SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 20-F

(Mark One)

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2020

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____

OR

☐ **SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Date of event requiring this shell company report _____

Commission file number 001-38097

CALLIDITAS THERAPEUTICS AB

(Exact name of registrant as specified in its charter and translation of Registrant's name into English)

Sweden
(Jurisdiction of
Incorporation or Organization)

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

Title of each class:	Trading Symbol:	Name of each exchange on which registered:
American Depositary Shares, each representing two common shares, quota value SEK 0.04 per share	CALT	Nasdaq Global Select Market
Common shares, quota value SEK 0.04 per share *		Nasdaq Global Select Market*

* Not for trading, but only in connection with the registration of the American Depositary Shares.

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

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act: None.

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report:

As of December 31, 2020, 49,941,584 common shares were outstanding, including common shares represented by American Depositary Shares.

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

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Yes ☐ No ☒

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

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

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

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

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

† The term “new or revised financial accounting standard” refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

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

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☐ International Financial Reporting Standards as issued by the International Accounting Standards Board ☒ Other ☐

If “Other” has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow.
Item 17 ☐ Item 18 ☐

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b 2 of the Exchange Act). Yes ☐ No ☒

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This annual report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are based on our management's beliefs and assumptions and on information currently available to our management. In some cases, you can identify forward-looking statements by the words "may," "might," "will," "could," "would," "should," "expect," "intend," "plan," "is designed to," "objective," "anticipate," "believe," "estimate," "predict," "potential," "continue," "ongoing or the negative of these and similar expressions identify forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. The forward-looking statements and opinions contained in this annual report are based upon information available to our management as of the date of this annual report and, while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. Forward-looking statements contained in this annual report include, but are not limited to, statements about:

- the timing, progress and results of our ongoing Phase 3 clinical trial for Nefecon and development plans for setanaxib or any other future indications or product candidates;
- the potential attributes and benefits of Nefecon, setanaxib and any other product candidates and their competitive position with respect to alternative treatments;
- the timing, scope or likelihood of domestic and foreign regulatory marketing application submissions, acceptance for review and approvals;
- the potential benefit of orphan drug designation for Nefecon and setanaxib, and likelihood of obtaining orphan drug exclusivity for any other product candidates, the U.S. Food and Drug Administration's, or the FDA's, accelerated approval pathway, the European Medicines Agency's, or the EMA's, conditional approval pathway, the FDA's Section 505(b)(2) pathway and the EMA's hybrid application pathway for Nefecon or any other future product candidates;
- the acceptance of proteinuria data as the primary endpoint for our Phase 3 clinical trial for Nefecon to support approval by the FDA, EMA or comparable foreign regulatory authorities;
- our ability to successfully identify and develop other potential product candidates;
- the impact of the COVID-19 pandemic to our business and clinical trials as well as supply of our product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our product candidates, if approved for commercial use;
- our manufacturing, commercialization and marketing capabilities and strategy;
- the rate and degree of market acceptance and clinical utility of Nefecon, setanaxib and any future product candidates;
- the timing of our submission of marketing applications to the FDA and EMA for Nefecon;
- the anticipated benefits of our acquisition of Genkyotex S.A., or Genkyotex;

- our ability to integrate Genkyotex's operations, pipeline of product candidates and personnel with our business;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals, including sales and marketing personnel if Nefecon or other future product candidates are approved;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights, the validity of intellectual property rights held by third parties, and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights;
- our competitive position, and developments and projections relating to our competitors and our industry, including estimates of the size and growth potential of the markets for our product candidates;
- our plans to enter into collaborations for commercialization of Nefecon, setanaxib or any future product candidates;
- whether we are classified as a passive foreign investment company for current and future periods;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our exposure to additional scrutiny as a U.S. public company;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act; and
- the impact of laws and regulations.

You should refer to the section of this annual report titled "Item 3.D.—Risk Factors" for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this annual report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

You should read this annual report and the documents that we reference in this annual report and have filed as exhibits to the annual report completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

Information regarding market and industry statistics contained in this annual report is included based on information available to us that we believe is accurate. Forecasts and other forward looking information obtained from this available information is subject to the same qualifications and the additional uncertainties accompanying any estimates of future market size, revenue and market acceptance of products and services.

SUMMARY OF RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous material and other risks and uncertainties, including those described in "Item 3.D.—Risk Factors" in this annual report. The principal risks and uncertainties affecting our business include the following:

- The outbreak of the novel strain of coronavirus disease, COVID-19, could adversely impact our business, including our clinical trials, and the supply 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.
- 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 use of proteinuria as a surrogate endpoint with an accelerated approval pathway to enable the advancement of Nefecon is a novel approach in nephrology.
- 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.
- 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.
- 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 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.
- 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.
- 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 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.
- We may fail to realize the anticipated benefits of our acquisition of Genkyotex, or those benefits may take longer to realize than expected.

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

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 NeflgArd 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 outof-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, filling 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 enforceable. 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 disapplied 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.

The dual listing of our common shares and the ADSs may adversely affect the liquidity and value of the ADSs.

Our ADSs are listed on The Nasdaq Global Select Market and our common shares are listed on Nasdaq Stockholm. Trading of the ADSs or common shares, as applicable, in these markets will take place in different currencies (U.S. dollars on Nasdaq and Swedish Kronor on Nasdaq Stockholm), and at different times (resulting from different time zones, different trading days and different public holidays in the United States and Sweden). The trading prices of our common shares or ADSs, as applicable, on these two markets may differ due to these and other factors. Any decrease in the price of our common shares on Nasdaq Stockholm could cause a decrease in the trading price of the ADSs on Nasdaq. Investors could seek to sell or buy our common shares or ADSs to take advantage of any price differences between the markets through a practice referred to as arbitrage. Any arbitrage activity could create unexpected volatility in both the trading prices on one exchange and the common shares or Ads available for trading on the other exchange. In addition, holders of ADSs will not be immediately able to surrender their ADSs and withdraw the underlying common shares for trading on the other market without effecting necessary procedures with the depositary. This could result in time delays and additional cost for holders of ADSs. We cannot predict the effect of this dual listing on the value of our common shares and the ADSs. However, the dual listing of our common shares and the ADSs may reduce the liquidity of these securities in one or both markets and may adversely affect the development of an active trading market for the ADSs in the United States.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant securities price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices. Defending against litigation is costly and time-consuming, and could divert our management's attention and our resources. Furthermore, during the course of litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our ADSs.

ITEM 4. INFORMATION ON THE COMPANY

A. HISTORY AND DEVELOPMENT OF THE COMPANY

We were formed in 2004 in order to develop and commercialize Nefecon, which we acquired from Nefecon's inventors, Professors Bengt Fellström and Roger Hällgren at Uppsala University, Sweden. We are led by an experienced and dedicated management team with more than 15 years of prior experience on average in the pharmaceutical industry, including at leading pharmaceutical companies such as GlaxoSmithKline, Novo Nordisk, Pfizer and UCB. Our board of directors includes highly qualified researchers, pharmaceutical sector executives and experts in the fields of drug development, corporate development and pharmaceutical commercialization. We are supported by a highly regarded network of leading experts within the field of IgAN, including prominent IgAN specialists throughout the world that serve as external advisors and investigators on clinical trials of Nefecon.

The legal and commercial name of the company is Calliditas Therapeutics AB. We were founded as a public limited company under the laws of Sweden on February 20, 2004 under the name Pharmalink AB and were registered with the Swedish Companies Registration Office on April 15, 2004. On September 19, 2017, we changed our name to Calliditas Therapeutics AB.

In June 2018, we completed an initial public offering of our common shares on Nasdaq Stockholm, pursuant to which we raised gross proceeds of SEK 738.7 million. Our common shares trade on Nasdaq Stockholm under the ticker "CALTX."

In July 2019, we completed a private placement of our common shares, pursuant to which we raised gross proceeds of SEK 210.3 million.

In June 2020, we completed an initial public offering of our American Depositary Shares, or ADSs, on The Nasdaq Global Select Market in the United States and sold 924,000 common shares in Europe and countries outside of the United States in a concurrent private placement to qualified investors for gross proceeds of approximately $90 million (approximately SEK 828 million) before deduction of issuance costs, underwriting commissions and expenses. In July 2020, the underwriters in the U.S. IPO exercised a portion of their over-allotment option, whereby we received additional gross proceeds of approximately $6.9 million (approximately SEK 63 million) before deduction of issuance costs, underwriting commissions and expenses. Our ADSs trade on The Nasdaq Global Select Market under the ticker "CALT."

Our registered office is located at Kungsbron 1, C8, SE-111 22, Stockholm, Sweden, and our telephone number is +46 (0) 8 411 3005. Our website address is *www.calliditas.se*. The information contained on our website is not a part of this annual report.

We have three wholly owned subsidiaries, located in Sweden and the United States. The U.S. subsidiary is Calliditas Therapeutics, Inc. (renamed Calliditas NA Enterprises Inc. effective July 1, 2021) and Calliditas Therapeutics US Inc. and the Swedish subsidiary is Nefecon AB. We have two additional subsidiaries, Genkyotex S.A., located in France, and Genkyotex Suisse S.A., located in Switzerland.

In November 2020, we acquired a controlling interest in Genkyotex S.A., or Genkyotex, a biopharmaceutical company specializing in NOX therapies with offices in France and Switzerland. Genkyotex's unique platform enables the identification of orally available small molecules which selectively inhibit specific NOX enzymes that amplify multiple disease processes such as fibrosis and inflammation. The acquisition of Genkyotex adds a late-stage orphan pipeline asset and platform in inflammation and fibrosis to our product portfolio in orphan diseases. In March 2021, we participated in a rights issue in Genkyotex, and increased our ownership percentage to 90.2% of the share capital of Genkyotex.

The SEC maintains an Internet site (*www.sec.gov*) that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC.

B. BUSINESS OVERVIEW

Overview

We are a clinical-stage biopharmaceutical company focused on identifying, developing and commercializing novel treatments in orphan indications, with an initial focus on renal and hepatic diseases with significant unmet medical needs. Our lead product candidate, Nefecon, is a proprietary, novel oral formulation of budesonide, an established, highly potent local immunosuppressant, for the treatment of the autoimmune renal disease IgA nephropathy, or IgAN, for which there is a high unmet medical need and there are no approved treatments. IgAN is a progressive, chronic disease that over time results in deterioration of kidney function in patients, many of whom end up at risk of developing end-stage renal disease, or ESRD, with the need for dialysis or kidney transplant. Nefecon is currently the only pharmaceutical candidate in development for IgAN that is intended to be disease-modifying. Nefecon targets the ileum, the distal region of the small intestine, which is the presumed origin of IgAN due to the ileum being the location of the highest concentration of the Peyer's patches, which are responsible for the production of secretory immunoglobulin A, or IgA, antibodies. Nefecon is the only compound in development for IgAN that has met the primary and key secondary endpoint in a randomized, double-blind, placebo-controlled Phase 3 clinical trial. Nefecon has been granted orphan drug designation for the treatment of IgAN in the United States and the European Union. We also recently acquired a controlling interest in Genkyotex S.A., or Genkyotex, providing us with access to a novel platform of Nicotinamide adenine dinucleotide phosphate, oxidase, or NOX, inhibitors, which we intend to primarily develop for orphan diseases with fibrotic components, with a main focus on kidney and liver diseases.

In November 2020, we reported positive topline data from Part A of our global, pivotal Phase 3 clinical trial, which we refer to as NefIgArd. In this trial of 200 patients, treatment with Nefecon was associated with a statistically significant and clinically meaningful reduction of protein in the urine, or proteinuria, and stabilization of kidney function. The primary endpoint analysis showed a 31% mean reduction in the treatment arm versus baseline, with placebo showing a 5% mean reduction versus baseline, resulting in a 27% mean reduction at nine months of the treatment arm versus placebo (p=0.0005). The key secondary endpoint, eGFR, showed a treatment benefit of 7% versus placebo at nine months, reflecting stabilization in the treatment arm and a 7% decline of eGFR in the placebo arm (p=0.0029). This reflected an absolute decline of 4.04 ml/min/1.73m2 in the placebo group over 9 months compared to a 0.17 ml/min/1.73m2 decline in the treatment arm. In addition, the trial showed that Nefecon was generally well-tolerated. On the basis of the positive results of Part A of NefIgArd, we submitted a New Drug Application, or NDA, in March 2021 for accelerated approval by the FDA. In April 2021, Nefecon was granted accelerated assessment by the EMA, and we intend to submit a Marketing Authorisation Application, or MAA, for conditional approval by the EMA in the second quarter of 2021. In January 2021, we completed the enrollment of all 360 patients in NefIgArd, which includes 200 patients previously enrolled in Part A and another 160 patients enrolled for Part B. In February 2021, we announced dosing of the first patient in the global open-label extension, or OLE, of NeflgArd, which is open to all qualifying patients who have completed NeflgArd. We also previously conducted a Phase 2b trial with 150 patients, which also met the identical primary and key secondary endpoint.

Although we observed a statistically significant and clinically meaningful reduction of proteinuria, the FDA and EMA have not provided a specific level of reduction of proteinuria that would be required to obtain marketing approvals. Accordingly, there can be no assurance that the level of reduction of proteinuria that we observed in Part A of our NefIgArd trial will be sufficient to satisfy the FDA and EMA. The FDA accelerated approval pathway, and the accelerated assessment process of the EMA, may not lead to a faster development process and does not increase the likelihood that our product candidates will receive marketing approval. If approved, we expect that Nefecon will be the first treatment on the market indicated for IgAN. We believe that if Nefecon can successfully treat IgAN patients, their kidney function will be preserved. We retain worldwide rights to Nefecon other than in Greater China and Singapore where we have established a strategic collaboration.

IgAN, sometimes referred to as Berger’s disease, is a serious progressive autoimmune disease of the kidney in which up to 50% of patients end up at risk of developing ESRD within ten to twenty years. The standard of care for ESRD is dialysis or kidney transplant, which represents a significant health economic burden as well as a material impact on patients’ quality of life. IgAN is an orphan disease that we estimate affects approximately 130,000 to 150,000 people in the United States and approximately 200,000 people in Europe. A significantly higher prevalence has been observed in Asia, including in Greater China, where IgAN has historically been a leading cause of ESRD. We estimate that IgAN affects approximately two million people in Greater China and approximately 180,000 people in Japan. We estimate the U.S. market opportunity for IgAN to be approximately $9.0 billion to $10.0 billion annually, based on our estimate of the prevalence of the disease in the United States and primary market research conducted by IQVIA that we commissioned to assess preliminary reimbursement levels perceived acceptable by U.S.-based payors. In this market, we intend to primarily focus on treating those IgAN patients that are at risk of progressing to ESRD.

Although IgAN manifests in the kidney, most scientific studies have found that the pathogenesis of IgAN begins in the ileum. Masses of lymphatic tissue, known as Peyer’s patches, are predominantly found in the ileum where they produce secretory IgA antibodies. IgA antibodies play a key role in the immune system by protecting the body from foreign substances, such as food-derived factors, bacteria and viruses. Patients with IgAN have elevated levels of a subclass of IgA antibodies produced in the gut that lack units of galactose, a type of sugar, at their hinge region. The hinge region is a flexible amino acid stretch in the central part of the heavy chains of the IgA antibody. In IgAN patients, a combination of genetic predisposition and environmental, bacterial or dietary factors are presumed to lead to an increased production of these galactose-deficient IgA antibodies, potentially in combination with increased intestinal permeability, leading to these antibodies appearing in the blood. The galactose-deficient IgA antibodies are immunogenic when found in the circulation, which triggers autoantibodies, or antibodies created by the body in response to a constituent of its own tissue. This in turn leads to the formation of pathogenic immune complexes, or clusters of antibodies, which deposit in the membranes of the glomeruli, the kidney’s filtration apparatus. These trapped immune complexes initiate an inflammatory cascade that damages the membranes, resulting in protein and blood leaking into the urine. Ultimately the glomeruli are destroyed, reducing the kidney’s ability to remove waste products from the blood. As the disease progresses, waste products that are normally removed from the blood accumulate, resulting in potentially life-threatening complications that in many patients will lead to the need for dialysis or kidney transplant.

Despite a need for new therapies, there have been few new drugs developed for chronic kidney diseases during the last decade and there is no approved therapy for IgAN. Patients with IgAN are typically initially given antihypertensive medications as recommended by the non-profit organization Kidney Disease: Improving Global Outcome consortium, or KDIGO. This treatment regimen initially attempts to manage the symptoms of IgAN by decreasing blood pressure and reducing proteinuria but does not address the underlying cause of IgAN. Over time, physicians attempt to control disease progression with a variety of off-label treatments, as a significant proportion of patients experience continued deterioration of kidney function, with no approved treatment options currently available. For IgAN patients whose disease has progressed, clinicians may treat patients with systemic immunosuppressive agents, primarily consisting of high doses of systemic corticosteroids, such as prednisone, prednisolone and methylprednisolone. While some published reports indicate that these agents may reduce proteinuria, this high dosing of systemic corticosteroids is also associated with a wide range of adverse events, including high blood pressure, weight gain, diabetes, serious infections and osteoporosis.

Nefecon is currently the only pharmaceutical candidate in development that is designed to target the ileum, with the goal of being a disease-modifying treatment. Nefecon is designed to release a high dose of a locally acting immunosuppressive agent in the ileum, where the highest concentration of Peyer's patches exists, to reduce the formation of secretory galactose-deficient IgA antibodies and their appearance in the blood.

Nefecon's active ingredient is budesonide, an established, highly potent locally acting corticosteroid. After the active ingredient has been released and has had its effect in the intestinal mucosa, it enters the liver, where 90% is cleared in first pass metabolism, resulting in the inactivation of a majority of the active ingredient before the substance reaches the systemic circulation. This high metabolism may limit systemic immunosuppressive activity and decrease the significant side effects associated with systemic corticosteroids that are currently used off-label to treat IgAN, of which only 20% to 30% are cleared in first pass metabolism. Other locally delivered approved therapies where budesonide is the active ingredient include those for asthma, allergic rhinitis, Crohn's disease and ulcerative colitis. Based on the written minutes from our End-of-Phase 2 meeting, the FDA has indicated alignment on a pathway toward accelerated approval in the United States based on the evaluation of a surrogate endpoint rather than a clinical outcome endpoint. We have received similar feedback from the EMA on a conditional market access pathway in the European Union and Nefecon was granted accelerated assessment by the EMA.

Additionally, since Nefecon is a reformulation of the active ingredient in an existing approved drug, we are pursuing the Section 505(b)(2) pathway for regulatory approval by the FDA in the United States and the hybrid application pathway for conditional approval by the EMA in the European Union. Nefecon is the current name for our lead product; the final proprietary name has not yet been determined.

Nefecon Phase 3 Clinical Trial Results

Nefecon is the most advanced clinical-stage product candidate for the treatment of IgAN. In November 2020, we reported positive topline data from our global, pivotal Phase 3 clinical trial in IgAN, which we refer to as NefIgArd. NefIgArd is designed to evaluate reduction of the surrogate marker proteinuria as its primary endpoint, which is the same endpoint used in our previously completed NEFIGAN clinical trial. We randomized our first patient in NefIgArd in November 2018. NefIgArd is a double-blind, placebo-controlled, two-part Phase 3 clinical trial. The first part of NefIgArd, which we refer to as Part A, is a pivotal efficacy and safety trial. The primary endpoint of Part A is the decrease in proteinuria in the first 200 randomized and dosed patients. In addition, a secondary endpoint of Part A is the difference in kidney function between treated and placebo patients as measured by eGFR. The key secondary endpoint in Part A, which is a measure of eGFR over a nine-month period, is also expected to be informative of the primary endpoint of Part B, as discussed below. On the basis of the positive Part A results, we submitted an NDA in March 2021 for accelerated approval by the FDA. In April 2021, Nefecon was granted accelerated assessment by the EMA, and we intend to submit an MAA for conditional approval by the EMA in the second quarter of 2021.

The second part, which we refer to as Part B, is a post-approval confirmatory trial designed to provide evidence of long-term renal benefit. Following completion of enrollment in Part A in December 2019, completed enrollment for Part B of another 160 patients in January 2020 and the beginning of 2021 in order to power Part B to assess the difference in kidney function between treated and placebo patients as measured by eGFR over a two-year period from the start of dosing of each patient. We experienced a reduced enrollment rate over the last several months of 2020 due to the impact of the COVID-19 pandemic, and we did not complete full enrollment until January of 2021. Having successfully completed enrollment, we expect to report data from Part B in early 2023. Across both parts, NefIgArd has enrolled a total of 360 patients and will generate nine months of dosing data, as well as an aggregate of 15 months of follow-up data. If approved by the FDA, we intend to market and commercialize Nefecon in the United States as a treatment specifically designed to have a disease-modifying effect for IgAN by preserving kidney function and thereby avoiding progression to ESRD.

In our completed pan-European Phase 2b clinical trial, Nefecon was also observed to statistically significantly reduce proteinuria and to provide clinical benefit by preserving kidney function, as measured by estimated glomerular filtration rate, eGFR, which is considered a key metric for measuring kidney disease progression. This trial, known as NEFIGAN, was a double-blind, placebo-controlled trial in 150 patients randomized to receive either 8 mg or 16 mg per day of Nefecon or placebo, each on top of optimized RAS blockade to lower blood pressure, the predominant current standard of care. NEFIGAN achieved its primary endpoint of reduction in proteinuria for the 16 mg dose cohort. As measured by the urine protein creatinine ratio, or UPCR, patients in the placebo cohort exhibited an increase in proteinuria of 2.7%, while patients in the 16 mg dose cohort also exhibited statistically significant and clinically meaningful reductions in proteinuria of 27.3%. Patients treated with Nefecon also exhibited stabilization of eGFR, reflecting preservation of kidney function, while patients administered with placebo continued to show deterioration.

Nefecon Phase 2 Clinical Trial Results

In order to approve a drug, the FDA generally requires one or more clinical trials demonstrating that the product candidate meets an endpoint that represents a direct clinical outcome, such as survival, decreased pain or the absence of disease, which we refer to as a clinical endpoint. However, in certain circumstances, the FDA selectively allows the use of surrogate endpoints that are reasonably likely to predict clinical benefit in clinical trials to permit a more rapid development and approval path of treatments for serious or life-threatening diseases. For treatments related to chronic kidney disease, clinical trials have generally relied on clinical endpoints such as time to dialysis or transplantation. Due to the significant expense associated with the large patient numbers and extended clinical trial duration required to adequately measure such clinical endpoints, few new therapeutic drug candidates have emerged over the past two decades to treat renal disease. In 2012, the FDA and the American Society of Nephrology, or ASN, founded the Kidney Health Initiative, or KHI, with the goal of supporting research and innovation for the development of safe and efficacious treatments for kidney disease. We funded a collaboration with Tufts University and the University of Utah to conduct a meta-analysis based on selected, well-defined clinical trials in IgAN patients in order to provide regulatory authorities with a data-driven basis to accept a novel surrogate marker for potentially accelerated approval of treatments for IgAN. The final analytical framework from this collaboration showed a robust statistical relationship between reduction in proteinuria and reduction of the risk of progression to ESRD. We believe that this framework, together with the research and analysis conducted by the KHI and spearheaded by ASN, the National Kidney Foundation and the FDA, led to the FDA's acceptance of an accelerated approval pathway at our End-of-Phase 2 meeting in January 2017. This change in regulatory approach was fundamental to our decision to commence our ongoing Phase 3 clinical trial for Nefecon in IgAN.

Genkyotex Acquisition

In 2020, we acquired a controlling interest in Genkyotex, which provides us with access to a novel platform of NOX inhibitors that we intend to develop for orphan diseases with fibrotic components, primarily focused on kidney and liver disease. Examples of fibrotic indications include primary biliary cholangitis, or PBC, primary sclerosing cholangitis, or PSC, and idiopathic pulmonary fibrosis, or IPF, and non-alcoholic steatohepatitis, or NASH. The lead compound, setanaxib has shown clinically relevant activity across a variety of biomarkers related to fibrosis as well as Fibroscan in a recently completed Phase 2 trial in PBC, despite not achieving its primary endpoint. In addition, two investigator led studies are underway, exploring setanaxib in IPF and diabetic kidney disease, or DKD. 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 positive data, Genkyotex plans to initiate a Phase 2/3 trial 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 the second half of 2021.

Clinical Development Plans for Nefecon and Setanaxib

Beyond IgAN, we are exploring applications of Nefecon or its active ingredient for other autoimmune diseases in which it may have therapeutic potential, such as PBC and autoimmune hepatitis, or AIH. We are planning to evaluate setanaxib as our first candidate in PBC, but will also continue to evaluate Nefecon for the treatment of PBC, a progressive and chronic autoimmune disease of the liver, that causes damage to the small bile ducts that drain bile from the liver, which can result in cholestasis and ultimately destruction of the bile ducts, leading to liver cell damage and ultimately liver failure, resulting in the need for a liver transplant. There are currently no approved therapies that specifically address the autoimmune response that is believed to drive PBC or the inflammatory consequences of the autoimmune response. Nefecon is designed to deliver high peak concentrations of its active ingredient to the intestine, which is then transported directly to the liver in order to locally reduce the autoimmune processes that drive PBC. We have received orphan drug designation for the treatment of PBC by the FDA. In addition, through our recent acquisition of a controlling interest in Genkyotex, we have acquired access to a novel NOX inhibitor platform from which the lead compound, setanaxib, has completed a Phase 2 trial in PBC and recently received orphan drug designation for the treatment of PBC in the U.S. and Europe. Based on its Phase 2 results indicating clinically relevant anti-fibrotic activity despite not achieving its primary endpoint in a trial in PBC, 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 positive data, Genkyotex plans to initiate a Phase 2/3 trial in PBC, incorporating higher dosing than that used in the Phase 2 trial and using alkaline phosphatase, or ALP, as a primary endpoint. The final design and protocol are subject to further feedback and commentary by the FDA. Genkyotex plans to initiate the trial 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 the second half of 2021 which will study administration of setanaxib in conjunction with immunotherapy targeting cancer associated fibroblasts, or CAFs.

We have also in-licensed Budenofalk 3 mg oral capsules from the German pharmaceutical company Dr. Falk Pharma GmbH, or Falk Pharma, in order to obtain regulatory approval and commercialize Budenofalk in the United States for the treatment of AIH, another rare immune inflammatory liver indication. Budenofalk has been tested in a large randomized, controlled clinical trial in AIH patients and is approved for the treatment of AIH in several countries in Europe, but there has been no clinical development or regulatory approval in the United States. Budenofalk is a formulation of budesonide originally developed to treat Crohn’s disease. We believe Budenofalk has the potential to complement our activities in the United States. We have received orphan drug designation for the treatment of AIH using budesonide by the FDA. We discussed our development plans with the FDA for AIH during 2020 and have received helpful feedback as to the potential regulatory pathway forward. However, we expect to have further interactions with FDA in 2021 before we are in a position to affirmatively decide on the design and timing of a clinical program.

If approved by the FDA, we intend to commercialize Nefecon independently in the United States by establishing a targeted commercial sales infrastructure with a primary focus on IgAN patients at risk of progressing to ESRD. We intend to launch Nefecon in the United States in the first half of 2022, if approved. We are currently focused on disease education, interaction with patient advocacy groups and market access, with the goal of educating physicians about the disease origin, understanding patient needs and preparing our market access strategy for Nefecon. We believe this market can be addressed by a small and dedicated number of marketing and medical sales specialists, initially approximately 40, to efficiently cover the approximately 3,700 nephrologists focused on our target patient population in the United States.

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 IgAN in Greater China and Singapore. 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.

NOX inhibitors is a fairly new drug class focused on inhibiting the overproduction of reactive oxygen species, or ROS, which can drive fibrogenesis across multiple organs. We believe that this platform has several potential applications across orphan indications, focusing on anti-fibrotic and anti-inflammatory applications. Setanaxib is the lead compound, complemented by a research effort focused on developing follow up compounds. Potential indications include PBC, PSC, IPF, NASH and various kidney indications with a fibrotic component. There is also a potential to explore oncology indications, using setanaxib administered with checkpoint inhibitors to address tumor drug resistance related to fibroblasts.

Our Company and Management Team

We were formed in 2004 in order to develop and commercialize Nefecon, which we acquired from Nefecon's inventors, Professors Bengt Fellström and Roger Hällgren at Uppsala University, Sweden. We are led by an experienced and dedicated management team with more than 15 years of prior experience on average in the pharmaceutical industry, including at leading pharmaceutical companies such as GlaxoSmithKline, Novo Nordisk, Pfizer and UCB. Our board of directors includes highly qualified researchers, pharmaceutical sector executives and experts in the fields of drug development, corporate development and pharmaceutical commercialization. We are supported by a highly regarded network of leading experts within the field of IgAN, including prominent IgAN specialists throughout the world that serve as external advisors and investigators on clinical trials of Nefecon.

COVID-19 Pandemic

As of the date of this annual report, the impact of the COVID-19 pandemic to our business has been limited. 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 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 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. With sites in 19 countries participating in the trial, there are several geographies facing challenging situations in their healthcare systems, but we believe were able to put in place effective measures designed to address patient safety and preserve trial data integrity, in close cooperation with national coordinators, primary investigators, study nurses and our contract research organization. In January 2021, we completed the enrollment of all 360 patients in NefIgArd, which includes 200 patients previously enrolled in Part A and another 160 patients enrolled for Part B. We intend to report data from Part B in early 2023, subject to any further impact from the COVID-19 pandemic to our business. There are, however, 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.

Although we believe we have implemented strategies to potentially minimize the impact of the COVID-19 pandemic to our business, we expect that we may experience delays with respect to the initiation of certain additional trials. The extent to which the COVID-19 outbreak impacts the timing of these additional 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. We will continue to evaluate the impact of the COVID-19 pandemic to our business.

Our Strategy

We aim to apply our interdisciplinary expertise in pharmaceutical product development to identify, develop and commercialize novel treatments in orphan indications, with an initial focus on renal and hepatic diseases with significant unmet medical needs. To achieve this objective, we intend to pursue the following strategies:

Rapidly and efficiently advance Nefecon through Phase 3 clinical development and regulatory approval in order to establish a new standard of care for IgAN. We reported positive topline results from Part A of NefIgArd in November of 2020, where the trial met the primary and key secondary endpoint. On the basis of the positive results of Part A of NefIgArd, we submitted an NDA in March 2021 for accelerated approval by the FDA. In April 2021, Nefecon was granted accelerated assessment by the EMA, and we intend to submit an MAA for conditional approval by the EMA in the second quarter of 2021.

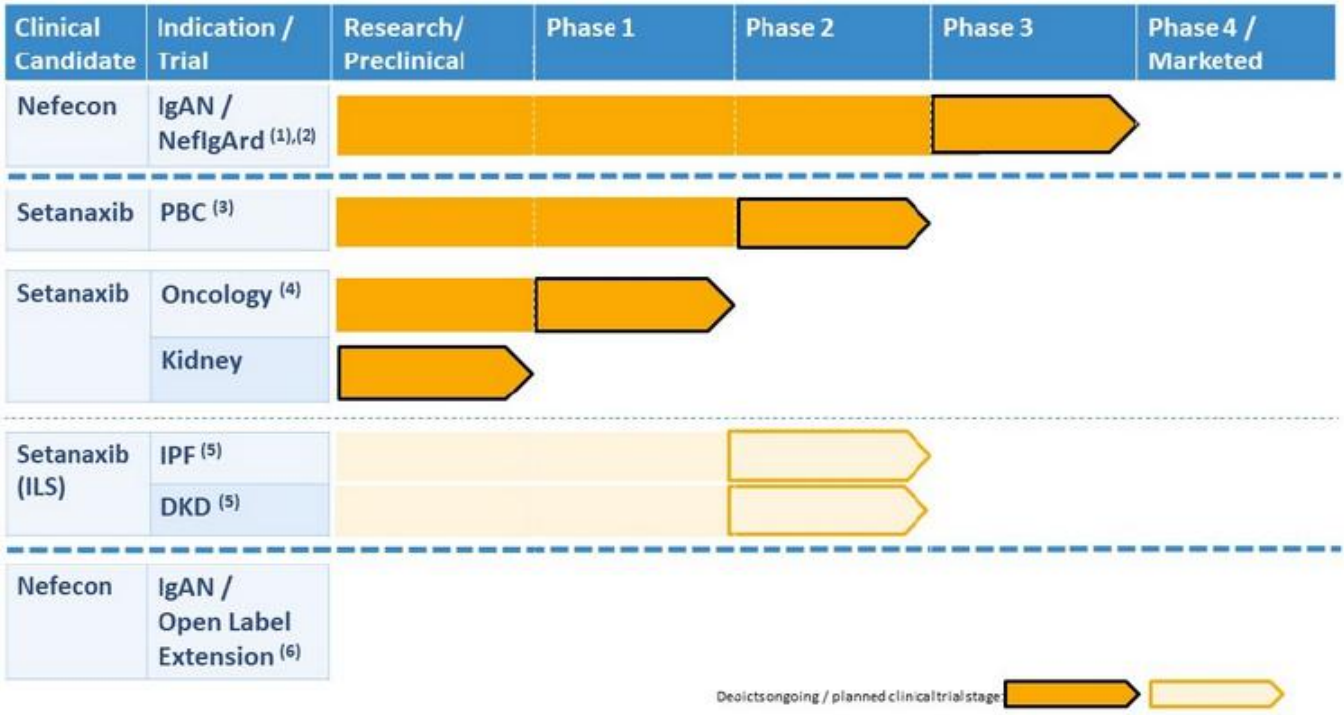
Maximize the potential of Nefecon, if approved, through commercialization independently and through collaborations with third parties. We retain worldwide rights to Nefecon other than in Greater China and Singapore. If approved by the FDA, we intend to commercialize Nefecon independently in the United States by establishing a targeted commercial sales infrastructure with a primary focus on IgAN patients at risk of progressing to ESRD. We intend to launch Nefecon in the United States in the first half of 2022, if approved. Based on third party research we commissioned to assess the U.S. nephrologist IgAN market, we believe this market can be served by a small and dedicated number of marketing and medical sales specialists to efficiently cover the approximately 3,700 nephrologists focused on our target patient population in the United States. In 2019, we granted a license to Everest to develop and commercialize Nefecon for IgAN and other potential indications in Greater China and Singapore. 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.

Leverage our existing pipeline, proprietary formulations and significant experience with drug release technology to explore treatments in select orphan hepatic diseases. We believe that our proprietary technology has the potential to treat orphan hepatic diseases in which therapeutic benefits can be achieved by a local release of a potent immunosuppressant targeted at the liver while limiting systemic side effects. We are exploring additional indications to apply Nefecon or its active ingredient, and are prioritizing conditions in which there is a strong scientific and clinical rationale and an attractive commercial opportunity, such as PBC and AIH. There are currently no approved therapies that specifically address the autoimmune response that is believed to drive PBC or the inflammatory consequences of the autoimmune response. In addition, there are no approved therapies in the United States for AIH. We discussed our development plans with the FDA for AIH during 2020 and have received helpful feedback as to the potential regulatory pathway forward. However, we expect to have further interactions with FDA in 2021 before we are in a position to affirmatively decide on a clinical program.

Leverage and enhance our product pipeline complemented by selective acquisitions or in-licensing of product candidates focused on nephrology or orphan diseases. In addition to building partnerships to enhance broad commercialization of Nefecon, we actively seek to exploit and leverage our existing pipeline as well as acquire or in-license additional product candidates that present a strong strategic and commercial fit. We believe that our team is well-positioned to identify attractive assets and accelerate their development. In particular, we seek to expand our pipeline with product candidates with an attractive risk/reward profile, such as those that have demonstrated proof-of-concept in patients, are in late-stage clinical development and can be rapidly advanced to market approval. We currently focus on, and we expect to continue to focus on, nephrology and orphan diseases for our clinical development efforts. In 2020, we acquired a controlling interest in Genkyotex, a leader in NOX inhibition therapies. Genkyotex's lead product candidate, setanaxib, is an example of a late stage asset with potential for application in a variety of orphan indications, which adds to and complements our focus on inflammatory disease and provides us with a platform with anti-fibrotic and anti-inflammatory compounds.

Our Pipeline

The following table summarizes the development stage and status of our portfolio of key product candidates:



(1) Pursuing accelerated approval pathway in the United States, an expedited pathway, and conditional approval pathway in the European Union.

(2) Pursuing under the Section 505(b)(2) pathway in the United States and, as applicable, the hybrid application pathway in the European Union.

(3) Phase 2/3 trial planned to start in the second half of 2021.

(4) Phase 2 trial in head and neck cancer planned to start in the second half of 2021.

(5) Investigator-led trial. Not controlled or funded by Calliditas.

(6) Open label extension of the NefIgArd study.

We submitted an NDA for Nefecon for accelerated approval by the FDA in March 2021. In April 2021, Nefecon was granted accelerated assessment by the EMA, and we intend to submit an MAA for conditional approval by the EMA in the second quarter of 2021.

In addition, we have in-licensed Budenofalk 3 mg oral capsules and intend to develop Budenofalk in the United States for the treatment of AIH, subject to regulatory feedback. We have discussed the development plans with the FDA for AIH during 2020, but additional interaction is required before establishing any definitive clinical development plans.

Genkyotex's lead product candidate, setanaxib, was granted orphan drug designation by the FDA in October 2020, and by the European Commission in December 2020, in each case for the treatment of PBC. Genkyotex has discussed its registration strategy for setanaxib in PBC with the FDA and the EMA and expects further interactions in 2021.

Our Product Candidates

Nefecon for the Treatment of IgAN

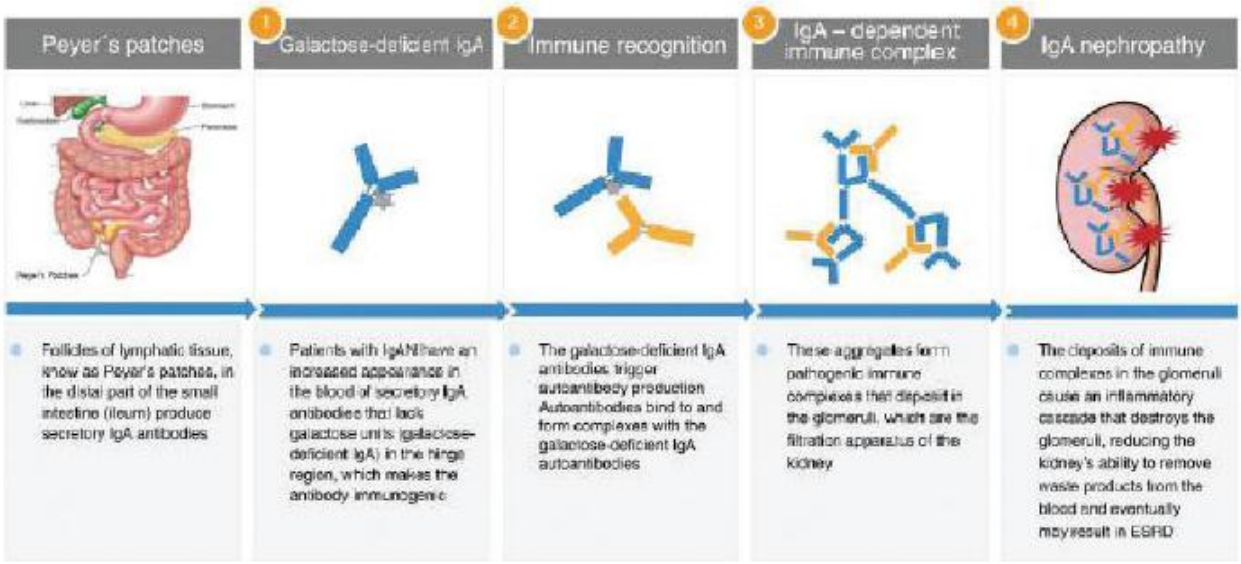
Our lead product candidate, Nefecon, is a proprietary, novel oral formulation of budesonide, an established, highly potent local immunosuppressant, for the treatment of IgAN, for which there are no approved treatments. Nefecon, which is the most advanced clinical-stage product candidate for the treatment of IgAN, has been granted orphan drug designation. Nefecon is designed to slow the progression of IgAN and delay kidney failure in patients affected by the disease. Nefecon is currently the only pharmaceutical candidate in development that is intended to be disease-modifying. Nefecon is the only compound in development for IgAN that has met the primary and key secondary endpoint in a randomized, double-blind, placebo-controlled Phase 3 clinical trial. In November 2020, we reported positive topline data of this global, pivotal Phase 3 clinical trial, which we refer to as NefIgArd. In this trial, treatment with Nefecon was associated with a statistically significant and clinically meaningful reduction of protein in the urine, or proteinuria, and stabilization of kidney function. We also previously conducted a Phase 2b trial with 150 patients, which also met the identical primary and key secondary endpoint. We believe that if Nefecon can successfully treat IgAN patients, their kidney function will be preserved.

IgAN Disease Background

IgAN is a serious progressive autoimmune disease of the kidney, in which up to 50% of patients end up at risk of developing ESRD within ten to twenty years. The standard of care for ESRD is dialysis or kidney transplant, which represents a significant health economic burden as well as a material impact on patients' quality of life. IgAN is an orphan disease that we estimate affects approximately 130,000 to 150,000 people in the United States and approximately 200,000 people in Europe. A significantly higher prevalence of IgAN has been observed in Asia, including in Greater China, where it has historically been a leading cause of ESRD. We estimate that IgAN affects approximately two million people in Greater China. These estimates 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 Greater China. According to large Chinese epidemiology studies, IgAN represents around 40% of renal biopsies in China.

Although IgAN manifests in the kidney, most scientific studies have found that the pathogenesis of IgAN begins in the ileum, the distal part of the small intestine. The intestine represents the largest component of the immune system in the body, a site of continuous exposure to antigens and pathogens. Masses of lymphatic tissue, known as Peyer's patches, are predominantly found in the ileum where they produce secretory IgA antibodies. IgA antibodies play a key role in the immune system by protecting the body from foreign substances such as food-derived factors, bacteria and viruses. Patients with IgAN have elevated levels of a subclass of IgA antibodies produced in the gut that lack units of galactose, a type of sugar, at their hinge region. The hinge region is a flexible amino acid stretch in the central part of the heavy chains of the IgA antibody. In IgAN patients, a combination of genetic predisposition, environmental, bacterial or dietary factors are presumed to lead to an increased production of these galactose-deficient IgA antibodies, potentially in combination with increased intestinal permeability, which leads to these antibodies appearing in the blood. The galactose-deficient IgA antibodies are immunogenic when found in the circulation, which triggers autoantibodies, or antibodies created by the body in response to a constituent of its own tissue. This in turn leads to the formation of pathogenic immune complexes, or clusters of antibodies, which deposit in the membranes of the glomeruli, the kidney's filtration apparatus. These trapped immune complexes initiate an inflammatory cascade that damages the membranes, resulting in protein and blood leaking into the urine. Ultimately the glomeruli will be destroyed, reducing the kidney's ability to remove waste products from the blood. As the disease progresses, waste products that are normally removed from the blood will accumulate and will lead to potentially life-threatening complications that in many patients will lead to the need for dialysis or kidney transplant. Dialysis is estimated to cost between $70,000 and $200,000 per patient per year, with a total estimated annual hemodialysis cost in the United States of $42.0 billion. The average cost of a kidney transplant is approximately $415,000 with a total estimated annual cost in the United States of $7.0 billion. The graphic below shows the pathogenesis of IgAN.

IgA production in the Peyer's patches in the ileum is believed to cause IgAN in the kidney.



Treatment Landscape for IgAN Patients

There are currently no approved treatment options for IgAN. KDIGO recommends the use of blood pressure-lowering agents that inhibit or block the renin-angiotensin system, or RAS, using either angiotensin converting enzyme, or ACE, inhibitors or angiotensin receptor blockers, or ARBs. RAS inhibition reduces pressure in the kidney glomeruli, thereby lowering leakage and protein excretion in urine. Treatment via RAS inhibition is primarily symptomatic and does not address the underlying cause of IgAN. Over time, physicians attempt to control disease progression with a variety of off-label treatments, as a significant proportion of patients experience continued deterioration of kidney function, with no approved treatment options currently available.

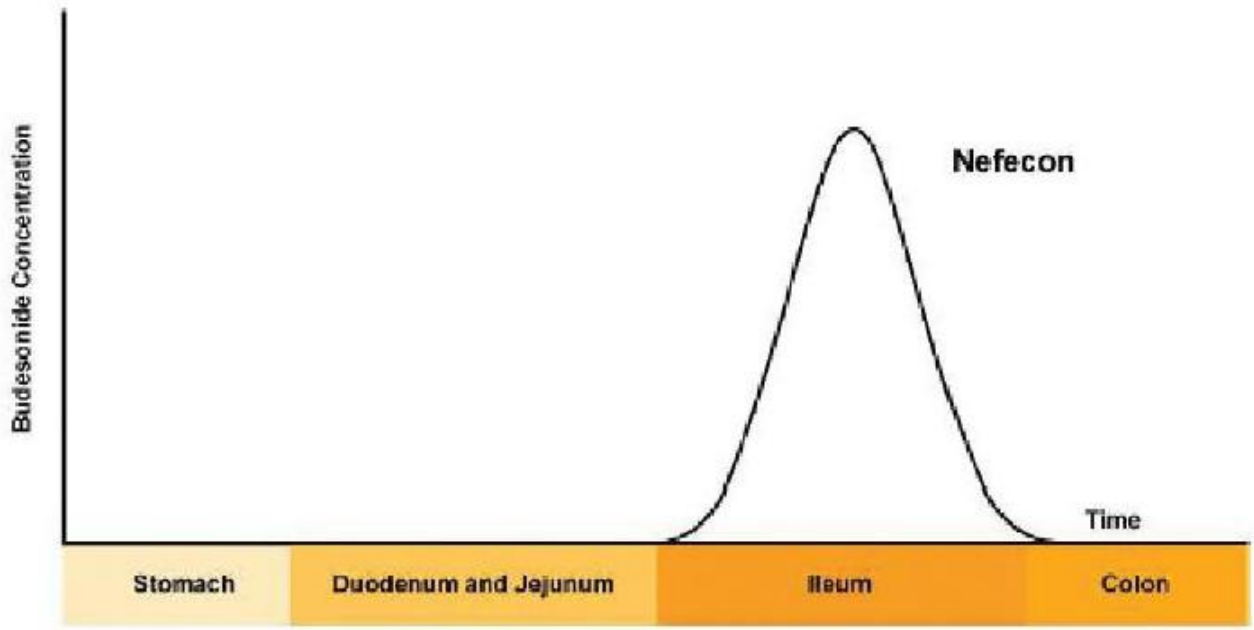
For IgAN patients whose disease has progressed, clinicians may treat patients with systemic immunosuppressive agents, primarily consisting of high doses of systemic corticosteroids, such as prednisone, prednisolone and methylprednisolone. While some published reports indicate that these agents may reduce proteinuria, high dosing of systemic corticosteroids is also associated with a wide range of adverse events, including high blood pressure, weight gain, diabetes, serious infections and osteoporosis.

The seriousness of these adverse events in patients with IgAN has been documented in two independent clinical trials investigating the safety and efficacy of systemic corticosteroids in IgAN. In the Therapeutic Evaluation of Steroids in IgA Nephropathy Global, or TESTING, clinical trial conducted by The George Institute for Global Health based in Sydney, Australia, 262 patients who had progressive IgAN despite treatment with RAS blockade agents were randomized to receive the systemic corticosteroid methylprednisolone or placebo. A significantly higher rate of serious infections and two infection-related deaths were observed in patients receiving methylprednisolone, leading to the suspension of the trial. While patients receiving methylprednisolone appeared to have improved outcomes compared to those receiving placebo, the early termination of the trial prevented a full efficacy analysis. In the open-label Supportive Versus Immunosuppressive Therapy for the Treatment of Progressive IgA Nephropathy, or STOP IgAN, trial conducted by Rheinisch Westfälische Technische Hochschule of Aachen University, there was also an increase in the rate of serious infections in the 82 patients who received the systemic corticosteroid prednisolone, as well as one infection-related death in the treatment cohort. In this trial, high-dose systemic corticosteroids were not observed to have a lasting effect on proteinuria and there was no significant difference in the decline in eGFR. The STOP IgAN trial concluded that the addition of immunosuppression, including systemic corticosteroids, to comprehensive supportive care was not beneficial in IgAN.

Our Solution: Nefecon

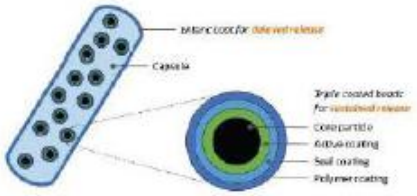
Nefecon is a proprietary, novel oral formulation of budesonide, designed to deliver a targeted and highly concentrated dose directly to the Peyer's patches that are predominantly found in the ileum. The high first pass metabolism of the active ingredient limits the adverse events typically associated with systemic corticosteroids, due to its limited spillover to the circulation. We have formulated Nefecon as a capsule with an enteric coating that prevents dissolution or disintegration in the gastric environment. The capsules are designed to travel intact through the stomach and intestine until they reach the ileum. Upon reaching the ileum, chemical and physical changes, such as acidity, trigger the disintegration of the Nefecon capsules and the release of the capsule's contents.

Nefecon is designed to release a locally acting immunosuppressant in the ileum to provide peak drug concentrations to immune cells in the Peyer's patches.



As illustrated below, Nefecon capsules contain triple coated sustained-release beads that are designed to provide a potent exposure of the active ingredient when it is released in the ileum, which we believe will locally suppress IgA antibody formation in the Peyer's patches and impair the appearance of the immune complexes in the blood. Nefecon is designed to block the initial step in the development of IgAN by preventing the formation of immune complexes that would otherwise become trapped in the glomerular membranes of the kidney, thereby having a disease-modifying effect and preserving kidney function.

Nefecon has two components: an enteric-coated capsule to deliver a local immunosuppressant to the ileum and sustained release beads that provide highly targeted local exposure of the active ingredient.



Budesonide is an established, highly potent locally acting corticosteroid that can be used for local treatment with limited systemic side effects. This active ingredient was selected because of its local potency

and high metabolization by the liver, with 90% being cleared in first pass metabolism, resulting in the inactivation of a majority of the active ingredient before the substance reaches the systemic circulation. This high metabolism limits systemic immunosuppressive activity and avoids the significant side effects associated with systemic corticosteroids that are currently used off-label to treat IgAN, of which only 20% to 30% are cleared in first pass metabolism.

Nefecon is differentiated in its properties, profile and mechanism of action as compared to certain currently marketed products that deliver budesonide to the intestine. Uceris is formulated to deliver a 9 mg tablet of budesonide specifically to the colon for the treatment of ulcerative colitis. Entocort is formulated to deliver 3 mg capsules at a maximum dose of 9 mg throughout the entire approximately eight meters of the intestine in a continuous release for the treatment of Crohn's disease. Unlike Nefecon, neither of these two formulations are designed to, or are capable of, delivering the required concentration of budesonide to the ileum to treat the cause of IgAN. We believe that any attempts to use these drugs to address IgAN would either be ineffective or would require dosing patients at levels several times higher than the doses approved, which may result in significant side effects. We have combined our proprietary formulation technology with know-how developed internally to create Nefecon. We believe this proprietary formulation will constitute a barrier to entry that would require significant time, focus and investment for a competitor to overcome. In addition, Nefecon has been granted orphan drug designation in the United States and the European Union, which will provide marketing exclusivity for seven and ten years after approval, respectively. In December 2019, we received a positive opinion from the EMA's Paediatric Committee on the pediatric investigation plan for Nefecon for the treatment of IgAN. If the pediatric investigation plan is successfully completed, Nefecon, if approved, may be eligible for an additional two years of marketing exclusivity in the European Union, on top of the potential ten years of market exclusivity provided by orphan drug designation in the European Union.

Genkyotex's Product Candidates

Genkyotex's lead product candidate, setanaxib, or GKT831, is designed to target inhibition of NOX 1 and NOX 4, which are major drivers of fibrogenesis in multiple organs. They produce reactive oxygen species, or ROS, and modulate signaling by oxidizing signaling proteins, which drive multiple inflammatory and fibrogenic pathways. 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, resulting in alignment on a regulatory pathway in the form of a pivotal and potentially registrational Phase 2/3 design incorporating higher dosing than that used in the Phase 2 trial, using alkaline phosphatase, or ALP, as a primary endpoint. The final design and protocol are subject to further feedback and commentary by the FDA. Genkyotex plans to initiate the Phase 2/3 trial in the second half of 2021.

Setanaxib is also being evaluated in a Phase 2 clinical trial initiated by researchers investigating type 1 diabetes and diabetic kidney disease, or DKD. A grant from the United States National Institutes of Health, or NIH, of $8.9 million was also awarded to Professor Victor Thannickal at the University of Alabama at Birmingham to fund a multi-year research program evaluating the role of NOX enzymes in idiopathic pulmonary fibrosis, or IPF, a chronic lung disease that results in fibrosis of the lungs. The core component of this program is a Phase 2 trial with setanaxib in patients suffering from IPF for which the enrollment of a first patient was announced in September 2020. In October 2020, setanaxib was granted orphan drug designation by the FDA, and in December 2020, setanaxib was granted orphan drug designation by the European Commission, in each case for the treatment of PBC.

Based on preclinical animal models, setanaxib has also shown promising results in combination with immunotherapies, specifically checkpoint inhibitors targeting PD-1. The studies have investigated the ability of setanaxib to affect cancer associated fibroblasts, or CAFs, which has resulted in publications of study results indicating that setanaxib might be used to reduce the negative effects of CAFs in certain tumors, including in head and neck cancer. Genkyotex is planning to initiate a Phase 2 proof of concept study in head and neck cancer in 2021, involving approximately 30 to 40 patients in order to further explore setanaxib's anti-fibrotic effects and characteristics related to CAFs.

Genkyotex also has a polyvalent platform, Vaxiclase, which is suited to the development of immunotherapies. Genkyotex has out-licensed all rights for the use of Vaxiclase as an antigen per se, or GTL003, to Serum Institute of India Pvt. Ltd., or SIIL, the world's largest producer of vaccine doses, for the development by SIIL of cellular multivalent combination vaccines against a variety of infectious diseases.

Clinical Development of Nefecon

Initial Proof of Concept Observed in a Phase 2a Clinical Trial in IgAN Patients

In 2010, we completed a single-cohort, open-label Phase 2a clinical trial at three sites in Sweden. In this trial, 16 biopsy-confirmed IgAN patients received 8 mg of Nefecon orally daily for six months, with a three-month follow-up period after discontinuation of treatment. The primary objective was an assessment of the effect of Nefecon on the presence of the protein albumin in the urine, or albuminuria, which is a sign of kidney disease, and the secondary objective was to evaluate the effect of Nefecon on eGFR. Patients in this trial had a mean reduction in albuminuria of 23% at the end of treatment, with a further reduction to 40% two months after the end of treatment, and an increase in eGFR of 8%. Nefecon was associated with a statistically significant and clinically meaningful effect on albuminuria, serum creatinine and eGFR.

The FDA utilizes the reported statistical measures when evaluating the results of a clinical trial, including statistical significance as measured by p-values, to evaluate the reported evidence of a product candidate's safety and efficacy. A result is considered to be statistically significant when the probability of the result occurring by random chance, rather than from the efficacy of the treatment, is sufficiently low. The conventional method for determining the statistical significance of a result is known as the "p-value," which represents the probability that random chance caused the result (e.g., a p-value=0.05 means that there is a 5% probability that the difference between the control arm and the treatment arm is purely due to random chance). Generally, a p-value less than 0.05 is considered statistically significant and, if not otherwise specified, we have used this conventional standard to define statistical significance for the clinical trials and data presented in this annual report.

Nefecon was observed to be well tolerated, with no serious adverse events reported. Adverse events reported in the clinical trial included abdominal pain, acne, nausea, sleep disturbances, depression and mood swings. Of the adverse events reported, 76% were classified as mild and 24% were classified as moderate. Of the adverse events reported, 56% were determined by the investigator not to be related to Nefecon. Three patients withdrew from the trial due to adverse events.

Confirmatory Proof of Concept Observed in a Phase 2b Clinical Trial in IgAN Patients

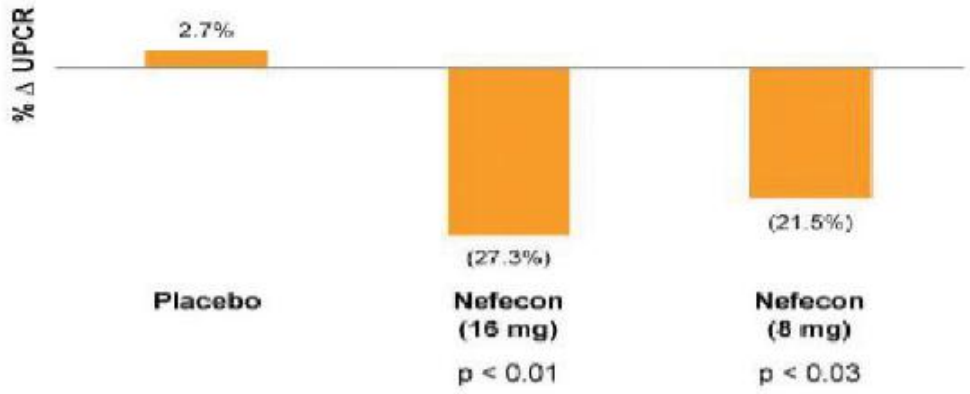
In 2015, we completed a double-blind, placebo-controlled clinical trial, known as NEFIGAN, in 150 adult patients. In this trial, patients were randomized to receive either 8 mg or 16 mg per day of Nefecon or placebo, each on top of optimized RAS blockade to lower blood pressure, the predominant current standard of care. This trial involved 62 sites across ten countries in Europe, and was the largest double-blind trial ever conducted with an investigational candidate in IgAN patients.

All patients with biopsy-confirmed IgAN were included in a run-in period of six months. During this period, patients were treated with RAS blockade therapies, including ACE inhibitors and ARBs. The objective of this run-in period was to ensure that patients were on an individually optimized and stable dose of RAS blockade therapy sustainable for the duration of the treatment period. The enrolled patients on a stable dose were then re-screened based on specific inclusion criteria, including, among other things, proteinuria and eGFR levels, in order to be randomized into the trial. The trial was initially designed to include 90 patients, based on an expected conversion ratio of 40% to 45% from enrollment in the run-in period to randomization into the trial. However, the actual conversion ratio was 70% to 75%, resulting in 150 patients being randomized, as optimization of RAS blockade therapies had less impact than initially expected. The patients were then randomized to receive 8 mg Nefecon, 16 mg Nefecon or placebo once a day for nine months. At the end of nine months, treatment was discontinued and the patients were observed for an additional three months.

The primary endpoint evaluated in NEFIGAN was mean reduction in proteinuria as measured by UPCR. As contemplated by the trial design, we conducted a predefined analysis after the first 90 patients had completed their nine-month treatment phase. This predefined analysis was conducted on 149 randomized patients in the trial who received at least one dose of Nefecon or placebo and underwent at least one post-dose efficacy measurement (one patient randomized into the trial was unable to swallow the capsule containing the study drug). For those patients who had not yet completed the nine months in the trial, we conducted the predefined analysis using an industry-standard statistics approach, known as the Mixed-Effect Model Repeated Measure model, or MMRM. MMRM is a statistical technique that is often utilized by trial sponsors, where necessary, in data packages submitted to both the FDA and the EMA in cases where the full dataset is not available for analysis. This approach used the data from the completed cohorts to impute data for those not yet completed in order to arrive at statistically validated results that would have been expected to be observed had such individuals completed the full nine months of dosing.

The primary endpoint was achieved during this planned predefined analysis, and under the predefined protocol, no further analysis of the primary endpoint was to be conducted. In the interim analysis, patients in the placebo cohort exhibited an increase in proteinuria of 2.7%. Results from the 16 mg dose cohort, indicated that Nefecon was associated with statistically significant and clinically meaningful reductions in proteinuria. Results from the 16 mg dose cohort indicated that Nefecon was associated with a mean reduction in proteinuria of 27.3% ($p<0.01$). Based on these results, we selected 16 mg as the dose for our Phase 3 clinical trial. Patients in the 8 mg dose cohort also exhibited a mean reduction in proteinuria of 21.5% ($p<0.03$), but this reduction was not statistically significant for purposes of the predefined analysis. The total availability of p-value for this analysis was 0.025, or half of the typical 0.05, as it was designed as a one-sided test. This availability had no impact on the approach, as all numerical results can be doubled to achieve the typical 0.05 p-value test. As it was unknown as to whether the predefined analysis would achieve statistical significance, or whether a subsequent analysis of the complete population would be required, the alpha was split, resulting in a lower p-value of 0.0158 to define statistical significance rather than the conventional 0.025. Despite this higher hurdle for statistical significance, the predefined analysis met the endpoint.

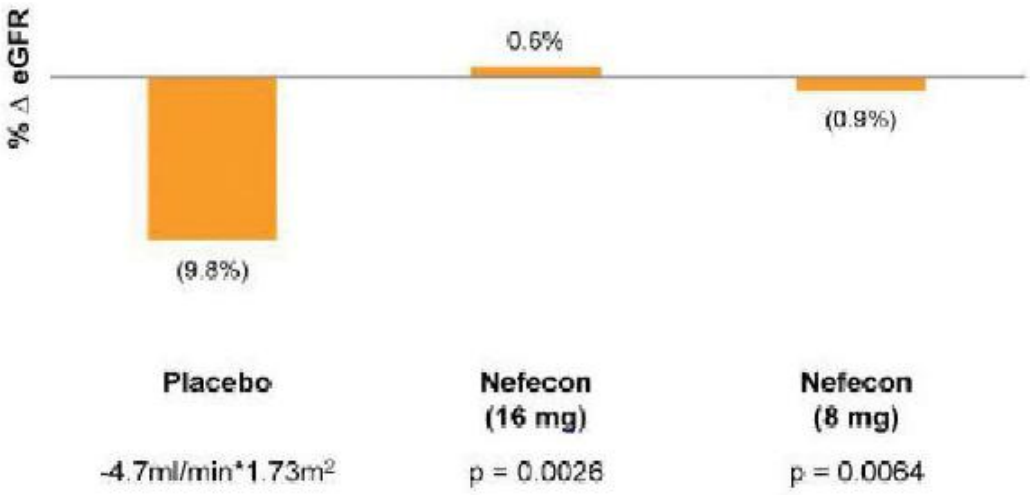
In the interim analysis of the primary endpoint for NEFIGAN, 16 mg of Nefecon was associated with statistically significant and clinically meaningful reductions in UPCR compared to placebo in NEFIGAN at nine months.



After all subjects had completed the trial, we analyzed secondary and tertiary endpoints, such as eGFR, based on the complete data set. We also performed an analysis of the full UPCR data. Results from this dataset conducted in accordance with the statistical plan indicated that patients from the 16 mg dose cohort exhibited a statistically significant and clinically meaningful reduction of 32.0% (p=0.0005) at 12 months, which was three months after the discontinuation of dosing. Results analyzed outside of the statistical plan indicated that patients from this cohort exhibited a reduction in proteinuria of 25.4% at nine months.

Key secondary endpoints, including change in 24-hour urine protein, urine albumin creatinine ratio, or UACR, 24-hour urine albumin and eGFR, were also met. As a measure of kidney function, statistically significant and clinically meaningful differences in eGFR between Nefecon and the placebo groups were observed. Patients in the placebo group exhibited a 9.8% decrease in eGFR, corresponding to -4.7 ml/min*1.73m2, which reflects the worsening of kidney function during the nine months of placebo dosing, while eGFR was stabilized in Nefecon-treated patients. The 16 mg Nefecon cohort had a increase in eGFR of 0.6%, which reflected a difference from placebo of 10.4% (p=0.0026) and the 8 mg Nefecon cohort had a decrease in eGFR of 0.9% (p=0.0064, compared to placebo). The eGFR levels in patients that received the 16 mg Nefecon dose remained stable during the three-month follow-up period post treatment. In contrast, the placebo cohort, over the same time period, exhibited a continuous decline to 10.7% in eGFR levels compared to baseline, which represented a difference versus the 16 mg cohort of 11.4% (p=0.0134). Nefecon was associated with stabilization of kidney function during the trial, which supports our belief that Nefecon may have a disease-modifying effect.

Nefecon was associated with a stabilization of eGFR in NEFIGAN.



As illustrated in the table below, results observed in additional tertiary endpoints evaluated in NEFIGAN were consistent with the results observed in the primary endpoint of proteinuria reduction.

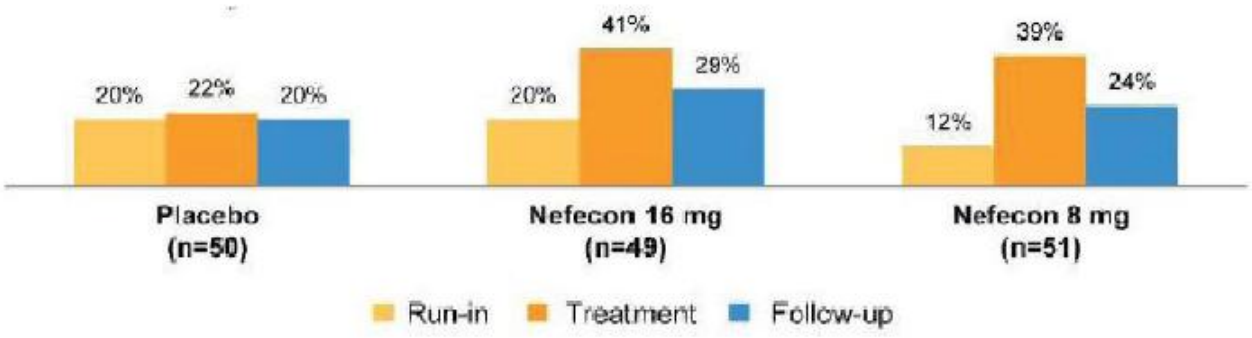
Mean change from baseline in proteinuria variables, p-creatinine and microhematuria proportion in NEFIGAN after nine months.

	9 Months		
	Placebo	Nefecon (16 mg)	Nefecon (8 mg)
UPCR (interim)	3%	(27%)	(22%)
Total 24-hour urine protein	1%	(30%)	(20%)
UACR	6%	(28%)	(14%)
Total 24-hour urine albumin	2%	(33%)	(18%)
P-Creatinine	7%	(2%)	(1%)
Microhematuria proportion	86%	63%	82%

Nefecon was observed to be generally well tolerated. We observed no clinically meaningful changes in blood pressure, body weight or hemoglobin A1C, a measure of blood sugar metabolism, from baseline, and there were no serious infections reported in the trial. Only four possibly drug-related serious adverse events were reported, one in each of the 8 mg and 16 mg cohorts, and two in the placebo cohort (which classification was made by the investigator at the time when the safety results were blinded).

To collect safety data, we used solicited adverse event reporting in addition to the typical spontaneous adverse event reporting, which is known to result in some degree of overreporting of adverse events as compared to spontaneous adverse event reporting. In the trial, all patients completed a questionnaire with several questions related to potential steroid-related side effects and gastrointestinal side effects at every visit, including during the run-in and follow-up periods when no active drug was administered. As illustrated in the graphic below, approximately 20% of patients in both the placebo and treatment cohorts reported This response data was consistent in the run-in, treatment and follow-up periods for the placebo cohort. An incremental 20% of patients reported side effects in the 8 mg and 16 mg treatment cohorts during the treatment period.

Summary of solicited corticosteroid-related adverse events observed in NEFIGAN.



Adverse events observed in NEFIGAN were consistent with those known to be associated with non-systemic corticosteroids such as budesonide. The most commonly reported adverse events in the treatment cohorts included nasopharyngitis, acne, joint swelling, cushingoid, insomnia, muscle spasms, dyspepsia, headache, peripheral edema, mood swings and hypertension. Of these events, 75.8% were categorized as mild, 22.6% as moderate and 1.6% as severe.

In the treatment cohorts, eight patients experienced serious treatment emergent adverse events: seven patients in the 16 mg group reported eight serious adverse events (aggravated condition, nephrotic syndrome, aortic dissection, deep vein thrombosis, menorrhagia, proteinuria, appendicitis and spinal pain) and one patient in the 8 mg group reported a serious adverse event (aggravated condition). In the placebo cohorts, three patients reported four serious adverse events (two events of proteinuria, sciatica and aggravated condition).

All serious adverse events in the treatment cohorts were determined by the investigator to be unrelated to Nefecon, except for one 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 one patient in the 8 mg treatment cohort with aggravation of renal condition, which was classified by the investigator as possibly being treatment-related. In the placebo cohort, two serious adverse events (proteinuria and aggravated condition) were classified by the investigator as possibly being treatment-related at the time when the safety results were blinded.

Patient discontinuations were higher among patients in the Nefecon 16 mg cohort as compared to the 8 mg cohort. Most of the patients who discontinued treatment experienced mild to moderate symptoms including, most frequently, acne and other transitory cosmetic side effects.

We believe that the results of the NEFIGAN trial support the further development of Nefecon for the treatment of IgAN. We discussed these results with the FDA in our End-of-Phase 2 meeting in January 2017 and, based on the FDA's positive feedback on the use of decrease in proteinuria at nine months as compared to baseline as a surrogate endpoint, we proceeded to initiate our Phase 3 clinical trial for Nefecon.

Phase 3 Clinical Development

Proteinuria as a Surrogate Marker for IgAN

In order to approve a drug, the FDA generally requires one or more clinical trials demonstrating that the product candidate meets an endpoint that represents a direct clinical outcome, such as survival, decreased pain or the absence of disease, which we refer to as a clinical endpoint. There are, however, exceptions where the FDA accepts the use of surrogate endpoints rather than clinical endpoints when evaluating a product candidate for approval. The FDA selectively allows the use of surrogate endpoints in clinical trials to permit a more rapid development and approval path of treatments for serious or life-threatening diseases. The FDA permits the use of such surrogate endpoints only if they are reasonably likely to predict clinical benefit and constitute a clinical endpoint that can be measured earlier than irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability of alternative treatments or lack thereof. When the FDA accepts novel surrogate endpoints for approval in pivotal trials, the pivotal trials are required to be followed by confirmatory post-approval trials to verify the clinical benefit. For treatments related to chronic kidney disease, clinical trials have generally relied on clinical endpoints, such as time to dialysis or transplantation. Due to the significant expense associated with the large patient numbers and extended clinical trial duration required to adequately measure such clinical endpoints, few new therapeutic drug candidates have emerged over the past two decades to treat renal disease.

In 2012, the FDA and the American Society of Nephrology, or ASN, founded the Kidney Health Initiative, or KHI, with the goal of supporting research and innovation for the development of safe and efficacious treatments for kidney disease. We have participated in this initiative since 2014. In 2011, we funded a collaboration with Tufts University and the University of Utah to conduct a meta-analysis based on selected, well-defined clinical trials in IgAN patients in order to provide regulatory authorities with a data-driven basis to accept a novel surrogate marker for potentially accelerated approval of treatments for IgAN. The final analytical framework from this collaboration showed a robust statistical relationship between reduction in proteinuria and reduction of the risk of progression to ESRD. We believe that this framework, together with the research and analysis conducted by the KHI and spearheaded by ASN, the National Kidney Foundation and the FDA, led to the FDA's acceptance of an accelerated approval pathway at our End-of-Phase 2 meeting in January 2017. This change in regulatory approach was fundamental to our decision to commence the Phase 3 trial for Nefecon in IgAN.

Phase 3 Clinical Trial in IgAN Patients

We are currently conducting global pivotal Phase 3 clinical trial in IgAN, which we refer to as NefIgArd. NefIgArd is designed to evaluate reduction of the surrogate marker proteinuria as its primary endpoint, which is the same endpoint used in NEFIGAN. NefIgArd is a randomized, double-blind, placebo-controlled, two-part Phase 3 clinical trial. The first part, which we refer to as Part A, is a pivotal efficacy and safety trial, the results of which form the basis for submission of an NDA to the FDA and a planned MAA submission to the EMA. The primary endpoint of Part A is the decrease in proteinuria in the first 200 randomized and dosed patients. In addition, a secondary endpoint of Part A is the difference in kidney function between treated and placebo patients as measured by eGFR. The secondary endpoint in Part A, which is a measure of eGFR over a nine-month period, is also expected to be informative of the primary endpoint of Part B, as discussed below. We reported positive topline results from Part A in the fourth quarter of 2020, where the trial met the primary and key secondary endpoint. On the basis of the positive Part A results, we submitted an NDA in March 2021 for accelerated approval by the FDA. In April 2021, Nefecon was granted accelerated assessment by the EMA, and we intend to follow this with an MAA submission for conditional approval by the EMA in the second quarter of 2021.

The second part of NefIgArd, which we refer to as Part B, is a post-approval confirmatory trial designed to provide evidence of long-term renal benefit. Following completion of enrollment in Part A in December 2019, we completed the enrollment of an additional 160 patients in January 2021, in order to power Part B to assess the difference in kidney function between treated and placebo patients as measured by eGFR over a two-year period from the start of dosing of each patient. Having successfully completed enrollment, we expect to report data from Part B in early 2023. Across both parts, NefIgArd will enroll a total of 360 patients and generate nine months of dosing data, as well as an aggregate of 15 months of follow-up data from Parts A and B. If approved, we intend to market and commercialize Nefecon in the United States as a treatment specifically designed to have a disease-modifying effect for IgAN by preserving kidney function and thereby avoiding progression to ESRD.

Phase 3 Clinical Trial Results from Part A of NefIgArd

In November 2020, we reported positive topline results from Part A of NefIgArd. The trial met its primary objective of demonstrating a statistically significant reduction in the urine protein creatinine ratio, or UPCR, after nine months of treatment with 16 mg of Nefecon compared to placebo, with significant continued improvement at 12 months. The trial also met the key secondary endpoint showing a statistically significant difference in eGFR after nine months of treatment with Nefecon compared to placebo. Collectively, the efficacy data from nine months' treatment with 16 mg of Nefecon indicated a significant and beneficial effect on key factors correlated to the progression to ESRD for IgAN patients.

Topline Results

The analysis set included 199 patients diagnosed with primary IgAN and who were on a background of optimized and stable renin-angiotensin system, or RAS inhibitor therapy. The patients were randomized in a 1:1 ratio into one of two arms—Nefecon 16 mg/day or placebo—and treated orally for nine months daily.

24-hour UPCR (Proteinuria) Data

The primary endpoint analysis showed a 31% mean reduction in the treatment arm versus baseline, with placebo showing a 5% mean reduction versus baseline, resulting in a 27% mean reduction at nine months of the treatment arm versus placebo (p=0.0005). Based on the trends from the data observed from those patients who had reached 12 months at the time of the database lock, the company would expect the proteinuria reduction versus baseline to end up between 42% and 48% at 12 months for the 16 mg treatment cohort.

eGFR Data

The key secondary endpoint, eGFR, showed a mean treatment benefit of 7% versus placebo at nine months, reflecting stabilization in the treatment arm and a 7% decline of eGFR in the placebo arm (p=0.0029). This represented an absolute decline of 4.04 ml/min/1.73 m2 in the placebo arm over nine months compared to a 0.17 ml/min/1.73 m2 decline in the treatment arm.

Safety Profile

The results indicate that Nefecon was generally well-tolerated, with adverse events similar to those observed in the Phase 2b, including no clinically relevant changes in weight, blood pressure or HbA1c in the treatment arm. There were also no severe infections, and overall, it was consistent with the known safety profile of Nefecon's active ingredient, Budesonide. The withdrawal rate in this trial was significantly less than what was seen in the Phase 2b NEFIGAN trial.

On the basis of the positive results of Part A of NefIgArd, we submitted an NDA in the first quarter of 2021 for accelerated approval by the FDA. In April 2021, Nefecon was granted accelerated assessment by the EMA, and we plan to submit an MAA for conditional approval by the EMA in the second quarter of 2021.

The NefIgArd trial is continuing on a blinded basis with patients continuing in the observational Part B of the trial for a 12 month period following the completion of Part A. In January 2021, we completed the enrollment of all 360 patients in NefIgArd, which includes 200 patients previously enrolled in Part A and another 160 patients enrolled in Part B. Having successfully completed enrollment, we intend to report data from Part B in early 2023, subject to any further impact from the COVID-19 pandemic to our business.

Additional Trials

Open-Label Extension Trial

We have initiated an open-label extension trial or the OLE trial, for eligible patients who have completed treatment in Part A and Part B of NefIgArd. The OLE trial commenced when the first patient completed both Part A and Part B of NefIgArd, which occurred in the fourth quarter of 2020, and we reported dosing of the first patient in February 2021.

The continuation of the COVID-19 pandemic may impact our ability to initiate or complete the OLE trial according to plan.

Commercialization Plan

We retain worldwide rights to Nefecon other than in Greater China and Singapore. If approved, we intend to commercialize Nefecon in the United States independently. We estimate the total U.S. market opportunity to be approximately $9.0 billion to $10.0 billion annually, based on our estimate of the prevalence of the disease in the United States and primary market research conducted by IQVIA that we commissioned to assess preliminary reimbursement levels perceived acceptable by U.S.-based payors. Such primary market research indicated that the estimated pricing of a course of treatment of Nefecon could range from $55,000 to $85,000 per patient. In that IQVIA market research, 68% of nephrologists also indicated that they would prescribe Nefecon for their IgAN patients within the first year of commercial availability. A majority of nephrologists also indicated that they would prescribe Nefecon as the first agent after, or in conjunction with, treatment with ACEs or ARBs. Payor feedback from our market research indicated that payors generally did not anticipate managing reimbursement of Nefecon in a different manner from other therapies approved for their indications.

Out of the estimated U.S. IgAN market, we intend to commercialize Nefecon in the United States with a targeted commercial infrastructure and with a primary focus on specialist physicians treating IgAN patients at risk of progressing to ESRD. We intend to launch Nefecon in the United States in the first half of 2022, if approved. We are currently focused on disease education, patient advocacy and market access, with the goal of facilitating access to Nefecon, if approved and commercialized, to the patients for which Nefecon can fulfill an unmet medical need. We believe this market can be addressed by a small and dedicated number of marketing and medical sales specialists, initially approximately 40, to efficiently cover the approximately 3,700 nephrologists focused on our target patient population in the United States. In the United States, we estimate that approximately 200 key opinion leaders have direct, first-degree contacts with 90% of practicing nephrologists in the IgAN community.

In 2019, we entered into an agreement with Everest, pursuant to which we granted Everest an exclusive license to develop and commercialize Nefecon for IgAN in Greater China and Singapore. Everest may exercise its option to develop Nefecon in additional indications subject to additional payment by Everest. We have recently reported positive topline data from the ongoing Phase 3 NefIgArd trial. If Nefecon is approved by Chinese regulatory authorities, we expect to achieve commercial access to the Chinese market could be achieved in 2024, which potentially positions Nefecon to be the first approved medication for IgAN in China. 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.

Setanaxib and Nefecon for Primary Biliary Cholangitis

We are exploring applications of setanaxib and Nefecon for other autoimmune diseases in which it may have therapeutic potential such as primary biliary cholangitis, or PBC, a progressive and chronic autoimmune disease of the liver. Based on available Phase 2 clinical data and recent Phase 1 data, combined with interactions with the FDA related to setanaxib, we presently favor proceeding with setanaxib in this indication and plan to launch a Phase 2/3 trial in the second half of 2021. We believe that setanaxib is differentiated from other approved or late stage development candidates in PBC, due to its effect on fibrosis, inflammation and significant impact on fatigue, as seen in the Phase 2 trial. However, we continue to explore stand alone or combination therapies involving Nefecon in this indication, as there are currently no approved therapies that specifically address the autoimmune response that is believed to drive PBC or the inflammatory consequences of the autoimmune response. Nefecon is designed to deliver high peak concentrations of the local immunosuppressant budesonide to the intestine, where it is then transported directly to the liver in order to locally suppress the autoimmune response associated with PBC and counteract the inflammation resulting from increased and toxic levels of bile acid. We have received orphan drug designation for the treatment of PBC by the FDA.

PBC Disease Background

PBC is a progressive and chronic autoimmune disease of the liver that causes a cycle of immune injury to biliary epithelial cells, resulting in cholestasis and fibrosis. The origin of the autoimmune response is believed to be the production of cytotoxic T-cells and B-cell derived autoantibodies directed towards the epithelial cells of the small bile ducts in the liver, resulting in inflammation and damage to the duct cells and eventually destroying the bile ducts. This destruction results in the accumulation of increased bile acid in the liver, a condition known as cholestasis, to levels that are toxic to the liver cells, resulting in destruction of liver cells and fibrosis. PBC can culminate in liver failure, necessitating the need for a liver transplant. PBC is an orphan disease and, based on its known prevalence rates, we estimate that there are approximately 140,000 patients in the United States. The annual incidence for PBC ranges from 0.3 to 5.8 cases per 100,000 in the United States.

Early symptoms include fatigue, itchy skin, dry eyes and mouth dryness. As the disease progresses, there is pain in the upper right abdomen, musculoskeletal pain, edema, jaundice, osteoporosis, elevated cholesterol and hypothyroidism. If untreated, the active liver tissue is destroyed and replaced by fibrous tissue, leading to liver failure and the need for a liver transplant. Individuals with PBC are also at a greater risk than the general population of developing hepatocellular carcinoma.

Current Treatments for PBC

Ursodeoxycholic acid, a generic drug also known as ursodiol, or UDCA, and obeticholic acid, marketed as Ocaliva by Intercept Pharmaceuticals, are the only FDA-approved treatments for PBC. Both of these agents are bile acid analogs whose mechanisms of action aim to protect the liver from damage caused by endogenous bile acids and inhibition of bile acid synthesis. These drugs are primarily anticholestatic. Neither of these drugs specifically addresses the autoimmune response that is believed to drive PBC or the inflammatory consequences of the autoimmune response. Despite adequate dosing of UDCA, approximately one-third of PBC patients do not respond adequately and are at risk of requiring liver transplant. Despite showing improvements in liver values in the blood, Ocaliva has not been proven in clinical testing to delay or avoid the need for liver transplant. Although systemic corticosteroids have been shown to alleviate PBC symptoms, their adverse event profile limits their treatment potential.

Our Solution: Setanaxib

Setanaxib is our favored drug candidate to pursue in PBC. NOX inhibitors are a fairly new drug class focused on inhibiting the overproduction of ROS, which can drive fibrogenesis across multiple organs. Based on earlier Phase 2 data and recent positive Phase 1 data, we plan to launch a pivotal and potentially registrational Phase 2/3 trial in PBC in the second half of 2021. We believe that setanaxib is differentiated from other approved or late stage development candidates in PBC, due to its effect on fibrosis, inflammation and significant impact on fatigue, as seen in the Phase 2 trial.

In the Phase 2 trial concluded in 2019, setanaxib did not reach its primary endpoint; however, it showed clinical activity and effect on fibrosis as measured by a variety of biomarkers as well as Fibroscan. It also resulted in a statistically significant impact on fatigue, the most commonly reported symptom of PBC, and is the only drug candidate, to our knowledge, to achieve this to date in this patient population.

In January 2021, Genkyotex reported positive data from its Phase 1 clinical trial to evaluate the safety and pharmacokinetics of setanaxib. The Phase 1 trial assessed the safety and pharmacokinetics of oral setanaxib at selected doses in 46 healthy adult male and female subjects. The trial consisted of a single ascending dose, or SAD, part and a multiple ascending dose, or MAD, part with dosing up to 1600 mg/day. The trial demonstrated that setanaxib was generally well tolerated at the doses tested, with no safety signal or dose-limiting toxicity being identified. Based on this positive data, Genkyotex plans to initiate a Phase 2/3 trial in PBC in the second half of 2021, incorporating higher dosing than that used in the Phase 2 trial and using alkaline phosphatase, or ALP, as a primary endpoint. The final design and protocol are subject to further feedback and commentary by the FDA.

This platform also has several potential applications across orphan indications, focusing on anti-fibrotic and anti-inflammatory applications. Setanaxib is the lead compound, complemented by a research effort focused on developing follow up compounds. Potential indications include PBC, PSC, IPF, NASH and various kidney indications with a fibrotic component. We also intend to explore oncology indications involving fibrotic components such as CAFs and head and neck cancer using setanaxib administered with checkpoint inhibitors to address tumor drug resistance related to fibroblasts. To this end, Genkyotex plans to initiate a Phase 2 proof-of-concept study in head and neck cancer in 2021, which will study administration of setanaxib in conjunction with immunotherapy targeting CAFs.

We also continue to explore application of Nefecon in PBC, as based on current knowledge of PBC's pathophysiology, we believe that targeted exposure to budesonide in the liver may counteract the original autoimmune response that is believed to drive PBC, as well as the inflammation resulting from increased and toxic levels of bile acid. In addition, while historical trials have shown that systemic corticosteroids may alleviate symptoms and improve biochemical and histologic parameters, no targeted immunosuppressive anti-inflammatory therapy is currently approved for PBC in the United States or Europe. Nefecon is designed to deliver high peak concentrations of budesonide to the intestine that is then transported directly to the liver, where it can have a local anti-inflammatory effect to reduce the inflammation associated with PBC, while minimizing systemic exposure and reducing systemic corticosteroid-related adverse events. We believe that Nefecon has the potential to address the significant unmet medical need to improve outcomes for PBC patients as a second line therapy.

Budenofalk for Autoimmune Hepatitis

We have exclusively in-licensed Budenofalk 3 mg oral capsules for the U.S. market from Falk Pharma. Budenofalk is a formulation of budesonide originally developed to treat Crohn's disease. Our license covers all indications for the United States market, excluding orphan indications outside of liver targets.

Budenofalk has been tested in a large, randomized, controlled clinical trial in AIH patients and is approved for the treatment of AIH in several countries in Europe, but there has been no clinical development or regulatory approval in the United States. In addition, Budenofalk has been approved for the treatment of Crohn's disease and acute episodes of collagenous colitis in several countries in Europe, but regulatory approval was never pursued in the United States. We therefore believe Budenofalk also has the potential to address AIH for patients in the United States. We have received orphan drug designation for the treatment of AIH using budesonide by the FDA. We have discussed the development plans with the FDA for AIH during 2020, but additional interaction is required before establishing any definitive clinical development plans. In these discussions with the FDA, if appropriate, we intend to share the data we obtained pursuant to the license agreement with Falk Pharma to support seeking approval of Budenofalk for AIH in the United States through the Section 505(b)(2) abbreviated approval pathway. If there is limited added value perceived by the FDA with regards to the Budenofalk data related to a regulatory pathway, we will need to assess whether to proceed with Budenofalk or alternatively Nefecon utilizing the Section 505(b)(2) pathway. Without yet having had any discussions with the FDA in this regard, we believe that the time and effort under such a scenario might be identical, irrespective of whether we elect to proceed with Budenofalk or Nefecon.

AIH Disease Background

AIH is a rare disease associated with chronic inflammation of the liver. Based on current knowledge of AIH's pathophysiology, the origin of the autoimmune response is believed to be production of cytotoxic T-cells and B-cell derived autoantibodies directed towards liver cells or its components, resulting in inflammation of the liver cells that eventually destroys the cell and leads to fibrosis. AIH often presents as a slow progressing disease of the liver, leading to cirrhosis at variable rates with complications such as liver failure and liver cancer. Typical symptoms are fatigue, abdominal discomfort, jaundice, enlarged liver, skin rashes, joint pains and, in women, loss of menstruation. Some patients have no obvious symptoms and are diagnosed based on liver problems identified during routine blood tests. AIH is an orphan disease and based on its known prevalence rates, we estimate that there are approximately 50,000 to 80,000 patients in the United States. The annual incidence of AIH ranges from 0.1 to 1.9 cases per 100,000 in the United States. The disease is at least three times as common in women as in men and can occur at any time during life.

Current Treatments for AIH

There are currently no approved therapies for treatment of AIH in the United States. The standard of care includes immunosuppressive systemic corticosteroids, typically prednisone, alone or in combination with azathioprine. A common modality is to use a high-dose induction period followed by a lower-dose maintenance therapy. The clinical outcome target is to prevent development of cirrhosis or prevent progression if cirrhosis has occurred. Many patients respond well to standard of care and achieve disease remission, in which case the prognosis is favorable. However, up to 80% of treated patients report steroid-related side effects after two years and 15% discontinue treatment due to drug-related adverse events. Furthermore, 50% to 90% of patients relapse if treatment is stopped. In addition, the high risk of adverse events in some patient groups (where systemic steroid treatment may be contraindicated) such as patients with osteoporosis, hypertension, diabetes or underlying mental illness, results in non-treatment, which leads to an increased risk of cirrhosis. Given the high rates of standard-of-care treatment adverse events and high rates of relapse after discontinuation of standard-of-care treatment among AIH patients, there is a significant unmet need among AIH patients.

Our Solution: Budenofalk

Based on our current knowledge of AIH's pathophysiology, we believe that targeted exposure to budesonide in the liver may counteract the original autoimmune response that is believed to drive AIH, as well as the inflammation resulting from the damage to the liver cells. Budenofalk was studied in a randomized clinical trial and was observed to have greater clinical activity and fewer side effects compared to treatment with systemic corticosteroids, which may drive patient compliance and benefit. We believe that Budenofalk has the potential to address the significant unmet medical need to improve outcomes for AIH patients for whom there are no currently approved therapies in the United States.

Collaborations and License Agreements

License Agreement with Everest Medicines

In 2019, we entered into a license agreement with Everest Medicines, or Everest, pursuant to which we granted Everest an exclusive, royalty-bearing, non-transferable (other than in connection with a change of control transaction) license to develop, manufacture and commercialize Nefecon for IgAN, which Everest may exercise its option to develop Nefecon in other potential indications, if and when we initiate a registrational clinical study in such indications, which we collectively refer to as the Licensed Product. The territories covered by the Everest license are Greater China, including mainland China, Taiwan, Hong Kong and Macau, and Singapore which we collectively refer to as the Territories.

Pursuant to the terms of the Everest license, Everest must use commercially reasonable efforts to develop the Licensed Product and to obtain, support and maintain approval of the Licensed Product in the Territories. Everest is also entitled to sublicense the rights granted under the Everest license to its affiliates and to other third-parties with our prior consent.

As initial consideration for the license, Everest paid us an upfront payment of $15.0 million. Additionally, Everest is required to pay us aggregate milestone payments of up to $106.0 million upon the achievement of specific clinical, regulatory and commercial milestones. Of the milestone payments described above, a $5.0 million milestone payment from Everest was triggered upon approval of Everest's IND in China in December 2019. Everest is also required to pay tiered royalties of a high single digit to mid-teens percentage on annual net sales of the Licensed Product, subject to customary reductions.

Unless earlier terminated, the Everest license will expire upon the expiration of the last-to-expire royalty term for the Licensed Product in the Territory. The royalty term will terminate on a country-by-country basis on the later of (i) twelve years from the first commercial sale of the Licensed Product in such country, (ii) the expiration of the last to expire valid claim of the licensed patents and any patents covering licensed intellectual property in such country or region, or (iii) the expiration of all regulatory exclusivity for such Licensed Product in such country or region. Upon expiration of the Everest license, the licenses granted to Everest will be considered fully paid-up, perpetual and irrevocable. Either party may terminate the Everest license upon a material breach by the other party and failure to cure such breach within a specified period. The Everest license is also terminable in the event of bankruptcy, insolvency, dissolution or winding up of the other party. Everest has the right to terminate the license agreement for convenience by providing 12 months written notice to us. We have the right to terminate the license agreement in full upon 30 days prior written notice to Everest in the event that Everest, their affiliates or sublicensees directly challenge the patentability, enforceability or validity of any licensed patents.

Genkyotex Out-licensing Agreements

Through our acquisition of a controlling interest in Genkyotex, we became a party to a license agreement with Serum Institute of India Pvt. Ltd., or the SIIL, the world's largest producer of vaccine doses, pursuant to which we granted SIIL the use of Vaxiclase as an antigen per se, or GTL003, for the development of cellular multivalent combination vaccines against a variety of infectious diseases. In 2018, Genkyotex and SIIL entered into a revised agreement expanding the territories from emerging pharmaceutical markets to certain developed world territories, including the U.S., Canada, E.U. member states, and the U.K.

Since the beginning of the agreement, Genkyotex has received a total of $2.1 million in upfront and extension payments and from the achievement of a pre-specified development milestone in November 2016. According to the terms of the initial agreement, Genkyotex is eligible to receive $57 million in milestone payments. Following the expansion of the agreement to the developed world territories, Genkyotex becomes eligible to receive an additional €100 million, bringing the overall agreement to approximately €150 million in upfront payment, development and commercial milestones. Genkyotex is also eligible to receive single digit royalties on any future sales.

Manufacturing

We rely on third parties to manufacture Nefecon. We have an agreement with a third-party vendor to produce drug substance and drug product for Nefecon for our ongoing and planned clinical trials.

We require all of our contract manufacturing organizations, or CMOs, to conduct manufacturing activities in compliance with current good manufacturing practice, or cGMP, requirements. We currently rely solely on these CMOs for scale-up and process development work and to produce sufficient quantities of our product candidates for use in clinical trials. We anticipate that these CMOs will have the capacity to support both clinical supply and commercial-scale production, but we do not have any formal agreements at this time to cover commercial production. We may also elect to enter into agreements with other CMOs to manufacture supplies of drug substance and finished drug product.

Competition

The pharmaceutical industry is characterized by rapid evolution of technologies and intense competition. While we believe that our product candidates, technology, knowledge, experience and scientific resources provide us with competitive advantages, we face competition from major pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions, among others.

Smaller or earlier-stage companies, may also prove to be significant competitors, particularly through collaborative arrangements with large established companies. These companies may also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites, enrolling patients in clinical trials and acquiring technologies complementary to, or necessary for, our programs.

A competitor may obtain FDA or other regulatory approvals for their products more rapidly than we may obtain approvals for our product candidates, which could result in such competitor establishing a strong market position before we are able to commercialize our product candidates. In addition, the availability of reimbursement from government and private payors will also significantly impact the pricing and competitiveness of our products.

Nefecon, if approved, along with any other product candidates that we successfully develop and commercialize, will compete with approved treatment options, including off-label therapies, and new therapies that may become available in the future. Key considerations that would impact our ability to effectively compete with other therapies include the efficacy, safety, method of administration, cost, level of promotional activity, regulatory market exclusivity and intellectual property protection of our products. Many of the companies against which we may compete have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products.

While there are no approved therapies for the treatment of IgAN, we are aware that other companies are developing product candidates for this indication, including four product candidates in Phase 3 clinical development. Omeros Corporation is developing narsoplimab, a monoclonal antibody administered through intravenous infusion and Travere Therapeutics, Inc. (previously Retrophin Inc.) is developing sparsentan, an orally-administered small molecule. Chinook Therapeutics, Inc. recently initiated enrollment in a Phase 3 trial with an orally administered small molecule, atrasentan. Novartis AG is developing iptacopan (LNP023), an orally-administered small molecule and have announced that they also recently started a Phase 3 trial. In addition, we are aware of product candidates in Phase 2 clinical development. Alnylam Pharmaceuticals Inc. is developing cemdisiran, an investigational RNAi therapeutic, Vera Therapeutics, Inc. (originator Merck KGaA) is developing atacicept, a recombinant protein and Alexion Pharmaceuticals Inc. is developing ravulizumab, a monoclonal antibody. Further, we are aware that Visterra, Inc. has started a dose-finding Phase 2 trial with a systemic B-cell inhibitor, and that open label Phase 2 trials recently were announced by DiaMedica Therapeutics, Inc. and Ionis Pharmaceuticals Inc. All of these trials use either intravenous infusion or subcutaneous injection as mode of administration. In addition, Apellis Pharmaceuticals, Inc. and Reata Pharmaceuticals, Inc. have conducted smaller open-label Phase 2 clinical trials but have not yet announced any intention to proceed with further development activities in IgAN. We are also aware of several therapies that are used off-label for the treatment of IgAN, including a variety of systemic immunosuppressive agents, including systemic corticosteroids like prednisone, prednisolone and methylprednisolone.

With respect to PBC, UDCA, a generic drug, and obeticholic acid, marketed as Ocaliva by Intercept Pharmaceuticals, Inc., are the only FDA-approved treatments for PBC. Additionally, we are aware that other companies are developing product candidates with pharmacologies distinct from Nefecon and setanaxib for this indication, the most advanced being peroxisome proliferator-activating receptor, or PPAR, agonists in Phase 3 clinical development by Cymabay Therapeutics, Inc. and GENFIT SA. Intercept Pharmaceuticals, Inc. and Zydus Pharmaceuticals (USA) Inc. also have projects exploring PPAR agonists but are in Phase 2 development. Gilead Sciences, Inc. and Novartis AG are potentially continuing their farnesoid X receptor, or FXR, agonists and are in Phase 2 clinical development. Additionally, systemic corticosteroids, like prednisone, have been shown to alleviate symptoms associated with PBC but is associated with increased rates of osteoporosis.

There are currently no approved therapies for the treatment of AIH in the United States and there are few product candidates in development for this indication. We are aware of an injectable immunosuppressive monoclonal antibody under Phase 2 clinical development by Novartis AG and a repurposed oral anti-inflammatory small molecule under Phase 2 clinical development by TaiwanJ Pharmaceuticals Co., Ltd. F. Hoffmann-La Roche AG recently announced a Phase 2 trial with an immunomodulator. The standard of care includes immunosuppressive systemic corticosteroids, typically prednisone, alone or in combination with azathioprine.

Intellectual Property

We strive to protect the proprietary technologies that we believe are important to our business, including pursuing and maintaining patent protection intended to cover the technologies incorporated into, or used to produce, our product candidates, including compositions of matter of our product candidates and their methods of use, as well as other inventions that are important to our business. In addition to patent protection, we also rely on trade secrets to protect aspects of our business that we do not consider appropriate for patent protection, including certain aspects of our technology and drug product manufacturing. Our commercial success depends in part upon our ability to obtain and maintain patent and other proprietary protection for commercially important technologies, inventions and know-how related to our business, defend and enforce our intellectual property rights, particularly our patent rights, preserve the confidentiality of our trade secrets and operate without infringing valid and enforceable intellectual property rights of others.

Patents

The patent positions for biotechnology companies like us are generally uncertain and can involve complex legal, scientific and factual issues. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any of our technologies and product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the inventions and patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

With regards to Nefecon, we co-own one patent family with Kyowa Kirin Services Ltd., f/k/a Archimedes Development Ltd., to which we have a sole and exclusive global license, even in relation to the other co-owner, in any field of use. This patent family protects a formulation for the oral delivery of budesonide and the medicinal use thereof. The patents in this patent family expire in 2029. The patents in this family include a United States patent, a patent in each of China, Hong Kong and Japan and a European patent that has been validated in 15 countries. The patents in this family are not eligible for extension in the United States because the active ingredient is used in existing approved drugs. In Europe, extension of the patents is not likely subject to the recent judgement of litigation in the European Union, CJEU C-443/17, related to the degree to which it is possible to obtain a Supplementary Protection Certificate for a previously authorized active ingredient.

With regards to the NOX estate, there are three patent families covering various aspects of the setanaxib asset derived from three PCT applications. The composition of matter and certain methods of therapy are covered in two of these patent families. The third covers the use of setanaxib in certain oncology indications, including head and neck cancer. There are seven further patent families that cover other NOX inhibitors and their use. As these patents and applications cover new chemical entities, the territorial coverage is generally quite wide, and as the compounds do not yet form part of an approved drug product, patent life may potentially be extended in countries where legislation provides for patent term extension. The two families covering setanaxib’s composition of matter have projected expiry dates in 2028 and 2029, excluding potential extensions.

The vaccine patent estate is a combination of licensed, wholly owned and jointly owned patent families. This estate stems from the French company Genticel S.A., or Genticel, with which Genkyotex entered into a strategic combination. The vaccine technology is based on technologies from Institut Pasteur and Genticel. Later, Genticel entered into a partnership, also covering licenses to technology controlled by Genticel, with the Serum Institute of India, Pvt. Ltd. or SIIL. The partnership with the SIIL was continued and re-negotiated after the Genticel/Genkyotex strategic combination. The vaccine technology covers certain immune-cell targeting and immune system stimulating methods and delivery of certain antigens to antigen presenting cells. The most recent patent family, co-owned by Genkyotex and SIIL, has a projected expiry date in 2035.

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. For example, we believe we have gained significant know-how related to the composition, manufacturing process and the drug release performance of Nefecon through our extensive product development work. We typically rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for patent protection. We protect trade secrets and know-how by establishing confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and partners. These agreements generally provide that all confidential information developed or made known during the course of an individual or entity's relationship with us must be kept confidential during and after the relationship. These agreements also generally provide that all inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary information by third parties.

Government Regulation

Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States and by the European Commission following a positive opinion provided by the EMA through the marketing authorization application process for a drug falling within the scope of the centralized procedure or by a national Competent Authority through other marketing authorization application processes (national procedure, mutual recognition or decentralized procedure) before they may be legally marketed in the European Union. Medicines with orphan designation fall within the mandatory scope of the centralized procedure. Our product candidates will be subject to similar requirements in other countries prior to marketing in those countries. The process of obtaining regulatory approvals and the compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

United States Government Regulation

In the United States, the FDA regulates drugs under the FDCA and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the drug development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including imposition of a clinical hold, refusal by the FDA to approve applications, withdrawal of an approval, import/export delays, issuance of warning letters and other types of enforcement letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

The clinical testing, manufacturing, labeling, storage, distribution, record keeping, advertising, promotion, import, export and marketing, among other things, of our product candidates are governed by extensive regulation by governmental authorities in the United States and other countries. The steps required by the FDA before a drug may be approved for marketing in the United States generally include:

- completion of extensive preclinical, laboratory tests, animal studies and formulation studies in accordance with applicable regulations, including the FDA's Good Laboratory Practice, or GLP, regulations;
- the submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials commence;
- approval by an IRB representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials, in accordance with applicable IND and GCP requirements, to establish the safety and efficacy of the drug for each proposed indication;
- preparation and submission to the FDA of an NDA;
- FDA acceptance, review and approval of the NDA, which might include an advisory committee review;
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the drug, or components thereof, are made to assess compliance with current good manufacturing practices, or cGMPs;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data; and agreement for compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and any post-approval studies required by the FDA.

The testing and approval process requires substantial time, effort and financial resources, and the receipt and timing of any approval is uncertain. The FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

Preclinical and Human Clinical Trials in Support of an NDA

Preclinical studies include laboratory evaluations of the product candidate, as well as *in vitro* and animal studies to assess the potential safety and efficacy of the product candidate. The conduct of preclinical studies is subject to federal regulations and requirements including GLP regulations. The results of the preclinical studies, together with manufacturing information and analytical data, among other things, are submitted to the FDA as part of the IND, which must become effective before human clinical trials may commence. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concerns or questions about the conduct of the trials as outlined in the IND prior to that time and places a clinical hold on the IND. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. The FDA may nevertheless initiate a clinical hold after the 30 days if, for example, significant public health risks arise.

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, subject selection and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Each clinical trial must be reviewed and approved by an IRB at or servicing each of the sites at which the trial will be conducted. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completion.

Clinical trials are typically conducted in three sequential phases prior to approval, but the phases may overlap or be combined. These phases generally include the following:

Phase 1. Phase 1 clinical trials represent the initial introduction of a product candidate into human subjects, frequently healthy volunteers. In Phase 1, the product candidate is usually tested for safety, including adverse effects, dosage tolerance, absorption, distribution, metabolism, excretion and pharmacodynamics.

Phase 2. Phase 2 clinical trials usually involve studies in a limited patient population to (1) evaluate the efficacy of the product candidate for specific indications, (2) determine dosage tolerance and optimal dosage and (3) identify possible adverse effects and safety risks.

Phase 3. If a product candidate is found to be potentially effective and to have an acceptable safety profile in Phase 2 clinical trials, the clinical trial program will be expanded to Phase 3 clinical trials to further demonstrate clinical efficacy, optimal dosage and safety within an expanded patient population at geographically dispersed clinical trial sites.

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations, or when otherwise requested by the FDA in the form of post-market requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in enforcement action or withdrawal of approval. Companies that conduct certain clinical trials also are required to register them and post the results of completed clinical trials on a government-sponsored database, such as ClinicalTrials.gov in the United States, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Progress reports detailing the results of clinical trials, among other information, must be submitted at least annually to the FDA. Within 15 calendar days after the sponsor determines that the information qualifies for reporting, written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk to humans exposed to the drug and any clinically important increase in the rate of a serious adverse reaction over that listed in the protocol or investigator brochure. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within 7 calendar days after the sponsor's initial receipt of the information.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must have in place methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and testing and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Submission and FDA Review of an NDA

The results of preclinical studies and clinical trials, together with detailed information on the drug's manufacture, composition, quality, controls and proposed labeling, among other things, are submitted to the FDA in the form of an NDA, requesting approval to market the drug for one or more indications. The application must be accompanied by a significant user fee payment, which typically increases annually, although waivers may be granted in limited cases. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. The FDA has substantial discretion in the approval process and may refuse to file or approve any application or decide that the data is insufficient for approval and require additional preclinical, clinical or other studies.

Once an NDA has been accepted for filing, the FDA sets a user fee goal date that informs the applicant of the specific date by which the FDA intends to complete its review. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has 10 months from the receipt of an NDA for a non-new molecular entity in which to complete its initial review of a standard NDA and respond to the applicant. The review process can be extended by FDA requests for additional information or clarification. The FDA reviews NDAs to determine, among other things, whether the proposed drug is safe and effective for its intended use, and whether the drug is being manufactured in accordance with cGMPs to assure and preserve the drug's identity, strength, quality and purity. Before approving an NDA, the FDA typically will inspect the facilities at which the drug is manufactured and will not approve the drug unless the manufacturing facilities comply with cGMPs. Additionally, the FDA will typically inspect one or more clinical trial sites for compliance with GCP and integrity of the data supporting safety and efficacy.

During the approval process, the FDA also will determine whether a REMS is necessary to assure the safe use of the drug. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patent registries. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS, and the FDA will not approve the application without an approved REMS, if required. A REMS can substantially increase the costs of obtaining approval. The FDA may also convene an advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical trial data. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information.

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities and clinical trial sites, the FDA will issue either an approval of the NDA or a Complete Response Letter, detailing the deficiencies in the submission and the additional testing or information required for reconsideration of the application. FDA may also issue a Complete Response Letter or defer action on an application if the agency has determined that a pre-approval inspection of an applicant's manufacturing facilities is necessary and the agency is unable to complete such an inspection due to the COVID-19 pandemic. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, withdraw the application or request a hearing. Even with submission of this additional information, the FDA may ultimately decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a new drug, it may limit the approved indications for use of the drug. It may also require that contraindications, warnings or precautions be included in the drug labeling, such as a special warning, known as a boxed warning, to highlight a particular safety risk. In addition, the FDA may call for post-approval studies, including Phase 4 clinical trials, to further assess the drug's safety after approval. The agency may also require testing and surveillance programs to monitor the drug after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the drug outweigh the potential risks. The FDA may prevent or limit further marketing of a drug based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved drug, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Section 505(b)(2) NDAs

As an alternative path to FDA approval for modifications to formulations or uses of drugs previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA.

Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments. A Section 505(b)(2) NDA is an application that contains full reports of investigations of safety and effectiveness, but where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This type of application permits reliance for such approvals on literature or on an FDA finding of safety, effectiveness or both for an approved drug product. As such, under Section 505(b)(2), the FDA may rely, for approval of an NDA, on data not developed by the applicant. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the approved branded reference drug. The FDA may then approve the new product candidate for the new indication sought by the 505(b)(2) applicant.

Fast Track and Breakthrough Designations and Priority Review

The FDA is authorized to designate certain drugs for expedited programs, including fast track designation, breakthrough therapy designation, and priority review, if they demonstrate the potential to address an unmet medical need and are intended for the treatment of a serious or life-threatening disease or condition. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

The FDA may designate a drug for fast track designation if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. For fast track designated drugs, sponsors may have a higher number of interactions with the FDA during preclinical and clinical development. In addition, the FDA may review sections of the NDA for a fast track designated drug on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A product is eligible for priority review if it has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the new PDUFA agreement, these six and ten month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

The FDA may designate a drug for breakthrough designation if the drug, alone or in combination with one or more other drugs, is intended to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies. The feature of this program allows the same advantages of the fast track designation, but also intensive FDA guidance to promote efficient development and FDA organizational commitment.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon adequate and well-controlled clinical trials establishing that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the drug has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. The benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, confirmatory studies to verify and describe the drug's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the drug.

All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Post-Approval Requirements

In additional to the post-approval requirements specific to an accelerated approval pathway, there are other post-approval requirements whatever the registration pathway.

Approved drugs that are manufactured or distributed in the United States pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, drug sampling and distribution, advertising and promotion and reporting of adverse experiences with the drug. After approval, most changes to the approved drug, such as adding new indications or other labeling claims and some manufacturing and supplier changes are subject to prior FDA review and approval. There also are continuing, annual program user fee requirements for marketed drugs, as well as new application fees for certain supplemental applications.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance programs to further assess and monitor the drug's safety and effectiveness after commercialization. The FDA may also require a REMS, which could involve requirements for, among other things, medication guides, special trainings for prescribers and dispensers, patient registries, and elements to assure safe use.

In addition, entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. The FDA has promulgated specific requirements for drug cGMPs. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may issue enforcement letters or withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the drug reaches the market. Corrective action could delay drug distribution and require significant time and financial expenditures. Later discovery of previously unknown problems with a drug, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the drug, suspension of the approval, complete withdrawal of the drug from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of drug approvals;

- drug seizure or detention, or refusal to permit the import or export of drugs; or

- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of drugs that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent FDA from approving a different product for the same disease or condition, or the same product for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the application user fee. A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than or different from the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

FDA Marketing Exclusivity Provisions for Drugs

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA, submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, as amended, certain NDAs or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the drug for use in adults, or full or partial waivers from the pediatric data requirements if certain criteria are met.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent marketing and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the drug to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of FDA-requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the drug are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, which is commonly referred to as Brexit. Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty and the United Kingdom formally left the European Union on January 31, 2020. A transition period began on February 1, 2020, during which European Union pharmaceutical law remained applicable to the United Kingdom, which ended on December 31, 2020. Since the regulatory framework in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union Directives and Regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom, now that United Kingdom legislation has the potential to diverge from European Union legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the United Kingdom in the long-term. The MHRA, the UK medicines and medical devices regulator, has recently published detailed guidance for industry and organizations to follow from January 1, 2021 now the transition period is over, which will be updated as the UK's regulatory position on medicinal products evolves over time.

European Union Regulation for Drug Development and Registration

Preclinical and Clinical Development

In the European Union, our product candidates are also subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the European Union clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the Member State regimes. To improve the current system, Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use, which repealed Directive 2001/20/EC, was adopted on April 16, 2014. The Regulation aims at harmonizing and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials, and increasing their transparency. It is expected that the new Regulation will apply following confirmation of full functionality of the Clinical Trials Information System (CTIS), the centralized EU portal and database for clinical trials foreseen by the Regulation, through an independent audit, currently expected to occur in December 2021. The new Regulation will be directly applicable in all Member States (and so does not require national implementing legislation in each Member State), and aims at simplifying and streamlining the approval of clinical studies in the EU, for instance by providing for a streamlined application procedure via a single point and strictly defined deadlines for the assessment of clinical study applications.

Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU Member States where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions, or SUSARs, to the investigated drug that occur during the clinical trial have to be reported to the NCAs and ECs of the Member States where the clinical trial is conducted.

European Drug Review and Approval

In the European Economic Area, or EEA (which is currently still comprised of the Member States of the European Union plus Norway, Iceland and Liechtenstein, with the United Kingdom having left the European Union on January 31, 2020), medicinal products can only be commercialized after obtaining a marketing authorization, or MA. MAs may be granted either centrally (centralized MA) or nationally (national MA).

The centralized MA is issued centrally by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA. It is valid throughout the entire territory of the EEA. The centralized procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicinal products (i.e. gene-therapy, somatic cell-therapy or tissue-engineered medicines) and medicinal products containing a new active substance indicated for the treatment of HIV or AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union. Under the centralized procedure the maximum timeframe for the evaluation of a MA application by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of a MA application considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who make the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of a MA application under the accelerated assessment procedure is of 150 days, excluding stop-clocks, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

National MAs are issued nationally by the competent authorities of the Member States of the EEA and only cover their respective territory. National MAs are available for products not falling within the mandatory scope of the centralized procedure. We do not foresee that any of our current product candidates will be suitable for a national MA as they fall within the mandatory criteria for the centralized procedure. Therefore, our product candidates should be approved through centralized MAs.

Under the above-described procedures, before granting the MA, the EMA makes an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, Great Britain will no longer be covered by centralized MAs (under the Northern Irish Protocol, centralized MAs will continue to be recognized in Northern Ireland). All medicinal products with a current centralized MA were automatically converted to Great Britain MAs on January 1, 2021. 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 MA. A separate application will, however, still be required.

Pursuant to Regulation (EC) No 1901/2006, all applications for marketing authorization for new medicines must include the results of studies as described in a pediatric investigation plan, or PIP, agreed between the EMA's Pediatric Committee, or PDCO, and the applicant, unless the medicine is exempt because of a deferral or waiver. In case of no waiver or deferral, applicants can request that a PIP compliance check is carried out before submitting a marketing-authorization application. Alternatively, a compliance check will be carried out as part of the validation of the application but this may delay the validation phase. The applicant and the EMA may, where such a step is adequately justified, agree to modify a pediatric investigation plan to assist validation. Modifications are not always possible; may take longer to agree than the period of validation permits; and may still require the applicant to withdraw its marketing authorization application and to conduct additional non-clinical and clinical studies. Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP (even where such results are negative) are eligible for six months' supplementary protection certificate extension (if any is in effect at the time of approval). This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Orphan Drugs

In the EEA, Regulation (EC) No 141/2000, as amended, states that a drug will be designated as an orphan drug if its sponsor can establish:

- that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition and either (i) such condition affects not more than five in ten thousand persons in the European Union when the application is made, or (ii) without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment in its development; and

- that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, that the drug will be of significant benefit to those affected by that condition.

Regulation (EC) No 847/2000 sets out further provisions for implementation of the criteria for designation of a drug as an orphan drug. An application for the designation of a drug as an orphan drug must be submitted at any stage of development of the drug but before filing of a MA application. A MA for an orphan drug may only include indications designated as orphan. For non-orphan indications treated with the same active pharmaceutical ingredient, a separate MA has to be sought.

If a centralized MA in respect of an orphan drug is granted pursuant to Regulation (EC) No 726/2004, regulatory authorities will not, for a period of usually 10 years, accept another application for a MA, or grant a MA or accept an application to extend an existing MA, for the same therapeutic indication, in respect of a "similar medicinal product". A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. This period may however be reduced to six years if, at the end of the fifth year, it is established, in respect of the drug concerned, that the criteria for orphan drug designation are no longer met, in other words, when it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity.

The exclusivity period may increase to 12 years if the MA application includes the results of studies from an agreed pediatric investigation plan. Notwithstanding the foregoing, a MA may be granted, for the same therapeutic indication, to a similar medicinal product if:

- the holder of the MA for the original orphan drug has given its consent to the second applicant;
- the holder of the MA for the original orphan drug is unable to supply sufficient quantities of the drug; or
- the second applicant can establish in the application that the second drug, although similar to the orphan drug already authorized, is safer, more effective or otherwise clinically superior.

The European Commission is currently looking into the experience gathered with the orphan and pediatric regulations and may propose changes to the incentives and rewards as they exist today.

Regulation (EC) No 847/2000 lays down definitions of the concepts ‘similar drug’ and ‘clinical superiority’. Other incentives available to orphan drugs in the European Union include financial incentives such as a reduction of fees or fee waivers and protocol assistance. Orphan drug designation in itself does not shorten the duration of the regulatory review and approval process but an applicant’s request for an accelerated review may be granted in case the medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation.

Data and marketing exclusivity

The EEA also provides opportunities for market exclusivity. Upon receiving a marketing authorization in the EEA, innovative medicinal products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents generic or biosimilar applicants from referencing the innovator’s pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization during a period of eight years from the date on which the reference product was first authorized in the EEA. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator’s data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity period. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies.

Coverage, Pricing, and Reimbursement

Significant uncertainty exists in the United States as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. Sales of our products will depend, in part, on the extent to which our products, once approved, will be covered and reimbursed by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. Adequate coverage and reimbursement from third party payors are critical to new product acceptance. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent our products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third party payors. Third-party payors decide which therapeutics they will pay for and establish reimbursement levels. These third-party payors are increasingly reducing reimbursement levels for medical products and services. The process for determining whether a third-party payor will provide coverage for a drug product typically is separate from the process for setting the price of a drug product or for establishing the reimbursement rate that a payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the approved drugs for a particular indication. 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 therapeutic 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.

To secure coverage and reimbursement for any product candidate that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product candidate, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Whether or not we conduct such studies, our product candidates may not be considered medically necessary or cost-effective. A third-party payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Further, no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor. One payor's determination to provide coverage for a product does not assure that other payors will also provide coverage, and adequate reimbursement, for the product. Third-party reimbursement may not be sufficient to enable us to realize an appropriate return on our investment in product development.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. The United States federal government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, utilization management and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of the product candidates and could have a material adverse effect on our sales, results of operations and financial condition. 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 not clear what effect the Special Enrollment Period may have.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, in the EU Member States can restrict the range of medicinal products for which their national health insurance systems provide reimbursement and they can control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. 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. Approaches between Member States are diverging. For example, in France, effective market access will be supported by agreements with hospitals and products may be reimbursed by the Social Security Fund. The price of medicines is negotiated with the Economic Committee for Health Products, or CEPS. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if third party payors fail to provide coverage and adequate reimbursement. In addition, emphasis on managed care, the increasing influence of health maintenance organizations, and additional legislative changes in the United States has increased, and we expect will continue to increase, the pressure on healthcare pricing. The downward pressure on the rise in healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. Coverage policies and third party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

The European Commission has issued a proposal for health technology assessment building on efforts of Member States for common health technology assessments on a voluntary basis under the umbrella of the European Network for Health Technology Assessment. The proposal provides for the mandatory use by Member States of joint clinical assessments conducted at EU level which is considered controversial. It is uncertain if the proposed legislation will be adopted. Health technology assessments are used by most Member States to inform reimbursement decisions. The proposed legislation, if adopted may have an impact on health technology assessment and reimbursement decisions taken at national level.

Healthcare Reform

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 the ability to profitably sell product candidates for which marketing approval is obtained. Among policy makers and payors 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.

For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, ACA, enacted in the United States in March 2010, has already had, and is expected to continue to have, a significant impact on the healthcare industry. The ACA has expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, the ACA: (i) created an annual, nondeductible fee on entities that manufacture or import certain branded pharmaceutical products; (ii) expanded and increased industry rebates for drugs covered under Medicaid programs; and (iii) made changes to the coverage requirements under the Medicare Part D program.

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.

The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole”, and increased the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D. In December 2018, CMS published a new 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 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. 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. 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 cost sharing reductions, or 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. It is unclear what impact these rulings will have on our business. It is unclear what impact these rulings will have on our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, on August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. Specifically, the Joint Select Committee on Deficit Reduction was created to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, started in April 2013 and which, due to subsequent legislative amendments, including the BBA, will stay in effect through 2030 unless additional Congressional action is taken. The CARES Act, and subsequent legislation, suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2021, and extended the sequester by one year, through 2030. Proposed legislation, if passed, would extend this suspension until the end of the pandemic. Additionally, on January 2, 2013, former President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA. The ATRA, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare and reform government program reimbursement methodologies for drug products. The former Trump administration's budget proposal for fiscal year 2021 included 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. Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. 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. 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 it is unclear whether President Joseph Biden will work to reverse these measures or pursue similar policy initiatives, 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. Although a number of these, and other measures may require additional authorization to become effective, and it is unclear whether President Joseph Biden will work to reverse these measures or pursue similar policy initiatives, 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.

We also expect that additional state and federal healthcare reform measures will be adopted in the future, particularly as a result of the recent presidential election. In addition, it is possible that additional governmental action is taken to address the COVID-19 pandemic.

Other U.S. Healthcare Laws and Compliance Requirements

Our business operations in the United States and our arrangements with clinical investigators, healthcare providers, consultants, third-party payors and patients expose us to broadly applicable federal and state fraud and abuse and other healthcare laws. These laws may impact, among other things, our research, and if approved, proposed sales, marketing and education programs of our product candidates. The laws that may affect our ability to operate include, among others:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order, or recommendation of, an item, good, facility or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. The term remuneration has been interpreted broadly to include anything of value. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. A violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA. 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, including the FCA, which can be enforced by private individuals through civil whistleblower or qui tam actions, and civil monetary penalty laws, which prohibit individuals and entities from, among other things, knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, or making a false statement or record material to payment of a false claim or avoiding, decreasing, or concealing an obligation to pay money to the federal government, including for example, providing inaccurate billing or coding information to customers or promoting a product off-label;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willingly falsifying, concealing or covering up a material fact or making materially false statements, fictitious, or fraudulent statements in connection with the delivery of or payment for healthcare benefits, items, or services. A person or entity does not have to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which imposes certain requirements on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, and their business associates, which are individuals and entities that perform functions or activities on behalf of covered entities that involve protected health information as well as their covered subcontractors, relating to the privacy, security and transmission of protected health information; HITECH also created four 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 HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions;

- the federal Physician Payments Sunshine Act, enacted as part of the ACA, which requires applicable manufacturers of drugs for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to track and annually report to CMS payments and other transfers of value provided to physicians (as defined by such law) and teaching hospitals and certain ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made during the previous year to certain non-physician providers, including physician assistants and nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives; and

- state and foreign equivalents of each of the above federal laws and regulations, such as: state anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state and local marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements; state laws that require the reporting of information related to drug pricing; state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state and local laws that require the registration of pharmaceutical sales representatives; and state and/or foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as HIPAA, thus complicating compliance efforts.

The ACA broadened the reach of the federal fraud and abuse laws by, among other things, amending the intent requirement of the U.S. federal Anti-Kickback Statute and certain federal criminal healthcare fraud statutes. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation. In addition, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA or the civil monetary penalties laws.

We may be subject to data privacy and security regulations by both the federal government and the states in which we conduct our business, including HIPAA, as amended by HITECH, and their implementing regulations, as well as the California Consumer Privacy Act of 2018, or the CCPA, which became effective on January 1, 2020. The CCPA establishes a new privacy framework for covered businesses by creating an expanded definition of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. The California State Attorney General has commenced enforcement actions against violators as of July 1, 2020. Further, a new California privacy law, the California Privacy Rights Act, or CPRA, was passed by California voters on November 3, 2020. The CPRA will create additional obligations with respect to processing and storing personal information that are scheduled to take effect on January 1, 2023 (with certain provisions having retroactive effect to January 1, 2022). Many of the state laws differ from each other in significant ways and are often not preempted by HIPAA, and may have a more prohibitive effect than HIPAA, thus complicating compliance efforts.

We may develop products that, once approved, may be administered by a physician. Under currently applicable U.S. law, certain products not usually self-administered (including injectable drugs) may be eligible for coverage under Medicare through Medicare Part B. Medicare Part B is part of original Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain pharmaceutical products, that are medically necessary to treat a beneficiary's health condition. As a condition of receiving Medicare Part B reimbursement for a manufacturer's eligible drugs, the manufacturer is required to participate in other government healthcare programs, including the Medicaid Drug Rebate Program and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of HHS as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities that participate in the program.

In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors.

In order to distribute any approved products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws involves substantial costs. 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. 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, for example, significant administrative, civil, and/or criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to administrative, civil, and/or criminal sanctions, including exclusions from government funded healthcare programs.

Employees and Human Capital Resources

As of December 31, 2020, we had 46 full-time employee equivalents. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. Other objectives include diversity and inclusion, employee development, training and safety. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.

As the COVID-19 pandemic continues, we have followed the recommendations of domestic public health authorities calling for employees to work from home if possible. We have supported and implemented a work-from-home policy for our employees, while the office remains open for ongoing necessary activities as permitted by relevant government orders. As our workforce is accustomed to working from home, we have not seen any significant impact of remote working arrangements to our operations to date.

None of our personnel are covered by a collective bargaining agreement. Collective bargaining agreements, or CBAs, can be entered into in Swedish law at the national, industry, or company levels. These CBAs are binding on both employers and employees. We have no trade union representation or CBAs at the company level, but CBAs may, however, change the employment conditions of our employees in the future and hence adversely affect our employment relationships.

Facilities

Our principal office is located at Kungsbron 1, C8, SE-111 22 Stockholm, Sweden. We lease approximately 4,585 square feet of office space at this location, under one lease agreement, and our leases for this location extend through May 2022. We hold an option to extend our leases for three additional years. We believe that suitable additional or substitute space will be available as needed to accommodate any future expansion of our operations.

C. ORGANIZATIONAL STRUCTURE

As of December 31, 2020, we had four subsidiaries. The following table sets out for each of our principal subsidiaries, the country of incorporation, and percentage ownership and voting interest held by us (directly or indirectly through subsidiaries) as of December 21, 2020:

Company	Country of incorporation	Percentage ownership and voting interest	Main activity
Calliditas Therapeutics, Inc.	United States	100%	Biopharmaceutical company
Nefecon AB	Sweden	100%	Biopharmaceutical company
Genkyotex S.A.	France	86.2%	Biopharmaceutical company
Genkyotex Suisse S.A.	Switzerland	86.2%	Biopharmaceutical company

D. PROPERTY, PLANTS AND EQUIPMENT

We lease our operational office, which consists of approximately 4,585 square feet, located in Stockholm, Sweden. The lease for this facility expires in 2022.

We have a total of 3 facilities worldwide owned or leased as of December 31, 2020, as set forth in the following table:

Facility location	Use	Approx. size (m^2)	Lease expiry
Sweden	Principal office	426	May 2022
France	Laboratory	140	January 2023
Switzerland	Office	281	December 2022

Environment, Health and Safety

Our research and development activities take place in our facilities in Stockholm, Sweden, Geneva, Swtitzerland and Archamps, France. For these activities we have obtained the necessary environmental and biohazard permits from the responsible governments. See “Item 3.D.—Risk Factors—Risks Related to Our Business and Industry.”

E. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

A. OPERATING RESULTS

Overview

We are a clinical-stage biopharmaceutical company focused on identifying, developing and commercializing novel treatments in orphan indications, with an initial focus on renal and hepatic diseases with significant unmet medical needs. Our lead product candidate, Nefecon, is a proprietary, novel oral formulation of budesonide, an established, highly potent local immunosuppressant, for the treatment of the autoimmune renal disease IgA nephropathy, or IgAN, for which there is a high unmet medical need and there are no approved treatments. IgAN is a progressive, chronic disease that over time results in deterioration of kidney function in patients, many of whom end up at risk of developing end-stage renal disease, or ESRD, with the need for dialysis or kidney transplant. Nefecon is currently the only pharmaceutical candidate in development for IgAN that is intended to be disease-modifying. Nefecon targets the ileum, the distal region of the small intestine, which is the presumed origin of IgAN due to the ileum being the location of the highest concentration of the Peyer’s patches, which are responsible for the production of secretory immunoglobulin A, or IgA, antibodies. Nefecon is the only compound in development for IgAN that has met the primary and key secondary endpoints in a randomized, double-blind, placebo-controlled Phase 3 clinical trial. Nefecon has been granted orphan drug designation for the treatment of IgAN in the United States and the European Union. We also recently acquired Genkyotex S.A., or Genkyotex, providing us with access to a novel platform of nicotinamide adenine dinucleotide phosphate oxidase, or NOX, inhibitors, which we intend to primarily develop for orphan diseases with fibrotic components, with a main focus on kidney and liver diseases.

In November 2020, we reported positive topline data from Part A of our global, pivotal Phase 3 clinical trial, which we refer to as NefIgArd. In this trial of 200 patients, treatment with Nefecon was associated with a statistically significant and clinically meaningful reduction of protein in the urine, or proteinuria, and stabilization of kidney function. The primary endpoint analysis showed a 31% mean reduction in the treatment arm versus baseline, with placebo showing a 5% mean reduction versus baseline, resulting in a 27% mean reduction at nine months of the treatment arm versus placebo (p=0.0005). The key secondary endpoint, eGFR, showed a treatment benefit of 7% versus placebo at nine months, reflecting stabilization in the treatment arm and a 7% decline of eGFR in the placebo arm (p=0.0029). This reflected an absolute decline of 4.04 ml/min/1.73m2 in the placebo group over 9 months compared to a 0.17 ml/min/1.73m2 decline in the treatment arm. In addition, the trial showed that Nefecon was generally well-tolerated. On the basis of the positive results of Part A of NefIgArd, we submitted a New Drug Application, or NDA, in March 2021 for accelerated approval by the FDA. In April 2021, Nefecon was granted accelerated assessment by the EMA, and we intend to submit a Marketing Authorisation Application, or MAA, for conditional approval by the EMA in the second quarter of 2021. In January 2021, we completed the enrollment of all 360 patients in NefIgArd, which includes 200 patients previously enrolled in Part A and another 160 patients enrolled in Part B. In February 2021, we announced dosing of the first patient in the global open-label extension, or OLE, of NeflgArd, which is open to all qualifying patients who have completed NeflgArd. We also previously conducted a Phase 2b trial with 150 patients, which also met the identical primary and key secondary endpoint.

Although we observed a statistically significant and clinically meaningful reduction of proteinuria, the United States Food and Drug Administration, or the FDA, and the European Medicines Agency, or the EMA, have not provided a specific level of reduction of proteinuria that would be required to obtain marketing approvals. Accordingly, there can be no assurance that the level of reduction of proteinuria that we observed in our Phase 3 clinical trial will be sufficient to satisfy the FDA and EMA. The FDA accelerated approval pathway and the EMA accelerated assessment pathway, may not lead to a faster development process and does not increase the likelihood that our product candidates will receive marketing approval. If approved, we expect that Nefecon will be the first treatment on the market indicated for IgAN. We believe that if Nefecon can successfully treat IgAN patients, their kidney function will be preserved. We retain worldwide rights to Nefecon other than in Greater China and Singapore where we have established a strategic collaboration.

Since our inception in 2004, we have devoted substantially all of our resources to conducting research and development of our product candidates, in-licensing and acquiring rights to our product candidates, business planning, raising capital and providing general and administrative support for our operations. To date, we have financed our operations primarily with proceeds from the sale of our equity and the upfront payment from the out-license of Nefecon to Everest Medicines, or Everest. Through December 31, 2020, we had received net proceeds of SEK 2,124.4 million from the issuance of equity securities. In June and July 2020, we completed a new share issuance of 9.2 million shares, in connection with the U.S. IPO and concurrent private placement, for gross proceeds of SEK 891.4 million from U.S. and international institutional investors. In July 2019, we completed a directed new share issuance of 3.5 million shares for gross proceeds of SEK 210.3 million from Swedish and international institutional investors. We believe that our cash as of December 31, 2020 will be sufficient to fund our operations 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. There can be no assurance that Nefecon will be approved by regulatory authorities, or that we will be successful in marketing Nefecon, if approved. See “Item 3.D.—Risk Factors—Risks Related to Our Financial Position and Need for Additional Capital—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.”

We have incurred significant operating losses since our inception in 2004. For the years ended December 31, 2020 and 2019, we had a net loss of SEK 436.5 million and SEK 32.6 million, respectively. As of December 31, 2020 and 2019, we had an accumulated loss of SEK 918.6 million and SEK 488.1 million, respectively. These losses have resulted primarily from costs incurred in connection with research and development activities and administrative and selling activities associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future, and we expect our expenses to increase in connection with our ongoing development and planned commercialization activities.

In June 2019, we received an upfront payment from Everest in connection with the execution of the license agreement, as discussed below under “—License Agreement with Everest Medicines.” We do not expect to generate substantial revenue from product sales or otherwise unless and until we successfully complete clinical development of and obtain regulatory approval for Nefecon or our other product candidates. In addition, if we obtain regulatory approval for Nefecon, we expect to incur significant expenses related to developing our commercialization capabilities to support sales, marketing and distribution activities, either independently or in collaboration with others.

Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations or other strategic transactions.

We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back, or discontinue the development and commercialization of one or more of our development programs.

Basis of Presentation

License Agreement with Everest Medicines

In 2019, we entered into a license agreement with Everest, pursuant to which we granted Everest an exclusive, royalty-bearing, non-transferable license to develop, manufacture and commercialize Nefecon for IgAN, which at Everest's option, may be extended to other potential indications if and when we initiate a registrational clinical trial in such indications, which we collectively refer to as the Licensed Product. The territories covered by the Everest license are Greater China, including mainland China, Taiwan, Hong Kong and Macau, and Singapore, which we collectively refer to as the Territories.

Under the terms of the agreement, we received an initial upfront payment of $15.0 million upon signing the agreement, and we are eligible to receive future payments upon the satisfaction of specific clinical, regulatory and commercial milestones of up to an additional $106.0 million, inclusive of option payments for the development of Nefecon in other potential indications. In December 2019, we announced that of the milestone payments described above, a $5.0 million milestone payment from Everest was triggered upon approval of Everest's investigational new drug application, or IND, in China. Everest is also required to pay typical tiered royalties on annual net sales of the Licensed Product, subject to customary reductions. See "Item 4.B.—Business Overview—License Agreement with Everest Medicines."

Initial Public Offering

In June 2020, we completed an initial public offering, of our American Depositary Shares on The Nasdaq Global Select Market in the United States and sold 924,000 common shares in Europe and countries outside of the United States in a concurrent private placement to qualified investors for gross proceeds of approximately $90 million (approximately SEK 828 million) before deduction of issuance costs, underwriting commissions and expenses. In July 2020, the underwriters in the U.S. IPO exercised a portion of their over-allotment option, whereby we received additional gross proceeds of approximately $6.9 million (approximately SEK 63 million) before deduction of issuance costs, underwriting commissions and expenses.

Acquisition of a Controlling Interest in Genkyotex S.A.

In November 2020, we acquired a controlling interest in Genkyotex S.A., or Genkyotex, a biopharmaceutical company specializing in NOX therapies with offices in France and Switzerland. Genkyotex's unique platform enables the identification of orally available small molecules which selectively inhibit specific NOX enzymes that amplify multiple disease processes such as fibrosis and inflammation. The acquisition of Genkyotex adds a late-stage orphan pipeline asset and platform in inflammation and fibrosis to our product portfolio in orphan diseases. We acquired 7,236,515 ordinary shares of Genkyotex from Genkyotex's largest shareholders and management team, or the Block Sellers, representing 62.7% of the share capital and voting rights for EUR 19.7 million in cash at EUR 2.73 per share. On November 26, 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. In March 2021, we participated in a rights issue in Genkyotex, and increased our ownership percentage to 90.2% of the share capital of Genkyotex.

The Acquisition costs in 2020, 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. See our Annual Report 2020 for more information.

Components of our Results of Operations

Revenue

From inception through December 31, 2020, we have not generated revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. In 2019, we recognized revenue in connection with the execution of the license agreement with Everest and additionally upon triggering a payment to us resulting from the satisfaction of a regulatory milestone under such agreement, and we are eligible to receive future payments upon the satisfaction of specific clinical, regulatory and commercial milestones, as well as typical tiered royalties. We refer to revenue received from our license agreement with Everest as "net sales" in our consolidated financial statements. If our development efforts for Nefecon, setanaxib and future product candidates are successful and result in approved and marketed products, or if we enter into additional collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments such collaboration or license agreements.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our development activities, including the development of Nefecon, setanaxib and our other product candidates, and include:

- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct clinical trials on our behalf, as well as contract manufacturing organizations, or CMOs, that manufacture drug products for use in our clinical trials;
- salaries, benefits and other related costs for our personnel engaged in research and development functions;
- costs of outside consultants, including their fees and related travel expenses, directly related to our research and development functions; and
- costs related to compliance with regulatory requirements.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as a prepaid expense or accrued expense. Swedish research and development tax credits on social security costs are recorded as an offset to research and development expense. See "—Income Taxes" below for further details.

From inception through December 31, 2020, our research and development expenses have primarily been for the development of Nefecon for the treatment of IgAN. As such, we do not track our internal research and development expenses on a product-by-product or indication-by-indication basis for product candidates. Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase for the foreseeable future 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.

The process of conducting the necessary clinical trials to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

We also expect to incur additional expenses related to milestone and royalty payments payable to third parties with whom we have entered into license agreements. See “Item 5.B.—Liquidity and Capital Resources—Contractual Obligations and Commitments.”

Administrative and Selling Expenses

Administrative and selling expenses consist of salaries and other related costs for personnel in our executive, finance, corporate, commercialization and business development and administrative functions. Administrative and selling expenses also include professional fees for legal, intellectual property, accounting, auditing, tax and consulting services, related travel expenses and facility-related expenses, which include expenses for rent and maintenance of facilities and other operating costs.

We expect that our administrative and selling expenses will increase in the future as we increase our headcount to support our continued development and potential commercialization of our portfolio of product candidates. We also expect to incur increased expenses associated with being a dual-listed public company in the United States and Sweden, including costs of accounting, audit, legal, regulatory and tax compliance services, director and officer insurance costs and investor and public relations costs.

Other Operating Income

Other operating income consists primarily of realized and unrealized foreign currency transaction gains on operating receivables and liabilities.

Other Operating Expenses

Other operating expenses consist primarily of realized and unrealized foreign currency transaction gains and losses on operating receivables and liabilities.

Financial Income

Financial income consists primarily of interest income earned on cash accounts, realized and unrealized gains on foreign exchange derivative instruments, and realized and unrealized foreign currency transaction gains on financial receivables and liabilities.

Financial Expenses

Financial expenses consist primarily of realized and unrealized losses on foreign exchange derivative instruments and realized and unrealized foreign currency transaction losses on financial receivables and liabilities.

Income Tax

We are subject to corporate taxation in Sweden and taxation in the United States, France and Switzerland for our subsidiaries. Due to the nature of our business, we have generated losses since inception and have therefore not paid Swedish corporation tax to date. The research and development tax credit on social security costs for personnel within research and development received in Sweden and France is recorded as a credit against research and development expenses. The Swedish and France research and development tax credit on social security costs for personnel within research and development is fully refundable to us and is not dependent on current or future taxable income..

As of December 31, 2020, we had SEK 2,704.8 million of tax losses carried forward for which deferred tax assets have not been recognized in the statement of financial position. Deferred tax assets will be recognized for unused tax losses to the extent that it is probable that taxable profit will be available against which the losses can be utilized.

Results of Operations

Comparison of Years Ended December 31, 2020 and 2019

	Year ended December 31,		
	2020	**2019**	**% Change**
	(In thousands of SEK)		
Net sales	874	184,829	(99.5)%
Operating expenses	(380,594)	(212,848)	78.8%
Research and development	(241,371)	(149,826)	61.1%
Administrative and selling	(141,724)	(62,882)	125.4%
Other operating income	2,501	4,385	(43.0)%
Other operating expenses	-	(4,525)	(100)%
Operating loss	**(379,720)**	**(28,019)**	1,255.2%
Financial income	547	926	(40.9)%
Financial expenses	(56,978)	(5,408)	953.6%
Loss before taxes	**(436,151)**	**(32,501)**	1242.0%
Income taxes	(360)	(77)	367.5%
Net loss for the year attributable to shareholders	**(433,494)**	**(32,578)**	1,230.6%
Non-controlling interest	(3,017)	-	-%
Loss per share before and after dilution, SEK	(9.66)	(0.88)	997.7%

Net Sales

Net sales decreased by SEK 184.0 million for the twelve months ended December 31, 2020 compared to the twelve months ended December 31, 2019. This decrease was mainly due to the out-licensing of Nefecon for China as part of the license agreement with Everest Medicines, which occurred in 2019.

Research and Development Expenses

Research and development expenses increased by SEK 91.5 million for the twelve months ended December 31, 2020 compared to the twelve months ended December 31, 2019. This increase was primarily due to increased cost for clinical trials of SEK 45.9 million. Additionally, we had a SEK 17.8 million increase in third party consultant costs engaged in research and development functions and a SEK 5.9 million increase in personnel costs due to increased headcount for personnel engaged in research and development functions.

Selling, General and Administrative Expenses

Administrative and selling expenses increased by SEK 78.8 million for the twelve months ended December 31, 2020 compared to the twelve months ended December 31, 2019. This increase was primarily due to a SEK 24.3 million increase in third party consultant costs engaged in selling, general and administrative functions and an SEK 14.5 million increase in costs related to U.S. listing fees and insurances. Additionally, we had a SEK 16.0 million increase in costs for our pre-commercial activities incl. personnel in the U.S. and a SEK 16.0 million increase in costs for non-U.S. personnel, whereof SEK 8.6 million is related to incentive programs.

Other Operating Income

Other operating income decreased by SEK 1.9 million for the twelve months ended December 31, 2020 compared to the twelve months ended December 31, 2019, primarily due to disadvantageous exchange rate development on operating receivables and liabilities.

Financial Income (Expense)

Financial income decreased by SEK 0.4 million for the twelve months ended December 31, 2020 compared to the twelve months ended December 31, 2019, primarily due to reduced unrealized foreign currency transaction gains on cash accounts. Financial expense increased by SEK 51.6 million for the twelve months ended December 31, 2020 compared to the twelve months ended December 31, 2019, primarily due to unrealized foreign currency transaction losses on cash accounts held in USD, due to a weakened USD against SEK.

B. LIQUIDITY AND CAPITAL RESOURCES

Sources of Funds

From inception through December 31, 2020, we have not generated revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. In June 2019, we received the upfront payment of $15.0 million from Everest in connection with the execution of the license agreement, and we are eligible to receive future payments upon the satisfaction of specific clinical, regulatory and commercial milestones, as well as typical tiered royalties. In December 2019, we announced that a $5.0 million milestone payment from Everest was triggered upon approval of Everest's IND in China. If our development efforts for Nefecon and future product candidates are successful and result in approved and marketed products, or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from collaboration or license agreements.

Through December 31, 2020, we had received net proceeds of SEK 2,124.4 million from the issuance of equity securities. In June and July 2020, we completed a new share issuance of 9.2 million shares, in connection with the U.S. IPO and a concurrent private placement, for gross proceeds of SEK 891.4 million from U.S. and international institutional investors. In July 2019, we completed a directed new share issuance of 3.5 million shares for gross proceeds of SEK 210.3 million from Swedish and international institutional investors. We believe that our cash as of December 31, 2020 will be sufficient to fund our operations and capital expenditure requirements into the third quarter of 2022. There can be no assurance that Nefecon will be approved by regulatory authorities, or that we will be successful in marketing Nefecon, if approved. See "Item 3.D.—Risk Factors—Risks Related to Our Financial Position and Need for Additional Capital—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."

We currently have no ongoing material financing commitments, such as lines of credit or guarantees, that are expected to affect our liquidity over the next five years, other than our lease obligations described below under "Item 5.B.—Liquidity and Capital Resources—Contractual Obligations and Commitments."

In addition to the foregoing, based on our current assessment, we do not expect any material impact on our long-term liquidity due to the COVID-19 pandemic. However, we will continue to assess the effect of the pandemic to our operations. The extent to which the COVID-19 pandemic will impact our business and operations will depend on future developments that 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. While the potential economic impact brought by 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 in the future. In addition, a recession or long-term market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

Cash Flows

Comparison for the Years Ended December 31, 2020 and 2019

The table below summarizes our cash flows for the years ended December 31, 2020 and 2019.

	Year ended December 31,		
	2020	**2019**	**Variance**
	(In thousands of SEK)		
Cash and cash equivalents at beginning of the period	**753.5**	**646.2**	**107.4**
Net cash flows (used in) / from operating activities	(309.2)	(71.0)	(238.2)
Net cash flows (used in) / from investing activities	(172.6)	(18.1)	(154.5)
Net cash flows (used in) / from financing activities	768.6	198.8	569.7
Net increase (decrease) in cash	286.8	109.8	177.0
Exchange-rate difference in cash	(44.0)	(2.4)	(41.6)
Cash and cash equivalents at end of the period	**996.3**	**753.5**	**242.8**

Operating Activities

During the year ended December 31, 2020, net cash used in operating activities was SEK 309.2 million, primarily resulting from our operating loss of SEK 379.7 million and positive net cash changes in our operating assets and liabilities of SEK 54.1 million. Net changes in our operating assets and liabilities for the year ended December 31, 2020 consisted mainly of a SEK 46.6 million decrease in account receivables due to payments received from Everest.

During the year ended December 31, 2019, net cash used in operating activities was SEK 71.0 million, primarily resulting from our operating loss of SEK 28.0 million and negative net cash changes in our operating assets and liabilities of SEK 45.9 million. Net changes in our operating assets and liabilities for the year ended December 31, 2019 consisted mainly of a SEK 46.6 million increase in account receivables due to the timing of payments associated with the license agreement with Everest.

Investing Activities

During the year ended December 31, 2020, net cash used for investing activities was SEK 172.6 million for the acquisition of shares in Genkyotex SA.

During the year ended December 31, 2019, net cash used for investing activities was SEK 18.1 million, consisting of SEK 16.1 million for the acquisition of a license from Dr. Falk Pharma to develop a product in the United States, SEK 1.9 million for a lease security deposit and SEK 0.1 million in capital expenditures.

Financing Activities

During the year ended December 31, 2020, net cash provided by financing activities was SEK 768.6 million, mainly consisting of net SEK 795.5 million from our IPO in the United States and SEK 59.3 million from exercise of warrants less SEK 82.1 million used for acquisition of shares in Genkyotex SA in a simplified public mandatory cash offer.

During the year ended December 31, 2019, net cash provided by financing activities was SEK 198.8 million, primarily consisting of SEK 199.4 million net proceeds from a new share issuance and SEK 2.8 million attributable to warrant premiums from our Warrant Program 2019/2022, partially offset by paid transaction costs of SEK 1.7 million and lease payments of SEK 1.7 million.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities. We will need additional funds to meet operational needs and capital requirements for clinical trials, other research and development expenditures, and business development activities. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

We believe that our cash as of December 31, 2020 will be sufficient to fund our operations 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 exhaust our available capital resources sooner than we expect. There can be no assurance that Nefecon will be approved by regulatory authorities, or that we will be successful in marketing Nefecon, if approved. See “Item 3.D.—Risk Factors—Risks Related to Our Financial Position and Need for Additional Capital—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.”

Because of the numerous risks and uncertainties associated with the development of product candidates and programs, and because the extent to which we may enter into collaborations with third parties for development of our product candidates is unknown, we are unable to estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements will depend on many factors, including our:

- conducting and fully enrolling clinical trials in the development of Nefecon and our other product candidates;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we complete registrational clinical trials that achieve their primary and/or secondary endpoints;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval by acquiring sales force, marketing and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- completing development of our product candidates and in-licensing or otherwise acquiring new product candidates;

- qualifying for and maintaining, adequate coverage and reimbursement by government and payors for our product candidates for which we obtain marketing approval;
- establishing and maintaining supply and manufacturing processes and relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development of our product candidates and the commercial supply of our product candidates for which we obtain marketing approval;
- obtaining market acceptance of our product candidates, if approved, as viable treatment options with acceptable safety profiles;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed, including robust quality systems and compliance systems;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations under such arrangements;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

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 the 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.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2020 and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments due by Period				
	Total	Less than 1 Year	1-3 years	4-5 Years	More than 5 years
			(in thousands)		
Lease obligations(1)	5,626	4,521	1,105	—	—
Total	5,626	4,521	1,105	—	—

(1) Amounts reflect minimum payments due for our office space and laboratory lease as of December 31, 2020.

We enter into contracts in the normal course of business with CROs and CMOs and other third parties for clinical trials and manufacturing. There are no obligations associated with cancellation provisions, non-cancelable portions of agreement terms or minimum cancellation fees.

License Agreements with Archimedes and Dr. Falk Pharma

We are required to pay Kyowa Kirin Services Ltd., f/k/a Archimedes Development Ltd, or Archimedes, a fixed royalty of 3% of net sales of all products, including Nefecon, if approved, covered by the license granted to us pursuant to our agreement with Archimedes pursuant to which we were granted (i) an exclusive license to certain patents and joint intellectual property developed with Archimedes and (ii) a non-exclusive license to certain of Archimedes' know-how as necessary or useful to develop and commercialize Nefecon or other product candidates.

Additionally, pursuant to our agreement with Dr. Falk Pharma, we may incur potential milestone payments totaling up to €38.5 million upon our achievement of specific clinical, regulatory and commercial milestones, as applicable and royalties on annual net sales of licensed products at a low- to mid-teens percentage, subject to reductions in certain circumstances, on annual net sales of licensed products. These royalty payments are subject to certain minimum annual dollar requirements in the amount of six to seven figures.

Due to the uncertainty of the achievement and timing of the events requiring various payments under these agreements, the amounts to be paid by us are not fixed or determinable at this time and are excluded from the table above.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with International Financial Reporting Standards, or IFRS, issued by the International Accounting Standards Board, or IASB. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, costs and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in greater detail in our consolidated financial statements appearing at the end of this annual report, the following accounting policies are the judgments and estimates used in the preparation of our consolidated financial statements.

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and communicating with our personnel to identify services that have been performed on our behalf by third-party service providers and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our third-party service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing clinical trials on our behalf;
- CMOs in connection with the production of clinical trial materials;
- investigative sites or other service providers in connection with clinical trials;
- vendors in connection with clinical development activities; and
- vendors related to product manufacturing and development and distribution of clinical supplies.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs, CMOs and vendors that supply, conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Intangible Assets

Development expenditures are capitalized when they meet the criteria for capitalization. The most important criteria for capitalization are that the final product of the development process has a probable future earnings or cost-savings capacity, and that the technical and financial conditions exist for completing the development work. Research and development expenditures are otherwise expensed as operating expenses. We capitalize expenditures for the development of pharmaceuticals to the extent that it is expected to meet the criteria in accordance with IAS 38. The decision to capitalize is based on significant judgments made by management, including the technical feasibility of completing the intangible asset so that it will be available for use or sale and assumptions used to demonstrate that the asset will generate probable future economic benefits (e.g., projected cash flow projections, discount rate). Our expenditures for the development of pharmaceuticals were not deemed to meet the capitalization criteria for the twelve months ended December 31, 2020 or December 31, 2019 and were thus expensed. Capitalization of expenditures for the development of pharmaceuticals typically takes place late in Phase 3 clinical trials, or alternatively in conjunction with the initiation of pivotal trials, depending on when the criteria are deemed to have been met. The reason for this is that before then it is uncertain whether the expenditure will generate future economic benefits and that financing the completion of the asset is not yet guaranteed. Market approval has not yet been obtained for any products and, accordingly, the conditions for capitalizing development expenditures are not met.

Intangible assets with a finite useful life are recognized at initial recognition at cost less accumulated amortization and any accumulated impairment losses. Intangible assets with finite lives are amortized over the useful economic life and assessed for impairment whenever there is an indication that the intangible asset may be impaired. When determining the amortized amount of the assets, the residual value of the asset is taken into account, when applicable.

Our intangible assets are essentially attributable to us acquiring the rights to the NOX platform and the vaccine platform (SIIL agreement), as well as goodwill in connection with the acquisition of Genkyotex SA. In addition, to the previous in-licensing agreement of Budenofalk 3mg oral capsule from the German pharmaceutical company Dr Falk Pharma GmbH. For goodwill and intangible assets not yet available for use the Group assesses for impairment at each reporting date based on their recoverable amounts, including key assumptions such as the timing of potential commercialization, market size, market share, probability of reaching the market and the discount ratesAmortization of the intangible assets begins when the asset can be used, that is, when it is in the place and in the condition required to be able to use it in the manner intended by the Group’s management.

The Group's expected finite useful life is:

– Licenses and similar rights – 6-15 years

Until market approval from regulatory authorities has been granted, amortization of "Licenses and Similar Rights" will not commence. As market approval has not yet been obtained, no other costs have been capitalized. Following market approval from regulatory authorities, "Licenses and Similar Rights" will be amortized on a straight-line basis over the expected useful life. Until a market approval of the product has been obtained, the asset is assessed for impairment at least once a year, or when there is an indication that the asset may be impaired

The acquisition of Genkyotex SA resulted in the Group acquiring the rights to the NOX platform and the vaccine platform (SIIL agreement), as well as goodwill. Goodwill arising in a business combination comprises the difference between the cost of the business combination and the fair value of identifiable assets acquired, liabilities assumed, and any contingent liabilities recognized at the acquisition date. Goodwill on business combinations is included in intangible assets and measured at cost less any accumulated impairment losses. Goodwill is allocated to the cash-generating units, which is the full Group, and tested annually for impairment requirement, or whenever there is any indication of impairment. There is no amortization of goodwill and impairment of goodwill is not reversed.

Revenue

Revenue is recognized when a promised product or service is transferred to the counterparty, which can be done over time or at a point in time. Revenue is the amount that we expect to receive as compensation for transferred goods or services.

Revenue for out-licensing is recognized at a point in time that occurs when control over the intangible asset is transferred to the counterparty. Variable remuneration (for example, attributable to future regulatory milestones) is recognized when there is no longer any significant uncertainty as to whether these will occur. Compensation attributable to sales-based milestones or royalties are not recognized until the sale that results in the right to milestones or royalties arises. Revenue attributable to the sale of approved products recognized at the point in time when control of the goods is transferred to the counterparty.

Income Tax

Income tax comprises current tax and deferred tax. Income tax is recognized in net profit for the period, except when the underlying transaction is recognized in other comprehensive income or equity with the related tax effect recognized in other comprehensive income and in equity. Current tax is the tax that is to be paid or received in the current year, with the application of the tax rates that are decided or decided in practice on the closing date. Current tax also includes adjustments of current tax attributable to prior periods. Deferred tax is calculated based on temporary differences between the tax bases of assets and liabilities and their carrying amounts. Temporary differences attributable to participations in subsidiaries that are not expected to be reversed in the foreseeable future are not taken into account. Deferred tax is calculated with the application of the tax rates and tax rules decided or announced on the closing date, and that are expected to apply when the deferred tax asset in question is realized or the deferred tax liability is settled. Deferred tax liabilities and deferred tax assets are offset as far as possible within the framework of local laws and regulations on taxation. Deferred tax assets on deductible temporary differences and loss carryforwards are recognized only to the extent that it is likely that it will be possible to utilize these. The value of deferred tax assets is reduced when it is no longer deemed likely that they can be utilized. Our loss carryforwards have not been measured and are not recognized as a deferred tax asset. Loss carryforwards are measured when we have established a level of earnings that management is certain will result in a tax surplus.

Warrants

Accounting for warrants requires us to make significant judgments, estimates and assumptions. We estimate the fair value of warrants granted using the Black-Scholes option-pricing model, which requires the input of subjective assumptions, including volatility, risk-free interest rate, expected dividends, and expected term. We have only issued warrants that were transferred at fair value. Premiums received for warrants granted to acquire our shares are recognized as an addition to equity, based on the warrant premium, at the date when the warrant was transferred to the counterparty.

Option Program

We have issued an option program which constitutes share-based payments. The cost for the remuneration that is recognized in a period is dependent on the original valuation that was made on the date on which the contracts with the participants in the incentive programs were concluded, the number of months of service required for vesting of their options (accruals are made over this period), the number of options that are expected to be vested under the terms of the plans and a continuous reassessment of the value of the tax benefits for the participants under the plans (for determining provisions for social security expenses). Those estimates which affect the cost in a period and the corresponding increase in equity mainly refer to inputs for the valuation of the options. All the options are classified as equity-settled, as vested options are settled in equity. When the options are exercised, the company issues new shares.

Quantitative and Qualitative Disclosures about Market Risks

Market risk is the risk that the fair value of, or future cash flows from, a financial instrument will vary due to changes in market prices. The type of market risk that primarily impacts us is foreign currency risk.

Foreign Currency Risk

Translation Exposure

We maintain our consolidated financial statements in our functional currency Swedish Kronor, which is also our functional currency. All amounts, unless otherwise stated, are rounded to the nearest thousand.

Transactions in foreign currency are translated to the functional currency at the exchange rate on the date of the transaction. Monetary assets and liabilities in foreign currency are translated to the functional currency at the exchange rate that applies on the closing date. Exchange rate differences arising on translation are recognized in net profit for the year. Foreign exchange gains and losses on operating receivables and liabilities are recognized in operating profit, while foreign exchange gains and losses on financial receivables and liabilities are recognized as financial items.

Assets and liabilities in foreign operations are translated from the functional currency of the operations to the Group’s presentation currency at the exchange rate applicable on the closing date. Income and expenses in a foreign operation are translated to SEK at the average exchange rate which corresponds to an approximation of the exchange rates prevailing on each individual transaction date. Translation differences arising in the translation of foreign operations’ functional currencies are recognized in the consolidated statements of comprehensive income.

We recorded foreign currency transaction gains of SEK 2.5 million and foreign currency transaction losses of SEK 0.1 million for the twelve months ended December 31, 2020 and 2019, respectively. These foreign currency transaction gains and losses are included in other operating income and other operating expenses in our consolidated financial statements.

We recorded foreign exchange rate difference translation losses of SEK 53.3 million and SEK 2.4 million for the twelve months ended December 31, 2020 and 2019, respectively. These foreign currency translation losses are included in financial expenses in our consolidated financial statements.

Transaction Exposure

Our transaction exposure from contracted payment flows in foreign currency is limited. However, our transaction exposure has been increasing year by year. The table below sets forth our exposure in each currency for the years ended December 31, 2020 and December 31, 2019.

Currency Exposure 2020 (%)	Revenue	Operating expenses
USD	100%	35%
EUR	—	36%
GBP	—	6%
SEK	—	23%

Currency Exposure 2019 (%)	Revenue	Operating expenses
USD	100%	22%
EUR	—	54%
GBP	—	3%
SEK	—	21%

Our primary transaction exposure is in Euros and U.S. dollars. A 10% stronger Euro against the Swedish Krona would have a negative impact on profit after tax and equity of approximately SEK 10.2 million and SEK 10.2 million for 2020 and 2019, respectively. A 10% stronger U.S. dollar against the Swedish Krona would have a negative impact on profit after tax and equity of approximately SEK 10.0 million and positive impact of SEK 14.4 million for 2020 and 2019, respectively.

Interest Rate Risk

We are currently not exposed to significant interest rate risk. Our only variable interest-bearing financial assets are cash at Swedish banks. Certain European countries have recently experienced (or currently are expected to experience) negative interest rates on certain fixed-income instruments, and similar interest rate conditions may be experienced in other regions. Negative interest rates may magnify our susceptibility to interest rate risk and diminish yield and performance on our investments. Changing interest rates may have unpredictable effects on securities markets in general, directly or indirectly impacting our investments and yield.

Given the short-term nature of these investments, the sensitivity towards interest rate fluctuations is deemed not to be significant. Therefore, the effect of an increase or decrease in interest rates would only have an immaterial effect on our financial results.

As of December 31, 2020 and 2019, we had no debt outstanding and are therefore not subject to interest rate risk related to debt.

C. RESEARCH AND DEVELOPMENT, PATENTS AND LICENSES

For a discussion of our research and development activities, see the sections of this annual report titled “Item 4.B.—Business Overview” and “Item 5.A.—Operating Results.”

D. TREND INFORMATION

Other than as disclosed elsewhere in this annual report, we are not aware of any trends, uncertainties, demands, commitments or events for the period from January 1, 2020 to December 31, 2020 that are reasonably likely to have a material effect on our net revenues, income, profitability, liquidity or capital resources, or that caused the disclosed financial information to be not necessarily indicative of future operating results or financial conditions. For a discussion of trends, see the sections of this annual report titled “Item 4.B.—Business Overview,” “Item 5.A.—Operating Results”, and “Item 5.B.—Liquidity and Capital Resources.”

E. OFF-BALANCE SHEET ARRANGEMENTS

We did not have any off-balance sheet arrangements, as defined in the rules and regulations of the SEC, as of or during the periods presented.

Recently Adopted Accounting Pronouncements and Accounting Pronouncements Not Yet Adopted

A description of recently adopted accounting pronouncements and accounting pronouncements not yet adopted that may potentially impact our financial position and results of operations is disclosed in our consolidated financial statements appearing at the end of this annual report.

JOBS Act

On April 5, 2012, the Jumpstart Our Business Startups Act, or the JOBS Act, was enacted. Subject to certain conditions set forth in the JOBS Act, we are entitled to rely on certain exemptions as an "emerging growth company." We are not required to, among other things, (i) provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b), (ii) provide all of the compensation disclosure that may be required of non-emerging growth public companies under the Dodd-Frank Wall Street Reform and Consumer Protection Act, (iii) comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (auditor discussion and analysis) and (iv) disclose certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the chief executive officer's compensation to median employee compensation. These exemptions will apply for a period of five years following the completion of the global offering or until we no longer meet the requirements of being an emerging growth company, whichever is earlier.

Internal Control Over Financial Reporting

As a public company listed on Nasdaq, the Sarbanes-Oxley Act will require, among other things, that we assess the effectiveness of our internal control over financial reporting at the end of each fiscal year. We anticipate being first required to issue management's assessment of internal control over financial reporting pursuant to Section 404(a) of the Sarbanes-Oxley Act in connection with issuing our consolidated financial statements as of and for the year ending December 31, 2021.

In connection with our financial statement preparation process 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), or PCAOB, in our internal control over financial reporting. Under the standards established by the PCAOB, 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 experience 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.

F. TABULAR DISCLOSURE OF CONTRACTUAL OBLIGATIONS

For information regarding our contractual obligations, see "Item 5.B.—Liquidity and Capital Resources—Contractual Obligations and Commitments."

G. SAFE HARBOR

This annual report contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act and as defined in the Private Securities Litigation Reform Act of 1995. See "Cautionary Statement with Respect to Forward Looking Statements" at the beginning of this annual report.

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. DIRECTORS AND SENIOR MANAGEMENT

Our Board of Directors

Our board of directors is currently comprised of five members, who we refer to individually as a director. Less than a majority of the directors of our board of directors are citizens or residents of the United States.

The following table sets forth certain information with respect to the current members of our board of directors, including their ages as of December 31, 2020:

Name	Age	Position
Elmar Schnee	61	Chairman of the Board of Directors
Hilde Furberg	62	Director
Lennart Hansson, Ph.D.	64	Director
Diane Parks	68	Director
Molly Henderson	50	Director

The address for our directors is our registered office, care of Calliditas Therapeutics AB, Kungsbron 1, C8, SE-11 22, Stockholm, Sweden.

Under the rules and regulations of Nasdaq a director will qualify as "independent" if our board of directors affirmatively determines that he or she has no material relationship with us (either directly or as a partner, stockholder or officer of an organization that has a relationship with us). Our board of directors has determined that, of our five directors, no director has a relationship that would interfere with the exercise of independent judgment in carrying out his or her responsibilities as a director and that each of these directors is "independent" as that term is defined under Nasdaq rules. The Swedish Code includes certain independence requirements for the directors, and requires a majority of the directors to be independent of the company and at least two directors to also be independent of major shareholders.

The following is the biographical information of the members of our board of directors:

Elmar Schnee has served as the chairman of our board of directors since May 2019. Since 2012, Mr. Schnee has served as a managing director at Caljem GmbH, a consulting company. From May 2017 to August 2018, Mr. Schnee served as a management advisor to MindMaze SA, a neuro-technology company, where he also served as chief operating officer from June 2016 to April 2017. From October 2011 to November 2013, Mr. Schnee served as chairman and chief executive officer of Cardiorentis Ltd., a biopharmaceutical company. From January 2003 to June 2011, Mr. Schnee held various positions in senior management at Merck KGaA, a global pharmaceutical and chemical group. From November 2005 to June 2006, Mr. Schnee served as Deputy Member of the Executive Board of Merck KGaA responsible for the global pharmaceuticals business. From July 2006 to June 2011, he served as a member of the Executive Board and General Partner of Merck KGaA, with responsibility for global pharmaceutical activities. Prior to Merck KGaA, Mr. Schnee held senior positions in strategy, business development and marketing at UCB SA, Sanofi-Synthélabo SA, Migliara/Kaplan Associates, Inc. and Fisons Pharmaceuticals PLC. Since August 2014, Mr. Schnee served as a member of the board of directors of Jazz Pharmaceuticals plc and previously served as a director of Gentium (now a subsidiary of Jazz Pharmaceuticals plc) from May 2012 until April 2014. Since April 2017, Mr. Schnee has served as Chairman of the board of Santhera Pharmaceuticals Holding AG, a specialty pharmaceutical company. From June 2016 until May 2019, he served on the board of directors of Stallergenes-Greer plc. From November 2013 to August 2015, Mr. Schnee served on the board of directors of Cardiorentis Ltd. In addition, he currently serves on the boards of directors of three privately-held life sciences companies, Damian Pharma AG, Noorik Biopharmaceuticals AG and Moleac Pte Ltd. Mr. Schnee holds both a bachelor's degree in marketing and a master's degree in marketing and general management from the Swiss Institute of Business administration in Zurich.

We believe that Mr. Schnee is qualified to serve on our board of directors because of his experience, qualifications, attributes and skills, including his extensive experience in leadership roles at other biotechnology and pharmaceutical companies.

Hilde Furberg has served as a member of our board of directors since September 2014, and also served as our Chairperson from December 2015 to December 2016. Ms. Furberg has served as an independent consultant and professional board member since December 2018, including as advisor to Investinor AS since December 2018. Prior to that, Ms. Furberg served as SVP and General Manger/European Head of Rare Diseases at Sanofi Genzyme from November 2010 to November 2018. Ms. Furberg previously worked in companies such as Genzyme and Baxter. Ms. Furberg currently serves on the board of directors of Tappin AS, PCI Biotech Holding ASA, OncoZenge Bio-Me and Herantis Pharma. Ms. Furberg previously served on the board of directors of Blueprint Genetics, Probi, Pronova, Clavis, Bergenbio and Algeta. She received her Master of Science in Chemistry from Oslo University, Norway.

We believe that Ms. Furberg is qualified to serve on our board of directors because of her experience, qualifications, attributes and skills, including her extensive experience in biotechnology and pharmaceutical companies.

Lennart Hansson, Ph.D. has served as a member of our board of directors since May 2009. Dr. Hansson served as Head of Life Science at Industrifonden from 2008 to 2016. Dr. Hansson has also held various leadership roles at KabiGen AB, Symbicom AB, AstraZeneca, Biovitrum AB and as CEO of Arexis AB. Dr. Hansson serves as the chairman of the board of directors of Sixera Pharma AB and Ignitus AB. Dr. Hansson serves as a member of the Board of Directors of Cinclus AB, InDex Pharmaceuticals Holding AB (publ), and Medivir AB (publ). Dr. Hansson received his Ph.D. in Genetics from the University of Umea.

We believe that Dr. Hansson is qualified to serve on our board of directors because of his experience, qualifications, attributes and skills, including his broad experience from leading positions within pharmaceutical development and business development in both biotechnology and pharmaceutical companies.

Diane Parks has served as a member of our board of directors since May 2019. Ms. Parks previously served as the SVP Head of U.S. Commercial at Kite Pharma, Inc., from January 2016 to July 2018. Prior to that she served as the Vice President Marketing at Pharmacyclics from October 2014 to October 2015. She currently serves as a member of the board of directors for TriSalus Life Sciences, Kura Oncology, Inc. and Soligenix, Inc. Ms. Parks received her Bachelor of Science degree from Kansas State University and an MBA from Georgia State University.

We believe that Ms. Parks is qualified to serve on our board of directors because of her experience, qualifications, attributes and skills, including extensive sales and marketing experience in the United States.

Molly Henderson has served as a member of our board of directors since June 2020. Currently, Ms. Henderson is the Chief Financial Officer or UroGen Pharma LTD (Nasdaq: URGN) since October 2020. Prior to that role, Ms. Henderson was Chief Financial Officer, Executive Vice President and Corporate Secretary at Advaxis, Inc. Prior to serving at Advaxis, Inc., Ms. Henderson was Chief Financial Officer at Iovance Biotherapeutics, Inc. (formerly Lion Biotechnologies, Inc.) from June 2015 through August 2016. Ms. Henderson also served as the Chief Business and Financial Officer, Senior Vice President of VirtualScopics, Inc., a public company provider of imaging solutions to the pharmaceutical, biotechnology, and medical device industries, from May 2008 to August 2013, and as that company's Chief Financial Officer from May 2003 to May 2008. From 2013 to 2015, Ms. Henderson relocated to Europe, during which time she advised start-up companies in Switzerland. Earlier in her career, Ms. Henderson served as the Corporate Controller of Ultralife, Inc., a publicly-held provider of high performance lithium battery solutions. Prior to serving at Ultralife, Inc., Ms. Henderson was a Manager in the audit division of PricewaterhouseCoopers LLP. Ms. Henderson received her M.B.A. and B.S. degrees from the State University of New York at Buffalo.

We believe that Ms. Henderson is qualified to serve on our board of directors because of her extensive experience in leadership roles at other biotechnology and pharmaceutical companies.

Family Relationships

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

Our Executive Management

The following table sets forth certain information with respect to the current members of our executive management, including their ages as of December 31, 2020:

Name	Age	Position
Renée Aguiar-Lucander	58	Chief Executive Officer
Fredrik Johansson	43	Chief Financial Officer
Richard Philipson, M.D.	56	Chief Medical Officer
Andrew Udell	50	Vice President, North America Commercial
Frank Bringstrup, M.D.	61	Vice President Regulatory Affairs
Katayoun Welin-Berger, Ph.D.	52	Vice President Operations

The address for our executive management is our registered office, care of Calliditas Therapeutics AB, Kungsbron 1, C8, SE-11 22, Stockholm, Sweden.

The following is a brief summary of the biographical information of the members of our executive management:

Renée Aguiar-Lucander has served as our Chief Executive Officer since May 2017. Prior to joining us, from June 2015 until April 2017, Ms. Aguiar-Lucander served as a non-executive director on a variety of boards. Prior to that, from January 2009 to June 2015, Ms. Aguiar-Lucander served as Partner of Omega Fund Management, an international venture capital company focused on investments within the life science sector. Ms. Aguiar-Lucander is the Chairman of the Board of Directors of Exenta Inc.. Ms. Aguiar-Lucander received her B.A. in Finance from Stockholm School of Economics and received her M.B.A. from INSEAD.

Fredrik Johansson has served as our Chief Financial Officer since August 2017. Prior to joining us, from March 2015 to January 2017, he was Chief Financial Officer and Chief Operating Officer of Techstep ASA (f/k/a Birdstep Technology), listed on the Oslo Stock Exchange, where he, among other tasks, was in charge of the acquisition and reversed listing of Teki Solutions. Prior to that, Mr. Johansson served as Chief Financial Officer of Phone Family from December 2012 to March 2015. Prior to that, Mr. Johansson served as Chief Financial Officer of Teligent Telecom from October 2009 to June 2012. Mr. Johansson serves as Chairman of the Board of Directors of Truference AB. He studied Business Law at Jönköping International Business School and studied Business and American Law, Economics and Finance at Georgia State University, University of South Carolina and Lund University.

Richard Philipson has served as our Chief Medical Officer since July 2020. Dr. Philipson is a physician with 24 years of experience in the pharmaceutical industry from both large pharmaceutical companies and smaller biotechs. Prior to joining us, Dr. Philipson worked as Chief Medical Officer with the U.K.-based biotech company Trizell from July 2016 to July 2020, where he led the Adstiladrin Phase 3 clinical program and Biologics License Application in non-muscle invasive bladder cancer, submitted to the FDA in September 2019. Before Trizell, Dr. Philipson worked for Takeda from June 2014 to July 2016 as an Executive Medical Director. Prior to Takeda, Dr. Philipson spent nearly 16 years at GlaxoSmithKline, where he held a number of senior positions, including Disease Area Head and Acting Chief Medical Officer for the Rare Diseases Unit. Dr. Philipson received a BSc in Biomedical Sciences at London University and an MB MS, from Middlesex Hospital Medical School. He is a Member of the Royal College of Physicians and Fellow of the Faculty of Pharmaceutical Medicine.

Andrew Udell has served as our Vice President, North America Commercial since January 2019. Prior to joining us, from March 2017 to June 2018, he served as Vice President North America Commercial at NeuroDerm, LTD, a biotechnology company. Mr. Udell also served as the Principal at Andrew B. Udell Consulting LLC, a marketing consulting company, from May 2012 to January 2019. Prior to that, Mr. Udell held several sales and marketing positions in the pharmaceutical industry. Mr. Udell received his BSc from Lehigh University and his M.B.A. from the University of Connecticut.

Frank Bringstrup, M.D. has served as our Vice President of Regulatory Affairs since February 2019. Prior to joining us, from October 2001 to January 2019, Dr. Bringstrup held various positions at Novo Nordisk A/S, including most recently as the Senior Global Regulatory Lead from October 2006 to January 2019. Dr. Bringstrup received his M.D. from University of Copenhagen. He holds a diploma in Managing Medical Product Innovation from the Copenhagen Business School, a diploma in Business Administration from Warwick University, and a post graduate specialist course in public health from the Danish Health Authority.

Katayoun Welin-Berger, Ph.D. has served as our Vice President Operations since January 2020. Prior to that, from January 2014 to December 2019, Dr. Welin-Berger served as Vice President of Operations at BioGaia AB. Prior to that, she served in various development and operations roles at AstraZeneca. Dr. Welin-Berger received her Ph.D. in Pharmacy from Uppsala University in Sweden.

General Information About Our Directors and Executive Management

As of the date of this annual report, none of the members of our board of directors and executive management has a family relationship with any other member of our board of directors or executive management.

As of the date of this Annual Report and except as set out below, none of the members of our board of directors and executive management for at least the previous five years:

- has been convicted of any fraudulent offenses;
- has been a senior manager or a member of the administrative, management or supervisory bodies of any company at the time of or preceding any bankruptcy, receivership or liquidation;
- has been subject to any official public incrimination and/or sanction by any statutory or regulatory authority (including any designated professional body); or
- has ever been disqualified by a court from acting as a member of the administrative, management or supervisory bodies of any company or from acting in the management or conduct of affairs of any company.

B. COMPENSATION

Compensation of Our Executive Officers and Directors

For the year ended December 31, 2020, the aggregate compensation accrued or paid to the members of our board of directors and executive officers serving during the year was SEK 24.7 million.

During and for the year ended December 31, 2020, our executive officers had performance-based compensation programs and amounts paid to provide pension and healthcare benefits.

Non-Executive Director Compensation

The remuneration of our non-executive directors is proposed by the remuneration committee and determined by our board as a whole, based on, inter alia, a review of current practices in other companies.

Equity Incentive Plans

Warrant Programs

We have established two warrant programs, as an incentive for our employees and consultants: the 2018/2022 Warrant Program, or the 2018 Program and the 2019/2022 Warrant Program, or the 2019 Program. We refer to the 2018 Program and the 2019 Program as the Programs. Warrants are issued by the board in accordance with authorizations given to it by our shareholders. Each warrant issued under the Programs entitle the holder to subscribe for shares at a specified exercise price during a specified subscription period. The material terms of the Programs are summarized below.

No further awards will be issued under either the 2018 Program or 2019 Program.

2018/2022 Warrant Program

In 2018, our shareholders approved the 2018 Program to permit the issuance of warrants to purchase up to 1,160,000 common shares to our certain employees and consultants. As of December 31, 2020, warrants to purchase up to an aggregate of 856,586 common shares were outstanding. The exercise price for these warrants is SEK 74.30 per share. The warrants issued under the 2018 Plan may be exercised from January 1, 2022 until March 31, 2022, or such earlier date as may be determined in accordance with the terms of the Program. All exercise prices must be paid in cash at the time of subscription. The 2018 Program is closed and no further warrants may be issued under this program.

Pursuant to the terms of the 2018 Program, warrantholders are entitled to an adjustment of the number of warrants issued and/or the exercise price applicable in the event of certain corporate changes. Events giving rise to an adjustment include, among other things, the issuance of bonus shares, a reverse share split or share split, issuance of new convertible bonds or warrants and payment of dividends in the form of our equity. Additionally, in the event of a “change of control event” as defined in the 2018 Program, each warrantholder will be permitted to exercise all of his or her warrants regardless of the fact that such warrants would otherwise only be exercisable during the specified subscription period. Any warrants not exercised prior to the change in control event are forfeited.

We may amend the 2018 Program at any time with respect to changes which are required by legislation, court decisions, or decisions by public authorities, or, if in our opinion, any such actions are appropriate or necessary and the rights of any warrantholders are in no way prejudiced without the consent of the affected holder.

2019/2022 Warrant Program

In 2019, our shareholders approved the 2019 Program to permit the issuance of warrants to purchase up to 1,160,000 common shares to certain of our employees and consultants. As of December 31, 2020, warrants to purchase up to an aggregate of 422,500 common shares were outstanding. The exercise price for these warrants is SEK 74.50 per share. The 2019 Program is limited to no more than 25 participants and includes caps on the number of warrants that may be issued to a consultant or certain categories of consultants. The warrants issued under the 2019 Plan may be exercised from October 1, 2022 until December 31, 2022, or such earlier date as may be determined in accordance with the terms of the Program. All exercise prices must be paid in cash at the time of subscription. The 2019 Program has concluded, and no further warrants may be issued under this program.

Pursuant to the terms of the 2019 Program, warrantholders are entitled to an adjustment of the number of warrants issued and/or the exercise price applicable in the event of certain corporate changes. Events giving rise to an adjustment include, among other things, the issuance of bonus shares, a reverse share split or share split, issuance of new convertible bonds or warrants and payment of dividends in the form of our equity. Additionally, in the event of a “change of control event” as defined in the 2019 Program, each warrantholder will be permitted to exercise all of his or her warrants regardless of the fact that such warrants would otherwise only be exercisable during the specified subscription period. Any warrants not exercised prior to the change in control event are forfeited.

We may amend the 2019 Program at any time with respect to changes which are required by legislation, court decisions, or decisions by public authorities, or, if in our opinion, any such actions are appropriate or necessary and the rights of any warrantholders are in no way prejudiced without the consent of the affected holder.

ESOP 2020

The ESOP 2020 is a program under which participants will be granted stock options to acquire common shares in our company. As of December 31, 2020, options to purchase up to an aggregate of 1,089,000 common shares were outstanding. Eligible participants in the ESOP 2020 include our executive officers, employees and consultants. We have initially reserved options to purchase up to a maximum of 1,500,000 common shares that may be allocated under the ESOP. Our board of directors may grant options, on one or several occasions, between the date of the 2020 annual general meeting and the date of the 2021 annual general meeting to up to 40 employees or consultants of the Company. The maximum allocation per individual in each category shall be 400,000 Options for Category 1 (CEO), 250,000 Options for Category 2 (Management) and 100,000 Options for Category 3 (Other key personnel and consultants).

The options under the ESOP 2020 are granted for no consideration, though grantees must pay the exercise price of such options to acquire their underlying common shares. The options generally will vest over a three-year period, with 20% vesting on the date of the first anniversary of the grant date, an additional 40% vesting during the second year following the grant date and the remaining 40% vesting during the third year following the grant date. The exercise price of the options will be set at 115% of the volume-weighted average price of the common shares on Nasdaq Stockholm during the ten trading days preceding each grant date. Following the conclusion of the vesting period, the options may be exercised during a one-year period thereafter. The options are not transferrable and may not be pledged. The number of options are subject to customary adjustment for corporate events affecting our capital structure, including a bonus issue, merger, rights issue, share split, reverse share split, reduction of share capital or similar measures. In the event of a public takeover offer, significant asset sale, liquidation, merger or similar transaction, all then unvested options will vest in their entirety following the completion of such transaction.

Our board of directors is responsible for preparing the detailed terms and conditions of the ESOP 2020, in accordance with the terms and guidelines of the ESOP 2020 approved by the shareholders. To this end, our board of directors shall be entitled to make adjustments to meet foreign regulations or market conditions, including resolving on cash or other settlement if deemed favorable for us based on foreign tax regulations. In particular, personnel in the United States may participate in the ESOP 2020 as modified by a U.S. sub-plan. Options granted under the U.S. sub-plan will vest in accordance with the schedules determined by our board of directors at the time of grant. All options granted under the U.S. sub-plan will be classified as "non-qualified stock options" under U.S. federal tax laws. No options granted under the U.S. sub-plan will be exercisable more than four years following the date on which such options were granted (subject to earlier expiration as provided in the ESOP 2020 or the optionee's award agreement). Any adjustments to the number of options and the applicable exercise price are permitted only to the extent and in a manner that complies with Section 409A of the U.S. Internal Revenue Code.

LTIP 2019

On May 8, 2019, our shareholders approved the Board Long Term Incentive Program 2019, or the LTIP 2019, to permit the grant of performance-based share awards, or Share Awards, to certain of our board members. Pursuant to the terms of the LTIP 2019, we were permitted to grant up to 70,000 shares in the form of Share Awards. As of December 31, 2020, 51,399 Share Awards had been granted. The Share Awards are subject to performance-based vesting, and vest in three equal annual installment based on the performance of our share price during the relevant measurement period, calculated in accordance with the terms of the LTIP 2019, subject to the board member's continued service through the applicable vesting date. Share Awards granted under the LTIP 2019 may not be transferred. In the event of a "take-over," "asset sale" or "merger" or other similar transaction as each term is defined in the terms of the LTIP 2019, all outstanding Share Awards will vest in their entirety upon the completion of such transaction and the Company shall have a right to repurchase all such Share Awards for fair market value.

LTIP 2020

On June 25, 2020, our shareholders approved the Board Long Term Incentive Program 2020, or the LTIP 2020, which permits the grant of performance-based share awards, or Share Awards, to our board members. Pursuant to the terms of the LTIP 2020, up to 40,000 shares in the form of Share Awards can be granted. As of December 31, 2020, 31,371 Share Awards had been granted. The Share Awards shall be subject to performance-based vesting, and vest in three equal annual installments based on the performance of our share price during the relevant measurement period, calculated in accordance with the terms of the LTIP 2020, subject to the board member's continued service through the applicable vesting date. Share Awards granted under the LTIP 2020 may not be transferred. In the event of a "take-over," "asset sale" or "merger" or other similar transaction as each term is defined in the terms of the LTIP 2020, all outstanding Share Awards would vest in their entirety upon the completion of such transaction and we shall have a right to repurchase all such Share Awards for fair market value.

Insurance and Indemnification

To the extent permitted by the Swedish Companies Act, we are empowered to indemnify our directors against any liability they incur by reason of their directorship. We maintain directors' and officers' insurance to insure such persons against certain liabilities.

Insofar as indemnification of liabilities arising under the Securities Act may be permitted to our board of directors, executive officers, or persons controlling us pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

C. BOARD PRACTICES

Director Independence

As a foreign private issuer, under the listing requirements and rules of Nasdaq, we are not required to have independent directors on our board of directors, except that our audit committee is required to consist fully of independent directors, subject to certain phase-in schedules. However, our board of directors has determined that, under current listing requirements and rules of Nasdaq and taking into account any applicable committee independence standards, all of our five directors are "independent directors." In making such determination, our board of directors considered the relationships that each non-executive director has with us and all other facts and circumstances our board of directors deemed relevant in determining the director's independence, including the number of common shares beneficially owned by the director and his or her affiliated entities (if any). The Swedish Code includes certain independence requirements for the directors, and requires a majority of the directors to be independent of the company and at least two directors to also be independent of major shareholders

Role of the Board in Risk Oversight

Our board of directors is responsible for the oversight of our risk management activities and has delegated to the audit committee the responsibility to assist our board in this task. While our board oversees our risk management, our management is responsible for day-to-day risk management processes. Our board of directors expects our management to consider risk and risk management in each business decision, to proactively develop and monitor risk management strategies and processes for day-to-day activities and to effectively implement risk management strategies adopted by the board of directors. We believe this division of responsibilities is the most effective approach for addressing the risks we face.

Composition of Our Board of Directors

Our board of directors is currently composed of five members. Under the rules and regulations of Nasdaq a director will qualify as "independent" if our board of directors affirmatively determines that he or she has no material relationship with us (either directly or as a partner, stockholder or officer of an organization that has a relationship with us). Our board of directors has determined that, of our six directors, no director has a relationship that would interfere with the exercise of independent judgment in carrying out his or her responsibilities as a director and that each of these directors is "independent" as that term is defined under Nasdaq rules. The Swedish Code includes certain independence requirements for the directors, and requires a majority of the directors to be independent of the company and at least two directors to also be independent of major shareholders.

Our board of directors performs its duties in accordance with the rules of procedure of the board of directors. The rules of procedure are reviewed and adopted by the board of directors annually. Our board of directors, including the chairman is elected by our shareholders at the annual general meeting up until the end of the next annual general meeting, with the possibility of re-election. In addition, our employees may, pursuant to statutory rules regarding the representation of employees on the board of directors, elect employee representatives to the board of directors. Currently the board of directors has no employee representatives. The majority of our board members are considered to be independent under the corporate governance standards of Nasdaq and Nasdaq Stockholm.

Committees of Our Board of Directors

Our board of directors has two standing committees: an audit committee and a remuneration committee.

Audit Committee

Our audit committee currently consists of Molly Henderson, Hilde Furberg and Lennart Hansson, and assists the board of directors in overseeing our accounting and financial reporting processes. Molly Henderson serves as chairperson of the audit committee.

The audit committee consists exclusively of members of our board who are financially literate, and Lennart Hansson and Molly Henderson are each considered an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq rules and regulations. Our board of directors has determined that all of the members of the audit committee satisfy the "independence" requirements set forth in Rule 10A-3 under the Exchange Act.

The audit committee is governed by a charter that complies with Nasdaq rules. The audit committee's responsibilities include:

- monitoring our financial reporting;
- monitoring the efficiency of our internal controls, internal auditing and risk management;
- keeping informed of the auditing of the annual report and the consolidated accounts; and
- reviewing and monitoring the impartiality and independence of our auditors and paying close attention to whether our auditors are providing other services besides audit services for us.

Our audit committee reports regularly to our board of directors on the exercise of its functions. It informs our board of directors about all areas in which action or improvement is necessary in its opinion and produces recommendations concerning the necessary steps that need to be taken. The audit review and the reporting on that review cover us and our subsidiaries as a whole. The members of the audit committee are entitled to receive all information which they need for the performance of their function, from our board of directors and employees. Every member of the audit committee shall exercise this right in consultation with the chairperson of the audit committee.

The audit committee has deliberated four times in the course of 2020. At these meetings, the main points of discussion were review of the 2019 financial statements, Ernst & Young AB's 2019 audit report, 2020 audit fee proposal, review of interim consolidated financial statements and press releases, Ernst & Young AB's report on interim financial statements, updates on internal control activities, updates on corporate audit activities, review of the 2020-2023 business plan and discussions on financing options.

The meeting attendance rate for our directors in the audit committee is set out in the table below:

Audit Committee	Number of meetings attended in 2020	Attendance %
Molly Henderson (Chairperson, from June 2020))	2	100
Hilde Furberg	4	100
Lennart Hansson (from May 2020)	2	100
Thomas Eklund (until June 2020)	2	100

Remuneration Committee

Our remuneration committee consists of Diane Parks, Elmar Schnee and Lennart Hansson. Elmar Schnee serves as chairman of the remuneration committee.

The Remuneration committee's responsibilities include:

- identifying, reviewing and proposing policies relevant to the compensation and benefits of our directors and executive officers;
- reviewing and approving each executive officer's compensation in light of such policies and reporting to the board; and
- overseeing and administering our employee share option scheme or equity incentive plans in operation from time to time.

The remuneration committee has deliberated four times over the course of 2020. The main topics of discussion were management performance reviews, the 2020 long term incentive plan, and 2020 management targets and management remuneration proposals.

The meeting attendance rate for our directors in the remuneration committee is set out in the table below:

Remuneration and Nomination Committee	Number of meetings attended in 2020	Attendance %
Elmar Schnee (Chairperson)	4	100
Lennart Hansson (from May 2020)	2	100
Diane Parks	4	100

Nomination Committee

We are following the Swedish Code of Corporate Governance, or the Swedish Code, and are therefore required to have a nomination committee, which is not a standing committee of our board of directors. According to the Swedish Code, the general meeting shall appoint the members of the nomination committee or resolve on procedures for appointing the members. Such procedures were adopted by our 2020 annual general meeting. The nomination committee shall, pursuant to the Swedish Code, consist of at least three members of which a majority shall be independent in relation to us and our management. In addition, at least one member of the nomination committee shall be independent in relation to the largest shareholder in terms of voting rights or group of shareholders who cooperates in terms of our management.

Ahead of the 2021 annual general meeting, the nomination committee consists of Patrick Sobocki (appointed by Stiftelsen Industrifonden), Spike Loy (appointed by BVF), Karl Tobieson (appointed by Linc AB) and Elmar Schnee (chairman of our board of directors). Patrick Sobocki serves as chairman of the nomination committee.

The nomination committee's responsibilities include:

- preparing a proposal for the election of a chairman of the board of directors, the members of the board of directors, the election of a chairman of the annual general meeting, election of auditors, the determination of fees to board members and auditors, and matters pertaining thereto.

Corporate Governance Practices

We are a "foreign private issuer," as defined by the SEC. As a result, in accordance with Nasdaq listing requirements, we may rely on home country governance requirements and certain exemptions thereunder rather than complying with Nasdaq corporate governance standards. While we expect to voluntarily follow most Nasdaq corporate governance rules, we may choose to take advantage of the following limited exemptions:

- exemption from filing 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;

- exemption from Section 16 rules requiring insiders to file public reports of their securities ownership and trading activities and providing for liability for insiders who profit from trades in a short period of time;

- exemption from the Nasdaq requirement necessitating disclosure of any waivers of the Code of Business Conduct and Ethics for directors and executive officers;

- exemption from the requirement to obtain shareholder approval for certain issuances of securities, including shareholder approval of share option plans;

- exemption from the requirement that our audit committee have review and oversight responsibilities over all "related party transactions," as defined in Item 7.B of Form 20-F;

- exemption from the requirement that our board of directors have a compensation committee that is composed entirely of independent directors with a written charter addressing the committee's purpose and responsibilities; and

- exemption from the requirement to have independent director oversight of director nominations.

Furthermore, Nasdaq Rule 5615(a)(3) provides that a foreign private issuer may rely on home country corporate governance practices in lieu of certain of the rules in the Nasdaq Rule 5600 Series and Rule 5250(d). We intend to follow Swedish corporate governance practices in lieu of Nasdaq corporate governance requirements as follows:

- We do not intend to follow Nasdaq Rule 5620(c) regarding quorum requirements applicable to meetings of shareholders. Such quorum requirements are not required under Swedish law. The Swedish Companies Act (SFS 2005:551) and our articles of association, which were approved by our shareholders on March 3, 2020 and are currently in effect, provide alternative quorum requirements that are generally applicable to meetings of shareholders.

- We do not intend to follow Nasdaq Rule 5605(b)(2), which requires that independent directors regularly meet in executive sessions where only independent directors are present. Our independent directors may choose to meet in executive sessions at their discretion.

- We do not intend to follow Nasdaq Rule 5605(e) regarding the composition of the nominating committee.

Although we may rely on certain home country corporate governance practices, we must comply with Nasdaq's Notification of Noncompliance requirement (Nasdaq Rule 5625) and the Voting Rights requirement (Nasdaq Rule 5640). Further, we must have an audit committee that satisfies Nasdaq Rule 5605(c)(3), which addresses audit committee responsibilities and authority and requires that the audit committee consist of members who meet the independence requirements of Nasdaq Rule 5605(c)(2)(A)(ii).

Because we are a foreign private issuer, our directors and executive officers are not subject to short-swing profit and insider trading reporting obligations under Section 16 of the Exchange Act. They will, however, be subject to the obligations to report changes in securities ownership under Section 13 of the Exchange Act and related SEC rules.

We intend to take all actions necessary for us to maintain compliance as a foreign private issuer under the applicable corporate governance requirements of the Sarbanes-Oxley Act, the rules adopted by the SEC and Nasdaq listing rules.

Accordingly, our shareholders will not have the same protections afforded to shareholders of companies that are subject to all of the corporate governance requirements of Nasdaq.

D. EMPLOYEES

For information regarding our employees, see "Item 4.B.—Business Overview—Employees and Human Capital Disclosure."

E. SHARE OWNERSHIP

For information regarding the share ownership of our directors and members of our executive committee, see "Item 6.B.—Compensation" and "Item 7.A.—Major Shareholders."

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. MAJOR SHAREHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common shares as of March 31, 2021 for:

- each person who is known by us to own beneficially more than 5% of our total outstanding common shares;
- each member of our board of directors and our executive management;
- all members of our board of directors and our executive management as a group.

Beneficial ownership is determined in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities and include common shares that can be acquired within 60 days of March 31, 2021. The percentage ownership information shown in the table is based upon 49,941,584 common shares outstanding as of March 31, 2021.

Except as otherwise indicated, all of the shares reflected in the table are common shares and all persons listed below have sole voting and investment power with respect to the shares beneficially owned by them, subject to applicable community property laws. The information is not necessarily indicative of beneficial ownership for any other purpose.

In computing the number of common shares beneficially owned by a person and the percentage ownership of that person, we deemed outstanding common shares subject to options held by that person that are immediately exercisable or exercisable within 60 days of March 31, 2021. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person. The information in the table below is based on information known to us or ascertained by us from public filings made by the shareholders.

Name of beneficial owner	Shares beneficially owned	
	Number	Percentage
5% or Greater Shareholders:		
BVF Partners LP[(1)]	6,331,562	12.7%
Stiftelsen Industrifonden [(2)]	5,772,995	11.6%
Linc AB [(3)]	5,036,450	10.1%
Handelsbanken Fonder AB[(4)]	3,106,160	6.2%
Executive Officers and Directors:		
Renée Aguiar-Lucander[(5)]	412,000	*
Fredrik Johansson[(6)]	21,250	*
Richard Philipson, M.D.	—	—
Andrew Udell	—	—
Frank Bringstrup, M.D.	—	—
Elmar Schnee	—	—
Hilde Furberg[(7)]	44,750	*
Lennart Hansson, Ph.D. [(8)]	12,000	*
Diane Parks	—	—
Molly Henderson	—	—
All directors and executive management as a group (12 persons)	490,000	*

* Indicates beneficial ownership of less than 1% of the total outstanding common shares.

(1) Based on shareholder information as of November 9 , 2020 but does not reflect an unknown number of warrants granted by Industrifonden and Investinor AS to purchase additional common shares of the Company exercisable within 60 days of September 30, 2020. BVF Inc., as the general partner of BVF Partners L.P., may be deemed to beneficially own the shares that are beneficially owned by such funds. Mark Lampert, as a director and officer of BVF Inc., may be deemed to beneficially own the shares that are beneficially owned by BVF Inc. The address of the above persons and entities is 44 Montgomery St. 40th floor, San Francisco, CA 94104.

(2) Consists of 5,772,995 common shares, held directly by Stiftelsen Industrifonden (of which 233,197 are subject to a call option exercisable by the holder). David Sonnek is the Chief Executive Officer of Stiftelsen Industrifonden and has voting and dispositive power with respect to the shares reported in the table above. The address of Stiftelsen Industrifonden is Vasagatan 11, 111 91 Stockholm, Sweden.

(3) Consists of 5,036,450 common shares, held directly by Linc AB. Bengt Julander is the Chief Executive Officer of Linc AB and, as a result, may be deemed to have voting and dispositive power with respect to the shares reported in the table above. The address of Linc AB is Cronhamns gata 6A, 185 32 Vaxholm, Sweden.

(4) Consists of 3,106,160 common shares, held directly by Handelsbanken Fonder AB. Magdalena Wahlqvist Alveskog is the Chief Executive Officer of Handelsbanken Fonder AB and, as a result, may be deemed to have voting and dispositive power with respect to the shares reported in the table above. Voting and dispositive power with respect to such shares are made by the board of directors of Handelsbanken Fonder AB, of whom there are three or more and none of whom individually has the power to direct such decisions. The address of Handelsbanken Fonder AB is SE-10670 Stockholm, Sweden.

(5) Consists of 412,000 common shares.

(6) Consists of 21,250 common shares.

(7) Consists of 44,750 common shares.

(8) Consists of 12,000 common shares.

Each of our shareholders is entitled to one vote per ordinary share. None of the holders of our shares have different voting rights from other holders of shares. We are not aware of any arrangement that may, at a subsequent date, result in a change of control of our company.

As of March 31, 2021, we had one holder of record of our ADSs in the United States, which is CITIBANK ADR. This shareholder held in the aggregate 11.7% of the 49,941,584 common shares outstanding as of March 31, 2021. The number of record holders in the United States is not representative of the number of beneficial holders nor is it representative of where such beneficial holders are resident since many of these common shares were held by brokers or other nominees. As of March 31, 2021, assuming that all of our common shares represented by ADSs are held by residents of the United States, we estimate that approximately 23.8% of our outstanding common shares were held in the United States by approximately 21 institutional holders of record.

To our knowledge, and other than changes in percentage ownership as a result of the shares issued in connection with our initial U.S. public offering, there has been no significant change in the percentage ownership held by the major shareholders listed above.

B. RELATED PARTY TRANSACTIONS

Other than compensation arrangements described in "Management" elsewhere in this annual report, since January 1, 2020, we have not engaged in any transactions with our executive officers, directors or holders of more than 5% of our share capital, including their affiliates, which we refer to as our related parties.

Agreements with Our Executive Officers and Directors

We have entered into employment agreements with certain of our executive officers. These agreements contain customary provisions and representations, including confidentiality, non-competition, non-solicitation and inventions assignment undertakings by the executive officers and non-executive directors. The enforceability of the non-competition provisions may be limited under applicable law.

Related Party Transactions Policy

We have adopted a related party transaction policy requiring that all related party transactions required to be disclosed by a foreign private issuer pursuant to the Exchange Act be approved by the audit committee or another independent body of our board of directors.

C. INTERESTS OF EXPERTS AND COUNSEL

Not applicable.

ITEM 8. FINANCIAL INFORMATION

A. CONSOLIDATED STATEMENTS AND OTHER FINANCIAL INFORMATION

Consolidated financial statements

The consolidated financial statements required by this item accompany this Annual Report on Form 20-F in the form of our Annual Report 2020.

Legal proceedings

From time to time we may become involved in legal, governmental or arbitration proceedings or be subject to claims arising in the ordinary course of our business. We are not presently a party to any legal, governmental or arbitration proceeding. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

B. SIGNIFICANT CHANGES

Except as disclosed elsewhere in this annual report, we have not experienced any significant changes since the date of our audited consolidated financial statements included in this annual report.

ITEM 9. THE OFFER AND LISTING

A. OFFER AND LISTING DETAILS

Our ADSs have traded on The Nasdaq Global Select Market under the symbol “CALT” since June 5, 2020. Prior to that date, there was no public trading market for our ADSs. Our common shares have traded on Nasdaq Stockholm under the symbol “CALTX” since June 29, 2018. Prior to that date, there was no public trading market for our ADSs or our common shares. Our initial U.S. public offering in June 2020 was priced at $19.50 per ADS.

B. PLAN OF DISTRIBUTION

Not applicable.

C. MARKETS

The ADSs have been listed on The Nasdaq Global Select Market under the symbol “CALT” since June 5, 2020, and our common shares have been listed on Nasdaq Stockholm under the symbol “CALTX” since June 29, 2018.

D. SELLING SHAREHOLDERS

Not applicable.

E. DILUTION

Not applicable.

F. EXPENSES OF THE ISSUE

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. SHARE CAPITAL

Not applicable.

B. MEMORANDUM AND ARTICLES OF ASSOCIATION

We are a Swedish public limited company registered with the Swedish Companies Registration Office (corporate registration number 556659-9766). Below are summaries of the material provisions of our articles of association and of related material provisions of the Swedish Companies Act.

Articles of Association

Object of the Company

Our object is set forth in Section 3 of our articles of association and is to, directly or through subsidiaries, conduct research and development as well as the manufacture and sale of pharmaceuticals and medical devices, own and manage shares and other securities as well as other tangible and intangible property, as well as any other business associated therewith.

Powers of the Directors

Our board of directors shall direct our policy and shall supervise the performance of our chief executive officer and his or her actions. Our board of directors may exercise all powers that are not required under the Swedish Companies Act or under our articles of association to be exercised or taken by our shareholders.

Number of Directors

Our articles of association provide that our board of directors shall consist of three to ten members. Our board of directors currently has five members, with no deputy members.

Rights Attached to Shares

All of the common shares have equal rights to our assets and earnings, and are entitled to one vote at the general meeting. At the general meeting, every shareholder may vote to the full extent of their shares held or represented, without limitation. Each common share entitles the shareholder to the same preferential rights related to issues of shares, warrants and convertible bonds relative to the number of shares they own and have equal rights to dividends and any surplus capital upon liquidation. Shareholders' rights can only be changed in accordance with the procedures set out in the Swedish Companies Act. Transfers of shares are not subject to any restrictions. There are no limitations on the rights to own securities.

Exclusive Forum

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, 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.

Preemptive Rights

Under the Swedish Companies Act, shareholders of any class of shares will generally have a preemptive right to subscribe for shares or warrants issued of any class in proportion to their shareholdings. Shareholders will have preferential rights to subscribe for new shares in proportion to the number of shares they own. If an offering is not fully subscribed for based on subscription rights, shares may be allocated to subscribers without subscription rights. The preemptive right to subscribe does not apply in respect of shares issued for consideration by payment in kind or of shares issued pursuant to convertible debentures or warrants previously issued by the company.

The preemptive right to subscribe for new shares may be set aside. A share issue with deviation from the shareholders' preemptive rights may be resolved either by the shareholders at a general meeting, or by the board of directors if the board resolution is preceded by an authorization therefor from the general meeting. A resolution to issue shares with deviation from the shareholders' preemptive rights and a resolution to authorize the board of directors to do the same must be passed by two-thirds of both the votes cast and the shares represented at the general meeting resolving on the share issue or the authorization of the board of directors.

Voting at Shareholder Meetings

Under the Swedish Companies Act, shareholders entered into the shareholders' register as of the record date are entitled to vote at a general meeting (in person or by appointing a proxyholder). In accordance with our articles of association, shareholders must give notice of their intention to attend the general meeting no later than the date specified in the notice. Shareholders who have their shares registered through a nominee and wish to exercise their voting rights at a general meeting must request to be temporary registered as a shareholder and entered into the shareholders' register four business days prior to the date of the general meeting. The rights described herein do not apply to holders of ADSs. See "Item 12.D.—American Depositary Shares."

Shareholder Meetings

The general meeting of shareholders is our highest decision-making body and serves as an opportunity for our shareholders to make decisions regarding our affairs. Shareholders who are registered in the share register held by Euroclear Sweden AB six business days before the meeting and have notified us no later than the date specified in the notice described below have the right to participate at our general meetings, either in person or by a representative. All shareholders have the same participation and voting rights at general meetings. At the annual general meeting, *inter alia*, members of the board of directors are elected, the principles for the appointment of the nomination committee are established, and a vote is held on whether each individual board member and the chief executive officer will be discharged from any potential liabilities for the previous fiscal year. Auditors are elected as well. Decisions are made concerning adoption of annual reports, allocation of earnings, fees for the board of directors and the auditors, guidelines for executive remuneration and other essential matters that require a decision by the meeting. Most decisions require a simple majority but the Swedish Companies Act dictates other thresholds in certain instances. See "—Differences in Corporate Law—Shareholder Vote on Certain Transactions."

Shareholders have the right to ask questions to our board of directors and managers at general meetings which pertain to the business of the company and also have an issue brought forward at the general meeting. In order for us to include the issue in the notice of the annual general meeting, a request of issue discussion must be received by us normally seven weeks before the meeting. Any request for the discussion of an issue at the annual general meeting shall be made to the board of directors and any request within the nomination committee's competence shall be made to the nomination committee. The board shall convene an extraordinary general meeting if shareholders who together represent at least 10% of all shares in the company so demand in writing to discuss or resolve on a specific issue.

The arrangements for the calling of general meetings are described below in "—Differences in Corporate Law—Annual General Meeting" and "—Differences in Corporate Law—Special Meeting."

Notices

The Swedish Companies Act requirements for notice are described below in "—Differences in Corporate Law—Notices."

Subject to our articles of association and Nasdaq Stockholm's Rulebook for Issuers, we must publish the full notice of a general meeting by way of press release, on our website and in the Swedish Official Gazette, and must also publish in the Svenska Dagbladet, a daily Swedish newspaper, that such notice has been published. The notice of the annual general meeting will be published six to four weeks before the meeting. The notice must include an agenda listing each item that shall be voted upon at the meeting. The notice of any extraordinary general meetings will be published six to three weeks before the meeting. Pursuant to the Swedish Code of Corporate Governance, which does not carry the force of law but is considered ideal corporate governance practice for Swedish companies whose shares trade on a regulated market, we shall, as soon as the time and venue for the annual general meeting have been decided, and no later than in conjunction with the third quarter report, publish such information on our website.

Record Date

Under the Swedish Companies Act, in order for a shareholder to participate in a shareholders' meeting, the shareholder must have its shares registered in its own name in the share register four business days. In accordance with section 8 of our articles of association, shareholders must give notice of their intention to attend the shareholders' meeting no later than the date specified in the notice.

Amendments to the Articles of Associations

Under the Swedish Companies Act, an amendment of our articles of association requires a resolution passed at a shareholders' meeting. The number of votes required for a valid resolution depends on the type of amendment, however, any amendment must be approved by not less than two-thirds of the votes cast and represented at the meeting. The board of directors is not allowed to make amendments to the articles of association absent shareholder approval.

Provisions Restricting Change in Control of Our Company

Neither our articles of association nor the Swedish Companies Act contains any restrictions on change of control.

Differences in Corporate Law

The applicable provisions of the Swedish Companies Act differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of, inter alia, the Swedish Companies Act applicable to us and the Delaware General Corporation Law relating to shareholders' rights and protections. We are not subject to Delaware law but are presenting this description for comparative purposes. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to Delaware law and Swedish law.

Number of Directors

Sweden. Under the Swedish Companies Act, a public company shall have a board of directors consisting of at least three directors. More than half of the directors shall be resident within the European Economic Area (unless otherwise approved by the Swedish Companies Registration Office). The actual number of board members shall be determined by a shareholders' meeting, within the limits set out in the company's articles of association. Under the Swedish Code of Corporate Governance, only one director may also be a senior executive of the relevant company or a subsidiary. The Swedish Code of Corporate Governance includes certain independence requirements for the directors, and requires a majority of the directors to be independent of the company and at least two directors to also be independent of major shareholders.	*Delaware*. Under the Delaware General Corporation Law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws. The Delaware General Corporation Law does not address director independence, though Delaware courts have provided general guidance as to determining independence, including that the determination must be both an objective and a subjective assessment.

Removal of Directors

Sweden. Under the Swedish Companies Act, directors appointed at a general meeting may be removed by a resolution adopted at a general meeting, upon the affirmative vote of a simple majority of the votes cast.	*Delaware*. Under the Delaware General Corporation Law, unless otherwise provided in the certificate of incorporation, directors may be removed from office, with or without cause, by a majority stockholder vote, though in the case of a corporation whose board is classified, stockholders may effect such removal only for cause.

Vacancies on the Board of Directors

Sweden. Under the Swedish Companies Act, if a director's tenure should terminate prematurely, the election of a new director may be deferred until the time of the next annual general meeting, providing there are enough remaining directors to constitute a quorum.	*Delaware*. Under the Delaware General Corporation Law, vacancies on a corporation's board of directors, including those caused by an increase in the number of directors, may be filled by a majority of the remaining directors.

Annual General Meeting

Sweden. Under the Swedish Companies Act, within six months of the end of each fiscal year, the shareholders shall hold an annual general meeting at which the board of directors shall present the annual report and auditor's report and, for a parent company which is obliged to prepare group accounts, the group accounts and the auditor's report for the group. Shareholder meetings shall be held in the city stated in the articles of association. The minutes of a shareholders' meeting must be made available on the company's website no later than two weeks after the meeting.	*Delaware*. Under the Delaware General Corporation Law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws. If a company fails to hold an annual meeting or fails to take action by written consent to elect directors in lieu of an annual meeting for a period of 30 days after the date designated for the annual meeting, or if no date was designated, 13 months after either the last annual meeting or the last action by written consent to elect directors in lieu of an annual meeting, whichever is later, the Delaware Court of Chancery may summarily order a meeting to be held upon the application of any stockholder or director. The Delaware General Corporation Law does not require minutes of stockholders' meetings to be made public.

Special Meeting

Sweden. Under the Swedish Companies Act, the board of directors shall convene an *extraordinary general meeting* if a shareholder minority representing at least ten per cent of the company's shares or the auditor of the company so demands, and the board of directors may convene an extraordinary general meetings whenever it believes reason exists to hold an extraordinary general meeting prior to the next annual general meeting.	*Delaware*. Under the Delaware General Corporation Law, special meetings of the stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.

Notices

Sweden. Under the Swedish Companies Act, a shareholders' meeting must be preceded by a notice. The notice of the annual general meeting of shareholders must be issued no sooner than six weeks and no later than four weeks before the date of an annual general meeting. In general, notice of other extraordinary general meetings must be issued no sooner than six weeks and no later than three weeks before the meeting. Publicly listed companies must always notify shareholders of a general meeting by advertisement in a Swedish newspaper, the Swedish Official Gazette, by press release, and on the company's website.	*Delaware*. Under the Delaware General Corporation Law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour, and purpose or purposes of the meeting.

Preemptive Rights

Sweden. Under the Swedish Companies Act, shareholders of any class of shares have a preemptive right (*Sw. företrädesrätt*) to subscribe for shares issued of any class in proportion to their shareholdings. The preemptive right to subscribe does not apply in respect of shares issued for consideration other than cash or of shares issued pursuant to convertible debentures or warrants previously granted by the company. The preemptive right to subscribe for new shares may also be set aside by a resolution passed by two thirds of the votes cast and shares represented at the shareholders' meeting resolving upon the issue.

Delaware. Under the Delaware General Corporation Law, unless otherwise provided in a corporation's certificate of incorporation, a stockholder does not, by operation of law, possess preemptive rights to subscribe to additional issuances of the corporation's stock.

Shareholder Vote on Certain Transactions

Sweden. In matters which do not relate to elections and are not otherwise governed by the Swedish Companies Act or the articles of association, resolutions shall be adopted at the general meeting by a simple majority of the votes cast. In the event of a tied vote, the chairman shall have the casting vote. For matters concerning securities of the company, such as new share issuances, and other transactions such as private placements, mergers, and a change from a public to a private company (or vice-versa), the articles of association may only prescribe thresholds which are higher than those provided in the Swedish Companies Act.

Unless otherwise prescribed in the articles of association, the person who receives the most votes in an election shall be deemed elected. In general, a resolution involving the alteration of the articles of association shall be valid only when supported by shareholders holding not less than two-thirds of both the votes cast and the shares represented at the general meeting. The Swedish Companies Act lays out numerous exceptions for which a higher threshold applies, including restrictions on certain rights of shareholders, limits on the number of shares shareholders may vote at the general meeting, directed share issues to directors, employees and other closely related parties, and changes in the legal relationship between shares.

Delaware. Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: (i) the approval of the board of directors; and (ii) approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of a corporation entitled to vote on the matter.

C. MATERIAL CONTRACTS

We have not entered into any material contracts other than in the ordinary course of business and other than those described in "Item 4. Information on the Company," "Item 7. Major Shareholders and Related Party Transactions—B. Related Party Transactions," or elsewhere in this annual report on Form 20-F.

D. EXCHANGE CONTROLS

There is no Swedish legislation affecting the import or export of capital or the remittance of dividends, interest or other payments to non-resident holders of our securities, except that, subject to the provisions in any tax treaty, dividends are subject to withholding tax.

E. TAXATION

General

The taxation discussion set forth below does not purport to be a complete analysis or listing of all potential tax effects relevant to the acquisition, ownership or disposition of our common shares or ADSs. The statements of United States and Swedish tax laws set forth below are based on the laws in force as of the date of this report and may be subject to any changes in United States or Swedish law, and in any double taxation convention or treaty between the United States and Sweden, occurring after that date, which changes may then have retroactive effect.

Specific tax provisions may apply for certain categories of taxpayers. Your tax treatment if you are a holder of our common shares or ADSs depends in part on your particular situation. If you are a holder of our common shares or ADSs, you should therefore consult a tax advisor as to the tax consequences relating to your particular circumstances resulting from the ownership of our common shares or ADSs.

Certain United States Federal Income Tax Consequences

The following is a description of certain material U.S. federal income tax considerations for U.S. Holders (defined below) with respect to their ownership and disposition of our common shares or ADSs. It is not a comprehensive description of all tax considerations that may be relevant to a particular person's decision to acquire common shares or ADSs. This discussion applies only to a U.S. Holder that holds our common shares or ADSs as a capital asset for tax purposes (generally, property held for investment). In addition, it does not describe all of the tax consequences that may be relevant in light of a U.S. Holder's particular circumstances, including state and local tax consequences, estate tax consequences, alternative minimum tax consequences, the potential application of the Medicare contribution tax, and tax consequences applicable to U.S. Holders subject to special rules, such as:

- banks, insurance companies, and certain other financial institutions;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons required for U.S. federal income tax purposes to conform the timing of income accruals to their financial statements under Section 451(b) of the Code;
- persons holding common shares or ADSs as part of a hedging transaction, "straddle," wash sale, conversion transaction or integrated transaction or persons entering into a constructive sale with respect to common shares or ADSs;
- persons whose "functional currency" for U.S. federal income tax purposes is not the U.S. dollar;
- brokers, dealers or traders in securities, commodities or currencies;
- tax-exempt entities or government organizations;

- S corporations, partnerships, or other entities or arrangements classified as partnerships for U.S. federal income tax purposes;
- regulated investment companies or real estate investment trusts;
- persons who acquired our common shares or ADSs pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons holding our common shares or ADSs in connection with a trade or business, permanent establishment, or fixed base outside the United States; and
- persons who own (directly, constructively or through attribution) 5% or more (by vote or value) of our outstanding common shares or ADS.

If an entity that is classified as a partnership for U.S. federal income tax purposes holds common shares or ADSs, the U.S. federal income tax treatment of a partner will generally depend on the status of the partner and the activities of the partnership. Partnerships holding common shares or ADSs and partners in such partnerships are encouraged to consult their tax advisors as to the particular U.S. federal income tax consequences of holding and disposing of common shares or ADSs.

The discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury Regulations, and the Convention Between the Government of the United States and the Government of Sweden for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income, signed on September 1, 1994 or the U.S.-Sweden Tax Treaty, all as of the date hereof, changes to any of which may affect the tax consequences described herein—possibly with retroactive effect.

A "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of common shares or ADSs and is:

(i) An individual who is a citizen or individual resident of the United States;

(ii) a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia;

(iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

(iv) a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

The discussion below assumes that the representations contained in the deposit agreement are true and that the obligations in the deposit agreement and any related agreement will be complied with in accordance with their terms. Accordingly, a holder of an ADS should be treated for U.S. federal income tax purposes as holding the common shares represented by the ADS.

PERSONS CONSIDERING AN INVESTMENT IN COMMON SHARES OR ADSs SHOULD CONSULT THEIR TAX ADVISORS AS TO THE PARTICULAR TAX CONSEQUENCES APPLICABLE TO THEM RELATING TO THE ACQUISITION, OWNERSHIP AND DISPOSITION OF THE COMMON SHARES OR ADSs, INCLUDING THE APPLICABILITY OF U.S. FEDERAL, STATE AND LOCAL TAX LAWS.

PFIC Rules

A non-U.S. corporation will be classified as a PFIC for any taxable year in which, after applying certain look-through rules, either:

- at least 75% of its gross income is passive income (such as interest income); or
- at least 50% of its gross assets (determined on the basis of a quarterly average) is attributable to assets that produce passive income or are held for the production of passive income.

We will be treated as owning our proportionate share of the assets and earning our proportionate share of the income of any other entity treated as a corporation for U.S. federal income tax purposes, the equity of which we own, directly or indirectly, 25% or more (by value).

A separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. As a result, our PFIC status may change from year to year. 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 the global offering. 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 years. It is uncertain whether we will be a PFIC for the 2021 taxable year or any subsequent taxable years.

Our status as a PFIC is a fact-intensive determination made on an annual basis applying principles and methodologies that in some circumstances are unclear and subject to varying interpretation. Because of the uncertainties involved in determining our PFIC status, we cannot provide any assurances regarding our PFIC status.

If we are classified as a PFIC in any year with respect to which a U.S. Holder owns the common shares or ADSs, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns the common shares or ADSs, regardless of whether we continue to meet the tests described above unless we cease to be a PFIC and the U.S. Holder has made a "deemed sale" election under the PFIC rules. If the "deemed sale" election is made, a U.S. Holder will be deemed to have sold the common shares or ADSs the U.S. Holder holds at their fair market value and any gain from such deemed sale would be subject to the rules described below. After the deemed sale election, so long as we do not become a PFIC in a subsequent taxable year, the U.S. Holder's common shares or ADSs with respect to which such election was made will not be treated as shares in a PFIC and the U.S. Holder will not be subject to the rules described below with respect to any "excess distribution" the U.S. Holder receives from us or any gain from an actual sale or other disposition of the common shares or ADSs.

For each taxable year we are treated as a PFIC with respect to U.S. Holders, U.S. Holders will be subject to special tax rules with respect to any "excess distribution" such U.S. Holder receives and any gain such U.S. Holder recognizes from a sale or other disposition (including, under certain circumstances, a pledge) of common shares or ADSs, unless (i) such U.S. Holder makes a "qualified electing fund" election, or QEF Election, with respect to all taxable years during such U.S. Holder's holding period in which we are a PFIC or (ii) our common shares or ADSs constitute "marketable" securities, and such U.S. Holder makes a mark-to-market election as discussed below. Distributions a U.S. Holder receives in a taxable year that are greater than 125% of the average annual distributions a U.S. Holder received during the shorter of the three preceding taxable years or the U.S. Holder's holding period for the common shares or ADSs will be treated as an excess distribution. Under these special tax rules:

- the excess distribution or gain will be allocated ratably over a U.S. Holder's holding period for the common shares or ADSs;
- the amount allocated to the current taxable year, and any taxable year prior to the first taxable year in which we became a PFIC, will be treated as ordinary income; and
- the amount allocated to each other year will be subject to the highest tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year.

The tax liability for amounts allocated to years prior to the year of disposition or "excess distribution" cannot be offset by any net operating losses for such years, and gains (but not losses) realized on the sale of the common shares or ADSs cannot be treated as capital, even if a U.S. Holder holds the common shares or ADSs as capital assets. In addition, if we are a PFIC, a U.S. Holder will generally be subject to similar rules with respect to distributions we receive from, and our dispositions of the stock of, any of our direct or indirect subsidiaries that also are PFICs, as if such distributions were indirectly received by, and/or dispositions were indirectly carried out by, such U.S. Holder. U.S. Holders should consult their tax advisors regarding the application of the PFIC rules to our subsidiaries.

If a U.S. Holder makes an effective QEF Election, the U.S. Holder will be required to include in gross income each year, whether or not we make distributions, as capital gains, such U.S. Holder's pro rata share of our net capital gains and, as ordinary income, such U.S. Holder's pro rata share of our earnings in excess of our net capital gains. However, a U.S. Holder can only make a qualified electing fund election with respect to common shares in a PFIC if such company agrees to furnish such U.S. Holder with certain tax information annually. We do not currently intend to provide U.S. Holders with the information necessary for U.S. Holders to make a QEF Election. Therefore you should assume that you will not receive such information from us and would therefore be unable to make a QEF Election with respect to any of our common shares or ADSs were we to be or become a PFIC.

U.S. Holders can avoid the interest charge on excess distributions or gain relating to the common shares or ADSs by making a mark-to-market election with respect to the common shares or ADSs, provided that the common shares or ADSs are "marketable." Common shares or ADSs will be marketable if they are "regularly traded" on certain U.S. stock exchanges or on a foreign stock exchange that meets certain conditions. For these purposes, the common shares or ADSs will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. Any trades that have as their principal purpose meeting this requirement will be disregarded. We intend to list our ADSs on The Nasdaq Global Select Market, which is a qualified exchange for these purposes. Each U.S. Holder should consult its tax advisor as to the whether a mark-to-market election is available or advisable with respect to the common shares or ADSs.

A U.S. Holder that makes a mark-to-market election must include in ordinary income for each year an amount equal to the excess, if any, of the fair market value of the common shares or ADSs at the close of the taxable year over the U.S. Holder's adjusted tax basis in the common shares or ADSs. An electing holder may also claim an ordinary loss deduction for the excess, if any, of the U.S. Holder's adjusted basis in the common shares or ADSs over the fair market value of the common shares or ADSs at the close of the taxable year, but this deduction is allowable only to the extent of any net mark-to-market gains for prior years. Gains from an actual sale or other disposition of the common shares or ADSs will be treated as ordinary income, and any losses incurred on a sale or other disposition of the shares will be treated as an ordinary loss to the extent of any net mark-to-market gains for prior years. Once made, the election cannot be revoked without the consent of the Internal Revenue Service, or the IRS, unless the common shares or ADSs cease to be marketable.

However, a mark-to-market election generally cannot be made for equity interests in any lower-tier PFICs that we own, unless shares of such lower-tier PFIC are themselves "marketable." As a result, even if a U.S. Holder validly makes a mark-to-market election with respect to our common shares or ADSs, the U.S. Holder may continue to be subject to the PFIC rules (described above) with respect to its indirect interest in any of our investments that are treated as an equity interest in a PFIC for U.S. federal income tax purposes. U.S. Holders should consult their tax advisors to determine whether any of these elections would be available and if so, what the consequences of the alternative treatments would be in their particular circumstances. Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to make an annual filing containing such information as the U.S. Treasury may require. U.S. Holders should consult their tax advisors regarding the requirements of filing such information returns under these rules.

WE STRONGLY URGE YOU TO CONSULT YOUR TAX ADVISOR REGARDING THE IMPACT OF OUR PFIC STATUS ON YOUR INVESTMENT IN THE COMMON SHARES OR ADSs AS WELL AS THE APPLICATION OF THE PFIC RULES TO YOUR INVESTMENT IN THE COMMON SHARES OR ADSs.

Taxation of Distributions

Subject to the discussion above under "PFIC rules," distributions paid on common shares or ADSs, other than certain pro rata distributions of common shares or ADSs, will generally be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we do not intend to calculate our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. Non-corporate U.S. Holders may qualify for the preferential rates of taxation with respect to dividends on our common shares or ADSs applicable to long-term capital gains (i.e., gains from the sale of capital assets held for more than one year) applicable to qualified dividend income (as discussed below) if we are a "qualified foreign corporation" and certain other requirements (discussed below) are met. A non-U.S. corporation (other than a corporation that is classified as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year) generally will be considered to be a qualified foreign corporation (a) if it is eligible for the benefits of a comprehensive tax treaty with the United States which the Secretary of Treasury of the United States determines is satisfactory for purposes of this provision and which includes an exchange of information provision, or (b) with respect to any dividend it pays on common shares or ADSs that are readily tradable on an established securities market in the United States. We intend to list our ADSs on The Nasdaq Global Select Market, which is an established securities market in the United States, and we expect the ADSs to be readily tradable on The Nasdaq Global Select Market. However, there can be no assurance that the ADSs will be considered readily tradable on an established securities market in the United States. We are incorporated under the laws of Sweden, and we believe that we qualify as a resident of Sweden for purposes of, and are eligible for the benefits of, the U.S.-Sweden Tax Treaty, although there can be no assurance in this regard. Further, the IRS has determined that the U.S.-Sweden Tax Treaty is satisfactory for purposes of the qualified dividend rules and that it includes an exchange-of-information program. Therefore, subject to the discussion regarding PFIC, such dividends will generally be expected to be "qualified dividend income" in the hands of individual U.S. Holders, provided that a holding period requirement (more than 60 days of ownership, without protection from the risk of loss, during the 121-day period beginning 60 days before the ex-dividend date) and certain other requirements are met. However, the qualified dividend income treatment will not apply if we are treated as a PFIC with respect to the U.S. Holder.

The amount of any dividend will be treated as foreign-source dividend income to U.S. Holders and will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will generally be included in a U.S. Holder's income on the date of the U.S. Holder's receipt of the dividend. The amount of any dividend income paid in foreign currency will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of actual or constructive receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt. Such gain or loss would generally be treated as U.S.-source ordinary income or loss.

Subject to applicable limitations, some of which may vary depending upon your circumstances, Swedish income taxes withheld from dividend payments on shares at a rate not exceeding an applicable rate under the U.S.-Sweden Tax Treaty will be creditable against your U.S. federal income tax liability. Swedish income taxes withheld in excess of the applicable t rate under the U.S.-Sweden Tax Treaty will not be eligible for credit against your U.S. federal income tax liability. The rules governing foreign tax credits are complex and U.S. Holders should therefore consult their tax advisors regarding the effect of the receipt of dividends for foreign tax credit limitation purposes.

Sale or Other Taxable Disposition of Common Shares and ADSs

Subject to the discussion above under "PFIC rules," gain or loss realized on the sale or other taxable disposition of common shares or ADSs will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder held the common shares or ADSs for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder's tax basis in the common shares or ADSs disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations.

If the consideration received by a U.S. Holder is not paid in U.S. dollars, the amount realized will be the U.S. dollar value of the payment received determined by reference to the spot rate of exchange on the date of the sale or other disposition. However, if the common shares or ADSs are treated as traded on an "established securities market" and you are either a cash basis taxpayer or an accrual basis taxpayer that has made a special election (which must be applied consistently from year to year and cannot be changed without the consent of the IRS), you will determine the U.S. dollar value of the amount realized in a non-U.S. dollar currency by translating the amount received at the spot rate of exchange on the settlement date of the sale. If you are an accrual basis taxpayer that is not eligible to or does not elect to determine the amount realized using the spot rate on the settlement date, you will recognize foreign currency gain or loss to the extent of any difference between the U.S. dollar amount realized on the date of sale or disposition and the U.S. dollar value of the currency received at the spot rate on the settlement date.

Information Reporting and Backup Withholding

Payments of dividends and sales proceeds that are made within the United States or through certain U.S.-related financial intermediaries generally are subject to information reporting, and may be subject to backup withholding, unless (i) the U.S. Holder is a corporation or other exempt recipient or (ii) in the case of backup withholding, the U.S. Holder provides a correct taxpayer identification number and certifies that it is not subject to backup withholding on a duly executed IRS Form W-9 or otherwise establishes an exemption.

Backup withholding is not an additional tax. The amount of any backup withholding from a payment to a U.S. Holder will be allowed as a credit against the U.S. Holder's U.S. federal income tax liability and may entitle the U.S. Holder to a refund, provided that the required information is timely furnished to the IRS.

Information with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals (and, under regulations, certain entities) may be required to report information relating to the common shares or ADSs, subject to certain exceptions (including an exception for common shares or ADSs held in accounts maintained by certain U.S. financial institutions), by filing IRS Form 8938 (Statement of Specified Foreign Financial Assets) with their federal income tax return. Such U.S. Holders who fail to timely furnish the required information may be subject to a penalty. Additionally, if a U.S. Holder does not file the required information, the statute of limitations with respect to tax returns of the U.S. Holder to which the information relates may not close until three years after such information is filed. U.S. Holders should consult their tax advisors regarding their reporting obligations with respect to their ownership and disposition of the common shares or ADSs.

Material Swedish Tax Considerations

The following is a summary of certain material Swedish tax issues for holders of common shares or ADSs that are not resident in Sweden for tax purposes. The summary is based on current legislation and is intended to provide general information only. The summary does not cover, inter alia, the special rules regarding tax-free dividends that may be applicable when investors hold common shares or ADSs that are deemed to be held for business purposes (for tax purposes), foreign companies conducting business through a permanent establishment in Sweden, or foreign companies that have been Swedish companies. Each person considering an investment in common shares or ADSs is advised to consult an independent tax advisor as to the tax consequences that could arise from the acquisition, ownership and disposition of the common shares or ADSs.

Taxation of Dividends

For holders not resident in Sweden for tax purposes that receive dividends on common shares or ADSs of a Swedish limited liability company, Swedish withholding tax is normally withheld. The same withholding tax applies to certain other payments made by a Swedish limited liability company, such as payments as a result of redemption of shares and repurchase of shares through an offer directed to all shareholders or all holders of a certain class. The withholding tax rate is 30%. The tax rate is, however, generally reduced under an applicable tax treaty. For example, under the U.S.-Sweden Tax Treaty the tax rate on dividends paid to U.S. holders entitled to the benefits of the U.S.-Sweden Tax Treaty should not exceed 15%. In Sweden, withholding tax deductions are normally carried out by Euroclear Sweden AB or, in respect of nominee-registered shares, by the nominee. The tax treaties Sweden has entered into generally enable the withholding tax deduction to be made in accordance with the tax rate stipulated in the treaty, provided that Euroclear Sweden AB or the nominee, as applicable, has received the required information concerning the tax residency of the investor entitled to the dividend (this applies also under the U.S.—Sweden tax treaty). Furthermore, investors entitled to reduced tax rates under applicable tax treaties may claim a refund from the Swedish tax authorities within five calendar years following the year the dividend was distributed if the full withholding tax rate at 30% has been withheld.

Taxation of Capital Gains

Holders not resident in Sweden for tax purposes are normally not liable for capital gains taxation in Sweden upon disposals of common shares or ADSs. Holders of common shares or ADSs may, however, be subject to taxation in their state of residence.

According to a special rule, private individuals not resident in Sweden for tax purposes are, however, subject to Swedish capital gains taxation upon disposals of common shares or ADSs if they have been residents of Sweden due to a habitual abode in Sweden or a stay in Sweden for six consecutive months at any time during the calendar year of disposal or the ten calendar years preceding the year of disposal. In a number of cases though, the applicability of this rule is limited by tax treaties. For example, under the U.S.-Sweden Tax Treaty this rule applies for ten years from the date the private individuals became non-resident of Sweden for tax purposes.

F. DIVIDENDS AND PAYING AGENTS

Not applicable.

G. STATEMENT BY EXPERTS

Not applicable.

H. DOCUMENTS ON DISPLAY

We are subject to the information reporting requirements of the Exchange Act applicable to foreign private issuers and under those requirements will file reports with the SEC. Those reports may be inspected without charge at the locations described below. As a foreign private issuer, we are exempt from the rules under the Exchange Act related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as United States companies whose securities are registered under the Exchange Act. Nevertheless, we will file with the SEC an annual report containing financial statements that have been examined and reported on, with and opinion expressed by an independent registered public accounting firm.

We maintain a corporate website at *www.calliditas.se*. We intend to post a link to our annual report on Form 20-F as filed with the SEC on our website promptly following it being filed with the SEC. Information contained on, or that can be accessed through, our website does not constitute a part of this annual report. We have included our website address in this annual report solely as an inactive textual reference.

The SEC maintains a website (*www.sec.gov*) that contains reports, proxy and information statements and other information regarding registrants, such as us, that file electronically with the SEC.

With respect to references made in this annual report to any contract or other document of Calliditas Therapeutics AB, such references are not necessarily complete and you should refer to the exhibits attached or incorporated by reference to this annual report for copies of the actual contract or document.

I. SUBSIDIARY INFORMATION

Not applicable.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

For information about market risks, see "Item 5.B.—Liquidity and Capital Resources—Quantitative and Qualitative Disclosures about Market Risks."

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. DEBT SECURITIES

Not applicable.

B. WARRANTS AND RIGHTS

Not applicable.

C. OTHER SECURITIES

Not applicable.

D. AMERICAN DEPOSITARY SHARES

Citibank, N.A. is the depositary bank for the American Depositary Shares, also referred to as ADSs. Each ADS represents two common shares (or a right to receive two common shares) deposited with Citibank Europe plc**,** as custodian for the depositary located at 1 North Wall Quay, Dublin 1, Ireland. Each ADS also represents any other securities, cash or other property which may be held by the depositary. The deposited shares, together with our other securities, cash and other property held by the depositary, are referred to as the deposited securities. The depositary's office at which the ADSs are administered is located at 388 Greenwich Street, New York, New York 10013.

A deposit agreement among us, the depositary, ADS holders and all other persons indirectly or beneficially holding ADSs sets out ADS holder rights as well as the rights and obligations of the depositary. New York law governs the deposit agreement and the ADSs. A copy of the deposit agreement is incorporated by reference as an exhibit to this annual report.

Fees and Charges

Persons depositing or withdrawing shares or ADS holders must pay:	**For:**
$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)	Issuance of ADSs, including issuances resulting from a distribution of shares or rights or other property Cancellation of ADSs for the purpose of withdrawal, including if the deposit agreement terminates
$.05 (or less) per ADS	Any cash distribution to ADS holders
A fee equivalent to the fee that would be payable if securities distributed to you had been shares and the shares had been deposited for issuance of ADSs	Distribution of securities distributed to holders of deposited securities (including rights) that are distributed by the depositary to ADS holders
$.05 (or less) per ADS per calendar year	Depositary services

Registration or transfer fees	Transfer and registration of shares on our share register to or from the name of the depositary or its agent when you deposit or withdraw shares
Expenses of the depositary	Cable, telex and facsimile transmissions (when expressly provided in the deposit agreement) converting foreign currency to U.S. dollars
Taxes and other governmental charges the depositary or the custodian has to pay on any ADSs or shares underlying ADSs, such as stock transfer taxes, stamp duty or withholding taxes	As necessary
Any charges incurred by the depositary or its agents for servicing the deposited securities	As necessary

The depositary collects its fees for delivery and surrender of ADSs directly from investors depositing shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions or by directly billing investors or by charging the book-entry system accounts of participants acting for them. The depositary may collect any of its fees by deduction from any cash distribution payable (or by selling a portion of securities or other property distributable) to ADS holders that are obligated to pay those fees. The depositary may generally refuse to provide fee-attracting services until its fees for those services are paid.

From time to time, the depositary may make payments to us to reimburse us for costs and expenses generally arising out of establishment and maintenance of the ADS program, waive fees and expenses for services provided to us by the depositary or share revenue from the fees collected from ADS holders. In performing its duties under the deposit agreement, the depositary may use brokers, dealers, foreign currency dealers or other service providers that are owned by or affiliated with the depositary and that may earn or share fees, spreads or commissions.

The depositary may convert currency itself or through any of its affiliates and, in those cases, acts as principal for its own account and not as agent, advisor, broker or fiduciary on behalf of any other person and earns revenue, including, without limitation, transaction spreads, that it will retain for its own account. The revenue is based on, among other things, the difference between the exchange rate assigned to the currency conversion made under the deposit agreement and the rate that the depositary or its affiliate receives when buying or selling foreign currency for its own account. The depositary makes no representation that the exchange rate used or obtained in any currency conversion under the deposit agreement will be the most favorable rate that could be obtained at the time or that the method by which that rate will be determined will be the most favorable to ADS holders, subject to the depositary's obligations under the deposit agreement. The methodology used to determine exchange rates used in currency conversions is available upon request.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

Not applicable.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

Not applicable.

ITEM 15. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

Our management, with the participation of our chief executive officer and chief financial officer, has performed an evaluation of the effectiveness of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act) as of the end of the period covered by this report, as required by Rule 13a-15(b) under the Exchange Act.

Based on that evaluation, our management has concluded that, as of December 31, 2020, our disclosure controls and procedures are not effective due to the material weaknesses described below.

Management's Annual Report on Internal Control over Financial Reporting

This annual report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report by our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Attestation Report of the Registered Public Accounting Firm

Since we are an "emerging growth company" as defined under the JOBS Act, we are exempt from the requirement to comply with the auditor attestation requirements that our independent registered public accounting firm attest to and report on the effectiveness of our internal control structure and procedures for financial reporting.

Changes in Internal Control Over Financial Reporting

We and our independent registered public accounting firm identified a material weakness in our internal control over financial reporting in connection with the audit of our consolidated financial statements for the years ended December 31, 2020 and 2019. The material weakness 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 intend 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.

Except as described above, there were no other changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the twelve months ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 16. RESERVED

Not applicable.

ITEM 16A. AUDIT COMMITTEE FINANCIAL EXPERT

The audit committee consists exclusively of members of our board who are financially literate, and Lennart Hansson and Molly Henderson are each considered an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq rules and regulations. Our board of directors has determined that all of the members of the audit committee satisfy the "independence" requirements set forth in Rule 10A-3 under the Exchange Act.

ITEM 16B. CODE OF ETHICS

Our board of directors adopted a code of business conduct and ethics that applies to our directors, officers and employees in March 2020. We have posted a copy of our code of business conduct and ethics on our website at: *www.calliditas.se*, where you can obtain a copy without charge.

ITEM 16C. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Ernst & Young AB has served as our independent registered public accounting firm for 2019 and 2020. Our accountants billed the following fees to us for professional services in each of those fiscal years:

	Year Ended December 31,	
Fees	**2020**	**2019**
	in thousands of SEK	
Audit Fees	4,449	645
Audit-Related Fees	3,774	3,348
Tax Fees	-	-
All Other Fees	-	98
Total	**8,223**	**4,086**

"Audit Fees" are the aggregate fees billed for the audit of our annual financial statements. This category also includes services that generally the independent accountants provide, such as consents and assistance with and review of documents filed with the SEC.

"Audit-Related Fees" are the aggregate fees billed for assurance and related services that are reasonably related to the performance of the audit and are not reported under Audit Fees. In 2020 and 2019, "Audit-Related Fees" also include fees billed for assurance and audit-related services regarding our public offerings on Nasdaq.

"Tax Fees" are the aggregate fees billed for professional services rendered by the principal accountant for tax compliance, tax advice and tax planning related services.

"All Other Fees" are any additional amounts billed for products and services provided by the principal accountant. No other fees were paid to Ernst & Young AB for the fiscal years ended December 31, 2020.

Audit Committee's Pre-Approval Policies and Procedures

The audit committee has responsibility for, among other things, appointing, setting compensation of and overseeing the work of our independent registered public accounting firm, or external auditor. In recognition of these responsibilities, the audit committee has adopted a policy governing the pre-approval of all audit and permitted non-audit services performed by our external auditor to ensure that the provision of such services does not impair the external auditor's independence from us and our management. Unless a type of service to be provided by our external auditor has received general pre-approval from the audit committee, it requires specific pre-approval by the audit committee. The payment for any proposed services in excess of pre-approved cost levels requires specific pre-approval by the audit committee.

Pursuant to its pre-approval policy, the audit committee may delegate its authority to pre-approve services to the chairperson of the Audit Committee. The decisions of the chairperson to grant pre-approvals must be presented to the full audit committee at its next scheduled meeting. The audit committee may not delegate its responsibilities to pre-approve services to the management.

The audit committee has considered the non-audit services provided by Ernst & Young AB as described above and believes that they are compatible with maintaining Ernst & Young AB's independence as our external auditor. In accordance with Regulation S-X, Rule 2-01, paragraph (c)(7)(i), no fees for services were approved pursuant to any waivers of the pre-approval requirement.

ITEM 16D. EXEMPTIONS FROM THE LISTING STANDARDS FOR AUDIT COMMITTEES

Not applicable.

ITEM 16E. PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS

Not applicable.

ITEM 16F. CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT

Not applicable.

ITEM 16G. CORPORATE GOVERNANCE

We qualify as a foreign private issuer. The Listing Rules of the Nasdaq Stock Market include certain accommodations in the corporate governance requirements that allow foreign private issuers to follow "home country" corporate governance practices in lieu of the otherwise applicable corporate governance standards of the Nasdaq Stock Market. While we expect to voluntarily follow most Nasdaq corporate governance rules, we may choose to take advantage of the following limited exemptions:

- exemption from filing 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;
- exemption from Section 16 rules requiring insiders to file public reports of their securities ownership and trading activities and providing for liability for insiders who profit from trades in a short period of time;
- exemption from the Nasdaq requirement necessitating disclosure of any waivers of the Code of Business Conduct and Ethics for directors and executive officers;
- exemption from the requirement to obtain shareholder approval for certain issuances of securities, including shareholder approval of share option plans;
- exemption from the requirement that our audit committee have review and oversight responsibilities over all "related party transactions," as defined in Item 7.B of Form 20-F;
- exemption from the requirement that our board of directors have a compensation committee that is composed entirely of independent directors with a written charter addressing the committee's purpose and responsibilities; and
- exemption from the requirement to have independent director oversight of director nominations.

Furthermore, Nasdaq Rule 5615(a)(3) provides that a foreign private issuer may rely on home country corporate governance practices in lieu of certain of the rules in the Nasdaq Rule 5600 Series and Rule 5250(d). We intend to follow Swedish corporate governance practices in lieu of Nasdaq corporate governance requirements as follows:

- We do not intend to follow Nasdaq Rule 5620(c) regarding quorum requirements applicable to meetings of shareholders. Such quorum requirements are not required under Swedish law. The Swedish Companies Act (SFS 2005:551) and our articles of association, which were approved by our shareholders on March 3, 2020 and are currently in effect, provide alternative quorum requirements that are generally applicable to meetings of shareholders.

- We do not intend to follow Nasdaq Rule 5605(b)(2), which requires that independent directors regularly meet in executive sessions where only independent directors are present. Our independent directors may choose to meet in executive sessions at their discretion.

- We do not intend to follow Nasdaq Rule 5605(e) regarding the composition of the nominating committee.

Although we may rely on certain home country corporate governance practices, we must comply with Nasdaq's Notification of Noncompliance requirement (Nasdaq Rule 5625) and the Voting Rights requirement (Nasdaq Rule 5640). Further, we must have an audit committee that satisfies Nasdaq Rule 5605(c)(3), which addresses audit committee responsibilities and authority and requires that the audit committee consist of members who meet the independence requirements of Nasdaq Rule 5605(c)(2)(A)(ii).

Because we are a foreign private issuer, our directors and executive officers are not subject to short-swing profit and insider trading reporting obligations under Section 16 of the Exchange Act. They will, however, be subject to the obligations to report changes in securities ownership under Section 13 of the Exchange Act and related SEC rules.

We intend to take all actions necessary for us to maintain compliance as a foreign private issuer under the applicable corporate governance requirements of the Sarbanes-Oxley Act, the rules adopted by the SEC and Nasdaq listing rules. Accordingly, our shareholders will not have the same protections afforded to shareholders of companies that are subject to all of the corporate governance requirements of Nasdaq.

ITEM 16H. MINE SAFETY DISCLOSURE

Not applicable.

PART III

ITEM 17. FINANCIAL STATEMENTS

Not applicable.

ITEM 18. FINANCIAL STATEMENTS

The financial statements required by this item are incorporated herein by reference to pages 40 to 67 of our Annual Report 2020.

ITEM 19. EXHIBITS

Annual Report

Pages 40 to 67 of our Annual Report 2020, furnished to the SEC as Exhibit 99.1 to Form 6-K, dated April 27, 2021, are incorporated by reference into this Form 20-F. The content of websites, scientific articles and other sources referenced on these pages are not incorporated by reference into this Annual Report on Form 20-F.

Exhibits

The Exhibits listed in the Exhibit Index at the end of this annual report are filed as Exhibits to this annual report.

EXHIBIT INDEX

Exhibit	Description	Incorporated by Reference Schedule/ Form	File Number	Exhibit	File Date (mm/dd/yyyy)
1.1	Articles of Association of the Registrant	Form F-1	333-238244	3.1	05/14/2020
2.1	Form of Deposit Agreement	Form F-1/A	333-238244	4.1	06/01/2020
2.2	Form of American Depositary Receipt (included in Exhibit 2.1)				
2.3	Share Purchase Agreement, dated August 13, 2020, by and between the Registrant and the Block Sellers	Form F-1	333-252436	2.1	01/26/2021
2.4*	Description of Securities				
4.1†	License Agreement regarding NEFECON, dated June 10, 2019, by and between the Registrant and Everest Medicines II Limited.	Form F-1	333-238244	10.1	05/14/2020
4.2	English translation of Lease Agreement, dated as of March 20, 2019, by and between Vasaterminalen AB and the Registrant	Form F-1	333-238244	10.2	05/14/2020
4.3#	English Translation of Warrants 2018/2022 in Calliditas Therapeutics AB (publ)	Form F-1	333-238244	10.4	05/14/2020
4.4#	English Translation of Warrants 2019/2022 in Calliditas Therapeutics AB (publ)	Form F-1	333-238244	10.5	05/14/2020
4.5#	Board Long Term Incentive Program 2019	Form F-1	333-238244	10.6	05/14/2020
4.6#	Board Long Term Incentive Program 2020	Form F-1	333-252436	10.6	01/26/2021
4.7#	English Translation of Principles for the 2020 ESOP for the Registrant's management and key personnel	Form F-1	333-238244	10.7	05/14/2020
4.8#	ESOP 2020 United States Sub-Plan	Form S-8	333-240126	99.1	07/27/2020
4.9#	Employment Agreement, by and between the Registrant and Renée Aguiar-Lucander, dated May 1, 2017	Form F-1	333-238244	10.8	05/14/2020
4.10#	Employment Agreement, by and between the Registrant and Fredrik Johansson, dated August 1, 2017	Form F-1	333-238244	10.10	05/14/2020
4.11#	Employment Agreement, by and between the Registrant and Frank Bringstrup, dated February 1, 2019	Form F-1	333-238244	10.11	05/14/2020
4.12#	Employment Agreement, by and between the Registrant and Andrew B. Udell, dated March 1, 2019	Form F-1	333-238244	10.12	05/14/2020
4.13#	Employment Agreement, by and between the Registrant and Katayoun Welin-Berger, dated September 17, 2019	Form F-1	333-252436	10.13	01/26/2021
4.14#	Employment Agreement, by and between the Registrant and Richard Philipson, dated March 26, 2020	Form F-1	333-252436	10.14	01/26/2021
8.1*	Subsidiaries of the Registrant				
12.1*	Certification by the Principal Executive Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				
12.2*	Certification by the Principal Financial Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				
13.1**	Certification by the Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
13.2**	Certification by the Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
15.1*	Consent of independent registered public accounting firm				
101.INS	XBRL Instance Document	Form 6-K	001-39308	101.INS	4/27/2021
101.SCH	XBRL Taxonomy Extension Schema Document	Form 6-K	001-39308	101.SCH	4/27/2021
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	Form 6-K	001-39308	101.CAL	4/27/2021
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	Form 6-K	001-39308	101.DEF	4/27/2021
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	Form 6-K	001-39308	101.LAB	4/27/2021
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	Form 6-K	001-39308	101.PRE	4/27/2021

* Filed herewith.

** Furnished herewith.

# Indicates a management contract or any compensatory plan, contract or arrangement.

† Confidential treatment status has been granted as to certain portions thereto, which portions are omitted and filed separately with the U.S. Securities and Exchange Commission.

SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

Date: April 27, 2021

CALLIDITAS THERAPEUTICS AB

By: /s/ Renée Aguiar-Lucander
Name: Renée Aguiar-Lucander
Title: Chief Executive Officer

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Calliditas Therapeutics AB

Opinion on the Financial Statements

We have audited the accompanying consolidated statements of financial position of Calliditas Therapeutics AB and subsidiaries (the Company) as of December 31, 2020 and 2019, the related consolidated statements of income, comprehensive income, changes in equity, and cash flows for each of the two years in the period ended December 31, 2020, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019 and the results of its operations and its cash flows in each of the two years in the period ended December 31, 2020, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young AB

We have served as the Company’s auditor since 2004.
Stockholm, Sweden
April 27, 2021

Exhibit 2.4

DESCRIPTION OF SECURITIES

The following description of the capital stock of Calliditas Therapeutics AB ("us," "our," "we" or the "Company") is a summary of the rights of our ordinary shares and certain provisions of our articles of association in effect as of December 31, 2020. This summary does not purport to be complete and is qualified in its entirety by the provisions of our articles of association previously filed with the Securities and Exchange Commission and incorporated by reference as an exhibit to the Annual Report on Form 20-F of which this Exhibit 2.4 is a part, as well as to the applicable provisions of Swedish legislation on stock corporations. We encourage you to read our articles of association and applicable Swedish legislation on stock corporations carefully.

General

We were founded in accordance with Swedish law on February 20, 2004 under the name Pharmalink AB and were registered with the Swedish Companies Registration Office on April 15, 2004. On September 19, 2017, we changed our name to Calliditas Therapeutics AB. Our common shares have been listed for trading on Nasdaq Stockholm since June 29, 2018 under the ticker "CALTX." Our ADSs have been listed for trading on The Nasdaq Global Select Market since June 5, 2020 under the ticker "CALT."

We have two wholly owned subsidiaries, located in Sweden and the United States. The U.S. subsidiary is Calliditas Therapeutics Inc. and the Swedish subsidiary is Nefecon AB. We have two additional subsidiaries, Genkyotex S.A., located in France, and Genkyotex Suisse S.A., located in Switzerland.

Our registered office is located at Kungsbron 1, C8, SE-111 22, Stockholm, Sweden, and our telephone number is +46 (0) 8 411 3005. Our website address is www.calliditas.com. We have included our website address in this prospectus solely as an inactive textual reference. The information contained on or accessible through our website is not incorporated by reference into this prospectus.

Common Shares

4,500,000 common shares have been issued, each with a quota (par) value SEK 0.04, entailing an increase of our share capital of up to SEK 180,000. All of our outstanding common shares have been validly issued, fully paid and non-assessable, and are not redeemable and do not have any preemptive rights other than under the Swedish Companies Act as described below. In accordance with our articles of association, all of the common shares are in one class of shares, denominated in SEK. As of March 31, 2021, we had issued and outstanding 49,941,584 common shares.

The development in the number of shares since our foundation in 2004 is shown below.

Year	Transaction	Nominal Value	Subscription Price per Share (SEK)	Increase in Number of Shares	Increase in Share Capital (SEK)	Total Number of Shares	Total Share Capital (SEK)
2004	Foundation	100	-	1,000	100,000	1,000	100,000
2004	New share issue	100	25,000	12	1,200	1,012	101,200
2005	New share issue	100	50,562	178	17,800	1,190	119,000
2009	New share issue	100	60,000	132	13,200	1,322	132,000
2012	New share issue	100	52,950	664	66,400	1,986	198,600
2013	New share issue	100	52,950	813	81,300	2,799	279,900
2014	New share issue	100	52,950	189	18,900	2,988	298,800
2014	New share issue	100	52,950	809	80,900	3,797	379,700
2015	New share issue	100	52,950	756	75,600	4,553	455,300
2016	New share issue	100	52,950	752	75,200	5,305	530,500
2017	New share issue	100	52,950	605	60,500	5,910	591,000
2017	Share split (1:10)	10	-	53,190	-	59,100	591,000
2017	New share issue	10	5,295	7,026	70,260	66,126	661,260
2017	New share issue	10	5,295	566	5,660	66,692	666,920
2017	Share split (1:250)	0.04		16,606,308	-	16,673,000	666,920
2018	Conversion of bridge loans in connection with offering	0.04	45.00	2,114,903	84,596.12	18,787,903	751,516.12
2018	New share issue in connection with listing	0.04	45.00	16,414,444	656,577.76	35,202,347	1,408,093.88
2019	New share issue	0.04	60.00	3,505,291	140,211.64	38,707,638	1,548,305.52
2020	New share issue in connection with listing	0.04	89.70	9,937,446	397,497.80	48,645,084	1,945,803.40
2020	Exercise of Warrant program	0.04	42.36	1,296,500	52,860.00	49,941,584	1,997,663.40

There were no special terms or installment payments for any of the transactions listed above. There have been two changes in voting rights since we were listed on Nasdaq Stockholm in 2018 through a directed share issue in July 2019, entailing an increase of the number of shares and votes with 3,505,291 and share capital with SEK 140,211.64, and the initial public offering on the Nasdaq Global Select Market in June 2020, entailing an increase of the number of shares with 9,937,446 and share capital with SEK 397,497.80. During the period as a listed company, there has not been any reduction of amount of share capital.

At the 2020 annual general meeting held on June 25, 2020, our shareholders resolved that for the period until the 2021 annual general meeting, our board of directors would be authorized to, at one or several occasions, increase our share capital by issuing new shares. Such share issue resolution may be made with or without deviation from the shareholders' preferential rights, where payment for new share can be made in cash, contribution in kind, debt conversion or in accordance with certain other conditions. The authorization may only be utilized to the extent that it corresponds to a dilution of not more than 20% of the total number of outstanding shares outstanding as per the time of the annual general meeting. The authorization was proposed by the board of directors to increase its financial flexibility. Should the board of directors resolve on an issue with deviation from the shareholders' preferential rights, the reason for such deviation shall be to finance an acquisition, to procure capital to finance the continued development of projects or to commercialize our products.

Any share issue under the authorization must be made at market terms and conditions. The subscription price will be determined by the board of directors. Any new shares issued on the basis of the authorization will rank pari passu with our existing shares.

On the date of the 2020 annual general meeting, we had 47,938,408 shares outstanding. As such, under the authorization, the board of directors is authorized to issue up to 11,984,602 new shares.

Below are summaries of the material provisions of our articles of association and of related material provisions of the Swedish Companies Act.

Share Capital

Articles of Association

Object of the Company

Our object is set forth in Section 3 of our articles of association and is to, directly or through subsidiaries, conduct research and development as well as the manufacture and sale of pharmaceuticals and medical devices, own and manage shares and other securities as well as other tangible and intangible property, as well as any other business associated therewith.

Powers of the Directors

Our board of directors shall direct our policy and shall supervise the performance of our chief executive officer and his or her actions. Our board of directors may exercise all powers that are not required under the Swedish Companies Act or under our articles of association to be exercised or taken by our shareholders.

Number of Directors

Our articles of association provide that our board of directors shall consist of three to ten members. Our board of directors currently has five members, with no deputy members.

Rights Attached to Shares

All of the common shares have equal rights to our assets and earnings, and are entitled to one vote at the general meeting. At the general meeting, every shareholder may vote to the full extent of their shares held or represented, without limitation. Each common share entitles the shareholder to the same preferential rights related to issues of shares, warrants and convertible bonds relative to the number of shares they own and have equal rights to dividends and any surplus capital upon liquidation. Shareholders' rights can only be changed in accordance with the procedures set out in the Swedish Companies Act. Transfers of shares are not subject to any restrictions.

Exclusive Forum

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, 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.

Preemptive Rights

Under the Swedish Companies Act, shareholders of any class of shares will generally have a preemptive right to subscribe for shares or warrants issued of any class in proportion to their shareholdings. Shareholders will have preferential rights to subscribe for new shares in proportion to the number of shares they own. If an offering is not fully subscribed for based on subscription rights, shares may be allocated to subscribers without subscription rights. The preemptive right to subscribe does not apply in respect of shares issued for consideration by payment in kind or of shares issued pursuant to convertible debentures or warrants previously issued by the company.

The preemptive right to subscribe for new shares may be set aside. A share issue with deviation from the shareholders' preemptive rights may be resolved either by the shareholders at a general meeting, or by the board of directors if the board resolution is preceded by an authorization therefor from the general meeting. A resolution to issue shares with deviation from the shareholders' preemptive rights and a resolution to authorize the board of directors to do the same must be passed by two-thirds of both the votes cast and the shares represented at the general meeting resolving on the share issue or the authorization of the board of directors.

Voting at Shareholder Meetings

Under the Swedish Companies Act, shareholders entered into the shareholders' register as of the record date are entitled to vote at a general meeting (in person or by appointing a proxyholder). In accordance with our articles of association, shareholders must give notice of their intention to attend the general meeting no later than the date specified in the notice. Shareholders who have their shares registered through a nominee and wish to exercise their voting rights at a general meeting must request to be temporary registered as a shareholder and entered into the shareholders' register four business days prior to the date of the general meeting. The rights described herein do not apply to holders of ADSs. See "Description of American Depositary Shares."

Shareholder Meetings

The general meeting of shareholders is our highest decision-making body and serves as an opportunity for our shareholders to make decisions regarding our affairs. Shareholders who are registered in the share register held by Euroclear Sweden AB six business days before the meeting and have notified us no later than the date specified in the notice described below have the right to participate at our general meetings, either in person or by a representative. All shareholders have the same participation and voting rights at general meetings. At the annual general meeting, *inter alia*, members of the board of directors are elected, the principles for the appointment of the nomination committee are established, and a vote is held on whether each individual board member and the chief executive officer will be discharged from any potential liabilities for the previous fiscal year. Auditors are elected as well. Decisions are made concerning adoption of annual reports, allocation of earnings, fees for the board of directors and the auditors, guidelines for executive remuneration and other essential matters that require a decision by the meeting. Most decisions require a simple majority but the Swedish Companies Act dictates other thresholds in certain instances. See "-Differences in Corporate Law-Shareholder Vote on Certain Transactions."

Shareholders have the right to ask questions to our board of directors and managers at general meetings which pertain to the business of the company and also have an issue brought forward at the general meeting. In order for us to include the issue in the notice of the annual general meeting, a request of issue discussion must be received by us normally seven weeks before the meeting. Any request for the discussion of an issue at the annual general meeting shall be made to the board of directors and any request within the nomination committee's competence shall be made to the nomination committee. The board shall convene an extraordinary general meeting if shareholders who together represent at least 10% of all shares in the company so demand in writing to discuss or resolve on a specific issue.

The arrangements for the calling of general meetings are described below in "—Differences in Corporate Law—Annual General Meeting" and "—Differences in Corporate Law—Special Meeting."

Notices

The Swedish Companies Act requirements for notice are described below in "—Differences in Corporate Law-Notices."

Subject to our articles of association and Nasdaq Stockholm's Rulebook for Issuers, we must publish the full notice of a general meeting by way of press release, on our website and in the Swedish Official Gazette, and must also publish in the Svenska Dagbladet, a daily Swedish newspaper, that such notice has been published. The notice of the annual general meeting will be published six to four weeks before the meeting. The notice must include an agenda listing each item that shall be voted upon at the meeting. The notice of any extraordinary general meetings will be published six to three weeks before the meeting. Pursuant to the Swedish Code of Corporate Governance, which does not carry the force of law but is considered ideal corporate governance practice for Swedish companies whose shares trade on a regulated market, we shall, as soon as the time and venue for the annual general meeting have been decided, and no later than in conjunction with the third quarter report, publish such information on our website.

Record Date

Under the Swedish Companies Act, in order for a shareholder to participate in a shareholders' meeting, the shareholder must have its shares registered in its own name in the share register four business days. In accordance with section 8 of our articles of association, shareholders must give notice of their intention to attend the shareholders' meeting no later than the date specified in the notice.

Amendments to the Articles of Associations

Under the Swedish Companies Act, an amendment of our articles of association requires a resolution passed at a shareholders' meeting. The number of votes required for a valid resolution depends on the type of amendment, however, any amendment must be approved by not less than two-thirds of the votes cast and represented at the meeting. The board of directors is not allowed to make amendments to the articles of association absent shareholder approval.

Provisions Restricting Change in Control of Our Company

Neither our articles of association nor the Swedish Companies Act contains any restrictions on change of control.

Differences in Corporate Law

The applicable provisions of the Swedish Companies Act differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of certain differences between the provisions of, inter alia, the Swedish Companies Act applicable to us and the Delaware General Corporation Law relating to shareholders' rights and protections. We are not subject to Delaware law but are presenting this description for comparative purposes. This summary is not intended to be a complete discussion of the respective rights and it is qualified in its entirety by reference to Delaware law and Swedish law.

Number of Directors

Sweden. Under the Swedish Companies Act, a public company shall have a board of directors consisting of at least three directors. More than half of the directors shall be resident within the European Economic Area (unless otherwise approved by the Swedish Companies Registration Office). The actual number of board members shall be determined by a shareholders' meeting, within the limits set out in the company's articles of association. Under the Swedish Code of Corporate Governance, only one director may also be a senior executive of the relevant company or a subsidiary. The Swedish Code of Corporate Governance includes certain independence requirements for the directors, and requires a majority of the directors to be independent of the company and at least two directors to also be independent of major shareholders.

Delaware. Under the Delaware General Corporation Law, a corporation must have at least one director and the number of directors shall be fixed by or in the manner provided in the bylaws. The Delaware General Corporation Law does not address director independence, though Delaware courts have provided general guidance as to determining independence, including that the determination must be both an objective and a subjective assessment.

Removal of Directors

Sweden. Under the Swedish Companies Act, directors appointed at a general meeting may be removed by a resolution adopted at a general meeting, upon the affirmative vote of a simple majority of the votes cast.

Delaware. Under the Delaware General Corporation Law, unless otherwise provided in the certificate of incorporation, directors may be removed from office, with or without cause, by a majority stockholder vote, though in the case of a corporation whose board is classified, stockholders may effect such removal only for cause.

Vacancies on the Board of Directors

Sweden. Under the Swedish Companies Act, if a director's tenure should terminate prematurely, the election of a new director may be deferred until the time of the next annual general meeting, providing there are enough remaining directors to constitute a quorum.

Delaware. Under the Delaware General Corporation Law, vacancies on a corporation's board of directors, including those caused by an increase in the number of directors, may be filled by a majority of the remaining directors.

Annual General Meeting

Sweden. Under the Swedish Companies Act, within six months of the end of each fiscal year, the shareholders shall hold an annual general meeting at which the board of directors shall present the annual report and auditor's report and, for a parent company which is obliged to prepare group accounts, the group accounts and the auditor's report for the group. Shareholder meetings shall be held in the city stated in the articles of association. The minutes of a shareholders' meeting must be made available on the company's website no later than two weeks after the meeting.

Delaware. Under the Delaware General Corporation Law, the annual meeting of stockholders shall be held at such place, on such date and at such time as may be designated from time to time by the board of directors or as provided in the certificate of incorporation or by the bylaws. If a company fails to hold an annual meeting or fails to take action by written consent to elect directors in lieu of an annual meeting for a period of 30 days after the date designated for the annual meeting, or if no date was designated, 13 months after either the last annual meeting or the last action by written consent to elect directors in lieu of an annual meeting, whichever is later, the Delaware Court of Chancery may summarily order a meeting to be held upon the application of any stockholder or director. The Delaware General Corporation Law does not require minutes of stockholders' meetings to be made public.

Special Meeting

Sweden. Under the Swedish Companies Act, the board of directors shall convene an *extraordinary general meeting* if a shareholder minority representing at least ten per cent of the company's shares or the auditor of the company so demands, and the board of directors may convene an extraordinary general meetings whenever it believes reason exists to hold an extraordinary general meeting prior to the next annual general meeting.

Delaware. Under the Delaware General Corporation Law, special meetings of the stockholders may be called by the board of directors or by such person or persons as may be authorized by the certificate of incorporation or by the bylaws.

Notices

Sweden. Under the Swedish Companies Act, a shareholders' meeting must be preceded by a notice. The notice of the annual general meeting of shareholders must be issued no sooner than six weeks and no later than four weeks before the date of an annual general meeting. In general, notice of other extraordinary general meetings must be issued no sooner than six weeks and no later than three weeks before the meeting. Publicly listed companies must always notify shareholders of a general meeting by advertisement in a Swedish newspaper, the Swedish Official Gazette, by press release, and on the company's website.

Delaware. Under the Delaware General Corporation Law, unless otherwise provided in the certificate of incorporation or bylaws, written notice of any meeting of the stockholders must be given to each stockholder entitled to vote at the meeting not less than ten nor more than 60 days before the date of the meeting and shall specify the place, date, hour, and purpose or purposes of the meeting.

Preemptive Rights

Sweden. Under the Swedish Companies Act, shareholders of any class of shares have a preemptive right (*Sw. företrädesrätt*) to subscribe for shares issued of any class in proportion to their shareholdings. The preemptive right to subscribe does not apply in respect of shares issued for consideration other than cash or of shares issued pursuant to convertible debentures or warrants previously granted by the company. The preemptive right to subscribe for new shares may also be set aside by a resolution passed by two thirds of the votes cast and shares represented at the shareholders' meeting resolving upon the issue.

Delaware. Under the Delaware General Corporation Law, unless otherwise provided in a corporation's certificate of incorporation, a stockholder does not, by operation of law, possess preemptive rights to subscribe to additional issuances of the corporation's stock.

Shareholder Vote on Certain Transactions

Sweden. In matters which do not relate to elections and are not otherwise governed by the Swedish Companies Act or the articles of association, resolutions shall be adopted at the general meeting by a simple majority of the votes cast. In the event of a tied vote, the chairman shall have the casting vote. For matters concerning securities of the company, such as new share issuances, and other transactions such as private placements, mergers, and a change from a public to a private company (or vice-versa), the articles of association may only prescribe thresholds which are higher than those provided in the Swedish Companies Act.

Unless otherwise prescribed in the articles of association, the person who receives the most votes in an election shall be deemed elected. In general, a resolution involving the alteration of the articles of association shall be valid only when supported by shareholders holding not less than two-thirds of both the votes cast and the shares represented at the general meeting. The Swedish Companies Act lays out numerous exceptions for which a higher threshold applies, including restrictions on certain rights of shareholders, limits on the number of shares shareholders may vote at the general meeting, directed share issues to directors, employees and other closely related parties, and changes in the legal relationship between shares.

Delaware. Generally, under Delaware law, unless the certificate of incorporation provides for the vote of a larger portion of the stock, completion of a merger, consolidation, sale, lease or exchange of all or substantially all of a corporation's assets or dissolution requires: (i) the approval of the board of directors; and (ii) approval by the vote of the holders of a majority of the outstanding stock or, if the certificate of incorporation provides for more or less than one vote per share, a majority of the votes of the outstanding stock of a corporation entitled to vote on the matter.

Stock Exchange Listing

Our common shares are currently traded on Nasdaq Stockholm under the symbol "CALTX." Our ADSs are currently traded on The Nasdaq Global Select Market under the symbol "CALT."

Transfer Agent and Registrar of Shares

Our share register is maintained by Euroclear. The share register reflects only record owners of our common shares. Holders of our ADSs will not be treated as our shareholders and their names will therefore not be entered in our share register. The depositary, the custodian or their nominees will be the holder of the common shares underlying our ADSs. Holders of our ADSs have a right to receive the common shares underlying their ADSs.

American Depository Shares

Citibank, N.A. is the depositary bank for the American Depositary Shares. Citibank's depositary offices are located at 388 Greenwich Street, New York, New York 10013. American Depositary Shares are frequently referred to as "ADSs" and represent ownership interests in securities that are on deposit with the depositary bank. ADSs may be represented by certificates that are commonly known as "American Depositary Receipts" or "ADRs." The depositary bank typically appoints a custodian to safekeep the securities on deposit. In this case, the custodian is Citibank Europe plc, located at 1 North Wall Quay, Dublin 1, Ireland.

We have appointed Citibank as depositary bank pursuant to a deposit agreement. A copy of the deposit agreement has been filed with the SEC under cover of a registration statement on Form F-6 (File No. 333-238726). You may obtain a copy of the deposit agreement from the SEC's website (www.sec.gov). Please refer to Registration Number 333-238726 when retrieving such copy.

We are providing you with a summary description of the material terms of the ADSs and of your material rights as an owner of ADSs. Please remember that summaries by their nature lack the precision of the information summarized and that the rights and obligations of an owner of ADSs will be determined by reference to the terms of the deposit agreement and not by this summary. We urge you to review the deposit agreement in its entirety. The portions of this summary description that are italicized describe matters that may be relevant to the ownership of ADSs but that may not be contained in the deposit agreement.

Each ADS represents two common shares, quota value SEK 0.04 per share. As a holder of ADSs, you will not be treated as one of our shareholders and you will not have shareholder rights. You will have the rights of an ADS holder or beneficial owner (as applicable) as provided in the deposit agreement among us, the depositary and holders and beneficial owners of ADSs from time to time.

Each ADS represents the right to receive, and to exercise the beneficial ownership interests in two common shares that are on deposit with the depositary bank and/or custodian. An ADS also represents the right to receive, and to exercise the beneficial interests in, any other property received by the depositary bank or the custodian on behalf of the owner of the ADS but that has not been distributed to the owners of ADSs because of legal restrictions or practical considerations. We and the depositary bank may agree to change the ADS-to-share ratio by amending the deposit agreement. This amendment may give rise to, or change, the depositary fees payable by ADS owners. The custodian, the depositary bank and their respective nominees will hold all deposited property for the benefit of the holders and beneficial owners of ADSs. The deposited property does not constitute the proprietary assets of the depositary bank, the custodian or their nominees. Beneficial ownership in the deposited property will under the terms of the deposit agreement be vested in the beneficial owners of the ADSs. The depositary bank, the custodian and their respective nominees will be the record holders of the deposited property represented by the ADSs for the benefit of the holders and beneficial owners of the corresponding ADSs. A beneficial owner of ADSs may or may not be the holder of ADSs. Beneficial owners of ADSs will be able to receive, and to exercise beneficial ownership interests in, the deposited property only through the registered holders of the ADSs, the registered holders of the ADSs (on behalf of the applicable ADS owners) only through the depositary bank, and the depositary bank (on behalf of the owners of the corresponding ADSs) directly, or indirectly, through the custodian or their respective nominees, in each case upon the terms of the deposit agreement.

If you become an owner of ADSs, you will become a party to the deposit agreement and therefore will be bound to its terms and to the terms of any ADR that represents your ADSs. The deposit agreement and the ADR specify our rights and obligations as well as your rights and obligations as owner of ADSs and those of the depositary bank. As an ADS holder you appoint the depositary bank to act on your behalf in certain circumstances. The deposit agreement and the ADRs are governed by New York law. However, our obligations to the holders of common shares will continue to be governed by the laws of Sweden, which may be different from the laws in the United States.

In addition, applicable laws and regulations may require you to satisfy reporting requirements and obtain regulatory approvals in certain circumstances. You are solely responsible for complying with such reporting requirements and obtaining such approvals. None of the depositary bank, the custodian, us or any of their or our respective agents or affiliates shall be required to take any actions whatsoever on your behalf to satisfy such reporting requirements or obtain such regulatory approvals under applicable laws and regulations.

As an owner of ADSs, we will not treat you as one of our shareholders and you will not have direct shareholder rights. The depositary bank will hold on your behalf the shareholder rights attached to the common shares underlying your ADSs. As an owner of ADSs you will be able to exercise the shareholders rights for the common shares represented by your ADSs through the depositary bank only to the extent contemplated in the deposit agreement. To exercise any shareholder rights not contemplated in the deposit agreement you will, as an ADS owner, need to arrange for the cancellation of your ADSs and become a direct shareholder.

The manner in which you own the ADSs (e.g., in a brokerage account vs. as registered holder, or as holder of certificated vs. uncertificated ADSs) may affect your rights and obligations, and the manner in which, and extent to which, the depositary bank's services are made available to you. As an owner of ADSs, you may hold your ADSs either by means of an ADR registered in your name, through a brokerage or safekeeping account, or through an account established by the depositary bank in your name reflecting the registration of uncertificated ADSs directly on the books of the depositary bank, commonly referred to as the direct registration system, or DRS. The direct registration system reflects the uncertificated (book-entry) registration of ownership of ADSs by the depositary bank. Under the direct registration system, ownership of ADSs is evidenced by periodic statements issued by the depositary bank to the holders of the ADSs. The direct registration system includes automated transfers between the depositary bank and The Depository Trust Company, or DTC, the central book-entry clearing and settlement system for equity securities in the United States. If you decide to hold your ADSs through your brokerage or safekeeping account, you must rely on the procedures of your broker or bank to assert your rights as ADS owner. Banks and brokers typically hold securities such as the ADSs through clearing and settlement systems such as DTC. The procedures of such clearing and settlement systems may limit your ability to exercise your rights as an owner of ADSs. Please consult with your broker or bank if you have any questions concerning these limitations and procedures. All ADSs held through DTC will be registered in the name of a nominee of DTC. This summary description assumes you have opted to own the ADSs directly by means of an ADS registered in your name and, as such, we will refer to you as the holder. When we refer to you, we assume the reader owns ADSs and will own ADSs at the relevant time.

The registration of the common shares in the name of the depositary bank or the custodian shall, to the maximum extent permitted by applicable law, vest in the depositary bank or the custodian the record ownership in the applicable common shares with the beneficial ownership rights and interests in such common shares being at all times vested with the beneficial owners of the ADSs representing the common shares. The depositary bank or the custodian shall at all times be entitled to exercise the beneficial ownership rights in all deposited property, in each case only on behalf of the holders and beneficial owners of the ADSs representing the deposited property.

Dividends and Distributions

As a holder of ADSs, you generally have the right to receive the distributions we make on the securities deposited with the custodian. Your receipt of these distributions may be limited, however, by practical considerations and legal limitations. Holders of ADSs will receive such distributions under the terms of the deposit agreement in proportion to the number of ADSs held as of the specified record date, after deduction of the applicable fees, taxes and expenses.

Distributions of Cash

Whenever we make a cash distribution for the securities on deposit with the custodian, we will deposit the funds with the custodian. Upon receipt of confirmation of the deposit of the requisite funds, the depositary bank will arrange for the funds received in a currency other than U.S. dollars to be converted into U.S. dollars and for the distribution of the U.S. dollars to the holders, subject to the Swedish laws and regulations.

The conversion into U.S. dollars will take place only if practicable and if the U.S. dollars are transferable to the United States. The depositary bank will apply the same method for distributing the proceeds of the sale of any property (such as undistributed rights) held by the custodian in respect of securities on deposit.

The distribution of cash will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. The depositary bank will hold any cash amounts it is unable to distribute in a non-interest bearing account for the benefit of the applicable holders and beneficial owners of ADSs until the distribution can be effected or the funds that the depositary bank holds must be escheated as unclaimed property in accordance with the laws of the relevant states of the United States.

Distributions of Shares

Whenever we make a free distribution of common shares for the securities on deposit with the custodian, we will deposit the applicable number of common shares with the custodian. Upon receipt of confirmation of such deposit, the depositary bank will either distribute to holders new ADSs representing the common shares deposited or modify the ADS-to-share ratio, in which case each ADS you hold will represent rights and interests in the additional common shares so deposited. Only whole new ADSs will be distributed. Fractional entitlements will be sold and the proceeds of such sale will be distributed as in the case of a cash distribution.

The distribution of new ADSs or the modification of the ADS-to-share ratio upon a distribution of common shares will be made net of the fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes or governmental charges, the depositary bank may sell all or a portion of the new common shares so distributed.

No such distribution of new ADSs will be made if it would violate a law (*e.g.*, the U.S. securities laws) or if it is not operationally practicable. If the depositary bank does not distribute new ADSs as described above, it may sell the common shares received upon the terms described in the deposit agreement and will distribute the proceeds of the sale as in the case of a distribution of cash.

Distributions of Rights

Whenever we intend to distribute rights to subscribe for additional common shares, we will give prior notice to the depositary bank and we will assist the depositary bank in determining whether it is lawful and reasonably practicable to distribute rights to subscribe for additional ADSs to holders.

The depositary bank will establish procedures to distribute rights to subscribe for additional ADSs to holders and to enable such holders to exercise such rights if it is lawful and reasonably practicable to make the rights available to holders of ADSs, and if we provide all of the documentation contemplated in the deposit agreement (such as opinions to address the lawfulness of the transaction). You may have to pay fees, expenses, taxes and other governmental charges to subscribe for the new ADSs upon the exercise of your rights. The depositary bank is not obligated to establish procedures to facilitate the distribution and exercise by holders of rights to subscribe for new common shares other than in the form of ADSs.

The depositary bank will *not* distribute the rights to you if:

- we do not timely request that the rights be distributed to you or we request that the rights not be distributed to you; or
- we fail to deliver satisfactory documents to the depositary bank; or
- it is not reasonably practicable to distribute the rights.

The depositary bank will sell the rights that are not exercised or not distributed if such sale is lawful and reasonably practicable. The proceeds of such sale will be distributed to holders as in the case of a cash distribution. If the depositary bank is unable to sell the rights, it will allow the rights to lapse.

Elective Distributions

Whenever we intend to distribute a dividend payable at the election of shareholders either in cash or in additional shares, we will give prior notice thereof to the depositary bank and will indicate whether we wish the elective distribution to be made available to you. In such case, we will assist the depositary bank in determining whether such distribution is lawful and reasonably practicable.

The depositary bank will make the election available to you only if it is reasonably practicable and if we have provided all of the documentation contemplated in the deposit agreement. In such case, the depositary bank will establish procedures to enable you to elect to receive either cash or additional ADSs, in each case as described in the deposit agreement.

If the election is not made available to you, you will receive either cash or additional ADSs, depending on what a shareholder in Sweden would receive upon failing to make an election, as more fully described in the deposit agreement.

Other Distributions

Whenever we intend to distribute property other than cash, common shares or rights to subscribe for additional common shares, we will notify the depositary bank in advance and will indicate whether we wish such distribution to be made to you. If so, we will assist the depositary bank in determining whether such distribution to holders is lawful and reasonably practicable.

If it is reasonably practicable to distribute such property to you and if we provide to the depositary bank all of the documentation contemplated in the deposit agreement, the depositary bank will distribute the property to the holders in a manner it deems practicable.

The distribution will be made net of fees, expenses, taxes and governmental charges payable by holders under the terms of the deposit agreement. In order to pay such taxes and governmental charges, the depositary bank may sell all or a portion of the property received.

The depositary bank will *not* distribute the property to you and will sell the property if:

- we do not request that the property be distributed to you or if we request that the property not be distributed to you; or
- we do not deliver satisfactory documents to the depositary bank; or
- the depositary bank determines that all or a portion of the distribution to you is not reasonably practicable.

The proceeds of such a sale will be distributed to holders as in the case of a cash distribution.

Redemption

Whenever we decide to redeem any of the securities on deposit with the custodian, we will notify the depositary bank in advance. If it is practicable and if we provide all of the documentation contemplated in the deposit agreement, the depositary bank will provide notice of the redemption to the holders.

The custodian will be instructed to surrender the shares being redeemed against payment of the applicable redemption price. The depositary bank will convert into U.S. dollars upon the terms of the deposit agreement the redemption funds received in a currency other than U.S. dollars and will establish procedures to enable holders to receive the net proceeds from the redemption upon surrender of their ADSs to the depositary bank. You may have to pay fees, expenses, taxes and other governmental charges upon the redemption of your ADSs. If less than all ADSs are being redeemed, the ADSs to be retired will be selected by lot or on a *pro rata* basis, as the depositary bank may determine.

Changes Affecting Common Shares

The common shares held on deposit for your ADSs may change from time to time. For example, there may be a change in nominal or par value, split-up, cancellation, consolidation or any other reclassification of such common shares or a recapitalization, reorganization, merger, consolidation or sale of assets of the Company.

If any such change were to occur, your ADSs would, to the extent permitted by law and the deposit agreement, represent the right to receive the property received or exchanged in respect of the common shares held on deposit. The depositary bank may in such circumstances deliver new ADSs to you, amend the deposit agreement, the ADRs and the applicable Registration Statement(s) on Form F-6, call for the exchange of your existing ADSs for new ADSs and take any other actions that are appropriate to reflect as to the ADSs the change affecting the Shares. If the depositary bank may not lawfully distribute such property to you, the depositary bank may sell such property and distribute the net proceeds to you as in the case of a cash distribution.

Transfer, Combination and Split Up of ADRs

As an ADR holder, you will be entitled to transfer, combine or split up your ADRs and the ADSs evidenced thereby. For transfers of ADRs, you will have to surrender the ADRs to be transferred to the depositary bank and also must:

- ensure that the surrendered ADR is properly endorsed or otherwise in proper form for transfer;
- provide such proof of identity and genuineness of signatures as the depositary bank deems appropriate;
- provide any transfer stamps required by the State of New York or the United States; and

- pay all applicable fees, charges, expenses, taxes and other government charges payable by ADR holders pursuant to the terms of the deposit agreement, upon the transfer of ADRs.

To have your ADRs either combined or split up, you must surrender the ADRs in question to the depositary bank with your request to have them combined or split up, and you must pay all applicable fees, charges and expenses payable by ADR holders, pursuant to the terms of the deposit agreement, upon a combination or split up of ADRs.

Withdrawal of Common Shares Upon Cancellation of ADSs

As a holder of ADSs, you will be entitled to present your ADSs to the depositary bank for cancellation and then receive the corresponding number of underlying common shares at the custodian's offices. Your ability to withdraw the common shares held in respect of the ADSs may be limited by U.S. and Swedish legal considerations applicable at the time of withdrawal. In order to withdraw the common shares represented by your ADSs, you will be required to pay to the depositary bank the fees for cancellation of ADSs and any charges and taxes payable upon the transfer of the common shares. You assume the risk for delivery of all funds and securities upon withdrawal. Once canceled, the ADSs will not have any rights under the deposit agreement.

If you hold ADSs registered in your name, the depositary bank may ask you to provide proof of identity and genuineness of any signature and such other documents as the depositary bank may deem appropriate before it will cancel your ADSs. The withdrawal of the common shares represented by your ADSs may be delayed until the depositary bank receives satisfactory evidence of compliance with all applicable laws and regulations. Please keep in mind that the depositary bank will only accept ADSs for cancellation that represent a whole number of securities on deposit.

You will have the right to withdraw the securities represented by your ADSs at any time except for:

- temporary delays that may arise because (i) the transfer books for the common shares or ADSs are closed, or (ii) common shares are immobilized on account of a shareholders' meeting or a payment of dividends;

- obligations to pay fees, taxes and similar charges; or

- restrictions imposed because of laws or regulations applicable to ADSs or the withdrawal of securities on deposit.

The deposit agreement may not be modified to impair your right to withdraw the securities represented by your ADSs except to comply with mandatory provisions of law.

Voting Rights

As a holder, you generally have the right under the deposit agreement to instruct the depositary bank to exercise the voting rights for the common shares represented by your ADSs.

At our request, the depositary bank will distribute to you any notice of shareholders' meeting received from us together with information explaining how to instruct the depositary bank to exercise the voting rights of the securities represented by ADSs. In lieu of distributing such materials, the depositary bank may distribute to holders of ADSs instructions on how to retrieve such materials upon request.

If the depositary bank timely receives valid voting instructions from a holder of ADSs as of the applicable record date(s), it will endeavor to vote the securities (in person or by proxy) represented by the holder's ADSs in accordance with such voting instructions and in accordance with Swedish law (which may include temporary registration of the securities in the name of the applicable beneficial owner or designated nominee). In order to provide valid voting instructions, an ADS holder may be required to provide us and the depositary with such information about, and documents pertaining to, the applicable holders and beneficial owners of the ADSs being voted.

Securities for which no voting instructions have been received will not be voted (except as otherwise contemplated in the deposit agreement). Please note that the ability of the depositary bank to carry out voting instructions may be limited by practical and legal limitations and the terms of the securities on deposit. We cannot assure you that you will receive voting materials in time to enable you to return voting instructions to the depositary bank in a timely manner.

Fees and Charges

As an ADS holder, you will be required to pay the following fees under the terms of the deposit agreement:

Service	**Fees**
· Issuance of ADSs (e.g., an issuance of ADS upon a deposit of common shares, upon a change in the ADS-to-share ratio, or for any other reason), excluding ADS issuances as a result of distributions of common shares	Up to $0.05 per ADS issued
· Cancellation of ADSs (e.g., a cancellation of ADSs for delivery of deposited property, upon a change in the ADS-to-share ratio, or for any other reason)	Up to $0.05 per ADS cancelled
· Distribution of cash dividends or other cash distributions (e.g., upon a sale of rights and other entitlements)	Up to $0.05 per ADS held
· Distribution of ADSs pursuant to (i) stock dividends or other free stock distributions, or (ii) exercise of rights to purchase additional ADSs	Up to $0.05 per ADS held
· Distribution of securities other than ADSs or rights to purchase additional ADSs (e.g., upon a spin-off)	Up to $0.05 per ADS held
· ADS Services	Up to $0.05 per ADS held on the applicable record date(s) established by the depositary bank
· Registration of ADS transfers (e.g., upon a registration of the transfer of registered ownership of ADSs, upon a transfer of ADSs into DTC and *vice versa*, or for any other reason)	Up to $0.05 per ADS (or fraction thereof) transferred
· Conversion of ADSs of one series for ADSs of another series (e.g., upon conversion of Partial Entitlement ADSs for Full Entitlement ADSs, or upon conversion of Restricted ADSs (each as defined in the Deposit Agreement) into freely transferable ADSs, and *vice versa*)	Up to $0.05 per ADS (or fraction thereof) converted

As an ADS holder you will also be responsible to pay certain charges such as:

- taxes (including applicable interest and penalties) and other governmental charges;
- the registration fees as may from time to time be in effect for the registration of common shares on the share register and applicable to transfers of common shares to or from the name of the custodian, the depositary bank or any nominees upon the making of deposits and withdrawals, respectively;
- certain cable, telex and facsimile transmission and delivery expenses;
- the fees, expenses, spreads, taxes and other charges of the depositary bank and/or service providers (which may be a division, branch or affiliate of the depositary bank) in the conversion of foreign currency;
- the reasonable and customary out-of-pocket expenses incurred by the depositary bank in connection with compliance with exchange control regulations and other regulatory requirements applicable to common shares, ADSs and ADRs; and
- the fees, charges, costs and expenses incurred by the depositary bank, the custodian, or any nominee in connection with the ADR program.

ADS fees and charges for (i) the issuance of ADSs, and (ii) the cancellation of ADSs are charged to the person for whom the ADSs are issued (in the case of ADS issuances) and to the person for whom ADSs are cancelled (in the case of ADS cancellations). In the case of ADSs issued by the depositary bank into DTC, the ADS issuance and cancellation fees and charges may be deducted from distributions made through DTC, and may be charged to the DTC participant(s) receiving the ADSs being issued or the DTC participant(s) holding the ADSs being cancelled, as the case may be, on behalf of the beneficial owner(s) and will be charged by the DTC participant(s) to the account of the applicable beneficial owner(s) in accordance with the procedures and practices of the DTC participants as in effect at the time. ADS fees and charges in respect of distributions and the ADS service fee are charged to the holders as of the applicable ADS record date. In the case of distributions of cash, the amount of the applicable ADS fees and charges is deducted from the funds being distributed. In the case of (i) distributions other than cash and (ii) the ADS service fee, holders as of the ADS record date will be invoiced for the amount of the ADS fees and charges and such ADS fees and charges may be deducted from distributions made to holders of ADSs. For ADSs held through DTC, the ADS fees and charges for distributions other than cash and the ADS service fee may be deducted from distributions made through DTC, and may be charged to the DTC participants in accordance with the procedures and practices prescribed by DTC and the DTC participants in turn charge the amount of such ADS fees and charges to the beneficial owners for whom they hold ADSs. In the case of (i) registration of ADS transfers, the ADS transfer fee will be payable by the ADS Holder whose ADSs are being transferred or by the person to whom the ADSs are transferred, and (ii) conversion of ADSs of one series for ADSs of another series, the ADS conversion fee will be payable by the Holder whose ADSs are converted or by the person to whom the converted ADSs are delivered.

In the event of refusal to pay the depositary bank fees, the depositary bank may, under the terms of the deposit agreement, refuse the requested service until payment is received or may set off the amount of the depositary bank fees from any distribution to be made to the ADS holder. Certain depositary fees and charges (such as the ADS services fee) may become payable shortly after the closing of the ADS offering. Note that the fees and charges you may be required to pay may vary over time and may be changed by us and by the depositary bank. You will receive prior notice of such changes. The depositary bank may reimburse us for certain expenses incurred by us in respect of the ADR program, by making available a portion of the ADS fees charged in respect of the ADR program or otherwise, upon such terms and conditions as we and the depositary bank agree from time to time.

Amendments and Termination

We may agree with the depositary bank to modify the deposit agreement at any time without your consent. We undertake to give holders 30 days' prior notice of any modifications that would materially prejudice any of their substantial rights under the deposit agreement. We will not consider to be materially prejudicial to your substantial rights any modifications or supplements that are reasonably necessary for the ADSs to be registered under the Securities Act or to be eligible for book-entry settlement, in each case without imposing or increasing the fees and charges you are required to pay. In addition, we may not be able to provide you with prior notice of any modifications or supplements that are required to accommodate compliance with applicable provisions of law.

You will be bound by the modifications to the deposit agreement if you continue to hold your ADSs after the modifications to the deposit agreement become effective. The deposit agreement cannot be amended to prevent you from withdrawing the common shares represented by your ADSs (except as permitted by law).

We have the right to direct the depositary bank to terminate the deposit agreement. Similarly, the depositary bank may in certain circumstances on its own initiative terminate the deposit agreement. In either case, the depositary bank must give notice to the holders at least 30 days before termination. Until termination, your rights under the deposit agreement will be unaffected.

After termination, the depositary bank will continue to collect distributions received (but will not distribute any such property until you request the cancellation of your ADSs) and may sell the securities held on deposit. After the sale, the depositary bank will hold the proceeds from such sale and any other funds then held for the holders of ADSs in a non-interest bearing account. At that point, the depositary bank will have no further obligations to holders other than to account for the funds then held for the holders of ADSs still outstanding (after deduction of applicable fees, taxes and expenses).

In connection with any termination of the deposit agreement, the depositary bank may make available to owners of ADSs a means to withdraw the common shares represented by ADSs and to direct the depositary of such common shares into an unsponsored American depositary share program established by the depositary bank. The ability to receive unsponsored American depositary shares upon termination of the deposit agreement would be subject to satisfaction of certain U.S. regulatory requirements applicable to the creation of unsponsored American depositary shares and the payment of applicable depositary fees.

Books of Depositary

The depositary bank will maintain ADS holder records at its depositary office. You may inspect such records at such office during regular business hours but solely for the purpose of communicating with other holders in the interest of business matters relating to the ADSs and the deposit agreement.

The depositary bank will maintain in New York facilities to record and process the issuance, cancellation, combination, split-up and transfer of ADSs. These facilities may be closed from time to time, to the extent not prohibited by law.

Limitations on Obligations and Liabilities

The deposit agreement limits our obligations and the depositary bank's obligations to you. Please note the following:

- we and the depositary bank are obligated only to take the actions specifically stated in the deposit agreement without negligence or bad faith;
- the depositary bank disclaims any liability for any failure to carry out voting instructions, for any manner in which a vote is cast or for the effect of any vote, provided it acts in good faith and in accordance with the terms of the deposit agreement;
- the depositary bank disclaims any liability for any failure to determine the lawfulness or practicality of any action, for the content of any document forwarded to you on our behalf or for the accuracy of any translation of such a document, for the investment risks associated with investing in common shares, for the validity or worth of the common shares, for any tax consequences that result from the ownership of ADSs, for the credit-worthiness of any third party, for allowing any rights to lapse under the terms of the deposit agreement, for the timeliness of any of our notices or for our failure to give notice;
- we and the depositary bank will not be obligated to perform any act that is inconsistent with the terms of the deposit agreement;
- we and the depositary bank disclaim any liability if we or the depositary bank are prevented or forbidden from or subject to any civil or criminal penalty or restraint on account of, or delayed in, doing or performing any act or thing required by the terms of the deposit agreement, by reason of any provision, present or future of any law or regulation, or by reason of present or future provision of any provision of our Articles of Incorporation and By-laws or any provision of or governing the securities on deposit, or by reason of any act of God or war or other circumstances beyond our control;
- we and the depositary bank disclaim any liability by reason of any exercise of, or failure to exercise, any discretion provided for in the deposit agreement or in our Articles of Incorporation and By-laws or in any provisions of or governing the securities on deposit;
- we and the depositary bank further disclaim any liability for any action or inaction in reliance on the advice or information received from legal counsel, accountants, any person presenting Shares for deposit, any holder of ADSs or authorized representatives thereof, or any other person believed by either of us in good faith to be competent to give such advice or information;

- we and the depositary bank also disclaim liability for the inability by a holder to benefit from any distribution, offering, right or other benefit that is made available to holders of common shares but is not, under the terms of the deposit agreement, made available to you;

- we and the depositary bank may rely without any liability upon any written notice, request or other document believed to be genuine and to have been signed or presented by the proper parties;

- we and the depositary bank also disclaim liability for any consequential or punitive damages for any breach of the terms of the deposit agreement;

- no disclaimer of any Securities Act liability is intended by any provision of the deposit agreement;

- nothing in the deposit agreement gives rise to a partnership or joint venture, or establishes a fiduciary relationship, among us, the depositary bank and you as ADS holder; and

- nothing in the deposit agreement precludes Citibank (or its affiliates) from engaging in transactions in which parties adverse to us or the ADS owners have interests, and nothing in the deposit agreement obligates Citibank to disclose those transactions, or any information obtained in the course of those transactions, to us or to the ADS owners, or to account for any payment received as part of those transactions.

As the above limitations relate to our obligations and the depositary's obligations to you under the deposit agreement, we believe that, as a matter of construction of the clause, such limitations would likely to continue to apply to ADS holders who withdraw the common shares from the ADS facility with respect to obligations or liabilities incurred under the deposit agreement before the cancellation of the ADSs and the withdrawal of the common shares, and such limitations would most likely not apply to ADS holders who withdraw the common shares from the ADS facility with respect to obligations or liabilities incurred after the cancellation of the ADSs and the withdrawal of the common shares and not under the deposit agreement.

In any event, you will not be deemed, by agreeing to the terms of the deposit agreement, to have waived our or the depositary's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder. In fact, you cannot waive our or the depositary's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

Taxes

You will be responsible for the taxes and other governmental charges payable on the ADSs and the securities represented by the ADSs. We, the depositary bank and the custodian may deduct from any distribution the taxes and governmental charges payable by holders and may sell any and all property on deposit to pay the taxes and governmental charges payable by holders. You will be liable for any deficiency if the sale proceeds do not cover the taxes that are due.

The depositary bank may refuse to issue ADSs, to deliver, transfer, split and combine ADRs or to release securities on deposit until all taxes and charges are paid by the applicable holder. The depositary bank and the custodian may take reasonable administrative actions to obtain tax refunds and reduced tax withholding for any distributions on your behalf. However, you may be required to provide to the depositary bank and to the custodian proof of taxpayer status and residence and such other information as the depositary bank and the custodian may require to fulfill legal obligations. You are required to indemnify us, the depositary bank and the custodian for any claims with respect to taxes based on any tax benefit obtained for you.

Foreign Currency Conversion

The depositary bank will arrange for the conversion of all foreign currency received into U.S. dollars if such conversion is practical, and it will distribute the U.S. dollars in accordance with the terms of the deposit agreement. You may have to pay fees and expenses incurred in converting foreign currency, such as fees and expenses incurred in complying with currency exchange controls and other governmental requirements.

If the conversion of foreign currency is not practical or lawful, or if any required approvals are denied or not obtainable at a reasonable cost or within a reasonable period, the depositary bank may take the following actions in its discretion:

- convert the foreign currency to the extent practical and lawful and distribute the U.S. dollars to the holders for whom the conversion and distribution is lawful and practical;

- distribute the foreign currency to holders for whom the distribution is lawful and practical; or

- hold the foreign currency (without liability for interest) for the applicable holders.

Governing Law/Waiver of Jury Trial

The deposit agreement, the ADRs and the ADSs will be interpreted in accordance with the laws of the State of New York. The rights of holders of common shares (including common shares represented by ADSs) are governed by the laws of Sweden.

The deposit agreement provides that, to the extent permitted by law, ADS 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 common shares, the ADSs or the deposit agreement, including any claim under U.S. federal securities laws. If we or the depositary opposed a jury trial demand based on the waiver, the court would determine whether the waiver was enforceable in the facts and circumstances of that case in accordance with applicable case law. However, you will not be deemed, by agreeing to the terms of the deposit agreement, to have waived our or the depositary's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder.

Exhibit 8.1

List of Subsidiaries

Subsidiary	**Jurisdiction of incorporation or organization**
Calliditas Therapeutics, Inc.*	Delaware
Calliditas Therapeutics US Inc.	Delaware
Nefecon AB	Sweden
Genkyotex S.A.	France
Genkyotex Suisse S.A.	Switzerland

* Renamed Calliditas NA Enterprises Inc. effective July 1, 2021.

Exhibit 12.1

CERTIFICATION BY THE PRINCIPAL EXECUTIVE OFFICER PURSUANT TO SECURITIES EXCHANGE ACT RULES 13A-14(A) AND 15D-14(A) AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Renée Aguiar-Lucander, certify that:

1. I have reviewed this Annual Report on Form 20-F of Calliditas Therapeutics AB;

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

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

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

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

(b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

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

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

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

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

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

Date: April 27, 2021

By: /s/ Renée Aguiar-Lucander
Name: Renée Aguiar-Lucander
Title: Chief Executive Officer
(Principal Executive Officer)

Exhibit 12.2

CERTIFICATION BY THE PRINCIPAL FINANCIAL OFFICER PURSUANT TO SECURITIES EXCHANGE ACT RULES 13A-14(A) AND 15D-14(A) AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Fredrik Johansson, certify that:

1. I have reviewed this Annual Report on Form 20-F of Calliditas Therapeutics AB;

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

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

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

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

(b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

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

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

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

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

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

Date: April 27, 2021

By: /s/ Fredrik Johansson
Name: Fredrik Johansson
Title: Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 13.1

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

In connection with the Annual Report of Calliditas Therapeutics AB (the "Company") on Form 20-F for the period ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Renée Aguiar-Lucander, in my capacity as Chief Executive Officer and Chairman of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: April 27, 2021

By: /s/ Renée Aguiar-Lucander
Name: Renée Aguiar-Lucander
Title: Chief Executive Officer
(Principal Executive Officer)

Exhibit 13.2

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

In connection with the Annual Report of Calliditas Therapeutics AB (the "Company") on Form 20-F for the period ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Fredrik Johansson, in my capacity as Chief Financial Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: April 27, 2021

By: /s/ Fredrik Johansson
Name: Fredrik Johansson
Title: Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statement Form S-8 (333-240126) pertaining to the ESOP 2020 United States Sub-Plan (the "U.S. Sub-Plan") and the Long-term Performance Based Incentive Program (the "Board LTIP 2020") of Calliditas Therapeutics AB of our report dated April 27, 2021, with respect to the consolidated financial statements of Calliditas Therapeutics AB, included in this Annual Report (Form 20-F) for the year ended December 31, 2020.

/s/ Ernst & Young AB

Stockholm, Sweden
April 27, 2021