital may cause dilution to holders of our common shares or ADSs, restrict our operations or require us to relinquish rights to our technologies or product candidates.***

We do not have any committed external source of funds or other support for our development efforts and we cannot be certain that additional funding will be available on acceptable terms, or at all. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our operations through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements.

If we undertake financing arrangements in the future, the terms of any financing may adversely affect the holdings or the rights of holders of our common shares or ADSs and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common shares or ADSs to decline. The sale of additional equity or convertible securities would dilute all of our existing shareholders and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of ADSs. The incurrence of indebtedness could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, financial condition and results of operations. Further, any additional fundraising efforts may divert our management from its day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our development programs or the commercialization of any of our product candidates, if approved, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

***Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.***

Since we began operations in 2004, we have invested most of our resources in developing our lead product candidate Nefecon, our technology, building our intellectual property portfolio, conducting business operations, raising capital and providing administrative support for these operations. Consequently, we have limited operations upon which to evaluate our business, and predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing drug products. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate activity or an acceptable safety profile, gain regulatory approval, secure market access and reimbursement and become commercially viable.

Nefecon is being investigated in an ongoing Phase 3 clinical trial for the treatment of IgAN. We have not yet demonstrated an ability to successfully conduct any Phase 3 clinical trials, obtain regulatory approvals, manufacture a commercial-scale product or conduct sales and marketing activities necessary for successful product commercialization or obtain reimbursement in the countries of sale. In addition, given our limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors in achieving our business objectives. Additionally, we expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control.

In addition, we will need to transition at some point from a company with a development focus to a company capable of supporting commercial activities, and we may not be successful in such a transition.

#### **Risks Related to Our Acquisition of Genkyotex**

***We may fail to realize the anticipated benefits of our acquisition of Genkyotex, or those benefits may take longer to realize than expected.***

In November 2020, we acquired a controlling interest in Genkyotex. Our ability to realize the anticipated benefits of such acquisition will depend, to a large extent, on our ability to integrate Genkyotex and its NOX inhibitor platform into our business and business strategy and realize anticipated growth opportunities and synergies. The integration process has been, and we expect will continue to be, complex and time-consuming. The expected benefits may not be achieved within the anticipated time frame, or at all. The failure to meet the challenges involved and to realize the anticipated benefits of the acquisition could cause an interruption of, or a loss of momentum in, our development, and could adversely affect our business, financial condition and results of operations.

In addition, in November 2020, we submitted a simplified public mandatory cash offer, or the Tender Offer, to the remaining shareholders in Genkyotex. The Tender Offer closed on December 11, 2020. As a result of the Tender Offer, we increased our ownership percentage to 86.2% of the share capital of Genkyotex. Additionally, in March 2021, we participated in a EUR 5.0 million rights issue and increased our ownership to 90.2%. Collectively, the transactions above are referred to as the "Acquisition."

Our ability to realize the anticipated benefits of the Acquisition is expected to entail numerous additional material potential difficulties, including, among others:

- any delay or failure in progressing setanaxib in clinical development and manufacturing, or any delay or failure to ultimately obtain marketing approval for commercialization of setanaxib in the United States and Europe thereafter;
- changes in laws or regulations that adversely impact the anticipated benefits of the Acquisition;
- increased complexity of compliance and cost of operations due to any delay in reaching 90% ownership of Genkyotex or failure to delist Genkyotex from Euronext;

- challenges related to the perception by patients, the medical community and third-party payors of setanaxib for the treatment of PBC, idiopathic pulmonary fibrosis, or IPF, nonalcoholic steatohepatitis, or NASH, and other fibrotic indications;
- disruptions to our manufacturing arrangements with third-party manufacturers, including our manufacturing and supply arrangements with respect to setanaxib and disruptions to our third-party distribution channel;
- difficulties in achieving the anticipated business opportunities and growth prospects from the Acquisition;
- the size of the treatable patient population for setanaxib may be smaller than we believe it is; and
- potential unknown liabilities, adverse consequences, unforeseen increased expenses or other unanticipated problems associated with the Acquisition.

We do not own or control all of the outstanding shares of Genkyotex, which may limit our ability to take certain actions, other than on an arms' length basis in the ordinary course of business. As a French listed company, Genkyotex is subject to conflict of interest rules arising from French corporate law and codified in the French Commercial Code has adopted the corporate governance code recommended by MiddleNext, a French association of mid-cap listed companies, and follows recommendations adopted by the French Financial Markets Authority. If, under these provisions, directors of Genkyotex who are directors, officers or employees of Calliditas cannot vote on certain matters (such as those where there is a disqualifying conflict of interest), we may not be able to obtain required board approval of decisions that we favor.

Similarly, if there are transactions requiring the approval of Genkyotex shareholders and as to which Calliditas has a disqualifying conflict of interest, such transactions would require the approval of Genkyotex's minority shareholders, who may not approve a transaction that we favor.

Many of these factors are outside of our control, and any one of them could result in increased costs, decreased expected revenues and further diversion of management time and energy, which could materially adversely impact our business, financial condition and results of operations.

The Acquisition cost, excluding transaction costs, amounted to EUR 27.8 million. In addition, we may owe shareholders of Genkyotex consideration of up to EUR 55 million, based on all shares of Genkyotex outstanding, contingent upon the achievement of certain milestones related to regulatory approvals of setanaxib in the U.S. and Europe. We also expect to incur expenses related to the continued development, regulatory approval process and commercialization with respect to setanaxib. Because we have limited financial resources, by investing in the Acquisition, we may forgo or delay pursuit of other opportunities that may have proven to have greater commercial potential.

All of these factors could decrease or delay the expected accretive effect of the Acquisition and negatively impact our stock price. As a result, it cannot be assured that the Acquisition will result in the full realization of the benefits anticipated from the Acquisition or in the anticipated time frames or at all.

***The work required to integrate Genkyotex may divert management resources from operational matters and other strategic opportunities.***

We expect that the successful integration of Genkyotex's operations, pipeline of product candidates and personnel will require management time and attention. The amount of time that our management will be required to devote to the integration may divert their attention from the day to day operation of the business or other strategic opportunities. In addition, uncertainty regarding the Acquisition and its impact on our results of operations, employees, regulatory compliance may create additional demands on management's time and resources. The trading price for our ADSs and common shares is predicated in part by investor expectations for our future growth, including organic growth and other potential opportunities for growth through strategic acquisitions. If diversion of management's impairs our results of operations, our share price could be negatively impacted.

***The Acquisition will result in the combined company operating in additional jurisdictions, increasing our exposure to international business risks.***

We have focused our operations primarily in Sweden, with some operations in the United States. Genkyotex primarily operates in France and Switzerland. The Acquisition will result in our operations in a number of additional jurisdictions worldwide exposing our business to additional risks related to:

- challenges caused by distance as well as language and cultural differences;
- general economic conditions in each country or region;
- political unrest, terrorism and the potential for other hostilities;
- complexities in compliance overlapping or changes in tax regimes;
- difficulties in transferring funds from certain countries;
- increased exposure to currency fluctuations; and
- increased compliance costs associated with local regulatory compliance.
- If we are unable to adequately manage our operations in these new jurisdictions, we could experience decreased revenues or increased operating expenses, any of which could adversely affect our business, financial condition, and results of operations.

#### **Risks Related to Our Dependence on Third Parties**

***We rely, and expect to continue to rely, on third parties, including independent clinical investigators and contract research organizations, or CROs, to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.***

We have relied upon, and plan to continue to rely upon third parties, including independent clinical investigators and third-party CROs, to conduct our clinical trials and to monitor and manage data for our clinical programs. We rely on these parties for execution of our clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third party contractors and CROs are required to comply GCP requirements, which are regulations and guidelines enforced by the FDA, the EMA and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we, our investigators or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Further, these investigators and CROs are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. If independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if their performance is substandard or not in conformance with our clinical trial protocols or GCP regulations, it may delay or compromise the prospects for approval and commercialization of any product candidates that we develop. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated.



Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated.

The COVID-19 pandemic and government measures taken in response may also have an impact on our CRO, including due to travel or quarantine policies or prioritization of resources toward the pandemic, and any disruption in their performance would affect our ability to complete our clinical trials.

There is a limited number of third-party service providers that specialize or have the expertise required to achieve our business objectives. If any of our relationships with these third-party CROs or clinical investigators terminate, we may not be able to enter into arrangements with alternative CROs or investigators or to do so on commercially reasonable terms. If CROs or clinical investigators do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they cannot perform their contractual duties or obligations due to the impacts of the COVID-19 pandemic on their operations or at the sites they are overseeing, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs or investigators involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and results of operations.

In addition, clinical investigators may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA. Any such delay or rejection could prevent us from commercializing our clinical-stage product candidates or any future product candidates.

***We rely on third parties to manufacture Nefecon and setanaxib, and we expect to continue to rely on third parties for the clinical and commercial supply of Nefecon, setanaxib and other future product candidates. The development of Nefecon, setanaxib or such other product candidates, and the commercialization of any approved products, could be stopped, delayed or made less profitable if any such third party fails to provide us with sufficient clinical or commercial quantities of such product candidates or products, fails to do so at acceptable quality levels or prices or fails to achieve or maintain satisfactory regulatory compliance.***

We do not currently have, and we do not plan to build, the infrastructure or capability internally to manufacture Nefecon, setanaxib or any other product candidate for use in the conduct of our clinical trials or, if approved, for commercial supply. We rely on, and expect to continue to rely on, contract manufacturing organizations, or CMOs. Reliance on third-party providers may expose us to more risk than if we were to manufacture our product candidates ourselves. We do not control the manufacturing processes of the CMOs we contract with and are dependent on those third parties for the production of our product candidates in accordance with relevant regulations such as cGMP, which includes, among other things, quality control, quality assurance and the maintenance of records and documentation.

If we were to experience an unexpected loss of supply of or if any supplier were unable to meet our clinical or commercial demand for any of our product candidates, we could experience delays in our planned clinical studies or commercialization. For example, the COVID-19 pandemic may impact our ability to procure sufficient future supplies for Nefecon, setanaxib and our other product candidates, and the extent of any impacts will depend on the severity and duration of the spread of the virus, and the actions undertaken to contain COVID-19 or treat its effects; however, we do not currently anticipate any interruptions in our supply of Nefecon and setanaxib for our ongoing and planned clinical trials. We could be unable to find alternative suppliers of acceptable quality that can produce appropriate volumes at an acceptable cost. Moreover, our suppliers are often subject to strict manufacturing requirements and rigorous testing requirements, which could limit or delay production. The long transition periods necessary to switch manufacturers and suppliers, if necessary, would significantly delay our clinical studies and the commercialization of our products, if approved, which would materially adversely affect our business, financial condition and results of operation. Additionally if any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our product candidates. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

In complying with the manufacturing regulations of the FDA, the EMA and comparable foreign regulatory authorities, we and our third-party suppliers must spend significant time, money and effort in the areas of design and development, testing, production, record-keeping and quality control to assure that the products meet applicable specifications and other regulatory requirements. The failure to comply with these requirements could result in an enforcement action against us, including the seizure of products and shutting down of production. We and any of these third-party suppliers may also be subject to audits by the FDA, the EMA or comparable foreign regulatory authorities. If any of our third-party suppliers fails to comply with cGMP or other applicable manufacturing regulations, our ability to develop and commercialize our product candidates could suffer significant interruptions. We face risks inherent in relying on a single CMO, as any disruption, such as a fire, natural hazards, pandemic, epidemic, or outbreak of an infectious disease or vandalism at the CMO could significantly interrupt our manufacturing capability. We currently do not have alternative production plans in place or disaster-recovery facilities available. In case of a disruption, we will have to establish alternative manufacturing sources. This would require substantial capital on our part, which we may not be able to obtain on commercially acceptable terms or at all. Additionally, we would likely experience months of manufacturing delays as we build or locate replacement facilities and seek and obtain necessary regulatory approvals. If this occurs, we will be unable to satisfy manufacturing needs on a timely basis, if at all. Also, operating any new facilities may be more expensive than operating our current facility. Further, business interruption insurance may not adequately compensate us for any losses that may occur and we would have to bear the additional cost of any disruption. For these reasons, a significant disruptive event of the manufacturing facility could have drastic consequences, including placing our financial stability at risk.

***We are dependent on a single supplier for the manufacture of the active pharmaceutical ingredient in Nefecon.***

We currently depend on a single supplier for the active ingredient in Nefecon. We cannot ensure that this supplier will remain in business or have sufficient capacity or supply to meet our needs, or that it will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. While we believe we can identify and transition to alternate suppliers for the active ingredient if necessary, our use of a single supplier exposes us to several risks, including disruptions in supply, price increases or late deliveries, including any disruptions resulting from factors related to the COVID-19 pandemic. For example, government-issued priority orders for COVID-19 vaccines may have a rippling effect on the manufacturing industry which could produce production and shipping delays for our product candidates in the future. We do not currently anticipate any interruptions in our supply of the active ingredient for our ongoing and planned clinical trials. Our current vendor may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Finding a suitable replacement supplier, materials and processes could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption or delay in supply could compromise our ability to pursue development and eventual commercialization of our product candidates.

***We have not yet manufactured on a commercial scale and expect to rely on third parties to produce and process commercial quantities of Nefecon, setanaxib or future product candidates, if approved.***

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for Nefecon, setanaxib or future product candidates. We have not yet entered into any arrangement with a third party for the supply of commercial quantities of Nefecon or setanaxib. To the extent that we enter into future manufacturing arrangements with third parties for commercial supply of Nefecon, setanaxib or future product candidates, if approved, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA, EMA or comparable foreign regulatory authorities following inspections that will be conducted after we submit an application to such regulatory authorities. We do not directly control the manufacturing process of, and will be completely dependent on, our contract manufacturing partners for compliance with cGMP requirements for the manufacture of our product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA or comparable foreign regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, EMA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

***We may collaborate with third parties for the commercialization of Nefecon, setanaxib or future product candidates, if approved, in select jurisdictions. If we are unable to establish such collaborations, we may not be successful in our commercialization efforts.***

In order to market and successfully commercialize any product candidate we develop, if approved, we must build our sales and marketing capabilities or enter into collaborations with third parties for these services. We currently have no sales, marketing or distribution capabilities and as a company have no experience in marketing products. If approved by the FDA, we intend to commercialize Nefecon for IgAN and setanaxib in the United States independently. In other key territories, including Europe, we may commercialize Nefecon or setanaxib through a broad regional partnership. For example, in 2019 we entered into an agreement with Everest Medicines, or Everest, pursuant to which we granted Everest an exclusive license to develop and commercialize Nefecon for the treatment of IgAN in Greater China and Singapore.

To the extent that we depend on collaborators for sales and marketing activities, any revenues we receive will depend upon the success of those collaborators' sales and marketing teams and the collaborators' prioritization of our product and compliance with applicable regulatory requirements, and there can be no assurance that the collaborators' efforts will be successful.

If we are unable to enter into a collaboration for the commercialization of product candidates we develop, if approved, we may be forced to delay the commercialization of our product candidates or reduce the scope of our sales or marketing activities in such jurisdictions, which would have an adverse effect on our business, operating results and prospects.

***If our third-party providers, including our CMOs and CROs, fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.***

Our third-party manufacturers are subject to numerous environmental, health and safety laws and regulations, including those governing the handling, use, storage, treatment and disposal of hazardous materials and wastes. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations.

Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological waste or hazardous waste insurance coverage, workers compensation or property and casualty and general liability insurance policies that include coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

#### **Risks Related to Intellectual Property**

***We rely on patents and other intellectual property rights to protect Nefecon, setanaxib and our other product candidates, the enforcement, defense and maintenance of which may be challenging and costly. Failure to enforce or protect these rights adequately could harm our ability to compete and impair our business.***

Our commercial success depends in part on obtaining and maintaining patents and other forms of intellectual property rights for Nefecon, setanaxib and our other product candidates, methods used to manufacture those products and the methods for treating patients using those products, or on licensing in such rights. Patent law relating to the scope of claims in the fields in which we operate is complex and uncertain, and we cannot make any assurances that we will be able to obtain or maintain patent or other intellectual property rights, or that the patent and other intellectual property rights we may obtain will be valuable, provide an effective barrier to competitors or otherwise provide competitive advantages. For example, although we co-own a single patent family relating to the formulation of Nefecon, which expires in 2029, such rights may not provide adequate protection against competitors. Failure to protect or to obtain, maintain or extend adequate patent and other intellectual property rights could materially adversely affect our ability to develop and market our products and product candidates. Patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover the technology at issue. We cannot be certain that patents will be issued or granted with respect to future patent applications, or that issued or granted patents will not later be found to be invalid or unenforceable. The patent position of biopharmaceutical companies is generally uncertain because it involves complex legal and factual considerations.

The standards applied by the United States Patent and Trademark Office, or USPTO, the European Patent Office or EPO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biopharmaceutical patents. Consequently, patents may not issue from future patent applications.

The patent prosecution process is expensive and time-consuming, and we and our future licensors, licensees or collaboration partners may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our future licensors, licensees or collaboration partners will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Further, the issuance, scope, validity, enforceability and commercial value of our and our current or future licensors', licensees' or collaboration partners' patent rights are highly uncertain. Our future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors, licensees or collaboration partners. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If our current or future licensors, licensees or collaboration partners fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors, licensees or collaboration partners are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. The patent examination process may require us or our licensors, licensees or collaboration partners to narrow the scope of the claims of our or our licensors', licensees' or collaboration partners' future patent applications, which may limit the scope of patent protection that may be obtained. We cannot assure you that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent from issuing from a pending patent application.

Even if patents do successfully issue, third parties may initiate an opposition, interference, re-examination, post-grant review, *inter partes* review, nullification or derivation action in court or before patent offices, or similar proceedings challenging the validity, enforceability or scope of such patents, which may result in the patent claims being narrowed or invalidated. For example, opposition proceedings at the EPO are increasingly common, and are costly and time consuming to defend. Furthermore, it is possible that we will need to defend other patents from challenges by others from time to time. It is possible that one or more of our U.S. patents may be challenged by parties who file a request for post-grant review or *inter partes* review or *ex parte* reexamination. Post-grant proceedings are increasingly common in the United States and are costly to defend. Our patent rights may not provide us with a proprietary position or competitive advantages against competitors. Furthermore, even if the outcome is favorable to us, the enforcement of our intellectual property rights can be extremely expensive and time consuming.

Because patent applications are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file any patent application related to a product candidate. Furthermore, if third parties have filed such patent applications on or before March 15, 2013, an interference proceeding can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such applications after March 15, 2013, a derivation proceeding can be initiated by such third parties to determine whether our invention was derived from theirs. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing our invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license.

***Issued patents covering Nefecon, setanaxib or our future product candidates could be found invalid or unenforceable if challenged in court.***

To protect our competitive position, we may from time to time need to resort to litigation in order to enforce or defend any patents or other intellectual property rights owned by or licensed to us, or to determine or challenge the scope or validity of patents or other intellectual property rights of third parties. Enforcement of intellectual property rights is difficult, unpredictable and expensive, and many of our or our licensors' or collaboration partners' adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensors or collaboration partners can. Accordingly, despite our or our licensors' or collaboration partners' efforts, we or our licensors or collaboration partners may not prevent third parties from infringing upon or misappropriating intellectual property rights we own or control, particularly in countries where the laws may not protect those rights as fully as in the United States and Europe. We may fail in enforcing our rights, in which case our competitors may be permitted to use our technology without being required to pay us any license fees. In addition, however, litigation involving our patents carries the risk that one or more of our patents will be held invalid (in whole or in part, on a claim-by-claim basis) or held unenforceable. Such an adverse court ruling could allow third parties to commercialize our product candidates, and then compete directly with us, without payment to us.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our products, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States or in Europe, defendant counterclaims alleging invalidity or unenforceability are commonplace. A claim for a validity challenge may be based on failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. A claim for unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or the EPO or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our product candidates. Such a loss of patent protection could have a material adverse impact on our business. Further, litigation could result in substantial costs and diversion of management resources, regardless of the outcome, and this could harm our business and financial results. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights.

***If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.***

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell Nefecon or future product candidates without infringing the intellectual property and other proprietary rights of third parties. However, our development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Third parties may have U.S. and non-U.S. issued patents and pending patent applications relating to compounds, methods of manufacturing compounds and/or methods of use for the treatment of the disease indications for which we are developing our product candidates. If any third-party patents or patent applications are found to cover our product candidates or their methods of use or manufacture, we may not be free to manufacture or market our product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our products candidates, including patent infringement lawsuits in Europe, United States or abroad, as well as interference, derivation, *inter partes* review, and post-grant proceedings before the EPO or USPTO and opposition or other proceedings before foreign patent offices. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the composition, use or manufacture of our product candidates. We cannot guarantee that any of our patent searches or analyses including, but not limited to, the identification of relevant patents, the scope of patent claims or the expiration of relevant patents are complete or thorough, nor can we be certain that we have identified each and every patent and pending application in the United States, Europe and other jurisdictions that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may be accused of infringing. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Accordingly, third parties may assert infringement claims against us based on intellectual property rights that exist now or arise in the future. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use or manufacture. The scope of protection afforded by a patent is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources, and we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate or product. If we were required to obtain a license to continue to manufacture or market the affected product, we may be required to pay substantial royalties or grant cross-licenses to our patents. We cannot, however, be certain you that any such license will be available on acceptable terms, if at all. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations as a result of claims of patent infringement or violation of other intellectual property rights. Further, the outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance, including the demeanor and credibility of witnesses and the identity of any adverse party. This is especially true in intellectual property cases that may turn on the testimony of experts as to technical facts upon which experts may reasonably disagree. Furthermore, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us; alternatively or additionally it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

***We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.***

Our former, present and future employees may have had prior employment at universities or at other biotechnology or pharmaceutical companies. Some of these employees may have executed proprietary rights, non-disclosure, non-competition or other similar agreements, in connection with such previous employment. Although we try to ensure that our employees 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 these employees have used or disclosed third-party intellectual property, including trade secrets or other proprietary information. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may sustain damages or lose key personnel, valuable intellectual property rights or the personnel's work product, which could hamper or prevent commercialization of our technology, which could materially affect our commercial development efforts. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

***We may become involved in lawsuits to protect or enforce our patent or other intellectual property, which could be expensive, time consuming and unsuccessful.***

Competitors may infringe our patent, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving our patent could limit our ability to assert those patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the trademarks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could adversely affect the price of shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Additionally, for certain of our existing and future in-licensed patent rights, we may not have the right to bring suit for infringement and may have to rely on third parties to enforce these rights for us. If we cannot or choose not to take action against those we believe infringe our intellectual property rights, we may have difficulty competing in certain markets where such potential infringers conduct their business, and our commercialization efforts may suffer as a result.

***Our ability to compete may be adversely affected if we are unsuccessful in defending against any claims by competitors or others that we are infringing upon their intellectual property rights.***

The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, biopharmaceutical companies have employed intellectual property litigation as a means to gain an advantage over their competitors. As a result, we may be required to defend against claims of intellectual property infringement that may be asserted by our competitors against us and, if the outcome of any such litigation is adverse to us, it may affect our ability to compete effectively.

Our involvement in litigation, and in any interference, derivation, reexamination, *inter partes* review opposition or post-grant proceedings or other intellectual property proceedings inside and outside of the United States or Europe may divert management time from focusing on business operations, could cause us to spend significant amounts of money and may have no guarantee of success. Any current and potential intellectual property litigation also could force us to do one or more of the following:



- stop selling, incorporating, manufacturing or using our products in the United States, Europe or other jurisdictions that use the subject intellectual property;
- obtain from a third party asserting its intellectual property rights, a license to sell or use the relevant technology, which license may not be available on reasonable terms, or at all, or may be non-exclusive thereby giving our competitors access to the same technologies licensed to us;
- redesign those products or processes that use any allegedly infringing or misappropriated technology, which may result in significant cost or delay to us, or which redesign could be technically infeasible; or
- pay damages, including the possibility of treble damages in a patent case if a court finds us to have willfully infringed certain intellectual property rights.

***Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.***

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, we could have a substantial adverse effect on our share price. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

***We may become dependent on intellectual property licensed from third parties for certain of our product candidates, and termination of any of these licenses could result in the loss of significant rights, which would substantially harm our business.***

If we in-license additional product candidates in the future, we might become dependent on proprietary rights from third parties with respect to those product candidates. Any termination of such licenses could result in the loss of significant rights and would cause material adverse harm to our ability to develop and commercialize any product candidates subject to such licenses.

Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of licensed technology in relation to our development and commercialization of our product candidates and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we own, as we are for intellectual property that we license, which are described below. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could materially suffer.

***We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.***

Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire or in-license such proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain a license to third-party intellectual property rights necessary for the development of a product candidate or program, we may have to abandon development of that product candidate or program and our business and financial condition could suffer.

***If our trademarks and trade names are not adequately protected, then 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, which we need to build name recognition by potential partners or customers in our markets of interest. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. If other entities use trademarks similar to ours in different jurisdictions, or have senior rights to ours, it could interfere with our use of our current trademarks throughout the world. Both the FDA and EMA have indicated that we will not be able to use the name Nefecon for our product candidate, and the FDA has conditionally accepted an alternative name for commercial use. Any goodwill and recognition that we have built for the name Nefecon will therefore be lost.

***We enjoy only limited geographical protection with respect to certain patents and may face difficulties in certain jurisdictions, which may diminish the value of intellectual property rights in those jurisdictions.***

We often file our first patent application (i.e., priority filing) with the USPTO, the EPO, or more typically, in the national office of a European country (e.g., in the United Kingdom or Sweden). International applications under the Patent Cooperation Treaty, or PCT, are filed within twelve months after the priority filing. Based on the PCT filing, national and regional patent applications may be filed in additional jurisdictions where we believe our product candidates may be marketed. We have so far not filed for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant proceeding of each national/regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant patent offices, while granted by others. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

Competitors may use our and our licensors' or collaboration partners' technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors or collaboration partners have patent protection, but enforcement is not as strong as that in the United States and Europe. These products may compete with our product candidates, and our and our licensors' or collaboration partners' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in the United States and Europe, and companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions.

Some countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired and our business and results of operations may be adversely affected.

Proceedings to enforce our and our licensors' or collaboration partners' patent rights in foreign jurisdictions could result in substantial costs and divert our and our licensors' or collaboration partners' efforts and attention from other aspects of our business, could put our and our licensors' or collaboration partners' patents at risk of being invalidated or interpreted narrowly and our and our licensors' or collaboration partners' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors or collaboration partners. We or our licensors or collaboration partners may not prevail in any lawsuits that we or our licensors or collaboration partners initiate and the damages or other remedies awarded, if any, may not be commercially meaningful.

***Intellectual property rights do not necessarily address all potential threats to our competitive advantage.***

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make product candidates that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or have licensed;
- the patents of third parties may have an adverse effect on our business;
- we or our licensors or any current or future strategic partners might not have been the first to conceive or reduce to practice the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or any future strategic partners might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;

- our competitors might conduct development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- third parties performing manufacturing or testing for us using our products or technologies could use the intellectual property of others without obtaining a proper license; and
- we may not develop additional technologies that are patentable.

***Changes in patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our products.***

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, the America Invents Act, or the AIA, has been enacted in the United States, resulting in significant changes to the U.S. patent system.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Additionally, the U.S. Supreme Court and the Court of Appeals for the Federal Circuit have ruled on patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

We consider proprietary trade secrets, confidential know-how and unpatented know-how to be important to our business. We may rely on trade secrets or confidential know-how to protect our technology, especially where patent protection is believed to be of limited value. However, trade secrets and confidential know-how are difficult to maintain as confidential.

To protect this type of information against disclosure or appropriation by competitors, our policy is to require our employees, consultants, contractors and advisors to enter into confidentiality agreements with us. However, current or former employees, consultants, contractors and advisers may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Enforcing a claim that a third party obtained illegally and is using trade secrets or confidential know-how is expensive, time consuming and unpredictable. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. Furthermore, if a competitor lawfully obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Failure to obtain or maintain trade secrets or confidential know-how trade protection could adversely affect our competitive position. Moreover, our competitors may independently develop substantially equivalent proprietary information and may even apply for patent protection in respect of the same. If successful in obtaining such patent protection, our competitors could limit our use of our trade secrets or confidential know-how.

Under certain circumstances, we may also decide to publish some know-how to attempt to prevent others from obtaining patent rights covering such know-how.

***We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.***

Many of our employees, including our senior management, were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees 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 these employees have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we successfully prosecute or defend against such claims, litigation could result in substantial costs and distract management.

***Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.***

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO, the EPO and national patent offices in several stages over the lifetime of the patent. The USPTO, the EPO and various foreign governmental patent offices require compliance with a number of procedural, documentaries, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors or collaboration partners fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market, which would have an adverse effect on our business.

## Risks Related to Our Employee Matters, Managing Our Growth and Other Risks Relating to Our Operations

### *The outbreak of the novel coronavirus disease, COVID-19, could adversely impact our business, including our clinical trials.*

In December 2019, a novel strain of the coronavirus disease, COVID-19, was identified in Wuhan, China. This virus continues to spread globally and has spread to a number of countries, including the United States, and the World Health Organization declared the COVID-19 virus a global pandemic. The outbreak and government measures taken in response to contain the spread of the virus have had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. Governments have instituted travel and other restrictions in order to reduce the spread of the disease that, among other things, direct individuals to shelter at their places of residence, direct businesses and governmental agencies to cease non-essential operations at physical locations, prohibit certain non-essential gatherings and events and order cessation of non-essential travel. In response to the spread of COVID-19, we have instituted a work-from-home policy for most of our administrative employees.

Remote work policies, quarantines, shelter-in-place and similar government orders, shutdowns or other restrictions on the conduct of business operations related to the COVID-19 pandemic may negatively impact productivity, disrupt our ongoing research and development activities and impact our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course.

As a result of the COVID-19 pandemic, we may experience disruptions that could severely impact our clinical trials, including:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures deemed non-essential, which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA or other regulatory authorities, including the potential inability of the FDA or other regulatory authorities to conduct pre-approval inspections of our manufacturing facilities, which may impact review and approval timelines as well as delay our ability to continue development of our programs in PBC, AIH or head and neck cancer;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems; and
- limitations on employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people.

In addition, federal, local and other governmental authorities, such as those in the United States, have imposed orders restricting travel and gathering of individuals that have the impact of impairing normal business operations. Such orders may also impact personnel at third-party manufacturing facilities, or the availability or cost of materials, which would disrupt our supply chain; however, we do not currently anticipate any interruptions in our supply of Nefecon for our ongoing and planned clinical trials.

To date, we do not anticipate that the COVID-19 pandemic will significantly impact the ongoing clinical activities related to NefIgArd, our Phase 3 pivotal trial in IgAN. We reported positive topline results from Part A of NefIgArd in the fourth quarter of 2020. We fully recruited Part A in December 2019, and because Nefecon is orally-administered by patients at home at home and the trial is conducted globally and designed to require only limited interaction among patients and the healthcare system, the impact of the COVID-19 pandemic to Part A of the trial was limited. Having successfully completed enrollment for Part B in January 2021, we expect to report data from Part B in early 2023.

Additionally, three vaccines for COVID-19 were granted Emergency Use Authorization by the FDA in late 2020 and early 2021, and more are likely to be authorized in the coming months. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials and commercial product, if approved, which could lead to delays in these trials and issues with our commercial supply, if we obtain regulatory approval. There are still uncertainties with regard to the continued development of COVID-19 and its implications, such as the potential inability of regulatory authorities to conduct pre-approval inspections of our manufacturing facilities, if required, and we will continue to assess the situation and seek to put in place relevant mitigating measures where necessary.

The spread of COVID-19, which has caused a broad impact globally, may materially affect our financial position. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common shares and ADSs.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the outbreak impacts our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, any restrictions on the ability of hospitals and trial sites to conduct trials that are not designed to address the COVID-19 pandemic and the perceived effectiveness of actions taken in the United States and other countries to contain and treat the disease.

In addition, to the extent the ongoing COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this "Risk Factors" section.

***Our business depends on retaining our key personnel and recruiting additional qualified personnel.***

Our success depends upon the continued contributions of our key management, scientific and technical personnel, including Renée Aguiar-Lucander, Fredrik Johansson, Richard Philipson, Katayoun Welin-Berger, Frank Bringstrup and Andrew Udell, who have been instrumental for us and have substantial experience with Nefecon and our other product candidates. The loss of key managers and senior scientists could delay our development activities, and we do not carry key person insurance. In addition, our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified management, scientific and medical personnel. Many other biotechnology and pharmaceutical companies and academic institutions that we compete with for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. Therefore, we might not be able to attract new qualified personnel or retain our key persons on conditions that are economically acceptable. Furthermore, we will need to recruit new managers and qualified scientific personnel to develop our business if we expand into fields that will require additional skills. Our inability to attract qualified personnel and retain our key persons could prevent us from achieving our objectives and implementing our business strategy, which could have a material adverse effect on our business and prospects. Given the stage of our programs and our plans to expand operations, our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior personnel across our organization.

***We expect to expand our development, regulatory and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, manufacturing, regulatory affairs and sales and marketing. To manage our anticipated future growth, 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. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

***Our business is subject to economic, political, regulatory and other risks associated with international operations.***

As a company incorporated and based in Sweden, our business is subject to risks associated with conducting business in Sweden, the United States and internationally. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing regulatory requirements for product candidate approvals;
- differing jurisdictions could present different issues for securing, maintaining or obtaining freedom to operate in such jurisdictions;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates of the Swedish Krona, U.S. dollar and Euro and currency controls;
- changes in a specific country's or region's political or economic environment, including the implications of the United Kingdom's withdrawal from the European Union;
- trade protection measures, import or export licensing requirements or other restrictive actions by governments;
- differing reimbursement regimes and price controls in certain international markets;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad, including, for example, the variable tax treatment in different jurisdictions of stock options granted under our employee stock plan or equity incentive plan;



- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- an outbreak of a contagious disease, such as coronavirus, which may cause us or our distributors, third party vendors and manufacturers and/or customers to temporarily suspend our or their respective operations in the affected city or country;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

***The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business, which could reduce the price of our common shares.***

Following the result of a referendum in 2016, the United Kingdom left the European Union on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom was subject to a transition period until December 31, 2020, or the Transition Period, during which European Union rules continued to apply. The United Kingdom and the European Union have signed a EU-UK Trade and Cooperation Agreement, which became provisionally applicable on January 1, 2021 and will become formally applicable once ratified by both the United Kingdom and the European Union. This agreement provides details on how some aspects of the United Kingdom and European Union's relationship will operate going forwards however there are still many uncertainties.

Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our product candidates is derived from European Union Directives and Regulations, Brexit, following the Transition Period, could materially impact the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom or the European Union, now that United Kingdom legislation has the potential to diverge from European Union legislation. For example, the United Kingdom is now no longer be covered by the centralized procedures for obtaining EEA-wide marketing and manufacturing authorizations from the EMA and a separate process for authorization of drug products is required in the United Kingdom. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. In addition, we may be required to pay taxes or duties or be subjected to other hurdles in connection with the importation of our product candidates into the European Union, or we may incur expenses in establishing a manufacturing facility in the European Union in order to circumvent such hurdles. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom or the European Union for our product candidates, or incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the United Kingdom. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the European Union.

***Exchange rate fluctuations may materially affect our results of operations and financial condition.***

Due to the international scope of our operations, our assets, earnings and cash flows are affected by fluctuations in the exchange rates of several currencies, particularly the Swedish Krona, the U.S. dollar and the Euro. The functional currency of Calliditas Therapeutics AB and our consolidated subsidiaries is the Swedish Krona and a significant portion of our operating expenses are paid in Swedish Krona.

Additionally, although we are based primarily in Sweden, we may receive payments from our business partners in U.S. dollars and Euros, and we regularly acquire services, consumables and materials in U.S. dollars and Euros. Further, potential future revenue may be derived from the United States, countries within the Euro zone and various other countries around the world. These future revenues may also be affected by fluctuations in foreign exchange rates which may, in turn, have a significant impact on our results of operations and cash flows from period to period. As a result, to the extent we continue our expansion on a global basis, we expect that increasing portions of our revenue, cost of revenue, assets and liabilities will be affected by fluctuations in currency valuations. We may, therefore, experience economic loss and a negative impact on earnings or net assets solely as a result of currency exchange rate fluctuations.

***Our internal computer systems, or those used by our CROs or other contractors or consultants, may fail or suffer security breaches.***

Despite the implementation of security measures, our internal computer systems and those of our current and future CROs and other contractors and consultants are vulnerable to damage from computer viruses and unauthorized access. For example, companies have experienced an increase in phishing and social engineering attacks from third parties in connection with the COVID-19 pandemic. While we have not to our knowledge experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our future product candidates could be delayed.

***Failure to comply with health and data protection laws and regulations could lead to government enforcement actions, including civil or criminal penalties, private litigation, and adverse publicity and could negatively affect our operating results and business.***

We and any potential collaborators may be subject to U.S. federal and state and foreign data protection laws and regulations, such as laws and regulations that address privacy and data security. In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws, including Section 5 of the Federal Trade Commission Act, that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third parties, including research institutions from which we obtain clinical trial data, that are subject to privacy and security requirements under HIPAA, as amended by HITECH. To the extent that we act as a business associate to a healthcare provider engaging in electronic transactions, we may also be subject to the privacy and security provisions of HIPAA, as amended by HITECH, which restricts the use and disclosure of patient-identifiable health information, mandates the adoption of standards relating to the privacy and security of patient-identifiable health information, and requires the reporting of certain security breaches to healthcare provider customers with respect to such information. Additionally, many states have enacted similar laws that may impose more stringent requirements on entities like ours. Depending on the facts and circumstances, we could be subject to significant civil, criminal, and administrative penalties if we violate HIPAA.

Further, California recently passed the California Consumer Protection Act, or CCPA, which went into effect January 2020 and provides broad rights to CCPA California consumers with respect to the collection and use of their information by businesses. In March 2020, the California State Attorney General proposed varying versions of companion draft regulations which are not yet finalized. Despite the delay in adopting regulations, the California State Attorney General will commence enforcement actions against violators beginning July 1, 2020. The CCPA further expands the privacy and process enhancements and commitment of resources in support of compliance with California's regulatory requirements and may lead to similar laws in other U.S. states or at a national level.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

***European data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.***

Because we are conducting clinical trials in the European Union, we are subject to additional privacy restrictions. The collection and use of personal health data in the European Economic Area, or EEA (being the European Union plus Norway, Iceland and Liechtenstein) is governed by the General Data Protection Regulation 2016/679, or GDPR, which became effective May 25, 2018. The GDPR applies to the processing of personal data by any company established in the EEA and to companies established outside the EEA to the extent they process personal data in connection with the offering of goods or services to data subjects in the EEA or the monitoring of the behavior of data subjects in the EEA. The GDPR enhances data protection obligations for data controllers of personal data, including stringent requirements relating to the consent of data subjects, expanded disclosures about how personal data is used, requirements to conduct privacy impact assessments for "high risk" processing, limitations on retention of personal data, mandatory data breach notification and "privacy by design" requirements, and creates direct obligations on service providers acting as processors. The GDPR also imposes strict rules on the transfer of personal data outside of the EEA to countries that do not ensure an adequate level of protection, like the United States (which, while deemed a third country, has the benefit of the Privacy Shield regime for transatlantic data transfers). Failure to comply with the requirements of the GDPR and the related national data protection laws of the EU Member States and Norway, Iceland and Liechtenstein may result in fines up to €20 million or 4% of a company's global annual revenues for the preceding financial year, whichever is higher. Moreover, the GDPR grants data subjects the right to claim material and non-material damages resulting from infringement of the GDPR. Given the breadth and depth of changes in data protection obligations, maintaining compliance with the GDPR will require significant time, resources and expense, and we may be required to put in place additional controls and processes ensuring compliance with the new data protection rules. This may be onerous and adversely affect our business, financial condition and results of operations. There has been limited enforcement of the GDPR to date, particularly in biopharmaceutical development, so we face uncertainty as to the exact interpretation of the new requirements on our trials and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the new law. In addition, further to the United Kingdom's exit from the EU on January 31, 2020, the GDPR ceased to apply in the UK at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law (referred to as the 'UK GDPR'). The UK GDPR and the UK Data Protection Act 2018 set out the UK's data protection regime, which is independent from but aligned to the EU's data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. The UK, however, is now regarded as a third country under the EU's GDPR which means that transfers of personal data from the EEA to the UK will be restricted unless an appropriate safeguard, as recognised by the EU's GDPR, has been put in place. Although, under the EU-UK Trade Cooperation Agreement it is lawful to transfer personal data between the UK and the EEA for a 6 month period following the end of the transition period, with a view to achieving an adequacy decision from the European Commission during that period. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection (this means that personal data transfers from the UK to the EEA remain free flowing).

***The increasing use of social media platforms presents new risks and challenges.***

Social media is increasingly being used to communicate about our clinical development programs and the diseases our therapeutics are being developed to treat, and we intend to utilize appropriate social media in connection with our commercialization efforts following approval of our product candidates, if any. Social media practices in the biotechnology and biopharmaceutical industry continue to evolve and regulations and regulatory guidance relating to such use are evolving and not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business, resulting in potential regulatory actions against us, along with the potential for litigation related to off-label marketing or other prohibited activities and heightened scrutiny by the FDA, the SEC and other regulators. For example, patients may use social media channels to comment on their experience in an ongoing blinded clinical trial or to report an alleged adverse event. If such disclosures occur, there is a risk that trial enrollment may be adversely impacted, that we may fail to monitor and comply with applicable adverse event reporting obligations or that we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our product candidates. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. In addition, we may encounter attacks on social media regarding our company, management, product candidates or products. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business.

***Our business operations and current and future relationships with investigators, health care professionals, consultants, third-party payors and customers may be subject, directly or indirectly, to U.S. federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.***

Although we do not currently have any products on the market, our current and future operations may be directly, or indirectly through our relationships with investigators, health care professionals, customers and third-party payors, subject to various U.S. federal and state healthcare laws and regulations, including, without limitation, the U.S. federal Anti-Kickback Statute. Healthcare providers, including physicians and others play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. These laws impact, among other things, our proposed sales, marketing and education programs and constrain our business and financial arrangements and relationships with third-party payors, healthcare professionals and others who recommend, purchase, or provide our approved products, and other parties through which we research as well as market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to patient data privacy and security regulation by both the U.S. federal government and the states in which we conduct our business. Finally, our current and future operations are subject to additional healthcare-related statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. The laws that may affect our ability to operate include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act, or FCA. The definition of the "remuneration" under the federal Anti-Kickback Statute has been interpreted to include anything of value. Further, courts have found that if "one purpose" of remuneration is to induce referrals, the federal Anti-Kickback Statute is violated. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution; but the exceptions and safe harbors are drawn narrowly and require strict compliance in order to offer protection. On December 2, 2020, the Office of Inspector General, or OIG, published further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. This rule (with exceptions) became effective January 19, 2021. Implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed. We continue to evaluate what effect, if any, the rule will have on our business;

- federal civil and criminal false claims laws and civil monetary penalty laws, including the FCA, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal healthcare programs, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or an obligation to pay or transmit money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. For example, manufacturers have been prosecuted for causing false claims to be submitted because of off-label promotion purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal healthcare programs for the product. The FCA also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, and as amended again by the Final HIPAA Omnibus Rule, published in January 2013, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers, and business associates that perform certain services involving the use or disclosure of individually identifiable health information as well as their covered subcontractors. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs;

- the U.S. federal legislation commonly referred to as Physician Payments Sunshine Act, and its implementing regulations, which requires certain manufacturers of drugs, that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the CMS information related to certain payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held by physicians (as defined by such law) and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value in the previous year made to certain non-physician providers, including physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives;
- analogous state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral source, state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities, state and local laws that require the registration of pharmaceutical sales representatives, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal and state enforcement bodies have continued their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry.

It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant sanctions, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in 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, reputational harm and the curtailment or restructuring of our operations. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

***Our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.***

We are exposed to the risk that our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA, EMA and comparable foreign regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the United States and abroad; or laws that require the reporting of financial information or data accurately. 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 may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted, a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. 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 civil, criminal and administrative penalties, damages, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, 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 adversely affect our ability to operate our business, financial condition and results of operations.

***We are subject to the U.S. Foreign Corrupt Practices Act of 1977, and other anti-corruption laws, as well as export control laws, import and customs laws, trade and economic sanctions laws and other laws governing our operations.***

Our operations are subject to anti-corruption laws, including the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. §201, the U.S. Travel Act, and other anti-corruption laws that apply in countries where we do business. The FCPA and these other laws generally prohibit us and our employees and intermediaries from authorizing, promising, offering, or providing, directly or indirectly, a financial or other advantage to government officials or other persons to induce them to improperly perform a relevant function or activity (or reward them for such behavior).

We, along with those acting on our behalf and our commercial partners, operate in a number of jurisdictions that pose a high risk of potential FCPA violations, and we participate in collaborations and relationships with third parties whose corrupt or illegal activities could potentially subject us to liability under the FCPA or local anti-corruption laws, even if we do not explicitly authorize or have actual knowledge of such activities. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

Compliance with the FCPA and these other laws is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, anti-corruption laws present particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of Sweden, Norway and the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions and embargoes on certain countries and persons, anti-money laundering laws, import and customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses. Such liabilities could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the FCPA, other anti-corruption laws or Trade Control laws could also have an adverse impact on our reputation, business, results of operations and financial condition. Further, the failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting.

***We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our third-party contract manufacturers, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. Earthquakes or other natural disasters could further disrupt our operations and have a material and adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters or our development operations, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. Disaster recovery and business continuity plans may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management approach, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third-party contract manufacturers, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our development programs may be harmed. Any business interruption may have a material and adverse effect on our business, financial condition, results of operations and prospects.

#### **Risks Related to the Ownership of our Securities**

***The price of our equity securities may be volatile and may fluctuate due to factors beyond our control.***

The price of the securities of publicly traded clinical-stage biopharmaceutical companies has been highly volatile and is likely to remain highly volatile in the future. The price of the securities of publicly traded clinical-stage biopharmaceutical companies has been highly volatile and is likely to remain highly volatile in the future. Since the ADSs were sold at our initial U.S. public offering in June 2020 at a price of \$19.50 per ADS, the price per ADS has ranged as low as \$19.00 and as high as \$38.00 through December 31, 2020. During this same period, common share prices have ranged from as low as SEK 89.50 to as high as SEK 165.80. The market price of the ADSs and our common shares may fluctuate significantly due to a variety of factors, including:

- the commencement, enrollment or results of our planned and future clinical trials, including NefIgArd;
- positive or negative results from, or delays in, testing and clinical trials by us, strategic partners or competitors;



- delays in entering into strategic relationships with respect to development or commercialization of our product candidates or entry into strategic relationships on terms that are not deemed to be favorable to us;
- technological innovations or commercial product introductions by us or competitors;
- changes or developments in laws or regulations applicable to our product candidates;
- developments concerning proprietary rights, including patents and litigation matters;
- public concern relating to the commercial value or safety of any of our product candidates;
- the loss of any of our key scientific or management personnel;
- announcements concerning our competitors or the biopharmaceutical industry in general;
- actual or anticipated fluctuations in our operating results;
- financing or other corporate transactions;
- publication of research reports or comments by securities or industry analysts;
- general market conditions in the biopharmaceutical industry or in the economy as a whole , including the COVID-19 pandemic and related global economic uncertainty;
- the trading volume or our ADSs on The Nasdaq Global Select Market or our common shares on Nasdaq Stockholm;
- sales of our ADSs or common shares by us, members of our senior management and directors or our shareholders or the anticipation that such sales may occur in the future;
- general economic, political, and market conditions and overall fluctuations in the financial markets in the United States or Sweden;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry;
- investors' general perception of us and our business; and
- other events and factors, many of which are beyond our control.

COVID-19 has spread rapidly around the world since December 2019 and has negatively affected the stock market and investor sentiment. The stock market in general, and The Nasdaq Global Select Market and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, following periods of volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Due to the potential volatility of our stock price, we may therefore be the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

These and other market and industry factors may cause the market price and demand for our securities to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their ADSs at or above the price paid for the ADSs and may otherwise negatively affect the liquidity of the ADSs. In addition, the stock market in general, and biopharmaceutical 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 will continue to incur increased costs as a result of operating as a U.S.-listed public company, and our board of directors will be required to devote substantial time to new compliance initiatives and corporate governance practices.***

As a U.S.-listed public company, and particularly after we no longer qualify as an emerging growth company, we will continue to incur significant legal, accounting and other expenses that we did not incur as a public company listed on Nasdaq Stockholm. The Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Stock Market, or Nasdaq, and other applicable securities rules and regulations impose various requirements on non-U.S. reporting public companies, including the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our board of directors and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

However, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, we are required to furnish a report on our internal control over financial reporting beginning with our second annual report on Form 20-F. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404.

***We have no present intention to pay dividends on our common shares in the foreseeable future and, consequently, your only opportunity to achieve a return on your investment during that time is if the price of the ADSs or common shares, as applicable, appreciates.***

We have no present intention to pay dividends in the foreseeable future. Any recommendation by our board of directors to pay dividends will depend on many factors, including our financial condition (including losses carried-forward), results of operations, legal requirements and other factors. Furthermore, pursuant to Swedish law, the calculation of amounts available for distribution to shareholders, as dividends or otherwise, must be determined on the basis of our non-consolidated statutory accounts prepared in accordance with Swedish accounting rules. If the price of the ADSs or the common shares declines before we pay dividends, you will incur a loss on your investment, without the likelihood that this loss will be offset in part or at all by potential future cash dividends.

***We have identified a material weakness in our internal control over financial reporting. If our remediation of this material weakness is not effective, or if we experience additional material weaknesses or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately report our financial condition or results of operations.***

In connection with our preparation and the audits of our financial statements as of and for the years ended December 31, 2020 and 2019, we have identified a material weakness as defined under the Exchange Act and by the Public Company Accounting Oversight Board (United States) in our internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's financial statements will not be prevented or detected on a timely basis. The material weakness relates to our financial statement closing process, primarily related to the lack of sufficient skilled personnel with SEC reporting knowledge and experiences for purposes of timely and reliable financial reporting. Specifically, the material weakness identified relates to a lack of resources sufficient to prepare and review our consolidated financial statements and related disclosures in accordance with the requirements set forth by the SEC.

We intend to continue to implement measures designed to remediate this material weakness, including hiring or engaging additional accounting personnel with knowledge and experience in SEC reporting requirements in order to timely and reliably report our financial results in accordance with the requirements of the SEC. However, the implementation of these measures may not fully address these material weaknesses in our internal control over financial reporting in which case we would not be able to conclude that they have been fully remedied. Our failure to correct this material weakness or our failure to discover and address any other control deficiencies could result in inaccuracies in our financial statements and could also impair our ability to comply with applicable financial reporting requirements and make related regulatory filings on a timely basis. As a result, our business, financial condition, results of operations and prospects, as well as the trading price and listing of our ADSs may be materially and adversely affected. We cannot assure you that all of our existing material weaknesses have been identified, or that we will not identify additional material weaknesses in the future.

Neither our management nor an independent registered public accounting firm has performed an evaluation of our internal control over financial reporting in accordance with the provision of the Sarbanes-Oxley Act because no such evaluation has been required. Had we or our independent registered public accounting firm performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act, additional material weaknesses may have been identified.

We are subject to reporting obligations under U.S. securities laws and the Sarbanes-Oxley Act. Section 404 of the Sarbanes-Oxley Act requires that we include a report from management on the effectiveness of our internal control over financial reporting in our annual report on Form 20-F beginning with our annual report for the fiscal year ending December 31, 2021. If we fail to remediate the material weakness identified above, our management may conclude that our internal control over financial reporting is not effective. This conclusion could adversely impact the market price of our ADSs due to a loss of investor confidence in the reliability of our reporting processes. Although Section 404(b) of the Sarbanes-Oxley Act requires our independent registered public accounting firm to issue an annual report that addresses the effectiveness of our internal control over financial reporting, we have opted to rely on the exemptions provided in the JOBS Act, and consequently will not be required to comply with SEC rules that implement Section 404(b) until such time as we are no longer an emerging growth company.

***If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of the ADSs.***

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, including as a result of remote working policies due to the COVID-19 pandemic, could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of the ADSs. For example, we have identified material weaknesses in our internal control over financial reporting related to our financial statement closing process, primarily related to the lack of sufficient skilled personnel with SEC reporting knowledge and experiences for purposes of timely and reliable financial reporting. Specifically, the material weakness identified relates to a lack of resources sufficient to prepare and review our consolidated financial statements and related disclosures in accordance with the requirements set forth by the SEC.

We will be required to disclose changes made in our internal controls and procedures on a bi-annual basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an “emerging growth company” under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an “emerging growth company” for up to five years. An independent assessment of the effectiveness of our internal controls could detect problems that our management’s assessment might not. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

***Concentration of ownership of our common shares (including common shares in the form of ADSs) among our existing executive officers, directors and principal shareholders may prevent new investors from influencing significant corporate decisions.***

Our executive officers, directors, greater than five percent shareholders and their affiliates beneficially own approximately 41.5% of our outstanding common shares (including common shares in the form of ADSs). Depending on the level of attendance at our general meetings of shareholders, these shareholders either alone or voting together as a group may be in a position to determine or significantly influence the outcome of decisions taken at any such general meeting. Any shareholder or group of shareholders controlling more than 50% of the share capital present and voting at our general meetings of shareholders may control any shareholder resolution requiring a simple majority, including the appointment of board members, certain decisions relating to our capital structure, and the approval of certain significant corporate transactions. Among other consequences, this concentration of ownership may prevent or discourage unsolicited acquisition proposals that you may believe are in your best interest as one of our shareholders. Some of these persons or entities may have interests different than yours. For example, to the extent certain shareholders purchased their shares or ADSs at prices below those at which other shareholders purchased theirs and have held their common shares for a longer period, they may be more interested in selling our company to an acquirer than other investors or they may want us to pursue strategies that deviate from the interests of other shareholders.

Currently, we are not aware that any of our existing shareholders have entered or will enter into a shareholders’ agreement with respect to the exercise of their voting rights. Nevertheless, depending on the level of attendance at our general meetings of shareholders, or the General Meeting, these significant shareholders could, alone or together, have the ability to determine the outcome of decisions taken at any such General Meeting. Any such voting by these shareholders may not be in accordance with our interests or those of our shareholders. Among other consequences, this concentration of ownership may have the effect of delaying or preventing a change in control and might therefore negatively affect the market price of the ADSs.

***Fluctuations in exchange rates may increase the risk of holding ADSs and common shares.***

Due to the international scope of our operations, our assets, earnings and cash flows are influenced by movements in exchange rates of several currencies, particularly the Swedish Krona, U.S. dollar and Euro. Our functional currency is the Swedish Krona, and some of our operating expenses are paid in Swedish Krona, but we also receive payments and pay expenses in U.S. dollars and Euro. Further, potential future revenue may be derived from abroad, particularly from the United States. As a result, our business and the price of the ADSs and common shares on The Nasdaq Global Select Market and Nasdaq Stockholm, respectively, may be affected by fluctuations in foreign exchange rates between these currencies, which may also have a significant impact on our reported results of operations and cash flows from period to period. Currently, we hold foreign exchange call options on the Euro.

Moreover, because our common shares currently trade on Nasdaq Stockholm in Swedish Krona, and the ADSs trade on The Nasdaq Global Select Market in U.S. dollars, fluctuations in the exchange rate between the U.S. dollar and the Swedish Krona may result in temporary differences between the value of the ADSs and the value of our common shares, which may result in heavy trading by investors seeking to exploit such differences.

***Holders of ADSs are not treated as holders of our common shares.***

Holders of ADSs are not treated as holders of our common shares unless they withdraw the common shares underlying their ADSs in accordance with the deposit agreement and applicable laws and regulations. The depositary is the holder of the common shares underlying the ADSs. Holders of ADSs therefore do not have any rights as holders of our common shares, other than the rights that they have pursuant to the deposit agreement. See “Item 12.D.—American Depositary Shares.”

***Holders of ADSs may be subject to limitations on the transfer of their ADSs and the withdrawal of the underlying common shares.***

ADSs 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 a governmental body, or under any provision of the deposit agreement, or for any other reason, subject to the right of ADS holders to cancel their ADSs and withdraw the underlying common shares. Temporary delays in the cancellation of your ADSs and withdrawal of the underlying common shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of common shares is blocked to permit voting at a shareholders’ meeting or we are paying a dividend on our common shares. In addition, ADS holders may not be able to cancel their ADSs and withdraw the underlying common shares when they owe 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 common shares or other deposited securities. See “Item 12.D.—American Depositary Shares.”

***Holders of ADSs will not have the same voting rights as the holders of our common shares and may not receive voting materials in time to be able to exercise your right to vote.***

Except as described in this annual report and the deposit agreement, which is filed as an exhibit to the registration statement, holders of the ADSs will not be able to exercise voting rights attaching to the common shares represented by the ADSs. Under the terms of the deposit agreement, holders of the ADSs may instruct the depositary to vote the common shares underlying their ADSs. Otherwise, holders of ADSs will not be able to exercise their right to vote unless they withdraw the common shares underlying their ADSs to vote them in person or by proxy in accordance with applicable laws and regulations and our articles of association. Even so, ADS holders may not know about a meeting far enough in advance to withdraw those common shares. If we ask for the instructions of holders of the ADSs, the depositary, upon timely notice from us, will notify ADS holders of the upcoming vote and arrange to deliver our voting materials to them. Upon our request, the depositary will mail to holders a shareholder meeting notice that contains, among other things, a statement as to the manner in which voting instructions may be given. We cannot guarantee that ADS holders will receive the voting materials in time to ensure that they can instruct the depositary to vote the common shares underlying their ADSs. A shareholder is only entitled to participate in, and vote at, the meeting of shareholders, provided that it holds our common shares as of the record date set for such meeting and otherwise complies with our articles of association. In addition, the depositary’s liability to ADS holders for failing to execute voting instructions or for the manner of executing voting instructions is limited by the deposit agreement. As a result, holders of ADSs may not be able to exercise their right to give voting instructions or to vote in person or by proxy and they may not have any recourse against the depositary or us if their common shares are not voted as they have requested or if their shares cannot be voted.

***Claims of U.S. civil liabilities may not be enforceable against us.***

We are incorporated under Swedish law. Certain members of our board of directors and senior management 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. As a result, it may not be possible for investors to effect service of process within the United States upon such persons or to enforce judgments obtained in U.S. courts against them or us, including judgments predicated upon the civil liability provisions of the U.S. federal securities laws.

The United States and Sweden do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters. Consequently, a final judgment for payment given by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in Sweden. In addition, uncertainty exists as to whether the courts in Sweden would entertain original actions brought in Sweden against us or our directors or senior management predicated upon the securities laws of the United States or any state in the United States. Any final and conclusive monetary judgment for a definite sum obtained against us in U.S. courts would not be automatically recognized. Instead, new proceedings would need to be initiated before the competent court in Sweden. However, a judgment obtained in the U.S. may still have a strong evidentiary weight in the Swedish proceedings, depending on the circumstances and the assessment of the court. If a Swedish court gives judgment for the sum payable under a U.S. judgment, the Swedish judgment will be enforceable by methods generally available for this purpose. These methods generally permit the Sweden court discretion to prescribe the manner of enforcement. As a result, U.S. investors may not be able to enforce against us or certain of our directors any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

***We qualify as a foreign private issuer and, as a result, we are not subject to U.S. proxy rules and are subject to reporting obligations under the Securities Exchange Act of 1934, as amended, that, to some extent, permit less detailed and frequent reporting than that of a U.S. domestic public company.***

We report under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer under the Exchange Act, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including (i) the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act, (ii) the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time and (iii) the rules under the Exchange Act requiring the filing with the Securities and Exchange Commission, or SEC, of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K, upon the occurrence of specified significant events. In addition, foreign private issuers are not required to file their annual report on Form 20-F until 120 days after the end of each fiscal year, while U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers are also exempt from the Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

***As a foreign private issuer and as permitted by the listing requirements of Nasdaq, we will rely on certain home country governance practices rather than the corporate governance requirements of Nasdaq.***

We are entitled to rely on a provision in Nasdaq's corporate governance rules that allows us to follow Swedish law with regard to certain aspects of corporate governance. This allows us to follow certain corporate governance practices that differ in significant respects from the corporate governance requirements applicable to U.S. companies listed on Nasdaq. For example, we are exempt from Nasdaq regulations that require a listed U.S. company and intend to follow home country practice with respect to (i) the minimum quorum requirement for a meeting of shareholders, (ii) the requirement that non-management directors to meet on a regular basis without management present and (iii) the composition of the nominating and corporate governance committee.

In accordance with our Nasdaq listing, our audit committee is required to comply with the provisions of Section 301 of the Sarbanes-Oxley Act, and Rule 10A-3 of the Exchange Act. Because we are a foreign private issuer, however, our audit committee is not subject to additional Nasdaq requirements applicable to listed U.S. companies, including an affirmative determination that all members of the audit committee are "independent" using more stringent criteria than those applicable to us as a foreign private issuer. Furthermore, Nasdaq's corporate governance rules require listed U.S. companies to, among other things, seek shareholder approval for the implementation of certain equity compensation plans and issuances of common shares, which we are not required to follow as a foreign private issuer. Therefore, our shareholders may be afforded less protection than they otherwise would have under corporate governance listing standards applicable to U.S. domestic issuers.

***We may in the future lose our foreign private issuer status which would then require us to comply with the Exchange Act's domestic reporting regime and cause us to incur significant legal, accounting and other expenses.***

We are a foreign private issuer and therefore we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers. In order to maintain our current status as a foreign private issuer, either (a) a majority of our common shares must be either directly or indirectly owned of record by non-residents of the United States or (b)(i) a majority of our executive officers or directors may not be U.S. citizens or residents, (ii) more than 50 percent of our assets cannot be located in the United States and (iii) our business must be administered principally outside the United States. We are required to evaluate our foreign private issuer status as of June 30 of each year. If we lose foreign private issuer status, we would be required to comply with the Exchange Act reporting and other requirements applicable to U.S. domestic issuers, which are more detailed and extensive than the requirements for foreign private issuers. We may also be required to make changes in our corporate governance practices in accordance with various SEC and Nasdaq rules. The regulatory and compliance costs to us under U.S. securities laws if we are required to comply with the reporting requirements applicable to a U.S. domestic issuer may be significantly higher than the cost we would incur as a foreign private issuer. As a result, we expect that a loss of foreign private issuer status would increase our legal and financial compliance costs and would make some activities highly time consuming and costly. We also expect that if we were required to comply with the rules and regulations applicable to U.S. domestic issuers, it would make it more difficult and expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified members of our management team.

***We are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to "emerging growth companies" will make the ADSs less attractive to investors.***

We are an "emerging growth company," as defined in the U.S. Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an "emerging growth company," we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including not being required to comply with the auditor attestation requirements of Section 404, exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. As an "emerging growth company," we are required to report only two years of financial results and selected financial data compared to three and five years, respectively, for comparable data reported by other public companies. We may take advantage of these exemptions until we are no longer an "emerging growth company." We could be an "emerging growth company" for up to five years following completion of our initial public offering in the United States, although circumstances could cause us to lose that status earlier, including if the aggregate market value of our common shares held by non-affiliates exceeds \$700 million as of any June 30 (the end of our second fiscal quarter) before that time, in which case we would no longer be an "emerging growth company" as of the following December 31 (our fiscal year-end). We cannot predict if investors will find the ADSs less attractive because we may rely on these exemptions. If some investors find the ADSs less attractive as a result, there may be a less active trading market for the ADSs and the price of the ADSs may be more volatile.

***If securities or industry analysts cease coverage of us, or publish inaccurate or unfavorable research about our business, the price of the ADSs and our trading volume could decline.***

The trading market for the ADSs will depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. Securities or industry analysts may elect not to provide research coverage of our ADSs, and such lack of research coverage may negatively impact the market price of our ADSs. If one or more of the analysts who cover us downgrade the ADSs or publish inaccurate or unfavorable research about our business, the price of the ADSs would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for the ADSs could decrease, which might cause the price of the ADSs and trading volume to decline.

***Holders of ADSs 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 common shares provides that, to the fullest extent permitted by applicable law, ADSs holders 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. The waiver to right to a jury trial of the deposit agreement is not intended to be deemed a waiver by any holder or beneficial owner of ADSs of our or the depositary's compliance with the U.S. federal securities laws and the rules and regulations promulgated thereunder.

If we or the depositary oppose 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. 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. 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 you consult legal counsel regarding the jury waiver provision before investing in the ADSs.

If you or any other holders or 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, you or such other holder or beneficial owner 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/or the depositary. If a lawsuit is brought against us and/or 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 outcome than a trial by jury would have had, including results that could be less favorable to the plaintiffs in any such action.

Nevertheless, if this jury trial waiver 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 our ADSs serves as a waiver by any holder or beneficial owner of ADSs or by us or the depositary of compliance with any provision of the U.S. federal securities laws and the rules and regulations promulgated thereunder.

***If we were to be classified as a passive foreign investment company, there could be adverse U.S. tax consequences to certain U.S. holders.***

Under the Internal Revenue Code of 1986, as amended, we will be a "passive foreign investment company" for U.S. federal income tax purposes, or a PFIC, for any taxable year in which (1) 75% or more of our gross income consists of passive income or (2) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, passive income. If we are a PFIC for any taxable year during which a U.S. Holder (as defined below in "Material Income Tax Considerations— Material U.S. federal income tax considerations for U.S. holders") holds our common shares, or ADSs, the U.S. Holder may be subject to adverse tax consequences regardless of whether we continue to qualify as a PFIC, including ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred and additional reporting requirements.

A separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. Our status as a PFIC depends on the value of our assets and the composition of our income and assets. The total value of our assets for purposes of the asset test generally will be calculated using the market price of the common shares or ADSs, which may fluctuate considerably. Fluctuations in the market price of the common shares or ADSs may result in our being a PFIC for any taxable year. In addition, the composition of our assets will also be affected by how, and how quickly, we spend the cash we raise in any offering, including our initial public offering in the United States. Our income for a taxable year will be affected by whether we receive certain milestone payments in such year, and whether certain gains from foreign currency exchanges are treated as qualifying income for purposes of the PFIC income test. Based upon the value of our assets and the composition of our income and assets, we do not believe we were a PFIC for the 2019 or 2020 taxable year. It is uncertain whether we will be a PFIC for the 2021 taxable year or any subsequent taxable years. Because of the uncertainties involved in determining our PFIC status, we cannot provide any assurances regarding our PFIC status.



***Future changes to tax laws could materially adversely affect our company and reduce net returns to our shareholders.***

The tax treatment of the company is subject to changes in tax laws, regulations and treaties, or, in each case, the interpretation thereof, tax policy initiatives and reforms under consideration and the practices of tax authorities in jurisdictions in which we operate, as well as tax policy initiatives and reforms related to the Organisation for Economic Co-Operation and Development's, Base Erosion and Profit Shifting, Project, the European Commission's state aid investigations and other initiatives. Such changes may include (but are not limited to) the taxation of operating income, investment income, dividends received or (in the specific context of withholding tax) dividends paid. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our financial position and overall or effective tax rates in the future in countries where we have operations, reduce post-tax returns to our shareholders, and increase the complexity, burden and cost of tax compliance.

***Tax authorities may disagree with our positions and conclusions regarding certain tax positions, resulting in unanticipated costs, taxes or non-realization of expected benefits.***

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, a tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a "permanent establishment" under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

***The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation.***

Under Swedish corporate law, except in certain limited circumstances, which require at a minimum that a proposal for special review of accounts or a review of a specific item/topic as defined by shareholders requesting such review, has been supported by a minimum of 10% of the shareholders voting and being present at a general meeting, our shareholders may not ask for an inspection of our corporate records, while under Delaware corporate law any shareholder, irrespective of the size of such shareholder's shareholdings, may do so. Shareholders of a Swedish limited company are also unable to initiate a derivative action, a remedy typically available to shareholders of U.S. companies, in order to enforce a right of our company, in case we fail to enforce such right ourselves, other than in certain cases of board member/management liability under limited circumstances. In addition, a majority of our shareholders may release a member of our board of directors or our executive management from any claim of liability we may have, including if such board member or manager has acted in bad faith or has breached his or her duty of loyalty. However, a shareholder may bring a derivative action on behalf of our company against, among other persons, a member of our board of directors or our executive management, provided that the circumstances of the act or omission giving rise to the claim of liability were not known to the shareholders at the time of such shareholder resolution, or if shareholders representing at least 10% of the share capital represented at the relevant general meeting has opposed such shareholder resolution. In contrast, most U.S. federal and state laws prohibit a company or its shareholders from releasing a board member from liability altogether if such board member has acted in bad faith or has breached such board member's duty of loyalty to our company. Additionally, distribution of dividends from Swedish companies to foreign companies and individuals can be subject to non-refundable withholding tax, and not all receiving countries allow for deduction. See "Item 10.E.—Taxation—Material Swedish Tax Considerations" for a more detailed description of the withholding tax. Also, the rights as a creditor may not be as strong under Swedish insolvency law as under U.S. law or other insolvency law, and consequently creditors may recover less in the event our company is subject to insolvency compared to a similar case including a U.S. debtor. In addition, the use of the tax asset consisting of the accumulated tax losses requires that we are able to generate positive taxable income and the use of tax losses carried forward to offset against future income is subject to certain restrictions and can be restricted further by future amendments to Swedish tax law. Finally, Swedish corporate law may not provide appraisal rights in the case of a business combination equivalent to those generally afforded a shareholder of a U.S. company under applicable U.S. laws. As a result of these differences between Swedish corporate law and our articles of association, on the one hand, and U.S. federal and state laws, on the other hand, in certain instances, you could receive less protection as an equity holder of our company than you would as a shareholder of a U.S. company.

***Holders of the ADSs will not be able to exercise the pre-emptive subscription rights related to the shares that they represent and may suffer dilution of their equity holding in the event of future issuances of our shares.***

Under the Swedish Companies Act, our shareholders benefit from a pre-emptive subscription right on the issuance of shares for cash consideration only and not in the event of issuance of shares against non-cash contribution or debt conversion. Shareholders' pre-emptive subscription rights, in the event of issuances of shares against cash payment, may be disappplied by a resolution of the shareholders at a general meeting of our shareholders and/or the shares may be issued on the basis of an authorization granted to the board of directors pursuant to which the board may disapply the shareholders' pre-emptive subscription rights. For example, at the extraordinary general meeting held on March 3, 2020, our shareholders agreed to waive their pre-emptive subscription rights with respect to the proposed authorization to our board of directors to effect the capital increase necessary to effectuate our initial public offering in the United States. The absence or waiver of pre-emptive rights for existing equity holders may cause dilution to such holders.

Furthermore, the ADS holders would not be entitled, even if such rights accrued to our shareholders in any given instance, to receive such pre-emptive subscription rights related to the shares that they represent. Rather, the depositary is required to endeavor to sell any such subscription rights that may accrue to the shares underlying the ADSs and to remit the net proceeds therefrom to the ADS holders pro rata. In addition, if the depositary is unable to sell rights, the depositary will allow the rights to lapse, in which case you will receive no value for these rights. Further, if we offer holders of our shares the option to receive dividends in either cash or shares, under the deposit agreement, ADS holders will not be permitted to elect to receive dividends in shares or cash, but will receive whichever option we provide as a default to shareholders who fail to make such an election.

***We are a Swedish company with limited liability. The rights of our shareholders may be different from the rights of shareholders in companies governed by the laws of U.S. jurisdictions.***

We are a Swedish company with limited liability. Our corporate affairs are governed by our articles of association and by the laws governing companies incorporated in Sweden. The rights of shareholders and the responsibilities of members of our board of directors may be different from the rights and obligations of shareholders and boards of directors in companies governed by the laws of U.S. jurisdictions. In the performance of its duties, our board is required by Swedish law to consider the interests of our company, its shareholders, its employees and other stakeholders, in all cases with due observation of the principles of reasonableness and fairness. It is possible that some of these parties will have interests that are different from, or in addition to, the interests of our shareholders.

***Our articles of association designate specific courts in the United States as the exclusive forum for certain U.S. litigation that may be initiated by our shareholders, which could limit our shareholders' ability to obtain a favorable judicial forum for disputes with us.***

Our articles of association provide that, unless we consent in writing to the selection of an alternative forum and without any infringement on Swedish forum provisions and without applying Chapter 7, Section 54 of the Swedish Companies Act (2005:551), the United States District Court for the Southern District of New York shall be the sole and exclusive forum for resolving any complaint filed in the United States asserting a cause of action arising under the Securities Act, or the Federal Forum Provision.

We recognize that the proposed Federal Forum Provision may impose additional litigation costs on shareholders in pursuing any such claims, particularly if the shareholders do not reside in or near the State of New York. Additionally, proposed Federal Forum Provision may limit our shareholders' ability to bring a claim in a U.S. judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our shareholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other U.S. or Swedish courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on shareholders who assert that the provision is not enforceable or invalid. The United States District Court for the Southern District of New York may also reach different judgments or results than would other courts, including courts where a shareholder considering a U.S.-based action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our shareholders.