UNITED STATES
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, 2022

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: 001-36815

Ascendis Pharma A/S

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

The Kingdom of Denmark
(Jurisdiction of incorporation or organization)
Tuborg Boulevard 12
DK-2900 Hellerup, Denmark
(Address of principal executive offices)
Jan Møller Mikkelsen
President and Chief Executive Officer
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DK-2900 Hellerup, Denmark
Telephone: +45 70 22 22 44
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

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 one ordinary share, nominal value DKK 1 per share	ASND	The Nasdaq Stock Market LLC
Ordinary shares, nominal value DKK 1 per share*		The Nasdaq Stock Market LLC*

* 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:

57,152,295 ordinary shares
(as of December 31, 2022)

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

Note – Checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 from their obligations under those Sections.

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 definition of "large accelerated filer," "accelerated filer," and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

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. ☐

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. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

Auditor Firm ID:	**Auditor Name:**	**Auditor Location:**
1294	**Deloitte Statsautoriseret Revisionspartnerselskab**	**Copenhagen, Denmark**

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General

As used herein, references to "we", "us", the "company", "Ascendis", or "Ascendis Pharma", or similar terms in this annual report on Form 20-F shall mean Ascendis Pharma A/S and, as the context requires, its subsidiaries.

Our consolidated financial statements are presented in euros except where otherwise indicated, and are prepared in accordance with International Financial Reporting Standards ("IFRS"), as issued by the International Accounting Standards Board. All references in this annual report to "Dollars", "USD" and "$" are to U.S. Dollars, and all references to "euro", "EUR" or "€" are to European Union euro. Throughout this annual report, references to ADSs mean ADSs or ordinary shares represented by ADSs, as the case may be.

Special Note Regarding Forward-Looking Statements

This annual report contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "potential," "positioned," "seek," "should," "target," "will," "would," and other similar expressions that are predictions or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the timing or likelihood of regulatory filings and approvals for our product candidates;
- our expectations regarding the commercial availability of TransCon Growth Hormone ("TransCon hGH"), known by its brand name SKYTROFA® (lonapegsomatropin-tcgd), in the United States and related patient support services;
- the commercialization of our products and product candidates, if approved;
- our commercialization, marketing and manufacturing capabilities of our products and product candidates and associated devices;
- the scope, progress, results and costs of developing our product candidates or any other future product candidates, and conducting preclinical studies and clinical trials;
- our pursuit of oncology as our second of three independent therapeutic areas of focus and our development of a pipeline of product candidates related to oncology;
- our pursuit of ophthalmology as our third of three independent therapeutic areas of focus and our development of a pipeline of product candidates related to ophthalmology;
- our expectations regarding the potential market opportunities and patient populations for our products and product candidates, if approved for commercial use;
- our expectations regarding the potential advantages of our products and product candidates over existing therapies;
- our ability to enter into new collaborations;
- our expectations with regard to the ability to develop additional product candidates using our TransCon technologies and file Investigational New Drug Applications ("INDs") or similar for such product candidates;
- our expectations with regard to the ability to seek expedited regulatory approval pathways for our product candidates, including the potential ability to rely on the parent drug's clinical and safety data with regard to our product candidates;
- our expectations with regard to our current and future collaboration partners to pursue the development of our product candidates and submit INDs or similar for such product candidates;

- our development plans with respect to our products and product candidates;
- our pursuit of additional indications for TransCon hGH;
- our ability to develop, acquire and advance product candidates into, and successfully complete, clinical trials;
- the implementation of our business model and strategic plans for our business, our products and product candidates and technologies, including global commercialization strategies;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products and product candidates;
- our expectations regarding our ability to apply our technology platform and algorithm for product innovation to develop highly differentiated product candidates to address unmet medical needs;
- our ability to apply our platform technology to build a leading, fully integrated, global biopharmaceutical company;
- our use of our TransCon technologies to create new and potentially best-in-class therapies;
- estimates of our expenses, future revenue, capital requirements, our needs for additional financing and our ability to obtain additional capital;
- our financial performance;
- developments and projections relating to our market conditions, competitors and industry;
- the impact of international economic, political, legal, compliance, social and business factors, including inflation; and
- the effects on our business of the worldwide COVID-19 pandemic and the ongoing conflict in the region surrounding Ukraine and Russia.

These forward-looking statements are based on senior management's current expectations, estimates, forecasts and projections about our business and the industry in which we operate and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this annual report may turn out to be inaccurate. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section of this annual report titled "Item 3.D—Key Information—Risk Factors" and elsewhere in this annual report. You are urged to consider these factors carefully in evaluating the forward-looking statements. These forward-looking statements speak only as of the date of this annual report. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. Given these risks and uncertainties, you are cautioned not to rely on such forward-looking statements as predictions of future events.

You should read this annual report and the documents that we reference in this annual report and have filed as exhibits to this annual report completely and with the understanding that our actual future results may be materially different from what we expect. You should also review the factors and risks we describe in the reports we will file or submit from time to time with the U.S. Securities and Exchange Commission ("SEC") after the date of this annual report. We qualify all of our forward-looking statements by these cautionary statements.

Summary of Material Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties, including those described in "Item 3.D—Key Information—Risk Factors" in this annual report. You should carefully consider these risks and uncertainties when investing in our common stock. The principal risks and uncertainties affecting our business include the following:

- We have a limited operating history and we may incur significant losses in the future, which makes it difficult to assess our future viability.
- We may seek additional financing to achieve our goals, and a failure to obtain this capital if needed on acceptable terms, or at all, could force us to delay, limit, scale back or cease our commercialization activities, product development or any other or all operations.
- We are substantially dependent on the success of our products and product candidates, which may not be successful in nonclinical studies or clinical trials, receive regulatory approval or be successfully commercialized.
- Clinical drug development involves a lengthy and expensive process with uncertain outcomes, and we may encounter substantial delays in our clinical studies. Furthermore, results of earlier studies and trials may not be predictive of results of future trials.
- Interim, "top-line" 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.
- Our sales and marketing efforts may not be effective and we may not be successful in our commercial efforts.
- Competition in the biotechnology and pharmaceutical industries is intense and our competitors may discover, develop or commercialize products faster or more successfully than us. If we are unable to compete effectively our business, results of operations and prospects will suffer.
- We rely on third-parties to manufacture preclinical, clinical and commercial supplies of our products, product candidates and their device components.
- The parent drug, drug substance, drug product and other components of our products and product candidates are currently acquired from certain single-source suppliers. The loss of these suppliers, or their failure to supply could materially and adversely affect our business.
- Our operating results may vary significantly from period to period and these variations may be difficult to predict.
- The regulatory approval processes of the U.S. Food and Drug Administration, the European Medicines Agency and comparable authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.
- Failure to obtain or maintain adequate coverage and reimbursement for our product candidates could limit our ability to market those products and decrease our ability to generate revenue.
- If we are sued for allegedly infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in such litigation could harm our business.
- The potential effects of geopolitical conflicts, such as the military conflict between Russia and Ukraine could materially adversely impact our business, including our clinical trials, supply chain operation, regulatory timelines and commercial activities.
- The global pandemic caused by COVID-19 could materially adversely impact our business, including our clinical trials, supply chain operation, regulatory timelines and commercial activities.

The summary risk factors described above should be read together with the text of the full risk factors below in the section entitled "Risk Factors" and the other information set forth in this annual report on Form 20-F, including our consolidated financial statements and the related notes, as well as in other documents that we file with the SEC. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not precisely known to us or that we currently deem to be immaterial may also materially adversely affect our business, financial condition, results of operations, and future growth prospects.

PART I

Item 1 Identity of Directors, Senior Management and Advisers

Not applicable.

Item 2 Offer Statistics and Expected Timetable

Not applicable.

Item 3 Key Information

A. Reserved.

B. Capitalization and Indebtedness

Not applicable.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

Our business faces significant risks. You should carefully consider all of the information set forth in this annual report and in our other filings with 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 adversely affected by any of these risks. This report also contains forward-looking statements that involve risks and uncertainties. Our results could materially differ from those anticipated in these forward-looking statements, as a result of certain factors including the risks described below and elsewhere in this report and our other materials we file or furnish with the SEC. See "Special Note Regarding Forward-Looking Statements" above.

Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements

We have a limited operating history and we may incur significant losses in the future, which makes it difficult to assess our future viability.

We are applying our innovative TransCon technologies to build a leading, fully integrated, global biopharmaceutical company and develop a pipeline of product candidates with potential best-in-class profiles to address unmet medical needs. We currently have a pipeline of multiple independent endocrinology rare disease, oncology, and ophthalmology product candidates in development. We are also working to apply our TransCon technology platform in additional therapeutic areas to address unmet medical needs. On August 25, 2021, the U.S. Food and Drug Administration (the "FDA") approved TransCon hGH, known by its brand name SKYTROFA® and its international nonproprietary name lonapegsomatropin-tcgd in the U.S. for the treatment of pediatric patients one year and older who weigh at least 11.5 kg (25.4 lb) and have growth failure due to inadequate secretion of endogenous growth hormone. In addition, SKYTROFA (lonapegsomatropin), developed under the name TransCon hGH, was granted marketing authorisation by the European Commission ("EC") as a once-weekly subcutaneous injection for the treatment of children and adolescents ages 3 to 18 years with growth failure due to insufficient secretion of endogenous growth hormone on January 11, 2022.

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused substantially all of our efforts on our research and development activities relating to our product, TransCon hGH, and our lead product candidates, TransCon Parathyroid Hormone ("TransCon PTH") and its international nonproprietary name palopegteriparatide, TransCon C-Type Natriuretic Peptide ("TransCon CNP"), our product candidates in oncology and ophthalmology and our proprietary TransCon technologies. We have also focused significant efforts on the commercialization of TransCon hGH and in planning for the commercialization of TransCon PTH, if approved. We have a limited operating history upon which our shareholders and ADS holders can evaluate our business and prospects. Going forward, we may incur significant losses from our operations. We had a net loss of €583.2 million for the year ended December 31, 2022 and a net loss of €383.6 million for the year ended December 31, 2021. Our total equity was €263.3 million as of December 31, 2022 compared to €883.6 million as of December 31, 2021. Neither the net loss nor net profit we have experienced in prior years are necessarily indicative of our future results.

Apart from the FDA's approval of SKYTROFA and the EC's approval of SKYTROFA, none of our other product candidates have been approved for commercial sale by the FDA, the EC or similar non-U.S. regulatory authorities. The FDA has accepted for filing and granted Priority Review to our New Drug Application ("NDA") for use of TransCon PTH in adult patients with hypoparathyroidism and has set a Prescription Drug User Fee Act ("PDUFA") target action date of April 30, 2023. In the European Union ("EU"), a marketing authorisation application ("MAA") has also been submitted to the European Medicines Agency ("EMA") for TransCon PTH for use in adult patients with hypoparathyroidism. We expect that our annual operating expenses may increase over the next several years as we expand our research and development efforts and incur additional commercialization expenses, including those related to the potential commercialization of TransCon PTH. Although we have begun to receive revenue from commercial product sales, we may incur substantial operating losses for the foreseeable future as we execute our operating plan.

Possible future losses would have an adverse effect on our shareholders' equity. Further, the net losses or net income we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a reliable indication of our future performance.

We have limited revenue from commercial product sales and rely significantly on our TransCon technologies and TransCon product candidates.

We have limited revenue from commercial product sales of SKYTROFA in the U.S. and are yet to commercially launch SKYTROFA in the EU. Our ability to generate revenue will continue to depend significantly on our ability to successfully commercialize SKYTROFA in the U.S., to successfully launch and commercialize SKYTROFA in the EU, to successfully launch and commercialize TransCon PTH, if approved, to complete the research and development of our other product candidates and obtain the regulatory and marketing approvals necessary to commercialize such product candidates. Our ability to generate additional revenue from commercial product sales or pursuant to milestone payments or royalties from collaboration partners depends heavily on many factors, including but not limited to:

- completing research and preclinical and clinical development of our product candidates;
- obtaining additional regulatory approvals for our products and product candidates on our own, or together with our strategic collaboration partners;
- negotiating favorable terms of and entering into collaboration, licensing or other arrangements;
- our ability to commercialize or co-promote, and/or the ability of our collaboration partners to successfully commercialize, our products and product candidates;
- developing and sustaining a scalable manufacturing process for our products and product candidates, if approved;
- the market opportunities and patient populations for our products and product candidates, if approved, including with respect to TransCon hGH and TransCon PTH;
- obtaining market acceptance of our products and product candidates, if approved, as viable treatment options;

- addressing any competing technological and market developments;
- identifying, assessing, acquiring, in-licensing and/or developing new product candidates;
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how, and our ability to develop, manufacture and commercialize our product candidates and products without infringing intellectual property rights of others; and
- attracting, hiring, and retaining qualified personnel.

In cases where we are successful in obtaining regulatory approvals to market one or more of our product candidates (such as the approvals we have obtained for TransCon hGH), our revenue will be dependent, in part, upon the size of the markets in the territories for which regulatory approval is granted, the accepted price for the product, the availability of competing products, the ability to get reimbursement for our products at any price and the extent of our royalty rights for that territory. If the number of patients suitable for our product candidates is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect or the reasonably accepted population for treatment is narrowed by competition, physician choice, treatment guidelines or third-party payor restrictions, we may not generate significant revenue from the sale of such product candidates, even if approved. Limitations on our ability to generate revenue from commercial product sales or pursuant to up-front or milestone payments and royalties from collaboration partners would likely depress our market value and could impair our ability to raise capital, expand our business, discover or develop other product candidates or continue our operations.

We may seek additional financing to achieve our goals, and a failure to obtain this capital if needed on acceptable terms, or at all, could force us to delay, limit, scale back or cease our commercialization activities, product development or any other or all operations.

Since our inception, most of our resources have been dedicated to our research and development and commercialization activities. We have funded our operations primarily through issuance of preference shares, our ordinary shares and convertible debt securities and payments to us under collaboration agreements. For example, in March 2022, we received $557.9 million (€503.3 million) in net proceeds from an offering of convertible senior notes due 2028 after deducting the initial purchasers' discounts and commissions and estimated transaction costs. As of December 31, 2022, we had cash, cash equivalents and marketable securities totaling €742.9 million. We believe that we will continue to expend substantial resources for the foreseeable future, including costs associated with research and development and commercialization activities.

Based on our current operating plan, we believe that our existing cash, cash equivalents and marketable securities as of December 31, 2022 will be sufficient to meet our projected cash requirements for at least twelve months from the date of this annual report. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including, but not limited to:

- the manufacturing, selling and marketing costs associated with our products and product candidates, if approved, including the cost and timing of building our sales and marketing capabilities;
- the timing, receipt, and amount of sales of, or royalties on, TransCon hGH and any future products;
- the sales price and the availability of adequate third-party coverage and reimbursement for our products and product candidates, if approved;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- our ability to collect payments which are due to us from customers and collaboration partners (if any), which in turn is impacted by the financial standing of any such customers and collaboration partners;
- the progress, timing, scope, results and costs of our preclinical studies and clinical trials and manufacturing activities for our product candidates, including the ability to enroll patients in a timely manner for clinical trials;

- the time and cost necessary to obtain regulatory approvals for our product candidates and the costs of post-marketing studies that could be required by regulatory authorities;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the number and scope of preclinical and discovery programs that we decide to pursue or initiate;
- the potential acquisition and in-licensing of other technologies, products or assets;
- the time and cost necessary to respond to technological and market developments, including further development of our TransCon platform;
- the achievement of development, regulatory and commercial milestones resulting in the payment to us from collaboration partners of contractual milestone payments and the timing of receipt of such payments, if any;
- our progress in the successful commercialization and co-promotion of our products and product candidates, if approved, and our efforts to develop and commercialize our other existing product candidates;
- the market opportunities and patient populations for our products and product candidates, if approved, including with respect to TransCon PTH, and our ability to obtain market acceptance of our products and product candidates, if approved;
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of our product candidates;
- the extent to which we purchase ADSs prior to granting rights or awards for such shares under our equity incentive plans.

Additional funds may not be available if we need them or on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, scale back or cease our research and development and commercialization activities. Furthermore, uncertainty about the interest rate environment and rising interest rates, may make it more difficult, costly or dilutive for us to secure additional financing, which may have a negative impact on earnings and cash flow.

Raising additional capital may cause dilution to our holders of shares or ADSs, restrict our operations or require us to relinquish rights to our products or product candidates on unfavorable terms to us.

We may seek additional capital through a variety of means, including through public or private equity, debt financings or other sources, including up-front payments and milestone payments from strategic collaborations. To the extent that we raise additional capital through the issuance of convertible debt or equity securities, the ownership interest of our shareholders and ADS holders would be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our shareholders and ADS holders. Such financing may result in dilution to holders of shares or ADSs, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. If we raise additional funds through up-front payments or milestone payments pursuant to strategic partnerships with third-parties, we may have to relinquish valuable rights to our products or product candidates, or grant licenses on terms that are not favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Risks Related to Our Business

We are substantially dependent on the success of our products and product candidates, which may not be successful in nonclinical studies or clinical trials, receive regulatory approval or be successfully commercialized.

To date, we have invested a significant amount of our efforts and financial resources in research and development, including with respect to our proprietary TransCon technologies, and in commercialization activities. Our near-term prospects, including the extent of revenue from commercial product sales, will depend heavily on our successful development and commercialization of our products and product candidates, if approved. The clinical and commercial success of our products and product candidates and our TransCon technologies will depend on a number of factors, including the following:

- the outcome and successful execution of our ongoing and planned clinical trials of our products and product candidates;
- our ability and that of any collaboration partners to establish and maintain commercial-scale manufacturing processes for our products, product candidates and device components;
- whether our product candidates' safety, purity, potency, tolerability and/or efficacy profiles will be satisfactory to the EMA, the FDA and similar regulatory authorities to warrant marketing approval;
- whether the EMA, the FDA or similar regulatory authorities will require additional clinical trials prior to approving or issuing a positive opinion in order for our product candidates to be authorized, if ever;
- the prevalence and severity of adverse side effects of our products and product candidates;
- the occurrence of adverse events that implicate the TransCon technologies, including among any out-licensed product candidates;
- the timely receipt of necessary marketing authorizations or certifications for our product candidates and associated device components from the FDA, similar regulatory authorities and notified bodies;
- our ability and that of any collaboration partners to successfully commercialize our products or product candidates, if approved for marketing and sale by the FDA, the EC or similar regulatory authorities, including educating physicians and patients about the benefits, administration and use of such products;
- achieving and maintaining compliance with all applicable regulatory requirements;
- our expectations regarding the potential market opportunities and patient populations for our products and product candidates, including with respect to TransCon PTH;
- our progress in the successful commercialization and co-promotion of our products and product candidates, if approved, and our efforts to develop and commercialize our other existing product candidates;
- our ability to obtain market acceptance of our products or product candidates, if approved, including by patients and the medical community;
- our ability to obtain market acceptance of the device components of our combination products, such as the TransCon hGH auto-injector, and of our combination product candidates, if approved, such as the TransCon PTH drug delivery device, including by patients and the medical community;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments;
- obtaining and sustaining an adequate level of coverage and reimbursement for our products and product candidates by third-party payors;
- the effectiveness of our and any collaboration partners' marketing, sales and distribution strategies and operations;

- our ability and that of any collaboration partners, or any third-party manufacturer we contract with, to manufacture supplies of our products and product candidates and to develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practice ("cGMP"), or similar requirements;
- enforcing intellectual property rights in and to our products and product candidates;
- avoiding third-party interference, opposition, derivation or similar proceedings with respect to our patent rights, and avoiding other challenges to our patent rights and patent infringement claims; and
- continued acceptable safety profiles of our products and product candidates following any potential approval.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any collaboration partners.

We cannot be certain that we will be able to successfully commercialize any of our products or that such products will be approved in other jurisdictions, and we cannot be certain that any of our product candidates, including TransCon PTH, will ever be approved or successfully commercialized, or that we will ever generate revenue from sales of such product candidates. If we are not successful in completing the development of, obtaining approval for, and commercializing our product candidates, or are significantly delayed in doing so, our business will be harmed.

Our sales and marketing efforts may not be effective and we may not be successful in our commercial efforts.

Prior to launching our commercial sales in 2021, as a company we had no prior experience commercializing approved products. The success of our commercialization efforts is difficult to predict and subject to the effective execution of our business plan, including, among others, the continued development of our internal sales, marketing, and distribution capabilities and our ability to navigate the significant expenses and risks involved with the development and management of such capabilities. For example, our planned commercial launch of TransCon PTH, if approved, may not develop as planned or anticipated, which may require us to, among others, adjust or amend our business plan and incur significant expenses. Further, given our limited experience commercializing products, we do not have a long track record of successfully executing commercial launches. If we are unsuccessful in accomplishing our objectives and executing on our business plan, or if our commercialization efforts do not develop as planned, we may not be able to successfully commercialize our approved products and any future approved products, we may require significant additional capital and financial resources, we may not become profitable, and we may not be able to compete against more established companies in our industry.

Factors which may affect the success of our commercialization efforts include, but are not limited to:

- our ability to hire and retain required and qualified sales and marketing personnel, including in connection with any specialty sales organization for specific products or product candidates, if approved;
- our ability to provide sufficient training to develop and strengthen the technical expertise of our sales and marketing personnel;
- our ability to provide required support materials and resources to our sales personnel to help them educate physicians and healthcare providers regarding our products, including the proper administration of our products; and
- our resources to meet and timely fulfill supply obligations to our customers.

Additionally, we or any collaboration partners may be required to build and/or maintain marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third-parties to perform these services, and we or any collaboration partners may not be successful in doing so. Except for our license agreements with VISEN for Greater China and certain limited sales and distribution agreements with specialty distributors and specialty pharmacies in the United States for TransCon hGH, we have no sales, marketing or distribution agreements for TransCon hGH, TransCon PTH, TransCon CNP, or our other product candidates. We may enter into arrangements with third-parties to market and sell our products and product candidates, if approved, in one or multiple geographies. However, we may not be able to enter into such arrangements with others on acceptable terms, or at all. To the extent that we enter into such arrangements with other companies, our revenues, if any, will depend on the terms of any such arrangements and the efforts of others. These efforts may turn out not to be sufficient.

The acceptance and commercial success of our products and product candidates, if approved, will depend, in part, upon the degree of acceptance among physicians, patients, patient advocacy groups, third-party payors and the medical community.

Even after obtaining FDA or other regulatory approvals, our products and product candidates, if approved, may not achieve significant market acceptance among physicians, patients, patient advocacy groups, third-party payors and the medical community. The degree of market acceptance, if any, for our products for which marketing approval is obtained will depend on a number of factors, including:

- the safety, purity, potency and/or efficacy of the products as demonstrated in clinical trials;
- the prevalence and severity of any side effects and overall safety profile of the product;
- the perceived safety of the TransCon technologies;
- the convenience and features of the auto-injector or drug delivery device used to administer the drug;
- the clinical indications for which the product is approved;
- education of, and acceptance by, physicians, major operators of clinics and patients of the product as a safe and effective treatment and their willingness to pay for them;
- relative convenience and ease of administration of our products;
- the potential and perceived advantages of our products over current treatment options or alternative treatments, including future alternative treatments;
- the availability of supply of our products and their ability to meet market demand;
- marketing and distribution support for our products;
- the quality of our relationships with patient advocacy groups; and
- coverage and reimbursement policies of government and other commercial and third-party payors.

If our products or product candidates that obtain regulatory approval do not achieve significant market acceptance or commercial success, this could harm our business, results of operations and prospects, and the value of our shares or ADSs.

Our estimated market opportunities for our products and product candidates, if approved, are subject to numerous uncertainties and may prove to be inaccurate. If we have overestimated the size of our market opportunities, our future growth may be limited.

Our business plan is based in part on our estimated addressable markets and market opportunities for our products and product candidates, if approved, which are based on a variety of inputs, including data published by third parties, our own market insights and internal market intelligence, and internally generated data and assumptions. We have not independently verified any third-party information and there can be no assurance as to its accuracy or completeness. Such estimates, whether obtained or derived from third-party sources or developed internally, are subject to significant uncertainty and are based on assumptions and estimates that may not prove to be accurate. While we believe the market opportunity estimates underlying our business plan are reasonable, such information is inherently imprecise. In addition, our assumptions and estimates of market opportunities are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including but not limited to those described in this report. If this third-party or internally generated data prove to be inaccurate or we make errors in our assumptions based on that data, our actual market may be more limited than our estimates. In addition, these inaccuracies or errors may cause us to misallocate capital and other critical business resources, which could harm our business.

Clinical drug development involves a lengthy and expensive process with uncertain outcomes, and we may encounter substantial delays in our clinical studies. Furthermore, results of earlier studies and trials may not be predictive of results of future trials.

Before obtaining marketing approval from regulatory authorities for the sale of any product candidates, we must conduct extensive clinical studies to demonstrate the safety, purity, potency and/or efficacy of the product candidates in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process; the results of preclinical and clinical studies of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy despite having progressed through preclinical studies and initial clinical trials. A number of companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates.

We may experience delays or setbacks in our ongoing clinical trials, and we do not know whether future clinical trials will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure to:

- generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- reach consensus with regulatory authorities on study design or implementation of the clinical trials and/or obtain regulatory authorization to commence a trial;
- reach agreement on acceptable terms with prospective contract research organizations (“CROs”) and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- identify, recruit and train suitable clinical investigators;
- obtain institutional review board (“IRB”) or ethics committee approval at each site;
- manufacture, test, release, validate or import sufficient quantities of drug product for use in a trial;
- recruit, screen and enroll suitable patients to participate in a trial;
- have patients complete a trial or return for post-treatment follow-up;
- ensure that clinical sites observe trial protocol or continue to participate in a trial;
- address any patient safety concerns that arise during the course of a trial;

- address any conflicts with new or existing laws or regulations; or
- initiate or add a sufficient number of clinical trial sites.

The COVID-19 pandemic has had, and may continue to have an evolving impact on the conduct of clinical trials of investigational therapeutic candidates, and any challenges which may arise, for example, from quarantines, site closures, travel limitations, interruptions to the supply chain for our product candidates, or other considerations if site personnel or trial subjects become infected with COVID-19, which may lead to difficulties in meeting protocol-specified procedures, including administering or using the product candidate or adhering to protocol-mandated visits and laboratory/diagnostic testing, unavoidable protocol deviations due to COVID-19 illness and/or COVID-19 control measures, which will likely vary depending on many factors, including the nature of disease under study, the trial design, and in what region(s) the study is being conducted.

Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating. In addition, our Phase 3 foresiGHt Trial includes clinical sites located in Ukraine, and the invasion of Ukraine has impacted and may further impact our ability to monitor or collect data from patients at those clinical sites, which could affect the integrity of trial data obtained from those sites. We will continue to closely monitor the rapidly evolving geopolitical situation in Ukraine and Russia and its impact on our clinical trial operations and timelines.

We could also encounter delays if a clinical trial is suspended or terminated by us for a product candidate, by the IRBs of the institutions in which such trials are being conducted, by an independent data safety monitoring board, for such trial or by the FDA or similar regulatory authorities. Such authorities, or we, may suspend or terminate a clinical trial 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 or similar regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Further, we are conducting, and plan to conduct, clinical trials in sites outside of the United States. Conducting clinical trials in foreign countries presents additional risks that may delay completion of clinical trials. These risks include the failure of physicians or enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. In addition, the EMA or the FDA may determine that the clinical trial results obtained in foreign subjects do not establish the safety, purity, potency and/or efficacy of a product candidate when administered in EU or U.S. patients, and are thus not supportive of approval of a MAA in the EU or of an NDA, or Biologics License Application ("BLA"), in the United States. As a result, the EMA or the FDA may not accept data from clinical trials conducted outside the EU or the United States, respectively, and may require that we conduct additional clinical trials or obtain additional data before we can submit an NDA or BLA in the United States or a MAA in the EU. The EMA or the FDA may even require us to conduct additional clinical trials in the EU or the United States, respectively, before we are able submit an NDA, BLA, MAA or other marketing application for any of our product candidates.

If there are delays in the completion of, or termination of, any clinical trial of our product candidates or if we are required to conduct additional clinical trials in addition to those we have currently planned, the commercial prospects of our product candidates may be harmed, and our ability to generate revenue from commercial product sales from any of these product candidates will be delayed. In addition, any delays in completing the clinical trials will increase costs, slow down our product candidate development and approval process and jeopardize the ability to commence product sales and generate revenue from commercial product sales. Any of these occurrences may significantly harm our business, financial condition and prospects. Clinical trial delays may also allow our competitors to bring products to market before we do, which could impair our ability to obtain orphan exclusivity for our products that potentially qualify for orphan drug designation. 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.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

It is currently unclear to what extent the UK will seek to align its regulations with the EU. The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation). On January 17, 2022, the UK Medicines and Healthcare products Regulatory Agency ("MHRA") launched an eight-week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022 and aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The outcome of the consultation will be closely watched and will determine whether the UK chooses to align with the CTR or diverge from it to maintain regulatory flexibility. A decision by the UK not to closely align its regulations with the new approach that will be adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and/or make it harder to seek a marketing authorisation in the EU for our product candidates on the basis of clinical trials conducted in the UK.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be adversely impacted.

Certain of our product candidates are in various stages of preclinical development and we may not be successful in our efforts to successfully develop these products or expand our pipeline of product candidates.

A key element of our strategy is to expand our pipeline of product candidates utilizing our proprietary TransCon technologies, and to advance such product candidates through clinical development. Certain of our product candidates are in preclinical development and may require significant time and additional research and development before we can submit INDs or equivalent foreign regulatory applications to regulatory authorities to begin clinical studies. Of the large number of drugs and biologics in development, only a small percentage of such drugs successfully complete the EMA or FDA regulatory approval process and are commercialized. Accordingly, even if we are able to continue to fund such development programs, our product candidates may not be advanced to clinical studies or be successfully developed or commercialized. In addition, our preclinical product candidates may not demonstrate the advantages we expect from application of our TransCon technologies in preclinical studies. In such event, we may decide not to progress any such product candidates into clinical trials.

Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Although our research and development efforts to date have resulted in several development programs, we may not be able to develop product candidates that are safe, pure, potent and/or effective. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development or commercialization for many reasons, including the following:

- the research methodology used and our TransCon technologies may not be successful in creating potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may nevertheless be covered by third-parties' intellectual property rights or other types of exclusivity and we may not be able to obtain a license from such third-party or the license terms may not be acceptable to us;
- the market opportunity for a product candidate may change during our program or we may discover that such market opportunity was smaller than initially expected so that such a product may become financially unfeasible to continue to develop;
- a product candidate may be demonstrated to have harmful side effects or not to be effective, or otherwise not to meet other requirements for regulatory approval;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, or reimbursable by third-party payors, if applicable.

Even if we are successful in continuing to expand our pipeline, through our own research and development efforts or by pursuing in-licensing or acquisition of product candidates, the potential product candidates that we identify or acquire may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize a product pipeline, we may not be able to generate revenue from commercial product sales in future periods or achieve or sustain profitability.

Interim, "top-line" 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 publicly disclose preliminary or top-line data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line 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, top-line data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, top-line, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

By expending our limited resources to pursue particular product candidates and areas of focus we may fail to capitalize on product candidates or areas of focus that are more profitable or for which there is a greater likelihood of success.

We have focused on research programs and product candidates within the endocrinology, oncology and ophthalmology therapeutic areas. As a result, we may forego or delay pursuit of opportunities with other product candidates or in other therapeutic areas 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 research and 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.

We rely on third parties to conduct our nonclinical studies and clinical trials. If these third-parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for, or commercialize, our product candidates.

We do not currently have the ability to independently conduct clinical trials or IND-enabling nonclinical studies. We rely on medical institutions, clinical investigators, contract laboratories, collaboration partners and other third-parties, such as CROs, to conduct clinical trials of our products and product candidates. The third-parties with whom we contract for execution of our clinical trials play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, these third-parties are not our employees, and except for contractual duties and obligations, we control only certain aspects of their activities and have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely on these third-parties to conduct our nonclinical studies and our clinical trials, we remain responsible for ensuring that each of our nonclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on third-parties does not relieve us of our regulatory responsibilities. We and these third-parties are required to comply with current good laboratory practices ("GLPs"), for nonclinical studies, and good clinical practices ("GCPs"), for clinical studies. GLPs and GCPs are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our products in nonclinical and clinical development, respectively. Regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our third-party contractors fail to comply with applicable regulatory requirements, including GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the EMA, the FDA, or similar regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot be certain 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 products produced under cGMP or similar foreign regulations outside the United States. The failure of our contract manufacturers to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Our products and product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval, if any. If any of our product candidates receives marketing approval and subsequently causes undesirable side effects, the ability to market the product candidates could be compromised.

Undesirable side effects caused by any of our approved products or 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 or similar authorities. In the event that trials conducted by us or any collaboration partners, or trials we conduct with our product candidates, reveal a high and unacceptable severity and prevalence of side effects, such trials could be suspended or terminated and the FDA or similar regulatory authorities could order any collaboration partners or 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 prospects significantly.

Additionally, if we successfully develop a product candidate and it receives marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy ("REMS") to ensure that the benefits of treatment with such product candidate outweigh the risks for each potential patient, which may include, among other things, a communication plan to health care practitioners, patient education, extensive patient monitoring or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry. Foreign regulatory authorities may require us to adopt similar risk management measures.

In addition, in the event that any of our product candidates receives regulatory approval and we or others later identify undesirable side effects caused by one of our products, including TransCon hGH, a number of potentially significant negative consequences could occur, including:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or any collaboration partners, may be required to recall the product;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof, including the imposition of a REMS or requirements for similar actions, such as patient education, certification of health care professionals or specific monitoring;
- we, or any collaboration partners, may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require additional warnings on the label, including "boxed" warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

For example, a number of adverse reactions have been reported among users of daily somatropin, and we may observe and be required report similar adverse reactions for users of SKYTROFA. This reporting may result in Dear Healthcare Provider letters or other communications containing warnings or other safety information about the product.

Any of the foregoing events could prevent us, or any collaboration partners, from achieving or maintaining market acceptance of our products or product candidates, if approved, and could result in the loss of significant revenue to us, which would harm our results of operations and business.

Competition in the biotechnology and pharmaceutical industries is intense and our competitors may discover, develop or commercialize products faster or more successfully than us. If we are unable to compete effectively, our business, results of operations and prospects will suffer.

The markets in which we intend to compete are undergoing, and are expected to continue to undergo, rapid and significant technological changes. Some of our products and product candidates are for fields in which competitive products already exist and are established. We expect competition to intensify as technological advances are made or new drugs and biotechnology products are introduced. New developments by competitors may render our products and current or future product candidates and/or technologies non-competitive, obsolete or not economical. Our competitors' products may be more efficacious or marketed and sold more effectively than our products and product candidates.

We are aware of several pharmaceutical and biopharmaceutical companies that have commenced clinical studies of products or have successfully commercialized products addressing areas that we are targeting. A permanently PEGylated long-acting growth hormone (brand name Jintrolong) developed by GeneScience Pharmaceuticals Co., Ltd. is available in China and the Somatropin Biopartners product (LB03002), is available in Korea. Novo Nordisk has received regulatory approval in the United States, Japan, and Europe of once-weekly somapacitan (brand name Sogroya) for replacement of endogenous growth hormone in adult patients with GHD and filed somapacitan in the United States, Japan, and Europe for pediatric GHD. Pfizer (in collaboration with OPKO Health Inc.) has received regulatory approval of once-weekly somatrogon (brand name NGENLA) in the EU, Canada, Australia, Japan, Taiwan, the United Arab Emirates and Brazil for pediatric GHD. In January 2022, Pfizer (in collaboration with OPKO Health) announced the FDA issued a Complete Response Letter for the BLA for somatrogon. Other experimental growth hormone therapies based on permanent modification are in different stages of clinical development by various companies, including GeneScience Pharmaceuticals Co., Ltd., Genexine Inc., I-MAB, and JCR Pharmaceuticals Co., Ltd. In addition, Shire-NPS Pharmaceuticals Inc., a Takeda company owns the rights to parathyroid hormone (brand name NATPARA®), a treatment for hypoparathyroidism. Parathyroid hormone was voluntarily recalled in September 2019 in the U.S. and is now only available to a limited number of patients through a Special Use Program offered by its manufacturer, Shire-NPS Pharmaceuticals Inc., a Takeda company. In October 2022, Takeda announced manufacturing of all strengths of NATPARA will be discontinued globally at the end of 2024. In addition, we are aware of several academic groups and companies working on making longer-acting agonists of the PTH receptor, or PTH1R. Other companies and groups are developing or commercializing therapies for hypoparathyroidism, including Entera Bio, Extend Biosciences, Massachusetts General Hospital, Amolyt Pharma, MBX Biosciences and Eli Lilly and Company. Other companies are developing therapies for achondroplasia, including BioMarin, and QED Therapeutics. BioMarin Pharmaceutical, Inc. has received regulatory approval for vosoritide (brand name VOXZOGO) in the United States, EU and Japan for the treatment of achondroplasia. Rainier Therapeutics, Inc., QED Therapeutics, Sanofi, Ribomic, ProLynx, and Astellas, PhaseBio have achondroplasia programs in various clinical stages.

Other companies are developing toll like receptor agonists for cancer immunotherapy including: CureVac N.V., Seven and Eight Biopharmaceuticals Inc., Idera Pharmaceuticals, Inc., Checkmate Pharmaceuticals, Inc., Exicure, Inc., Bolt Therapeutics, Inc., and Silverback Therapeutics, Inc. In addition to product-based competition, our TransCon technologies face technology-based competition as we believe other companies are developing or evaluating enhanced drug delivery and sustained release technologies. In particular, we believe Nektar Therapeutics, OPKO Health, Inc., ProLynx LLC, MBX Biosciences and Serina Therapeutics, Inc. are developing technologies that use reversible linkers and that may be competitive with our TransCon technologies.

TransCon hGH is approved by the FDA in the U.S. under the brand name SKYTROFA for the treatment of pediatric patients one year and older who weigh at least 11.5 kg (25.4 lb) and have growth failure due to inadequate secretion of endogenous growth hormone. In addition, the EC has granted a marketing authorisation for SKYTROFA, developed under the name TransCon hGH, as a once weekly subcutaneous injection for the treatment of children and adolescents ages 3 to 18 years with growth failure due to insufficient secretion of endogenous growth hormone. However, it is also possible that our competitors will commercialize competing drugs or treatments before we can launch any other product candidates that are ultimately approved by regulatory authorities. We also anticipate that we will face increased competition in the future as new companies enter into our current and target markets.

Furthermore, to the extent we are developing TransCon product candidates that incorporate already approved drugs, we face competition from the pharmaceutical companies which are currently marketing such approved products. These pharmaceutical companies can generally be expected to seek to delay the introduction of competing products through a variety of means including:

- filing new formulation patent applications on drugs whose original patent protection is about to expire;
- filing an increasing number of patent applications that are more complex and costly to challenge;
- filing suits for alleged patent infringement that automatically delay FDA or foreign regulatory authorities' approval;
- filing suits that challenge our marketing and promotion efforts;
- developing patented controlled-release or other "next-generation" products, which may compete with TransCon product candidates;
- establishing exclusive contracts with third-party payors; or
- changing product claims and product labeling.

Any one of these strategies may increase the costs and risks associated with our efforts to develop and commercialize our products and product candidates and may delay or altogether prevent such development or commercialization.

Many of our competitors have:

- significantly greater name recognition, financial, marketing, research, drug portfolios, drug development and technical and human resources than we have at every stage of the discovery, development, manufacturing and commercialization process and additional mergers and acquisitions in the biotechnology industries may result in even more resources being concentrated in our competitors;
- more extensive experience in commercializing drugs, conducting preclinical testing, conducting clinical studies, obtaining regulatory approvals, challenging patents and in manufacturing and marketing pharmaceutical products;
- products that have been approved or are in late stages of development; and
- collaboration arrangements in our target markets with leading companies and research institutions.

With respect to our products and product candidates that we successfully develop, we will face competition based on many different factors, including:

- the safety and effectiveness of such product candidates;
- the timing of and specific circumstances relating to regulatory approvals for these product candidates;
- the availability and cost of manufacturing, marketing and sales capabilities;
- the effectiveness of our marketing and sales capabilities;
- the price of our product candidates;
- the availability and amount of third-party reimbursement for our product candidates;
- the product's convenience and ease of administration compared to alternative treatments; and
- the strength of our patent position.

In addition, academic institutions, government agencies, and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaborative or licensing relationships with our competitors.

Our competitors may develop or commercialize products with significant advantages in regard to any of these factors. Our competitors may therefore be more successful in commercializing their products than we are, which could adversely affect our business, results of operations and prospects, and the value of our shares or ADSs.

Our proprietary TransCon technologies include a new approach to extending the residence time and duration of action of a variety of drug products.

Our TransCon technologies have been developed to improve the delivery of a variety of drug products. TransCon hGH is approved by the FDA in the U.S. under the brand name SKYTROFA (lonapegsomatropin-tcgd) for the treatment of pediatric patients one year and older who weigh at least 11.5 kg (25.4 lb) and have growth failure due to inadequate secretion of endogenous growth hormone. The EC has granted a marketing authorisation for SKYTROFA, developed under the name TransCon hGH, as a once weekly subcutaneous injection for the treatment of children and adolescents ages 3 to 18 years with growth failure due to insufficient secretion of endogenous growth hormone. However, we cannot be certain that any of our other products or product candidates using our TransCon technologies will be deemed safe or efficacious (or that TransCon hGH will be deemed safe or effective for other indications), nor that any aspects of our TransCon technologies will yield additional product candidates that could be commercially valuable. Further, one of our two carrier systems, the TransCon hydrogel carrier system, has limited experience in humans. As a result, our TransCon hydrogel carriers, when dosed extensively in humans, may fail to perform as we expect. Failure of any of our product candidates to be successfully developed, approved and commercialized may result in our TransCon technologies being viewed as an ineffective approach to developing drug products which would harm our business and prospects.

We apply our TransCon technologies to both approved and unapproved parent drugs to extend the half-life of such drugs in the body, and to enhance the overall benefit of a given therapy. Even when applied to approved parent drugs, we have generated limited clinical data on our product candidates using our systemic TransCon technologies with respect to safety and efficacy for long-term treatment in humans. The long-term safety and efficacy of our TransCon technologies and the extended life in the body of our product candidates utilizing TransCon technologies is unknown, and it is possible that our product candidates may have an increased risk of unforeseen reactions following extended treatment relative to other approved products. If extended treatment with our products or product candidates utilizing TransCon in our ongoing or future clinical trials results in any concerns about the safety or efficacy of our TransCon technologies, we may be unable to successfully develop or commercialize our products or product candidates.

We have limited clinical data on product candidates utilizing our TransCon technologies to indicate whether they are safe or effective for long-term use in humans.

Our products and product candidates are designed to transiently link a parent drug molecule to select TransCon carriers via our TransCon linkers. Once injected, we believe that our prodrugs predictably release the unmodified parent drug molecule over time, thus preserving the parent drug's original mode of action, and, we believe, the parent drug's original safety and efficacy profile. We believe that our TransCon carriers remain bound to our TransCon linkers and that they are cleared from the body predominantly by renal filtration and biliary transport with fecal excretion. We have limited clinical data regarding utilizing the systemic TransCon technologies to indicate whether they are safe, pure, potent and/or effective for long-term use in humans, including the safety of any degradation products that may result after the TransCon carrier and TransCon linker are cleaved from the parent drug molecule. If treatment with any of our product candidates in our clinical trials results in concerns about their safety or efficacy, we and any collaboration partners may be unable to successfully develop or commercialize any or all of our TransCon technologies based on such product candidates or enter into collaborations with respect to our product candidates.

We depend on certain collaboration partners to develop and conduct clinical studies with, obtain regulatory approvals for, market and sell product candidates, and if such collaboration partners fail to perform as expected, or are unable to obtain the required regulatory approvals for such product candidates, the potential of such product candidates would be significantly reduced and our business would be significantly harmed.

We rely on our collaboration partners to conduct certain clinical studies. For example, in November 2018, we announced the formation of VISEN Pharmaceuticals ("VISEN"), a company established to develop, manufacture, and commercialize our endocrinology rare disease therapy candidates in Greater China. In connection with the formation of VISEN, we granted VISEN exclusive rights to develop and commercialize our rare disease endocrinology products based on our proprietary TransCon technologies, including TransCon hGH, TransCon PTH and TransCon CNP, in Greater China for use in all human indications, subject to certain exceptions. We may also enter into collaboration agreements with other parties in the future relating to our other product candidates.

If our collaboration partners do not perform in the manner we expect or fulfill their responsibilities in a timely manner, or at all, if our agreements with them terminate or if the quality or accuracy of the clinical data they obtain is compromised, the clinical development, regulatory approval and commercialization efforts related to our collaboration product candidates could be delayed or terminated and it could become necessary for us to assume the responsibility at our own expense for the clinical development of such product candidates. In that event, we would likely be required to limit the size and scope of efforts for the development and commercialization of such product candidate, to seek additional financing to fund further development, or to identify alternative collaboration partners, and our potential to generate future revenue from royalties and milestone payments from such product candidate would be significantly reduced or delayed and our business would be harmed. Our existing collaborations and any future collaboration arrangements that we may enter into with third-parties may not be scientifically or commercially successful. In addition to the risks inherent in the development of a drug product candidate, factors that may affect the success of our collaborations include the following:

- our collaboration partners have the unilateral ability to choose not to develop a collaboration product for one or more indications for which such product has been or is currently being evaluated, and our collaboration partners may choose to pursue an indication that is not in our strategic best interest or to forego an indication that they believe does not provide significant market potential even if clinical data is supportive of further development for such indication;
- our collaboration partners may choose not to develop and commercialize our collaboration products in certain relevant markets;
- our collaboration partners may take considerably more time advancing our product candidates through the clinical and regulatory process than we currently anticipate, which could materially delay the achievement of milestones and, consequently the receipt of milestone payments from our collaboration partners;
- our collaboration partners have substantial discretion under their respective agreements regarding how they structure their efforts and allocate resources to fulfill their obligations to diligently develop, obtain regulatory approval for and commercialize our collaboration products;
- our collaboration partners control all aspects of commercialization efforts under their respective license agreements and may change the focus of their development and commercialization efforts or pursue higher-priority programs and, accordingly, reduce the efforts and resources allocated to their collaborations with us;
- our collaboration partners are solely responsible for obtaining and maintaining all regulatory approvals and we or our collaboration partners may fail to develop a commercially viable formulation or manufacturing process for our product candidates, and we or our collaboration partners may fail to manufacture or supply sufficient drug substance for commercial use, if approved, which could result in lost revenue under such collaborations;

- our collaboration partners may not comply with all applicable regulatory requirements or may fail to report safety data in accordance with all applicable regulatory requirements;
- if any of our agreements with our collaboration partners terminate, we will no longer have any rights to receive potential revenue under such agreement, in which case we would need to identify alternative means to continue the development, manufacture and commercialization of the affected product candidates, alone or with others;
- our collaboration partners have the discretion to sublicense their rights with respect to our collaboration technology in connection with collaboration product candidates to one or more third-parties without our consent; and
- our collaboration partners may be pursuing alternative technologies or developing alternative products, either on their own or in collaboration with others, that may be competitive with products on which they are collaborating with us or which could affect our collaboration partners' commitment to the collaboration.

The timing and amount of any milestone and royalty payments we may receive under agreements with collaboration partners and the value of any equity we own in our collaboration partners (such as the equity we own in VISEN) will depend on, among other things, the efforts, allocation of resources, and successful development and commercialization of our product candidates by our collaboration partners. We cannot be certain that any development and regulatory milestones will be achieved or that we will receive any future milestone payments under agreements we may enter into with collaboration partners. In addition, in certain circumstances we may believe that we have achieved a particular milestone and the applicable collaboration partner may disagree with our belief. In that case, receipt of that milestone payment may be delayed or may never be received, which may require us to adjust our operating plans. We also cannot be certain that any equity we own in our collaboration partners (such as the equity we own in VISEN) will maintain its value or grow in value.

We may form additional strategic collaborations in the future with respect to our proprietary programs, but we may not realize the benefits of such collaborations.

We may form strategic collaborations, create joint ventures or enter into licensing arrangements with third-parties with respect to our independent programs that we believe will complement or augment our existing business. We have historically engaged, and intend to continue to engage, in partnering discussions with a range of biopharmaceutical companies and could enter into new collaborations at any time. For example, in November 2018, we announced the formation of VISEN, a company established to develop, manufacture, and commercialize our endocrinology rare disease therapies in Greater China. In connection with the formation of VISEN, we granted VISEN exclusive rights to develop and commercialize our rare disease endocrinology products based on our proprietary TransCon technologies, including TransCon hGH, TransCon PTH and TransCon CNP, in Greater China for use in all human indications, subject to certain exceptions. We face significant competition in seeking appropriate strategic partners, and the negotiation process to secure appropriate terms is time-consuming and complex. Any delays in identifying suitable development partners and entering into agreements to develop our product candidates could also delay the commercialization of our product candidates, which may reduce their competitiveness even if they reach the market. Moreover, we may not be successful in our efforts to establish such a strategic partnership for any future product candidates and programs on terms that are acceptable to us, or at all. This may be for a number of reasons. For example, under our collaboration with VISEN, VISEN has a right of first negotiation to develop certain of our endocrinology product candidates in Greater China, so our ability to negotiate such a collaboration with suitable third-parties may be hampered by such rights we granted to VISEN. Additionally, our product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort, our research and development pipeline may be viewed as insufficient, and/or third-parties may not view our product candidates and programs as having sufficient potential for commercialization, including the likelihood of an adequate safety and efficacy profile. Even if we are successful in entering into a strategic alliance or license arrangement, there is no guarantee that the collaboration will be successful, or that any future collaboration partner will commit sufficient resources to the development, regulatory approval, and commercialization of our product candidates, or that such alliances will result in us achieving revenues that justify such transactions.

We may seek orphan designation for some of our product candidates and we may be unsuccessful, or may be unable to maintain the benefits associated with orphan designation, including the potential for market exclusivity, for product candidates for which we obtain orphan designation.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs or biologics intended to treat relatively small patient populations as orphan drug products. Under the Orphan Drug Act, the FDA may designate a drug or biologic as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals 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 EU, orphan designation is granted by the EC based on a scientific opinion of the EMA's Committee for Orphan Medicinal Products. A medicinal product may be designated as orphan if its sponsor can establish that (i) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (ii) either (a) such condition affects no more than 5 in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (iii) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the medicinal product will be of significant benefit to those affected by the condition. Orphan designation must be requested before submitting a BLA or NDA in the United States or a MAA in the EU.

If a drug or biologic with an orphan designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug or biologic is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug or biologic for the same disease or condition for a seven-year period, except in limited circumstances. If our competitors are able to obtain orphan drug exclusivity prior to us, for products that constitute the "same drug" and treat the same diseases or conditions as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time. The applicable period is seven years in the United States. The applicable exclusivity period is ten years in the EU, but such exclusivity period can be reduced to six years if, at the end of the fifth year, a product no longer meets the criteria for orphan designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

As part of our business strategy, we intend to pursue orphan designation for certain of our product candidates. For example, in June 2018, we were granted orphan drug designation by the FDA for TransCon PTH for the treatment of hypoparathyroidism, in February 2019, we were granted orphan drug designation by the FDA for TransCon CNP for the treatment of achondroplasia, and in April 2020, we were granted orphan drug designation by the FDA for TransCon hGH for the treatment of GHD. Additionally, in July 2020, we were granted orphan designation by the EC for TransCon CNP for the treatment of achondroplasia and in October 2020, we were granted orphan designation by the EC for TransCon PTH for treatment of hypoparathyroidism. In October 2019, we were granted orphan designation by the EC for TransCon hGH for GHD. In July 2021, we were granted orphan drug designation from the Japanese Ministry of Health, Labour and Welfare for TransCon PTH. However, we may be unsuccessful in obtaining additional orphan designations, and may be unable to maintain the benefits associated with orphan designation, such as orphan drug exclusivity.

Even if we obtain orphan drug exclusivity for any of our product candidates, that exclusivity may not effectively protect those product candidates from competition because different drugs can be approved for the same condition, and orphan drug exclusivity does not prevent the FDA or foreign regulatory authorities from approving the same or a different drug in another indication. Even after an orphan drug is granted orphan exclusivity and approved, the FDA or foreign regulatory authorities can subsequently approve a later application for the same drug for the same condition before the expiration of the exclusivity period if the FDA or foreign regulatory authorities conclude that the later drug is clinically superior in that it is shown to be safer in a substantial portion of the target populations, 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 and in foreign jurisdictions may be lost if the FDA or foreign regulatory authorities later determine that the request for designation was materially defective or if we are unable to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan 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.

Any biological product for which we intend to seek approval may face competition sooner than anticipated.

The Affordable Care Act ("ACA") includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until twelve years from the date on which the reference product was first licensed. During this twelve-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product.

We believe that any of our future biological product candidates approved under a BLA should qualify for the twelve-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to Congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Jurisdictions in addition to the United States have established abbreviated pathways for regulatory approval of biological products that are biosimilar to earlier approved reference products. For example, the EU has had an established regulatory pathway for biosimilars since 2006. Moreover, the extent to which a biosimilar, once approved, could be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing.

We rely on third parties to manufacture preclinical, clinical, and commercial supplies of our products, product candidates and their device components.

We do not own facilities for manufacturing our products and product candidates. We depend on third-parties to manufacture and provide analytical services with respect to our products and product candidates and their respective device components.

In addition, to produce the quantities necessary to meet anticipated market demand, we and/or any collaboration partners will need to secure sufficient manufacturing capacity with third-party manufacturers. For TransCon hGH, we believe we have secured agreements to provide for sufficient manufacturing capacity with third-party manufacturers; however, our estimates of market demand may be inaccurate and third-party manufacturers may fail to produce sufficient quantities on a timely basis or at all. If we and/or any collaboration partners are unable to produce our products and product candidates in sufficient quantities to meet the requirements for the launch of the product or to meet future demand, our revenues and gross margins would be adversely affected. For example, public health epidemics or pandemics, such as COVID-19 currently impacting multiple jurisdictions worldwide may impact the ability of our existing or future manufacturers to perform their obligations under our manufacturing agreements with such parties. Such failure or substantial delay could materially harm our business. To be successful, our products and product candidates must be manufactured in commercial quantities in compliance with regulatory requirements and at acceptable costs. We and/or any collaboration partners will regularly need to maintain access to facilities to manufacture commercial supplies of our products and product candidates, if approved. All of this will require additional funds and successful completion of inspection or audits and approval by the FDA, other regulatory authorities and by notified bodies with respect to the device components. If we and/or any collaboration partners are unable to establish and maintain a manufacturing capacity within our planned time and cost parameters, the development and sales of our products and product candidates as well as our business, results of operations and prospects, and the value of our shares or ADSs could be adversely affected.

We and/or any collaboration partners may encounter problems with aspects of manufacturing our products and product candidates, including the following:

- production yields;
- quality control and assurance;
- shortages of qualified personnel;
- compliance with FDA and foreign regulations;
- production costs; and
- development of advanced manufacturing techniques and process controls.

We evaluate our options for clinical study supplies and commercial production of our products and product candidates on a regular basis, which may include use of third-party manufacturers, or entering into a manufacturing joint venture relationship with a third party. We are aware of only a limited number of companies on a worldwide basis who operate manufacturing facilities in which our products and product candidates can be manufactured under cGMP or similar foreign regulations, a requirement for all pharmaceutical products. We cannot be certain that we will be able to contract with any of these companies on acceptable terms, if at all, all of which could harm our business, results of operations and prospects, and the value of our shares or ADSs.

In addition, we, as well as any third-party manufacturer, will be required to register such manufacturing facilities with the FDA (and have a U.S. agent for the facility, if outside the United States) and other regulatory authorities. The facilities will be subject to inspections confirming compliance with the FDA, and other regulatory authority cGMP or similar foreign requirements. We do not control the manufacturing process of our product candidates, and we are dependent on our contract manufacturing partners for compliance with cGMPs or similar regulations for manufacture of both active drug substances and finished drug products. If we or any third-party manufacturer fails to maintain regulatory compliance, our business, financial condition and results of operations may be harmed, and the FDA or other regulatory authorities can impose regulatory sanctions that range from a warning letter to withdrawal of approval to seeking product seizures, injunctions and, where appropriate, criminal prosecution. Pursuant to our agreements with VISEN, we have and may in the future supply material to VISEN for use in clinical trials and commercial applications. In order to fulfill these supply, we rely on third-party manufacturers over which we have no or very limited control or power.

If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or similar regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a similar regulatory authority does not approve these facilities for the manufacture of our products or product candidates or if it withdraws any such 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 products or product candidates, if approved.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our products and product candidates. Any significant delay or discontinuation in the supply of such materials would delay commercialization and the completion of our clinical studies and harm our business.

There are a limited number of suppliers for raw materials that we use to manufacture our products and product candidates, and there may be a need to identify alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our products or product candidates for commercial sale and/or our clinical studies. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Although we generally do not begin a clinical study unless we believe we have on hand, or will be able to manufacture, a sufficient supply of a product candidate to complete such study, and we currently envision that VISEN, which relies on us for clinical supply of our product candidates, would do the same, any significant delay or discontinuity in the supply of a product candidate, or the raw material components thereof, for a clinical study due to the need to replace a third-party manufacturer could considerably delay completion of our or VISEN's clinical studies, product testing, and potential regulatory approval of our product candidates, which could harm our business and results of operations.

Any inability to obtain suppliers, including an inability to obtain, or delay in obtaining, approval of a supplier from the FDA or other regulatory authorities, would delay or prevent the clinical development and commercialization of our products and product candidates.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products and product candidates.

Our business exposes us to potential product liability risks which are inherent in research and development, preclinical and clinical studies, manufacturing, marketing and use of our products and product candidates. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. Product liability claims may be expensive to defend and may result in judgements against us which are potentially punitive. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products and product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products and product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize or co-promote our products or product candidates.

It is generally necessary for us to secure certain levels of insurance as a condition for the conduct of clinical studies. We believe that our product liability insurance for clinical studies is sufficient to cover claims. We currently maintain liability insurance with certain specified coverage limits. We cannot be certain that the insurance policies will be sufficient to cover all claims that may be made against us. Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of any products we develop. We currently carry product liability insurance covering use in our clinical trials in the amount of $20 million in the aggregate on our primary insurance policy and $100 million in the aggregate on our excess insurance policy. Any claim that may be brought against us could result in a court judgement or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various limits, exclusions and deductibles, and given these various limits, exclusions and deductibles, we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. Product liability insurance is expensive, difficult to obtain and may not be available in the future on acceptable terms.

We will need to continue to significantly increase the size of our organization and we may have difficulties in managing our growth and expanding our operations successfully.

As of December 31, 2022, we had 797 employees worldwide, with key facilities in Denmark, Germany, and the United States. As we advance our products and product candidates through the development and commercialization process, we will need to expand managerial, operational, financial, sales and marketing and other resources to manage our operations, preclinical and clinical trials, research and development activities, regulatory filings, manufacturing and supply activities, and any marketing and commercialization activities or contract with other organizations to provide these capabilities for us. As operations expand, we expect that we will need to manage additional relationships with various suppliers and other organizations. Our ability to manage our operations and growth requires us to continue to improve our operational, financial and management controls, reporting systems and procedures across a global organization. Such growth could place a strain on our administrative and operational infrastructure. We may not be able to make improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. Our management, personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively execute our growth strategy requires that we either internally, together with collaboration partners or through third-party contractors, as applicable:

- expand our general and administrative functions;
- identify, recruit, screen, retain, incentivize and integrate additional employees;
- manage our internal development efforts effectively while carrying out our contractual obligations to third-parties;
- establish and build a marketing and commercial organization; and
- continue to improve our operational, legal, financial, compliance and management controls, reporting systems and procedures.

If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

We incur significant costs as a result of operating as a public company, and our management devotes substantial time to compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would harm our business.

We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and regulations regarding corporate governance practices. Our senior management and other personnel need to devote a substantial amount of time to ensure that we maintain compliance with all of these requirements. Moreover, the reporting requirements, rules and regulations increase our legal and financial compliance costs and make some activities more time consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as members of our senior management, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms.

We are subject to Section 404 of The Sarbanes-Oxley Act of 2002 ("Section 404"), and the related rules of the SEC, which generally require our senior management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting, and we are required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal controls over financial reporting.

As we grow our business and enter into new activities, and as the reporting requirements increase, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our consolidated financial statements may be materially misstated. We may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of the ADSs to fall. In addition, as a public company we are required to file accurate and timely annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of the ADSs from The Nasdaq Global Select Market or other adverse consequences that would harm our business.

Our operating results may vary significantly from period to period and these variations may be difficult to predict.

Our operating results are expected to vary significantly from period to period due to a number of factors. Many of these factors are outside of our control. These factors include:

- the timing of regulatory approvals, if any, for our product candidates;
- the amount and timing of revenue from product sales;
- the potential market opportunities and patient populations for our products and product candidates, including with respect to TransCon PTH;
- the initiation of intellectual property litigation by third-parties or by us;
- the amount and timing of operating costs and capital expenditures relating to the expansion of our business operations and facilities;
- the timing of the commencement, completion or termination of collaboration agreements;
- the timing and amount of payments to us under collaboration agreements, if any;
- the introduction of new products and services by us, collaboration partners or our competitors;
- delays in preclinical testing and clinical studies;
- changes in regulatory requirements for clinical studies;

- costs and expenses associated with preclinical testing and clinical studies;
- exchange rate fluctuations;
- the regional and global effect of inflation;
- the adverse impact of multiple interest rate increases implemented and forecasted by the U.S. Federal Reserve; and
- payment of license fees for the right to use third-party proprietary rights, if any.

Our revenues in any particular period may be lower than we anticipate and, if we are unable to reduce spending in that period, our operating results will be harmed.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

We may consider strategic transactions, such as acquisitions of companies, asset purchases, and in-licensing or out-licensing of products, product candidates or technologies. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near- and long-term expenditures and may pose significant integration challenges or disrupt our senior management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- up-front, milestone and royalty payments, equity investments and financial support of new research and development candidates including increase of personnel, all of which may be substantial;
- exposure to unknown liabilities, including potential indemnification claims from a potential spin-off or out-license of certain of our intellectual property rights;
- disruption of our business and diversion of our management's time and attention to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;
- higher-than-expected acquisition and integration costs;
- lower-than-expected benefits, from out-licensing or selling our technology, intellectual property or any of our subsidiaries or, from in-licensing intellectual property or purchasing assets;
- write-downs of assets or goodwill or impairment charges;
- difficulty and cost in combining or separating the operations and personnel of any acquired or sold businesses with our existing operations and personnel;
- we may disagree with our strategic partners about decisions affecting the business, which could result in litigation or arbitration that increases our expenses, distracts our officers and directors and disrupts the day-to-day operations of the strategic venture, including by delaying important decisions until the dispute is resolved;
- our strategic partners may take actions that we oppose;
- our strategic partners might experience financial distress or become bankrupt;
- impairment of relationships with key suppliers or customers of any acquired or sold businesses due to changes in our senior management and ownership; and
- inability to retain key employees of any acquired businesses.

In addition, to the extent we enter into a strategic transaction that includes ongoing operations or shared ownership and management, our strategic partners may take actions that we oppose or we may disagree with our strategic partners about decisions affecting the business, which could result in litigation or arbitration, distract our officers and directors and otherwise disrupt the day-to-day operations of our business and the business of the strategic partner or entity. Furthermore, to the extent that our directors and officers serve on the boards of our strategic partners, such directors may be required to abstain from board decision-making in the event of a conflict of interest;

Accordingly, although we cannot be certain that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks, and could harm our business, results of operations, financial condition and prospects.

Exchange rate fluctuations or abandonment of the euro currency may harm our results of operations and financial condition.

Due to the international scope of our operations, fluctuations in exchange rates, particularly between the Euro, the Danish Krone and the U.S. Dollar, may adversely affect us. Although we are based in Denmark, we source research and development, manufacturing, consulting and other services from several countries. Further, potential future revenue may be derived from abroad, including from the United States. We currently attempt to limit our exposure to exchange rate risks by maintaining cash positions in the currencies in which we expect to incur the majority of our future expenses; however, for a variety of reasons we may be unable to maintain cash positions in the currencies in which we expect to incur the majority of our future expenses and we may fail to predict the currency of our future expenses, accurately or at all. As a result, our business and the price of the ADSs may be affected by fluctuations in foreign exchange rates between the Euro and these other currencies, which may also have a significant impact on our reported results of operations and cash flows from period to period. We currently do not enter into foreign exchange contracts to cover our exposure to exchange rate fluctuations, or any other form of exchange rate hedging arrangements. If we fail to manage foreign exchange risk adequately our business, results of operations and prospects, and the value of our shares or ADSs may be adversely affected.

In addition, the possible abandonment of the Euro by one or more members of the EU could harm our business in the future. Despite measures taken by the EU to provide funding to certain member states in financial difficulties and by a number of European countries to stabilize their economies and reduce their debt burdens, it is possible that the Euro could be abandoned in the future as a currency by countries that have adopted its use. This could lead to the re-introduction of individual currencies in one or more EU member states. The effects on our business of a potential dissolution of the EU, the exit of one or more EU member states from the EU or the abandonment of the Euro as a currency, are impossible to predict with certainty, and any such events could harm our business, financial condition and results of operations.

The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business.

The United Kingdom ("UK") left the EU on January 31, 2020, following which existing EU legislation continued to apply in the UK during a transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement ("Trade and Cooperation Agreement") which became effective on January 1, 2021. The Trade and Cooperation Agreement includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

The long-term effects of Brexit on our business in the UK, the EU and worldwide will depend on the implementation and application of the Trade and Cooperation Agreement and any other relevant agreements between the UK and the EU. EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law". However, under the Retained EU Law (Revocation and Reform) Bill 2022, which is currently before the UK parliament, any retained EU law not expressly preserved and "assimilated" into domestic law or extended by ministerial regulations (to no later than June 23, 2026) will automatically expire and be revoked by December 31, 2023. In addition, new EU legislation will not be applicable in Great Britain. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an 'appropriate authority' to amend or supplement existing regulations in the area of medicines and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps. There is a possibility that over time, national laws will be amended and that consequently the regulatory framework in Great Britain will diverge from that of the EU. As of January 1, 2021, the MHRA is the UK's standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain; broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA.

Brexit has resulted in the relocation of the EMA from the UK to the Netherlands. This relocation has caused, and may continue to cause, disruption in the administrative and medical scientific links between the EMA and the MHRA, including delays in granting clinical trial authorisation or marketing authorisation, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supply chain for clinical trial product and final authorized formulations. The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorisation and commercialization of products in the EU and/or the UK.

These developments, or the perception that any related developments could occur, have had and may continue to have a material adverse effect on global economic conditions and financial markets, and may significantly reduce global market liquidity, restrict the ability of key market participants to operate in certain financial markets or restrict our access to capital. Any of these factors could have a material adverse effect on our business, financial condition and results of operations and reduce the price of our ADSs.

Risks associated with our international operations, including seeking and obtaining approval to commercialize our product candidates in foreign jurisdictions, could harm our business.

We engage extensively in international operations, which include seeking marketing approval for certain of our product candidates in foreign jurisdictions. We expect that we are or will be subject to additional risks related to entering into these international business markets and relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing drug import and export rules;
- reduced protection for intellectual property rights in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems, and different competitive drugs;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from work conducted by these distributors;
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the Foreign Corrupt Practices Act, its books and records provisions, or its anti-bribery provisions; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

For example, we originally planned to conduct the Phase 3 foresiGHt trial utilizing sites in Belarus and Russia, but instead we engaged alternative sites for the study following the outbreak of conflict in Ukraine, which adversely affected patient enrollment. In addition, the manufacture of our products and product candidates is dependent upon third-party manufacturers that are based in other parts of the world, including the United States, Europe (including the UK and Switzerland), Japan and China. This manufacturing process requires that the components used in our products and product candidates are transported long distances, through multiple countries, which increases the risk that issues in the global supply chain or other disruptions to the international marketplace could harm our business.

The parent drug, drug substance, drug product and other components of our products and product candidates are currently acquired from certain single-source suppliers. The loss of these suppliers, or their failure to supply could materially and adversely affect our business.

Our growth hormone parent drug as well as our TransCon hGH drug substance are supplied by Fujifilm Diosynth Biotechnologies UK Limited ("Fujifilm"), pursuant to our agreement with Fujifilm. TransCon hGH drug product in vials is manufactured by Vetter Pharma Fertigung ("Vetter"), pursuant to our agreement with Vetter. TransCon hGH drug product in dual chamber cartridges is supplied by Vetter for use in our drug delivery device made by Philips Medisize A/S (formerly Medicom Innovation Partner A/S). The intermediates of our proprietary TransCon linkers are made by CARBOGEN AMCIS AG under an agreement with CARBOGEN AMCIS AG and accompanying purchase orders. For products that utilize soluble TransCon carriers, NOF Corporation (Japan) ("NOF"), supplies PEGs. Furthermore, NOF is responsible for coupling the TransCon linker used for TransCon hGH to methoxy PEG, under manufacturing agreements and accompanying purchase orders. Our PTH as well as our TransCon PTH drug substance is supplied by Bachem, Switzerland, pursuant to our agreement with Bachem. Vetter manufactures the TransCon PTH drug product in cartridges and assembles the cartridges with a drug delivery device made by Ypsomed AG. CNP drug substance is supplied by Wacker Biotech, Germany. Our TransCon CNP drug product in vials is manufactured by Vetter pursuant to our agreement with Vetter. With the exception of Lonza, who will be supplying TransCon hGH drug substance, we do not currently have any other suppliers for the drug substance, drug product or other components of our TransCon hGH, TransCon PTH and TransCon CNP, although we believe that there are alternate sources of supply that could satisfy our clinical and commercial requirements, we cannot provide assurance that identifying alternate sources and establishing relationships with such sources would not result in significant delays in the commercialization or development of our products and product candidates. Additionally, we may not be able to enter into supply arrangements with alternative suppliers on commercially reasonable terms or at all. A delay in the commercialization or development of our products or product candidates or having to enter into a new agreement with a different third-party on less favorable terms than we have with our current suppliers could have a material adverse impact upon on our business.

We may not be successful in our efforts to identify additional product candidates based on our TransCon technologies.

An important element of our strategy is to develop new products and product candidates based on our TransCon technologies. Research programs to identify new product candidates require substantial technical, financial and human resources. These research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including that:

- the research methodology used may not be successful in identifying potential product candidates; or
- potential product candidates may, on further study, be shown to have inadequate efficacy, harmful side effects or other characteristics suggesting that they are unlikely to be effective or safe products, or that they may not be sufficiently differentiated or offer substantial improvement over the currently available treatment options or standard of care in a given therapeutic category.

If we are unable to develop suitable product candidates through internal research programs or otherwise, we will not be able to increase our revenues in future periods, which could harm our business, results of operations and prospects, and the value of our shares or ADSs.

We are highly dependent on the services of our President and Chief Executive Officer, Jan Møller Mikkelsen, and if we are not able to retain this member of our senior management or recruit additional management, clinical and scientific personnel, our business will suffer.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified personnel. We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

In particular, we are highly dependent upon Jan Møller Mikkelsen, our President and Chief Executive Officer. The loss of services of this individual could result in delays in product development and harm our business.

We may have difficulties in attracting and retaining key personnel, and if we fail to do so our business may suffer.

We are highly dependent on the principal members of our senior management and scientific staff, the loss of whose services could adversely affect the achievement of planned development objectives. In addition, we could experience difficulties attracting and retaining qualified employees in the future. For example, competition for qualified personnel in the biotechnology and pharmaceuticals field is intense due to the limited number of individuals who possess the skills and experience required by our industry. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

For us to further expand our product development plans, we will need to hire additional qualified scientific personnel to perform research and development. We will also need to hire personnel with expertise in clinical testing, government regulation, sales and marketing, and finance, and might need to hire personnel with expertise in manufacturing. We may not be able to attract and retain personnel on acceptable terms, given the competition for such personnel among biotechnology, pharmaceutical and healthcare companies, universities and non-profit research institutions. Although we may be successful in attracting and retaining suitably qualified scientific personnel, there can be no assurance that we will be able to attract and retain such personnel on acceptable terms given the competition for experienced scientists from numerous pharmaceutical and chemical companies, specialized biotechnology firms, universities and other research institutions. Our failure to do so could adversely affect our business, results of operations and prospects, and the value of our shares or ADSs.

Our information technology systems, or those of our CROs or other contractors or consultants, may fail or suffer in the event of information technology system failures, cyberattacks or deficiencies in our cybersecurity, which could result in a material disruption of our product development programs and other critical business functions.

Despite the implementation of security measures, our information technology systems and those of our CROs and other contractors and consultants are vulnerable to attack and damage from computer viruses and malware (e.g., ransomware), unauthorized access, natural disasters, terrorism, war, telecommunication and electrical failures, malfeasance by external or internal parties, human error (e.g., social engineering, phishing). Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities.

We and certain of our service providers may from time to time be subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our and our critical third parties' operations, it could result in a material disruption of our programs, our operations, and ultimately, our financial results. For example, the loss of clinical trial data from completed or ongoing clinical trials for our products or product candidates could result in delays in our regulatory approval efforts, and the loss of research data could result in delays of our research and development efforts and it would be expensive to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our products or product candidates could be delayed.

If a security breach or other incident were to result in the unauthorized access to or unauthorized use, disclosure, release or other processing of personal information, it may be necessary to notify individuals, governmental authorities, supervisory bodies, the media and other parties pursuant to applicable privacy and security laws. Any security compromise affecting us, our service providers, strategic partners, other contractors, consultants, or our industry, whether real or perceived, could harm our reputation, erode confidence in the effectiveness of our security measures and lead to regulatory scrutiny. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary or personal information, we could incur liability, including litigation exposure, penalties and fines, we could become the subject of regulatory action or investigation, our competitive position could be harmed and the further development and commercialization of our products and services could be delayed. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our business. Furthermore, federal, state and international laws and regulations can expose us to enforcement actions and investigations by regulatory authorities, and potentially result in regulatory penalties, fines and significant legal liability, if our information technology security efforts fail. Laws around cybersecurity are also developing, and changes in such laws may require additional compliance costs. For example, in the EU, more stringent rules around cybersecurity are being adopted, such as the NIS2 Directive, which requires in-scope entities to implement heightened cybersecurity measures and responses, including with respect to security incident handling and reporting obligations. If a security breach or other incident were to result in the unauthorized access to or unauthorized use, disclosure, release or other processing of personal information, it may be necessary to notify individuals, governmental authorities, supervisory bodies, the media and other parties pursuant to privacy and security laws. We maintain cyber liability insurance ; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

The global pandemic caused by COVID-19 could materially adversely impact our business, including our clinical trials, supply chain operation, regulatory timelines and commercial activities.

In December 2019, a novel strain of coronavirus, COVID-19, was reported to have surfaced in Wuhan, China. Since then, the COVID-19 coronavirus has been declared by WHO to be a worldwide pandemic. As a result of the rapidly growing spread of COVID-19 throughout the areas we operate, we may experience disruptions that could severely impact our business, clinical trials and commercialization activities, including:

- delays or difficulties in enrolling and retaining patients in our clinical trials, which could potentially have a negative impact on clinical trial timelines;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- significant increases in expenses required to manage impacts to our business to complete our planned operations within our projected timelines;
- 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 monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials and commercialization activities, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials;
- interruption in global storage and shipping that may affect the supply of TransCon hGH or the transport of clinical trial materials, such as comparator drugs used in certain of our clinical trials;
- interruptions in our global supply chain with regards to clinical trials and commercial supply;
- changes in local regulations as part of a response to the COVID-19 outbreak which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- refusal of regulatory authorities to accept data from clinical trials in these affected geographies;
- in conducting our clinical trials, suppliers may experience delays in providing necessary equipment, consumables and services, which could cause temporary delays in clinical trial activities;
- global demand for COVID-19 vaccines or COVID-19 therapeutics could result in contract manufacturers not having sufficient capacity to meet scheduled manufacturing. In addition, sourcing of certain types of raw materials, consumables and equipment could result in scheduled manufacturing being delayed or postponed;
- travel restrictions and local outbreaks of COVID-19 could restrict authorities from performing site inspections in connection with their review procedures of marketing applications for TransCon products and product candidates, which could potentially delay the commercial launch in areas outside of the United States; and
- our commercial launch strategy, including for TransCon hGH, could be negatively impacted by patients not being able to see their physicians, and similarly, our commercial team not being able to meet in-person with physicians and payors, which could both have a negative impact on the commercial launch strategy.

In addition, the pandemic has caused, and may cause further, disruption to global financial markets. This may reduce our ability to access capital on favorable terms or to access capital at all. Furthermore, sustained adverse market events (such as a recession or depression) resulting from the pandemic could materially and adversely affect our business and the price of our ADSs.

The extent to which the COVID-19 pandemic further impacts our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the speed and extent of geographic spread of the disease, the duration of the outbreak, travel restrictions and social distancing in the affected areas, business closures or business disruptions and the effectiveness of actions taken in the affected areas to contain and treat the disease.

Unfavorable global and regional economic, political, health, climate and other conditions and events could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by global or regional economic, political, health, climate and other conditions and events. A global financial crisis or global or regional political and economic instability, wars, terrorism, civil unrest, outbreaks of disease, such as COVID-19, and other unexpected events, such as natural disasters, internet security threats, and damage to global communication networks, could cause extreme volatility, disrupt our business and increase our costs and expenses. Business disruptions could include, among others, disruptions to clinical enrollment, clinical site availability, patient accessibility, conduct of our clinical trials and commercialization activities, as well as temporary closures of our facilities and the facilities of suppliers or manufacturers in our supply chain.

For example, trade policies and geopolitical disputes (including as a result of China-Taiwan geo-political instability) and other international conflicts can result in tariffs, sanctions and other measures that restrict international trade, and can materially adversely affect our business, particularly if these measures occur in regions where our third-party contract manufacturers operate. Countries may also adopt measures, such as controls on imports or exports of goods, technology or data, that could adversely impact the Company’s operations and supply chain. These geopolitical risks could also adversely affect VISEN's activities in China.

For example, the military conflict between Russia and Ukraine has increased the likelihood of supply interruptions and made it difficult to conduct business operations, including clinical trials, in the region and in nearby countries. We originally planned to conduct the Phase 3 foresiGHt trial utilizing sites in Belarus and Russia, but instead we engaged with alternative sites for the study following the outbreak of conflict in Ukraine, which adversely affected patient enrollment. Such developments could negatively impact such operations or require use to delay or suspend clinical trial activities, which may increase product development costs and harm our business. In addition, the COVID-19 outbreak, including developments involving subsequent COVID-19 variants, significantly affected the financial markets of many countries and resulted and may in the future result in a variety of regulatory orders, guidance and restrictions. Similarly, global climate change could result in certain types of natural disasters occurring more frequently or with more intense effects. Some of our corporate and operational functions, including certain of our oncology research facilities, are located in California, which has experienced severe earthquakes, droughts, fires and other natural disasters in the past. We do not have multiple-site capacity for all of our operations in the event of a business disruption. Furthermore, parties in our supply chain and our customers are similarly vulnerable to these global or regional economic, political, health, climate and other conditions and events. Global or regional economic, political, health, climate and other conditions and events could result in a variety of risks to our business, including our ability to raise capital when needed on acceptable terms, if at all. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which such conditions and events could adversely impact our business.

Risks Related to Government Regulatory and Legal Requirements

The regulatory approval processes of the EMA, the FDA and comparable authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive regulation by the FDA, EU legislative bodies and other regulatory authorities in the United States, the EU and other jurisdictions, which regulations differ from country to country. We are not permitted to market any drug product in the United States until we receive marketing approval from the FDA. Equally, we are not permitted to market any drug product in the EU until we receive a marketing authorisation from the EC or EU member state competent authorities.

Obtaining regulatory approval of an NDA, BLA or MAA, can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable U.S., EU and foreign regulatory requirements may subject us to administrative or judicially imposed sanctions or other actions, including:

- warning letters;
- civil and criminal penalties;
- injunctions;
- withdrawal of regulatory approval of products;
- product seizure or detention;
- product recalls;
- total or partial suspension of production; and
- refusal to approve pending NDAs or BLAs, MAA, or supplements to approved NDAs or BLAs or extensions or variations to marketing authorizations.

Prior to obtaining approval to commercialize a drug or biological product candidate in the United States, the EU or other regions, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the EMA, the FDA or other similar regulatory authorities, that any drug product candidates are safe and effective for their intended uses, and that any biological product candidates are safe, pure and potent for their intended uses. The number of nonclinical studies and clinical trials that will be required for FDA, or EMA approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering drug or biological product candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials and result in the FDA or other regulatory authorities denying approval of a product candidate for any or all targeted indications.

The time required to obtain approval by the FDA and comparable authorities is unpredictable, typically takes many years following the commencement of clinical studies, and depends upon numerous factors. The EMA, the FDA and comparable authorities have substantial discretion in the approval process and we may encounter matters with the EMA, the FDA or such comparable authorities that requires us to expend additional time and resources and delay or prevent the approval of our product candidates. For example, the FDA or EMA may require us to conduct additional studies or trials for drug or biological product candidates either prior to or post-approval, such as additional drug-drug interaction studies or safety or efficacy studies or trials, or it may object to elements of our clinical development program such as the number of subjects in our current clinical trials from the United States or Europe. In addition, approval policies, 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, which may cause delays in the approval or result in a decision not to approve an application for regulatory approval. Despite the time and expense exerted, failure can occur at any stage. Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the EMA, the FDA or other comparable foreign regulatory authorities may disagree with the design or implementation of our, or any collaboration partners', clinical studies;
- the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which approval is sought;
- the EMA, the FDA or comparable foreign regulatory authorities may disagree with the interpretation of data from preclinical studies or clinical studies;
- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of an NDA or BLA, MAA, or other submission or to obtain regulatory approval in the United States, the EU or elsewhere;
- we, or any collaboration partners, may be unable to demonstrate to the EMA, the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers responsible for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

In addition, FDA and foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the EC in November 2020. A proposal for revision of several legislative instruments related to medicinal products (potentially revising the duration of regulatory exclusivity, eligibility for expedited pathways, etc.) is currently expected to be adopted by the EC by Q1 2023. The proposed revisions, once they are agreed and adopted by the European Parliament and European Council (not expected before the end of 2024) may have a significant impact on the pharmaceutical industry in the long term.

This lengthy approval process, as well as the unpredictability of the results of clinical studies, may result in our failure to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects. Additionally, if the EMA, the FDA or comparable foreign regulatory authorities require that we conduct additional clinical studies, place limitations on our label, delay approval to market our product candidates or limit the use of our products, our business and results of operations may be harmed.

In addition, even if we ultimately obtain approval for any product candidate, regulatory authorities may approve any of 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 impose a REMS or similar risk management measures, or 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 harm the commercial prospects for our product candidates.

Additional time may be required to obtain marketing authorizations for any of our product candidates that we develop as combination products.

We are developing a pen-injector device with Ypsomed to facilitate patient administration of TransCon PTH. We anticipate that, if successfully developed and approved, the pen-injector version of TransCon PTH would be regulated as a combination product by the FDA and other regulatory authorities. Combination products require coordination within the FDA and within comparable regulatory agencies for review of their drug and device components. For example, we expect the FDA's review of the TransCon PTH NDA will include the participation of both the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health. The EU regulates medical devices and medicinal products separately, through different legislative instruments, and the applicable requirements will vary depending on the type of drug-device combination product. For instance, drug-delivery products intended to administer a medicinal product where the medicinal product and the device form a single integral product are regulated as medicinal products in the EU. In such a case, the MAA must include – where available – the results of the assessment of the conformity of the device part with the EU Medical Devices Regulation contained in the manufacturer's EU declaration of conformity of the device or the relevant certificate issued by a notified body. If the MAA does not include the results of the conformity assessment and where for the conformity assessment of the device, if used separately, the involvement of a notified body is required, the EMA or the EU member state competent authority must require the applicant to provide a notified body opinion on the conformity of the device. By contrast, in case of drug-delivery products intended to administer a medicinal product where the device and the medicinal product do not form a single integral product (but are, e.g., co-packaged), the medicinal product is regulated in accordance with the rules for medicinal products described above while the device part is regulated as a medical device and will have to comply with all the requirements set forth by the Medical Devices Regulation.

Although the FDA and comparable foreign agencies have or may have systems in place for the review and approval of combination products, we may experience additional delays in the development and commercialization of such product candidates due to regulatory timing constraints and uncertainties in the product development and approval process. Moreover, although we anticipate that the device component of any combination product candidates we develop will be reviewed within the usual time frames expected for the underlying drug component application, and that no separate marketing application for the device components of such product candidates will be required in the United States, the FDA or comparable regulatory authorities may delay approval or require additional studies with the device which may delay the approval of the combination product.

Even after a regulatory approval for a product candidate, we are subject to ongoing regulatory obligations and review, which may result in significant additional expenses. Additionally, our products and product candidates, if approved, could be subject to labeling and other restrictions and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

The governmental regulation of the development of products, including SKYTROFA (lonapegsomatropin-tcgd) in the U.S., SKYTROFA (lonapegsomatropin) in the EU, and our other product candidates extend beyond clinical studies to approval required for their sale and monitoring of such products after sale. This regulation, approval and monitoring is the responsibility of numerous authorities in the United States, the EU and authorities in other territories. Following any regulatory approval of a product candidate, we, any collaboration partners and the manufacturers of our products will be subject to continuing regulatory obligations, including safety reporting requirements, regulatory oversight of product promotion and marketing, and cGMP or similar requirements. Furthermore, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These regulations cover all aspects of manufacturing, testing, quality control and recordkeeping of our products. If we or any collaboration partners or manufacturers fail to comply with applicable regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs or similar requirements and GCPs for any clinical trials that we conduct post-approval. As such, we and our third-party contract manufacturers will be subject to continual review and periodic inspections to assess compliance with regulatory requirements. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. Regulatory authorities may also impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-marketing studies. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs to assure compliance.

In addition, under the Federal Food, Drug, and Cosmetic Act, particular restrictions are placed on the distribution of human growth hormone products, including TransCon hGH. The distribution of product samples to physicians must also comply with the requirements of the Prescription Drug Marketing Act. Manufacturing facilities for our products remain subject to periodic inspection by regulatory authorities and must continue to adhere to International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use and the FDA's cGMP requirements. Application holders must obtain FDA approval for many product and manufacturing changes, depending on the nature of the change. Sales, marketing, and scientific/educational grant programs must comply with the U.S. Anti-Kickback Statute, the False Claims Act, as amended and similar state laws. Certain payments and other transfers of value to U.S. licensed physicians (as defined under statute) and teaching hospitals must be reported under the Physician Payments Sunshine Act. Pricing and rebate programs must comply with the Medicaid Drug Rebate Program requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Veterans Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to U.S. consumer protection and unfair competition laws.

We will also be required to report certain adverse reactions and production problems, if any, to the FDA or foreign regulatory authorities, and to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription pharmaceutical products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have FDA or foreign regulatory authorities approval.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- warning letters, fines or holds on clinical trials;
- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;

- injunctions or the imposition of civil or criminal penalties;
- suspension or revocation of existing regulatory approvals;
- suspension of any of our future or ongoing clinical trials;
- refusal to approve pending applications or supplements to approved applications submitted by us;
- restrictions on our or our contract manufacturers' operations; or
- product seizure or detention, or refusal to permit the import or export of products.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize our product candidates. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

In addition, the FDA's and foreign regulatory authorities' policies may change and additional government laws or regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability.

Within the EU, once a marketing authorisation is obtained, numerous post-approval requirements similar to the above ones also apply, and as in the United States, advertising and promotional activities for the product must be consistent with the approved summary of product characteristics and therefore off-label promotion of medicinal products is not permitted. Furthermore, the advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. The requirements are regulated by both EU regulations as well as national applicable regulations.

The regulatory requirements relating to the manufacturing, testing, marketing and sale of pharmaceutical products are subject to periodic change. This may impact our development plans. Changes in the regulations governing us could increase costs and adversely affect our business.

Furthermore, companies developing pharmaceutical products are facing increased demands to publish clinical trial results. Any such publication by us may, in addition to the additional cost of the publication, may lead to investors misinterpreting the published data due to its technical and scientific nature, which, in turn, may adversely affect our business, results of operations and prospects and the value of our shares or ADSs.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the EMA following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new drugs, medical devices and biologics or modifications to approved drugs, and biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections at domestic and foreign manufacturing facilities from March 2020 until July 2021. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic, and any resurgence of the virus may lead to further inspectional delays. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to hinder or prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Third-party payor coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates 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 in the United States are essential for most patients to be able to afford treatments such as our products or product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for drug treatments by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our products, and potentially attract additional collaboration partners to invest in the development of our product candidates. We cannot be sure that adequate coverage and reimbursement in the United States, the EU or elsewhere will be available for our products or any products 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, medical devices and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug is available. It is possible that a third-party payor may consider our products or product candidates, if approved, and the generic or biosimilar parent drug as substitutable and only offer to reimburse patients for the generic drug. Even if we show improved efficacy or improved convenience of administration with our products or product candidates, if approved, pricing of the existing parent drug may limit the amount we will be able to charge for such product. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our products or product candidates, and may not be able to obtain a satisfactory financial return on products that we may develop.

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, biologics and medical devices 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, biologics and medical devices. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our products or product candidates.

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 products and product candidates, if approved, and on related parent drugs. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Many countries, including the EU member states, established complex and lengthy procedures to obtain price approvals, coverage and reimbursement. These procedures vary from country to country but are commonly initiated after grant of the related marketing authorisation. More particularly, in the EU, potential reductions in prices and changes in reimbursement levels could be the result of different factors, including reference pricing systems. It could also result from the application of external reference pricing mechanisms, which consist of arbitrage between low-priced and high-priced countries. Reductions in the pricing of our medicinal products in one EU member state could affect the price in other EU member states and, thus, have a negative impact on our financial results. 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 products or 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. As an example, many EU member states review periodically their decisions concerning the pricing and reimbursement of medicinal products. The outcome of these reviews cannot be predicted and could have adverse effects on the pricing and reimbursement of our medicinal products in the EU member states.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our products or product candidates. We expect to experience pricing pressures in connection with the sale of our products and 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, medical devices 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.

We and contract manufacturers are subject to significant regulation with respect to manufacturing our products and product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements or may not be able to meet supply demands.

We depend on third-parties to manufacture products employing our TransCon technologies. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with cGMP or similar requirements outside the United States. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. All entities involved in the preparation of our products and product candidates for clinical studies or commercial sale, including our existing contract manufacturers for our products and product candidates, are subject to extensive regulation. Manufacturing facilities are subject to pre-approval and ongoing periodic inspection by the FDA and other corresponding governmental authorities, including unannounced inspections, and must be licensed before they can be used in commercial manufacturing of products employing our TransCon technologies. After regulatory approvals or licensure are obtained, the subsequent discovery of previously unknown manufacturing, quality control or regulatory documentation problems or failure to maintain compliance with the regulatory requirements may result in restrictions on the marketing of a product, revocation of the license, withdrawal of the product from the market, seizures, injunctions, or criminal sanctions. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of an NDA, BLA, MAA or comparable regulatory filing on a timely basis and must adhere to cGMP or similar regulations enforced by the FDA and other regulatory authorities through their facilities inspection programs. Some of our contract manufacturers have never produced a commercially approved pharmaceutical product and therefore have not obtained the requisite regulatory authority approvals to do so. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel.

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third-party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent suspension of production or closure of a facility. Any such remedial measures imposed upon us or third-parties with whom we contract could harm our business.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or other applicable regulatory authority can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new pharmaceutical product, withdrawal of an approval, or suspension of production. As a result, our business, financial condition, and results of operations may be harmed.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through submission and subsequent approval of a supplemental NDA or BLA, a marketing authorization variation application or equivalent foreign regulatory filing, which could result in further delay. The regulatory authorities may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. Furthermore, interruption or delay in supplies from one contract manufacturer may cause delays further down the supply chain, as certain contract manufacturers may rely on delivery of materials from other contract manufacturers.

These factors could cause us to incur higher costs and could cause the delay or termination of clinical studies, regulatory submissions, required approvals, or commercialization of our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed, or we could lose potential revenue.

Our operations involve hazardous materials and we and third-parties with whom we contract must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

As a pharmaceutical company, we are subject to environmental and safety laws and regulations, including those governing the use of hazardous materials. The cost of compliance with health and safety regulations is substantial. Our business activities involve the controlled use of hazardous materials. Our research and development activities involve the controlled storage, use and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. We and manufacturers and suppliers with whom we may contract are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of accidental contamination or injury from these materials, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. We cannot guarantee that the safety procedures utilized by third-party manufacturers and suppliers with whom we may contract will comply with the standards prescribed by laws and regulations or will 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 European, U.S. federal and state 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 the event of an accident or environmental discharge, we may be held liable for any consequential damage and any resulting claims for damages, which may exceed our financial resources and may materially adversely affect our business, results of operations and prospects, and the value of our shares or ADSs.

Our ability to effectively monitor and respond to the rapid and ongoing developments and expectations relating to environmental, social and governance matters, including related social expectations and concerns, may impose unexpected costs on us or result in reputational or other harm to us that could have a material adverse effect on our business, financial condition and results of operations.

There is an increasing focus and rapid and ongoing developments and changing expectations from certain investors, customers, consumers, employees and other stakeholders concerning environmental, social and corporate governance ("ESG") matters. Additionally, public interest and legislative pressure related to public companies' ESG practices continue to grow, which may result in increased regulatory, social or other scrutiny on us.

A variety of organizations measure the performance of companies on ESG topics, and the results of these assessments are widely publicized. In addition, investment in funds that specialize in companies that perform well in such assessments are increasingly popular, and major institutional investors have publicly emphasized the importance of such ESG measures to their investment decisions. Topics taken into account in such assessments include, among others, the company's efforts and impacts on climate change and human rights, ethics and compliance with law, and the role of the company's board of directors in supervising various sustainability issues.

We may be required to make investments in matters related to ESG, which could be significant. Our failure or perceived failure to meet the standards set by various constituencies could damage our reputation and our relationships with investors, governments, customers, employees, third parties and the communities in which we operate and expose us to increased regulatory risk, put us at a commercial disadvantage relative to our peers and materially adversely affect our business, financial condition, results of operations, ability to participate in debt and equity markets and the value of our shares or ADSs.

If we fail to comply or are found to have failed to comply with EU, FDA and other local regulations related to the promotion of our products for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other regulatory authorities, as well as courts. Our first product SKYTROFA (lonapegsomatropin-tcgd) was approved by the FDA on August 25, 2021 for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone, and we are restricted from marketing SKYTROFA and any other product candidate that receives marketing approval outside of its approved labeling, also referred to as off-label promotion. However, physicians may nevertheless lawfully prescribe an approved product to their patients in a manner that is inconsistent with the approved label, which is an off-label use. The FDA or other government authorities may allege or find that our practices constitute prohibited promotion of TransCon hGH for unapproved uses.

Over the past several years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the Food, Drug and Cosmetic Act, the False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "qui tam" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim, or caused a false claim to be submitted, to the government for payment. The person bringing a qui tam suit is entitled to a share of any recovery or settlement. Qui tam suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a qui tam suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

Our employees, independent contractors, principal investigators, CROs, consultants, vendors and collaboration partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants, vendors and collaboration partners may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate: (1) FDA or similar foreign regulations, including those laws that require the reporting of true, complete and accurate information to the FDA or foreign regulatory authorities; (2) manufacturing standards; (3) U.S. federal and state fraud and abuse and other healthcare laws and regulations including foreign requirements; or (4) laws that require the reporting of true and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, 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. These activities also include the improper use of information obtained in the course of clinical trials or falsification of clinical trial data, which could result in regulatory sanctions and serious harm to our reputation. 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 be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person or government 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 significant civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other U.S. federal or non U.S. healthcare programs, imprisonment, 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 and our results of operations.

We are subject to global anti-corruption laws, including but not limited to the U.S. Foreign Corrupt Practices Act, and non-compliance with such laws can subject us to criminal or civil liability and harm our business, financial condition and results of operations.

Our business activities may be subject to the Foreign Corrupt Practices Act (the "FCPA"), and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and, therefore, involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA.

There is no certainty that all of our employees, agents, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these requirements. We have adopted a code of conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from allegations, governmental investigations or other actions or lawsuits stemming from a failure to comply with these requirements. 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 civil or criminal fines and penalties, disgorgement of profits, injunctions and debarment from government contracts, as well as related stockholder lawsuits and other remedial measures, all of which could adversely affect our reputation, business, financial condition and results of operations. Investigations of alleged violations can also be disruptive and cause us to incur significant legal and investigatory fees.

Our failure to comply with trade compliance and economic sanctions laws and regulations of the United States and applicable international jurisdictions could materially adversely affect our reputation and results of operations.

Our business must be conducted in compliance with applicable economic and trade sanctions laws and regulations, such as those administered and enforced by the U.S. Department of Treasury's Office of Foreign Assets Control, the U.S. Department of State, the U.S. Department of Commerce, the United Nations Security Council and other relevant sanctions authorities. Our global operations expose us to the risk of violating, or being accused of violating, economic and trade sanctions laws and regulations. Our failure to comply with these laws and regulations may expose us to reputational harm as well as significant penalties, including criminal fines, imprisonment, civil fines, disgorgement of profits, injunctions and debarment from government contracts, as well as other remedial measures. Investigations of alleged violations can be expensive and disruptive. Despite our compliance efforts and activities we cannot assure compliance by our employees or representatives for which we may be held responsible, and any such violation could materially adversely affect our reputation, business, financial condition and results of operations.

Regulations related to "conflict minerals" may cause us to incur additional expenses and could limit the supply and increase the cost of certain metals used in manufacturing our products.

In August 2012, the SEC adopted a rule requiring disclosures of specified minerals, known as conflict minerals, that are necessary to the functionality or production of products manufactured or contracted to be manufactured by U.S.-listed companies. The conflict minerals rule requires companies annually to diligence, disclose and report whether or not such minerals originate from the Democratic Republic of Congo and/or adjoining countries of Angola, Burundi, Central African Republic, the Republic of the Congo, Rwanda, South Sudan, Tanzania, Uganda, and Zambia. The rule could affect sourcing at competitive prices and availability in sufficient quantities of certain minerals, including gold and tin, which are necessary to the functionality of our products, including our TransCon hGH auto-injector. The number of suppliers who provide conflict-free minerals may be limited. In addition, there may be material costs associated with complying with the disclosure requirements, such as costs related to determining the source of certain minerals used in our products, as well as costs of possible changes to products, processes, or sources of supply as a consequence of such verification activities. Due to the depth and complexity of the supply chain, we may not be able to sufficiently verify the origins of the relevant minerals used in our products through the due diligence procedures that we implement or the information that we receive from our suppliers may be inaccurate or inadequate, which may harm our reputation or subject us to SEC enforcement risks. In addition, we may encounter challenges to satisfy those customers who require that all of the components of our products be certified as conflict-free, which could place us at a competitive disadvantage if we are unable to do so.

Failure to obtain regulatory approvals in non-U.S. jurisdictions would prevent us from marketing our products outside of the United States.

In order to market our products outside of the United States, we, or any potential partner, must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our products. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed in these "Risk Factors", as well as other risks.

In the EU, medicinal products can only be commercialized after obtaining a marketing authorisation. For additional information, see "Item 4 B. Information on the Company – Business Overview – Foreign Regulation."

Outside the U.S. and the EU, approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA or EU approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA, EC, or EU member state competent authorities does not ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA, EC, or EU member states competent authorities. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval, EC, or EU member states competent authority. We may not be able to file for regulatory approvals or to do so on a timely basis, and even if we do file, we may not receive necessary approvals to commercialize our products in any market.

We are subject to healthcare laws, regulation and enforcement; our failure to comply with these laws could harm our results of operations and financial conditions.

We are subject to healthcare, statutory and regulatory requirements and enforcement by the U.S. federal government and the states and foreign governments in which we conduct our business. The laws that affect our ability to operate include:

- the U.S. Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under U.S. federal healthcare programs such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;
- U.S. false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent. In addition, 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 False Claims Act;
- U.S. federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U.S. federal Anti-Kickback Statute, 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;
- U.S. federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows, or should know, it is likely to influence the beneficiary’s selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies;
- the U.S. federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics, and medical supplies to report annually to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives) and teaching hospitals, and ownership and investment interests held by physicians (as defined under statute) and their immediate family members;
- U.S. federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- state law equivalents of each of the above U.S. federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers;
- state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources;
- state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; and
- European and other foreign law equivalents of each of the laws, including regulation regarding advertising of medicinal products and reporting requirements detailing interactions with and payments to healthcare providers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. The risk of our activities being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations.

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. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to significant penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in U.S. federal and state and/or foreign healthcare programs and imprisonment, any of which could adversely affect our ability to market our products and adversely impact our financial results.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention and security of personal data, such as information that we may collect in connection with clinical trials. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. Complying with these numerous, complex and often changing regulations is expensive and difficult, and any failure or perceived failure to comply with any data privacy laws or security laws, our policies and procedures, our contracts governing our processing of personal information or any security incident or breach involving the misappropriation, loss or other unauthorized use or disclosure of sensitive or confidential patient or consumer information, whether by us, one of our partners or another third-party, could adversely affect our business, financial condition and results of operations, and could result in negative publicity, government investigations and enforcement actions, claims by third-parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the U.S., HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. In addition, California enacted the California Consumer Privacy Act ("CCPA"), which went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the California Privacy Rights Act (the "CPRA") recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions went into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia, Connecticut, Utah and Colorado, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

Even when HIPAA or a state law does not apply, according to the Federal Trade Commission (the "FTC"), violating consumers' privacy rights or failing to take appropriate steps to keep consumers' personal information secure may constitute unfair and/or deceptive acts or practices in violation of Section 5(a) of the Federal Trade Commission Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities.

In Europe, the General Data Protection Regulation (the "GDPR") imposes strict requirements for processing the personal data of individuals within the EEA, including clinical trial data. For example, the GDPR requires us to make detailed disclosures to data subjects, requires disclosure of the legal basis on which we can process personal data, makes it harder for us to obtain valid consent for processing and in other cases prevents the use of consent as legal basis for processing of personal data, requires the appointment of data protection officers when sensitive personal data, such as health data, is processed on a large scale, provides robust rights for data subjects, imposes mandatory data breach notification through the EU and EEA, imposes additional obligations on us when contracting with service providers and requires us to adopt appropriate privacy governance including policies, procedures, training and data audit. If we do not comply with our obligations under the GDPR, we could be exposed to fines of up to the greater of €20 million or up to 4% of our total global annual revenue in the event of a significant breach. In addition, we may be the subject of litigation and/or adverse publicity, which could adversely affect our business, results of operations and financial condition. The law in this area is also developing rapidly. For example, in July 2020, the Court of Justice of the EU ("CJEU") invalidated the Privacy Shield, limiting how organizations could lawfully transfer personal data from the EEA to the U.S. and imposing further restrictions on the use of standard contractual clauses ("SCCs"). In March 2022, the U.S. and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU-U.S. Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for United States Signals Intelligence Activities. The EC also issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data transfers from September 27, 2021; existing SCC arrangements must be migrated to the revised clauses by December 27, 2022. The new SCCs apply only to the transfer of personal data outside of the EEA and not the UK. The UK's Information Commissioner's Office has published new data transfer standard contracts for transfers from the UK under the United Kingdom GDPR ("UK GDPR"). This new documentation will be mandatory for relevant data transfers from September 21, 2022; existing standard contractual clauses arrangements must be migrated to the new documentation by March 21, 2024. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non-EEA entities subject to the GDPR. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Relatedly, from January 1, 2021, companies have had to comply with both the GDPR and the UK GDPR, the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. The relationship between the UK and the EU in relation to certain aspects of data protection law remains unclear, for example around how data can lawfully be transferred between each jurisdiction, which exposes us to further compliance risk. The EC has adopted an adequacy decision in favor of the UK, enabling data transfers from EU member states to the UK without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the EC re-assesses and renews or extends that decision. In September 2021, the UK government launched a consultation on its proposals for wide-ranging reform of the UK's data protection laws following Brexit and the response to this consultation was published in June 2022. There is a risk that any material changes which are made to the UK data protection regime could result in the EC reviewing the UK adequacy decision, and the UK losing its adequacy decision if the EC deems the UK to no longer provide adequate protection for personal data. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

In addition, the Council of the European Union adopted the NIS2 Directive on November 28, 2022, which replaced and repealed the existing EU Directive on the Security of Network and Information Systems. The NIS2 Directive establishes cybersecurity risk management measures and reporting requirements for highly critical sectors, including for manufacturers of medical devices. This includes requirements to implement appropriate technical and operational measures to manage security risks, including measures with respect to business continuity, incident handling, encryption, and data access control. Important entities and essential entities will also be required to report cybersecurity incidents within specified timeframes. The NIS2 Directive was published in the Official Journal of the European Union on December 27, 2022, and will become effective on the twentieth day following its publication, with EU member states having 21 months from such effective date to then incorporate the NIS2 Directive into their national law. The NIS2 Directive requires EU members states to impose administrative fines for breaches of the NIS2 Directive of up to €7 million or 1.4% of the total worldwide turnover of the entity for the preceding financial year, whichever is greater for certain "important entities". Other entities, considered "essential entities" may be subject to administrative fines for breaches of the NIS2 Directive of up to €10 million or 2% of the total worldwide turnover of the entity for the preceding financial year, whichever is greater.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation and adversely affect our business and results of operations. Further, we cannot assure you that our third-party service providers with access to our or our customers', suppliers', trial patients', and employees' personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business including putting us in breach of our obligations under privacy laws and regulations and/or which could in turn adversely affect our business, results of operations and financial condition. In addition, if our practices are not consistent, or viewed as not consistent, with legal and regulatory requirements, including changes in laws, regulations and standards or new interpretations or applications of existing laws, regulations and standards, we may also become subject to audits, inquiries, whistleblower complaints, adverse media coverage, investigations, criminal or civil sanctions, all of which may harm our business, financial condition and results of operations.

Legislative or regulatory healthcare reforms in the United States and in foreign jurisdictions may make it more difficult and costly for us to obtain regulatory clearance or approval of our product candidates in the United States and in foreign jurisdictions and to produce, market and distribute our products in the United States and in foreign jurisdictions after clearance or approval is obtained.

From time to time, legislation is drafted and introduced in U.S. Congress that could significantly change the statutory provisions governing the regulatory clearance or approval, manufacture, and marketing of regulated products or the reimbursement thereof. In addition, FDA regulations and guidance are often revised or reinterpreted by the FDA in ways that may significantly affect our business. Similar risks exist in foreign jurisdictions. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recall, replacement, or discontinuance of one or more of our products; and
- additional record keeping.

Each of these would likely entail substantial time and cost and could harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any future products would harm our business, financial condition and results of operations.

In addition, the trend toward managed healthcare in the United States and the changes in health insurance programs, as well as legislative proposals to reform healthcare or reduce government insurance programs, may result in lower prices for pharmaceutical products, including any products that may be offered by us. In addition, any future regulatory change regarding the healthcare industry or third-party coverage and reimbursement may affect demand for any products that we may develop and could harm our sales and profitability. For example, in the United States, the ACA was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The ACA, among other things, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, addressed 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, established annual fees and taxes on manufacturers of certain branded prescription drugs and medical devices, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts, which, through subsequent legislative amendments, was increased to 70%, starting in 2019, 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 judicial, executive and Congressional challenges to certain provisions of the ACA. For example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace from February 15, 2021 through August 15, 2021. The executive order instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures will impact our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted, including reductions in Medicare payments to providers, which went into effect on April 1, 2013 and will stay in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. Further, the American Taxpayer Relief Act of 2012 reduced Medicare payments to several types of providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, in March 2021, the American Rescue Plan Act of 2021 was signed into law, which, among other things, eliminated the statutory cap on drug manufacturers' Medicaid Drug Rebate Program rebate liability effective January 1, 2024. Under current law enacted as part of the ACA, drug manufacturers' Medicaid Drug Rebate Program rebate liability is capped at 100% of the average manufacturer price for a covered outpatient drug. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for our products.

Recently, there has also been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. Most recently, in August 2022, the Inflation Reduction Act of 2022 (the "IRA") was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated, and the impact of the IRA on our business and the pharmaceutical industry cannot yet be fully determined. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including through constraints on reimbursement, imposition of mandatory discounts, discounts, restrictions on access to certain products, transparency measures, and programs for importation from other countries or bulk purchasing.

We expect that additional U.S. local and national healthcare reform measures will be adopted within and outside the United States in the future, any of which could limit the amounts that governments will pay for healthcare products and services, which could result in reduced demand for our products or product candidates or additional pricing pressures. The continuing efforts of the U.S. government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect the demand for any drug products for which we may obtain regulatory approval, including TransCon hGH, our ability to set a price that we believe is fair for our products, our ability to obtain coverage and reimbursement approval for a product, our ability to generate revenues and achieve or maintain profitability, and the level of taxes that we are required to pay.

In the EU, similar developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU 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 our product candidates, if approved. In markets outside of the United States and EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In December 2021, Regulation No 2021/2282 on Health Technology Assessment ("HTA") amending Directive 2011/24/EU, was adopted. This regulation, which entered into force in January 2022 and will become applicable from January 12, 2025 onwards, intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation foresees a three-year transitional period and will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

Risks Related to Our Intellectual Property

If our intellectual property related to our products and product candidates is not adequate, we may not be able to compete effectively in our market.

Our success depends in part on our ability to:

- protect our trade secrets;
- apply for, obtain, maintain and enforce patents; and
- operate without infringing upon the proprietary rights of others.

We will be able to protect our proprietary technologies from unauthorized use by third-parties only to the extent that such proprietary rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. Any non-confidential disclosure to or misappropriation by third-parties of our confidential or proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Where we elect to pursue patent protection on our proprietary technologies, we file, prosecute and maintain international and other national patent applications covering such technologies, including in the United States, Europe, China, and other jurisdictions.

As of December 31, 2022, 42 patents have been issued to us in the United States, 19 of which are directed to our TransCon technologies, seven of which are directed to TransCon hGH and seven of which are directed to TransCon CNP. In addition, as of December 31, 2022, we have over 238 issued patents in jurisdictions outside of the United States, at least 102 of which are directed to our TransCon technologies, and 85 of which are directed to TransCon hGH and/or our other product candidates. For additional information, see "Item 4 B. Information on the Company – Business Overview – Intellectual Property." We are not aware of any challenge to our issued patents, in the United States, Europe or in any other jurisdiction.

The patent application process, also known as patent prosecution, is expensive and time-consuming, and we and our current or future licensors and licensees 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 current licensors, or any future licensors or licensees, 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. Therefore, these and any of our patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, although we are unaware of any such defects. If we or our current licensors or licensees, or any future licensors or licensees, fail to establish, maintain or protect such patents and other intellectual property rights, including due to the impact of the COVID-19 pandemic on our or our licensors' business operations, such rights may be reduced or eliminated. If our current licensors or licensees, or any future licensors or licensees, 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. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Any of these outcomes could impair our ability to prevent competition from third-parties, which may harm our business.

It is expected that in 2023 European patent applications will have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unified Patent Court ("UPC"). In addition, conventional European patents, both already granted at the time the new system starts and granted thereafter, will be subject to the jurisdiction of the UPC, unless actively opted out. This will be a significant change in European patent practice and deciding whether to opt-in or opt-out of Unitary Patent practice will entail strategic and cost considerations. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation before the UPC. Moreover, the decision whether to opt-in or opt-out of Unitary Patent status will require coordinating with co-applicants, if any, adding complexity to any such decision.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be highly uncertain. The patent applications that we own or license may fail to result in issued patents in the United States or in other countries. Even if patents do issue on such patent applications, third-parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. For example, U.S. patents can be challenged by any person before the USPTO Patent Trial and Appeals Board at any time within the one-year period following that person's receipt of an allegation of infringement of the patents. Patents granted by the European Patent Office may be similarly opposed by any person within nine months from the publication of the grant. Similar proceedings are available in other jurisdictions, and in the United States, Europe and other jurisdictions third-parties can raise questions of validity with a patent office even before a patent has been granted. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. For example, a third-party may develop a competitive product that provides therapeutic benefits similar to one or more of our products or product candidates but that has a different composition that falls outside the scope of our patent protection. If the breadth or strength of protection provided by the patents and patent applications we hold or pursue with respect to our products or product candidates is successfully challenged, then our ability to commercialize our products or product candidates could be negatively affected, and we may face unexpected competition that could harm our business. Further, patents have a limited lifespan and patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date excluding U.S. provisional patent applications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such product candidates are commercialized. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. If we encounter delays in our clinical trials, the period of time during which we could market our products or product candidates under patent protection would be reduced. If we do not have sufficient patent life to protect our products, our business and results of operations will be adversely affected.

The degree of future protection of our proprietary rights is uncertain. Patent protection may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we might not have been the first to invent or the first to file the inventions covered by each of our pending patent applications and issued patents;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- the patents of others may have an adverse effect on our business;
- any patents we obtain or our in-licensed issued patents may not encompass commercially viable products, may not provide us with any competitive advantages or may be challenged by third-parties;
- any patents we obtain or our in-licensed issued patents may not be valid or enforceable; or
- we may not develop additional proprietary technologies that are patentable.

If we or our current licensors or licensees, or any future licensors or licensees, fail to prosecute, maintain and enforce patent protection for our products or product candidates, our ability to develop and commercialize our products or product candidates could be harmed and we might not be able to prevent competitors from making, using and selling competing products. This failure to properly protect the intellectual property rights relating to our products or product candidates could harm our business, financial condition and operating results. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

Even where laws provide protection, costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and the outcome of such litigation would be uncertain. If we were to initiate legal proceedings against a third-party to enforce a patent covering one of our products or product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Patents may be unenforceable if someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcomes of proceedings involving assertions of invalidity and unenforceability are unpredictable. It is possible that prior art of which we and the patent examiner were unaware during prosecution exists, which would render our patents invalid. Moreover, it is also possible that prior art may exist that we are aware of, but that we do not believe are relevant to our current or future patents, that could nevertheless be determined to render our patents invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability of our patents covering our products or product candidates, we would lose at least part, and perhaps all, of the patent protection on such product or product candidate. Such a loss of patent protection would harm our business. Moreover, our competitors could counterclaim in any suit to enforce our patents that we infringe their intellectual property. Furthermore, some of our competitors have substantially greater intellectual property portfolios, and resources, than we do.

We license intellectual property rights from third-parties. Such licenses may be subject to early termination if we fail to comply with our obligations in our licenses with third-parties, which could result in the loss of rights or technology that are material to our business.

We are or may become a party to licenses that give us rights to third-party intellectual property or technology that is necessary or useful for our business, and we may enter into additional licenses in the future. Under these license agreements, we are or may become obligated to pay the licensor fees, which may include annual license fees, milestone payments, royalties, a percentage of revenues associated with the licensed technology and a percentage of sublicensing revenue. These fees may be significant, which could make it difficult for us to achieve or maintain profitability. In addition, under certain of such agreements, we are or may become required to diligently pursue the development of products using the licensed technology. If we fail to comply with these obligations, including due to the impact of the COVID-19 pandemic on our business operations or our use of the intellectual property licensed to us in an unauthorized manner, and fail to cure our breach within a specified period of time, the licensor may have the right to terminate the applicable license, in which event we could lose valuable rights and technology that are material to our business, harming our ability to develop, manufacture and/or commercialize our platform, products or product candidates.

In addition, the agreements under which we license intellectual property or technology to or from third-parties can be complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire. The failure to obtain or in-license any compositions, methods of use, processes or other third-party intellectual property rights at a reasonable cost or on reasonable terms, could harm our business. If we fail to obtain licenses to necessary third-party intellectual property rights, we may need to cease use of the compositions or methods covered by such third-party intellectual property rights. Furthermore, we may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

If we are unable to prevent disclosure of our trade secrets or other confidential information to third-parties, our competitive position may be impaired.

In addition to patents, we rely on trade secrets and proprietary know-how. We seek protection, in part, through confidentiality and proprietary information clauses in agreements with our collaboration partners, employees, consultants, outside scientific collaboration partners and sponsored researchers and other advisors. Although we generally require all of our employees, consultants, advisors and any third-parties who have access to our proprietary know-how, information or technology to assign or grant similar rights to their inventions to us, and endeavor to execute confidentiality agreements with all such parties, we cannot be certain that we have executed such agreements with all parties who may have contributed to our intellectual property or who had access to our proprietary information, nor can we be certain that our agreements with such parties will not be breached. These agreements may not effectively prevent disclosure of confidential and proprietary information and may not provide an adequate remedy in the event of unauthorized use or disclosure of confidential and proprietary information. We cannot guarantee that our trade secrets and other confidential proprietary information will not be publicly disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. We may need to share our proprietary information, including trade secrets, with our current and future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. The failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

If we are sued for allegedly infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in such litigation could harm our business.

Our commercial success depends significantly on our ability to operate without infringing, violating or misappropriating the patents and other proprietary rights of third-parties. Our own technologies may infringe, violate or misappropriate the patents or other proprietary rights of third-parties, or we may be subject to third-party claims of such infringement. Numerous U.S. and foreign issued patents and pending patent applications owned by third-parties exist in the fields in which we are developing our products and product candidates. For example, we are aware of several issued patents related to auto-injection devices that may be relevant to our auto-injection device developed with Phillips-Medisize A/S (formerly Medicom Innovation Partner A/S); however, we believe that these (i) are invalid, and/or (ii) do not and will not cover our product or device. Additionally, we are aware of patents owned by a competitor that are related to CNP variants. Although we believe that these patents are not infringed by us and/or are invalid, we could be wrong in our assessment. We cannot be certain that our products and product candidates will not infringe these or other existing or future patents. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. Additionally, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our products or product candidates or our TransCon technologies. We may not be aware of patents that have already issued that a third-party might assert are infringed by our products or product candidates. It is also possible that patents of which we are aware, but which we do not believe are relevant to our products or product candidates, could nevertheless be found to be infringed by our products or product candidates. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect.

In addition, we may face costly and time-consuming intellectual property litigation with the NDA holders, BLA holders and Orange Book patentees of the products in respect of which we seek to obtain FDA approval. Companies that produce branded pharmaceutical products for which there are listed patents in the FDA's Orange Book routinely bring patent infringement litigation against applicants seeking FDA approval to manufacture and market branded and/or generic forms of their products. Accordingly, we may face patent litigation as a result of our submission of NDA and BLA applications to the FDA or as a result of submitting an MAA with the EMA.

Intellectual property litigation involves many risks and uncertainties, and there is no assurance that we will prevail in any lawsuit brought against us. Third-parties making claims against us for infringement, violation or misappropriation of their intellectual property rights may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our products and product candidates. Further, if a patent infringement suit were brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. Defense of these claims, regardless of their merit, would cause us to incur substantial expenses and, would be a substantial diversion of resources from our business. In the event of a successful claim of any such infringement, violation or misappropriation, we may need to obtain licenses from such third-parties and we may be prevented from pursuing product development or commercialization and/or may be required to pay damages. We cannot be certain that any licenses required under such patents or proprietary rights would be made available to us, or that any offer to license would be made available to us on commercially reasonable terms. If we cannot obtain such licenses, we may be restricted or prevented from manufacturing and selling products employing our technologies. These adverse results, if they occur, could adversely affect our business, results of operations and prospects, and the value of our shares or ADSs.

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

The biotechnology and pharmaceutical industries have been characterized by extensive litigation regarding patents and other intellectual property rights. The defense and prosecution of contractual or intellectual property lawsuits, USPTO interference or derivation proceedings, European Patent Office oppositions and related legal and administrative proceedings in the United States, Europe and other countries, involve complex legal and factual questions. As a result, such proceedings may be costly and time-consuming to pursue and their outcome is uncertain.

Litigation may be necessary to:

- protect and enforce our patents and any future patents issuing on our patent applications;
- enforce or clarify the terms of the licenses we have granted or may be granted in the future;
- protect and enforce trade secrets, know-how and other proprietary rights that we own or have licensed, or may license in the future; or
- determine the enforceability, scope and validity of the proprietary rights of third-parties and defend against alleged patent infringement.

Competitors may infringe our intellectual property. As a result, we may be required to file infringement claims to stop third-party infringement or unauthorized use. This can be expensive, particularly for a company of our size, and time-consuming. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings and some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. 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. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patent claims do not cover its technology or that the factors necessary to grant an injunction against an infringer are not satisfied. An adverse determination of any litigation or other proceedings could put one or more of our patents at risk of being invalidated, interpreted narrowly, or amended such that they do not cover our product candidates. Moreover, such adverse determinations could put our patent applications at risk of not issuing, or issuing with limited and potentially inadequate scope to cover our products or product candidates or to prevent others from marketing similar products.

Interference, derivation or other proceedings brought at the USPTO, may be necessary to determine the priority or patentability of inventions with respect to our patent applications or those of our licensors or potential collaboration partners. Litigation or USPTO proceedings brought by us may fail or may be invoked against us by third-parties. Even if we are successful, domestic or foreign litigation or USPTO or foreign patent office proceedings may result in substantial costs and distraction to our management and scientific personnel. We may not be able, alone or with our licensors or potential collaboration partners, to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other proceedings, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. In addition, during the course of this kind of litigation or these kind of proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for the ADSs could be significantly harmed.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act (the "Leahy-Smith Act") signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a "first to file" system. The Leahy-Smith Act could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

The U.S. Supreme Court has ruled on several 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. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technologies or our ability to enforce our proprietary technologies. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

It is expected that in 2023 European patent applications will have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the UPC. For additional information, see "If our intellectual property related to our products and product candidates is not adequate, we may not be able to compete effectively in our market."

Certain of our employees and patents are subject to German law.

As of December 31, 2022, 115 of our employees work in Germany and are subject to German employment law. Ideas, developments, discoveries and inventions made by such employees are generally subject to the provisions of the German Act on Employees' Inventions, which regulates the ownership of, and compensation for, inventions made by employees. Under this act, we face the risk that we may be required to pay additional compensation for assigned patent rights and disputes can occur between us and our employees or ex-employees pertaining to alleged non-adherence to the provisions of this act that may be costly to defend and consume our management's time and efforts whether we prevail or fail in such dispute. In addition, under the German Act on Employees' Inventions, certain employees may have retained rights to patents they invented or co-invented before October 2009. Although substantially all of these employees have assigned their interest in these patents to us, to the extent permitted by law, there is a risk that the compensation we provided to them may be deemed to be insufficient and we may be required under German law to increase the compensation due to such employees for the use of the patents. In those cases, where employees have not assigned their interests to us, we may need to pay compensation for the use of those patents. If we are required to pay additional compensation or face other disputes under the German Act on Employees' Inventions, our results of operations could be adversely affected.

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.

The USPTO and various foreign patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions to maintain patent applications and issued patents. Although an inadvertent lapse, including due to the effect of the COVID-19 pandemic on us or our patent maintenance vendors, 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 with these requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction.

Losing our patent rights could enable competitors to enter the market earlier than would otherwise have been the case.

Failure to secure trademark registrations for a commercial trade name for our products or product candidates in the United States or elsewhere could adversely affect our business.

We use various trademark rights in our business, including, Ascendis, Ascendis Pharma, TransCon and SKYTROFA. A trademark application for TransCon PTH has been filed in U.S. as well as the EU and other countries across the globe. However, our current or future trademarks and trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks, and we may not be able to obtain trademark protection in other territories that we consider of significant importance to us. Furthermore, other than for TransCon hGH, we have not yet registered trademarks for a commercial trade name for any other of our product candidates in the United States or elsewhere. During trademark registration proceedings, our trademark applications may be rejected. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third-parties can oppose pending trademark applications and seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing our products under new brands. We may license our trademarks and trade names to third-parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names.

The FDA has approved the use of SKYTROFA for TransCon hGH in the United States; however, any name we propose to use with TransCon PTH, or our other product candidates in the United States or any other country must be approved by the FDA, EMA or any other relevant health authority regardless of whether we have registered it, or applied to register it, as a trademark. For example, the FDA has approved the use of SKYTROFA in the United States and the EC has granted a marketing authorisation for the SKYTROFA in the EU. The FDA as well as EMA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA, EMA or any other relevant approval authority objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third-parties and be acceptable to the FDA, EMA or any other relevant approval authority.

We may not be able to enforce our intellectual property rights throughout the world.

Patents are of national or regional effect, and filing, prosecuting and defending patents on our products or product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. For example, patents with claims directed to dry pharmaceutical formulations of TransCon hGH have issued in the United States, Europe, and other jurisdictions, but related claims were rejected in China. An initial appeal upheld the rejection. We appealed this decision and vigorously advocate for the patentability of these claims. However, we may be unsuccessful, and our patent protection for TransCon hGH may expire sooner in China than in other jurisdictions. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and certain developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights in such countries. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third-parties. Consequently, we may not be able to prevent third-parties from practicing our inventions in certain countries outside the United States and many countries in Europe.

Competitors may use our 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 have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate.

These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

We may be subject to claims that we or our employees have misappropriated the intellectual property, including know-how or trade secrets, of a third-party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors were previously employed at or engaged by other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, consultants and contractors, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees, consultants and contractors do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may be subject to claims that we have wrongfully hired an employee from a competitor or that we or these employees, consultants and contractors have used or disclosed such third-party intellectual property, including know-how, trade secrets or other proprietary information. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, or access to consultants and contractors. 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 be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators, or other third-parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third-parties involved in developing our products or product candidates or as a result of questions regarding co-ownership of potential joint inventions. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our products or product candidates. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We or our licensors may have relied on third-party consultants or collaborators or on funds from third-parties, such as national governments, such that we or our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third-parties have ownership rights or other rights to our patents, including in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology.

This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Risks Related to Indebtedness

Our indebtedness and liabilities could limit the cash flow available for our operations, expose us to risks that could adversely affect our business, financial condition and results of operations, and impair our ability to satisfy our obligations under the Convertible Notes.

As of December 31, 2022, we had $575 million principal amount of indebtedness as a result of the 2.25% Convertible Senior Notes due 2028 ("Convertible Notes") offering. We may also incur additional indebtedness to meet future financing needs. Our indebtedness could have significant negative consequences for our shareholders and our business, results of operations, and financial condition by, among other things:

- increasing our vulnerability to adverse economic and industry conditions;
- limiting our ability to obtain additional financing;
- requiring the dedication of a substantial portion of our cash flow from operations to service our indebtedness, which will reduce the amount of cash available for other purposes;
- limiting our flexibility to plan for, or react to, changes in our business;
- diluting the interests of our existing shareholders as a result of issuing ADSs upon conversion of the Convertible Notes and the ordinary shares represented by such ADSs; and
- placing us at a possible competitive disadvantage with competitors that are less leveraged than us or have better access to capital.

Our ability to make scheduled payments of the principal of, to pay interest on or to refinance our indebtedness, including the Convertible Notes, depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate sufficient funds, and we may otherwise be unable to maintain sufficient cash reserves, to pay amounts due under our indebtedness, including the Convertible Notes, and our cash needs may increase in the future. In addition, future indebtedness that we may incur may contain financial and other restrictive covenants that limit our ability to operate our business, raise capital or make payments under our other indebtedness. If we fail to comply with these covenants or to make payments under our indebtedness when due, then we would be in default under that indebtedness, which could, in turn, result in that and our other indebtedness becoming immediately payable in full.

We may be unable to raise the funds necessary to redeem the Convertible Notes for cash following a fundamental change, and our future indebtedness may limit our ability to redeem the Convertible Notes in connection with such fundamental change.

Holders of the Convertible Notes may, subject to a limited exception described in the indenture, require us to redeem their Convertible Notes following a fundamental change under the indenture at a cash fundamental change redemption price generally equal to the principal amount of the Convertible Notes to be redeemed in connection with such fundamental change, plus accrued and unpaid interest, if any. We may not have enough available cash or be able to obtain financing at the time we are required to redeem the Convertible Notes in connection with a fundamental change. In addition, applicable law, regulatory authorities and the agreements governing our other indebtedness may restrict our ability to redeem the Convertible Notes in connection with a fundamental change. Our failure to redeem Convertible Notes in connection with a fundamental change when required will constitute a default under the indenture. A default under the indenture or the fundamental change itself could also lead to a default under agreements governing our other consolidated indebtedness (if any), which may result in that other indebtedness becoming immediately payable in full. If the repayment of such other indebtedness were to be accelerated after any applicable notice or grace periods, then we may not have sufficient funds to repay that indebtedness and redeem the Convertible Notes in connection with such fundamental change.

Provisions in the indenture could delay or prevent an otherwise beneficial takeover of us.

Certain provisions in the Convertible Notes and the indenture could make a third party attempt to acquire us more difficult or expensive. For example, a takeover will under certain circumstances constitute a fundamental change, and the noteholders will then have the right to require us to redeem their Convertible Notes for cash. In addition, if a takeover constitutes a make-whole fundamental change, then we may be required to temporarily increase the conversion rate. In either case, and in other cases, our obligations under the Convertible Notes and the indenture could increase the cost of acquiring us or otherwise discourage a third party from acquiring us or removing incumbent management, including in a transaction that noteholders or holders of the ADSs or our ordinary shares may view as favorable.

The accounting method for the Convertible Notes could adversely affect our reported financial condition and results.

The Convertible Notes are treated as a compound financial instrument with a foreign currency financial liability component ("host"), and an embedded derivative ("derivative") related to a written option to exchange a fixed number of our own shares for a fixed amount of Convertible Notes that is denominated in a foreign currency. The derivative is not closely related to the host, because it is exposed to dissimilar risks, such as volatility from the Company's own share price. Accordingly, the derivative is accounted for separately at fair value through profit or loss.

The initial fair value of the host was the residual amount after separating the embedded derivative at fair value, net of transaction costs attributable to the host component. Transaction costs were allocated to the host and the derivative in proportion to the allocation of proceeds. Transaction costs attributable to the derivative were recognized immediately in the profit or loss as a financial expense.

The difference between the principal amount of the Convertible Notes and the initial fair value of the host is amortized into interest expense over the expected lifetime of the Convertible Notes using the effective interest method. As a result of this amortization, the interest expense that we expect to recognize for the Convertible Notes for accounting purposes will be greater than the cash interest payments we will pay on the Convertible Notes, which will result in lower reported income or higher reported loss. The lower reported income or higher reported loss resulting from this accounting treatment could depress the trading price of our common stock and the Convertible Notes.

The fair value of the derivative cannot be measured based on quoted prices in active markets, or other observable input, and accordingly, the derivative is measured by using the Black-Scholes option pricing model, where the pricing is exposed from changes in the Company’s share price. Since the fair value is exposed to development in the Company's share price, the profit or loss is exposed to volatility from such development, which could result in lower reported income or higher reported loss. The lower reported income or higher reported loss resulting from this accounting treatment could have a negative effect on the trading price of the ADSs.

In addition, the accounting method for reflecting the ordinary shares represented by ADSs underlying the Convertible Notes in our diluted earnings per share may adversely affect our reported earnings and financial condition. We expect that, under applicable accounting principles, the ordinary shares represented by ADSs underlying the Convertible Notes will be reflected in our diluted earnings per share assuming that all the Convertible Notes were converted into ADSs at the beginning of the reporting period (or, if later, the date the Convertible Notes are first issued), unless the result would be antidilutive. Accounting for the Convertible Notes in this manner may reduce our diluted earnings per share.

Risks Related to Our Ordinary Shares and ADSs

The price of the ADSs may be volatile and the holders of the ADSs may not be able to resell ADSs at or above the price they paid.

The trading price of the ADSs has been and could continue to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include:

- our ability to commercialize or obtain regulatory approval for our products or product candidates, or delays in commercializing or obtaining regulatory approval;
- results from, or any delays in, clinical trial programs relating to our products or product candidates;
- our ability to apply our TransCon technologies to therapeutic areas other than endocrinology, including the therapeutic areas of oncology and ophthalmology;
- announcements of regulatory approval or a complete response letter to our product candidates, or specific label indications or patient populations for use, or changes or delays in the regulatory review process;
- announcements relating to current or future collaborations or joint ventures;
- announcements of therapeutic innovations or new products by us or our competitors;
- announcements regarding the parent drugs that we use in developing our product candidates;
- adverse actions taken by regulatory authorities with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to our products or product candidates;
- any adverse changes to our relationship with any manufacturers or suppliers;
- the success of our testing and clinical trials;
- the success of our efforts to acquire, license or discover additional products or product candidates;
- any intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our operating results;
- EMA, FDA or other similar regulatory actions affecting us or our industry or other healthcare reform measures in the EU, United States or in other markets;
- changes in the structure of healthcare payment systems;
- changes in financial estimates or recommendations by securities analysts;
- trading volume of the ADSs;
- sales or purchases of ordinary shares and/or ADSs by us, our senior management and board members, holders of the ADSs or our shareholders in the future;
- general economic and market conditions and overall fluctuations in the United States and international equity markets, including deteriorating market conditions due to investor concerns regarding inflation and hostilities between Russia and Ukraine;
- the effects on our business, operating results, prospects and financial condition of the worldwide COVID-19 pandemic; and
- the loss of any of our key scientific or senior management personnel.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of ADSs. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of the holders of ordinary shares or ADSs were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our senior management would be diverted from the operation of our business, which could seriously harm our financial position. Any adverse determination in litigation could also subject us to significant liabilities.

ADS holders do not directly hold our ordinary shares and do not have the rights of a holder of our ordinary shares.

Danish law governs shareholder rights. Our depositary, Bank of New York Mellon, is the holder of the ordinary shares underlying our ADSs. The deposit agreement among us, the depositary, and all other persons directly and indirectly holding ADSs, sets out ADS holder rights as well as the rights and obligations of the depositary. In addition, our depositary charges certain fees to holders of our ADSs.

ADS holders may not be able to exercise their right to vote the ordinary shares underlying their ADSs.

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

ADS holders may instruct the depositary of their ADSs to vote the ordinary shares underlying their ADSs. Otherwise, ADS holders are not able to exercise their right to vote, unless they withdraw the ordinary shares underlying the ADSs they hold. However, they may not know about the meeting far enough in advance to withdraw those ordinary shares. If we ask for instructions from ADS holders, the depositary, upon timely notice from us, will notify the ADS holders of the upcoming vote and arrange to deliver our voting materials to the ADS holders. We cannot guarantee that ADS holders will receive the voting materials in time to ensure that such holders can instruct the depositary to vote the ordinary shares underlying their ADSs or to withdraw the ordinary shares underlying their ADSs so that they can vote such shares directly. If the depositary does not receive timely voting instructions from an ADS holder, the depositary may give a proxy to a person designated by us to vote the ordinary shares underlying ADSs. In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for the manner of carrying out voting instructions. This means that ADS holders may not be able to exercise any right to vote, and there may be nothing an ADS holder can do if the ordinary shares underlying their ADSs are not voted as they requested.

An ADS holder may be subject to limitations on the transfer of their ADSs and the withdrawal of the underlying ordinary shares.

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

If we issue shares or ADSs in future financings, shareholders or holders of ADSs may experience immediate dilution and, as a result, the price of our ADSs may decline.

We may from time to time issue additional shares or ADS at a discount from the trading price of our ADSs. As a result, our shareholders and holders of ADSs would experience immediate dilution upon the issuance of ADSs at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preference shares, ADSs or ordinary shares. If we issue shares or securities convertible into shares of our share capital, our ordinary shareholders and holders of ADSs would experience additional dilution and, as a result, the price of our ADSs may decline.

Sales of a substantial number of our ordinary shares or ADSs in the public market could cause the price of the ADSs to fall.

If our existing shareholders or holders of ADSs sell, or indicate an intention to sell, substantial amounts of our ordinary shares or ADSs representing our ordinary shares in the public market, the trading price of our ADSs could decline. If our outstanding warrants are exercised or ADS subject to restricted stock units vest, additional ordinary shares or ADSs may become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act. If these additional ordinary shares or ADSs are sold, or if it is perceived that they will be sold, in the public market, the trading price of the ADSs could decline. Any sales of securities by these security holders could have a negative effect on the trading price of the ADSs.

Our principal shareholders and senior management own a significant percentage of our shares and are able to exert significant control over matters subject to shareholder approval.

As of February 1, 2023, our senior management, board members, holders of 5% or more of our share capital and their respective affiliates beneficially own approximately 70.6% of our outstanding voting securities. See "Item 7 A. Major Shareholders and Related Party Transactions - Major Shareholders" for information relating to the determination of the number of shares beneficially owned by an entity or a person. As a result, these security holders have the ability either alone or voting together as a group to determine and/or significantly influence the outcome of matters submitted to our shareholders for approval, including the election and removal of board members, payment of dividends, amendments to our articles of association, including changes to our share capital or any mergers, demergers, liquidations and similar transactions. This may prevent or discourage unsolicited acquisition proposals or offers for our ordinary shares or ADSs that our shareholders or ADS holders may feel are in their best interest as a shareholder or holder of ADSs. In addition, this group of shareholders may have the ability to control our management and affairs. Such control and concentration of ownership may affect the market price of the ADSs and may discourage certain types of transactions, including those involving actual or potential change of control of us (whether through merger, consolidation, take-over or other business combination), which might otherwise have a positive effect on the market price of the ADSs.

The rights of our shareholders may be different from the rights of shareholders in companies governed by the laws of U.S. jurisdictions.

Our corporate affairs are governed by our articles of association and by the laws governing companies incorporated in Denmark, including the Danish Companies Act. The rights of shareholders and the responsibilities of members of our board of directors may be different from the rights and obligations of shareholders in companies governed by the laws of U.S. jurisdictions. In the performance of its duties, our board of directors is required by Danish law to consider the interests of our company, its shareholders and its creditors. It is possible that some of these parties will have interests that are different from, or in addition to, the interests of our shareholders.

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

We are incorporated under the laws of Denmark. Substantially all of our assets are located outside the United States. A significant portion of our board members and employees reside outside 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 against them or us in U.S. courts, including judgements predicated upon the civil liability provisions of the U.S. securities laws of the United States.

The United States and Denmark currently do not have a treaty providing for the reciprocal recognition and enforcement of judgements, other than arbitration awards, in civil and commercial matters. Consequently, a final judgement 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 Denmark. To obtain a judgement which is enforceable in Denmark, the party in whose favor a final and conclusive judgement of the U.S. court has been rendered will be required to file its claim with a court of competent jurisdiction in Denmark. Such party may submit to the Danish court the final judgement rendered by the U.S. court. If and to the extent that the Danish court finds that the jurisdiction of the U.S. court has been based on grounds which are internationally acceptable and that proper legal procedures have been observed, the Danish court should, in principle, give binding effect to the judgement of the U.S. court, unless such judgement contravenes principles of public policy of Denmark. Danish courts are likely to deny the recognition and enforcement of punitive damages or other awards. Moreover, a Danish court may reduce the amount of damages granted by a U.S. court and recognize damages only to the extent that they are necessary to compensate for actual losses or damages. Enforcement and recognition of judgements of U.S. courts in Denmark are solely governed by the provisions of the Danish Administration of Justice Act.

Based on the lack of a treaty as described above, U.S. investors may not be able to enforce against us or members of our board of directors, our executive board, our senior management or certain experts named herein who are residents of Denmark or countries other than the United States any judgements obtained in U.S. courts in civil and commercial matters, including judgements under the U.S. federal securities laws.

As a foreign private issuer, we are not subject to U.S. proxy rules and are not subject to certain Exchange Act reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.

We report under 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 and although we are subject to Danish laws and regulations with regard to such matters and intend to furnish quarterly financial information to the SEC, 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 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 four months after the end of each fiscal year, while U.S. domestic issuers that are large accelerated filers are required to file their annual report on Form 10-K within 60 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, our shareholders and the holders of our ADS may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

Our status as a "foreign private issuer" allows us to adopt IFRS accounting principles, which are different than accounting principles under U.S. Generally Accepted Accounting Principles ("U.S. GAAP").

We have adopted and presented our consolidated financial statements in accordance with IFRS as issued by the International Accounting Standards Board and as adopted by the EU. IFRS is an internationally recognized body of accounting principles that are used by many companies outside of the United States to prepare their financial statements; and the SEC permits foreign private issuers such as our company to prepare and file their financial statements in accordance with IFRS rather than U.S. GAAP. IFRS accounting principles are different from those of U.S. GAAP, and SEC rules do not require us to provide a reconciliation of IFRS accounting principles to those of U.S. GAAP. Investors who are not familiar with IFRS may misunderstand certain information presented in our consolidated financial statements. Accordingly, we suggest that readers of our consolidated financial statements familiarize themselves with the provisions of IFRS accounting principles to better understand the differences between these two sets of principles.

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

As a foreign private issuer, in accordance with the listing requirements of The Nasdaq Global Select Market, we rely on home country governance requirements and certain exemptions thereunder rather than relying on the corporate governance requirements of The Nasdaq Global Select Market. For instance, the Listing Rules for The Nasdaq Stock Market, or The Nasdaq Listing Rules, for domestic U.S. issuers require listed companies to have, among other things, a majority of their board members be independent, and to have independent director oversight of executive compensation, nomination of board members and corporate governance matters. As a foreign private issuer, however, while we intend to comply with these requirements, we are permitted to follow home country practice in lieu of the above requirements. Danish law does not require that a majority of our board consist of independent directors or the implementation of a remuneration committee or nominating and corporate governance committee, and our board may thus in the future not include, or include fewer, independent directors than would be required if we were subject to The Nasdaq Listing Rules, or they may decide that it is in our interest not to have a remuneration committee or nominating and corporate governance committee, or have such committees governed by practices that would not comply with The Nasdaq Listing Rules. Since a majority of our board of directors may not consist of independent directors, if we decide to rely on the foreign private issuer exemption to The Nasdaq Listing Rules, our board's approach may, therefore, be different from that of a board with a majority of independent directors, and as a result, the management oversight of our company could, in the future, be more limited than if we were subject to The Nasdaq Listing Rules. We intend to follow home country practice with regard to, among other things, quorum requirements generally applicable to general meetings of shareholders.

Furthermore, Danish law does not have a regulatory regime for the solicitation of proxies and the solicitation of proxies is not a generally accepted business practice in Denmark, thus our practice varies from the requirement of Nasdaq Listing Rule 5620(b). In addition, our shareholders have authorized our board of directors to issue securities including in connection with certain events such as the acquisition of shares or assets of another company, the establishment of or amendments to equity-based compensation plans for employees, a change of control of us, rights issues at or below market price, certain private placements and issuance of convertible notes. To this extent, our practice varies from the requirements of Nasdaq Rule 5635, which generally requires an issuer to obtain shareholder approval for the issuance of securities in connection with such events. Accordingly, our shareholders and holders of our ADS may not have the same protections afforded to shareholders of companies that are subject to these Nasdaq requirements.

We may 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 qualify as 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. We may no longer be a foreign private issuer as of June 30, 2023, which would require us to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers as of January 1, 2024. To maintain our current status as a foreign private issuer, either (a) a majority of our ordinary shares or ADSs 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% of our assets cannot be located in the United States and (iii) our business must not be administered principally inside the United States. If we lost this 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 board of directors and members of our senior management.

We do not currently intend to pay dividends on our ordinary shares or ADSs, and, consequently, our shareholders' and ADS holders' ability to achieve a return on their investment will depend on appreciation in the price of the ADSs or our ordinary shares.

We do not currently intend to pay any cash dividends on our ordinary shares for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, our shareholders and ADS holders are not likely to receive any dividends on their investment for the foreseeable future. Because we do not intend to pay dividends, our shareholders' and ADS holders' ability to receive a return on their investment will depend on any future appreciation in the market value of our ADSs. There is no guarantee that our ordinary shares or ADSs will appreciate or even maintain the price at which our holders have acquired them.

Investors should be aware that the rights provided to our shareholders and holders of ADSs under Danish corporate law and our articles of association differ in certain respects from the rights that would typically be provided to a shareholder of a U.S. company under applicable U.S. federal and state laws.

Under Danish corporate law, except in certain limited circumstances (which require as a minimum that a proposal for inspection has been supported by a minimum of 25% 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 Danish limited liability company are also unable to initiate a derivative action, a remedy typically available to shareholders of U.S. companies, to enforce a right of our company, in case we fail to enforce such right ourselves, other than in certain cases of board member or management liability under limited circumstances. In addition, a majority of our shareholders may release a board member or manager 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 and only if a minority of at least 10% of the shareholders represented at the relevant general meeting have opposed the decision, may a shareholder bring a derivative action on behalf of our company. 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 Danish companies to foreign companies and individuals may be subject to non-refundable withholding tax, which may not be creditable or deductible under the tax laws of the country in which the recipient shareholder is resident for tax purposes. Also, the rights as a creditor may not be as strong under Danish 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 deficit requires that we are able to generate positive taxable income and can be restricted by future amendments to Danish tax law. Further, repurchases of ordinary shares or ADSs by Ascendis Pharma A/S may have adverse tax consequences to the Company or shareholders under applicable Danish law. Finally, Danish 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 Danish 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, shareholders and ADS holders could receive less protection as an equity holder of our company than they would as a shareholder of a U.S. company.

Holders of our ordinary shares or ADSs may not be able to exercise their pre-emptive subscription rights and may suffer dilution of their equity holding in the event of future issuances of our shares.

Under the Danish Companies Act, our shareholders benefit from a pre-emptive subscription right on the issuance of ordinary shares for cash consideration only and not in the event of issuance of shares against non-cash contribution or debt conversion. Even the 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 or ADSs 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. Such shares or ADSs may be issued above, or at market value. In addition, a shareholder may not be able to exercise the shareholder's pre-emptive right on a timely basis or at all, unless the shareholder complies with the Danish Companies Act and applicable laws in the jurisdiction in which the shareholder is resident. Furthermore, the use of pre-emptive subscription rights in relation to future capital increases in our company can be restricted for U.S. residents according to U.S. securities law. As a result, the shareholding or holding of ADSs of such shareholders or ADS holders may be materially diluted in the event shares or ADSs are issued in the future. Shares or ADSs may be issued at a discount to market price in rights offerings provided that the resolution is approved by two-thirds of the votes cast and the share capital represented at the general meeting and in these cases a restriction on the ability to exercise pre-emptive rights may materially dilute the value of the ordinary shares or ADSs held by the shareholder or ADS holder in question. Rights issues may also be carried out by the board of directors according to valid authorizations in our articles of association.

However, our ADS holders in the United States are not entitled to exercise or sell such pre-emptive subscription rights related to the ordinary shares, which they represent unless we register the pre-emptive subscription rights and the securities to which the pre-emptive subscription rights relate under the Securities Act or an exemption from the registration requirements is available. In addition, the deposit agreement provides that the depositary will not make rights available to ADS holders unless the distribution to ADS holders or both the rights and any related securities are either registered under the Securities Act or exempted from registration under the Securities Act. Further, if we offer holders of our ordinary shares the option to receive dividends in either cash or shares, under the deposit agreement the depositary may require satisfactory assurances from us that extending the offer to holders of ADSs does not require registration of any securities under the Securities Act before making the option available to holders of ADSs. We are under no obligation to file a registration statement with respect to any such rights or securities or to endeavor to cause such a registration statement to be declared effective. Moreover, we may not be able to establish an exemption from registration under the Securities Act. Accordingly, ADS holders may be unable to participate in our rights offerings or to elect to receive dividends in shares and may experience dilution in their holdings. In addition, if the depositary is unable to sell rights that are not exercised or not distributed or if the sale is not lawful or reasonably practicable, it will allow the rights to lapse, in which case our shareholders and ADS holders will receive no value for these rights.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our ordinary shares or ADSs, the price of the ADSs and trading volume could decline.

The trading market for the ADSs may be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or performance of the ADSs, or if our commercial sales, clinical trials or operating results fail to meet the expectations of analysts, 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, we could lose visibility in the financial markets, which in turn could cause the price of the ADSs or trading volume to decline.

We may be a "passive foreign investment company" for U.S. federal income tax purposes for our current taxable year and future taxable years, which could result in adverse U.S. federal income tax consequences to U.S. investors.

Under the Internal Revenue Code of 1986, as amended (the "Code"), and U.S. Treasury Regulations, the determination of passive foreign investment company ("PFIC") status is fact-specific, and generally cannot be made until after the close of the taxable year in question. Based on our market capitalization and the composition of our income, assets and operations, we do not believe we were a PFIC for U.S. federal income tax purposes for our taxable year ended December 31, 2022. However, this is a factual determination, and the application of the PFIC rules is subject to uncertainty in several respects, and we cannot assure you we will not be a PFIC for any taxable year. A non-U.S. corporation will be considered a PFIC for any taxable year if, after the application of certain look-through rules, either (1) at least 75% of its gross income for such taxable year is passive income (as defined in the relevant provisions of the Code) or (2) at least 50% of the value of its assets (generally based on an average of the quarterly values of the assets) during such year is attributable to assets that produce or are held for the production of passive income. A separate determination must be made each taxable year as to whether we are a PFIC (after the close of each such taxable year). If we are a PFIC for any taxable year during which a U.S. Holder (as defined in "Taxation—Material U.S. Federal Income Tax Consequences to U.S. Holders") holds ordinary shares or ADSs, the U.S. Holder may be subject to adverse tax consequences, including (i) the treatment of all or a portion of any gain on disposition as ordinary income, (ii) the application of an interest charge with respect to such gain and certain dividends and (iii) compliance with certain reporting requirements. Although we do not believe we were a PFIC for U.S. federal income tax purposes for our taxable year ended December 31, 2022, the application of the PFIC rules is subject to uncertainty in several respects. Whether we will be a PFIC in any year depends on the composition of our income and assets, and the relative fair market value of our assets from time to time, which we expect may vary substantially over time. In addition, because the value of our assets, including unbooked goodwill, for purposes of the asset test will generally be determined by reference to the market price of the ADSs, our PFIC status will depend in large part on the market price of the ADSs, which may fluctuate significantly. For these reasons, we cannot assure you we will not be a PFIC for any taxable year.

Each U.S. Holder is strongly urged to consult its tax advisor regarding these issues. See "Item 10 E. Additional Information—Taxation—Material U.S. Federal Income Tax Consequences to U.S. Holders."

If a United States person is treated as owning at least 10% of our ordinary shares or ADSs, such holder may be subject to adverse U.S. federal income tax consequences.

If a U.S. Holder (as defined in "Item 10 E. Additional Information—Taxation—Material U.S. Federal Income Tax Consequences to U.S. Holders.") is treated as owning (directly, indirectly or constructively) at least 10% of the value or voting power of our ordinary shares or ADSs, such U.S. Holder will be treated as a "United States shareholder" with respect to each "controlled foreign corporation" in our group. Because our group includes one or more U.S. subsidiaries, certain of our non-U.S. subsidiaries will be treated as "controlled foreign corporations" (regardless of whether we are treated as a "controlled foreign corporation"). A "United States shareholder" of a "controlled foreign corporation" may be required to report annually and include in its U.S. taxable income its pro rata share of "Subpart F income," "global intangible low-taxed income" and investments in U.S. property by "controlled foreign corporations," regardless of whether we make any distributions. Failure to comply with these reporting obligations may subject a "United States shareholder" to significant monetary penalties and may prevent the statute of limitations from starting with respect to such shareholder's U.S. federal income tax return for the year for which reporting was due. Further, an individual that is a "United States shareholder" with respect to a "controlled foreign corporation" generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a "United States shareholder" that is a U.S. corporation. We cannot provide any assurances that we will assist investors in determining whether any of our non-U.S. subsidiaries are treated as a "controlled foreign corporation" or whether such investor is treated as a "United States shareholder" with respect to any of such "controlled foreign corporations." Further, we cannot provide any assurances that we will furnish to any "United States shareholders" information that may be necessary to comply with the aforementioned reporting and tax payment obligations. U.S. Holders should consult their tax advisors regarding the potential application of these rules to their investment in our ordinary shares or ADSs.

Item 4 Information on the Company

A. History and Development of the Company

We were organized under the laws of the Kingdom of Denmark in September 2006 as a private limited liability company (*Anpartsselskab*, or ApS) and then transformed into a public limited liability company (*Aktieselskab*, or A/S), effective December 17, 2007. In connection with this conversion, our legal name changed from Ascendis Pharma ApS to Ascendis Pharma A/S. We commenced operations in December 2007 in connection with the acquisition of the company that invented our TransCon technologies, Complex Biosystems GmbH.

Our registered office and principal executive offices are located at Tuborg Boulevard 12, DK-2900 Hellerup, Denmark and our telephone number is +45 70 22 22 44. Our agent for service of process in the United States is Ascendis Pharma, Inc. Our corporate website address is www.ascendispharma.com. The information on, or that can be accessed through, our website is not part of and should not be incorporated by reference into this annual report or any other report we file or furnish to the U.S. Securities and Exchange Commission ("SEC"). We have included our website address as an inactive textual reference only. Our ADSs are traded on The Nasdaq Global Select Market under the symbol "ASND".

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

For additional information relating to the development of our company, see "Item 4 B. Information on the Company – Business Overview." For additional information relating to the Company's capital expenditures, see "Item 5 A. Operating and Financial Review and Prospects—Operating Results."

B. Business Overview

Overview

We are applying our innovative TransCon platform to build a leading, fully integrated, global biopharma company, focused on making a meaningful difference in patients' lives. Guided by our core values of patients, science, and passion, we use our TransCon technologies to create new and potentially best-in-class therapies.

Our Vision

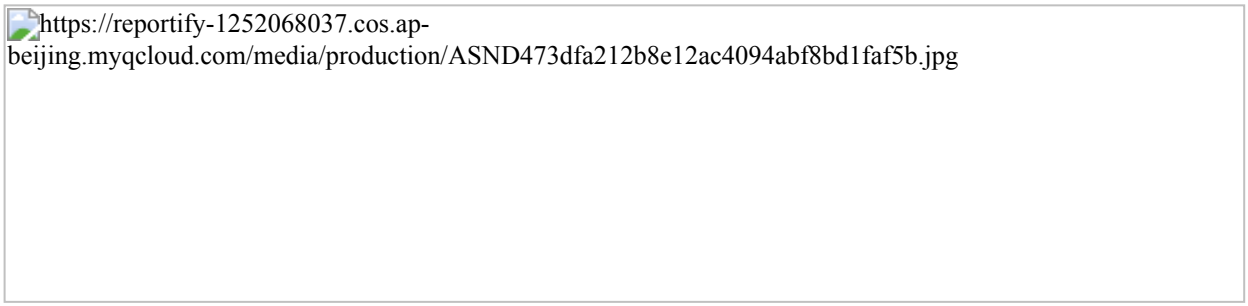
As announced in January 2019, Vision 3x3 is our vision to build a leading fully integrated, global, biopharma company and achieve sustainable growth through multiple approaches. This includes:

- Obtain regulatory approval for three independent Endocrinology Rare Disease products
  - TransCon hGH for pediatric growth hormone deficiency
  - TransCon PTH for adult hypoparathyroidism
  - TransCon CNP for achondroplasia
- Grow Endocrinology Rare Disease pipeline through
  - Global clinical reach
  - Pursuing 9 total indications, label optimization, and life cycle management
  - New endocrinology products
- Establish global commercial presence for our Endocrinology Rare Disease area
  - Build integrated commercial organization in North America and select European countries
  - Establish global commercial presence through partners with local expertise and infrastructure
- Advance a high-value oncology pipeline with one investigational new drug ("IND") or similar submission each year
- Create a third independent therapeutic area with a diversified pipeline

Our product candidates combine our TransCon technologies with clinically validated parent drugs and pathways, with the goal of optimizing efficacy, safety, tolerability and convenience.

We have applied these technologies in combination with clinically validated parent drugs or pathways using our algorithm with the goal of creating product candidates with the potential to be best-in-class in endocrinology rare diseases, oncology, and ophthalmology. In addition, we plan to apply this algorithm for product innovation in new therapeutic areas. We believe our approach to product innovation may reduce the risks associated with traditional drug development, and that our TransCon technologies have been validated by non-clinical and clinical programs completed to date.

Ascendis Algorithm for Product Innovation



When we apply our TransCon technologies to clinically validated parent drugs or pathways, we may benefit from established clinical safety and efficacy data, which we believe increases the probability of success compared to traditional drug development. As presented above, our algorithm for product innovation focuses on identifying indications that have an unmet medical need, have a clinically validated parent drug or pathway, are suitable to our TransCon technologies, have potential for creating a clearly differentiated product, have a potential established development pathway and have the potential to address a large market.

We currently have one marketed product and a diversified portfolio of five product candidates in clinical development in the areas of endocrinology rare diseases, and oncology and we are working to apply our TransCon technology platform in additional therapeutic areas, including ophthalmology.

- *First Marketed Product* – Our first marketed product is SKYTROFA® (lonapegsomatropin-tcgd), developed as TransCon Growth Hormone ("TransCon hGH"), which has received regulatory approval in the United States for the treatment of pediatric patients one year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone, also known as growth hormone deficiency ("GHD") and which is now commercially available for prescription in the United States. In addition, in the European Union ("EU"), TransCon hGH was granted marketing authorisation by the European Commission ("EC") as a once-weekly subcutaneous injection for the treatment of children and adolescents ages 3 to 18 years with growth failure due to insufficient secretion of endogenous growth hormone, known by its brand name SKYTROFA (lonapegsomatropin). In Europe, we plan to commercially launch SKYTROFA in Germany during the third quarter of 2023.
- *Endocrinology Rare Disease Pipeline* – We are developing three product candidates in our endocrinology rare disease portfolio spanning five potential indications across multiple geographies. These include TransCon hGH for pediatric GHD, adult GHD, and Turner Syndrome; TransCon PTH for adult patients with hypoparathyroidism; and TransCon CNP for achondroplasia ("ACH").
- *Oncology* – In oncology, we are leveraging our TransCon technologies in effort to enhance anti-tumor effects of clinically-validated parent drugs and pathways and to provide sustained modulation of tumor microenvironments and activate cytotoxic immune cells. We have initiated clinical development of two product candidates: TransCon TLR7/8 Agonist, an investigational, long-acting prodrug of resiquimod, a small molecule agonist of Toll like receptors ("TLR") 7 and 8 for intratumoral delivery and TransCon IL-2 ß/□ for systemic delivery, which is designed for prolonged exposure to an IL-2 variant that selectively activates the IL-2Rß/□, with minimal binding to IL-2Rα. Our clinical development program for these product candidates also includes evaluation of them as a potential combination therapy.
- *Ophthalmology* - In January 2023, we announced that we are establishing ophthalmology as our third independent therapeutic area of focus for our TransCon technologies. Ophthalmology intravitreal treatments ("IVT") represent an established, well-understood, and high-value therapeutic area, characterized by high unmet medical need. We are leveraging our TransCon hydrogel technology to create highly differentiated product candidates designed to provide continuous local release of clinically validated parent drugs over a period of months. TransCon RBZ (ranibizumab) is our first investigational pipeline candidate being developed to address vision loss caused by abnormal blood vessel growth and/or fluid build-up in the back of the eye. Our ophthalmology development pipeline includes other opportunities in various stages of development.

TransCon Products and Product Candidates Pipeline

1. *Not yet marketed in the EU*
2. *riGHt Trial*
3. *foresiGHt Trial*
4. *New InsiGHts Trial*
5. *NDA submitted to the FDA, PDUFA action date April 30, 2023; European MAA submitted November 2022, decision anticipated Q4 2023*
6. *PaTHway Japan Trial*
7. *ApproaCH Trial*
8. *transcendIT-101 Trial, includes 4 indication specific cohorts currently enrolling patients*
9. *IL-ßelie□e Trial*

We maintain an intellectual property portfolio comprising 282 issued patents and approximately 520 patent applications as of December 31, 2022 with claims directed to composition of matter, process, formulation and/or methods-of-use for our product candidates, including a product-specific device and core TransCon technologies. Other than the rights we have granted to VISEN Pharmaceuticals ("VISEN") as noted in this report, we hold worldwide rights to our TransCon technologies and owe no third-party royalty or milestone payment obligations with respect to our TransCon technologies, TransCon hGH or any of our other product candidates. While our TransCon prodrugs may incorporate already approved parent drugs, TransCon hGH and each of our other product candidates is a new molecular entity and is therefore eligible to be granted new intellectual property rights, including new composition of matter patents.

Global Commercialization Strategy

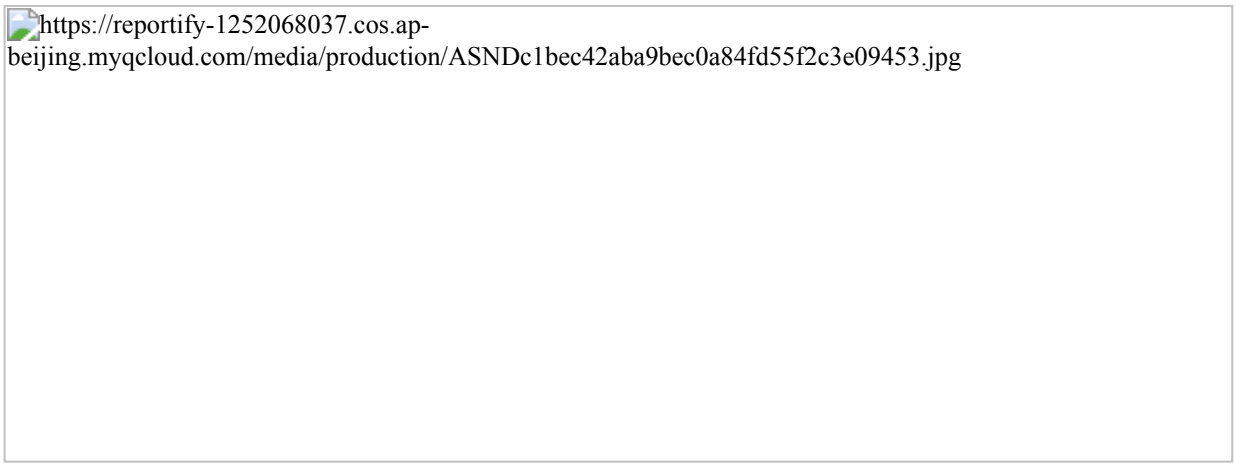
We are establishing a global presence to commercialize TransCon product candidates, if approved, to address patients' unmet medical needs. We have established a multi-faceted organization in the U.S. to support the ongoing commercialization of SKYTROFA which will also serve as the foundation for future endocrinology rare disease product launches in the U.S. We are expanding our presence in Europe by building integrated organizations in select countries beginning with the planned launch of SKYTROFA in Germany and through established distribution channels in others. In other markets, we plan to establish commercial presence through partners with local expertise and infrastructure.

TransCon Technologies

Overview

Our TransCon technologies are designed to combine the benefits of conventional prodrug and sustained release technologies to solve the fundamental limitations seen in other approaches to extending duration of a drug's action in the body with the goal of developing highly differentiated product candidates based on efficacy, safety, tolerability and convenience. In addition to retaining the original mode of action of the parent drug and potentially supporting dosing frequency from daily up to six months or more, we believe that predictable release over time can improve treatment efficacy, increase the likelihood of clinical development success, and provide intellectual property benefits.

TransCon molecules have three components: a parent drug, an inert carrier that protects it, and a linker that temporarily binds the two. When bound, the carrier inactivates and shields the parent drug from clearance. When injected into the body, physiologic pH and temperature conditions initiate the release of the active, unmodified parent drug in a predictable release manner. Depending upon the type of TransCon carrier we employ, we can design our TransCon prodrugs for sustained localized or systemic delivery.

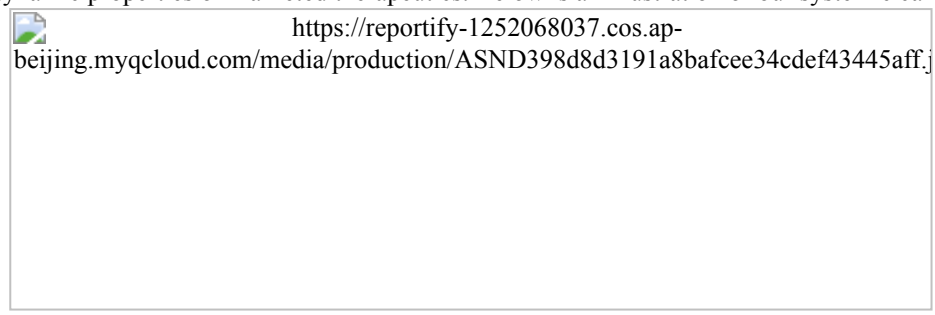


TransCon Technology Components

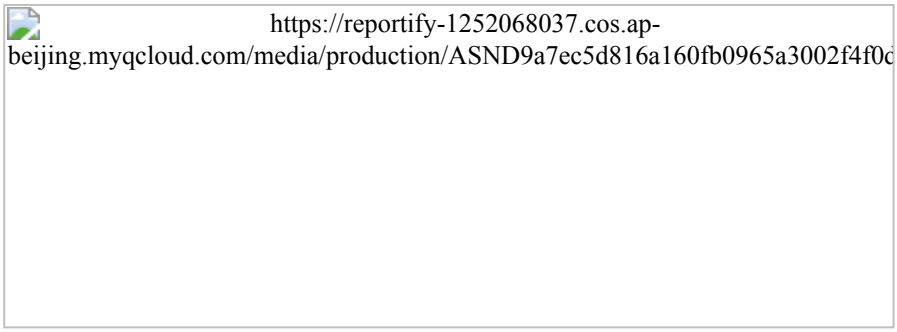
TransCon Carriers

Our TransCon technologies incorporate two carrier platforms that can be used for providing sustained localized or systemic drug exposure. These biocompatible carrier platforms include our TransCon systemic carriers, and our TransCon localized carriers, which are self-eliminating hydrogels. Our carriers inactivate and protect the drug through a shielding effect, which may prevent rapid excretion and degradation of the parent drug and enable benefits that include improved injection site tolerability, reduced systemic adverse effects and low immunogenicity.

- *Systemic* – Our TransCon systemic carriers are used for providing systemic drug exposure and are based on soluble compounds such as methoxy polyethylene glycol ("mPEG"), or other natural or synthetic polymers. Prodrugs created using our systemic carriers are readily absorbed into the bloodstream after administration, thus minimizing exposure of the subcutaneous tissue to active drug, which we believe may improve injection site tolerability. TransCon hGH, TransCon PTH and TransCon CNP, utilize mPEG as a carrier molecule. mPEG is widely used to improve the pharmacokinetic or pharmacodynamic properties of marketed therapeutics. Below is an illustration of our systemic carrier:



- *Localized* – Our TransCon localized carriers include TransCon hydrogels based on PEG, hyaluronic acid, or other biopolymers. TransCon hydrogel is designed to self-eliminate to soluble, biocompatible molecules after the drug payload has been released. When applied for localized delivery, the TransCon hydrogel enables the release of parent drug at high local concentrations within the target area while minimizing systemic exposure. We believe this may widen the therapeutic window for parent drugs that suffer from significant systemic side effects and toxicities, facilitating the development of highly efficacious product candidates with improved safety and tolerability profiles. Below is an illustration of our hydrogel carrier:



TransCon Linkers

Our reversible TransCon linkers are designed to enable the transient conjugation of a broad range of therapeutics, including proteins, peptides and small molecules, to our TransCon carriers. We have a large library of TransCon linkers that may be applicable to various types of parent drugs, and that can be tailored to potentially achieve half-life extension enabling daily, weekly, monthly, and half-yearly dosing, and customize the potential pharmacokinetic profile for each individual product candidate with the goal of optimizing the potential therapeutic effect. TransCon linkers are self-cleaving through a process called intra-molecular assisted cleavage, which causes the linker to release the unmodified parent drug. We can tailor the release properties of the linker to a given therapeutic indication and parent drug by modifying the linker structures. We believe the self-cleaving process of our linker avoids many of the shortcomings of conventional prodrug technologies, which often depend on metabolic processes, such as enzymatic degradation, to convert the prodrug into the active drug. The rate of metabolic conversion of prodrugs in these types of processes may differ between patients, and even within different tissues in the same patient. As a result, conventional prodrugs do not always offer predictable release of the parent drug. Our TransCon linkers are designed to predictably release an unmodified active parent drug at predetermined rates governed by physiological pH and temperature conditions, which are tightly regulated in the body. Consequently, we believe we can design our prodrugs to release the unmodified parent drug at predictable rates.

Parent Drugs

Our TransCon technologies are applicable across a broad range of therapeutic classes and are currently used to create potentially best-in-class long-acting product candidates based on proteins, peptides and small molecules. By primarily focusing on biological targets that have been clinically validated, we can leverage available knowledge regarding a target's activity. Based on this selective approach, we know what drug levels must be maintained in the body for optimal efficacy and safety, and we can design the release half-life and dosing frequency of our TransCon prodrugs to maintain these levels to achieve the desired pharmacological effect. We move a product candidate into development after it demonstrates the desired profile in non-clinical models. Furthermore, based on the established translational relationships between preclinical animal models and clinical efficacy, we believe experimental results generated in animal models are highly predictive of clinical results and reduce the development risk of our TransCon prodrugs. This strategy is designed to reduce risk and increase productivity.

This approach has enabled us to generate a pipeline of product candidates to address significant unmet medical needs and to become potential sources of significant revenue for our company. Because our TransCon technologies leverage clinically validated parent drugs or pathways, we believe we may benefit from a higher development and regulatory success rate as compared to development of drug compounds without established biology.

TransCon Products – Endocrinology Rare Disease

TransCon Growth Hormone (hGH)

Market Opportunity in Recombinant Human Growth Hormone

GHD is a serious orphan disease that affects both children and adults. Children with GHD are characterized by short stature, metabolic and cardiovascular abnormalities, cognitive deficiencies, and poor quality of life. GHD in adults is associated with increased adiposity, or fat mass, as well as psychiatric-cognitive, cardiovascular, muscular, metabolic and skeletal abnormalities. The current standard of care for GHD is daily subcutaneous injections of somatropin, a recombinant human growth hormone ("hGH"). Daily therapy with hGH has been shown to increase growth in children, and improve metabolic effects, including reducing adiposity and improving cardiovascular health in both children and adults. These daily hGH therapies have been shown to be safe and well-tolerated.

In both therapy-compliant children and adults with GHD, daily subcutaneous injections of hGH have resulted in improved body composition parameters, bone density, cardiovascular outcomes and quality of life. Growth hormone-deficient children who are fully adherent with their daily hGH treatment regimen may achieve a height in adulthood that is comparable to that of their family members and national norms.

Despite the demonstrated benefits of daily hGH therapy, many GHD patients are not adequately treated and adherence continues to be a challenge as reported in a 2021 paper published by Kaplowitz et al. in the *Journal of Managed Care and Specialty Pharmacy.* The observational retrospective cohort analysis utilized administrative claims data from two databases on over 20,000 pediatric patients diagnosed with GHD. Approximately 68% of commercial patients and approximately 63% of Medicaid patients received daily growth hormone treatment, whereas approximately 32% of commercial patients and approximately 37% of Medicaid patients were untreated. In addition, mean adherence as measured by proportions of days covered which is defined as the number of days covered by any daily growth hormone prescription during the follow-up period was approximately 60% in the commercial cohort and approximately 50% in the Medicaid cohort. Only 32% of commercial and 18% of Medicaid patients reported adherence rates greater than 80%.

Reducing injection frequency is associated with better adherence and thus may improve height velocity ("HV") for pediatric patients experiencing poor adherence with daily hGH injections. As shown in the figure below, for patients missing two or more injections per week, there was a clinically relevant reduction in their change in HV standard deviation score ("HVSDS") compared to high-compliance patients. A greater HVSDS indicates more rapid growth:

Figure: Negative impact of poor compliance on growth response. Patients missing two or more injections per week had a statistically significant reduction in height velocity; N=175. (Cutfield et al, 2011)

Since the introduction of hGH in 1981, a number of the world's largest pharmaceutical companies have developed and now market daily-prescribed hGH products. All currently marketed daily hGH products in the United States, Norditropin® (Novo Nordisk A/S), Humatrope® (Eli Lilly and Company), Nutropin AQ® (Genentech), Genotropin® (Pfizer Inc.), Zomacton® (Ferring Pharmaceuticals, Inc.) and Omnitrope® (Sandoz GmbH), contain unmodified somatropin (hGH) and are administered by subcutaneous injections. The global market for daily hGH products is dominated by Novo Nordisk, Pfizer, Eli Lilly, Sandoz, Merck KGaA and Roche, which together account for most of the global market share.

Primary indications for hGH in children are GHD, idiopathic short stature, chronic kidney disease, Prader-Willi syndrome, small for gestational age and Turner syndrome. In adults, primary indications for hGH include GHD and AIDS-induced weight loss. We estimate pediatric indications comprise up to 90% of the total hGH market, of which approximately half is for GHD.

Global annual sales from currently marketed hGH products are currently estimated at approximately $4 billion. We believe a significant market opportunity exists for a once-weekly hGH product with comparable efficacy, safety and tolerability as daily hGH products.

Competitive Landscape for Long-Acting Growth Hormone Therapies

Since the 1990s, the pharmaceutical industry has employed various approaches to develop long-acting growth hormone products to reduce the patient burden of daily injections and increase patient compliance with the dosing regimen. These approaches generally fall into two categories: unmodified somatropin (hGH) and permanent modification of growth hormone:

- Unmodified somatropin (hGH): Two long-acting growth hormone products using encapsulation technologies have previously received regulatory approval in U.S. and Europe and were subsequently discontinued due to commercial challenges. These include Nutropin Depot®, formerly marketed by Genentech, and Somatropin Biopartners, developed by LG Life Sciences and Biopartners GmbH. Nutropin Depot was approved in 1999 and later withdrawn; Somatropin Biopartners (LB03002), was approved by the European Medicines Agency (“EMA”) in 2013, and later withdrawn. We believe that the lack of market acceptance is a result of the various safety and tolerability issues that tend to arise with encapsulation technologies.
- Permanent modification of growth hormone: Modification technologies prolong activity in the body by creating analogs of growth hormone through permanent modification of the growth hormone molecule. This modification may alter the molecular size and interaction with the growth hormone receptor and/or change the natural association affinity to endogenous proteins, as well as the distribution in the body. These changes may alter and reduce the efficacy of these drugs compared to unmodified daily somatropin (hGH) and may also negatively impact the drug’s safety.

Novo Nordisk has received regulatory approval in the United States, Japan, and EU of once-weekly somapacitan (SOGROYA) for replacement of endogenous growth hormone in adult patients with GHD and submitted marketing applications seeking approval for somapacitan in the United States, Japan, and Europe for pediatric GHD.

Pfizer (in collaboration with OPKO Health Inc.) has received regulatory approval of once-weekly somatrogon (NGENLA) in the EU, Canada, Australia, Japan, Taiwan, the United Arab Emirates and Brazil for pediatric GHD. In January 2022, Pfizer (in collaboration with OPKO Health) announced the U.S. Food and Drug Administration ("FDA") issued a Complete Response Letter for the Biologics License Application (“BLA”) for somatrogon.

A permanently PEGylated long-acting growth hormone developed by GeneScience Pharmaceuticals Co., Ltd. (Jintrolong) is available in China and the Somatropin Biopartners product (LB03002) is available in Korea. Other experimental growth hormone therapies based on permanent modification are in different stages of clinical development by various companies, including GeneScience Pharmaceuticals Co., Ltd., Genexine Inc., I-MAB, and JCR Pharmaceuticals Co., Ltd.

Our Solution: TransCon hGH

TransCon hGH is a long-acting prodrug of somatropin (hGH) composed of an unmodified somatropin that is transiently bound to a carrier and proprietary linker. TransCon hGH is designed to maintain the same mode of action as daily therapies by releasing the same recombinant growth hormone molecule, somatropin, as used in extensively proven daily hGH therapy that is the current standard of care.

On August 25, 2021, the FDA approved TransCon hGH, known by its brand name SKYTROFA® (lonapegsomatropin-tcgd), for the treatment of pediatric patients one year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone, also known as GHD. SKYTROFA is the first FDA approved product that delivers somatropin, or growth hormone, by sustained release over one week.

The FDA approval of SKYTROFA (lonapegsomatropin-tcgd) was based on results from the Phase 3 heiGHt Trial, a 52-week, global, randomized, open-label, active-controlled, parallel-group trial that compared once-weekly TransCon hGH to daily somatropin (Genotropin®) in 161 treatment-naïve children with GHD. The primary endpoint was annualized height velocity ("AHV") at 52 weeks for weekly SKYTROFA (lonapegsomatropin-tcgd) and daily hGH treatment groups. Other endpoints included adverse events, injection-site reactions, incidence of anti-hGH antibodies, annualized height velocity, change in height standard deviation score ("SDS"), proportion of subjects with IGF-1 SDS (0.0 to +2.0), PK/PD in subjects < 3 years, and preference for and satisfaction with SKYTROFA (lonapegsomatropin-tcgd).

We believe SKYTROFA (lonapegsomatropin-tcgd) offers patients benefits compared to daily growth hormone:

- A national study has shown 66%, or 2/3 of patients miss more than one injection per week. We believe reducing injection frequency is associated with better adherence and thus may improve height velocity.
- In a Phase 3 clinical study, TransCon hGH demonstrated higher AHV compared to daily somatropin with similar safety profile in treatment-naïve children with GHD.
- With a weekly injection, patients switching from daily injections can experience up to 86% fewer injection days per year.
- After first removed from a refrigerator, SKYTROFA (lonapegsomatropin-tcgd) can be stored at room temperature for up to six months.

On January 11, 2022, the EC granted a marketing authorisation for SKYTROFA (lonapegsomatropin), developed under the name TransCon hGH, as a once-weekly subcutaneous injection for the treatment of children and adolescents ages 3 to 18 years with growth failure due to insufficient secretion of endogenous growth hormone.

In October 2019, we received Orphan Designation ("OD") from the EC for TransCon hGH for GHD. OD is granted to medicinal products that are (1) intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating, (2) provided that either (a) the disease affects no more than five in 10,000 persons in the EU, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment and (3) for which no satisfactory method of diagnosis, prevention, or treatment has been authorized for marketing in the EU (or if such a method exists, the product would provide significant additional benefit over existing therapies). We received Orphan Drug Designation ("ODD") from the FDA for TransCon hGH as a treatment for GHD in April 2020.

Results from the Phase 3 heiGHt Trial in Pediatric Subjects with GHD

The heiGHt Trial was a randomized, open-label, active-controlled Phase 3 registrational trial that enrolled 161 children with GHD who had not previously been treated. Subjects received either once-weekly TransCon hGH (0.24 mg/kg/week) or daily injections of Genotropin® at 34 µg/kg/day (0.24 mg/kg/week) with a 2:1 randomization. The primary endpoint was AHV at 52 weeks, with a non-inferiority analysis comparing the difference between the two treatment groups, followed by a test of superiority if non-inferiority was met. Two subjects, one from each arm, withdrew from the trial prior to the final visit.

Results showed that once-weekly TransCon hGH was superior to once-daily hGH on the primary endpoint of AHV at 52 weeks. In the primary analysis of the intent-to-treat population using least squared mean ("LS Mean") results from an ANCOVA model, TransCon hGH was associated with an AHV of 11.2 cm/year compared to 10.3 cm/year for the daily hGH. The treatment difference was 0.86 cm/year with a 95% confidence interval of 0.22 to 1.50 cm/year. The AHV for TransCon hGH was significantly greater than the daily hGH (p=0.0088).

Results from the trial indicated that TransCon hGH was generally safe and well-tolerated, with adverse events consistent with the type and frequency observed with daily hGH therapy and comparable between arms of the trial. No serious adverse events related to study drug were observed in either arm. No treatment-emergent adverse events leading to discontinuation of study drug were observed in either arm.

Additional Clinical Trials of TransCon hGH in Pediatric Subjects with GHD

In our ongoing Phase 3 riGHt Trial we are evaluating TransCon hGH in Japanese subjects for the treatment for pediatric GHD. The primary objective of the riGHt Trial is to evaluate and compare the annualized height velocity of 40 Japanese prepubertal treatment naïve children with GHD treated with weekly TransCon hGH to that of a commercially available daily hGH formulation at 52 weeks.

Proprietary Auto-injector

SKYTROFA includes the SKYTROFA® Auto-Injector and cartridges. The auto-injector provides for room temperature storage, includes an empty-all design and is expected to last for at least four years. The device has a single, low-volume injection for the majority of patients of less than 0.6 mL and requires a thin, 31-gauge needle that is only 4 millimeters in length, which is comparable to needles used to administer daily hGH. We are also working on strategies that will enable the auto-injector to integrate with the digital healthcare system, including Bluetooth connectivity features to allow for easy tracking of dosing adherence over time.

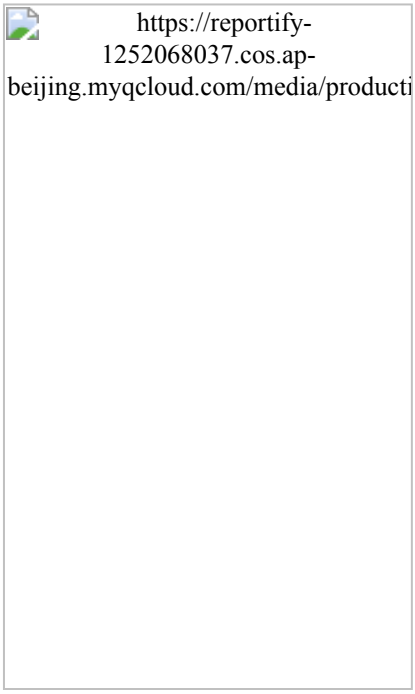


Figure: Our state-of-the-art auto-injector is designed to improve treatment compliance for children with GHD.

TransCon Product Candidates – Endocrinology Rare Diseases

TransCon Growth Hormone (hGH) for Other Indications

Clinical Development in Adults

We are currently conducting foresiGHt Trial, a global Phase 3 trial with the aim to demonstrate the metabolic benefits of TransCon hGH in adults and with the primary objective to evaluate change in trunk fat percentage. Patients in the trial are randomized in a 1:1:1 ratio into the three arms of the study—treatment with once-weekly TransCon hGH, once-weekly placebo, or daily hGH. The primary endpoint of the trial is a change from baseline in percentage trunk fat at 38 weeks. Following the 38-week main trial period, all patients will be eligible to receive once-weekly TransCon hGH during the 52-week open-label extension. During the fourth quarter, 2022, we completed recruitment into the Phase 3 foresiGHt Trial. Topline results from foresiGHt are expected in the fourth quarter of 2023.

Other Development Plans

In June 2022, we submitted a trial protocol to the FDA to evaluate TransCon hGH in Turner Syndrome. We are evaluating higher doses of TransCon hGH and daily hGH for Turner Syndrome compared to those doses for pediatric or adult GHD. In addition, we are also considering other potential indications for TransCon hGH where we believe a long-acting hGH therapy may offer benefits to patients with rare growth disorders.

TransCon PTH

Market Opportunity in Hypoparathyroidism

Hypoparathyroidism is a rare endocrine disorder characterized by insufficient levels of parathyroid hormone ("PTH"). Most hypoparathyroidism patients develop the condition following damage to or accidental removal of the parathyroid glands during thyroid surgery. Conventional therapy with calcium supplements and active vitamin D (also called calcitriol) does not effectively address the short-term symptoms, long-term complications, or quality-of-life impacts of hypoparathyroidism.

Short-term symptoms include weakness, severe muscle cramps (tetany), abnormal sensations such as tingling, burning and numbness (paresthesia), memory loss, impaired judgment, and headache. Patients often experience decreased quality of life, and, over the long term, prolonged use of conventional therapy may increase risk of major complications, such as calcium deposits in the brain, blood vessels, eye, and other soft tissues – including the kidneys, which can lead to impaired renal function. Hypoparathyroidism remains among the few hormonal insufficiency states without a replacement therapy that restores the missing hormone at physiologic levels.

Hypoparathyroidism also poses a high burden on the healthcare system despite current conventional therapy. For example, one survey of 374 patients showed that 72% experienced more than ten symptoms in the preceding twelve months, with symptoms experienced for a mean of 13 ± 9 hours a day. Other studies showed that 79% of HP cases require hospitalizations and that patients with the disease results have a four-fold increase in the risk of renal disease compared to healthy controls. Patients often experience decreased quality of life. We conducted a survey of 42 patients which found that 100% of subjects reported negative psychological impacts, interference with daily life and impact on physical functioning from HP, and that 76% were either no longer able to work or experienced interference with work productivity.

The latest clinical practice guideline addressing the prevention, diagnosis, and management of hypoparathyroidism was published in September 2022 in the Journal of Bone and Mineral Research and authored by leading clinicians from North America, Europe, and Asia. The authors suggest consideration of PTH replacement therapy in patients whose hypoparathyroidism is inadequately controlled with conventional therapy. Inadequate control is considered to be any one of the following: symptomatic hypocalcemia, hyperphosphatemia, renal insufficiency, hypercalciuria, or poor quality of life. In addition, the guideline indicate that individuals with poor compliance, malabsorption or who are intolerant of large dose of calcium and active vitamin D may also benefit from PTH replacement therapy. Based on this current guideline, we believe PTH replacement therapy could be applicable to most patients with hypoparathyroidism.

Currently, an effective PTH replacement therapy that fully addresses the condition is not widely available to patients with hypoparathyroidism in the U.S. In 2015, NATPARA (parathyroid hormone) for injection, was approved for once-daily subcutaneous injection as an adjunct to vitamin D and calcium in patients with hypoparathyroidism. NATPARA was voluntarily recalled in September 2019 in the U.S. and is now only available to a limited number of patients through a Special Use Program offered by its manufacturer, Shire-NPS Pharmaceuticals Inc., a Takeda company. In October 2022, Takeda announced that it will discontinue manufacturing NATPARA/NATPAR globally at the end of 2024.

We are also aware of several academic groups and companies working on making longer-acting agonists of the PTH receptor ("PTH1R"). In addition, other companies and groups are developing or commercializing therapies for hypoparathyroidism, including Entera Bio, Extend Biosciences, Massachusetts General Hospital, Amolyt Pharma, MBX Biosciences, and Eli Lilly and Company.

Teriparatide, PTH(1-34), approved since 2002 for the treatment of osteoporosis, has sometimes been used for treatment of hypoparathyroidism using multiple daily injections, despite not being approved for this indication. Clinical research conducted by the National Institutes of Health ("NIH") of subjects receiving continuous exposure to PTH(1-34), administered by an infusion pump, has demonstrated simultaneous normalization of sCa and urinary calcium, as well as normalization of bone turnover.

Hypoparathyroidism affects approximately 200,000 patients in the U.S., Europe, and Japan. In the U.S., we estimate hypoparathyroidism affects approximately 70,000 to 90,000 patients including 4,000 to 5,000 patients which we estimate have previously been treated with PTH therapy.

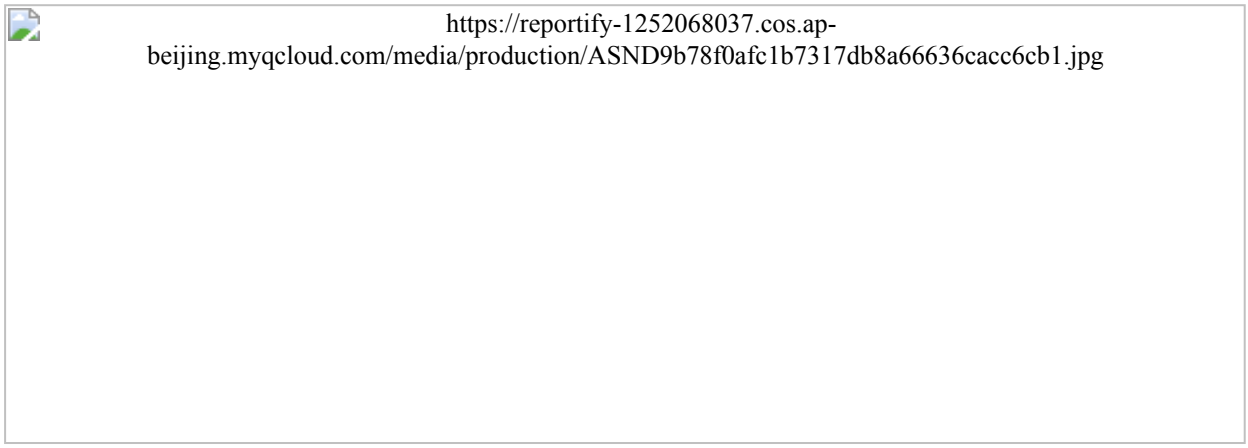


Figure:

1. *Ascendis internal estimates and Symphony Metys data*
2. *U.S. prevalence literature review and epi meta-analysis (Powers, Clarke, Milliman project, ipm.ai claims project; HCUPnet, Healthcare Cost and Utilization Project. Agency for Healthcare Research and Quality, Rockville, MD. for surgical cohort projection).*

Our Solution: TransCon PTH

TransCon PTH (palopegteriparatide) is an investigational prodrug of parathyroid hormone that is designed to be dosed once-daily to achieve and maintain a steady concentration of PTH in the bloodstream within the normal range, at levels similar to those observed in healthy individuals. TransCon PTH is designed to restore physiologic levels of PTH 24 hours per day, thereby more fully addressing all aspects of the disease including normalizing serum and urinary calcium and serum phosphate levels. Pharmacokinetic data from our Phase 1 trial of TransCon PTH in healthy subjects demonstrated a half-life of approximately 60 hours, supporting an infusion-like profile with daily administration.

With once-daily dosing, we believe this substantial half-life extension of PTH could more closely reflect the physiological levels of PTH observed in healthy individuals thereby maintaining blood calcium levels and normalizing urinary calcium excretion. Pharmacokinetic data from multiple ascending dose cohorts in our Phase 1 trial of TransCon PTH in healthy subjects demonstrated an infusion-like profile of free PTH. By providing steady levels of PTH in the physiological range, we believe TransCon PTH can address the fundamental limitations of short-acting PTH molecules and become a highly differentiated therapy for HP.

Clinical Development of TransCon PTH for Adult Hypoparathyroidism

Our ongoing Phase 3 PaTHway Trial, Phase 3 PaTHway Japan Trial, and Phase 2 PaTH Forward Trial evaluated TransCon PTH in adult patients with hypoparathyroidism. Following the primary outcome period, all three trials continue in the extension portion to collect long term data.

In January 2023, we announced topline data from PaTHway Japan Trial, a single-arm Phase 3 trial to evaluate the safety, tolerability, and efficacy of TransCon PTH. The study achieved its primary objective with topline results consistent with our trials in North America and EU. Twelve out of thirteen patients met the primary composite endpoint which was defined as serum calcium levels in the normal range (8.3–10.6 mg/dL) and independence from conventional therapy (active vitamin D and >600 mg/day of calcium supplements). TransCon PTH was generally well-tolerated, with no discontinuations related to study drug. Twelve patients continue in the ongoing 3-year extension portion of the PaTHway Japan Trial.

In December 2022, the FDA allowed Ascendis to initiate an expanded access program ("EAP") for TransCon PTH, for adult patients with hypoparathyroidism. To qualify for the EAP, patients must be adults diagnosed with hypoparathyroidism who live in the U.S., have prior PTH treatment experience, and meet other criteria. Requests for access to TransCon PTH under the U.S. EAP must be made by the treating physician. In January 2023, the online portal for physicians to request access to TransCon PTH through the U.S. EAP was opened.

In November 2022, we submitted a marketing authorisation application ("MAA") to the EMA for TransCon PTH in adult patients with hypoparathyroidism.

In October 2022, the FDA accepted for Priority Review our New Drug Application ("NDA") for TransCon PTH in adult patients with hypoparathyroidism and has set a Prescription Drug User Fee Act target action date of April 30, 2023. If approved by the PDUFA date, we expect U.S. commercial launch of TransCon PTH by the end of the second quarter of 2023.

In September 2022, we announced new Week 110 data from the Phase 2 PaTH Forward Trial showing that long-term therapy with TransCon PTH provided a durable response in adult patients with hypoparathyroidism, as evidenced by continued normalization of mean serum calcium levels and 93% of patients achieving independence from conventional therapy with active vitamin D and therapeutic levels of calcium. As of December 31, 2022, 57 out of the 59 patients continued in the open-label extension portion of the trial, where they receive a customized maintenance dose of TransCon PTH. In addition, all 57 subjects have exceeded two and a half years of follow-up in the PaTH Forward Trial. Two patients withdrew from the trial for reasons unrelated to safety or efficacy of the study drug.

In March 2022, we announced that top-line data from the randomized, double-blind, placebo-controlled portion of its Phase 3 PaTHway Trial of TransCon PTH in adults with hypoparathyroidism demonstrated statistically significant improvement with TransCon PTH compared to control on the primary composite endpoint and all key secondary endpoints. The primary endpoint, defined as serum calcium levels in the normal range (8.3–10.6 mg/dL) and independence from conventional therapy (active vitamin D and >600 mg/day of calcium supplements) with no increase in prescribed study drug within the 4 weeks prior to the Week 26 visit, was achieved by 78.7% of TransCon PTH-treated patients (48 of 61), compared to 4.8% for patients (1 of 21) in control group (p-value <0.0001). In addition, all key pre-specified secondary endpoints were met with statistical significance. TransCon PTH was generally well tolerated, with no discontinuations related to study drug. Three patients discontinued during the treatment period, two from the placebo arm and one from the TransCon PTH arm. TransCon PTH-treated patients showed a mean decrease in 24-hour urine calcium excretion into the normal range.

Following an initial blinded study period of 26 weeks all 79 patients completing the blinded period opted to receive treatment with TransCon PTH in the ongoing open-label extension portion of the study for up to 3 years (156 weeks). As of December 31, 2022, 77 out of 79 patients continued in the open label extension ("OLE") portion of the PaTHway Trial.

In April 2020, we announced top-line data from the four-week fixed dose, double-blinded portion of PaTH Forward, a global Phase 2 trial evaluating the safety, tolerability and efficacy of TransCon PTH in adult subjects with hypoparathyroidism. A total of 59 subjects were randomized in a blinded manner to receive fixed doses of TransCon PTH at 15, 18 or 21 µg/day or placebo for four weeks using a ready-to-use prefilled pen injector planned for commercial presentation. All doses of TransCon PTH were well-tolerated, and no serious or severe treatment-related adverse events ("TEAEs"), were observed at any point. No treatment-emergent adverse events led to discontinuation of study drug, and the overall incidence of TEAEs was comparable between TransCon PTH and placebo. Additionally, there were no drop-outs during the four-week fixed dose period.

In June 2018, we were granted ODD by the FDA, for TransCon PTH for the treatment of hypoparathyroidism. In October 2020, we were granted OD by the EC for TransCon PTH for the treatment of hypoparathyroidism. In July 2021, the Ministry of Health, Labour and Welfare granted ODD to TransCon PTH for the treatment of hypoparathyroidism.

TransCon CNP

Market Opportunity in Achondroplasia

ACH is the most common form of dwarfism, occurring in about one in 10,000 to 30,000 newborns or approximately 250,000 worldwide. ACH results in severe skeletal complications and comorbidities, including spinal stenosis due to premature fusion of the foramen magnum, sleep apnea, and chronic ear infections. Patients often face multiple surgeries to alleviate its many complications.

ACH is caused by an autosomal dominant activating mutation in fibroblast growth factor receptor 3 ("FGFR3") that leads to an imbalance in the effects of the FGFR3 and C-type natriuretic peptide ("CNP") signaling pathways. In ACH, mutations in FGFR3 result in constitutive activation, suppressing the proliferation and differentiation of chondrocytes resulting in improper cartilage to bone conversion in the growth plate.

Preclinical and clinical data show that the CNP pathway stimulates growth and increased CNP helps to counteract the effects of the FGFR3 mutation downstream.

In November 2021 BioMarin Pharmaceutical, Inc's VOXZOGO® (vosoritide) was approved by FDA and is indicated to increase linear growth in pediatric patients with ACH who are 5 years of age and older with open epiphyses. Other companies that are developing therapies for ACH include QED Therapeutics, Sanofi, Ribomic, PhaseBio, Astellas, and ProLynx.

Figure: The role of a defect in the FGFR3 signaling pathway in the development of ACH is well understood.

Our Solution: TransCon CNP

TransCon CNP is an investigational long-acting prodrug of C-type natriuretic peptide designed to provide continuous CNP exposure at therapeutic levels with a well-tolerated and convenient once-weekly dose. It is being developed for the treatment of children with ACH. TransCon CNP is designed to provide effective shielding of CNP from neutral endopeptidase degradation in subcutaneous tissue and the blood compartment, minimize binding of CNP to the NPR-C receptor to decrease clearance, reduce binding of CNP to the NPR-B receptor in the cardiovascular system to avoid hypotension, and release unmodified CNP, which is small enough in size to allow effective penetration into growth plates. Shorter acting CNP and CNP analogs in development have resulted in high C_{max} levels that may cause adverse cardiovascular events. We believe the therapeutically sustained release of TransCon CNP offers advantages that may mitigate this issue, leading to more constant CNP exposure at lower C_{max} to correlate with better therapeutic outcomes.

Clinical Development of TransCon CNP for ACH

TransCon CNP is currently being evaluated in a global Phase 2 trial, known as the ACcomplisH Trial, which is designed to evaluate the safety and efficacy of TransCon CNP in children (ages two to ten years) with ACH.

In November 2022, we announced topline results from ACcomplisH, a Phase 2 randomized, double-blind, placebo-controlled, dose-escalation trial evaluating the safety and efficacy of once-weekly TransCon CNP compared to placebo in children with ACH aged two to ten years old.

The ACcomplisH Trial evaluated 57 children with ACH aged 2 to 10 years old, randomized in a 3:1 ratio to receive either sequential ascending doses of once-weekly TransCon CNP or placebo for 52 weeks. All 57 randomized children completed the blinded portion of ACcomplisH and are currently continuing in the open label extension at the 100 µg/kg/week dose. The trial met its primary objectives, demonstrating that TransCon CNP at 100 µg/kg/week met the primary efficacy endpoint of AHV at 52 weeks (p=0.0218).

TransCon CNP Dose Group (n)	**AHV (cm/year)** LS Mean [95% CI]	**p-value** (TransCon CNP vs. Pooled Placebo)
6 µg/kg/week (n=10)	**4.09** [3.34, 4.84]	0.6004
20 µg/kg/week (n=11)	**4.52** [3.82, 5.22]	0.7022
50 µg/kg/week (n=10)	**5.16** [4.43, 5.90]	0.0849
100 µg/kg/week (n=11)	**5.42** [4.74, 6.11]	0.0218
Pooled Placebo (n=15)	**4.35** [3.75, 4.94]	NA

Additional highlights:

- TransCon CNP demonstrated a consistent dose-dependent increase in AHV across the four dose groups.
- Mean improvements in AHV for TransCon CNP-treated patients were consistent across age groups <5 years and >5 years, with dose response established.
- TransCon CNP at 100 µg/kg/week improved change in ACH-specific height SDS compared to placebo (p=0.0283).
- TransCon CNP was generally well tolerated, with no discontinuations.
- No serious adverse events ("SAEs") related to treatment were reported; two unrelated SAEs were reported.
- Injections were generally well tolerated with low frequency of injection site reactions ("ISRs"):
    - 11 mild ISRs (in 8 patients) out of >2,000 injections.
- Patients treated ≥6 months at 100 µg/kg/week in the blinded or OLE period demonstrated a consistent and sustained response, with mean AHV of 5.39 cm/year (n=40).

One year data from the OLE portion of the ACcomplisH Trial are expected during the fourth quarter of 2023.

In October 2022, we submitted protocols to initiate ApproaCH, global randomized, double-blind, placebo-controlled Phase 2b trial in children ages 2–11 years with ACH. The trial targets enrollment of ~80 patients. During the second quarter of 2023, we expect to complete enrollment in ApproaCH.

We are conducting the ACHieve Study, a multi-center natural history study designed to gain insight into the experiences of pediatric subjects with ACH. ACHieve will study growth velocity, body proportionality, and comorbidities over time in children with ACH up to eight years old. No study medication will be administered.

In addition, we are planning a trial to evaluate TransCon CNP in children under the age of 2 years. We plan to submit an IND or similar application for this trial in the third quarter of 2023.

In February 2019, we were granted ODD by the FDA for TransCon CNP for the treatment of ACH. In July 2020, we received OD from the EC for TransCon CNP for the treatment of ACH.

TransCon Product Candidates—Oncology

Market Opportunity in Oncology

Efficacy of many cancer treatments remains suboptimal and the incidence of cancer continues to rise. Improved understanding of the cellular and molecular mechanisms involved in anti-tumor immune responses has fueled the rapid growth of immuno-oncology therapeutics. Immune checkpoint inhibitors, such as anti-PD-(L)1 and anti-CTLA-4 antibodies, have provided new therapeutic options for patients. Supported by these and other advancements, oncology is now the largest therapy class in terms of revenue in pharmaceutical industry, with worldwide prescription drug and over-the-counter sales of $124 billion in 2018 and projected growth to $237 billion in 2024.

Despite recent advances, a high need for new treatment options remains for patients who do not respond or respond inadequately to current therapies. In addition to insufficient efficacy, many current treatments are limited by toxicities that result in dose reductions, treatment discontinuations, or long-term health risks to patients.

We believe that one approach to improving efficacy while limiting adverse events is to create long-acting product candidates using our sustained systemic release TransCon technology, allowing for more consistent circulating drug levels and potentially avoiding high peak concentrations that often associate with toxicity.

Another approach is to target the drug activity into tumors via intratumoral injection using our sustained localized release TransCon technology, aiming for high activity in the tumor microenvironment while limiting systemic adverse events. While one intratumoral treatment has been approved for the local treatment of recurrent melanoma, the overall success of intratumoral treatments has been limited to date. This is likely at least partly due to the short intratumoral retention of injected molecules, and, hence, the need for frequent, impractical dosing schedules.

Our Solution: TransCon Technologies for Oncology

We believe prolonging the therapeutic activity and targeting the drug activity to the relevant cell types and tissues have the potential to improve treatment outcomes. We believe TransCon is well-suited to improve cancer treatments given the large number of validated targets with known limitations. By applying our unique algorithm for product innovation to clinically validated targets and pathways, we believe TransCon has the potential to improve outcomes currently limited by suboptimal efficacy and systemic toxicity.

We believe TransCon technologies may have the potential to increase the efficacy of small molecules, peptides and proteins without increasing toxicity, which could offer the potential to treat more patients with new combination and multi-agent regimens that would not otherwise be feasible.

We are currently investigating two clinical-stage product candidates designed to activate the patient's own immune system to eradicate malignant cells. We believe our approach, if successfully developed, has the potential to optimize the efficacy of systemically administered, clinically validated therapies while limiting adverse effects.

Similarly, with the potential to achieve sustained local release at predictable levels, we believe TransCon product candidates may allow for improved efficacy and reduced dosing frequency of intratumorally administered therapies, potentially enabling treatments of multiple tumor types, including those that cannot be easily accessed for frequent injection.

Development of TransCon Product Candidates in Oncology

Our TransCon product candidates in oncology are designed to provide sustained systemic or intratumoral administration, which we believe could provide potent and durable anti-tumor efficacy. Our nonclinical studies have showed sustained activation of cytotoxic immune cells that resulted in robust anti-tumor responses by TransCon product candidates using infrequent administration.

Two of our oncology product candidates, TransCon TLR7/8 Agonist and TransCon IL-2 ß/□, are now in clinical development.

TransCon TLR7/8 Agonist for sustained localized release

TransCon TLR7/8 Agonist is an investigational long-acting prodrug, designed for sustained release of resiquimod, a small molecule agonist of TLR 7 and 8. It is designed to provide sustained and potent activation of the innate immune system in the tumor and tumor draining lymph node for weeks following a single intratumoral injection and to have a low risk of systemic toxicity. The transcendIT-101 Trial, a Phase 1/2 clinical trial to evaluate the safety and efficacy of TransCon TLR7/8 Agonist in locally advanced or metastatic solid tumors, alone or in combination with pembrolizumab, is enrolling patients in four indication-specific cohorts.

In October 2022, we announced completion of the dose-escalation portion and selection of the recommended Phase 2 dose in transcendIT-101. In the current portion of the trial, the recommended Phase 2 dose of TransCon TLR7/8 Agonist is being evaluated in four cohorts focused on cancers where increased TLR activity has potential to improve innate and adaptive immune activation and host defense against cancers. The cohorts include head and neck squamous-cell carcinoma; other HPV-associated cancers; melanoma; and cutaneous squamous cell carcinoma. In this portion of the study, all participants will be treated every three weeks with intratumoral TransCon TLR7/8 Agonist in combination with intravenous pembrolizumab. Limits on prior lines of therapy vary by cohort.

TransCon IL-2 ß/□ for sustained systemic release

TransCon IL-2 □/□ is an investigational long-acting prodrug designed to improve cancer immunotherapy through sustained release of an IL-2 variant that selectively activates IL-2Rß/□, with minimal binding to IL-2Rα. The Phase 1/2 IL-ßelie□e Trial evaluating TransCon IL-2 □/□ monotherapy in patients with advanced cancer is enrolling patients in dose escalation cohorts. During the second quarter of 2022, we dosed the first patient in the combination dose escalation cohort for TransCon IL-2 □/□ and checkpoint inhibitor, in the IL-ßelie□e Trial. Results from monotherapy dose escalation are expected during the first quarter of 2023 with dose escalation, combination therapy results expected during the third quarter of 2023.

Other Development Plans

We believe that a combination TransCon TLR7/8 Agonist and TransCon IL-2 □/□ may have the potential to produce greater anti-tumor activity than either candidate alone. We plan to evaluate clinical activity of the combination of TransCon TLR7/8 Agonist and TransCon IL-2 □/□ in 2023.

We are evaluating additional TransCon product candidates in nonclinical research studies with potential to enhance anti-tumor immune responses for the treatment of multiple tumor types. We are exploring product candidates using both systemic and intratumoral administration as monotherapies and as components of combination regimens. We believe these programs have the potential to make a positive impact to the lives of many patients with cancer.

TransCon Product Candidates—Ophthalmology

Market Opportunity in Ophthalmology

According to the Centers for Disease Control and Prevention, more than four million Americans aged 40 years and older are either legally blind or are with low vision. Age related eye diseases such as age-related macular degeneration, cataract, diabetic retinopathy, and glaucoma are the leading causes of blindness and low vision. Advances in technology have resulted in new treatment options for disorders such as wet AMD, diabetic macular edema, and retinal vein occlusion. Through intravitreal injections, medication is placed directly into a space in the back of the eye called the vitreous cavity.

The use of anti-vascular endothelial growth factor ("anti-VEGF") agents have transformed the treatment of wet AMD. Clinical studies have shown that anti-VEGF treatments are very successful in preventing vision loss as a result of wet AMD and may help to regain some lost vision. However, anti-VEGF treatment require repetitive intravitreal injections representing a high treatment burden for the patients. Lack of adherence and undertreatment remains a significant issue in real-world outcomes, and extending treatment duration remains a key unmet medical need. Intravitreal treatments represent an established, well-understood, and high-value therapeutic category, characterized by high unmet medical need. We estimate the global market for ophthalmology treatments exceeds $10 billion and is primed for disruption.

Our Solution: TransCon Technologies for Ophthalmology

TransCon Hydrogel platform has been designed to provide sustained levels of a drug at a localized site. It is designed to allow for prolonged, continuous release over months. In vivo data demonstrated that the TransCon Hydrogel platform provided continuous local drug release over at least six months supporting twice yearly administration. By reducing the frequency of intravitreal injection, we believe the TransCon Hydrogel platform could potentially increase patient adherence and persistence resulting in better outcomes.

Development of TransCon Ophthalmology Pipeline Candidates

TransCon RBZ (ranibizumab) has been selected as our lead pipeline candidate for ophthalmology. Lucentis® (ranibizumab) was first approved by the FDA in 2006 for the treatment of wet AMD. It has been studied extensively, and demonstrated efficacy following sustained infusion from an implantable osmotic minipump. Thus, we believe ranibizumab represents a clinically validated parent drug which we believe provides lower development risk compared to new candidate discovery.

In addition to TransCon RBZ, additional product candidates are under evaluation.

Strategic Collaborations

We also engage in strategic collaborations to further leverage our TransCon technologies in certain geographies with market-leading biopharmaceutical companies. These collaborations aim to make promising treatment options available to more patients and to further monetize both our TransCon technologies and our internal product candidates, particularly into therapeutic areas where we believe a partner may have more expertise, capability, and capital.

In addition, we may choose to pursue a collaboration to develop and market our internal, wholly owned product candidates in geographic markets outside our core focus areas of the United States and Europe.

Strategic Investment

VISEN Pharmaceuticals

In November 2018, we announced the formation of VISEN, a company established to develop and commercialize our endocrinology rare disease therapies in the People's Republic of China, Hong Kong, Macau, and Taiwan ("Greater China"). In connection with the formation of VISEN, we granted VISEN exclusive rights to develop and commercialize certain product candidates based on our proprietary TransCon technologies, including TransCon hGH, TransCon PTH and TransCon CNP, in Greater China for use in all human indications, subject to certain exceptions. As consideration for the rights granted to VISEN, we received 50% ownership in the outstanding shares of VISEN and concurrently with the rights we granted to VISEN, entities affiliated with Vivo Capital and Sofinnova Ventures purchased shares in VISEN for an aggregate purchase price of $40 million in cash. In January 2021, we invested additional $12.5 million in VISEN as part of VISEN's $150 million Series B financing. Following the Series B financing, we retained 43.93% of VISEN's issued and outstanding shares.

In November 2022, VISEN announced results from its pivotal Phase 3 study of TransCon hGH in children with GHD in China. The trial achieved its primary endpoint; patients treated with TransCon hGH demonstrated greater annualized height velocity at 52-weeks (p=0.0010) compared to patients treated with daily growth hormone with comparable safety and tolerability to daily growth hormone.

In June 2022, VISEN announced it had completed enrollment of the Phase 3 PaTHway China Trial of TransCon PTH. Results from PaTHway China are expected in first quarter of 2023.

In January 2021, China's National Medical Products Administration approved VISEN's application to conduct the ACcomplisH China Trial, a randomized, double-blind, placebo-controlled, Phase 2 dose expansion trial to evaluate the safety and efficacy of TransCon CNP in subjects with ACH. The aim is to enable patients to have continuous CNP exposure aiming to promote bone growth and ameliorate and prevent complications and comorbidities of ACH.

Market Opportunity in China

China is the second largest pharmaceutical market in the world after the United States and represents one of the fastest growing pharmaceutical markets worldwide. In recent years, the Chinese government has initiated a number of regulatory reforms that are expected to accelerate drug development, as well as drive growth and demand for new therapeutics in China. In addition to joining an international organization that standardizes regulations for clinical development, the National Medical Products Administration has introduced initiatives such as fast track review for drugs for unmet medical needs and adopted new rules that streamline the drug approval process in China for global companies.

The purpose of our investment in VISEN is to support our strategy to extend our endocrinology rare disease portfolio globally and establish a presence in China in partnership with collaborators who have significant experience and knowledge of the biopharmaceutical opportunity in China.

Rights Agreements

Under the Rights Agreements, VISEN must use diligent efforts to develop and commercialize licensed products in Greater China. Additionally, we and VISEN will conduct certain research and development activities allocated to the respective party under a research and technical development plan, and VISEN will reimburse us for costs of conducting such activities, including costs of our personnel committed to performing such activities in Greater China.

We will provide product supply to VISEN for use in conducting clinical trials in Greater China pursuant to separate clinical supply agreements entered into concurrently with the Rights Agreements in accordance with the terms and conditions set forth therein. Additionally, we may enter into a commercial supply agreement governing commercial supply of licensed product to VISEN on the terms and conditions set forth in the Rights Agreements.

Under the Rights Agreements, we agreed not to research, develop, or commercialize competing products in Greater China, and VISEN agreed not to grant certain rights under its interest in any inventions or intellectual property arising out of the activities conducted under the Rights Agreements to third-parties, in each case, under the terms and conditions specified in the Rights Agreements. We will have the right to exploit inventions and intellectual property arising out of the activities conducted under the Rights Agreements outside of Greater China. Additionally, we granted VISEN a right of first negotiation to develop and commercialize certain of its endocrinology products in Greater China.

The Rights Agreements continue in effect for as long as a valid claim of a licensed patent exists in Greater China. VISEN may terminate a Rights Agreement for convenience, for uncured material breach by us of a Rights Agreement and for our bankruptcy or insolvency-related events. We may terminate a Rights Agreement for certain specified material breaches thereof by VISEN, in the event VISEN undergoes a change of control in favor of a competitor, if VISEN challenges the validity of any of the licensed patents and for VISEN's bankruptcy or insolvency-related events.

Amended and Restated Shareholders Agreement

In connection with the Company's investment in VISEN, on January 8, 2021, the Company entered into an Amended and Restated Shareholders Agreement (the "Amended Shareholders Agreement"), amending and restating the Shareholders Agreement dated November 7, 2018, between the Company and the parties set forth therein (the "Shareholders Agreement"). In addition to rights previously granted under the Shareholders Agreement, under the Amended Shareholders Agreement, the Company has the right to designate two individuals for election to the board of directors of VISEN, which individuals are initially Jan Møller Mikkelsen and Michael Wolff Jensen. In addition, VISEN has agreed that certain specified events (including certain liquidation events) shall require the approval of (i) shareholders of VISEN holding at least 50% of VISEN's Series B preferred shares, (ii) shareholders of VISEN holding at least 60% of VISEN's Series A preferred shares and/or (iii) certain members of VISEN's board of directors. The Amended Shareholders Agreement can be terminated by written agreement among the holders of at least 60% of VISEN's Series A preferred shares and at least 50% of VISEN's Series B preferred shares.

Manufacturing

As we do not maintain the capability to manufacture finished drug products, we utilize contract manufacturers to manufacture finished drug product of our proprietary TransCon product candidates intended for clinical or commercial use. We source starting materials for our manufacturing activities from one or more suppliers. For the starting materials necessary for our proprietary TransCon product candidate development, we have agreements for the supply of such starting materials with drug manufacturers or suppliers that we believe have sufficient capacity to meet our demands. However, from time to time, we source critical raw materials and services from one or a limited number of suppliers and there is a risk that if such supply or services were interrupted, it would materially harm our business. In addition, we typically order raw materials and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements. We utilize the services of contract manufacturers to manufacture drug substance required for later phases of clinical development and eventual commercialization for us under all applicable laws and regulations and are subject to long term forecasting obligations and certain minimum purchase requirements for all parts of the commercial supply chain.

We have analytical and process development capabilities in our own facility. We generally perform analytical and process development for our proprietary TransCon product candidates internally and manufacture internally our TransCon product candidates necessary to conduct the non-GLP preclinical studies thereof. However, we occasionally outsource the manufacture of research and development-stage TransCon product candidates.

We do not have, and we do not currently plan to acquire or develop, the facilities or capabilities to manufacture bulk drug substance or filled drug product for use in human clinical trials. We rely on third-party manufacturers to produce the bulk drug substances required for our clinical trials and expect to continue to rely on third-parties to manufacture and test clinical trial drug supplies for the foreseeable future.

Our contract suppliers manufacture drug substance and finished drug product for our TransCon product candidates for clinical trial use in effort to comply with current good manufacturing practice ("cGMP") and applicable local regulations. cGMP and similar regulations include requirements relating to organization of personnel; buildings and facilities; equipment; control of components and drug product containers and closures; production and process controls; packaging and labeling controls; holding and distribution; laboratory controls; records and reports; and returned or salvaged products. The manufacturing facilities for our products must be in compliance with cGMP requirements, and for device and device components, the Quality System Regulation ("QSR") requirements, before any product is approved. Our third-party manufacturers may also be subject to periodic inspections of facilities by the FDA, the EU member states competent authorities, and other authorities, including reviews of procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations.

We also contract with additional third-parties for the filling, labeling, packaging, testing, storage and distribution of our TransCon product candidates. We employ personnel with the significant scientific, technical, production, quality and project management experience required to oversee our network of third-party suppliers and to manage manufacturing, quality data and information for regulatory compliance purposes.

NOF Manufacturing and Supply Agreement Related to TransCon hGH

On December 21, 2017, we entered into a multi-year Manufacturing and Supply Agreement (the "NOF Agreement") with NOF Corporation ("NOF"). Under the NOF Agreement, NOF has agreed to manufacture and supply the mPEG Linker (the "NOF hGH Product") for our TransCon hGH product candidate. We have agreed to purchase certain quantities of NOF hGH Product.

The NOF Agreement is effective as of December 21, 2017. The initial term of the NOF Agreement terminates on December 31, 2025 unless earlier terminated. After the expiration of the initial term of the NOF Agreement, the NOF Agreement continues until it is terminated. The NOF Agreement may be terminated (i) by either party for the other party's assignment for the benefit of creditors, insolvency, bankruptcy, liquidation, dissolution, or the taking of any action by the other party under an act for relief from creditors, (ii) by either party for the other party's uncured material breach, (iii) by us after the initial term of the NOF Agreement with one year written notice, or (iv) by mutual agreement of the parties. In addition, the NOF Agreement may be terminated by us in the event of a change of 50% or more of the direct or indirect ownership of NOF or manufacturing facilities relevant to the NOF Agreement, if such ownership goes to a third-party materially involved in the treatment of growth related disorders in humans. The NOF Agreement may also be terminated by either party for a continuing event of force majeure.

The NOF Agreement contains, among other provisions customary representations and warranties by us and NOF, grants of certain limited license rights related to either party's intellectual property in connection with the manufacturing and supply of NOF hGH Product, certain indemnification rights in favor of both parties and customary confidentiality provisions.

NOF Manufacturing and Supply Agreement Related to TransCon PTH

On August 31, 2020, we entered into a multi-year Manufacturing and Supply Agreement (the "NOF PTH Agreement") with NOF. Under the NOF PTH Agreement, NOF has agreed to manufacture and supply the PEG maleimide (the "NOF PTH Product") for our TransCon PTH product candidate. We have agreed to purchase certain quantities of NOF PTH Product. We may purchase NOF PTH Product from other manufacturers and are not obligated to purchase NOF PTH Product from NOF, other than certain quantities that have been forecasted by us in accordance with a mandatory rolling forecast that we must deliver to NOF from time to time.

The NOF PTH Agreement is effective as of August 31, 2020. The initial term of the NOF PTH Agreement terminates on December 31, 2027 unless earlier terminated. After the expiration of the initial term of the NOF PTH Agreement, the NOF PTH Agreement continues until it is terminated. The NOF PTH Agreement may be terminated (i) by either party for the other party's assignment for the benefit of creditors, insolvency, bankruptcy, liquidation, dissolution, or the taking of any action by the other party under an act for relief from creditors, (ii) by either party for the other party's uncured material breach, (iii) by us after the initial term of the NOF PTH Agreement with advance written notice, (iv) by NOF after the initial term of the NOF PTH Agreement with advance written notice, (v) by mutual agreement of the parties, or (vi) by us in the event of a change of fifty percent or more of the direct or indirect ownership of NOF or manufacturing facilities relevant to the NOF PTH Agreement, if such ownership goes to any of a pre-defined list of third parties. In addition, the NOF PTH Agreement may be terminated by NOF in the event of a change of fifty percent or more of the direct or indirect ownership of Ascendis, if such ownership goes to any of a pre-defined list of third parties. The NOF PTH Agreement may also be terminated by either party for a continuing event of force majeure.

The NOF PTH Agreement contains, among other provisions, customary representations and warranties by us and NOF, grants of certain limited license rights related to either party's intellectual property in connection with the manufacturing and supply of NOF PTH Product, certain indemnification rights in favor of both parties and customary confidentiality provisions.

Carbogen Manufacturing and Supply Agreement Related to TransCon hGH

On October 26, 2018, we entered into a multi-year Manufacturing and Supply Agreement (the "Carbogen Agreement") with Carbogen Amcis AG ("Carbogen"). Under the Carbogen Agreement, Carbogen has agreed to manufacture and supply Linker A (the "Carbogen Product") for our TransCon hGH product candidate. We may purchase Linker A from other manufacturers and are not obligated to purchase Carbogen Product from Carbogen, other than certain quantities that have been forecasted by us in accordance with a mandatory rolling forecast that we must deliver to Carbogen from time to time.

The Carbogen Agreement is effective as of October 26, 2018. The initial term of the Carbogen Agreement expires five years after the first commercial launch of our TransCon hGH product candidate (the "Carbogen Initial Term") unless earlier terminated. After the expiration of the Carbogen Initial Term of the Carbogen Agreement, the Carbogen Agreement continues until it is terminated. The Carbogen Agreement may be terminated (i) by either party for the other party's assignment of the Carbogen Agreement for the benefit of creditors, insolvency, bankruptcy, dissolution, or taking of any action under an act for relief from creditors, (ii) by either party for the other party's uncured material breach, (iii) by us after the Carbogen Initial Term of the Carbogen Agreement with one year written notice, (iv) by Carbogen after the Carbogen Initial Term of the Carbogen Agreement with four years written notice or (v) by mutual agreement of the parties. In addition, the Carbogen Agreement may be terminated by us in the event of a change of fifty percent or more of the direct or indirect ownership of Carbogen, if such ownership goes to a third-party materially involved in the treatment of growth-related disorders in humans. The Carbogen Agreement may also be terminated by either party for a continuing event of force majeure.

The Carbogen Agreement contains, among other provisions, certain representations and warranties by us and Carbogen, grants certain rights to intellectual property relating to, or inventions made in connection with, the manufacturing and supply of Carbogen Product, provides for certain indemnification rights in favor of both parties and includes confidentiality provisions.

Carbogen Manufacturing and Supply Agreement Related to TransCon PTH

On May 27, 2021, we entered into a multi-year Manufacturing and Supply Agreement (the "Carbogen PTH Agreement") with Carbogen. Under the Carbogen PTH Agreement, Carbogen has agreed to manufacture and supply Linker F (the "Carbogen PTH Product") for our TransCon PTH product candidate. We may purchase Carbogen PTH Product from other manufacturers and are not obligated to purchase Carbogen PTH Product from Carbogen, other than certain quantities that have been forecasted by us in accordance with a mandatory rolling forecast that we must deliver to Carbogen from time to time.

The Carbogen PTH Agreement is effective as of May 27, 2021. The initial term of the Carbogen PTH Agreement expires five years after the first commercial launch of our TransCon PTH product candidate (the "Carbogen PTH Initial Term") unless earlier terminated. After the expiration of the Carbogen PTH Initial Term of the Carbogen PTH Agreement, the Carbogen PTH Agreement continues until it is terminated. The Carbogen PTH Agreement may be terminated (i) by either party for the other party's assignment of the Carbogen PTH Agreement for the benefit of creditors, insolvency, bankruptcy, dissolution, or taking of any action under an act for relief from creditors, (ii) by either party for the other party's uncured material breach, (iii) by us after the Carbogen PTH Initial Term with one year written notice, (iv) by Carbogen after the Carbogen PTH Initial Term of the Carbogen PTH Agreement with four years written notice (subject to Carbogen's obligation to actively assist in technology transfer to an alternate supplier) or (v) by mutual agreement of the parties. In addition, the Carbogen PTH Agreement may be terminated by us in the event of a change of fifty percent or more of the direct or indirect ownership of Carbogen, if such ownership goes to a third-party materially involved in the treatment of growth-related disorders in humans. The Carbogen PTH Agreement may also be terminated by either party for a continuing event of force majeure.

The Carbogen PTH Agreement contains, among other provisions, certain representations and warranties by us and Carbogen, grants of certain rights to intellectual property relating to, or inventions made in connection with, the manufacturing and supply of Carbogen PTH Product, certain indemnification rights in favor of both parties and confidentiality provisions.

Philips Medisize (formerly B&O Medicom and Medicom Innovation Partner)

On January 12, 2017, we entered into a multi-year Manufacturing and Supply Agreement (the "Medicom Agreement") with Medicom Innovation Partner ("Medicom"). Under the Medicom Agreement, Medicom has agreed to exclusively manufacture and supply the auto injector injection device (the "Medicom Product") for our TransCon hGH product candidate. We are obligated to purchase certain quantities that have been forecasted by us in accordance with a mandatory rolling forecast that we must deliver to Medicom from time to time.

The Medicom Agreement is effective as of January 12, 2017. The term of the Medicom Agreement terminates on June 30, 2025 ("Medicom Initial Term") unless earlier terminated or unless extended unilaterally by us, with notice of extension to be given no later than June 30, 2024, by five years until June 30, 2030 ("Extended Term") after which date it shall continue indefinitely unless terminated. The Medicom Agreement may be terminated (i) by either party for the other party's bankruptcy or insolvency-related events, (ii) by either party for the other party's uncured material breach, (iii) by us by not extending the Medicom Initial Term into the Extended Term, (iv) by Medicom after the Extended Term of the Medicom Agreement with two year's advance written notice or by us after the Extended Term of the Medicom Agreement with one year's advance notice, or (v) by Medicom if we purchase less than an agreed volume of the Medicom Product (provided that we may avoid such termination by paying Medicom's lost profits up to such agreed minimum volume). In addition, the Medicom Agreement may be terminated by us in the event of a change of control of Medicom, if such control goes to a third-party materially involved in the treatment of certain defined endocrinology diseases in humans. In all events of termination Medicom is obligated to support a tech transfer of manufacture of Medicom Product to an alternate supplier.

The Medicom Agreement contains, among other provisions certain representations and warranties by us and Medicom, grants certain limited license rights related to either party's intellectual property in connection with the manufacturing and supply of Medicom Product, provides for certain indemnification rights in favor of both parties and includes confidentiality provisions.

Vetter Pharma International GmbH

On December 14, 2018, we entered into a multi-year Supply Agreement (the "Vetter Agreement") with Vetter Pharma International ("Vetter"). Under the Vetter Agreement, Vetter has agreed to manufacture and fill-and-finish drug product in dual-chamber cartridges (the "Ascendis Product") for our TransCon hGH product candidate. Vetter has agreed to supply in accordance with a long-term forecast in addition to a rolling forecast with a binding part that we must deliver to Vetter from time to time.

The Vetter Agreement is effective as of January 1, 2019. The term of the Vetter Agreement expires on the five-year anniversary of the date of first regulatory approval of the TransCon hGH product (the "Initial Term") after which term it shall be automatically renewed for subsequent two-year terms unless terminated. The Vetter Agreement may be terminated (i) by either party for the other party's uncured material breach, including certain enumerated events constituting material breach such as bankruptcy or insolvency-related events, (ii) by us with two years' notice, with effect no earlier than two years after expiry of the Initial Term or (iii) by either party if the other party is taken over by our or a Vetter competitor, as applicable.

The Vetter Agreement contains, among other provisions, certain representations and warranties by us and Vetter, grants certain limited license rights in connection with Vetter's manufacturing and supply, and our sale, distribution and other use, of Ascendis Product, provides for certain indemnification rights in favor of both parties and includes confidentiality provisions.

Fujifilm Commercial Supply Agreement

On January 9, 2019, we entered into a multi-year Commercial Supply Agreement (the "Fujifilm Agreement") with Fujifilm Diosynth Biotechnologies UK Ltd. ("Fujifilm"). Under the Fujifilm Agreement, Fujifilm has agreed to manufacture and supply TransCon hGH Drug Substance (the "Fujifilm Product") for our TransCon hGH product candidate. We may purchase TransCon hGH Drug Substance from other manufacturers and are not obligated to purchase Fujifilm Product from Fujifilm.

The Fujifilm Agreement is effective as of January 9, 2019. The initial term of the Fujifilm Agreement expires on December 31 in the year of the five-year anniversary of the first commercial sale of our TransCon hGH product candidate (the "Fujifilm Initial Term") unless earlier terminated. After the expiration of the Fujifilm Initial Term of the Fujifilm Agreement, the Fujifilm Agreement continues until it is terminated. The Fujifilm Agreement may be terminated (i) by either party for the other party's bankruptcy or insolvency-related events, (ii) by either party for the other party's uncured material breach or material breach that is not capable of remedy, (iii) by us after the Fujifilm Initial Term of the Fujifilm Agreement with two years written notice, or (iv) by Fujifilm after the Fujifilm Initial Term of the Fujifilm Agreement with five years written notice. We are entitled to terminate the Fujifilm Agreement with regards to the manufacture of recombinant hGH after one year following launch with two years written notice. In addition, the Fujifilm Agreement may be terminated by us in the event of a change in control of Fujifilm, where the new controlling entity is our competitor. The Fujifilm Agreement may also be terminated by either party for a continuing event of force majeure.

The Fujifilm Agreement contains, among other provisions, certain warranties by us and Fujifilm, grants certain limited license rights related to either party's intellectual property in connection with the manufacturing and supply of Fujifilm Product, provides for certain indemnification rights in favor of both parties and includes confidentiality provisions.

Lonza Tech Transfer and Manufacturing Agreement

On December 12, 2019, we entered into a multi-year commercial supply agreement (the "Lonza Agreement") with Lonza Ltd ("Lonza"). Under the Lonza Agreement, Lonza has agreed to manufacture and supply drug substance for our TransCon hGH product candidate (the "TransCon hGH Drug Substance"). Starting in 2023, we are obligated to purchase a certain minimum annual quantity of TransCon hGH Drug Substance from Lonza. We may also purchase TransCon hGH Drug Substance from other manufacturers.

The Lonza Agreement secures us a certain capacity of TransCon hGH Drug Substance per year.

The Lonza Agreement is effective as of December 12, 2019. The initial term of the Lonza Agreement expires seven years after first approval of a drug product manufactured using the TransCon hGH Drug Substance (the "Lonza Initial Term") unless earlier terminated. During the first five years of the Lonza Initial Term, we may decide, in our sole discretion, to extend the term of the Lonza Agreement by two years. The Lonza Agreement may be terminated (i) by either party for the other party's bankruptcy or insolvency-related events, (ii) by either party for the other party's uncured material breach, (iii) by either party for a continuing event of force majeure, (iv) by either party upon written notice after a specified time period in the event of our change of control, and (v) by either party in the event of the occurrence of certain conditions related to the manufacturing of the TransCon hGH Drug Substance as more fully described in the Lonza Agreement.

The Lonza Agreement contains, among other provisions, certain warranties by us and Lonza, grants certain limited license rights related to either party's intellectual property in connection with the manufacturing and supply of TransCon hGH Drug Substance, provides for certain indemnification rights in favour of both parties and includes confidentiality provisions.

Sharp Corporation Packaging and Supply Agreement

On December 1, 2019 we entered into a multi-year packaging agreement (the "Sharp Agreement") with Sharp Corporation ("Sharp"). Under the Sharp Agreement, Sharp will package, assemble, and label TransCon hGH for commercial use in certain territories, including the United States and the EU. We are non-exclusive to Sharp and may engage other manufacturers to package, assemble, and label TransCon hGH but we are obligated to meet certain minimum spend requirements for TransCon hGH during the first 12-month period after first shipment of TransCon hGH for commercial sale after regulatory approval thereof.

The Sharp Agreement is effective as of December 1, 2019. The initial term of the Sharp Agreement expires on December 31, 2025 and will be automatically extended for additional two-year periods unless earlier terminated. The Sharp Agreement may be terminated (i) by either party upon mutual consent, (ii) by either party for the other party's uncured material breach, (iii) by either party for the other party's bankruptcy or insolvency-related events, (iv) by either party for a continuing event of force majeure, (v) by either party after the initial term of the Sharp Agreement has been completed.

The Sharp Agreement contains, among other provisions, certain warranties by Sharp, provides for certain indemnification rights in favor of both parties and includes confidentiality provisions.

Bachem Manufacturing and Supply Agreement

On December 27, 2020, we entered into a multi-year Manufacturing and Supply Agreement (the "Bachem Agreement") with Bachem AG ("Bachem"). Under the Bachem Agreement, Bachem has agreed to manufacture and supply PTH drug substance (the "Bachem Product") for our TransCon PTH product candidate. We may purchase Bachem Product from other manufacturers and are not obligated to purchase Bachem Product from Bachem, other than certain quantities that have been forecasted by us in accordance with a mandatory rolling forecast that we must deliver to Bachem from time to time.

The Bachem Agreement is effective as of December 27, 2020. The initial term of the Bachem Agreement expires on December 31, 2027 (the "Bachem Initial Term") unless earlier terminated. After the expiration of the Bachem Initial Term, provided that market approval is received prior to expiration of the Bachem Initial Term, the Bachem Agreement continues until it is terminated. The Bachem Agreement may be terminated (i) by either party for the other party's assignment of the Bachem Agreement for the benefit of creditors, insolvency, bankruptcy, dissolution, or taking of any action under an act for relief from creditors, (ii) by either party for the other party's uncured material breach, (iii) by us after the Bachem Initial Term with two years' written notice, (iv) by Bachem after the Bachem Initial Term with four years' written notice or (v) by mutual agreement of the parties. In addition, the Bachem Agreement may be terminated by us prior to expiration of the Bachem Initial Term if Bachem is acquired by a company marketing a competing drug to TransCon PTH. The Bachem Agreement may also be terminated by either party for a continuing event of force majeure.

The Bachem Agreement contains, among other provisions, certain representations and warranties by us and Bachem, grants of certain rights to intellectual property relating to, or inventions made in connection with, the manufacturing and supply of Bachem Product, certain indemnification rights in favor of both parties and confidentiality provisions.

Competition

The pharmaceutical industry is very competitive and subject to rapid and significant innovation. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical and generic drug companies, universities, and other research institutions. Many of our competitors have greater resources, as well as larger research and development functions and more experienced marketing and manufacturing organizations. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products.

Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are superior to, or more effectively marketed than, the product candidates that we are currently developing or that we may develop, which could render our products obsolete and noncompetitive. For additional information regarding the companies that may be competitive with our product candidates currently in development, please see the descriptions of our current product candidates included above under the caption "TransCon Product Candidates."

In addition, many of our competitors have greater experience than we do in conducting preclinical and clinical trials and obtaining FDA and other regulatory approvals. Accordingly, our competitors may succeed in obtaining FDA or other regulatory approvals for drug candidates more rapidly than we do. Companies that complete clinical trials, obtain required regulatory authority approvals and commence commercial sale of their drugs before their competitors may achieve a significant competitive advantage. Drugs resulting from our research and development efforts or from our joint efforts with collaboration partners therefore may not be commercially competitive with our competitors' existing products or products under development.

We are aware that other companies are developing or evaluating enhanced drug delivery and sustained release technologies, which may be competitive with our TransCon technologies. In particular, we believe Nektar Therapeutics, OPKO Health, Inc., ProLynx LLC, MBX Biosciences and Serina Therapeutics, Inc. are developing technology platforms in the areas of enhanced drug delivery and reversible linkers that may be competitive with our TransCon technologies. We also expect that technological developments will occur at a rapid rate and that competition is likely to intensify as various enhanced delivery and sustained released technologies may achieve similar advantages.

Intellectual Property

We actively seek to protect the intellectual property and proprietary technology that we believe is important to our business, which includes seeking and maintaining patents covering our technology, *i.e.*, TransCon linkers and carriers, specific lead candidate structures, broad product concepts, proprietary processes and any other inventions that are commercially and/or strategically important to the development of our business. We also rely on trade secrets that may be important to the development of our business and actively seek to protect the confidentiality of such trade secrets.

Our success will depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third-parties. For more information, please see "Item 3 D. Key Information—Risk Factors—Risks Related to Our Intellectual Property."

As of December 31, 2022, we own a total of 83 patent families, of which 12 are currently in their priority year or international phase and we own several granted patents in the United States (42), Europe (27), Australia (39), Brazil (7), Canada (23), China (15), Israel (13), Indonesia (3), India (6), Korea (5), Malaysia (6), New Zealand (5), Japan (33), Mexico (14), Singapore (8), Russia (16), the United Arab Emirates (1) and South Africa (19) and have approximately 520 pending national/regional applications in a total of 26 jurisdictions (excluding the member states of the European Patent Convention in which our European patents were validated and Hong Kong, to which our EP and CN patents are extended).

So far none of our granted patents has been subject to opposition proceedings, appeals or similar actions aiming at revoking or restricting the scope of a granted patent.

The patent portfolios for the fields containing our most advanced product candidates as of December 31, 2022 are summarized below and the expected expiration dates included in the summary below do not give effect to patent term extensions that may be available.

TransCon hGH

Our patent portfolio related to TransCon hGH includes seven patent families relating to different aspects of TransCon hGH and an additional ten patent families covering various aspects of the auto-injector device for administration of TransCon hGH. The first of these patent families is a composition of matter patent family directed to the particular stoichiometry of TransCon hGH and a related TransCon carrier. As of December 31, 2022, this patent family included patents granted in Europe and the United States. We expect any patents granted in this patent family to expire in October 2024, absent any patent term adjustments or extensions.

The second of these patent families is a composition of matter patent family directed to a TransCon linker used in TransCon hGH. As of December 31, 2022, this patent family included patents granted in the United States, Europe, Australia, Brazil, Canada, Japan and Mexico and included a patent application in the United States. We expect any patents granted in this patent family to expire in March 2025, absent any patent term adjustments or extensions.

The third of these patent families is a composition of matter patent family directed to a broad class of TransCon hGH lead candidate structures. As of December 31, 2022, this patent family included patents granted in the United States, Europe, Australia, Brazil, Canada, China, Israel, India, Japan, Mexico, Russia and South Africa and included patent applications in Europe, the United States, Brazil and Russia. We expect any patents granted in this patent family to expire in April 2029, absent any patent term adjustments or extensions.

The fourth of these patent families is a composition of matter patent family directed to specific dry pharmaceutical compositions comprising TransCon hGH. As of December 31, 2022, this patent family included patents granted in the United States, Europe, Australia, Brazil, Canada, India, Israel, Mexico, Singapore and South Africa and included a patent application in Brazil. We expect any patents granted in this patent family to expire in December 2030, absent any patent term adjustments or extensions.

The fifth of these patent families is a composition of matter patent family directed to a broad class of TransCon hGH lead candidate structures. As of December 31, 2022, this patent family included patents granted in the United States, Australia, Europe, Japan, Russia, Singapore and South Africa and patent applications in the United States, Europe, Australia, Brazil, Canada, Israel, Japan, South Korea, Mexico, New Zealand, Russia and Singapore. We expect any patents granted in this patent family to expire in November 2035, absent any patent term adjustments or extensions. The EP patent in this family was also used as a basis for requesting a supplementary protection certificate (“SPC”) for SKYTROFA in Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Germany, Denmark, Estonia, Spain, Finland, France, Great Britain, Greece, Croatia, Hungary, Ireland, Iceland, Italy, Lithuania, Luxemburg, Latvia, Malta, The Netherlands, Norway, Poland, Portugal, Romania, Sweden, Slovenia and Slovakia. An SPC was already granted in Cyprus, Italy, Malta, The Netherlands and Slovenia, with an expiration date of January 16, 2037.

The sixth of these patent families is directed to a particular dosage regimen for long-acting growth hormone formulations. As of December 31, 2022, this patent family included a granted patent in Europe and patent applications in the United States and in Europe. We expect any patents granted in this patent family to expire in November 2035, absent any patent term adjustments or extensions.

The seventh of these patent families is directed to potential superior efficacy achieved with TransCon hGH treatment. As of December 31, 2022, this patent family included patent applications in the United States, Europe, Australia, Canada, China, Israel, Japan, Mexico and Singapore. We expect any patents granted in this family to expire in March 2040, absent any patent term adjustments or extensions.

Seven of the ten patent families covering the auto-injector device with a filing date of December 29, 2016, include patent applications in the United States, Europe, Australia, Canada, Japan and New Zealand and six granted patents in the United States, three granted patents in Europe, seven granted patents in Australia, and seven granted patents in Japan as of December 31, 2022. We expect any patents granted from these patent families to expire in December 2036, absent any patent term adjustments or extensions. As of December 31, 2022 the two patent families covering the auto-injector device with a filing date of May 23, 2018 and June 29, 2018, respectively, include patent applications in the United States, Europe, the United Arab Emirates, Australia, Brazil, Canada, China, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, Russia, Singapore and South Africa and two granted patents in China, one granted patent in Japan, two granted patents in Russia, one granted patent in Indonesia and one granted patent in South Africa. We expect any patents granted from these patent families to expire in March and June 2038, respectively, absent any patent term adjustments or extensions. The last patent family is currently in its international phase and also has one pending patent application in Taiwan. We expect any patents granted from this patent family to expire in September 2042, absent any patent term adjustments or extensions.

In addition to the SPCs, three requests for a patent term extension (“PTE”) for SKYTROFA were filed based on one granted U.S. patent from the third patent family and two granted patents from the fourth patent family, from which one will be selected for the PTE upon allowance. For two of the three requests a preliminary assessment that the patents would be eligible for extension was received from FDA.

TransCon PTH

Our patent portfolio related to TransCon PTH includes eleven patent families relating to different aspects of TransCon PTH. The first of these patent families is a composition of matter patent family directed to the TransCon linker used in TransCon PTH. As of December 31, 2022, this patent family included granted patents in the United States, Europe, the United Arab Emirates, Australia, Canada, China, Israel, Japan, Mexico, Russia and South Africa and included patent applications in Europe, the United States, Brazil and Russia. We expect any patents granted in this family to expire in January 2029, absent any patent term adjustments or extensions.

The second of these patent families is a composition of matter patent family directed to a broad class of TransCon PTH candidate structures. As of December 31, 2022, this patent family included patent applications in the United States, Europe, Australia, Brazil, Canada, China, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, Russia, Singapore and Thailand and granted patents in Australia, China, Japan, Korea, Russia, and South Africa. We expect any patents granted in this patent family to expire in February 2037, absent any patent term adjustments or extensions.

The third and fourth of these patent families are method of treatment patent families directed to a particular dosage regimen. As of December 31, 2022, one of these patent families includes patent applications in the United States, Europe, Australia, Brazil, Canada, China, Israel, Indonesia, Japan, South Korea, Mexico, Malaysia, New Zealand, Russia, Singapore and Thailand and a granted patent in Russia and South Africa. The other one of these patent families includes patent applications in the United States, Europe, Australia, Canada, China and Japan and a granted patent in China and Japan. We expect any patents granted in this patent family to expire in September 2037, absent any patent term adjustments or extensions.

The fifth of these patent families is a composition of matter family directed to PTH compounds exhibiting a beneficial pharmacokinetic profile. As of December 31, 2022, this patent family includes patent applications in the United States, Europe, Australia, Brazil, Canada, China, Israel, Japan, South Korea, Mexico, New Zealand, Russia and Singapore and a granted patent in Japan, Russia and South Africa. We expect any patents granted in this patent family to expire in September 2037, absent any patent term adjustments or extensions.

The sixth patent family relates to a starting dose for treatment with reversible PTH conjugates. As of December 31, 2022, this patent family includes patent applications in the United States, Europe, Australia, Brazil, Canada, China, Indonesia, Israel, Japan, South Korea, Mexico, Malaysia, New Zealand, Russia, Singapore, Thailand and South Africa. We expect any patents granted from this patent family to expire in May 2039, absent any patent term adjustments or extensions.

The seventh patent family relates to a pharmaceutical composition comprising reversible PTH conjugates. As of December 31, 2022, this patent family includes patent applications in the United States, Europe, Australia, Brazil, Canada, China, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, the Philippines, Russia, Singapore, Taiwan, Thailand, Vietnam and South Africa. We expect any patents granted from this patent family to expire in February 2040, absent any patent term adjustments or extensions.

The eighth and ninth patent families relate to a method of titrating hypoparathyroidism patients off of standard of care within four weeks from the beginning of daily treatment with a PTH compound and the treatment of the physical and mental well-being of hypoparathyroidism patients, respectively. As of December 31, 2022, the eighth family includes patent applications in the United States, Europe, Australia, Brazil, Canada, China, Indonesia, Israel, Japan, South Korea, Mexico, Malaysia, New Zealand, Russia, Singapore and South Africa. The ninth patent family is in Patent Cooperation Treaty phase. We expect any patents granted from this patent family to expire in September 2041, absent any patent term adjustments or extensions.

The tenth patent family relates to a reduction in bone mineral density in patients having increased bone mineral density. As of December 31, 2022, this patent family is in Patent Cooperation Treaty phase. We expect any patents granted from this patent family to expire in September 2042, absent any patent term adjustments or extensions.

The eleventh patent family covers treatment of hypoparathyroidism initially with a long-acting PTH compound, followed by treatment with an ultra-long-acting PTH compound. As of December 31, 2022, this patent family is in its priority year. We expect any patents granted from this patent to expire in September 2042, absent any patent term adjustments or extensions.

TransCon CNP

Our patent portfolio related to TransCon CNP includes thirteen patent families relating to different aspects of TransCon CNP. The first of these patent families is a composition of matter patent family directed to the particular stoichiometry of TransCon CNP and a related TransCon carrier. As of December 31, 2022, this patent family included patents granted in Europe and the United States and a patent application in Europe. We expect any patents granted in this patent family to expire in October 2024, absent any patent term adjustments or extensions.

The second of these patent families is a composition of matter patent family directed to the TransCon linker used in TransCon CNP. As of December 31, 2022, this patent family included granted patents in the United States, Europe, the United Arab Emirates, Australia, Brazil, Canada, China, Israel, Japan, Mexico and South Africa and included patent applications in Europe, the United States, Brazil, Mexico and Russia. We expect any patents granted in this family to expire in January 2029, absent any patent term adjustments or extensions.

The third of these patent families is a composition of matter patent family directed to a broad class of TransCon CNP candidate structures. As of December 31, 2022, this patent family included patent applications in the United States, Europe, Australia, Brazil, Canada, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, Russia, Singapore and Thailand and a granted patent in China, Russia, Singapore and South Africa. We expect any patents granted in this patent family to expire in January 2036, absent any patent term adjustments or extensions.

The fourth to the ninth patent families are composition of matter patent families directed various CNP compounds having beneficial properties. As of December 31, 2022, the first one of these six patent families included patent applications in the United States, Europe, Australia, Canada, Japan, Mexico and New Zealand and granted patents in the United States, Australia, Japan and South Africa. As of December 31, 2022, the second one included patent applications in the United States, Europe, Australia, Canada, Japan and New Zealand and a granted patent in the United States, Europe, Australia, Japan, and South Africa. As of December 31, 2022, the third one included patent applications in the United States, Europe, Australia, Brazil, Canada, China, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand and Singapore and a granted patent in the United States, Australia, China, Israel, Japan, and South Africa. As of December 31, 2022, the fourth one included patent applications in the United States, Europe, Australia, Canada, Israel and New Zealand and a granted patent in the United States and Australia. As of December 31, 2022, the fifth one included patent application in the United States, Europe, Australia, Brazil, Canada, China, Israel, South Korea, New Zealand and Singapore and a granted patent in the United States, Australia, China, and South Korea. As of December 31, 2022, the sixth one included patent applications in the United States, Europe, Australia, Canada, Israel and New Zealand and a granted patent in the United States. We expect any patents granted in these patent families to expire in January 2037, absent any patent term adjustments or extensions.

The tenth patent family covers a combination therapy of TransCon CNP. As of December 31, 2022, this patent family includes patent applications in the United States, Europe, Australia, Brazil, Canada, Indonesia, Israel, South Korea, Malaysia, New Zealand, Singapore and Thailand and a granted patent in China, Israel, Japan, Mexico, Russia, Singapore and South Africa. We expect any patents granted from this patent family to expire in September 2037, absent any patent term adjustments or extensions.

The eleventh patent family relates to a pharmaceutical composition comprising reversible CNP conjugates. As of December 31, 2022, this patent family includes patent applications in the United States, Europe, Australia, Brazil, Canada, China, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, the Philippines, Russia, Singapore, Taiwan, Thailand, Vietnam and South Africa. We expect any patents granted from this patent family to expire in February 2040, absent any patent term adjustments or extensions.

The twelfth patent family relates to a pharmacologically effective dose of TransCon CNP. As of December 31, 2022, this patent family was in Patent Cooperation Treaty phase. We expect any patents granted from this patent family to expire in December 2042, absent any patent term adjustments or extensions.

The thirteenth patent family relates to a liquid formulation of TransCon CNP. As of December 31, 2022, this patent family was in its priority year. We expect any patents granted from this patent family to expire in May 2043, absent any patent term adjustment or extensions.

TransCon TLR7/8

As of December 31, 2022, our patent portfolio related to TransCon TLR7/8 includes seven patent families. The first patent family relates to hydrogels, which are first synthesized and subsequently loaded with drug-linker conjugates. As of December 31, 2022, this patent family included granted patents in the United States and in Europe. We expect any patents granted in these patent families to expire in July 2025, absent any patent term adjustments or extensions.

The second patent family relates to a specific class of PEG-based hydrogels. As of December 31, 2022, this patent family included granted patents in the United States, Europe, Australia, Brazil, Canada, China, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, Russia, Singapore and South Africa and patent applications in the United States, Europe and Thailand. We expect any patents granted in this patent family to expire in July 2030, absent any patent term adjustments or extensions.

The third patent family relates to a broad class of TransCon TLR7/8 candidate structures. As of December 31, 2022, this patent family included patent applications in the United States, Europe, Argentina, the United Arab Emirates, Australia, Brazil, Canada, China, Eurasia, Egypt, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, the Philippines, Singapore, Taiwan, Thailand, Vietnam and South Africa. The fourth to sixth patent families relate to TransCon TLR7/8 compounds having beneficial properties. As of December 31, 2022, the fourth patent family included patent applications in the United States, Europe, Australia, Canada, Israel and Singapore. The fifth patent included as of December 31, 2022, patent applications in the United States, Europe, Australia, Brazil, Canada, China, Israel, Japan, South Korea, Mexico, Russia, Singapore and South Africa. As of December 31, 2022, the sixth patent family included patent applications in the United States, Europe, Australia, Canada, Israel and Singapore. We expect any patents granted in all four of these patent families to expire in January 2040, absent any patent term adjustments or extensions.

The seventh patent family relates to a pharmaceutical dose of TransCon TLR7/8. As of December 31, 2022, this application was in Patent Cooperation Treaty phase. We expect any patents granted from this patent family to expire in December 2042, absent any patent term adjustments or extensions.

TransCon IL-2

As of December 31, 2022, our patent portfolio related to TransCon IL-2 includes three patent families. The first of these patent families is a composition of matter patent family directed to a TransCon linker used in TransCon IL-2. As of December 31, 2022, this patent family included patents granted in the United States, Europe, Australia, Brazil, Canada, Japan and Mexico and included a patent application in the United States. We expect any patents granted in this patent family to expire in March 2025, absent any patent term adjustments or extensions.

The second and third patent family are composition of matter patent families directed to a broad class of TransCon IL-2 lead candidate structures. As of December 31, 2022, the second patent family included patent applications in the United States, Europe, Australia, Brazil, Canada, China, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, Russia, Singapore, Thailand and South Africa. We expect any patents granted in this patent family to expire in March 2039. As of December 31, 2022, the third patent family included patent applications in the United States, Europe, Argentina, the United Arab Emirates, Australia, Brazil, Canada, China, Eurasia, Egypt, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, the Philippines, Singapore, Taiwan, Thailand, Vietnam and South Africa. We expect any patents granted in this patent family to expire in June 2041, absent any patent term adjustments or extensions.

TransCon Technologies

Our patent portfolio also includes patents and patent applications generally relating to our TransCon technologies, including TransCon linkers, TransCon carriers and certain soluble conjugates. We own an aggregate of 15 patent families relating to TransCon linkers, the material components of which are described above. We own an aggregate of 11 patent families relating to TransCon carriers, the material components of which are described above. Finally, we own a composition of matter patent family that is directed to soluble conjugates in which one drug molecule is connected to one TransCon carrier molecule.

Laws and Regulations Regarding Patent Terms

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent term may be shortened if a patent is terminally disclaimed over another patent or if there are delays in patent prosecution by the patentee. A patent's term may be lengthened by a patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office in granting a patent. The patent term of a European patent is 20 years from its filing date, which, unlike in the United States, is not subject to patent term adjustments.

The term of a patent that covers an FDA-approved drug or biologic may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug or biologic is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We anticipate that some of our issued patents may be eligible for patent term extensions.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, safety surveillance, efficacy, quality control, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sale, import, export and the reporting of safety and other post-market information of pharmaceutical and medical device products such as those we are developing. A new drug must be approved by the FDA through the NDA process and a new biologic must be licensed by the FDA through the BLA process before it may be legally marketed in the United States. Our product candidates will be subject to similar requirements in other countries prior to marketing in those countries. The processes for obtaining regulatory approvals in the United States, the EU and in other foreign countries, along with subsequent compliance with appropriate federal, state, local and foreign statutes and regulations, require the expenditure of substantial time and resources.

U.S. Government Regulation

In the United States, we are subject to extensive regulation by the FDA, which regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and in the case of biologics, also under the Public Health Service Act ("PHSA") and their implementing regulations, and other federal, state, and local regulatory authorities. The FDCA, PHSA and their implementing regulations set forth, among other things, requirements for the research, testing, development, manufacture, quality control, safety, effectiveness, approval, labeling, storage, record keeping, reporting, distribution, import, export, advertising and promotion of our products. The process of obtaining regulatory approvals and the subsequent 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 product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs or BLAs, withdrawal of an approval, imposition of a clinical hold on clinical studies, issuance of warning letters or other notices of violation, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug or biologic may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's Good Laboratory Practice ("GLP") regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- approval by an independent institutional review board ("IRB"), at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice ("GCP"), requirements to establish the safety and efficacy of the proposed drug or biological product for each indication;
- submission to the FDA of an NDA or BLA after completion of all pivotal clinical trials;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's or biologic's identity, strength, quality and purity and of selected clinical investigation sites to assess compliance with GCP; and
- FDA review and approval of the NDA or BLA to permit commercial marketing of the product for particular indications for use in the United States.

Nonclinical Studies and Investigational New Drug Applications

Nonclinical studies include laboratory evaluations of product chemistry, toxicity and formulations, as well as animal studies to assess safety and efficacy. An IND is a request for authorization from the FDA to administer an investigational pharmaceutical product to humans. A sponsor must submit the results of the nonclinical tests, together with chemistry, manufacturing & control information, and any available clinical data or literature, to the FDA as part of an IND. Some nonclinical testing may continue after the IND is submitted. An IND automatically becomes effective and a clinical trial proposed in the IND may begin 30 days after the FDA receives the IND, unless during this 30-day waiting period, the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the sponsor must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence. The FDA may impose clinical holds on a product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA.

Clinical Trials

Clinical trials involve the administration of the investigational pharmaceutical product 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, 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. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA. In addition, written safety reports regarding serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar pharmaceutical products, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure must be submitted to the FDA.

Furthermore, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial. The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Information about certain clinical trials must be submitted within specific timeframes to the NIH, for public dissemination on their www.clinicaltrials.gov website.

Human clinical trials are typically conducted in three or four sequential phases, which may overlap or be combined:

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, optimal dosage, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The product candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific diseases and to determine optimal dosage.
- Phase 3: The product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, typically in well-controlled trials, to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

In some cases, the FDA may require, or sponsors may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be conducted after initial marketing approval, and may be used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA.

During the development of a new product candidate, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA or BLA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for FDA to provide advice, and for the sponsor and the FDA to reach consensus on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trial that they believe will support approval of the new product candidate.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product and 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 product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Marketing Approval in the U.S.

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA or BLA requesting approval or licensure to market the product for one or more indications. In most cases, the submission of an NDA or BLA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity or original BLA to review and act on the submission. This review typically takes twelve months from the date the NDA or BLA is submitted to the FDA because the FDA has sixty days from receipt to decide whether an application is accepted for filing, as described below.

The FDA conducts a preliminary review of all NDAs and BLAs 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 or BLA 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. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity. The FDA reviews a BLA to determine, among other things, whether the product is safe, pure and potent (which are analogous to the NDA safety and effectiveness requirements) and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency.

The FDA may refer an application for a novel drug or biologic to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts as well as consumer representatives, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA or BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

The FDA generally accepts data from foreign clinical trials in support of an NDA or BLA if the trials were conducted under an IND. If a foreign clinical trial is not conducted under an IND, the FDA nevertheless may accept the data in support of an NDA or BLA if the study was conducted in accordance with GCP requirements and the FDA is able to validate the data through an on-site inspection, if deemed necessary. The FDA may accept foreign data as the sole basis for marketing approval if (1) the foreign data are applicable to the U.S. population and U.S. medical practice, (2) the studies were performed by clinical investigators with recognized competence, and (3) the data may be considered valid without the need for an on-site inspection or, if the FDA considers the inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

After evaluating the NDA or BLA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA or BLA identified by the FDA and may require additional clinical data, such as an additional clinical trial or other significant and time-consuming requirements. If a Complete Response Letter is issued, the sponsor must resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug or biologic with specific prescribing information for specific indications.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA or BLA with a Risk Evaluation and Mitigation Strategy ("REMS") to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. The FDA may also require one or more Phase 4 post-marketing studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

In addition, the Pediatric Research Equity Act ("PREA") requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and BLAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Regulation of Combination Products in the United States

Certain products are comprised of components, such as drug components and device components, that would normally be subject to different regulatory frameworks by the FDA and frequently regulated by different centers at the FDA. These products are known as combination products. Under the FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. The determination of which center will be the lead center is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a drug-device combination product is attributable to the drug product, the FDA center responsible for premarket review of the drug product would have primary jurisdiction for the combination product. The FDA has also established the Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory review process. That office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible for developing guidance and regulations to clarify the regulation of combination products, and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute. A combination product with a primary mode of action attributable to the drug component generally would be reviewed and approved pursuant to the drug approval processes set forth in the FDCA or PHSA. In reviewing the NDA or BLA for such a product, however, FDA reviewers would consult with their counterparts in the FDA's Center for Devices and Radiological Health to ensure that the device component of the combination product met applicable requirements regarding safety, effectiveness, durability and performance. In addition, under FDA regulations, combination products are subject to cGMP requirements applicable to both drugs and devices, including the QSR applicable to medical devices.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. For example, the Fast Track program is intended to expedite or facilitate the process for reviewing new products that are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a fast track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA or BLA is submitted, the product candidate may be eligible for priority review. An NDA or BLA for a Fast Track product may also be eligible for rolling review, where the FDA may consider for review sections of the NDA or BLA 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 or BLA, 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 or BLA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A product candidate can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a drug or biologic submitted to the FDA for approval, including a product candidate with a Fast Track designation and/or Breakthrough Therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. An NDA or BLA is eligible for priority review if the product candidate is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. For new-molecular-entity NDAs or original BLAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date.

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled confirmatory clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required confirmatory studies in a timely manner or if such studies fail to verify the predicted clinical benefit. 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.

Fast Track designation, Breakthrough Therapy designation, priority review, and accelerated approval do not change the standards for approval but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Post-Approval Requirements

Drugs and biologics manufactured or distributed pursuant to FDA approvals and licenses are subject to pervasive and continuing regulation by the FDA and other government authorities, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes or other labeling claims are subject to prior FDA review and approval.

There also are continuing, annual program fee requirements for certain approved prescription drug or biologic products. The FDA may impose a number of post-approval requirements as a condition of approval of an NDA or BLA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug and biologics manufacturers and other entities involved in the manufacture and distribution of approved drugs and biologics are required to register their establishments with the FDA and state authorities and are subject to periodic unannounced inspections by the FDA and these state authorities for compliance with cGMP requirements. 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 withdraw the approval in accordance with the statute and regulations if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory 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 product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or BLAs or supplements to approved NDAs or BLAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. A company can make only those claims relating to safety and efficacy, purity and potency that are 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. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgement, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product 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 the product available in the United States for this type of disease or condition will be recovered from sales of the product in the United States. ODD must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. ODD does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. ODD entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user fee waivers.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same disease or condition for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different product for the same disease or condition or the same product for a different disease or condition.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the disease or condition 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.

Biosimilars and Exclusivity

The Affordable Care Act (“ACA”) includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (“BPCIA”), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. To date, relatively few biosimilars have been licensed under the BPCIA, although numerous biosimilars have been approved in Europe. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until twelve years from the date on which the reference product was first licensed. During this twelve-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor’s own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed “interchangeable” by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Drug Product Exclusivity

Market exclusivity provisions authorized under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent data 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 ("ANDA"), or an NDA submitted under Section 505(b)(2), 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 any preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric Exclusivity

Pediatric exclusivity is a type of non-patent 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 five-year and three-year non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA or BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data does not need to show the product to be effective in the pediatric population studied; rather, if the FDA has requested the study and the clinical study 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 product are extended by six months for purposes of the FDA approval process. This is not a patent term extension, but it effectively extends existing periods of regulatory exclusivity.

Foreign Regulation

To market any product outside of the United States, we need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorisation, commercial sales and distribution of our products. The foreign regulatory approval process includes all of the risks associated with FDA approval set forth above, as well as additional country and region-specific regulation.

Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. Approval by one regulatory authority does not ensure approval by regulatory authorities in other jurisdictions. The approval process varies from country to country, can involve additional testing beyond that required by FDA, and may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing, promotion, and reimbursement vary greatly from country to country.

Non-clinical Studies and Clinical Trials

Similar to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies (pharmaco-toxicological) must be conducted in compliance with the principles of GLP as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products – e.g., radio-pharmaceutical precursors for radio-labelling purposes). In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization ("ICH"), guidelines on GCP as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation ("EU CTR"), repeals the EU Clinical Trials Directive, and was adopted in April 2014 and became applicable on January 31, 2022. Unlike a Directive, the EU CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The EU CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via the Clinical Trials Information System, which is a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application ("CTA"), to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the EU CTR introduces a centralized process and only requires the submission of a single application for multi-center trials. The EU CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. One of the main aims of EU CTR is to increase transparency about clinical trials, which is done by making documents and data from the CTA publicly available through the Clinical Trials Information System at the time of decision about the clinical trial. There are few exceptions to this, and release of personal data and company confidential information is controlled through redaction and through requesting a trial-phase dependent deferral of disclosure.

The extent to which ongoing and new clinical trials will be governed by the EU CTR depends on the date of submission of the initial application, and whether the trial completes after the end of the transition period (31 January 2025). Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR.

Medicines used in clinical trials must be manufactured in accordance with GMP. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorisation

In order to market our future product candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorisation ("MA"). To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a MAA. The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MAs" are issued by the EC through the centralized procedure based on the opinion of the Committee for Medicinal Products for Human Use ("CHMP") of the EMA, and are valid throughout the EU. The centralized procedure is compulsory for certain types of medicinal products such as (i) medicinal products derived from biotechnological processes, (ii) designated orphan medicinal products, (iii) advanced therapy medicinal products ("ATMPs") (such as gene therapy, somatic cell therapy and tissue engineered products) and (iv) medicinal products containing a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases or autoimmune diseases and other immune dysfunctions, and viral diseases. The centralized procedure is optional for products containing a new active substance not authorized in the EU before May 20, 2004, or that represent a significant therapeutic, scientific or technical innovation, or whose authorisation would be in the interest of public health in the EU.
- "National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops.

Data and Marketing Exclusivity

In the EU, new products authorized for marketing (*i.e.*, reference products) generally receive eight years of data exclusivity and an additional two years of market exclusivity upon MA. If granted, the data exclusivity period prevents generic and biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial MA of the reference product in the EU. The overall ten-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the MA holder obtains an authorisation for one or more new therapeutic indications, which, during the scientific evaluation prior to their authorisation, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical or biological entity, and products may not qualify for data exclusivity.

Orphan Medicinal Products

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product can be designated as an orphan if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life threatening or chronically debilitating condition (2) either (a) such condition affects not more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from the orphan status, would not generate sufficient return in the EU to justify the necessary investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized for marketing in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition.

An EU orphan designation entitles a sponsor to incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized procedure. Upon grant of a MA, orphan medicinal products are entitled to a ten years of market exclusivity for the approved indication, which means that the competent authorities cannot accept another MAA, or grant a MA, or accept an application to extend a MA for a similar medicinal product for the similar indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan ("PIP"). No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. OD does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The orphan exclusivity period may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for which it received OD, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. OD must be requested before submitting an MAA. Additionally, MA may be granted to a similar product for the same indication at any time if (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant consents to a second orphan medicinal product application; or (iii) the applicant cannot supply enough orphan medicinal product.

Pediatric Development

In the EU, MAAs for new medicinal products have to include the results of studies conducted in the pediatric population, in compliance with a PIP agreed with the EMA's Paediatric Committee ("PDCO"). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all the EU member states and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted.

Post-Approval Requirements

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the EC and/or the competent regulatory authorities of the member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance ("QPPV") who is responsible for the establishment and maintenance of that system and oversees the safety profiles of medicinal products and any emerging safety concerns. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports ("PSURs").

All MAA must include a risk management plan ("RMP"), describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The RMP must be updated any time new information on the medicinal product becomes available which has a significant impact on the content of the RMP. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorisation obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorisation safety studies.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and differ from one country to another.

The aforementioned EU rules are generally applicable in the European Economic Area ("EEA"), which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom ("UK"), left the EU on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the UK during the transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement ("TCA"), and became effective on the January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law". The EU laws that have been transposed into UK law through secondary legislation remain applicable in Great Britain. However, under the Retained EU Law (Revocation and Reform) Bill 2022, which is currently before the UK parliament, any retained EU law not expressly preserved and "assimilated" into domestic law or extended by ministerial regulations (to no later than June 23, 2026) will automatically expire and be revoked by December 31, 2023. In addition, new legislation such as the EU CTR will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an 'appropriate authority' to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency ("MHRA"), is the UK's standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain ("GB"); broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a guidance on how various aspects of the UK regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, importing, exporting, and pharmacovigilance and is relevant to any business involved in the research, development, or commercialization of medicines in the UK. The new guidance was given effect via the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019, or the "Exit Regulations."

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder chooses to opt-out. In order to use the centralized procedure to obtain a MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore after Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to obtain a UK MA to commercialize products in the UK, an applicant must be established in the UK and must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the UK. The MHRA may rely on a decision taken by the EC on the approval of a new (centralized procedure) MA when determining an application for a GB authorisation (the so-called "EC Decision Reliance Procedure"); or use the MHRA's decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in GB (the so-called "MRDC Reliance Procedure").

There will be no pre-MA orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in GB, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in GB.

Regulation of Combination Products in the EU

The EU regulates medical devices and medicinal products separately, through different legislative instruments, and the applicable requirements will vary depending on the type of drug-device combination product. EU guidance has been published to help manufacturers select the right regulatory framework.

Drug-delivery products intended to administer a medicinal product where the medicinal product and the device form a single integral product are regulated as medicinal products in the EU. The EMA is responsible for evaluating the quality, safety and efficacy of MAAs submitted through the centralized procedure, including the safety and performance of the medical device in relation to its use with the medicinal product. The EMA or the EU member state national competent authority will assess the product in accordance with the rules for medicinal products described above but the device part must comply with the Medical Devices Regulation (including the general safety and performance requirements provided in Annex I). MAA must include—where available—the results of the assessment of the conformity of the device part with the Medical Devices Regulation contained in the manufacturer's EU declaration of conformity of the device or the relevant certificate issued by a notified body. If the MAA does not include the results of the conformity assessment and where for the conformity assessment of the device, if used separately, the involvement of a notified body is required, the competent authority must require the applicant to provide a notified body opinion on the conformity of the device.

By contrast, in case of drug-delivery products intended to administer a medicinal product where the device and the medicinal product do not form a single integral product (but are, e.g., co-packaged), the medicinal product is regulated in accordance with the rules for medicinal products described above while the device part is regulated as a medical device and will have to comply with all the requirements set forth by the Medical Devices Regulation.

The characteristics of non-integral devices used for the administration of medicinal products may impact the quality, safety and efficacy profile of the medicinal products. To the extent that administration devices are co-packaged with the medicinal product or, in exceptional cases, where the use of a specific type of administration device is specifically provided for in the product information of the medicinal product, additional information may need to be provided in the MAA for the medicinal product on the characteristics of the medical device(s) that may impact on the quality, safety and/or efficacy of the medicinal product.

The requirements regarding quality documentation for medicinal products when used with a medical device, including single integral products, co-packaged and referenced products, are outlined in the EMA guideline of July 22, 2021, which became applicable as of January 1, 2022.

The aforementioned EU rules are generally applicable in the EEA.

Other Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical products, other U.S. federal, state and foreign healthcare regulatory laws restrict business practices in the biopharmaceutical industry, which include, but are not limited to, state, federal and foreign anti-kickback, false claims, and transparency laws regarding drug pricing and payments or other items of value provided to physicians and other healthcare providers.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not meet the strict requirements of a statutory or regulatory exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances in light of the prohibitions in the statute. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation.

The federal civil False Claims Act prohibits any person or entity from, among other things, knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-covered, uses. Moreover, 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 federal civil False Claims Act.

In addition, the civil monetary penalties statute imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), created new federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. As with the Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Physician Payments Sunshine Act imposed, among other things, annual reporting requirements for covered manufacturers for certain payments and "transfers of value" provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician providers such as physician assistants and nurse practitioners, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Covered manufacturers must submit reports by the 90th day of each subsequent calendar year.

The majority of states also have anti-kickback and other fraud and abuse laws, which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers. Certain states also require implementation of compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on marketing practices, and/or tracking and reporting of marketing expenditures and pricing information as well as gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities.

Moreover, analogous state and foreign laws and regulations may be broader in scope than the provisions described above and may apply regardless of payor. These laws and regulations may differ from one another in significant ways, thus further complicating compliance efforts. For instance, in the EU, many EU member states have adopted specific anti-gift statutes that further limit commercial practices for medicinal products, in particular vis-à-vis healthcare professionals and organizations. Additionally, there has been a recent trend of increased regulation of payments and transfers of value provided to healthcare professionals or entities and many EU member states have adopted national "Sunshine Acts" which impose reporting and transparency requirements (often on an annual basis), similar to the requirements in the United States, on pharmaceutical companies. Certain countries also mandate implementation of commercial compliance programs, or require disclosure of marketing expenditures and pricing information.

Violation of any of such laws or any other governmental regulations that apply to drug manufacturers may result in significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug or medical device products for which we obtain regulatory approval. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of SKYTROFA or any other products for which we receive regulatory approval for commercial sale will therefore depend, in part, on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations.

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 FDA-approved drugs for a particular indication. A decision by a third-party payor not to cover SKYTROFA or our other product candidates could reduce physician utilization of our products and have a material adverse effect on our sales, results of operations and financial condition. Moreover, a third-party payor's decision to provide coverage for a drug or medical device product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for new products can differ significantly from payor to payor. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service or that they will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time-consuming process.

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. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of drugs, medical devices and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. In addition, in many foreign countries, 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. In the EU, governments influence the price of products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. 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 to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. 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 products. The downward pressure on healthcare costs in general, particularly prescription products, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from lower priced markets exert a commercial pressure on pricing within a country.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. For example, in 2010, the ACA and related legislation were enacted, which, among other things, (i) increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, (ii) addressed 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, (iii) extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans, (iv) imposed mandatory discounts for certain Medicare Part D beneficiaries, and (v) subjected drug manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace from February 15, 2021 through August 15, 2021. The executive order instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes include the Budget Control Act of 2011, which resulted in reductions in Medicare payments to providers, which went into effect on April 1, 2013 and will stay in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, reduced certain Medicare payments to several types of providers, including hospitals. The legislation also increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In addition, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

Further, on May 30, 2018, 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.

Moreover, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022 ("IRA") was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including through constraints on reimbursement, imposition of mandatory discounts, restrictions on access to certain products, transparency measures, and programs for importation from other countries or bulk purchasing.

Similar political, economic and regulatory developments are occurring in the EU and may affect the ability of pharmaceutical companies to profitably commercialize their products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could restrict or regulate post-approval activities and affect the ability of pharmaceutical companies to commercialize their products.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In the EU, potential reductions in prices and changes in reimbursement levels could be the result of different factors, including reference pricing systems, parallel distribution and parallel trade. It could also result from the application of external reference pricing mechanisms, which consist of arbitrage between low-priced and high-priced countries. Reductions in the pricing of our medicinal products in one EU member state could affect the price in other EU member states and, thus, have a negative impact on our financial results.

Health Technology Assessment ("HTA") of medicinal products in the EU is an essential element of the pricing and reimbursement decision-making process in a number of EU member states. The outcome of HTA has a direct impact on the pricing and reimbursement status granted to the medicinal product. A negative HTA by a leading and recognized HTA body concerning a medicinal product could undermine the prospects to obtain reimbursement for such product not only in the EU member state in which the negative assessment was issued, but also in other EU member states.

In 2011, Directive 2011/24/EU was adopted at the EU level. This Directive establishes a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states. The network facilitates and supports the exchange of scientific information concerning HTAs. Further to this, on December 13, 2021, Regulation No 2021/2282 on HTA, amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once the Regulation becomes applicable, it will have a phased implementation depending on the concerned products. This regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system and international healthcare systems. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures.

Data Privacy and Security

Privacy and data security have become significant issues in the United States, Europe and in many other jurisdictions where we may in the future conduct our operations. As we receive, collect, process, use and store personal and confidential data, we are or may become subject to diverse laws and regulations relating to data privacy and security, such as data breach notification laws, health information privacy and security laws, and consumer protection laws in the United States and abroad including the EU General Data Protection Regulation ("GDPR") and the U.K. GDPR. Privacy and security laws, regulations, and other obligations are complex and constantly evolving, and any unauthorized access, disclosure and other loss of personal data, including by third party vendors providing support services, can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties, restrictions on data processing and reputational damage.

Cybersecurity

In the normal course of business, we may collect and store personal information and certain sensitive company information, including proprietary and confidential business information, trade secrets, intellectual property, information regarding trial participants in connection with clinical trials, sensitive third-party information and employee information.

Despite the implementation of our cybersecurity program, our security measures cannot guarantee that a significant cyberattack will not occur. A successful attack on our information technology systems could have significant consequences to the business. While we devote resources to our security measures to protect our systems and information, these measures cannot provide absolute security. See "Item 3 D. Key Information—Risk Factors—Risks Related to Our Business" for additional information about the risks to our business associated with a breach or compromise to our information technology systems.

C. Organizational Structure

Certain of our operations are conducted through our following wholly-owned subsidiaries: Ascendis Pharma GmbH (Germany), Ascendis Pharma Endocrinology GmbH (Germany) Ascendis Pharma, Inc. (Delaware, United States), Ascendis Pharma Endocrinology, Inc. (Delaware, United States), Ascendis Pharma, Ophthalmology Division A/S (Denmark), Ascendis Pharma, Endocrinology Division A/S (Denmark), Ascendis Pharma Bone Diseases A/S (Denmark), Ascendis Pharma Growth Disorders A/S (Denmark) and Ascendis Pharma Oncology Division A/S (Denmark). These subsidiaries are also set forth in Exhibit 8.1 to this annual report.

D. Property, Plant and Equipment

Our material tangible fixed assets relate to leased facilities, which are recognized and measured as right-of-use assets in the consolidated financial statements. We do not own any of our facilities.

Our corporate headquarters is located in Hellerup, Denmark. In addition, we have offices and research and development facilities in Germany and the United States. We do not own facilities for manufacturing of our products and product candidates for the potential pivotal clinical studies, and/or for commercial manufacturing. Accordingly, we engage with Contract Manufacturing Organizations ("CMOs") to manufacture clinical trial supply, as well as we enter into long term collaborations with CMOs to establish and maintain commercial-scale manufacturing processes for our product candidates and devices.

The following table specifies our leased facilities and their related activities.

Location	Size (in square meters)	Primary usage	Enforceable lease period	Option to extend the lease beyond enforceable lease period
Denmark				
Tuborg Boulevard, Hellerup	7,775	Corporate headquarters, administration and R&D	July, 2029	No
Tuborg Boulevard, Hellerup	4,168	Administration	May, 2038	No
Germany				
Technologiepark, Heidelberg	2,134	R&D and laboratory facilities	January, 2025	Rolling 24 months option to extend
Technologiepark, Heidelberg	480	R&D and laboratory facilities	December, 2024	No
Technologiepark, Heidelberg	538	R&D and laboratory facilities	October, 2024	No
Max-Jarecki-Str., Heidelberg	2,321	Administration, R&D and laboratory facilities	January, 2026	No
United States				
Page Mill, Palo Alto, California	6,765	Administration	October, 2033	Option to extend for up to two periods of five years each
Redwood City, California	3,681	R&D and laboratory facilities	April, 2030	Option to extend for additional five years
West Windsor Township, New Jersey	1,097	Selling and administration	December, 2025	Option to extend for additional five years

In February 2022 we entered into a lease in Germany, comprising 11,390 square meters, with a term of 15 years, expected to commence in 2025, where its main activities will be administration, R&D and laboratory functions.

We believe that our existing facilities are adequate for our near-term needs. We believe that suitable additional or alternative space would be available if required in the future on commercially reasonable terms.

Item 4A Unresolved Staff Comments

Not applicable.

Item 5 Operating and Financial Review and Prospects

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our consolidated financial statements and related notes appearing elsewhere in this annual report. In addition to historical information, this discussion contains forward-looking statements based on our current expectations that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth in the "Item 3 D Key Information—Risk Factors" and "Special Note Regarding Forward-Looking Statements" sections and elsewhere in this annual report.

A. Operating Results

Refer to Part I, Item 5 in our Annual Report on Form 20-F for the financial year ended December 31, 2021 (filed with the SEC on March 2, 2022) for additional discussion of our financial condition and results of operations for the year ended December 31, 2020, as well as our financial condition and results of operations for the year ended December 31, 2021, compared to the year ended December 31, 2020.

Overview

For a description of business highlights in 2022, please refer to "Item 4B. Information on the Company—Business Overview".

Financial Operations Overview

Income and Expenses

Revenue from commercial product sales and clinical trial supply is recognized when the customer has obtained control of the goods and it is probable that we will collect the consideration to which we are entitled for transferring the goods. Control is transferred upon delivery. Service fees are recognized as revenue when the services have been performed.

Our operating expenses relate to research and development activities and to selling, general and administration activities. Research and development costs ("R&D costs") consist primarily of product development and pre-commercial manufacturing costs, preclinical and clinical study costs and costs for process optimizations and improvements performed by Clinical Research Organizations ("CROs") and Contract Manufacturing Organizations ("CMOs"), salaries and other personnel costs including pension and share-based payment, the cost of facilities, professional fees, cost of obtaining and maintaining our intellectual property portfolio, and depreciation of non-current assets used in research and development activities. Selling, general and administrative expenses ("SG&A expenses") comprise salaries and other personnel costs including pension and share-based payment, office supplies, cost of facilities, professional fees, and depreciation of non-current assets related to selling, general and administrative activities, and pre-commercial and commercial activities.

A material portion of our operating expenses are denominated in other currencies than the Euro, which expose our operating expenses to volatility. The cost increase for the year ended December 31, 2022 compared to the year ended December 31, 2021, also reflects the impact from foreign currency development, primarily with respect to the U.S. Dollar. We do not enter into derivative financial instruments to manage our exposure to foreign exchange risks.

Operating Assets and Liabilities

Our operating assets and liabilities primarily relate to property, plant and equipment including leased assets, inventories, receivables, prepayments and accruals for development costs, lease liabilities, trade payables, and contract liabilities (deferred income). Property, plant and equipment primarily relate to leased facilities, which are recognized and measured as right-of-use assets in the consolidated financial statements. Our receivables and liabilities are exposed to development in foreign currencies, primarily with respect to the U.S. Dollar. Please refer to the "Foreign Currency Risk" section under "Quantitative and Qualitative Disclosures about Market Risk" in this "Item 5 A Operating and Financial Review and Prospects—Operating Results" and to Note 16, "Financial Risk Management", for an analysis on our foreign currency exposure.

We have built up inventories to support the commercialization of SKYTROFA® (lonapegsomatropin-tcgd) and prepare for European launch in 2023. In addition to commercial inventories, manufacturing of pre-launch inventories is initiated for late-stage product candidates and is recognized as inventories. However, since pre-launch inventories are not realizable prior to obtaining marketing approvals, pre-launch inventories are immediately written down to zero through research and development costs. If the marketing approval is obtained, write-downs of pre-launch inventories will be reversed through research and development costs.

Capital Structure

The Company's capital structure comprises equity in form of issued capital, reserves, and convertible senior notes ("convertible notes"), which we issued for the first time in March 2022. For further details, please refer to "Item 5 B Operating and Financial Review and Prospects—Liquidity and Capital Resources".

Results of Operations

	Year Ended December 31,	
	2022	**2021**
	(EUR'000)	
Revenue	51,174	7,778
Cost of sales	12,137	3,523
Gross profit	**39,037**	**4,255**
Research and development costs	379,624	295,867
Selling, general and administrative expenses	221,227	160,180
Operating profit/(loss)	**(561,814)**	**(451,792)**
Share of profit/(loss) in associate	(17,697)	12,041
Finance income	52,181	59,718
Finance expenses	50,487	3,911
Profit/(loss) before tax	**(577,817)**	**(383,944)**
Tax on profit/(loss) for the year	(5,377)	367
Net profit/(loss) for the year	**(583,194)**	**(383,577)**

Comparison of the years ended December 31, 2022 and 2021

We had a net loss of €583.2 million for the year ended December 31, 2022 compared to a net loss of €383.6 million for the year ended December 31, 2021. Our total equity was €263.3 million as of December 31, 2022, compared to €883.6 million as of December 31, 2021. Further details about our results of operations are described in the following sections.

Revenue

The following table summarizes our revenue for the years ended December 31, 2022 and December 31, 2021:

	Year Ended December 31,	
	2022	2021
	(EUR'000)	
Sale of commercial products	35,659	943
Rendering of services	4,434	751
Sale of clinical supply	8,534	3,719
"Right-to-use" licenses	2,547	2,365
Total revenue	**51,174**	**7,778**

Revenue for the year ended December 31, 2022 was €51.2 million, representing an increase of €43.4 million compared to the year ended December 31, 2021. This increase was primarily attributable to the full year impact of revenue from the commercial sale of SKYTROFA, which reached €35.7 million for the year ended December 31, 2022. Quarterly revenue from sale of commercial products since launch in October 2021, was:

	Three Months Ended,					Year Ended,
	December 31, 2021	March 31, 2022	June 30, 2022	September 30, 2022	December 31, 2022	December 31, 2022
	(EUR'000)					
Sale of commercial products	**943**	**1,888**	**4,435**	**12,252**	**17,084**	**35,659**

Cost of Sales

Cost of sales for the year ended December 31, 2022 was €12.1 million, representing an increase of €8.6 million compared to the year ended December 31, 2021. This increase was primarily attributable to an increase in commercial products sold following the commercial launch of SKYTROFA in the U.S. in the fourth quarter of 2021. The increase in cost of sales was also due in part to clinical supply delivered to VISEN Pharmaceuticals ("VISEN").

Research and Development Costs

The following table specifies external project costs on the development pipeline and other R&D costs.

	2022	2021
	(EUR'000)	
External project costs		
TransCon hGH	98,483	65,658
TransCon PTH	41,537	36,079
TransCon CNP	42,133	35,728
TransCon IL-2 ß/γ	11,128	10,600
TransCon TLR7/8	25,110	13,499
Other project costs	6,698	2,201
Total external project costs	**225,089**	**163,765**
Other research and development costs		
Employee costs	119,904	106,558
Other costs	23,739	15,442
Depreciation	10,892	10,102
Total other research and development costs	**154,535**	**132,102**
Total research and development costs	**379,624**	**295,867**

The development of R&D costs reflects the advancement of our pipeline of endocrinology and oncology, where we have multiple prodrug therapies in development.

R&D costs for the year ended December 31, 2022 was €379.6 million representing an increase of €83.8 million compared to the year ended December 31, 2021. This increase was primarily due to reversal of a write-down (income) of pre-launch inventories of €53.7 million in 2021, following receipt of the marketing approval for SKYTROFA on the U.S. market in August 2021. In addition, the increase was driven by manufacturing of pre-launch inventories for TransCon PTH with a total amount of €12.3 million and a general increase in employee and other costs attributable to organizational growth.

Selling, General and Administrative Expenses

SG&A expenses for the year ended December 31, 2022 was €221.2 million representing an increase of €61.0 million compared to the year ended December 31, 2021. This increase was primarily attributable to an increase in external commercial expenses following the launch of SKYTROFA in the U.S. of €21.3 million, and an increase in employee and other general and administrative expenses attributable to organizational growth of €39.0 million.

Net Profit / (Loss) of Associate

Net loss of associate was €17.7 million for the year ended December 31, 2022, compared to a net profit of €12.0 million for the year ended December 31, 2021. For the year ended December 31, 2021, the net profit of associate comprised a non-cash gain of €42.3 million as a result of the Series B financing by VISEN in January 2021, and our share of loss of €30.3 million.

Finance Income and Finance Expenses

Finance income was affected by development in the U.S. Dollar compared to the Euro, where the strengthening of the U.S. Dollar remains the primary driver for the development in finance income. Finance expenses are significantly affected by convertible notes in form of interest and amortization charges. In addition, the conversion option embedded in the convertible notes is recognized and measured at fair value, where a non-cash fair value adjustment was recognized through finance expenses. Similarly, subsequent reporting periods may result in significant non-cash finance income or expenses. For further details, please refer to “Equity Risk” in section “Qualitative Disclosures about Market Risk” of this “Item 5 A Operating and Financial Review and Prospects—Operating Results” and Note 15, “Financial Assets and Financial Liabilities”.

Finance income for the year ended December 31, 2022 was €52.2 million representing a decrease of €7.5 million compared to the year ended December 31, 2021. This decrease was primarily attributable to a decrease of €14.3 million in net foreign exchange currency gains, primarily driven by foreign exchange loss on convertible notes, partly offset by an increase in foreign exchange gain from cash, cash equivalents and marketable securities, denominated in U.S. Dollars. In addition, the decrease is partly offset by an increase of €6.7 million in interest income from marketable securities and bank deposits.

Finance expenses for the year ended December 31, 2022 was €50.5 million representing an increase of €46.6 million compared to the year ended December 31, 2021. This increase was primarily driven by interest and amortization charges on convertible notes of €25.9 million, remeasurement loss on derivative liabilities of €15.5 million and transaction costs of €4.2 million, which represents a portion of the total transaction costs attributable to the derivative component of the convertible notes financing in March 2022.

Impact from COVID-19 Pandemic

The COVID-19 pandemic has affected countries where we are operating, where we have planned or have ongoing clinical trials, and where we rely on third-parties to manufacture preclinical, clinical and commercial supply.

While COVID-19 had an impact on how we work and conduct our activities, we have managed to avoid significant disruptions to our clinical and manufacturing operations.

As a result of governmental restrictions, field-based sales personnel primarily have worked under a remote engagement model with healthcare professionals and patient care organizations, and similarly, some patients have not been able to see their physicians. As restrictions cease, field-based sales personnel have begun in person engagements when interacting with healthcare professionals and patient care organizations, as well as patients having easier access to their physicians. The impact on the commercial product revenue is uncertain and difficult to quantify.

We monitor the risks from the pandemic closely, and work with relevant stakeholders to avoid and limit disruptions, and to develop and establish working measures. However, while COVID-19 continues to impact global societies, the uncertainty related to the duration and direction of the pandemic makes the future impact from COVID-19, including the magnitude of any impact on our operational results, highly uncertain and unpredictable.

For additional description related to COVID-19 related risks, please refer to "Item 3 D. Key Information—Risk Factors".

Critical Accounting Policies, Judgements and Estimates

The consolidated financial statements are prepared in accordance with the International Financial Reporting Standards ("IFRS"), as issued by the International Accounting Standards Board ("IASB"), and as adopted by the European Union ("EU"). A description of critical accounting policies is provided in Note 2 "Summary of Significant Accounting Policies" and Note 3 "Significant Accounting Judgements and Estimates" in the audited consolidated financial statements as of and for the years ended December 31, 2022, 2021 and 2020, of this annual report.

Critical Accounting Judgements

Critical accounting judgements which have a material impact on the consolidated financial statements are described in the following sections.

Internally Generated Intangible Assets

Development of Drug Candidates

IAS 38, "Intangible Assets" prescribes that intangible assets arising from development projects must be recognized in the consolidated statements of financial position if the criteria for capitalization are met. That means (1) that the development project is clearly defined and identifiable; (2) that technological feasibility, adequate resources to complete and a market for the product or an internal use of the project can be documented; (3) that the expenditure attributable to the development project can be measured reliably; and (4) that the Company has the intent to produce and market the product. Such an intangible asset shall be recognized if it can be demonstrated that the future income from the development project will exceed the aggregate cost of development, production, sale and administration of the product.

Due to the risk associated with drug development, future income from development projects related to drug candidates cannot be determined with sufficient certainty until the development activities have been completed and the necessary marketing approvals have been obtained. Accordingly, the Company does not recognize internally generated intangible assets at this time.

Critical Estimation Uncertainties

The key assumptions concerning the future and other key sources of estimation uncertainty at the reporting date, that have a risk of causing a material adjustment to the carrying amounts of assets and liabilities within the next financial year, are described below.

Revenue and Provisions

Provision for Sales Rebates and Product Returns

Sales deductions and product returns are considered variable consideration and constrained to the extent that a significant reversal in the amount of recognized revenue will not occur when the uncertainties associated with the rebate item are subsequently resolved, or for product returns, when the products are distributed to patients.

Provisions for unsettled sales deductions and product returns are estimated on the basis of a percentage of sales as defined by individual agreements and contracts, and for government rebates by individual state- and plan agreements. Further input in the calculations is based on payer channel mix, current contract prices under eligible programs, patient groups and current inventory levels in the distribution channels. Provisions are adjusted to absolute amounts and recognized as other liabilities when estimated sales rebates and returns are processed.

As of December 31, 2022, the provisions for sales rebates and product returns was €7.3 million compared to €1.2 million, as of December 31, 2021.

Share-Based Payment

Warrant Compensation Costs

IFRS 2, "Share-Based Payment" requires an entity to reflect in its consolidated statement of profit or loss and financial position, the effects of share-based payment transactions. Warrant compensation costs are recognized as cost of sales, research and development costs or selling, general and administrative expenses, as appropriate, over the vesting period, based on management's best estimate of the number of warrants that will ultimately vest, which is subject to uncertainty.

Warrant compensation costs are measured according to the grant date fair values of the warrants granted. Estimating fair values requires the Company to apply generally accepted valuation models and apply these models consistently according to the terms and conditions of the specific warrant program. Under all warrant programs, the Black-Scholes option-pricing model has been applied to determine the fair value of warrants granted. Subjective judgements and assumptions, which are subject to estimation uncertainties, need to be exercised in determining the appropriate input to the valuation model. These inputs include expected volatility of the Company's share price for a historic period equaling the expected lifetime of the warrants, reflecting the assumption that the historical volatility over a period similar to the life of the warrants is indicative of future trends, expected forfeitures and expected lifetime of warrants.

In 2021, the Company has for the first time, in connection with determining the grant date fair value of warrants and accordingly, warrant compensation costs, applied the price of the Company's ADSs, each representing one ordinary share of the Company, as input for expected volatility. Until December 31, 2020, the expected volatility was calculated using a simple average of daily historical data of comparable publicly traded companies, as the Company did not have sufficient data for the volatility of the Company's own share price. Refer to Note 7, "Share-based Payment", for additional details on the Company's warrant program and option-pricing model input.

Warrant compensation cost recognized in the consolidated statement of profit or loss was €55.2 million, €66.1 million and €53.2 million for the years ended December 31, 2022, 2021 and 2020, respectively.

Prepayments and Accruals

Project Development Costs

Development of drug candidates requires significant resources, and establishment of long-term working relationships with CROs and CMOs. Work performed by CROs and CMOs and other suppliers often comprise deliveries for more than one reporting period, and where payment terms for contractual work do not necessarily reflect the stage of completion of the individual projects and activities. Accordingly, determination of the stage of completion for ongoing project activities include estimation uncertainties as future efforts to complete the specific activity may be difficult to predict.

On each reporting date, all significant ongoing activities are reviewed to determine the stage of completion and compared to the invoices received. Accruals are recognized for individual projects where the stage of completion exceeds costs of invoices received. Similarly, prepayments are recognized for invoiced costs in excess of the stage of completion. The Company has implemented accrual calculation models and policies, to ensure that consistent accrual procedures are applied, which includes analyzing significant project stages and payment structures, comparing project milestones to planned performance, and revisiting prior periods estimates.

As of December 31, 2022, the consolidated statement of financial position included prepaid project costs of €4.4 million and accrued project costs of €38.0 million, compared to €8.0 million and €23.5 million, respectively, as of December 31, 2021.

Valuation of Embedded Derivatives

Foreign currency conversion options embedded in the convertible notes are accounted for separately as derivative liabilities at fair value through profit or loss.

Fair value cannot be measured based on quoted prices in active markets, or other observable input, and accordingly, derivative liabilities are measured by use of valuation techniques in form of the Black-Scholes Option Pricing model. Subjective judgements and assumptions, which are subject to estimation uncertainties, need to be exercised in determining the appropriate unobservable input to the valuation model (Level 3 in the fair value hierarchy). This includes volatility of the Company's share price for a historic period, reflecting the assumption that the historical volatility is indicative of a period similar to the expected lifetime of the options.

As of December 31, 2022, the valuation of the derivative liabilities was €158.0 million compared to €142.5 million at initial recognition on March 2022. Changes in assumptions relating to these factors could affect the reported fair value of derivative liabilities. Refer to Note 15 "Financial Assets and Liabilities", for additional details.

Quantitative and Qualitative Disclosures about Market Risk

Our activities expose us to the financial risks of changes in foreign currency exchange rates and interest rates. We do not enter into derivative financial instruments to manage our exposure to such risks.

Foreign Currency Risk

We are exposed to foreign exchange risk arising from various currency exposures, primarily with respect to the U.S. Dollar. For 2022 and 2021, revenue from commercial sale of products is solely related to the U.S. market where consideration received is in U.S. Dollar. Similarly, a material portion of our operating expenses are denominated in U.S. Dollar.

We have received payments in U.S. Dollar under our collaborations and the proceeds from our Series D financing in November 2014, our IPO in February 2015 and our follow-on offerings, the latest being in September 2021, were in U.S. Dollar. In addition, in March 2022, we issued an aggregate principal amount of $575.0 million of fixed rate 2.25% convertible notes.

We seek to minimize our exchange rate risk by maintaining cash positions in the currencies in which we expect to incur the majority of our future expenses and we make payments from those positions. As required under IFRS, we perform an analysis and report on our foreign currency exposure on an annual basis. Please refer to Note 16, "Financial Risk Management".

At December 31, 2022, the direct exposure from U.S. Dollar (U.S. Dollar monetary assets and liabilities held by non-U.S. Dollar entities) was €60.6 million, which primarily related to cash, cash equivalents and marketable securities, countered by convertible notes. A sensitivity analysis of our exposure to the U.S. Dollar based on outstanding foreign currency denominated monetary items as of December 31, 2022, shows that a strengthening of the U.S. Dollar against the Euro by 10% would increase profit or loss and equity before tax by €6.1 million.

A 10% weakening of the U.S. Dollar against the Euro would decrease profit or loss and equity before tax by a similar amount.

Interest Rate Risk

Our outstanding convertible notes have a 2.25% fixed rate coupon. In addition, the interest rate on our lease liabilities is fixed at the lease commencement date. Future indebtedness, including those related to lease arrangements, if any, may be subject to higher interest rates. In addition, future interest income from interest-bearing bank deposits and marketable securities may fall short of expectations due to changes in interest rates.

Derivative liabilities are measured at fair value through profit or loss. Since the fair value is exposed from the development in interest rates, the profit or loss is exposed to volatility from such development. For further details about our derivative liabilities, please refer to Note 15, “Financial Assets and Financial Liabilities”.

The effects of interest rate fluctuations are not considered a material risk to the Company’s financial position. Accordingly, no interest sensitivity analysis has been presented.

Credit Risk

We have adopted an investment policy with the primary purpose of preserving capital, fulfilling our liquidity needs and diversifying the risks associated with cash, cash equivalents and marketable securities. Our investment policy establishes minimum ratings for institutions with which we hold cash and cash equivalents, as well as rating and concentration limits for marketable securities held.

All material counterparties are considered creditworthy. While the concentration of credit risk may be significant, the credit risk for each individual counterpart is considered to be low. Our exposure to credit risk primarily relates to cash, cash equivalents and marketable securities. The credit risk on our bank deposits is limited because the counterparties, holding significant deposits, are banks with minimum credit-ratings of A3/A- assigned by international credit-rating agencies. The banks are reviewed on a regular basis and deposits may be transferred during the year to mitigate credit risk. In order to mitigate the concentration of credit risks on bank deposits and to preserve capital, a portion of the bank deposits have been placed into primarily U.S. government bonds, treasury bills, corporate bonds, and agency bonds. Our investment policy, approved by the board of directors, only allows investment in marketable securities having investment grade credit-ratings, assigned by international credit-rating agencies. Accordingly, the risk from probability of default is low. On each reporting date, the risk of expected credit loss on bank deposits and marketable securities, including the hypothetical impact arising from the probability of default is considered in conjunction with the expected loss caused by default by banks or securities with similar credit-ratings and attributes. In line with previous periods, this assessment did not reveal a material impairment loss, and accordingly no provision for expected credit loss has been recognized.

Marketable securities specified by investment grade credit rating are specified below:

	December 31, 2022		December 31, 2021	
	Carrying amount	Fair value	Carrying amount	Fair value
	(EUR’000)			
Marketable securities specified by investment grade credit rating				
High grade	203,530	202,048	144,307	144,030
Upper medium grade	94,650	93,795	196,909	196,566
Lower medium grade	—	—	2,142	2,135
Total marketable securities	**298,180**	**295,843**	**343,358**	**342,731**

Equity Risk

We are exposed to equity risk from changes in the Company’s share price, when remeasuring derivative liabilities at fair value.

Derivative liabilities relate to the foreign currency conversion option embedded in the convertible notes and are measured at fair value through profit or loss.

Fair value cannot be measured based on quoted prices in active markets, or other observable input, and accordingly, derivative liabilities are measured by using the Black-Scholes option pricing model, where the pricing is exposed from changes in the Company's share price. Since the fair value is exposed to the Company's share price, the profit or loss is exposed to volatility from such development. For further details about our derivative liabilities and for sensitivity analysis, please refer to Note 15, "Financial Assets and Liabilities".

B. Liquidity and Capital Resources

Our liquidity and capital resources comprise cash, cash equivalents and marketable securities.

As of December 31, 2022, these amounted to €742.9 million, and are specified as follows:

	Carrying amount	Fair value
	(EUR'000)	
December 31, 2022		
Liquidity and capital resources		
Marketable securities	298,180	295,843
Cash and cash equivalents	444,767	444,767
Total liquidity and capital resources	**742,947**	**740,610**
Classification in consolidated statement of financial position		
Non-current assets	7,492	7,201
Current assets	735,455	733,409
Total liquidity and capital resources	**742,947**	**740,610**

As of December 31, 2022, marketable securities had a weighted average duration of 3.0 and 12.6 months, for current (i.e., those maturing within twelve months after the reporting date) and non-current positions, respectively. The entire portfolio of marketable securities (current and non-current) had a weighted average duration of 3.2 months.

Historically, we have funded our operations primarily through issuance of preference shares, ordinary shares, including our initial public offering, follow-on offerings and exercise of warrants, convertible debt securities and payments to us made under collaboration agreements.

In February 2015, we announced the closing of our initial public offering, with net proceeds of $111.5 million (or €101.4 million). In addition, we have completed follow-on public offerings of American Depositary Shares ("ADSs") as specified below (all amounts disclosed after deducting underwriters' commissions and transaction costs):

- In 2016, with net proceeds of $127.1 million (or €116.6 million);
- In 2017, with net proceeds of $145.2 million (or €123.1 million);
- In 2018, with net proceeds of $242.5 million (or €198.6 million);
- In 2019, with net proceeds of $539.4 million (or €480.3 million);
- In 2020, with net proceeds of $654.6 million (or €580.5 million); and
- In 2021, with net proceeds of $436.3 million (or €367.9 million).

In March 2022, we issued an aggregate principal amount of $575.0 million of fixed rate 2.25% convertible notes. The net proceeds from the offering of the convertible notes were $557.9 million (€503.3 million), after deducting the initial purchasers' discounts and commissions, and transaction costs. The convertible notes rank equally in right of payment with all future senior unsecured indebtedness and are redeemable by us no earlier than on or after April 7, 2025. Unless earlier converted or redeemed, the convertible notes will mature on April 1, 2028.

For further description of the convertible notes, and a maturity analysis (on an un-discounted basis) for non-derivative financial liabilities, recognized on the consolidated statement of financial position as of December 31, 2022, please refer to Note 15, "Financial Assets and Liabilities".

We used $116.7 million (€105.3 million) of the net proceeds from the offering in March 2022 to repurchase 1,000,000 ADSs representing the Company's ordinary shares. Our holding of treasury shares is disclosed in Note 16, "Financial Risk Management".

Our expenditures primarily relate to research and development activities and selling, general and administrative activities to support our business, including our continued development of therapeutic areas within endocrinology and oncology, the commercialization of SKYTROFA and expenses made in anticipation of potential future product launches.

Cash requirements

We maintain cash-forecasts to ensure sufficient cash reserves are available to settle liabilities as they fall due.

As of December 31, 2022, our cash requirements primarily relate to the following:

- Semi-annual interest payments and potential repayment (April 1, 2028) of principal amount of convertible notes;
- Lease obligations related to our office and research and development facilities;
- Purchase obligations under our commercial supply agreements and related activities;
- Research and development activities related to clinical trials for our product candidates in clinical development.

Our cash requirements are determined in Euro applying foreign exchange rates at December 31, 2022. Accordingly, actual cash payments are exposed to development in foreign currencies, primarily with respect to the U.S. Dollar. Please refer to "Foreign Currency Risk" section under "Quantitative and Qualitative Disclosures about Market Risk", above, and to Note 16, "Financial Risk Management", for an analysis on our foreign currency exposure.

The convertible notes accrue interest at a rate of 2.25% per annum, payable semi-annually in arrears on April 1 and October 1 of each year, beginning on October 1, 2022. Unless earlier converted or redeemed, the convertible notes will mature on April 1, 2028. On an unconverted basis, short-term (payable within twelve months after the reporting date) and long-term (payable beyond twelve months after the reporting date) cash requirements (on an undiscounted basis) are €12.1 million and €593.7 million, respectively.

At December 31, 2022, the length of leases varies from one to ten years, without considering optional extension periods. Our cash requirements for lease obligations (on an undiscounted basis) are €14.0 million and €114.8 million, on short-term and long-term, respectively. In February 2022 we entered into a facility lease in Germany with an enforceable lease term of 15 years, which is expected to commence in 2025. At December 31, 2022, when including the impact of this new lease in Germany, which is not recognized as lease liabilities in the consolidated statement of financial position at December 31, 2022, our short-term and long-term cash requirements for lease obligations (on an undiscounted basis) were expected to be €14.0 million and €185.0 million, respectively. In addition, our lease obligations establish ancillary contractual commitments in relation to utilities, maintenance, levies, and other services. Costs relating to those commitments are recognized as services are received. Further, we have commitments related to short-term leases and leases of low value assets, IT and facility related services, which are expensed as incurred.

We have also entered into long-term commercial supply agreements, related to commercial manufacturing of SKYTROFA and manufacturing of pre-launch inventories related to TransCon PTH. Commercial supply agreements may include purchase obligations, usually determined on binding and non-binding supply forecasts, that are subject to continuous negotiation and adjustments according to individual contractual terms and conditions.

At December 31, 2022, our short-term and long-term cash requirements were €148.6 million and €49.7 million, respectively, excluding non-binding commitments for purchase of raw materials and intermediates used in the manufacturing process.

As part of our ordinary activities, we engage third-party CROs to perform clinical trial activities, which primarily are studies for more than one year. We are not subject to contingent liabilities from potential milestone payments related to licensing of intellectual property.

We have not entered into any off-balance sheet arrangements or any holdings in variable interest entities. In addition, we are not aware of any significant legal claims or disputes.

Based on our current operating plan, we believe that our existing cash, cash equivalents, and marketable securities are sufficient to meet our projected cash requirements for at least twelve months from the date of this annual report. However, our operating plan and actual cash requirements may change as a result of many factors. For example our future funding requirements will depend on many factors, including, but not limited to:

- the manufacturing, selling and marketing costs associated with our products and product candidates, if approved, including the cost and timing of building our sales and marketing capabilities;
- the timing, receipt, and amount of sales of, or royalties on, TransCon hGH and any future products;
- the sales price and the availability of adequate third-party coverage and reimbursement for our products and product candidates, if approved;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- our ability to collect payments which are due to us from customers and collaboration partners (if any), which in turn is impacted by the financial standing of any such customers and collaboration partners;
- the progress, timing, scope, results and costs of our preclinical studies and clinical trials and manufacturing activities for our product candidates that have not been licensed, including the ability to enroll patients in a timely manner for clinical trials;
- the time and cost necessary to obtain regulatory approvals for our product candidates and the costs of post-marketing studies that could be required by regulatory authorities;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the number and scope of preclinical and discovery programs that we decide to pursue or initiate;
- the potential acquisition and in-licensing of other technologies, products or assets;
- the time and cost necessary to respond to technological and market developments, including further development of our TransCon technologies;
- the achievement of development, regulatory and commercial milestones resulting in the payment to us from collaboration partners of contractual milestone payments and the timing of receipt of such payments, if any;
- our progress in the successful commercialization and co-promotion of our products and product candidates, if approved, and our efforts to develop and commercialize our other existing product candidates;
- the market opportunities and patient populations for our products and product candidates, if approved, including with respect to TransCon PTH, and our ability to obtain market acceptance of our products and product candidates, if approved; and
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of our product candidates.

Additional funds may not be available if we need them or on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, scale back or cease our research and development and commercialization activities, preclinical studies and clinical trials.

The following table summarizes our cash flows for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		
	2022	2021	Change
		(EUR'000)	
Cash flows from / (used in)			
Cash flows from/(used in) operating activities	(495,699)	(417,649)	(78,050)
Cash flows from/(used in) investing activities	61,732	(110,579)	172,311
Cash flows from/(used in) financing activities	396,773	351,387	45,386
Net increase in cash and cash equivalents	**(37,194)**	**(176,841)**	**139,647**

Cash flows from/(used in) Operating Activities

Cash flows used in operating activities for the year ended December 31, 2022 was €495.7 million, representing an increase of €78.1 million compared to the year ended December 31, 2021. This increase was primarily attributable to increase in net loss for the year adjusted for non-operating financial income and expense, taxes, and non-cash items. Working capital items contributed positively to change in operating cash flows by €30.3 million, primarily due to higher increase in inventories in 2021 as compared to 2022, following the launch of SKYTROFA. In addition, change in operating cash flow was negatively impacted by higher interest payments of €7.5 million, primarily related to convertible notes.

Cash flows from/(used in) Investing Activities

Cash flows from investing activities for the year ended December 31, 2022 was €61.7 million, compared to €110.6 million used for the year ended December 31, 2021, representing a decrease of €172.3 million in cash flows used in investing activities. This decrease was primarily attributable to:

- Additional net settlements of marketable securities of €142.8 million in line with our liquidity management strategy;
- Decrease in investments in property, plant and equipment of €9.2 million and receipt of reimbursements from leasehold improvements of €9.5 million in 2022. This was primarily related to leasehold improvements for our U.S. facilities, which were constructed in 2021; and
- The Series B investment in VISEN Pharmaceuticals of €10.2 million made in January 2021.

Cash Flows from/(used in) Financing Activities

Cash flows from financing activities for the year ended December 31, 2022, was €396.8 million, representing an increase of €45.4 million compared to the year ended December 31, 2021. This increase was primarily attributable to proceeds from issuance of convertible notes net of offering expenses of €503.3 million compared to our follow-on public offering in September 2021 of €367.9 million, partly offset by acquisition of treasury shares of €105.3 million in March 2022.

C. Research and Developments, Patents and Licenses, etc.

See "Item 4 B. Information on the Company—Business Overview" and "Item 5 A. Operating and Financial Review and Prospects – Operating Results—Financial Operations Overview—Research and Development Costs."

D. Trend Information

See "Item 5 A. Operating and Financial Review and Prospects—Operating Results."

E. Critical Accounting Estimates

See "Item 5 A. Operating and Financial Review and Prospects—Operating Results."

Item 6 Directors, Senior Management and Employees

A. Directors and Senior Management

We have a two-tier governance structure consisting of a board of directors and an executive board. The two bodies are separate; however, Jan Møller Mikkelsen, our President and Chief Executive Officer, is represented on both our board of directors and our executive board. Our executive board is supported by the other members of our senior management. Below is a summary of relevant information concerning our board of directors, executive board and senior management.

Members of Our Board of Directors, Executive Board and Senior Management

Board of Directors

The following table sets forth information with respect to each of our current board members and their respective ages as of the date of this annual report. Our board of directors is divided into two classes for purposes of election. One class is elected at each annual meeting of shareholders to serve for a two-year term. Our board of directors currently consists of seven members. All board members are eligible for re-election once their term expires.

The business address of our board members is our registered office address at Tuborg Boulevard 12, DK-2900 Hellerup, Denmark.

Name of Board Member	Age	Position(s)	Term Expires
Albert Cha, M.D., Ph.D.	50	Chairman and Board Member	2024
Lisa Bright	55	Board Member	2023
William Carl Fairey Jr.	58	Board Member	2023
Lars Holtug	64	Board Member	2024
Siham Imani	45	Board Member	2023
Jan Møller Mikkelsen	63	President, Chief Executive Officer and Board Member	2023
Rafaèle Tordjman, M.D., Ph.D.	53	Board Member	2024

The following is a brief summary of the business experience of our non-employee board members.

Albert Cha, M.D., Ph.D. has served as a member of our board of directors since November 2014 and as the Chairman of our board of directors since May 2021. Dr. Cha is a Managing Partner with Frazier Life Sciences. He previously was a managing partner at Vivo Capital LLC, a healthcare investment firm, where he has served in various positions, most recently as a managing partner. Dr. Cha currently serves as a member of the board of directors of KalVista Pharmaceuticals, Inc. In addition, Dr. Cha has previously served as a member of the board of directors of Aclaris Therapeutics, a publicly traded dermatology company, Sierra Oncology, Inc., a publicly traded oncology company, Biohaven Pharmaceutical Holding Company Ltd, a publicly traded clinical-stage biopharmaceutical company targeting neurological diseases and Menlo Therapeutics, Inc., a publicly traded late-stage biopharmaceutical company focused on the treatment of pruritus. Dr. Cha holds a B.S. and an M.S. from Stanford University and an M.D. and a Ph.D. from the University of California at Los Angeles.

Lisa Bright has served as a member of our board of directors since April 2017. Ms. Bright has over 30 years of executive experience in global life sciences companies and over five years' experience serving as a member of the board of directors of a number of public and private companies. Ms. Bright is currently Chair of the board of Resolution Therapeutics Ltd, a biotechnology company, and a Non-Executive Director of Dechra Pharmaceuticals PLC, a veterinary pharmaceutical company, and Immedica Pharma AB, a pharmaceutical company. She is also an Advisor to Syncona Limited, an investment trust dedicated to life science investments, and DRI Capital, a private equity fund. Previously, she served as President International for Intercept Pharmaceuticals, Inc., a biopharmaceutical company, from July 2016 to January 2021, and from November 2014 to July 2016 as Chief Commercial and Corporate Affairs Officer and Senior Vice President, Head of EUCA. During her tenure at Intercept, Ms. Bright oversaw the development of the global launch of an orphan medicine in the United States and Europe, including building the commercial organization in the United States and establishing legal affiliates and teams across Europe and Canada. From 2008 to November 2014, Ms. Bright held various leadership positions at Gilead Sciences Ltd., a biopharmaceutical company, including Vice President, Head of Government Affairs, Europe, Asia, Middle East and Australasia, Vice President and Head of HCV Launch Planning, Vice President and Head of Northern Europe and General Manager, UK and Ireland. Prior to Gilead Sciences, Ms. Bright served in various positions of increasing responsibility at GlaxoSmithKline plc from 1997 to 2006 including Vice President Commercial Planning and Operations and Vice President General Manager NZ and Vice President Head of Sales, UK and Ireland. Prior to that, Ms. Bright also worked at Sanofi from 1992 to 1996 and GlaxoSmithKline from 1989 to 1992. Ms. Bright received her B.Sc. in Pharmacology from University College London, United Kingdom.

William Carl Fairey Jr. has served as a member of our board of directors since September 2022. Mr. Fairey currently serves as Executive Chairman of Respira Therapeutics, Inc., a clinical-stage company developing inhaled therapeutics for cardiopulmonary diseases, a position he has held since January 2022. Since August 2021, Mr. Fairey has also served as a director of both Mirum Pharmaceuticals, a publicly-traded biotechnology company developing therapies for rare liver diseases, and Lung Therapeutics, Inc., a private clinical-stage biopharmaceutical company. Prior to Respira, Mr. Fairey was Executive Vice President and Chief Commercial Officer of MyoKardia, Inc., a publicly-traded clinical-stage biopharmaceutical company, from January 2019 until November 2020 when the company was acquired by Bristol-Myers Squibb. From January 2018 until January 2019, Mr. Fairey served as Executive Vice President and Chief Operating Officer of ChemoCentryx, Inc., a publicly-traded biopharmaceutical company developing therapeutics to treat autoimmune diseases, inflammatory disorders and cancer, primarily focused on orphan and rare diseases. Before ChemoCentryx, between 2001 and 2017, Mr. Fairey served in various positions of increasing responsibility at Actelion Pharmaceuticals, including as President of Actelion's U.S. division, as well as Vice President, Asia Pacific Region, Managing Director and Vice President, Australia Asia Pacific Region, President of Actelion Canada, and Vice President, US Sales and Managed Markets. Mr. Fairey began his pharmaceutical career as Business Director, Healthcare Management for the Parke-Davis Division of Warner-Lambert between 1988 and 2000. Mr. Fairey received a B.S. in Biology from the University of Oregon and an M.B.A. from Saint Mary's College of California.

Lars Holtug, M.Sc. has served as a member of our board of directors since November 2018. Mr. Holtug was a partner at PricewaterhouseCoopers Statsautoriseret Revisionspartnerselskab ("PwC") from 1993 to 2015. Mr. Holtug also currently serves as chairman of Gaming Investment A/S, a gaming solutions provider, and its eleven subsidiaries, and of MTI Caretag Invest A/S, a company investing in healthcare technology. Mr. Holtug also currently serves as a board member of Frida Forsikring Agentur A/S, Domus Forsikring A/S and Evaxion Biotech A/S, as well as the Audit Committee Chair of the board of Domus Forsikring A/S and Evaxion Biotech A/S. Previously, he was Chairman of PwC in Denmark from 2005 to 2009. From 2004 to 2015, Mr. Holtug was a member of the Danish Commercial Appeals Board (Erhvervsankenaevnet) and a board member of the Danish Company law association (Dansk Forening for Selskabsret). He was also a member of the Accounting Standards Board of the Federation of State Authorized Accountants in Denmark (Foreningen af Statsautoriserede Revisorer) from 1998 to 2002, and a member of the Auditing Standards Board from 1993 to 1998. Mr. Holtug holds an M.Sc. from Copenhagen Business School and is educated as a state authorized public accountant in Denmark.

Siham Imani has served as a member of our board of directors since September 2022. Ms. Imani currently serves as Executive Vice President Corporate Strategy and Business Development of Servier, a global pharmaceutical group headquartered in France, a position she has held since April 2019. Prior to her current role, Ms. Imani was Servier's Director of Corporate Strategy from April 2017 until April 2019. Before joining Servier, Ms. Imani held various positions of increasing responsibility at Ipsen, a French pharmaceutical company specializing in oncology, neuroscience and rare diseases, including Vice President European Business Unit Pediatric Endocrinology, Vice President Commercial Transformation & Support, Vice President Corporate Strategic Planning and Executive Committee Secretary, and Corporate Strategic Planning Director, from 2011 until April 2017. Ms. Imani also served as Projects Director of Pierre Fabre Medicament, a French pharmaceutical company, from 2010 to 2011, and as Marketing and Clinical Manager and European Marketing Manager of Biosense Webster, part of the Johnson & Johnson Family of Companies, from 2005 to 2010. Ms. Imani received a Master in Economics and a Master in Chemistry from École Polytechnique in Palaiseau, France and an M.B.A. from Stanford University.

Rafaèle Tordjman, M.D., Ph.D. has served as a member of our board of directors since November 2021, and previously served on our board of directors from 2007 until 2017. In 2018, Dr. Tordjman founded Jeito Capital, an independent investment company dedicated to biopharma/biotech to establish a model of continuous financing and to invest in the next generation of leaders in medical innovation. Dr. Tordjman was a Special Advisor at Sofinnova Partners from 2001 until March 2017, where she also served as Managing Partner specializing in life sciences investments from January 2011 to February 2017. Dr. Tordjman currently serves as the Chairperson of the board of InnoSkel, a biotechnology company, and Alentis Therapeutics, a clinical-stage biopharmaceutical company. Dr. Tordjman has also served on the boards of directors at several life sciences companies, including ObsEva SA, a Nasdaq-listed biopharmaceutical company, NuCana plc, a Nasdaq-listed clinical-stage pharmaceutical company, DBV Technologies SA, a publicly traded company specializing in allergy therapies, Flexion Therapeutics, Inc., a publicly traded company in clinical-stage pharmaceuticals, PregLem, a company specializing in reproductive female medicine, Lysogene, a public biopharmaceutical company developing treatments against central nervous system and genetic diseases, Medday Pharmaceuticals, a French company specializing in therapies against neurodegenerative diseases, and ENYO Pharma SA, a clinical stage biopharmaceutical company. Previously, Dr. Tordjman was a research scientist at the Institut National de la Santé et de la Recherche Médicale (INSERM) in Cochin Hospital, Paris, France. Dr. Tordjman has also practiced as a medical doctor, specializing in clinical hematology and internal medicine. Dr. Tordjman received an M.D. and completed a fellowship in hematology and internal medicine at the Paris University Hospitals, France. She received a Ph.D. in hematopoiesis and angiogenesis from and completed a post-doctoral fellowship in immunology at the University of Paris VII.

The table below provides certain information regarding the diversity of our board of directors.

Board Diversity Matrix (As of February 1, 2023)				
Country of Principal Executive Offices	Denmark			
Foreign Private Issuer	Yes			
Disclosure Prohibited under Home Country Law	No			
Total Number of Directors	7			
	Female	**Male**	**Non-Binary**	**Did Not Disclose Gender**
Part I: Gender Identity				
Directors	3	3	0	1
Part II: Demographic Background				
Underrepresented Individual in Home Country	1			
LGBTQ+	0			
Did Not Disclose Demographic Background	1			

Senior Management and Executive Board

The following table sets forth information with respect to each of the members of our senior management, their respective ages and their positions as of the date of this annual report. In addition to serving as members of our senior management, Mr. Mikkelsen, Mr. Smith, Mr. Wolff Jensen, and Ms. Sønderbjerg currently serve as the members of our executive board. The business address of these members of our senior management is our registered office address at Tuborg Boulevard 12, DK-2900 Hellerup, Denmark.

Name	Age	Position(s)
Jan Møller Mikkelsen	63	President, Chief Executive Officer and Board Member
Vibeke Miller Breinholt, Ph.D.	56	Executive Vice President, Nonclinical Development and Bioanalysis
Flemming Steen Jensen	61	Executive Vice President, Product Supply and Quality
Michael Wolff Jensen, L.L.M.	51	Executive Vice President, Chief Legal Officer
Sigurd Okkels, Ph.D.	63	Executive Vice President, Product Development
Peter Rasmussen	54	Vice President, Finance and Principal Accounting Officer
Stina Singel, M.D., Ph.D.	49	Executive Vice President, Head of Clinical Development, Oncology
Scott T. Smith	49	Executive Vice President, Chief Financial Officer
Lotte Sønderbjerg	62	Executive Vice President, Chief Administrative Officer
Kennett Sprogøe, Ph.D.	44	Executive Vice President, Head of Innovation and Research
Birgitte Volck, M.D., Ph.D.	60	Executive Vice President, Head of Clinical Development and Medical Affairs, Endocrinology Rare Diseases

The following is a brief summary of the business experience of our senior management and executive board.

Jan Møller Mikkelsen founded Ascendis Pharma and has served as President and Chief Executive Officer as well as Board member since December 2007 and currently serves on the board of VISEN Pharmaceuticals and as Chairman of the board of Hummingbird Bioscience. From 2002 to 2006, Mr. Mikkelsen served as President and Chief Executive Officer of LifeCycle Pharma A/S, now Veloxis Pharmaceuticals A/S, which was a publicly traded biotechnology company. From 2000 to 2002, Mr. Mikkelsen was President of the Pharmaceutical Division of Maxygen, Inc. Prior to that, Mr. Mikkelsen co-founded ProFound Pharma A/S, a biopharmaceutical company that was later acquired by Maxygen, Inc., and at ProFound, he served as Co-Chief Executive Officer from 1999 to 2000. From 1988 to 1999, Mr. Mikkelsen held various positions at Novo Nordisk A/S, a global healthcare company, including Vice President of Protein Discovery. Mr. Mikkelsen currently serves as a member of the advisory board of Inspirion Delivery Technologies, a specialty pharmaceutical company. Mr. Mikkelsen received a Cand. Scient. degree in Biochemistry from the University of Odense, Denmark, and pursued his post-doctoral research at Children's Hospital in Oakland, CA.

Vibeke Miller Breinholt, Ph.D. has served as our Executive Vice President of Nonclinical Development and Bioanalysis since January 2023 and previously served as our Senior Vice President of Nonclinical Development and Bioanalysis from January 2020 until January 2023 and as our Vice President of Nonclinical Development from January 2016 to January 2020. Dr. Breinholt has more than 15 years of experience within nonclinical development in the biopharmaceutical industry and more than seven years of experience in experimental cancer research. Prior to joining Ascendis, Dr. Breinholt served in roles of increasing responsibility at Novo Nordisk from November 2013 to December 2015, including serving as Head of Biopharm Toxicology and Safety Pharmacology, where she was responsible for overseeing more than 30 projects in early and late-stage development within diabetes, obesity, hemophilia and growth hormone deficiency. Prior to Novo Nordisk, she held positions of increasing responsibility at Genmab A/S from October 2007 to November 2013, ending her tenure as Senior Director of Preclinical Safety and Preclinical Regulatory Affairs. Dr. Breinholt began her industry career at Maxygen in October 2003, where she served as Head of Toxicology and Associate Director Regulatory affairs until October 2007. Dr. Breinholt received her M.S. and Ph.D. in Toxicology from Oregon State University within experimental cancer research and a B.S. in Bromatology from the Royal Veterinary and Agricultural University, Denmark. Dr. Breinholt also earned advanced diplomas in business administration and pharmaceutical regulatory affairs.

Flemming Steen Jensen has served as our Executive Vice President, Product Supply and Quality since January 2023 and previously served as our Senior Vice President, Product Supply and Quality from August 2015 until January 2023. Prior to this, Mr. Jensen served as Corporate Vice President for Global Pharma Consulting and Business Development and member of the management team at NNE Pharmaplan A/S, an engineering and consulting company (part of Novo Nordisk A/S), from October 2014 to July 2015. From 1999 to September 2014, Mr. Jensen served as Executive Vice President of Product Supply (Production, Supply Chain, Engineering and Maintenance, Business Improvements, Quality Assurance and Health, Safety and Environment) and member of the Board of Management of ALK-Abello A/S, a pharmaceutical company. From 1986 to 1999, Mr. Jensen held several management positions relating to development, manufacturing and engineering within Novo Nordisk A/S. Mr. Jensen is also a member of various boards of directors of companies in the life sciences industry. Mr. Jensen holds a M.Sc. in Pharmacy from the University of Copenhagen.

Michael Wolff Jensen, L.L.M. has served as our Executive Vice President, Chief Legal Officer since January 2023 and previously served as our Senior Vice President, Chief Legal Officer from June 2013 until January 2023. Mr. Jensen also currently serves as Chairman of the board of VISEN Pharmaceuticals. In addition, Mr. Jensen served as Chairman of our board of directors from January 2008 to May 2021 and as our Acting Chief Financial Officer from May 2008 to June 2013. From October 2010 to June 2013, Mr. Jensen served as Senior Legal Advisor and Head of Partnerships (France) for the renewable business division of Dong Energy A/S, the Danish State-owned utility company. Prior to Ascendis Pharma, Mr. Jensen served as Executive Vice President & Chief Financial Officer of LifeCycle Pharma, currently known as Veloxis Pharmaceuticals A/S, a publicly traded biotechnology company, from 2003 to 2008. Prior to joining Veloxis, Mr. Jensen served as Senior Vice President & Chief Financial Officer of Genmab A/S, a publicly traded biotechnology company from 2000 to 2003. Mr. Jensen received an L.L.M. degree from the University of Copenhagen.

Jens Sigurd Okkels, Ph.D. has served as our Executive Vice President of Product Development since January 2023 and previously served as our Senior Vice President of Product Development from April 2019 until January 2023. Most recently, Dr. Okkels led an independent consulting firm in the biopharmaceutical industry, Okkels Consulting, GmbH, from January 2018 until April 2019. Prior to this, from October 2011 until December 2017, he served as Vice President, Head of the Chemistry, Manufacturing and Controls Center in Europe at Takeda, where he was responsible for numerous projects at all stages of development, from preclinical and launch to life cycle management. Prior to his tenure at Takeda, Dr. Okkels held multiple VP roles at Nycomed, including Vice President of Technical Development, the Biologics Network and the International Pharmaceutical Affairs. Dr. Okkels also served as the Science and Technology Director at Maxygen after a merger with ProFound Pharma, a company which he co-founded in 1999. He launched his industry career at Novo Nordisk in 1992 after completing his postdoctoral training at the Royal Veterinary and Agricultural University (RVAU). Dr. Okkels received his Ph.D. in biochemistry and molecular biology from the RVAU in Copenhagen, Denmark.

Peter Rasmussen has served as our Vice President, Finance and Principal Accounting Officer since March 2014 and served as our Principal Financial Officer from February 2016 to August 2016. Prior to joining Ascendis, Mr. Rasmussen worked as a financial consultant for Ascendis from October 2013 to March 2014. From June 2008 to August 2012, Mr. Rasmussen served as the Chief Financial Officer of AdvanDx, Inc., a privately held medical device company. From 2007 to 2008, prior to AdvanDx, Mr. Rasmussen served as Head of Finance at Veloxis Pharmaceuticals A/S. Mr. Rasmussen is a state-authorized public accountant in Denmark and received an M.Sc. in Business Economics and Auditing from Copenhagen Business School.

Stina Singel, M.D., Ph.D. has served as our Executive Vice President, Head of Clinical Development, Oncology, since January 2023 and previously served as our Senior Vice President, Head of Clinical Development, Oncology, from January 2022 until January 2023 and as our Head of Clinical Development, Oncology, from May 2020 to January 2022. Prior to joining Ascendis, Dr. Singel served as Senior Vice President and Head of Clinical Development and Drug Safety at Nektar Therapeutics, a biopharmaceutical company, from April 2019 to May 2020. From March 2014 to April 2019, Dr. Singel held various positions of increasing responsibility at Genentech, a biotechnology company, ending her tenure as Senior Medical Director. From 2017 to 2019, Dr. Singel also served as an Adjunct Clinical Instructor at the Stanford University School of Medicine. Prior to Genentech, Dr. Singel was an Attending Physician and Clinical Translational Researcher focused on breast oncology at the University of Texas Southwestern Medical Center from 2010 to 2014 and was a Medical Oncologist at Washington Hematology Oncology, a community practice in Yakima, Washington, from 2008 to 2010.

Dr. Singel received her M.D. and Ph.D. degrees from the University of California, San Diego, where she also completed her internal medicine residency and medical oncology fellowship. She received her B.S. in Biology (magna cum laude) from Harvard University.

Scott T. Smith has served as our Executive Vice President and Chief Financial Officer since January 2023 and previously served as our Senior Vice President and Chief Financial Officer from August 2016 until January 2023. Previously, Mr. Smith served as Director of the Healthcare Investment Banking Group at Wedbush Securities, from 2012 to 2016, where he led the healthcare team, and, from 2009 to 2012, Mr. Smith served as a Managing Director at Wedbush. Prior to joining Wedbush, Mr. Smith served as a Director in the Global Healthcare Investment Banking Group at Merrill Lynch where he began his career in 1995. He has also worked in sales, marketing and strategy roles for various companies, including start-ups and a Fortune Global 500 company. Mr. Smith received his M.B.A. from the Stanford University Graduate School of Business and graduated magna cum laude with a B.A. in Economics/Accounting-Physics from Claremont McKenna College.

Lotte Sønderbjerg has served as our Executive Vice President, Chief Administrative Officer since January 2023 and previously served as our Senior Vice President, Chief Administrative Officer from December 2007 until January 2023. Mrs. Sønderbjerg is also Managing Director of Ascendis Pharma GmbH. Prior to joining Ascendis, Mrs. Sønderbjerg served as Senior Director of Human Resources and as Finance Director at Veloxis Pharmaceuticals A/S from 2003 to 2007. Prior to joining Veloxis Pharmaceuticals A/S, Mrs. Sønderbjerg served as Senior Director of Finance and Human Resources at Acadia Pharmaceuticals Inc., a publicly traded biotechnology company, from 1996 to 2003. Prior to her career in biotech, Mrs. Sønderbjerg was the Executive Secretary for the CEO and Board of Directors of Novo Nordisk A/S and PA to leading audit partner in PricewaterhouseCoopers LLP in Denmark. Mrs. Sønderbjerg received a Masters of Arts in International Business Communications from University of Aarhus.

Kennett Sprogøe, Ph.D. has held positions of increasing responsibility at Ascendis Pharma since December 2007, including serving as our Executive Vice President, Head of Innovation and Research since January 2023, Senior Vice President, Head of Innovation and Research from 2019 until January 2023, Senior Vice President of Product Innovation since January 2016 and Vice President Product Innovation since June 2014. Prior to joining Ascendis, Dr. Sprogøe conducted research at the University of Copenhagen, where he applied novel hyphenated screening technologies to expedite discovery of drug leads from natural sources. Dr. Sprogøe holds a Ph.D. in Natural Products Chemistry from the University of Copenhagen and a M.Sc. in Pharmacy from the Danish University of Pharmaceutical Sciences.

Birgitte Volck, M.D., Ph.D. has served as our Executive Vice President and Head of Clinical Development and Medical Affairs, Endocrinology Rare Diseases, since January 2023 and previously served as our Senior Vice President and Head of Clinical Development and Medical Affairs, Endocrinology Rare Diseases from July 2021 until January 2023. She also previously served as a member of our board of directors from May 2016 until July 2021. Dr. Volck served as the President of Research and Development at Avrobio Inc., a clinical-stage biotechnology company, from December 2018 to October 2020. From June 2016 to August 2018, Dr. Volck served as head of Research and Development, Rare Diseases for GlaxoSmithKline plc, a pharmaceutical company. From 2012 to 2016, Dr. Volck served as the Chief Medical Officer and Senior Vice President of Development at Swedish Orphan Biovitrum AB, a biopharmaceutical company. From 2007 to 2012, Dr. Volck held various positions at Amgen Inc., a biopharmaceutical company, including Executive Development Director, Bone, Neuroscience & Inflammation. Prior to Amgen, from 2004 to 2007, Dr. Volck served as Nordic Medical Director and Project Director at Genzyme A/S, a biotechnology company. From 2001 to 2004, Dr. Volck served as Head of Clinical Development at Pharmexa, a biotechnology company. Since June 2019, Dr. Volck has served as a non-executive director at Soleno Therapeutics, Inc., a clinical-stage biopharmaceutical company. Since May 2021, Dr. Volck has served as a non-executive director at Nykode AS (formerly Vaccibody AS), a clinical-stage biopharmaceutical company. From May 2017 to June 2018, Dr. Volck served as a non-executive director for Wilson Therapeutics AB, a biotechnology company. From May 2016 to April 2019, Dr. Volck has served as a director for TFS International, a clinical research organization. Dr. Volck received her M.D. and Ph.D. degrees from Copenhagen University, Denmark.

B. Compensation

Compensation of Members of Our Board of Directors and Senior Management

During 2022, Dr. Cha received board fees in the amount of €93,775 for his membership on our board and €29,293 for his tenure on the remuneration committee and the partial year of tenure on the audit committee and the nominating and corporate governance committee, Dr. Healy received €21,313 for his membership on our board and €10,320 for his tenure on the nominating and corporate governance committee and the audit committee, which reflected his partial year of service on our board, Ms. Bright received €51,150 for her membership on our board and €23,337 for her tenure on the audit committee and the remuneration committee and her partial year of tenure on the nominating and corporate governance committee, Mr. Holtug received €51,150 for his membership on our board and €30,264 for his tenure on the audit committee and the remuneration committee, Dr. Tordjman received €51,150 for her membership on our board and €7,460 for her partial year of tenure on the nominating and corporate governance committee, Ms. Imani received €15,888 for her membership on our board and €1,792 for her tenure of the nominating and corporate governance committee, which reflected her partial year of service on our board, and Mr. Fairey received €15,888 for his membership on our board, which reflected his partial year of service on our board. Mr. Mikkelsen did not receive any separate compensation in respect of his service on the board. His compensation under our senior management compensation program is described below.

On September 13, 2022, Ms. Imani and Mr. Fairey were each granted 9,160 warrants, in each case with an exercise price per share of $102.70 (€100.93) and an expiration date of September 13, 2032. The aggregate grant date fair value of the warrants granted to our board members in 2022 for their services as board members was €891,518.

The primary objective of our senior management's compensation program is to attract, motivate, reward and retain the managerial talent needed to achieve our business objectives. In addition, the compensation program is intended to compensate all employees at competitive market rates, while recognizing extraordinary accomplishments.

Compensation arrangements for our senior management have been designed to align a portion of their compensation with the achievement of our business objectives and growth strategy. Bonus payments for our senior management are determined with respect to a given year based on quantitative and qualitative goals set for our Company as a whole, as well as on an individual basis. Once the results of the year are known, bonus payments are determined at the discretion of our board and, with respect to senior management reporting to the CEO, in light of recommendations made by the CEO.

The aggregate compensation paid to our senior management who were employed by our company during 2022, consisting of Messrs. Mikkelsen, Smith, M. Jensen, Rasmussen, F. Jensen, and Høiland, Ms. Sønderbjerg and Drs. Sprogøe, Okkels, Punnonen, Breinholt, Pizzuti, Singel and Volck for the fiscal year ended December 31, 2022 was approximately €30.5 million. Mr. Høiland served as a member of our senior management until June 2022, and Dr. Punnonen and Dr. Pizzuti served as members of our senior management until June 2022 and September 2022, respectively. This amount consists of: (i) short-term employee benefits including salary and other in-kind benefits of approximately €6.7 million, (ii) bonuses of €3.2 million, (iii) share-based payments of approximately €20.3 million, and (iv) post-employment and other benefits of €0.3 million. Share-based payments reflect the 2022 expenses of warrants and RSUs granted in or before 2022. During 2022, no warrants or RSUs were granted to members of our senior management, as it was decided to change the time of yearly grants to the first quarter of 2023.

The total amount set aside or accrued by us to provide pension, retirement or similar benefits for the members of our board of directors and members of senior management for the year ended December 31, 2022 was €0.

Senior Management Agreements

We have entered into employment or service agreements with our senior management. The employment agreement with Mr. Mikkelsen contains a termination notice period of six months for a termination by Mr. Mikkelsen and twelve months for a termination by us. It also provides that during the 12-month period following a change of control ("change in control period"), we may only terminate Mr. Mikkelsen's employment with 18 months' notice. In addition, if during the change in control period, the position and responsibilities of Mr. Mikkelsen are changed (excluding insignificant changes), Mr. Mikkelsen will be entitled to regard his employment as having been terminated by us with twelve months' notice.

The agreements with Messrs. M. Jensen and F. Jensen and Ms. Lotte Sønderbjerg contain a termination notice period of three months for a termination by the employee and six months for a termination by us (except that in the case of Ms. Sønderbjerg, the notice period may be no less than the notice required pursuant to the rules of the Danish Salaried Employees Act with the addition of two months). The agreement with Mr. Rasmussen contains a termination notice period of one month for a termination by the employee and three months for a termination by us (except that the notice period may be no less than the notice required pursuant to the rules of the Danish Salaried Employees Act). The agreement with Dr. Sprogøe contains a termination notice period of one month for a termination by the employee and six months for a termination by us. The agreements with Drs. Volck, Okkels and Breinholt provide that the notice period may be no less than the notice required pursuant to the rules of the Danish Salaried Employees Act, which is at any time mutually extended by both parties with two months' notice to the end of a month, provided that the executive may terminate with one month's notice in the case of certain conditions related to sickness. The agreement with Dr. Singel provides that the employment is at-will and may be terminated by either the executive or us at any time. The agreements with certain of the foregoing senior management contain post-termination non-competition covenants that generally may last for a period of twelve months post-termination and entitle the executives to their base salary, or portion thereof, during the period.

The agreement with Mr. Smith provides that the employment is at-will and may be terminated by either the executive or us at any time. However, the agreement with Mr. Smith provides that in the event the executive is terminated by us without "cause" or he resigns for "good reason" (as defined in the agreement), the executive will be eligible to receive continued base salary during a certain severance period following termination and continued healthcare coverage up until the end of the month in which the severance period ends. Such severance period commences on the date of termination and ends on the six-month anniversary of the date of termination. In addition, in the event of the executive's termination due to disability, he will be eligible to receive continued base salary and healthcare coverage for 120 days following termination, and in the event of his death, we will pay his estate a lump sum amount equal to three months of his base salary.

Warrant Incentive Program

Our employees, consultants, advisors and board members are eligible to participate in our warrant incentive program. Warrants have been issued by the general meeting or by our board of directors pursuant to valid authorizations in our articles of association and the terms and conditions have, in accordance with the Danish Companies Act, been incorporated in our articles of association as in effect from time to time. Each warrant grants the holder the right to subscribe for one ordinary share against cash payment of the exercise price. The exercise price is determined by our board of directors and historically has not been less than the estimated fair value of our ordinary shares on the date of grant. As of December 31, 2022, our board of directors is authorized to issue an additional 1,959,496 warrants in the period ending May 29, 2027.

The grant of warrants to any participant is at the discretion of our board of directors and based on the recommendation of our management. The board of directors may determine the terms and conditions of the warrants issued, including exercise periods, subscription price and adjustments caused by changes to our company's situation.

Subject to earlier vesting upon the occurrence of certain exit events, warrants granted under the program between December 2012 and until and including November 2021 generally vest 1/48th per month from the date of grant subject to continued service for employees, consultants and grants to board members. However, effective from December 2015, subsequent grants to board members vest 1/24th per month from the date of grant. With respect to employees, in the event that a holder resigns due to our breach of employment terms or we terminate the employment relationship and the holder has not given us good reason to do so, the warrants will continue to vest post-termination in accordance with the same vesting schedule. Otherwise, warrants will cease vesting upon termination of service with respect to employees, board members and consultants.

Subject to earlier vesting upon the occurrence of certain exit events, for warrants granted under the program as in effect since December 9, 2021, the following applies: 25% of the warrants granted to employees and consultants generally vest one year after the time of grant, and the remaining 75% of the warrants granted generally vest with 1/36 per month from one year after the time of grant. As regards warrants which board members are granted in connection with appointment, 25% of the warrants granted generally vest one year after the time of the grant (the initial grant after the board member's accession), and the remaining 75% of the warrants granted generally vest with 1/36 per month from one year after the time of the grant. Regarding any subsequent grants of warrants to board members ("Subsequent Warrants") 50% of the Subsequent Warrants generally vest one year after the time of such subsequent grant and the remaining 50% of the Subsequent Warrants shall generally vest with 1/12 per month from one year after the time of such subsequent grant. Warrants will generally cease vesting upon termination of service with respect to employees, consultants and board members.

Vested warrants may be exercised during certain exercise periods each year. For 299,830 outstanding warrants, granted in the period 2012 to 2014, there are two annual exercise periods that continue for 21 days from and including the day after the publication of (i) the annual report notification—or if such notification is not published, the annual report—and (ii) our interim report (six-month report). For these warrants, the last exercise period is 21 days from and including the day after the publication of our interim report for the first half of 2023. For 15,732 outstanding warrants granted in connection with our preference D financing, there are four annual exercise periods that continue for 21 days following the day of publication of (i) our interim report (three-month report); (ii) the annual report notification—or if such notification is not published—the annual report; (iii) our interim report (six-month report); and (iv) our interim report (nine-month report). For these warrants, the last exercise period is 21 days following the publication of our interim report (nine-month report) in 2023. For 6,548,449 outstanding warrants granted on or after December 18, 2015, there are four annual exercise periods; each exercise period begins two full trading days after the publication of the public release of our earnings data of a fiscal quarter and continues until the end of the second-to-last trading day in which quarter the relevant earnings release is published. The warrants granted on or after December 18, 2015 expire ten years after the grant date.

The table below sets forth information regarding outstanding warrants held by those members of our board of directors and senior management who, assuming the exercise of warrants, beneficially own 1% or more of our total outstanding ordinary shares as of February 1, 2023.

Name	Grant Date	Awards granted and outstanding	Awards granted and outstanding, but unvested as of April 1, 2023		Award Exercise Price(s)	Award Expiration Date
Jan Møller Mikkelsen	December 3, 2012	249,372	—	€	7.9962	21 days following our interim report (six-month report) in 2023
	November 26, 2014	—	—	€	6.4775	21 days following our interim report (nine-month report) in 2023
	December 18, 2015	217,000	—	€	15.6750	December 18, 2025
	December 14, 2016	180,000	—	€	19.4194	December 14, 2026
	December 12, 2017	200,000	—	€	31.5995	December 12, 2027
	December 11, 2018	200,000	—	€	54.6357	December 11, 2028
	December 10, 2019	120,000	22,500	€	97.4993	December 10, 2029
	December 10, 2020	101,145	44,251	€	145.5045	December 10, 2030
	December 9, 2021	69,466	47,758	€	123.4637	December 9, 2031

RSU Program

In December 2021, we implemented a restricted stock units program. Under this program, Restricted Stock Units ("RSUs") may be granted to members of the senior management team, non-executive directors and other employees ("Participants") employed by the company or another company within the company's group. Our board of directors may also at its sole discretion decide to grant RSUs to consultants or members of our board of directors who are then also deemed Participants.

One RSU represents a right for the Participant to receive one Ascendis Pharma A/S American Depositary Share ("ADS") upon vesting. One Ascendis Pharma A/S ADS represents one (1) ordinary share in our company with a nominal value of DKK 1.00. ADSs underlying restricted stock units are treasury shares that have been repurchased in the market and, upon vesting, our company may at its sole discretion choose to make a cash settlement instead of delivering ADSs.

Our board of directors may in its sole discretion, at any given point in time, decide to grant RSUs and may at its discretion and on an individual basis decide to deviate from the vesting principles and/or the vesting conditions as set forth in our RSU Program.

RSUs are issued and granted to the Participant free of charge.

It is a condition for vesting that the Participant is still either employed or retained as consultant within our company or another company within our company's group or appointed as member of the board of directors on the vesting date. Subject to earlier vesting upon the occurrence of certain exit events, for each award of RSUs 1/3 of such RSUs will vest on each anniversary of the date of grant, subject to continued service and, in the case of the RSUs granted to our chief executive officer, subject to the achievement of a performance condition as determined by our board of directors.

On December 9, 2021, our board of directors granted an aggregate of (i) 5,352 restricted stock units to certain non-employee board members of the company, (ii) 104,886 restricted stock units to certain members of senior management of the company, and (iii) 37,910 restricted stock units to certain other employees of our company under the terms of our restricted stock unit program. On December 9, 2022, 41,685 RSUs vested and an equivalent number of ADSs were transferred to the Participants. As of December 31, 2022, a total of 82,492 RSUs were outstanding and unvested.

Insurance and Indemnification

According to the Danish Companies Act, the general meeting is allowed to discharge our board members and members of our senior management from liability for any particular financial year based on a resolution relating to the financial statements. This discharge means that the general meeting will discharge such board members and members of our senior management from liability to our company; however, the general meeting cannot discharge any claims by individual shareholders or other third-parties.

Additionally, we have entered into agreements with our board members and members of our senior management, pursuant to which, subject to limited exceptions, we have agreed to indemnify such board members and members of our senior management from civil liability, including (i) any damages or fines payable by them as a result of an act or failure to act in the exercise of their duties currently or previously performed by them; (ii) any reasonable costs of conducting a defense against a claim; and (iii) any reasonable costs of appearing in other legal proceedings in which such individuals are involved as current or former board members or members of our senior management.

There is a risk that such agreement will be deemed void under Danish law, either because the agreement is deemed contrary to the rules on discharge of liability in the Danish Companies Act, as set forth above, because the agreement is deemed contrary to sections 19 and 23 of the Danish Act on Damages, which contain mandatory provisions on recourse claims between an employee (including members of our senior management) and the company, or because the agreement is deemed contrary to the general provisions of the Danish Contracts Act.

In addition to such indemnification, we provide our board members and senior management with directors' and officers' liability insurance.

Insofar as indemnification of liabilities arising under the Securities Act may be permitted to board members and senior management 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

Board of Directors

Our board of directors is responsible for our overall and strategic management and must ensure proper organization of our business. In addition, our board is obligated to ensure that (i) bookkeeping and financial reporting procedures are satisfactory; (ii) adequate risk management and internal control procedures have been established; (iii) our board of directors receives ongoing information as necessary about our financial position; (iv) our executive board performs its duties properly and as directed by our board of directors; and (v) the financial resources of our company are adequate at all times, and that our company has sufficient liquidity to meet its current and future liabilities as they become due.

In performing its duties, our board of directors is required to act in the interests of our company (including our shareholders) and our associated business as a whole. Our board of directors may generally make any decisions in furtherance of our objectives that are not reserved for either the executive board or the shareholders either by virtue of the articles of association or by operation of Danish law. Typical shareholder decisions that our board of directors cannot resolve alone are: changes to the articles of association, elections of board members, elections of auditors, decisions to scrutinize our company's affairs, capital increases and decreases, payment of dividends, purchase of treasury shares, and decisions to merge, demerge or liquidate our company.

The general meeting of shareholders must elect no fewer than three and no more than ten members to our board of directors. The board of directors is classified into two classes as nearly equal in number as possible with respect to the duration of the term in which they severally hold office. Such classes consist of one class of directors ("Class I") who were elected at the annual general meeting held in 2021 for a term expiring at the annual general meeting to be held 2023; and a second class of directors ("Class II") who were elected at the annual general meeting held in 2022 for a term expiring at the annual general meeting to be held in 2024. The shareholders shall increase or decrease the number of directors, to ensure that the two classes shall be as nearly equal in number as possible; provided, however, that no decrease shall have the effect of shortening the term of any other director. At each annual general meeting, the successors of the class of directors whose term expires at that meeting shall be elected to hold office for a term expiring at the annual general meeting held in the second year following the year of their election.

Board members may be dismissed at any time at a general meeting of shareholders. A resolution by the general meeting of shareholders to appoint or dismiss board members requires a simple majority of the votes cast and there is no requirement for a specific quorum.

Under Danish corporate law, employees of companies that have employed at least 35 employees for the preceding three years are entitled to elect members of their board of directors corresponding to one-half of the members of their board of directors elected by the general meeting of shareholders. Board members elected by the employees are elected for terms of four years, and they hold the same rights and obligations as any board member elected by the shareholders. We do not currently have employee representatives on our board of directors.

Our board of directors elects its chairman. Our board of directors forms a quorum when more than half of the members of our board of directors are represented. Resolutions of our board of directors are passed by simple majority. Each board member is entitled to cast one vote. For a complete description of these board governance matters, you should refer to our articles of association, which are incorporated by reference as an exhibit to this annual report.

Our board of directors may also adopt resolutions without a meeting, provided that such resolutions are adopted in writing and submitted to all members of our board of directors and provided that no board member objects to adopting resolutions without conducting a meeting.

As a foreign private issuer, our board of directors is not required to hold regularly scheduled meetings at which only independent board members are present and we intend to comply with home country practices, which do not require executive sessions, in lieu of complying with Nasdaq Rule 5605(b)(2).

Mr. Mikkelsen is a member of our senior management and a member of our board of directors and has an employment agreement that provides for benefits upon termination of employment in certain circumstances. For information about such agreements, see "Item 6 B. Directors, Senior Management and Employees—Compensation—Senior Management Agreements."

In accordance with the exemption available to foreign private issuers under Nasdaq rules, we do not follow the requirements of the Nasdaq rules with regard to the process of nominating board members, and instead, follow Danish law and practice, in accordance with which our board of directors (or a committee thereof) is authorized to recommend to our shareholders director nominees for election. Under the Danish Companies Act, nominations for directors also may be made upon the request of any shareholder.

Executive Board

Our executive board is in charge of the day-to-day management of our operations and is assisted in this respect by the other members of our senior management. The executive board must follow the guidelines and directions issued by the board of directors. Day-to-day management does not include decisions of an unusual nature or of major importance, having regard to the circumstance. Such decisions may only be made by the executive board if specifically authorized by the board of directors, unless it will cause considerable inconvenience to our company's activities to wait for authorization by the board of directors. If so, the board of directors must be notified of the decision as soon as possible.

Director Independence

Our board of directors has undertaken a review of the independence of the directors and considered whether any director has a material relationship with us that could compromise their ability to exercise independent judgement in carrying out the responsibilities of a director. As a result of this review, our board of directors determined that Lisa Bright, Albert Cha, M.D., Ph.D., William Carl Fairey Jr., Lars Holtug, Siham Imani and Rafaèle Tordjman, M.D., Ph.D., representing six of our seven directors, are "independent directors" as that term is defined under the applicable rules and regulations of the SEC and the listing requirements and rules of Nasdaq. In making such determination, our board of directors considered the relationships that each non-employee 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 ordinary shares beneficially owned by the director and his or her affiliated entities (if any).

Committees of the Board of Directors

We have an audit committee, a remuneration committee and a nominating and corporate governance committee. We have adopted a charter for each of these committees. Under Danish corporate law, it is not possible to delegate the decision making authority of the entire board of directors to board committees.

Audit Committee

Our audit committee consists of Lars Holtug (Chair), Lisa Bright, Albert Cha, M.D., Ph.D. and William Carl Fairey Jr. Each member satisfies the independence requirements of the Nasdaq listing standards, and Lars Holtug qualifies as an "audit committee financial expert," as defined in Item 16A(b) of Form 20-F and as determined by our board of directors. Our audit committee oversees our accounting and financial reporting processes and the audits of our consolidated financial statements. As a foreign private issuer, we are not required to have a formal written audit committee charter that complies with Nasdaq Rule 5605(c)(1) and, although we have adopted an audit committee charter, we comply with home country practices in lieu of Nasdaq Rule 5605(c)(1). Nasdaq Rule 5605(c)(2)(A) requires that U.S. listed companies have an audit committee composed of at least three members, each of whom is an independent director, as defined in the Nasdaq rules. As a foreign private issuer, we are exempt from complying with the Nasdaq requirement to have an audit committee with at least three members, and we comply with home country practices in lieu of Nasdaq Rule 5605(c)(2)(A). However, our audit committee currently comprises four members, all of whom meet the relevant criteria for independence under Nasdaq rules and under Rule 10A-3 of the Exchange Act. Our audit committee is responsible for, among other things:

- making recommendations to our board of directors regarding the appointment by the general meeting of shareholders of our independent auditors;
- overseeing the work of the independent auditors, including making recommendations to the board of directors and resolving disagreements between the executive board and the independent auditors relating to financial reporting;
- reviewing the independence and quality control procedures of the independent auditors;
- discussing material off-balance sheet transactions, arrangements and obligations with the executive board and the independent auditors;
- reviewing all proposed related-party transactions;
- discussing the annual audited consolidated and statutory financial statements with the executive board;
- annually reviewing and reassessing the adequacy of our audit committee charter;
- meeting separately with the independent auditors to discuss critical accounting policies, recommendations on internal controls, the auditor's engagement letter and independence letter and other material written communications between the independent auditors and the executive board; and
- attending to such other matters as are specifically delegated to our audit committee by our board of directors from time to time.

Remuneration Committee

Our remuneration committee consists of Albert Cha, M.D., Ph.D. (Chair), Lisa Bright and Lars Holtug. Each member satisfies the independence requirements of the Nasdaq listing standards. Our remuneration committee assists our board of directors in reviewing and approving or recommending our compensation structure, including all forms of compensation relating to our board of director and the executive board. As a foreign private issuer, we are not required to have a formal written remuneration committee charter that complies with Nasdaq Rule 5605(d)(1) and, although we have adopted a remuneration committee charter, we comply with home country practices in lieu of Nasdaq Rule 5605(d)(1). Our remuneration committee is responsible for, among other things:

- reviewing and making recommendations to our board of directors with respect to compensation of our executive board and members of our board of directors;
- reviewing and approving the compensation, including equity compensation, change-of-control benefits and severance arrangements, of our chief executive officer, chief financial officer and such other members of our executive board as it deems appropriate;
- overseeing and making recommendations to our board of directors regarding the evaluation of our executive board;

- reviewing periodically and making recommendations to our board of directors with respect to any incentive compensation and equity plans, programs or similar arrangements; and
- attending to such other matters as are specifically delegated to our compensation committee by our board of directors from time to time.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee consists of Rafaèle Tordjman, M.D., Ph.D. (Chair), Lisa Bright and Siham Imani. Each member satisfies the independence requirements of the Nasdaq listing standards. Our nominating and corporate governance committee assists the board of directors in selecting individuals qualified to become our board members and in determining the composition of the board of directors and its committees. Our nominating and corporate governance committee is responsible for, among other things:

- recommending to our board of directors, persons to be nominated for election or re-election to our board of directors at any meeting of the shareholders;
- overseeing our board of director's annual review of its own performance and the performance of its committees; and
- considering, preparing and recommending to our board of directors a set of corporate governance guidelines.

For information on current term of office and the period during which the members of our board of directors, executive board and our senior management have served in office see "Item 6 A. Directors, Senior Management and Employees—Directors and Senior Management."

D. Employees

The following tables specify number of employees at the end of period, per their main activity function and geographic location for the past three financial years.

	Selling, General and Administration [1]	Research and Development, and Commercial Manufacturing	Total
December 31, 2022			
Denmark (Domicile country)	101	271	372
Germany	34	81	115
United States	170	140	310
Total	**305**	**492**	**797**

Of full-time employees, 220 (27.6%) hold a Ph.D., M.D., and/or equivalent degrees.

	Selling, General and Administration [1]	Research and Development, and Commercial Manufacturing	Total
December 31, 2021			
Denmark (Domicile country)	74	205	279
Germany	25	80	105
United States	137	118	255
Total	**236**	**403**	**639**

Of full-time employees, 198 (31.0%) hold a Ph.D., M.D., and/or equivalent degrees.

	Selling, General and Administration [1]	Research and Development	Total
December 31, 2020			
Denmark (Domicile country)	50	167	217
Germany	—	96	96
United States	63	106	169
Total	**113**	**369**	**482**

Of full-time employees, 121 (36.7%) hold a Ph.D., M.D., and/or equivalent degrees.

(1) Selling, General and Administration function includes business and corporate development, and commercial activities.

In 2022, employees engaged with research and development have increased, primarily due to advancement of our pipeline of endocrinology and oncology. In addition, number of employees has increased due to pre-launch and launch activities, and extension of corporate functions to support those activities.

None of our employees are represented by a labor union or covered under a collective bargaining agreement. We consider our employee relations to be good.

E. Share Ownership

See "Item 7 A. Major Shareholders and Related Party Transactions—Major Shareholders." Our employees are eligible to own shares of the company through a warrant incentive plan. For information on the plan, see "Item 6 B. Directors, Senior Management and Employees—Compensation—Warrant Incentive Program."

F. Disclosure of a Registrant's Action to Recover Erroneously Awarded Compensation

Not applicable.

Item 7 Major Shareholders and Related Party Transactions

A. Major Shareholders

The following table sets forth information relating to the beneficial ownership of our shares as of February 1, 2023, by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding ordinary shares;
- each of our board members; and
- each member of our senior management, including members of our executive board.

The number of shares beneficially owned by each entity, person, member of our board of directors or senior management is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power, as well as any shares that the individual has the right to subscribe for within 60 days of February 1, 2023, through the exercise of any warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares owned by that person.

The percentage of shares beneficially owned is computed on the basis of 57,152,295 ordinary shares outstanding as of February 1, 2023. Ordinary shares that a person has the right to subscribe for within 60 days of February 1, 2023 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights but are not deemed outstanding for purposes of computing the percentage ownership of any other person. Additionally, a person is considered to have the right to subscribe for ordinary shares which are subject to outstanding warrants and vested within 60 days of February 1, 2023, although such warrants may only be exercised in prescribed exercise periods. A person is considered to beneficially own ordinary shares which are subject to restricted stock units that vest within 60 days of February 1, 2023. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Ascendis Pharma A/S, at Tuborg Boulevard 12, DK-2900 Hellerup, Denmark.

Name and Address of Beneficial Owner	Number of Outstanding Shares Beneficially Owned	Number of Warrants Exercisable and RSUs to be Settled Within 60 Days	Number of Shares Beneficially Owned	Percentage of Beneficial Ownership
Entities affiliated with Artisan Partners LP [1]	7,940,434	—	7,940,434	13.9%
Entities affiliated with RA Capital Management, L.P. [2]	7,567,900	—	7,567,900	13.2%
Entities affiliated with FMR LLC [3]	5,355,943	—	5,355,943	9.4%
T. Rowe Price Associates, Inc. [4]	4,761,193	—	4,761,193	8.3%
Baker Bros. Advisors LP [5]	4,541,604	—	4,541,604	7.9%
Entities affiliated with Wellington Management Group LLP [6]	4,068,476	—	4,068,476	7.1%
Entities affiliated with Janus Henderson Group plc [7]	3,219,965	—	3,219,965	5.6%
Senior Management and Board Members				
Jan Møller Mikkelsen [8]	328,716	1,222,474	1,551,190	2.7%
Vibeke Miller Breinholt, Ph.D. [9]	927	64,539	65,466	*
Flemming Steen Jensen [10]	927	135,768	136,695	*
Michael Wolff Jensen, L.L.M. [11]	1,927	124,268	126,195	*
Sigurd Okkels, Ph.D. [12]	927	108,793	109,720	*
Peter Rasmussen [13]	195	51,075	51,270	*
Stina Singel, M.D, Ph.D. [14]	1,267	43,554	44,821	*
Scott T. Smith [15]	2,555	174,268	176,823	*
Lotte Sønderbjerg [16]	927	177,304	178,231	*
Kennett Sprogøe, Ph.D. [17]	1,957	154,581	156,538	*
Birgitte Volck, M.D., Ph.D. [18]	663	82,086	82,749	*
Albert Cha, M.D., Ph.D. [19]	195	93,828	94,023	*
Lisa Bright [20]	195	48,933	49,128	*
Lars Holtug, M.Sc. [21]	446	50,828	51,274	*
Rafaèle Tordjman, M.D., Ph.D. [22]	—	15,674	15,674	*
William Carl Fairey Jr.	—	—	—	*
Siham Imani	—	—	—	*

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

(1) Consists of an aggregate of 7,940,434 ADSs beneficially owned, or that may be deemed to be beneficially owned, by Artisan Partners Limited Partnership ("APLP"), Artisan Investments GP LLC ("Artisan Investments"), Artisan Partners Holdings LP ("Artisan Holdings"), Artisan Partners Asset Management Inc. ("APAM"), and Artisan Partners Funds, Inc. ("Artisan Funds") as reported by Amendment No. 2 to Schedule 13G filed on February 4, 2022. Artisan Holdings is the sole limited partner of APLP and the sole member of Artisan Investments; Artisan Investments is the general partner of APLP; APAM is the general partner of Artisan Holdings. APLP, Artisan Investments, Artisan Holdings and APAM have shared voting power over 6,830,520 shares and shared dispositive power over 7,940,434 shares. Artisan Funds has shared voting and dispositive power over 3,453,421 shares. The address of APLP, Artisan Investments, Artisan Holdings, APAM, and Artisan Funds is 875 East Wisconsin Avenue, Suite 800, Milwaukee, WI 53202.

(2) Consists of 7,567,900 ADSs held by RA Capital Healthcare Fund, L.P. (the "RA Fund") as reported by Amendment No. 11 to Schedule 13G filed with the SEC on February 14, 2022 by RA Capital Management, L.P. ("RA Capital"). RA Capital Healthcare Fund GP, LLC is the general partner of the RA Fund. The general partner of RA Capital is RA Capital Management GP, LLC, of which Peter Kolchinsky and Rajeev Shah are the controlling persons. RA Capital serves as investment adviser for the RA Fund and may be deemed a beneficial owner of ADSs held by the RA Fund. The RA Fund has delegated to RA Capital the sole power to vote and the sole power to dispose of all securities held in the RA Fund's portfolio. Because the RA Fund has divested voting and investment power over the reported securities it holds and may not revoke that delegation on less than 61 days' notice, the RA Fund disclaims beneficial ownership of the securities it holds and therefore disclaims any obligation to report ownership of the reported securities. As managers of RA Capital, Dr. Kolchinsky and Mr. Shah may be deemed beneficial owners of the ADSs beneficially owned by RA Capital. The address of the RA Fund, the RA Capital, Dr. Kolchinsky and Mr. Shah is c/o RA Capital Management, L.P., 200 Berkeley Street, 18th Floor, Boston, MA 02116.

(3) Consists of an aggregate of 5,355,943 ADSs beneficially owned, or that may be deemed to be beneficially owned, by FMR LLC, certain of its affiliates and other companies as reported on Amendment No. 8 to Schedule 13G filed on February 9, 2022 by FMR LLC. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act ("Fidelity Funds") advised by Fidelity Management & Research Company LLC ("FMR Co"), a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. FMR Co carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. FMR LLC has its principal business office at 245 Summer Street, Boston, MA 02210.

(4) Consists of 4,761,193 ordinary shares and ADSs held by T. Rowe Price Associates, Inc. ("Price Associates") as reported by Amendment No. 4 to Schedule 13G filed on February 14, 2022 by Price Associates. Price Associates, may be deemed to have sole power to vote over 1,596,799 shares and sole power to dispose of 4,761,193 shares. The address of Price Associates is 100 E. Pratt Street, Baltimore, Maryland 21202.

(5) Consists of (i) 4,195,958 ADSs held by Baker Brothers Life Sciences, L.P. ("Life Sciences") and (ii) 345,646 ADSs held by 667, L.P. ("667" and together with Life Sciences, the "Funds") as reported on Amendment No. 4 to Schedule 13G filed on February 14, 2022 by Baker Bros. Advisors LP (the "Adviser"), Baker Bros. Advisors (GP) LLC (the "Adviser GP"), Felix J. Baker and Julian C. Baker (collectively, "Baker Bros."). The Adviser GP, Felix J. Baker and Julian C. Baker as managing members of the Adviser GP, and the Adviser may be deemed to be beneficial owners of the ADSs directly held by the Funds. The Adviser GP is the sole general partner of the Adviser. Pursuant to the management agreements, as amended, among the Adviser, Life Sciences and 667 and their respective general partners, the Funds' respective general partners relinquished to the Adviser all discretion and authority with respect to the investment and voting power of the securities held by the Funds, and thus the Adviser has complete and unlimited discretion and authority with respect to the Funds' investments and voting power over investments. The address of Baker Bros. is c/o Baker Bros. Advisors LP, 860 Washington Street, 3rd Floor, New York, NY 10014.

(6) Consists of an aggregate of 4,068,476 ADSs beneficially owned, or that may be deemed to be beneficially owned, by Wellington Management Group LLP ("Management Group"), certain of its affiliates and other companies as reported by Amendment No. 1 to Schedule 13G filed on February 4, 2022 by Management Group, Wellington Group Holdings LLP, Wellington Investment Advisors Holdings LLP and Wellington Management Global Holdings, Ltd. The address of the Management Group is 280 Congress Street, Boston, MA 02210.

(7) Consists of an aggregate of 3,219,965 ADSs beneficially owned, or that may be deemed to be beneficially owned, by Janus Henderson Group plc ("Janus Henderson") as reported on Amendment No. 1 to Schedule 13G filed on February 10, 2022. The address of Janus Henderson is 201 Bishopsgate, EC2M 3AE, United Kingdom.

(8) Consists of (i) 328,716 ordinary shares and ADSs beneficially owned by Mr. Mikkelsen, and (ii) 1,222,474 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Mr. Mikkelsen.

(9) Consists of (i) 64,539 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Dr. Breinholt and (ii) 927 ADSs held by Dr. Breinholt.

(10) Consists of (i) 135,768 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Mr. Jensen and (ii) 927 ADSs held by Mr. Jensen.

(11) Consists of (i) 124,268 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Mr. Jensen, (ii) 927 ADSs held by Mr. Jensen and (iii) 1,000 ADSs held by MiWo Invest Aps ("MiWo Invest"). MiWo Invest is a personal investment company wholly-owned by Mr. Jensen.

(12) Consists of (i) 108,793 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Dr. Okkels and (ii) 927 ADSs held by Dr. Okkels.

(13) Consists of (i) 51,075 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Mr. Rasmussen and (ii) 195 ADSs held by Mr. Rasmussen.

(14) Consists of (i) 43,554 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Dr. Singel and (ii) 1,267 ADSs held by Dr. Singel.

(15) Consists of (i) 2,555 ordinary shares and ADSs held by Mr. Smith and (ii) 174,268 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Mr. Smith.

(16) Consists of (i) 177,304 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Ms. Sønderbjerg and (ii) 927 ADSs held by Ms. Sønderbjerg.

(17) Consists of (i) 1,927 ordinary shares and ADSs held by Dr. Sprogøe, (ii) 154,581 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Dr. Sprogøe and (iii) 30 ADSs held by family members of Dr. Sprogøe.

(18) Consists of (i) 82,086 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Dr. Volck, (ii) 463 ADSs held by Dr. Volck and (iii) 200 ADSs held by family members of Dr. Volck.

(19) Consists of (i) 93,828 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Dr. Cha and (ii) 195 ADSs held by Dr. Cha.

(20) Consists of (i) 48,933 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Ms. Bright and (ii) 195 ADSs held by Ms. Bright.

(21) Consists of (i) 50,828 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Mr. Holtug and (ii) 446 ADSs held by Mr. Holtug.

(22) Consists of 15,674 ordinary shares that may be subscribed pursuant to the exercise of warrants within 60 days of February 1, 2023 by Dr. Tordjman.

Record Holders

As of February 1, 2023, assuming that all of our ordinary shares represented by ADSs are held by residents of the United States, 100% of our outstanding ordinary shares were held in the United States by two holders of record and none of our outstanding ordinary shares were held outside of the United States. At such date, there were outstanding 56,944,171 ADSs, each representing one of our ordinary shares, and in the aggregate representing 99.64% of our outstanding ordinary shares. At such date, there were two holders of record registered with the Bank of New York Mellon, depositary of the ADSs. The actual number of holders is greater than these numbers of record holders and includes beneficial owners whose ADSs are held in street name by brokers and other nominees. This number of holders of record also does not include holders whose shares may be held in trust by other entities.

B. Related Party Transactions

The following is a description of related party transactions we have entered into since January 1, 2022 with any of our board members, our senior management, the owners of more than five percent of our share capital, and any other related parties.

Employment Agreements and Warrant Grants

We have entered into employment agreements with members of our senior management. Further, we have issued warrants to two new members of the board of directors. In addition, we are paying fees for board tenure and board committee tenure to the independent members of our board of directors. See “Item 6 B. Directors, Senior Management and Employees—Compensation” for more information.

Indemnification Agreements

We have entered into indemnification agreements with our board members and members of our senior management. See "Item 6 B. Directors, Senior Management and Employees—Compensation—Insurance and Indemnification" for a description of these indemnification agreements.

VISEN Pharmaceuticals

We have provided research and development services to VISEN Pharmaceuticals ("VISEN") under our Rights Agreements which will be reimbursed by VISEN. Further, under our Rights Agreements and clinical supply agreements, we have provided and agreed to provide product supply to VISEN for use in Greater China. In addition, under our cost sharing and volume commitment agreement with VISEN, we have invoiced VISEN's share of project costs as stipulated by the contract.

For quantitative details regarding transactions and outstanding balances with VISEN, please refer to Note 12, "Investment in Associate".

C. Interests of Experts and Counsel

Not applicable.

Item 8 Financial Information

A. Consolidated Statements and Other Financial Information

See the financial statements beginning on page F-1.

Legal Proceedings

From time to time, we may be involved in various claims and legal proceedings relating to claims arising out of our operations. We are not currently a party to any legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Dividends

We do not at present plan to pay cash dividends on our ordinary shares. Under Danish law, the distribution of ordinary and extraordinary dividends requires the approval of a company's shareholders at a company's general meeting. Under the Danish Companies Act the general meeting may authorise the board of directors to resolve to distribute extraordinary dividends after presentation of a company's first financial statements. The authorisation may be subject to financial and time restrictions. The shareholders may not distribute dividends in excess of the recommendation from the board of directors and may only pay out dividends from our distributable reserves, which are defined as results from operations carried forward and reserves that are not bound by law after deduction of loss carried forward. The decision to pay out extraordinary dividends shall be accompanied by a balance sheet, and the board of directors determine whether it will be sufficient to use the balance sheet from the annual report or if an interim balance sheet for the period from the annual report period until the extraordinary dividend payment shall be prepared. If extraordinary dividends are paid out later than six months following the financial year for the latest annual report, an interim balance sheet showing that there are sufficient funds shall always be prepared.

B. Significant Changes

See Note 21 "Subsequent Events" to the audited consolidated financial statements included elsewhere in this annual report.

Item 9 The Offer and Listing

A. Offer and Listing Details

The ADS have been listed on The Nasdaq Global Select Market under the symbol “ASND” since January 28, 2015. Prior to that date, there was no public trading market for ADSs or our ordinary shares.

B. Plan of Distribution

Not applicable.

C. Markets

The ADS have been listed on The Nasdaq Global Select Market under the symbol “ASND” since January 28, 2015.

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

Authorizations to Our Board of Directors

As of February 1, 2023, our board of directors is authorized to increase the share capital as follows:

- Our board of directors is authorized to increase our share capital by up to 9,000,000 shares with pre-emptive subscription rights for existing shareholders in connection with cash contributions. This authorization is valid until May 28, 2024.
- Our board of directors is authorized at one or more times to increase our share capital by up to nominal DKK 6,125,000 without pre-emptive subscription rights for existing shareholders. Capital increases according to this authorization can be carried out by our board of directors by way of contributions in kind, conversion of debt and/or cash contributions, and must be carried out at market price. This authorization is valid until May 27, 2026.
- Our board of directors is authorized to issue 578,717 warrants and to increase our share capital by up to 578,717 shares without pre-emptive subscription rights for existing shareholders in connection with the exercise, if any, of said warrants and to determine the terms and conditions thereof. This authorization is valid until May 28, 2025.

- Our board of directors is, without pre-emptive rights for existing shareholders, authorized to obtain loans against issuance of convertible bonds which confer the right to subscribe up to 9,000,000 shares. The convertible bonds shall be offered at a subscription price and a conversion price that correspond in aggregate to at least the market price of the shares at the time of the decision of our board of directors to issue the convertible bonds. The loans shall be paid in cash and our board of directors shall determine the terms and conditions for the convertible bonds. This authorization is valid until May 29, 2027.
- Our board of directors is on one or more occasions authorized to issue 333,414 warrants to members of the executive management and employees, advisors and consultants of the company or our subsidiaries and to increase our share capital by up to 333,414 shares, without pre-emptive subscription rights for existing shareholders in connection with the exercise, if any, of said warrants and to determine the terms and conditions thereof. The exercise price for the warrants shall at least be equal to the market price of the shares at the time of issuance. This authorization is valid until May 27, 2026.
- Our board of directors is on one or more occasions authorized to issue 1,000,000 warrants to members of the executive management and employees, advisors and consultants of the company or our subsidiaries and to increase our share capital by up to 1,000,000 shares, without pre-emptive subscription rights for existing shareholders in connection with the exercise, if any, of said warrants and to determine the terms and conditions thereof. The exercise price for the warrants shall be determined by the board of directors in consultation with the company's advisors and shall at least be equal to the market price of the shares at the time of issuance. This authorization is valid until May 29, 2027.

If our board of directors exercises its authorizations in full, and all warrants and convertible debt instruments are exercised fully (not including already issued warrants), then our share capital will amount to 83,189,426 shares consisting of 83,189,426 shares with a nominal value of DKK 1 each.

Owners' Register

We are obligated to maintain an owners' register (in Danish: *ejerbog*). The owners' register is maintained by Computershare A/S (Company Registration (CVR) no. 27088899), our Danish share registrar. It is mandatory that the owners' register is maintained within the European Union and that it is available to public authorities.

Pursuant to the Danish Companies Act, public and private limited liability companies are required to register with the Danish Business Authority information regarding shareholders who own at least 5% of the share capital or the voting rights. Pursuant to this provision, we file registrations with the Public Owners' Register of the Danish Business Authority. Shareholders that exceed the ownership threshold must notify us and we will subsequently file the information with the Danish Business Authority. Reporting is further required when thresholds of 5%, 10%, 15%, 20%, 25%, 50%, 90% or 100%, or 1/3 or 2/3 are reached or no longer reached.

Articles of Association and Danish Corporate Law

With respect to our articles of association, the following should be emphasized:

Objects Clause

Our corporate object, as set out in article 3 of our articles of association, is to develop ideas and preparations for the combating of disease medically, to manufacture and sell such preparations or ideas, to own shares of companies with the same objects and to perform activities in natural connection with these objects.

Summary of Provisions Regarding the Board of Directors and the Executive Board

Pursuant to our articles of association, our board of directors shall be elected by our shareholders at the general meeting and shall be composed of not less than three and no more than ten members. With respect to the duration of the term which our board members severally hold office, the board of directors is classified into two classes as nearly equal in number as possible. Such classes consist of one class of directors ("Class I") who were elected at the annual general meeting held in 2021 for a term expiring at the annual general meeting to be held in 2023; and a second class of directors ("Class II") who were elected at the annual general meeting held in 2022 for a term expiring at the annual general meeting to be held in 2024. Member of Class I Dr. James I. Healy, M.D., Ph.D., resigned from the board of directors with effect as of May 30, 2022. On September 9, 2022 Siham Imani and William Carl Fairey Jr. were elected as new members of the board of directors in Class I for a term expiring at the annual general meeting to be held in 2023. The shareholders shall increase or decrease the number of directors, in order to ensure that the two classes shall be as nearly equal in number as possible; provided, however, that no decrease shall have the effect of shortening the term of any other director. At each annual general meeting, the successors of the class of directors whose term expires at that meeting shall be elected to hold office for a term expiring at the annual general meeting held in the second year following the year of their election. Board members must retire from the board of directors at the annual general meeting following their 75th birthday. Board members are not required to own any shares of our share capital.

The board of directors shall appoint and employ an executive board consisting of one to five members to attend to our day-to-day management, and the board of directors shall determine the terms and conditions of the employment.

Voting Rights

Each shareholder is entitled to one vote for each share owned at the time of any general meeting. As compared with Danish citizens, there are no limitations under the articles of association or under Danish law on the rights of foreigners or non-Danish citizens to hold or vote our shares.

Dividend Rights

Our shareholders may at general meetings authorize the distribution of ordinary and extraordinary dividends. Our shareholders may not distribute dividends in excess of the recommendation from our board of directors and may only pay out dividends from our distributable reserves, which are defined as results from operations carried forward and reserves that are not bound by law after deduction of loss carried forward.

Our shareholders are eligible to receive any dividends declared and paid out. However, we have not to date declared or paid any dividends and we currently intend to retain all available financial resources and any earnings generated by our operations for use in the business and we do not anticipate paying any dividends in the foreseeable future. The payment of any dividends in the future will depend on a number of factors, including our future earnings, capital requirements, financial condition and future prospects, applicable restrictions on the payment of dividends under Danish law and other factors that our board of directors may consider relevant.

See "Item 10 E. Additional Information—Taxation" for a summary of certain tax consequences in respect of dividends or distributions to holders of our ordinary shares or the ADSs.

Pre-emptive Subscription Rights

Under Danish law, all shareholders have pre-emptive subscription rights in connection with capital increases that are carried out as cash contributions. An increase in share capital can be resolved by the shareholders at a general meeting or by the board of directors pursuant to an authorization given by the shareholders. In connection with an increase of a company's share capital, the shareholders may, by resolution at a general meeting, approve deviations from the general Danish pre-emptive rights of the shareholders. Under the Danish Companies Act, such resolution must be adopted by the affirmative vote of shareholders holding at least a two-thirds majority of the votes cast and the share capital represented at the general meeting.

The board of directors may resolve to increase our share capital without pre-emptive subscription rights for existing shareholders pursuant to the authorizations set forth above under the caption "Authorizations to Our Board of Directors."

Unless future issuances of new shares and/or pre-emptive rights are registered under the Securities Act or with any authority outside Denmark, U.S. shareholders and shareholders in jurisdictions outside Denmark may be unable to exercise their pre-emptive subscription rights.

Rights on Liquidation

Upon a liquidation or winding-up of our company, shareholders will be entitled to participate, in proportion to their respective shareholdings, in any surplus assets remaining after payment of our creditors.

Limitations on Holding of Shares

There are no limitations on the right to hold shares under the articles of association or Danish law.

Liability to Capital Calls by Us

Under our articles of association as well as the Danish Companies Act, our shareholders are not obligated to pay further amounts to us. All our shares are fully-paid.

Sinking Fund Provisions

There are no sinking fund provisions or similar obligations relating to our ordinary shares.

Disclosure Requirements

Pursuant to Section 55 of the Danish Companies Act, a shareholder is required to notify us when such shareholder's stake represents 5% or more of the voting rights in our company or the nominal value accounts for 5% or more of the share capital, and when a change of a holding already notified entails that the 5%, 10%, 15%, 20%, 25%, 50%, 90% or 100%, or 1/3 or 2/3 are reached or no longer reached. The notification shall be given within two weeks following the date when the limits are reached or are no longer reached.

The notification shall provide information on the date of the acquisition or disposal of the shares, the full name, civil registration (CPR) number, and address of the shareholder or, in the case of an enterprise, registered office and business registration (CVR) number, the number of shares and their nominal value and share classes (if applicable) as well as information about the basis on which the calculation of the holdings has been made. In the event that the shareholder is a non-resident company or citizen of Denmark, the notification shall include documentation, which clearly identifies the owner. The company shall cause the notification to be entered in the owners' register.

Pursuant to section 58a, we are obligated to collect and store for a period of at least five years certain information regarding the beneficial owners of shares in the Company. A beneficial owner is a physical person who ultimately holds or controls, directly or indirectly, a sufficient part of the ownership interests or voting rights or exercises control by other means, except for owners of companies whose ownership interests are traded on a regulated market or a similar market which is subject to a duty of disclosure in accordance with EU law or similar international standards.

The legal status of the notification obligations is not fully clarified in relation to ADS holders and an ADS holder may be subject to such obligations.

General Meetings

The general meeting of shareholders is the highest authority in all matters, subject to the limitations provided by Danish law and the articles of association. The annual general meeting shall be held in the Greater Copenhagen area not later than the end of May in each year.

At the annual general meeting, the audited annual report is submitted for approval, together with the proposed appropriation of profit/treatment of loss, the election of the board of directors and election of our auditors. In addition, the board of directors reports on our activities during the past year.

General meetings are convened by the board of directors with a minimum of two weeks' notice and a maximum of four weeks' notice. A convening notice will be forwarded to shareholders recorded in our owners' register, who have requested such notification and by publication in the Danish Business Authority's computerized information system and on the Company's website.

At the latest, two weeks before a general meeting (inclusive of the day of the general meeting), we shall make the following information and documents available on our website:

- the convening notice,
- the documents that shall be presented at the general meeting, which will in case of the annual general meeting include the annual report, and
- the agenda and the complete proposals.

Shareholders are entitled to attend general meetings, either in person or by proxy, and they or their proxy may be accompanied by one advisor. A shareholder's right to attend general meetings and to vote at general meetings is determined on the basis of the shares that the shareholder holds on the registration date. The registration date shall be one week before the general meeting is held. The shares which the individual shareholder holds are calculated on the registration date on the basis of the registration of ownership in the owners' register as well as notifications concerning ownership which the Company has received with a view to update the ownership in the owners' register. In addition, any shareholder who is entitled to attend a general meeting and who wishes to attend must have requested an admission card from us no later than three days in advance of the general meeting.

Any shareholder is entitled to submit proposals to be discussed at the general meetings. However, proposals by the shareholders to be considered at the annual general meeting must be submitted in writing to the board of directors not later than six weeks before the annual general meeting.

Extraordinary general meetings must be held upon resolution of an annual general meeting to hold such a meeting or upon request of the board of directors, our auditors or shareholders representing at least 1/20 of the registered share capital or such lower percentage as our articles of association may provide. Our articles of association do not state such lower percentage.

Holders of ADSs are not entitled to directly receive notices or other materials or to attend or vote at general meetings.

Resolutions in General Meetings

Resolutions made by the general meeting generally may be adopted by a simple majority of the votes cast, subject only to the mandatory provisions of the Danish Companies Act and our articles of association. Resolutions concerning all amendments to the articles of association must be passed by two-thirds of the votes cast as well as two-thirds of the share capital represented at the general meeting. Certain resolutions, which limit a shareholder's ownership or voting rights, are subject to approval by a nine-tenth majority of the votes cast and the share capital represented at the general meeting. Decisions to impose or increase any obligations of the shareholders towards the company require unanimity.

Quorum Requirements

There are no quorum requirements generally applicable to general meetings of shareholders. To this extent, our practice varies from the requirement of Nasdaq Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting shares.

Squeeze Out

According to Section 70 of the Danish Companies Act, shares in a company may be redeemed by a shareholder holding more than nine-tenths of the shares and the corresponding voting rights in the company. Furthermore, according to Section 73 of the Danish Companies Act, a minority shareholder may require a majority shareholder holding more than nine-tenths of the shares and the corresponding voting rights to redeem the minority shareholder's shares.

Danish Rules Intended to Prevent Market Abuse

As of July 3, 2016, EU Regulation No 596/2014 on market abuse entered into force and Chapter 10 of the Danish Securities Trading Act was repealed. Pursuant to said Chapter 10, we had adopted an internal code on inside information in respect of the holding of and carrying out of transactions by our board of directors and executive officers and employees in the shares or ADSs or in financial instruments the value of which is determined by the value of the ordinary shares or ADSs, and we had drawn up a list of those persons working for us who could have access to inside information on a regular or incidental basis and had informed such persons of the rules on insider trading and market manipulation, including the sanctions which could be imposed in the event of a violation of those rules. However, said EU Regulation No 596/2014 on market abuse imposes no such requirements on us and we have therefore taken steps to abandon our previous practice.

Limitation on Liability

Under Danish law, members of the board of directors or senior management may be held liable for damages in the event that loss is caused due to their negligence. They may be held jointly and severally liable for damages to the company and to third-parties for acting in violation of the articles of association and Danish law.

The general meeting is allowed to discharge our board members and members of our senior management from liability for any particular financial year based on a resolution relating to the financial statements. This discharge means that the general meeting will discharge such board members and members of our senior management from liability to us; however, the general meeting cannot discharge any claims by individual shareholders or other third-parties.

Additionally, we intend to enter, or have entered, into agreements with our board members and members of our senior management, pursuant to which, subject to limited exceptions, we will agree, or have agreed, to indemnify such board members and members of senior management from civil liability, including (i) any damages or fines payable by them as a result of an act or failure to act in the exercise of their duties currently or previously performed by them; (ii) any reasonable costs of conducting a defense against a claim; and (iii) any reasonable costs of appearing in other legal proceedings in which such individuals are involved as current or former board members or members of senior management.

There is a risk that such agreement will be deemed void under Danish law, either because the agreement is deemed contrary to the rules on discharge of liability in the Danish Companies Act, as set forth above, because the agreement is deemed contrary to sections 19 and 23 of the Danish Act on Damages, which contain mandatory provisions on recourse claims between an employee (including members of our senior management) and us, or because the agreement is deemed contrary to the general provisions of the Danish Contracts Act.

In addition to such indemnification, we provide our board members and senior management with directors' and officers' liability insurance.

Comparison of Danish Corporate Law and Our Articles of Association and Delaware Corporate Law

The following comparison between Danish corporate law, which applies to us, and Delaware corporate law, the law under which many publicly traded companies in the United States are incorporated, discusses additional matters not otherwise described in this annual report. This summary is subject to Danish law, including the Danish Companies Act, and Delaware corporate law, including the Delaware General Corporation Law.

Duties of Board Members

Denmark. Public limited liability companies in Denmark are usually subject to a two-tier governance structure with the board of directors having the ultimate responsibility for the overall supervision and strategic management of the company in question and with an executive board/management being responsible for the day-to-day operations.

Each board member and member of the executive board/management is under a fiduciary duty to act in the interest of the company but shall also take into account the interests of the creditors and the shareholders. Under Danish law, the members of the board of directors and executive management of a limited liability company are liable for losses caused by negligence whether shareholders, creditors or the company itself suffers such losses. They may also be liable for wrongful information given in the annual financial statements or any other public announcements from the company. An investor suing for damages is required to prove its claim with regard to negligence, loss, and causation. Danish courts, when assessing negligence, have been reluctant to impose liability unless the directors and officers neglected clear and specific duties. This is also the case when it comes to liability with regard to public offerings or liability with regard to any other public information issued by the company.

Delaware. The board of directors bears the ultimate responsibility for managing the business and affairs of a corporation. In discharging this function, directors of a Delaware corporation owe fiduciary duties of care and loyalty to the corporation and to its stockholders. Delaware courts have decided that the directors of a Delaware corporation are required to exercise informed business judgement in the performance of their duties. Informed business judgement means that the directors have informed themselves of all material information reasonably available to them. Delaware courts have also imposed a heightened standard of conduct upon directors of a Delaware corporation who take any action designed to defeat a threatened change in control of the corporation. In addition, under Delaware law, when the board of directors of a Delaware corporation approves the sale or break-up of a corporation, the board of directors may, in certain circumstances, have a duty to obtain the highest value reasonably available to the stockholders.

Terms of the Members of Our Board of Directors

Denmark. Under Danish law, the members of the board of directors of a limited liability company are generally appointed for an individual term of one year. There is no limit on the number of consecutive terms the board members may serve. Pursuant to our articles of association, our board members are appointed by the general meeting of shareholders for a term of two years and are divided into two classes. Election of board members is, according to our articles of association, an item that shall be included on the agenda for the annual general meeting.

At the general meeting, shareholders are entitled at all times to dismiss a board member by a simple majority vote.

It follows from Section 140 of the Danish Companies Act that in limited liability companies that have employed an average of at least 35 employees in the preceding three years, the employees are entitled to elect a minimum of two representatives and alternate members to the company's board of directors up to one half the number of the shareholder elected directors. If the number of representatives to be elected by the employees is not a whole number, such number must be rounded up.

Our company currently employs more than an average of 35 employees and has done so since 2016. Consequently, from 2018, our employees will be entitled to demand representation on our board of directors. The question will, upon request from the employees, be put to a popular vote among the employees. If more than half of the employees (regardless whether they participate in the vote) vote in favor of having representation, we must organize an election process.

Additionally, Section 141 of the Danish Companies Act allows for group representation on the board of directors of our Company, i.e. that employees of our Danish subsidiaries may demand representation on our board. However, our Danish subsidiaries do not currently have employees. The employees of Ascendis Pharma, Inc., Ascendis Pharma Endocrinology, Inc., Ascendis Pharma GmbH, and Ascendis Pharma Endocrinology GmbH may only demand representation on our board of directors provided that our general meeting adopts a resolution to that effect.

Delaware. The Delaware General Corporation Law generally provides for a one-year term for directors, but permits directorships to be divided into up to three classes, of relatively equal size, with up to three-year terms, with the years for each class expiring in different years, if permitted by the certificate of incorporation, an initial bylaw or a bylaw adopted by the stockholders. A director elected to serve a term on a "classified" board may not be removed by stockholders without cause. There is no limit in the number of terms a director may serve.

Board Member Vacancies

Denmark. Under Danish law, in the event of a vacancy, new board members are elected by the shareholders in a general meeting. Thus, a general meeting will have to be convened to fill a vacancy on the board of directors. However, the board of directors may choose to wait to fill vacancies until the next annual general meeting of the company, provided that the number of the remaining board members is more than two, and provided that the remaining board members can still constitute a quorum. It is only a statutory requirement to convene a general meeting to fill vacancies if the number of remaining members on the board is less than three.

Delaware. The Delaware General Corporation Law provides that vacancies and newly created directorships may be filled by a majority of the directors then in office (even though less than a quorum) unless (1) otherwise provided in the certificate of incorporation or bylaws of the corporation or (2) the certificate of incorporation directs that a particular class of stock is to elect such director, in which case any other directors elected by such class, or a sole remaining director elected by such class, will fill such vacancy.

Conflict-of-Interest Transactions

Denmark. Under Danish law, board members may not take part in any matter or decision-making that involves a subject or transaction in relation to which the board member has a conflict of interest with us.

Delaware. The Delaware General Corporation Law generally permits transactions involving a Delaware corporation and an interested director of that corporation if:

- The material facts as to the director's relationship or interest are disclosed and a majority of disinterested directors' consent;
- The material facts are disclosed as to the director's relationship or interest and a majority of shares entitled to vote thereon consent; or
- The transaction is fair to the corporation at the time it is authorized by the board of directors, a committee of the board of directors or the stockholders.

Proxy Voting by Board Members

Denmark. In the event that a board member in a Danish limited liability company is unable to participate in a board meeting, the elected alternate, if any, shall be given access to participate in the board meeting. Unless the board of directors has decided otherwise, or as otherwise is set out in the articles of association, the board member in question may in special cases grant a power of attorney to another board member, provided that this is considered safe considering the agenda in question.

Delaware. A director of a Delaware corporation may not issue a proxy representing the director's voting rights as a director.

Shareholder Rights

Notice of Meeting

Denmark. According to the Danish Companies Act, general meetings in limited liability companies shall be convened by the board of directors with a minimum of two weeks' notice and a maximum of four weeks' notice as set forth in the articles of association. A convening notice shall be forwarded to shareholders recorded in the company's owners' register, who have requested such notification. There are specific requirements as to the information and documentation required to be disclosed in connection with the convening notice.

Delaware. Under Delaware 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.

Voting Rights

Denmark. Each ordinary share confers the right to cast one vote at the general meeting of shareholders, unless the articles of association provide otherwise. Each holder of ordinary shares may cast as many votes as it holds shares. Shares that are held by the company or its subsidiaries do not confer the right to vote.

Delaware. Under the Delaware General Corporation Law, each stockholder is entitled to one vote per share of stock, unless the certificate of incorporation provides otherwise. In addition, the certificate of incorporation may provide for cumulative voting at all elections of directors of the corporation, or at elections held under specified circumstances. Either the certificate of incorporation or the bylaws may specify the number of shares and/or the amount of other securities that must be represented at a meeting in order to constitute a quorum, but in no event can a quorum consist of less than one third of the shares entitled to vote at a meeting.

Stockholders as of the record date for the meeting are entitled to vote at the meeting, and the board of directors may fix a record date that is no more than 60 nor less than ten days before the date of the meeting, and if no record date is set then the record date is the close of business on the day next preceding the day on which notice is given, or if notice is waived then the record date is the close of business on the day next preceding the day on which the meeting is held. The determination of the stockholders of record entitled to notice or to vote at a meeting of stockholders shall apply to any adjournment of the meeting, but the board of directors may fix a new record date for the adjourned meeting.

Shareholder Proposals

Denmark. According to the Danish Companies Act, extraordinary general meetings of shareholders will be held whenever required by the board of directors or the appointed auditor. In addition, one or more shareholders representing at least 1/20th of the registered share capital of the company may, in writing, require that a general meeting be convened. If such a demand is forwarded, the board of directors shall convene the general meeting within two weeks thereafter.

All shareholders have the right to present proposals for adoption at the annual general meeting, provided that the proposals are made in writing and forwarded at the latest six weeks prior thereto. In the event that the proposal is received at a later date, the board of directors will decide whether the proposal has been forwarded in due time to be included on the agenda.

Delaware. Delaware law does not specifically grant stockholders the right to bring business before an annual or special meeting of stockholders.

However, if a Delaware corporation is subject to the SEC's proxy rules, a stockholder who owns at least $2,000 in market value, or 1% of the corporation's securities entitled to vote, may propose a matter for a vote at an annual or special meeting in accordance with those rules.

Action by Written Consent

Denmark. Under Danish law, it is permissible for shareholders to take action and pass resolutions by written consent in the event of unanimity; however, this will normally not be the case in listed companies and for a listed company, this method of adopting resolutions is generally not feasible.

Delaware. Although permitted by Delaware law, publicly listed companies do not typically permit stockholders of a corporation to take action by written consent.

Appraisal Rights

Denmark. The concept of appraisal rights does not exist under Danish law, except in connection with statutory redemptions rights according to the Danish Companies Act.

According to Section 73 of the Danish Companies Act, a minority shareholder may require a majority shareholder that holds more than 90% of the company's registered share capital and votes to redeem his or her shares. Similarly, a majority shareholder holding more than 90% of the company's share capital and votes may, according to Section 70 of the same act, squeeze out the minority shareholders. In the event that the parties cannot agree to the redemption squeeze out price, this shall be determined by an independent evaluator appointed by the court. Additionally, there are specific regulations in Sections 249, 267, 285 and 305 of the Danish Companies Act that require compensation in the event of national or cross-border mergers and demergers. Moreover, shareholders who vote against a cross-border merger or demerger are, according to Sections 286 and 306 of the Danish Companies Act, entitled to have their shares redeemed.

Delaware. The Delaware General Corporation Law provides for stockholder appraisal rights, or the right to demand payment in cash of the judicially determined fair value of the stockholder's shares, in connection with certain mergers and consolidations.

Shareholder Suits

Denmark. Under Danish law, only a company itself can bring a civil action against a third-party; an individual shareholder does not have the right to bring an action on behalf of a company. An individual shareholder may, in its own name, have an individual right to take action against such third party in the event that the cause for the liability of that third party also constitutes a negligent act directly against such individual shareholder.

Delaware. Under the Delaware General Corporation Law, a stockholder may bring a derivative action on behalf of the corporation to enforce the rights of the corporation. An individual also may commence a class action suit on behalf of himself and other similarly situated stockholders where the requirements for maintaining a class action under Delaware law have been met. A person may institute and maintain such a suit only if that person was a stockholder at the time of the transaction which is the subject of the suit. In addition, under Delaware case law, the plaintiff normally must be a stockholder at the time of the transaction that is the subject of the suit and throughout the duration of the derivative suit. Delaware law also requires that the derivative plaintiff make a demand on the directors of the corporation to assert the corporate claim before the suit may be prosecuted by the derivative plaintiff in court, unless such a demand would be futile.

Repurchase of Shares

Denmark. Danish limited liability companies may not subscribe for newly issued shares in their own capital. Such company may, however, according to the Danish Companies Act Sections 196-201, acquire fully paid shares of its own capital provided that the board of directors has been authorized thereto by the shareholders acting in a general meeting. Such authorization can only be given for a maximum period of five years and the authorization shall fix (i) the maximum value of the shares and (ii) the minimum and the highest amount that the company may pay for the shares. Shares may generally only be acquired using distributable reserves.

Delaware. Under the Delaware General Corporation Law, a corporation may purchase or redeem its own shares unless the capital of the corporation is impaired or the purchase or redemption would cause an impairment of the capital of the corporation. A Delaware corporation may, however, purchase or redeem out of capital any of its preferred shares or, if no preferred shares are outstanding, any of its own shares if such shares will be retired upon acquisition and the capital of the corporation will be reduced in accordance with specified limitations.

Anti-takeover Provisions

Denmark. Under Danish law, it is possible to implement limited protective anti-takeover measures. Such provisions may include, among other things, (i) different share classes with different voting rights, (ii) specific requirements to register the shares named in the company's owners register and (iii) notification requirements concerning participation in general meetings. The Company has currently not adopted any such provisions.

Delaware. In addition to other aspects of Delaware law governing fiduciary duties of directors during a potential takeover, the Delaware General Corporation Law also contains a business combination statute that protects Delaware companies from hostile takeovers and from actions following the takeover by prohibiting some transactions once an acquirer has gained a significant holding in the corporation.

Section 203 of the Delaware General Corporation Law prohibits "business combinations," including mergers, sales and leases of assets, issuances of securities and similar transactions by a corporation or a subsidiary with an interested stockholder that beneficially owns 15% or more of a corporation's voting stock, within three years after the person becomes an interested stockholder, unless:

- the transaction that will cause the person to become an interested stockholder is approved by the board of directors of the target prior to the transaction;
- after the completion of the transaction in which the person becomes an interested stockholder, the interested stockholder holds at least 85% of the voting stock of the corporation not including shares owned by persons who are directors and officers of interested stockholders and shares owned by specified employee benefit plans; or
- after the person becomes an interested stockholder, the business combination is approved by the board of directors of the corporation and holders of at least 66.67% of the outstanding voting stock, excluding shares held by the interested stockholder.

A Delaware corporation may elect not to be governed by Section 203 by a provision contained in the original certificate of incorporation of the corporation or an amendment to the original certificate of incorporation or to the bylaws of the company, which amendment must be approved by a majority of the shares entitled to vote and may not be further amended by the board of directors of the corporation. Such an amendment is not effective until twelve months following its adoption.

Inspection of Books and Records

Denmark. According to Section 150 of the Danish Companies Act, a shareholder may request an inspection of the company's books regarding specific issues concerning the management of the company or specific annual reports. If approved by shareholders with simple majority, one or more investigators are elected. If the proposal is not approved by simple majority but 25% of the share capital votes in favor, then the shareholder can request the court to appoint an investigator.

Delaware. Under the Delaware General Corporation Law, any stockholder may inspect certain of the corporation's books and records, for any proper purpose, during the corporation's usual hours of business.

Pre-emptive Rights

Denmark. Under Danish law, all shareholders have pre-emptive subscription rights in connection with capital increases that are carried out as cash contributions. In connection with an increase of a company's share capital, the shareholders may, by resolution at a general meeting, approve deviations from the general Danish pre-emptive rights of the shareholders. Under the Danish Companies Act, such resolution must be adopted by the affirmative vote of shareholders holding at least a two-thirds majority of the votes cast and the share capital represented at the general meeting.

The board of directors may resolve to increase the company's share capital without pre-emptive subscription rights for existing shareholders pursuant to the authorizations described above under the caption "Authorizations to Our Board of Directors."

Unless future issuances of new shares are registered under the Securities Act or with any authority outside Denmark, U.S. shareholders and shareholders in jurisdictions outside Denmark may be unable to exercise their pre-emptive subscription rights.

Delaware. Under the Delaware General Corporation Law, stockholders have no pre-emptive rights to subscribe for additional issues of stock or to any security convertible into such stock unless, and to the extent that, such rights are expressly provided for in the certificate of incorporation.

Dividends

Denmark. Under Danish law, the distribution of ordinary and extraordinary dividends requires the approval of a company's shareholders at a company's general meeting. Under the Danish Companies Act the general meeting may authorize the board of directors to resolve to distribute extraordinary dividends after presentation of a company's first financial statements. The authorization may be subject to financial and time restrictions. The shareholders may not distribute dividends in excess of the recommendation from the board of directors and may only pay out dividends from the company's distributable reserves, which are defined as results from operations carried forward and reserves that are not bound by law after deduction of loss carried forward. The decision to pay out extraordinary dividends shall be accompanied by a balance sheet, and the board of directors determine whether it will be sufficient to use the balance sheet from the annual report or if an interim balance sheet for the period from the annual report period until the extraordinary dividend payment shall be prepared. If extraordinary dividends are paid out later than six months following the financial year for the latest annual report, an interim balance sheet showing that there are sufficient funds shall always be prepared.

Delaware. Under the Delaware General Corporation Law, a Delaware corporation may pay dividends out of its surplus (the excess of net assets over capital), or in case there is no surplus, out of its net profits for the fiscal year in which the dividend is declared and/or the preceding fiscal year (provided that the amount of the capital of the corporation is not less than the aggregate amount of the capital represented by the issued and outstanding stock of all classes having a preference upon the distribution of assets). In determining the amount of surplus of a Delaware corporation, the assets of the corporation, including stock of subsidiaries owned by the corporation, must be valued at their fair market value as determined by the board of directors, without regard to their historical book value. Dividends may be paid in the form of shares, property or cash.

Shareholder Vote on Certain Reorganizations

Denmark. Under Danish law, all amendments to the articles of association shall be approved by the general meeting of shareholders with a minimum of two-thirds of the votes cast and two-thirds of the represented share capital. The same applies to solvent liquidations, mergers with the company as the discontinuing entity, mergers with the company as the continuing entity if shares are issued in connection therewith, demergers with the company as the transferor company and demergers with the company as the existing transferee if amendment of the articles of association for any purpose other than the adoption of the transferor company's name or secondary name as the transferee company's secondary name is required to be made. Under Danish law, it is debatable whether the shareholders must approve a decision to sell all or virtually all of the company's business/assets.

Delaware. Under the Delaware General Corporation Law, the vote of a majority of the outstanding shares of capital stock entitled to vote thereon generally is necessary to approve a merger or consolidation or the sale of all or substantially all of the assets of a corporation. The Delaware General Corporation Law permits a corporation to include in its certificate of incorporation a provision requiring for any corporate action the vote of a larger portion of the stock or of any class or series of stock than would otherwise be required.

However, under the Delaware General Corporation Law, no vote of the stockholders of a surviving corporation to a merger is needed, unless required by the certificate of incorporation, if (1) the agreement of merger does not amend in any respect the certificate of incorporation of the surviving corporation, (2) the shares of stock of the surviving corporation are not changed in the merger and (3) the number of shares of common stock of the surviving corporation into which any other shares, securities or obligations to be issued in the merger may be converted does not exceed 20% of the surviving corporation's common stock outstanding immediately prior to the effective date of the merger. In addition, stockholders may not be entitled to vote in certain mergers with other corporations that own 90% or more of the outstanding shares of each class of stock of such corporation, but the stockholders will be entitled to appraisal rights.

Amendments to Governing Documents

Denmark. All resolutions made by the general meeting may be adopted by a simple majority of the votes, subject only to the mandatory provisions of the Danish Companies Act and the articles of association. Resolutions concerning all amendments to the articles of association must be passed by two-thirds of the votes cast as well as two-thirds of the share capital represented at the general meeting. Certain resolutions, which limit a shareholder's ownership or voting rights, are subject to approval by a nine-tenth majority of the votes cast and the share capital represented at the general meeting. Decisions to impose any or increase any obligations of the shareholders towards the company require unanimity.

Delaware. Under the Delaware General Corporation Law, a corporation's certificate of incorporation may be amended only if adopted and declared advisable by the board of directors and approved by a majority of the outstanding shares entitled to vote, and the bylaws may be amended with the approval of a majority of the outstanding shares entitled to vote and may, if so provided in the certificate of incorporation, also be amended by the board of directors.

C. Material Contracts

Except as otherwise disclosed in this annual report (including the Exhibits), we are not currently party to any material contract, other than contracts entered into in the ordinary course of business.

D. Exchange Controls

There are no laws or regulation in Denmark that restrict the export or import of capital (except for certain investments in certain domains in accordance with applicable resolutions by the United Nations or the European Union), including, but not limited to, foreign exchange controls, or which affect the remittance of dividends, interest or other payments to non-resident holders of our ordinary shares.

E. Taxation

Danish Tax Considerations

The following discussion describes the material Danish tax consequences under present law of an investment in the ADSs (representing our ordinary shares). The summary is for general information only and does not purport to constitute exhaustive tax or legal advice. It is specifically noted that the summary does not address all possible tax consequences relating to an investment in the ADSs. The summary is based solely on the tax laws of Denmark in effect on the date of this annual report. Danish tax laws may be subject to change, possibly with retroactive effect.

The summary does not cover investors to whom special tax rules apply, and, therefore, may not be relevant, for example, to investors subject to the Danish Tax on Pension Yields Act (*i.e.*, pension savings), professional investors, certain institutional investors, insurance companies, pension companies, banks, stockbrokers and investors with tax liability on return on pension investments. The summary does not cover taxation of individuals and companies who carry on a business of purchasing and selling shares. The summary only sets out the tax position of the direct owners of the ADSs and further assumes that the direct investors are the beneficial owners of the ADSs and any dividends thereon. Sales are assumed to be sales to a third party.

Potential investors in the ADSs are advised to consult their tax advisors regarding the applicable tax consequences of acquiring, holding and disposing of the ADSs based on their particular circumstances.

Investors who may be affected by the tax laws of other jurisdictions should consult their tax advisors with respect to the tax consequences applicable to their particular circumstances as such consequences may differ significantly from those described herein.

Tax Characterization of the ADSs

It is currently not clear under the Danish tax legislation how listed ADSs issued by Danish resident companies in general are to be treated for Danish tax purposes.

However, we obtained a tax ruling on June 21, 2022, from the Danish Tax Council which confirmed that ADSs issued by us are shares for Danish tax purposes. Based on an analysis of the terms of the Deposit Agreement between 1) the holders of ADSs, 2) Ascendis Pharma A/S and 3) Bank of New York Mellon, the Danish Tax Council found that the voting and economic rights attached to the underlying shares had effectively been transferred to the ADS holders and therefore, the ADSs qualified as shares for Danish tax purposes. The ruling is binding on the Danish tax authorities for 5 years as long as the facts remain as described in the ruling for the duration of the 5-year period and in the absence of a change of law. The ruling further confirmed that the ADSs are to be considered listed shares, as the ADSs are listed on Nasdaq. Accordingly, the remainder of this Danish tax discussion assumes that the ADSs will be treated as listed shares for Danish tax purposes.

Taxation of Danish Tax Resident Holders of the ADSs

Sale of the ADSs (Individuals)

For individual investors in 2022, gains from the sale of shares are included in the computation of the annual share income subject to 27% tax on the first DKK 58,900 (for cohabiting spouses, a total of DKK 117,800) and at a rate of 42% on share income exceeding DKK 58,900 (for cohabiting spouses over DKK 117,800). Such amounts are subject to annual adjustment and include all share income (*i.e.*, all capital gains and dividends derived by the individual or cohabiting spouses, respectively). The realization principle applies; i.e. the gains or losses are included in the income in the year of disposal.

Gains and losses on the sale of shares are calculated as the difference between the purchase price and the sales price. The purchase price is generally determined using the average method (in Danish “gennemsnitsmetoden”) as a proportionate part of the aggregate purchase price for all the shareholder’s shares in the company.

As the ADSs, for the purpose of this tax description, are considered listed shares for Danish tax purposes, losses may be offset against received dividends and capital gains on listed shares. Unused losses will automatically be offset against a cohabiting spouse's dividends and capital gains on listed shares. Any unused losses can be carried forward. It is a requirement for offsetting of losses, that the ADS holder (or the ADS holder's custodian bank) has declared the acquisition of the shares in the tax return for the year of acquisition. Such declaration must specify the identity of the ADS, the number of ADS acquired, the acquisition sum and the date of acquisition.

Sale of the ADSs (Companies)

For the purpose of taxation of sales of shares made by shareholders (Companies), a distinction is made between Subsidiary Shares, Group Shares, Tax-Exempt Portfolio Shares and Taxable Portfolio Shares (note that the ownership threshold described below is applied on the basis of the number of all shares issued by the company, and not on the basis of the number of the ADSs issued):

"Subsidiary Shares" are generally defined as shares owned by a shareholder holding at least 10% of the nominal share capital of the issuing company.

"Group Shares" are generally defined as shares in a company in which the shareholder of the company and the issuing company are subject to Danish joint taxation or fulfill the requirements for international joint taxation under Danish law (i.e., the company is controlled by the shareholder).

"Tax-Exempt Portfolio Shares" are defined as shares not admitted to trading on a regulated market owned by a shareholder holding less than 10% of the nominal share capital of the issuing company.

"Taxable Portfolio Shares" are defined as shares that do not qualify as Subsidiary Shares, Group Shares or Tax-Exempt Portfolio Shares.

Gains or losses on disposal of Subsidiary Shares and Group Shares and Tax-Exempt Portfolio Shares are not included in the taxable income of the shareholder.

Special rules apply with respect to Subsidiary Shares and Group Shares to prevent exemption through certain holding company structures just as other anti-avoidance rules may apply. These rules will not be described in further detail.

Capital gains from the sale of Taxable Portfolio Shares are taxable at a rate of 22% irrespective of ownership period. Losses on such shares are generally deductible. Gains and losses on Taxable Portfolio Shares are generally taxable according to the mark-to-market principle (in Danish "lagerprincippet").

According to the mark-to-market principle, each year's taxable gain or loss on Taxable Portfolio Shares is calculated as the difference between the market value of the shares at the beginning and end of the tax year. Thus, taxation will take place on an accrual basis even if no shares have been disposed of and no gains or losses have been realized.

If the Taxable Portfolio Shares are sold or otherwise disposed of before the end of the income year, the taxable income of that income year equals the difference between the value of the Taxable Portfolio Shares at the beginning of the income year and the value of the Taxable Portfolio Shares at realization. If the Taxable Portfolio Shares are acquired and realized in the same income year, the taxable income equals the difference between the acquisition sum and the realization sum. If the Taxable Portfolio Shares are acquired in the income year and not realized in the same income year, the taxable income equals the difference between the acquisition sum and the value of the shares at the end of the income years.

A change of status from Subsidiary Shares/Group Shares/Tax-Exempt Portfolio Shares to Taxable Portfolio Shares (or vice versa) is for tax purposes deemed to be a disposal of the shares and a reacquisition of the shares at market value at the time of change of status.

Dividends (Individuals)

Dividends on listed shares are taxed as share income, as described above. All share income must be included when calculating whether the amounts described above are exceeded. Dividends paid to individuals are generally subject to 27% withholding tax.

Dividends (Companies)

For corporate investors, dividends paid on Subsidiary Shares and Group Shares are tax-exempt irrespective of ownership period.

Dividends paid on Tax-Exempt Portfolio Shares are partly taxable as 70% of the dividends received are included in the taxable income, which is equivalent to an effective taxation of 15.4% (70% of 22%) irrespective of ownership period.

Dividends paid on Taxable Portfolio Shares are subject to the standard corporation tax rate of 22% irrespective of ownership period.

The actual withholding tax rate is as a starting point 27%, while it can be reduced (0%, 15.4%, 22%) if certain requirements are met. A claim for repayment can be made within two months or the excess tax will offset the corporation income tax for the year. The statute of limitations is three years.

Taxation of Shareholders Residing Outside Denmark

Holders of ADSs issued by Ascendis Pharma A/S are treated as holding listed ordinary shares in the company for Danish tax purposes.

Sale of the ADSs (Individuals and Companies)

Holders of the ADSs not resident in Denmark are normally not subject to Danish taxation on any gains realized on the sale of ADSs, irrespective of the ownership period, subject to certain anti-avoidance rules seeking to prevent that taxable dividend payments are converted to tax exempt capital gains.

No Danish share transfer tax or stamp duties are payable on transfer of ADSs.

If an investor holds the ADSs in connection with a trade or business conducted from a permanent establishment in Denmark, gains on shares may be included in the taxable income of such activities pursuant to the rules applying to Danish tax residents as described above.

Dividends (Individuals)

Dividends are generally subject to 27% Danish withholding tax. Individuals residing in certain black-listed countries and holding 25% or more of the share capital in the company are subject to 44% withholding tax.

Non-residents of Denmark are not subject to additional Danish income tax in respect to dividends received on shares.

Holders of ADSs are entitled to apply for a full or partial refund of Danish withholding tax on dividends withheld by the company, in the situations described below:

If the holders of the ADSs are considered beneficial owners of the dividends according to the applicable double tax treaty between Denmark and the tax residence country of the ADS holder, the withholding tax rate under such double tax treaty may apply to the extent the tax residency of the ADS holder can be documented.

For holders of ADSs (as beneficial owners of the dividends on the ordinary shares), if the withholding tax rate applied is higher than the applicable final tax rate (as reduced according to Danish law or an applicable double tax treaty) for the holder of ADSs, a request for a refund of Danish tax in excess hereof can be made in the following situations:

Reduction according to a tax treaty

In the event that the ADS holder is a resident of a state with which Denmark has entered into a tax treaty, the holder may generally, through certain certification procedures, seek a refund from the Danish tax authorities of the tax withheld in excess of the applicable treaty rate, which is typically 15%. Denmark has entered into tax treaties with approximately 80 countries, including the United States, Switzerland and almost all members of the European Union. The tax treaty between Denmark and the United States generally provides for a 15% tax rate.

Individuals residing in certain black-listed countries and holding 25% or more of the share capital in the company are not eligible for refund of dividend withholding taxes.

Reduction according to Danish tax law

If the ADS holder holds less than 10% of the nominal share capital (in the form of ordinary shares in the company and not on the basis of the number of the ADSs issued) of the company and the ADS holder is tax resident in a state which has a tax treaty or an international agreement, convention or other administrative agreement on assistance in tax matters according to which the competent authority in the state of the ADS holder is obligated to exchange information with Denmark, dividends are subject to tax at a rate of 15%. If the ADS holder is tax resident outside the European Union, it is an additional requirement for eligibility for the 15% tax rate that the ADS holder together with related ADS holders holds less than 10% of the nominal share capital of the company.

Note that the reduced tax rate does not affect the withholding rate, which is why the holder must claim a refund as described above in order to benefit from the reduced rate.

Where a non-resident of Denmark holds shares which can be attributed to a permanent establishment in Denmark, dividends are taxable pursuant to the rules applying to Danish tax residents described above.

Individuals residing in certain black-listed countries and holding 25% or more of the share capital in the company are not eligible for refund of dividend withholding taxes.

Dividends (Companies)

Dividends paid to companies are generally subject to 27% withholding tax.

Companies residing in certain black-listed countries and holding Subsidiary Shares or Group Shares are not eligible for refund of dividend withholding taxes.

Non-residents of Denmark are not subject to additional income tax with respect to dividends received on shares. Holders of ADSs are entitled to apply for a refund of Danish withholding tax on dividends paid by the company.

If the holder of the ADSs is considered the beneficial owner of the dividends according to the applicable double tax treaty between Denmark and the tax residence country of the ADS holder, the withholding tax rate under such double tax treaty may apply to the extent the tax residency of the ADS holder can be documented.

Dividends from Subsidiary Shares are tax exempt provided that the taxation of the dividends is to be waived or reduced in accordance with the Parent-Subsidiary Directive (2011/96/EEC) or in accordance with a tax treaty with the jurisdiction in which the company investor is resident. If Denmark is to reduce taxation of dividends to a foreign company under a tax treaty, Denmark will not—as a matter of domestic law—exercise such right and will in general not impose any tax at all. Further, dividends from Group Shares—not also being Subsidiary Shares—are exempt from Danish tax provided the company investor is a resident of the European Union or the EEA and provided the taxation of dividends should have been waived or reduced in accordance with the Parent-Subsidiary Directive (2011/96/EEC) or in accordance with a tax treaty with the country in which the company investor is resident had the shares been Subsidiary Shares.

Dividends paid on both Tax-Exempt and Taxable Portfolio Shares are generally subject to tax at a rate of 22% irrespective of ownership period. While the actual withholding tax rate is as a starting point 27%, it can be reduced if certain requirements are met. If the withholding tax rate applied is higher than the applicable final tax rate for the ADS holder, a request for a refund of Danish tax in excess hereof can be made by the ADS holder in the following situations:

Reduction according to a tax treaty

In the event that the ADS holder is a resident of a state with which Denmark has entered into a tax treaty, the holder may generally, through certain certification procedures, seek a refund from the Danish tax authorities of the tax withheld in excess of the applicable treaty rate, which is typically 15%. Denmark has entered into tax treaties with approximately 80 countries, including the United States and almost all members of the European Union. The tax treaty between Denmark and the United States generally provides for a 15% rate.

Companies residing in certain black-listed countries and holding Subsidiary Shares or Group Shares are not eligible for refund of dividend withholding taxes.

Reduction according to Danish tax law

If the ADS holder holds less than 10% of the nominal share capital (in the form of ordinary shares in the company and not on the basis of the number of the ADSs issued) in the company and the ADS holder is resident in a jurisdiction which has a tax treaty or an international agreement, convention or other administrative agreement on assistance in tax according to which the competent authority in the state of the ADS holder is obligated to exchange information with Denmark, dividends are generally subject to a tax rate of 15%. If the ADS holder is tax resident outside the European Union, it is an additional requirement for eligibility for the 15% tax rate that the ADS holder together with related ADS holders holds less than 10% of the nominal share capital of the company. Note that the reduced tax rate does not affect the withholding rate, hence, in this situation the ADS holder must also in this situation claim a refund as described above in order to benefit from the reduced rate.

Where a non-resident company of Denmark holds ADSs which can be attributed to a permanent establishment in Denmark, dividends are taxable pursuant to the rules applying to Danish tax residents described above. Companies residing in certain black-listed countries and holding Subsidiary Shares or Group Shares are not eligible for refund of dividend withholding taxes.

Share Transfer Tax and Stamp Duties

No Danish share transfer tax or stamp duties are payable on transfer of the shares.

Material U.S. Federal Income Tax Consequences to U.S. Holders

The following discussion describes the material U.S. federal income tax consequences to U.S. Holders (as defined below) under present law of an investment in the ADSs. The effects of any applicable state or local laws, or other U.S. federal tax laws such as estate and gift tax laws, any alternative minimum taxes, or the Medicare contribution tax on net investment income, are not discussed. This summary applies only to investors who hold the ADSs as capital assets (generally, property held for investment) and who have the U.S. dollar as their functional currency for U.S. federal income tax purposes. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, U.S. Treasury regulations promulgated thereunder, or the Treasury Regulations, judicial decisions, published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or the IRS, and the income tax treaty between the United States and Denmark, or the Treaty, all as in effect as of the date of this annual report. All of the foregoing authorities are subject to change, which change could apply retroactively and could affect the tax consequences described below.

The following discussion does not address all U.S. federal income tax consequences relevant to a U.S. Holder's particular circumstances or to U.S. Holders subject to particular rules, including:

- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons whose functional currency is not the U.S. dollar;
- persons holding the ADSs as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- real estate investment trusts or regulated investment companies;
- brokers, dealers or traders in securities, commodities or currencies;
- partnerships, S corporations or other entities or arrangements treated as partnerships or pass-through entities for U.S. federal income tax purposes, and persons that hold ADSs through such entities or arrangements;
- tax-exempt organizations, "individual retirement accounts" or "Roth IRAs";
- governmental organizations;
- persons who acquired the ADSs pursuant to the exercise of any employee share option or otherwise as compensation;
- persons that own or are deemed to own 10% or more of the company's equity by vote or value;
- persons that hold their ADSs through a permanent establishment or fixed base outside the United States; and
- persons deemed to sell the ADSs under the constructive sale provisions of the Code.

U.S. HOLDERS ARE URGED TO CONSULT THEIR TAX ADVISORS REGARDING THE APPLICATION OF THE U.S. FEDERAL INCOME TAX RULES TO THEIR PARTICULAR CIRCUMSTANCES AS WELL AS THE U.S. FEDERAL GIFT AND ESTATE AND U.S. STATE AND LOCAL AND NON-U.S. TAX CONSEQUENCES TO THEM OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF THE ADSs.

For purposes of this discussion, a "U.S. Holder" is a beneficial owner of the ADSs that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity taxable as a corporation, created or organized under the laws of the United States, any state thereof or the District of Columbia;

- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the supervision of a U.S. court and the control of one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code) or (2) has a valid election in effect under applicable Treasury Regulations to be treated as a United States person for U.S. federal income tax purposes.

If you are a partner in a partnership (or other entity or arrangement taxable as a partnership for U.S. federal income tax purposes) that holds the ADSs, your tax treatment generally will depend on your status and the activities of the partnership. Partnerships holding the ADSs and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences applicable to them.

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. Generally, a holder of an ADS should be treated for the U.S. federal income tax purposes as holding the ordinary shares represented by the ADS. Accordingly, no gain or loss will be recognized upon an exchange of ADSs for ordinary shares. The U.S. Treasury has expressed concerns that intermediaries in the chain of ownership between the holder of an ADS and the issuer of the security underlying the ADS may be taking actions that are inconsistent with the beneficial ownership of the underlying security. Accordingly, the creditability of foreign taxes, if any, as described below, could be affected by actions taken by intermediaries in the chain of ownership between the holders of ADSs and our company if as a result of such actions the holders of ADSs are not properly treated as beneficial owners of underlying ordinary shares.

Taxation of Dividends and Other Distributions on the ADSs

Subject to the passive foreign investment company, or PFIC, rules discussed below, the gross amount of any distribution to you with respect to the ADSs will be included in your gross income as dividend income when actually or constructively received to the extent that the distribution is paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). To the extent the amount of the distribution exceeds our current and accumulated earnings and profits, it will be treated first as a return of your tax basis in the ADSs, and to the extent the amount of the distribution exceeds your tax basis, the excess will be taxed as capital gain. However, we do not intend to calculate our earnings and profits under U.S. federal income tax principles. Therefore, a U.S. Holder should expect a distribution will generally be reported as ordinary dividend income for such purposes. Any dividends will not be eligible for the dividends-received deduction allowed to corporations in respect of dividends received from other U.S. corporations.

If we are eligible for benefits under the Treaty, or if the ADSs are readily tradable on an established securities market in the United States, dividends a U.S. Holder receives from us generally will be "qualified dividend income." If certain holding period and other requirements, including a requirement that we are not a PFIC in the year of the dividend or the immediately preceding year, are met, qualified dividend income of an individual or other non-corporate U.S. Holder generally will be subject to preferential tax rates. ADSs representing ordinary shares generally are considered for these purposes to be readily tradable on an established securities market in the United States if they are listed on The Nasdaq Global Select Market, as our ADSs currently are. You should consult your tax advisor regarding the availability of these preferential tax rates under your particular circumstances.

As discussed in "Item 10 E.—Taxation—Danish Tax Considerations," payments of dividends by us may be subject to Danish withholding tax. The rate of withholding tax applicable to U.S. Holders that are eligible for benefits under the Treaty is reduced to a maximum of 15%. For U.S. federal income tax purposes, U.S. Holders will be treated as having received the amount of withheld Danish taxes, and as then having paid over the withheld taxes to the Danish taxing authorities. As a result of this rule, the amount of dividend income included in gross income for U.S. federal income tax purposes by a U.S. Holder with respect to a payment of dividends may be greater than the amount of cash actually received (or receivable) by the U.S. Holder from us with respect to the payment.

Dividends will generally constitute foreign source income for foreign tax credit limitation purposes. Subject to the discussion of the PFIC rules below, any tax withheld with respect to distributions on the ADSs at the rate applicable to a U.S. Holder may, subject to a number of complex limitations, be claimed as a foreign tax credit against such U.S. Holder's U.S. federal income tax liability or may be claimed as a deduction for U.S. federal income tax purposes. Any amount withheld in excess of the tax rate applicable to a U.S. Holder generally is not eligible to be claimed as a foreign tax credit, regardless of whether such amount is actually refunded or reclaimed. The limitation on foreign taxes eligible for credit is calculated separately with respect to specific classes of income. For this purpose, dividends distributed by us with respect to the ADSs generally will constitute "passive category income." The rules with respect to the foreign tax credit are complex and involve the application of rules that depend upon a U.S. Holder's particular circumstances. Furthermore, recently issued Treasury Regulations have imposed additional requirements that must be met for a foreign tax to be creditable (including requirements that a "covered withholding tax" be imposed on nonresidents in lieu of a generally imposed tax that satisfies the regulatory definition of a "net income tax," which may be unclear or difficult to determine). You are urged to consult your tax advisor regarding the availability of the foreign tax credit under your particular circumstances.

Taxation of Disposition of the ADSs

Subject to the PFIC rules discussed below, you will recognize gain or loss on any sale, exchange or other taxable disposition of an ADS equal to the difference between the amount realized (in U.S. dollars) on the disposition of the ADS and your tax basis (in U.S. dollars) in the ADS. Any such gain or loss will be capital gain or loss, and will be long-term capital gain or loss if you have held the ADS for more than one year at the time of sale, exchange or other taxable disposition. Otherwise, such gain or loss will be short-term capital gain or loss. Long-term capital gains recognized by certain non-corporate U.S. Holders, including individuals, generally will be taxable at a reduced rate. The deductibility of capital losses is subject to limitations. Any such gain or loss you recognize generally will be treated as U.S.-source income or loss for foreign tax credit limitation purposes. You should consult your tax advisor regarding the proper treatment of gain or loss in your particular circumstances.

Passive Foreign Investment Company

Under the Code and Treasury Regulations, the determination of PFIC status is fact-specific and generally cannot be made until after the close of the taxable year in question. Based on our market capitalization and the composition of our income, assets and operations, we do not believe we were a PFIC for U.S. federal income tax purposes for our taxable year ended December 31, 2022. However this is a factual determination, and the application of the PFIC rules is subject to uncertainty in several respects, and we cannot assure you we will not be a PFIC for any taxable year. A non-U.S. corporation will be considered a PFIC for any taxable year if either:

- at least 75% of its gross income for such taxable year is passive income (as defined in the relevant provisions of the Code), or
- at least 50% of the value of its assets (generally based on an average of the quarterly values of the assets during such taxable year) is attributable to assets that produce or are held for the production of passive income.

For purposes of the above calculations, if a non-U.S. corporation owns, directly or indirectly, 25% or more of the total value of the outstanding shares of another corporation, it will be treated as if it (a) held a proportionate share of the assets of such other corporation and (b) received directly a proportionate share of the income of such other corporation. Passive income generally includes dividends, interest, rents, royalties and capital gains, but generally excludes rents and royalties which are derived in the active conduct of a trade or business and which are received from a person other than a related person.

A separate determination must be made each taxable year as to whether we are a PFIC (after the close of each such taxable year). Because the value of our assets, including unbooked goodwill, for purposes of the asset test will generally be determined by reference to the market price of the ADSs, our PFIC status will depend in large part on the market price of the ADSs, which may fluctuate significantly. In addition, changes in the composition of our income or assets may cause us to become a PFIC. For these reasons, we cannot assure you we will not be a PFIC for any taxable year.

If we are a PFIC for any year during which you hold the ADSs, we generally will continue to be treated as a PFIC with respect to you for all succeeding years during which you hold the ADSs, regardless of whether we continue to meet the income or asset tests described above, unless we cease to be a PFIC and you make a "deemed sale" election with respect to the ADSs you hold. If such election is made, you will be deemed to have sold the ADSs you hold at their fair market value on the last day of the last taxable year in which we qualified as a PFIC, and any gain from such deemed sale would be subject to the consequences described below. After the deemed sale election, the ADSs with respect to which the deemed sale election was made will not be treated as shares in a PFIC unless we subsequently become a PFIC.

For each taxable year we are treated as a PFIC with respect to you, you will be subject to special tax rules with respect to any "excess distribution" (as defined below) you receive and any gain you realize from a sale or other disposition (including a pledge) of the ADSs, unless you make a "mark-to-market" election as discussed below. Distributions you receive in a taxable year that are greater than 125% of the average annual distributions you received during the shorter of the three preceding taxable years or your holding period for the ADSs will be treated as an "excess distribution." Under these special tax rules, if you receive any "excess distribution" or realize any gain from a sale or other disposition of the ADSs:

- the "excess distribution" or gain will be allocated ratably over your holding period for the ADSs,
- the amount allocated to the current taxable year, and any taxable year before the first taxable year in your holding period in which we were a PFIC, will be treated as ordinary income, and
- the amount allocated to each other year will be subject to the highest income 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.

Gains (but not losses) realized on the sale of the ADSs cannot be treated as capital gains, even if you hold the ADSs as capital assets.

If we are treated as a PFIC with respect to you for any taxable year, to the extent we own directly or indirectly equity in any non-U.S. corporations that are also PFICs, you will be deemed to own your proportionate share of any such lower-tier PFIC, and you may be subject to the rules described in the preceding two paragraphs with respect to the shares of such lower-tier PFICs you would be deemed to own. As a result, you may incur liability for any "excess distribution" described above if we receive a distribution from such lower-tier PFICs or if any shares in such lower-tier PFICs are disposed of (or deemed disposed of). You should consult your tax advisor regarding the application of the PFIC rules to any lower-tier PFICs.

Alternatively, a U.S. Holder of "marketable stock" (as defined below) in a PFIC may make a "mark-to-market" election for such stock to elect out of the general tax treatment for PFICs discussed above. If you make a "mark-to-market" election for the ADSs, you will include in income for each year we are a PFIC an amount equal to the excess, if any, of the fair market value of the ADSs as of the close of your taxable year over your adjusted basis in such ADSs. You are allowed a deduction for the excess, if any, of the adjusted basis of the ADSs over their fair market value as of the close of the taxable year. However, deductions are allowable only to the extent of any net "mark-to-market" gains on the ADSs included in your income for prior taxable years. Amounts included in your income under a "mark-to-market" election, as well as gain on the actual sale or other disposition of the ADSs, are treated as ordinary income. Ordinary loss treatment also applies to the deductible portion of any "mark-to-market" loss on the ADSs, as well as to any loss realized on the actual sale or disposition of the ADSs to the extent the amount of such loss does not exceed the net "mark-to-market" gains previously included for the ADSs. Your basis in the ADSs will be adjusted to reflect any such income or loss amounts. If you make a valid "mark-to-market" election, the tax rules that apply to distributions by corporations that are not PFICs would apply to distributions by us, except the lower applicable tax rate for qualified dividend income would not apply. If we cease to be a PFIC when you have a "mark-to-market" election in effect, gain or loss realized by you on the sale of the ADSs will be a capital gain or loss and taxed in the manner described above under "Taxation of Disposition of the ADSs."

The "mark-to-market" election is available only for "marketable stock," which is stock that is traded in other than de minimis quantities on at least 15 days during each calendar quarter, or regularly traded, on a qualified exchange or other market, as defined in applicable Treasury Regulations. Any trades that have as their principal purpose meeting this requirement will be disregarded. The ADSs are listed on The Nasdaq Global Select Market and, accordingly, provided the ADSs are regularly traded, if you are a holder of ADSs, the "mark-to-market" election would be available to you if we are a PFIC. Once made, the election cannot be revoked without the consent of the IRS unless the ADSs cease to be "marketable stock." If we are a PFIC for any year in which the U.S. Holder owns ADSs but before a "mark-to-market" election is made, the interest charge rules described above will apply to any "mark-to-market" gain recognized in the year the election is made. The "mark-to-market" election may not be available with respect to the shares of lower-tier PFICs that are treated as owned by you. Consequently, you could be subject to the PFIC rules with respect to income of the lower-tier PFICs the value of which already had been taken into account indirectly via "mark-to-market" adjustments. A U.S. Holder should consult its tax advisors as to the availability and desirability of a "mark-to-market" election, as well as the impact of such election on interests in any lower-tier PFICs.

In certain circumstances, a U.S. Holder of stock in a PFIC can make a "qualified electing fund election" to mitigate some of the adverse tax consequences of holding stock in a PFIC by including in income its share of the corporation's income on a current basis. However, we do not currently intend to prepare or provide the information that would enable you to make a "qualified electing fund election."

Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to file an annual report containing such information as the U.S. Treasury may require. A U.S. Holder's failure to file the annual report will cause the statute of limitations for such U.S. Holder's U.S. federal income tax return to remain open with regard to the items required to be included in such report until three years after the U.S. Holder files the annual report, and, unless such failure is due to reasonable cause and not willful neglect, the statute of limitations for the U.S. Holder's entire U.S. federal income tax return will remain open during such period. U.S. Holders should consult their tax advisors regarding the requirements of filing such information returns under these rules, taking into account the uncertainty as to whether we are currently treated as or may become a PFIC.

YOU ARE STRONGLY URGED TO CONSULT YOUR TAX ADVISOR REGARDING THE APPLICATION OF THE PFIC RULES TO YOUR INVESTMENT IN THE ADSs.

Information Reporting and Backup Withholding

Distributions with respect to the ADSs and proceeds from the sale, exchange or other disposition of the ADSs may be subject to information reporting to the IRS and U.S. backup withholding. Certain U.S. Holders are exempt from backup withholding, including corporations and certain tax-exempt organizations. A U.S. Holder will be subject to backup withholding if such holder is not otherwise exempt and such holder:

- fails to furnish the holder's taxpayer identification number, which for an individual is ordinarily his or her social security number;
- furnishes an incorrect taxpayer identification number;
- is notified by the IRS that the holder previously failed to properly report payments of interest or dividends; or
- fails to certify under penalties of perjury that the holder has furnished a correct taxpayer identification number and that the IRS has not notified the holder that the holder is subject to backup withholding.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against the U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS. U.S. Holders should consult their tax advisors regarding their qualification for an exemption from backup withholding and the procedures for obtaining such an exemption.

Additional Reporting Requirements

Tax return disclosure obligations (and related penalties for failure to disclose) apply to certain U.S. Holders who hold certain specified foreign financial assets in excess of certain thresholds. The definition of specified foreign financial assets includes not only financial accounts maintained in foreign financial institutions, but also may include the ADSs. U.S. Holders should consult their tax advisors regarding the possible implications of these tax return disclosure obligations.

F. Dividends and Paying Agents

Not applicable.

G. Statements by Experts

Not applicable.

H. Documents on Display

We are subject to the periodic reporting and other informational requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Under the Exchange Act, we are required to file reports and other information with the SEC. Specifically, we are required to file annually a Form 20-F no later than four months after the close of each fiscal year, which is December 31. The SEC maintains a web site at www.sec.gov that contains reports, proxy and information statements, and other information regarding registrants that make electronic filings with the SEC using its EDGAR system. As a foreign private issuer, we are exempt from the rules under the Exchange Act prescribing the furnishing and content of quarterly reports and proxy statements, and officers, directors and major shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act.

I. Subsidiary Information

Not applicable.

J. Annual Report to Security Holders

The Company intends to submit any annual report provided to security holders in electronic format as an exhibit to a current report on Form 6-K.

Item 11 Quantitative and Qualitative Disclosures About Market Risk

See "Item 5 A. Operating and Financial Review and Prospects—Operating Results—Quantitative and Qualitative Disclosures about Market Risk."

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.

The Bank of New York Mellon, as depositary, registers and delivers American Depositary Shares, also referred to as ADSs. Each ADS represents one ordinary share (or a right to receive one ordinary share) deposited with The Bank of New York Mellon, London Branch, or any successor, as custodian for the depositary. Each ADS also represents any other securities, cash or other property which may be held by the depositary in respect of the depositary facility. The depositary's corporate trust office at which the ADSs are administered and its principal executive office is located at 240 Greenwich Street, New York, New York 10286.

A deposit agreement among us, the depositary and you the ADS holders sets out ADS holder rights as well as the rights and obligations of the depositary. A copy of the deposit agreement is incorporated by reference as an exhibit to this annual report.

Fees and Expenses

Pursuant to the terms of the deposit agreement, the holders of ADSs will be required to pay the following fees:

Persons depositing or withdrawing ordinary shares or ADSs must pay:	***For:***
$5.00 (or less) per 100 ADSs (or portion of 100 ADSs)	• Issue of ADSs, including issues resulting from a distribution of ordinary shares or rights or other property • Cancellation of ADSs for the purpose of withdrawal, including if the deposit agreement terminates
$0.05 (or less) per ADS	• Any cash distribution to you
A fee equivalent to the fee that would be payable if securities distributed to you had been ordinary shares and the shares had been deposited for issue of ADSs	• Distribution of securities distributed to holders of deposited securities which are distributed by the depositary to you
$0.05 (or less) per ADS per calendar year	• Depositary services
Registration or transfer fees	• Transfer and registration of ordinary 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 have to pay on any ADS or share underlying an ADS, for example, share 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 ordinary 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 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 to ADS holders that are obligated to pay those fees. The depositary may generally refuse to provide for-fee services until its fees for those services are paid.

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

PART II

Item 13 Defaults, Dividend Arrearages and Delinquencies

Not applicable.

Item 14 Material Modification to the Rights of Security Holders and Use of Proceeds

A. Material Modifications to the Rights of Securities Holders

Not applicable.

B. Use of Proceeds

Not applicable.

Item 15 Control and Procedures

A. Disclosure Controls and Procedures

Our chief executive officer and principal financial and accounting officers, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act) as of December 31, 2022, have concluded that based on the evaluation of these controls and procedures required by Rule 13a-15(b) of the Exchange Act, our disclosure controls and procedures were effective.

B. Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting.

Internal control over financial reporting is defined in rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the Company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the Company's assets that could have a material effect on the audited consolidated financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect material misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022. This assessment was performed under the directions and supervision of our Chief Executive Officer and our principal financial and accounting officers and based on the criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations (COSO) of the Treadway Commission.

A material weakness is a control deficiency, or a combination of control deficiencies in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected. These control deficiencies could result in a misstatement of the financial statement accounts or related disclosures that would result in a material misstatement in the annual or interim consolidated financial statements that would not be prevented or detected on a timely basis. Based on management's assessment of those criteria, management has concluded that the design and operating effectiveness of our internal control over financial reporting was effective as of December 31, 2022.

The effectiveness of the Company's internal control over financial reporting has been audited by Deloitte Statsautoriseret Revisionspartnerselskab, our independent registered public accounting firm, as stated in their report on the Company's financial statements and internal control over financial reporting as of December 31, 2022, which is included under Item 18 below.

C. Attestation Report of the Registered Public Accounting Firm

The effectiveness of our internal control over financial reporting as of December 31, 2022 has been audited by Deloitte Statsautoriseret Revisionspartnerselskab, an independent registered public accounting firm, as stated in their report, which appears in Item 18 below.

D. Changes in Internal Control over Financial Reporting

During the year ended December 31, 2022, the Company has implemented new processes and controls related to convertible notes and derivative liabilities, following the financing completed in March 2022. There has been no other changes in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) that occurred during the period covered by this annual report that has materially affected, or is reasonably likely to materially affect, internal control over financial reporting.

Item 16A Audit Committee Financial Expert

Mr. Lars Holtug, an independent director under Nasdaq Rule 5605(a)(2) and Rule 10A-3 of the Exchange Act and a member of the Audit Committee, qualifies as an "audit committee financial expert," as defined in Item 16A(b) of Form 20-F and as determined by our board of directors.

Item 16B Code of Ethics

We have adopted a code of business conduct and ethics that applies to all of our employees, members of our senior management and members of our board of directors, including those members of our senior management responsible for financial reporting. Our code of ethics is posted on our Company website at: http://www.ascendispharma.com. We will disclose any substantive amendments to the code of business conduct and ethics, or any waiver of its provisions, on our website. The reference to our website does not constitute incorporation by reference of the information contained at or available through our website.

Item 16C Principal Accountant Fees and Services

The following table sets forth, for each of the years indicated, the fees billed by our independent public accountants and the percentage of each of the fees out of the total amount billed by the accountants.

	Year ended December 31, 2022		Year ended December 31, 2021	
	EUR'000	%	EUR'000	%
Audit Fees	814	85	771	89
Tax Fees	138	15	87	10
All Other Fees	—	—	13	1
Total	**952**	**100**	**871**	**100**

Audit Fees are defined as the standard audit work that needs to be performed each year to issue opinions on our consolidated financial statements and to issue reports on our local statutory financial statements. Also included are services that can only be provided by our auditor, such as reviews of quarterly financial results, consents and comfort letters and any other audit services required for SEC or other regulatory filings.

Audit Related Fees include those other assurance services provided by the independent auditor but not restricted to those that can only be provided by the auditor signing the audit report.

Tax Fees relate to the aggregate fees billed in each of the last two fiscal years for professional services rendered by the principal accountant for tax compliance, tax advice, and tax planning.

All Other Fees are any additional amounts billed for products and services provided by the principal accountant.

Pre-Approval Policies and Procedures for Non-Audit Services

Our Audit Committee has adopted a policy pursuant to which we will not engage our auditors to perform any non-audit services unless the audit committee pre-approves the service.

Item 16D Exemptions from the Listing Standards for Audit Committees

Not applicable.

Item 16E Purchases of Equity Securities by the Issuer and Affiliated Purchasers

In connection with the issuance of an aggregate principal amount of $575.0 million of fixed rate 2.25% convertible notes, we used $116.7 million (€105.3 million) of the net proceeds to repurchase 1,000,000 ADSs representing the Company's ordinary shares. Total holding of treasury shares is disclosed in Note 16, "Financial Risk Management".

The table below is a summary of the shares repurchased by us during the 2022 fiscal year. All ADSs were repurchased pursuant to the before mentioned convertible notes issuance.

Date	Total Number of ADSs Purchased	Weighted Average Price Paid per ADS (US$)*	Total Number of ADSs Purchased as Part of Publicly Announced Programs	Maximum Number of Shares that May Yet Be Purchased Under the Plans or Programs
March 25, 2022	1,000,000	$ 116.70	—	—

* Total value includes fees and costs associated with the repurchases.

Item 16F Change in Registrants Certifying Accountant

None.

Item 16G Corporate Governance

The Sarbanes-Oxley Act of 2002, as well as related rules subsequently implemented by the SEC, requires foreign private issuers, including our Company, to comply with various corporate governance practices. In addition, Nasdaq rules provide that foreign private issuers may follow home country practice in lieu of the Nasdaq corporate governance standards, subject to certain exceptions and except to the extent that such exemptions would be contrary to U.S. federal securities laws. In addition to the home country practices described under "Item 6 C. Directors, Senior Management and Employees—Board Practices", the home country practices followed by our Company in lieu of Nasdaq rules are described below:

- We do not intend to follow Nasdaq's quorum requirements applicable to meetings of shareholders. In accordance with Danish corporate law and generally accepted business practice, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders.
- We do not intend to follow Nasdaq's requirements regarding the provision of proxy statements for general meetings of shareholders. Danish corporate law does not have a regulatory regime for the solicitation of proxies and the solicitation of proxies is not a generally accepted business practice in Denmark. We do intend to provide shareholders with an agenda and other relevant documents for the general meeting of shareholders.
- We do not intend to follow Nasdaq's requirements regarding shareholder approval for certain issuances of securities under Nasdaq Rule 5635. Pursuant to Danish corporate law, our shareholders have authorized our board of directors to issue securities including in connection with certain events such as the acquisition of shares or assets of another company, the establishment of or amendments to equity-based compensation plans for employees, a change of control of us, rights issues at or below market price, certain private placements and issuance of convertible notes. 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 of 2002, the rules adopted by the SEC and Nasdaq's listing standards. As a Danish company not listed on a regulated market within the EU/EEA, we do not need to comply with the Danish corporate governance principles nor do we need to explain any deviation from these provisions in our Danish statutory annual report.
- We do not intend to follow Nasdaq's requirements regarding shareholder approval for all equity compensation plans. Generally, Nasdaq Rule 5635(c) requires each issuer to obtain shareholder approval of all equity compensation plans (including warrant incentive plans) and material amendments to such plans. However, pursuant to Nasdaq Rule 5615(a)(3), we have elected to follow our home country's practices (in this case, being Danish practices) in lieu of the requirements of Nasdaq Rule 5635(c). Our home country practices do not require us to obtain a shareholders' approval for amendments to our existing warrant incentive program.

Because we are a foreign private issuer, our members of our board of directors, executive board members and senior management are not subject to short-swing profit and insider trading reporting obligations under section 16 of the U.S. Securities Exchange Act of 1934, as amended, or the Exchange Act. They will, however, be subject to the obligations to report changes in share ownership under section 13 of the Exchange Act and related SEC rules.

Item 16H Mine Safety Disclosure

Not applicable.

Item 16I Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 17 Financial Statements

See “Item 18 Financial Statements.”

Item 18 Financial Statements

ASCENDIS PHARMA A/S

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and Board of Directors of Ascendis Pharma A/S

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated statements of financial position of Ascendis Pharma A/S and subsidiaries (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of profit or loss and other comprehensive income, the consolidated statements of changes in equity, and the consolidated cash flow statements for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board. Also, in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by COSO.

Basis for Opinions

The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on these financial statements and an opinion on the Company's internal control over financial reporting 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 audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the financial statements included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures to 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. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting

includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current-period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Derivative liabilities – Refer to Notes 2, 3 and 15 to the financial statements

Critical Audit Matter Description

In March 2022, the Company issued convertible senior notes, which were separated into a financial liability and an embedded derivative component on initial recognition. The financial liability is presented as part of Borrowings on the statement of financial position and accounted for at amortized cost. The embedded derivative component has been accounted for separately as it is deemed not closely related to the financial liability and is presented under Derivative liabilities in the statement of financial position. The embedded derivative component is measured at fair value, which requires the Company to make significant estimates regarding the determination of fair value. In measuring the fair value of the embedded derivative component, the Black-Scholes option pricing model is used, incorporating observable inputs and an assumption for expected volatility. As of December 31, 2022, the derivative liabilities totaled EUR 158 million.

We identified *Derivative liabilities* as a critical audit matter due to the judgment related to the initial and subsequent valuation of the embedded derivative component. Significant audit effort was required to audit the valuation of the embedded derivative component, including involvement of specialists.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to derivatives liabilities included the following, among others:

- We tested the effectiveness of controls over valuation of derivative liabilities;
- We obtained and read the purchase agreement and offering memorandum to understand the details of the transaction;
- We evaluated the accounting treatment of the derivative liabilities;
- We evaluated the valuation techniques used for the derivative liabilities;
- We traced the information from the purchase agreement and offering memorandum to the inputs used in the Company's calculations of the derivative liabilities;
- We traced the external inputs used in the Company's calculations of the derivative liabilities to reliable independent sources;

- We tested the mathematical accuracy of the Company's calculations of the derivative liabilities;
- We involved our internal fair value specialists to independently calculate the fair value and assess the reasonableness of the valuation assumptions of the derivative liabilities at initial recognition and at year-end.

/s/ Deloitte Statsautoriseret Revisionspartnerselskab

Copenhagen, Denmark

February 16, 2023

We have served as the Company's auditor since 2007.

Consolidated Statements of Profit or Loss and Other Comprehensive Income for the Years Ended December 31

	Notes	2022	2021	2020
			(EUR'000)	
Consolidated Statement of Profit or Loss				
Revenue	**4**	51,174	7,778	6,953
Cost of sales	**6, 11**	12,137	3,523	—
Gross profit		**39,037**	**4,255**	**6,953**
Research and development costs	**6, 11**	379,624	295,867	260,904
Selling, general and administrative expenses	**6, 11**	221,227	160,180	76,669
Operating profit/(loss)		**(561,814)**	**(451,792)**	**(330,620)**
Share of profit/(loss) of associate	**12**	(17,697)	12,041	(9,524)
Finance income	**15**	52,181	59,718	1,812
Finance expenses	**15**	50,487	3,911	80,842
Profit/(loss) before tax		**(577,817)**	**(383,944)**	**(419,174)**
Tax on profit/(loss) for the year	**9**	(5,377)	367	219
Net profit/(loss) for the year		**(583,194)**	**(383,577)**	**(418,955)**
Attributable to owners of the Company		(583,194)	(383,577)	(418,955)
Basic and diluted earnings/(loss) per share		€ (10.40)	€ (7.00)	€ (8.28)
Weighted average number of shares used for calculation (basic and diluted) [(1)]		56,071,793	54,771,763	50,616,528
			(EUR'000)	
Consolidated Statement of Comprehensive Income				
Net profit/(loss) for the year		**(583,194)**	**(383,577)**	**(418,955)**
Other comprehensive income/(loss)				
Items that may be reclassified subsequently to profit or loss:				
Exchange differences on translating foreign operations		(327)	3,855	(42)
Other comprehensive income/(loss) for the year, net of tax		**(327)**	**3,855**	**(42)**
Total comprehensive income/(loss) for the year, net of tax		**(583,521)**	**(379,722)**	**(418,997)**
Attributable to owners of the Company		**(583,521)**	**(379,722)**	**(418,997)**

(1) A total of 6,864,011 warrants outstanding as of December 31, 2022 (a total of 7,085,073 warrants and 6,148,004 warrants outstanding as of December 31, 2021 and 2020, respectively) can potentially dilute earnings per share in the future but have not been included in the calculation of diluted earnings per share because they are antidilutive for the periods presented. Similarly, 575,000 convertible senior notes which can potentially be converted into 3,456,785 ordinary shares, can potentially dilute earnings per share in the future but have not been included in the calculation of diluted earnings per share because they are antidilutive for 2022.

Consolidated Statements of Financial Position as of December 31,

	Notes	2022	2021
		(EUR'000)	
Assets			
Non-current assets			
Intangible assets	**5, 10**	4,828	5,272
Property, plant and equipment	**5, 11**	129,095	126,049
Investment in associate	**12**	22,932	38,345
Other receivables	**15**	1,920	1,808
Marketable securities	**15, 16**	7,492	107,561
		166,267	**279,035**
Current assets			
Inventories	**13**	130,673	75,405
Trade receivables	**15**	11,910	2,200
Income tax receivables		883	893
Other receivables	**15**	12,833	20,093
Prepayments		31,717	25,231
Marketable securities	**15, 16**	290,688	235,797
Cash and cash equivalents	**15, 16**	444,767	446,267
		923,471	**805,886**
Total assets		**1,089,738**	**1,084,921**
Equity and liabilities			
Equity			
Share capital	**16**	7,675	7,646
Distributable equity		255,673	875,989
Total equity		**263,348**	**883,635**
Non-current liabilities			
Borrowings	**15, 16**	482,956	97,966
Derivative liabilities	**15, 16**	157,950	—
Contract liabilities	**14**	14,213	2,964
		655,119	**100,930**
Current liabilities			
Borrowings	**15, 16**	25,421	6,995
Contract liabilities	**14**	—	2,601
Trade payables and accrued expenses	**15, 16**	101,032	59,417
Other liabilities		31,989	29,952
Income tax payables		5,490	198
Provisions		7,339	1,193
		171,271	**100,356**
Total liabilities		**826,390**	**201,286**
Total equity and liabilities		**1,089,738**	**1,084,921**

Consolidated Statements of Changes in Equity

		Distributable Equity				
	Share Capital	Share Premium	Treasury shares	Foreign Currency Translation Reserve	Accumulated Deficit	Total
			(EUR '000)			
Equity at January 1, 2020	**6,443**	**1,122,097**	**—**	**(34)**	**(531,392)**	**597,114**
Net profit / (loss) for the period	—	—	—	—	(418,955)	**(418,955)**
Other comprehensive income/(loss), net of tax	—	—	—	(42)	—	**(42)**
Total comprehensive income/(loss)	**—**	**—**	**—**	**(42)**	**(418,955)**	**(418,997)**
Transactions with Owners						
Share-based payment (Note 7)	—	—	—	—	53,170	**53,170**
Capital increase	774	638,023	—	—	—	**638,797**
Cost of capital increase	—	(31,373)	—	—	—	**(31,373)**
Equity at December 31, 2020	**7,217**	**1,728,747**	**—**	**(76)**	**(897,177)**	**838,711**
Net profit / (loss) for the period	—	—	—	—	(383,577)	**(383,577)**
Other comprehensive income/(loss), net of tax	—	—	—	3,855	—	**3,855**
Total comprehensive income/(loss)	**—**	**—**	**—**	**3,855**	**(383,577)**	**(379,722)**
Transactions with Owners						
Share-based payment (Note 7)	—	—	—	—	66,830	**66,830**
Acquisition of treasury shares	—	—	(21)	—	(21,584)	**(21,605)**
Capital increase	429	398,966	—	—	—	**399,395**
Cost of capital increase	—	(19,974)	—	—	—	**(19,974)**
Equity at December 31, 2021	**7,646**	**2,107,739**	**(21)**	**3,779**	**(1,235,508)**	**883,635**
Net profit / (loss) for the period	—	—	—	—	(583,194)	**(583,194)**
Other comprehensive income/(loss), net of tax	—	—	—	(327)	—	**(327)**
Total comprehensive income/(loss)	**—**	**—**	**—**	**(327)**	**(583,194)**	**(583,521)**
Transactions with Owners						
Share-based payment (Note 7)	—	—	—	—	64,180	**64,180**
Acquisition of treasury shares	—	—	(134)	—	(105,965)	**(106,099)**
Transfer under stock incentive programs			6		(6)	**—**
Capital increase	29	5,124	—	—	—	**5,153**
Equity at December 31, 2022	**7,675**	**2,112,863**	**(149)**	**3,452**	**(1,860,493)**	**263,348**

Consolidated Cash Flow Statements for the year Ended December 31

	Notes	2022	2021	2020
			(EUR'000)	
Operating activities				
Net profit/(loss) for the year		**(583,194)**	**(383,577)**	**(418,955)**
Reversal of finance income		(52,181)	(59,718)	(1,812)
Reversal of finance expenses		50,487	3,911	80,842
Reversal of gain and loss on disposal of property, plant and equipment		22	—	—
Reversal of tax charge		5,377	(367)	(219)
Increase/(decrease) in provisions		6,145	1,193	—
Adjustments for non-cash items:				
Non-cash consideration relating to revenue		(2,547)	(2,365)	(3,499)
Share of profit/(loss) of associate		17,697	(12,041)	9,524
Share-based payment		64,180	66,830	53,170
Depreciation		17,514	14,946	9,448
Amortization		444	445	—
Changes in working capital:				
Inventories		(55,268)	(75,405)	—
Receivables		(11,531)	(6,659)	(1,996)
Prepayments		(6,409)	(11,238)	(6,357)
Contract liabilities (deferred income)		8,648	5,202	(495)
Trade payables, accrued expenses and other payables		45,943	39,186	7,884
Cash flows generated from/(used in) operations		**(494,673)**	**(419,657)**	**(272,465)**
Finance income received		8,271	3,697	1,326
Finance expenses paid		(9,294)	(1,841)	(1,504)
Income taxes received/(paid)		(3)	152	1,095
Cash flows from/(used in) operating activities		**(495,699)**	**(417,649)**	**(271,548)**
Investing activities				
Investment in associate		—	(10,187)	—
Acquisition of property, plant and equipment		(14,489)	(23,704)	(19,860)
Reimbursement for acquisition of property, plant and equipment		9,535	—	5,054
Development expenditures (software)		—	(530)	(1,692)
Purchase of marketable securities		(213,842)	(226,038)	(537,752)
Settlement of marketable securities		280,528	149,880	263,051
Cash flows from/(used in) investing activities		**61,732**	**(110,579)**	**(291,199)**
Financing activities				
Payment of principal portion of lease liabilities		(6,356)	(6,429)	(4,774)
Net proceeds from convertible senior notes		503,281	—	—
Proceeds from exercise of warrants		5,153	11,537	26,882
Net proceeds from follow-on public offerings		—	367,884	580,542
Acquisitions of treasury shares, net of transactions costs		(105,305)	(21,605)	—
Cash flows from/(used in) financing activities		**396,773**	**351,387**	**602,650**
Increase/(decrease) in cash and cash equivalents		**(37,194)**	**(176,841)**	**39,903**
Cash and cash equivalents at January 1		446,267	584,517	598,106
Effect of exchange rate changes on balances held in foreign currencies		35,694	38,591	(53,492)
Cash and cash equivalents at December 31		**444,767**	**446,267**	**584,517**
Cash and cash equivalents include:				
Bank deposits		427,810	441,736	581,872
Short-term marketable securities		16,957	4,531	2,645
Cash and cash equivalents at December 31		**444,767**	**446,267**	**584,517**

Note 1—General Information

Ascendis Pharma A/S, together with its subsidiaries, is applying its innovative TransCon technologies to build a leading, fully integrated, global biopharma company. Ascendis Pharma A/S was incorporated in 2006 and is headquartered in Hellerup, Denmark. Unless the context otherwise requires, references to the "Company," "we," "us," and "our," refer to Ascendis Pharma A/S and its subsidiaries.

The address of the Company's registered office is Tuborg Boulevard 12, DK-2900 Hellerup, Denmark. The Company's registration number in Denmark is 29918791.

On February 2, 2015, the Company completed an initial public offering ("IPO"), which resulted in the listing of American Depositary Shares ("ADSs"), representing the Company's ordinary shares, under the symbol "ASND" in the United States on The Nasdaq Global Select Market.

The Company's Board of Directors approved these consolidated financial statements on February 16, 2023.

Note 2—Summary of Significant Accounting Policies

Basis of Preparation

The consolidated financial statements are prepared in accordance with the International Financial Reporting Standards ("IFRS"), as issued by the International Accounting Standards Board ("IASB"), and as adopted by the European Union (the "EU").

The accounting policies applied when preparing the consolidated financial statements are described in detail below and are applied for all entities. Significant accounting judgements and sources of estimation uncertainties used when exercising the accounting policies are described in Note 3 "Significant Accounting Judgements and Estimates".

These consolidated financial statements have been prepared under the historical cost convention, apart from certain financial instruments that are measured at fair value at initial recognition.

Changes in Accounting Policies and Disclosures

Several amendments to and interpretations of IFRS applied for the first time in 2022, which has not had an impact on the accounting policies applied by the Company. Thus, the accounting policies applied when preparing these consolidated financial statements have been applied consistently to all the periods presented.

Presentation of Distributable Equity Reserves

For the financial year ended December 31, 2020, and 2021, the "Share-based Payment Reserve" amounted to €133.1 million and €199.9 million, respectively, and was presented as a separate reserve within "Distributable Equity" in the consolidated statements of changes in equity, comprising accumulated corresponding entries to the share-based payment expense recognized in the consolidated statement of profit or loss, arising from warrant programs and RSU programs. For the financial year ended December 31, 2022, the "Share-based Payment Reserve" is presented as part of accumulated deficit.

For the financial year ended December 31, 2021, the "Treasury Shares Reserve" amounted to €21.6 million, and was presented as a separate reserve within "Distributable Equity" in the consolidated statements of changes in equity, comprising total costs of treasury shares acquired. For the financial year ended December 31, 2022, the "Treasury Shares Reserve" represents only the nominal amount of treasury shares acquired, whereas the treasury shares premium is presented as part of accumulated deficit. At December 31, 2021, nominal amount of treasury shares amounted to €0.02 million.

We have decided to change the presentation to simplify and rationalize disclosure in the consolidated financial statements. Comparative figures in the consolidated statements of changes in equity have been reclassified to reflect the change in presentations. The change in presentations had no other impact on the consolidated financial statements.

Going Concern

The Company's Board of Directors has at the time of approving the consolidated financial statements, a reasonable expectation that the Company has adequate resources to continue in operational existence for the foreseeable future. Thus, the Company continues to adopt the going concern basis of accounting in preparing the consolidated financial statements.

Basis of Consolidation

The consolidated financial statements include the parent company, Ascendis Pharma A/S, and all enterprises over which the parent company has control. Control of an enterprise exists when the Company has exposure, or rights to, variable returns from its involvement with the enterprise and has the ability to control those returns through its power over the enterprise. Accordingly, the consolidated financial statements include Ascendis Pharma A/S and the subsidiaries listed in Note 19, "Investment in Group Enterprises".

Consolidation Principles

Subsidiaries, which are enterprises the Company controls at the reporting date, are fully consolidated from the date upon which control is transferred to the Company. They are deconsolidated from the date control ceases.

Control over an enterprise is reassessed if facts and circumstances indicate that there are changes to one or more of the three elements of control, respectively:

- the contractual arrangement(s) with the other vote holders of the enterprise;
- the Company's voting rights and potential voting rights; and
- rights arising from other contractual arrangements.

All intra-group assets and liabilities, equity, income, expenses and cash flows relating to transactions between group enterprises are eliminated in full on consolidation.

Subsidiaries apply accounting policies in line with the Company's accounting policies. When necessary, adjustments are made to bring the entities' accounting policies in line with those of the Company.

Investment in Associates

An associate is an entity over which the Company has significant influence over financial and operational decisions but without having control or joint control. The Company's associate is accounted for using the equity method and is initially recognized at cost. Thereafter, the carrying amount of the investment is adjusted to recognize changes in the Company's share of net assets of the associate since the acquisition or establishment date.

The consolidated statements of profit or loss include the Company's share of result after tax of the associate after any adjustments made to bring the associates accounting policies in line with those of the Company. Transactions between the associate and the Company are eliminated proportionally according to the Company's interest in the associate. Unrealized gains and losses resulting from transactions between the Company and its associate is eliminated to the extent of the Company's interest in the associate.

On each reporting date, the Company determines whether there are indications that the investment is impaired. If there is such evidence, the amount of impairment is calculated as the difference between the recoverable amount of the associate and its carrying amount. Any impairment loss is recognized in the consolidated statements of profit or loss.

Foreign Currency

Functional and Presentation Currency

Items included in the consolidated financial statements are measured using the functional currency of each group entity. Functional currency is the currency of the primary economic environment in which the entity operates. The consolidated financial statements are presented in Euros ("EUR"), which is also the functional currency of the parent company.

Translation of Transactions and Balances

On initial recognition, transactions in currencies other than the individual entity's functional currency are translated applying the exchange rate in effect at the date of the transaction. Receivables, payables and other monetary items denominated in foreign currencies that have not been settled at the reporting date are translated using the exchange rate in effect at the reporting date. Monetary items carried at fair value that are denominated in foreign currencies are translated at the rates prevailing at the date when the fair value was determined.

Exchange rate differences that arise between the rate at the transaction date and the rate in effect at the payment date, or the rate at the reporting date, are recognized in profit or loss as finance income or finance expenses. Property, plant and equipment, intangible assets and other non-monetary items that are measured in terms of historical cost in a foreign currency are translated using the exchange rates as of the dates of the initial transactions.

Currency Translation of Group Enterprises

When subsidiaries or the associate present their financial statements in a functional currency other than EUR, their statements of profit or loss are translated at average exchange rates. Balance sheet items are translated using the exchange rates at the reporting date. Exchange rate differences arising from translation of foreign entities' balance sheet items at the beginning of the year to the reporting date exchange rates as well as from translation of statements of profit or loss from average rates to the exchange rates at the reporting date are recognized in other comprehensive income. Similarly, exchange rate differences arising from changes that have been made directly in a foreign subsidiary's equity are recognized in other comprehensive income.

Revenue

Revenue from Commercial Sale of Products

Revenue is recognized when the customer has obtained control of the goods and it is probable that the Company will collect the consideration to which it is entitled for transferring the goods. Control is transferred upon delivery.

Revenue is measured at the contractual sales price, reflecting the consideration received or receivable from customers, net of value added taxes, and provisions for a variety of sales deductions such as prompt pay discounts, shelf stock adjustments and applicable sales rebates attributable to various commercial arrangements, managed healthcare organizations, and government programs such as Medicaid and the 340B Drug Pricing Program (chargebacks), and co-pay arrangements. In addition, goods are principally sold on a "sale-or-return" basis, where customers may return products in line with the Company's return policy. Sales deductions and product returns are considered variable consideration and are estimated at the time of sale using the expected value method. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net contractual price only to the extent that it is probable that a significant reversal will not occur.

Unsettled sales rebates and product returns are recognized as provisions when timing or amount is uncertain. Payable amounts that are absolute are recognized as other liabilities. Sales discounts and rebates that are payable to customers are offset in trade receivables.

Other Revenue

Other revenue relates to collaboration and license agreements. In addition, other revenue is generated from feasibility studies for potential partners to evaluate if TransCon technologies enable certain advantages for their product candidates of interest. Such feasibility studies are often structured as short-term agreements with fixed fees for the work that the Company performs.

When contracts with customers are entered into, the goods and/or services promised in the contract are assessed to identify distinct performance obligations. A promise in the agreement is considered a distinct performance obligation if both of the following criteria are met:

- the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (i.e., the good or service is capable of being distinct); and
- the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (i.e., the promise to transfer the good or service is distinct within the context of the contract).

Under collaboration, license, and other agreements that contain multiple promises to the customer, the promises are identified and accounted for as separate performance obligations, if these are distinct. If promises are not distinct, those goods or services are combined with other promised goods or services until a bundle of goods or services that is distinct is identified.

The transaction price in the contract is measured at fair value and reflects the consideration the Company expects to be entitled to in exchange for those goods or services. The transaction price is allocated to each performance obligation according to their stand-alone selling prices and is recognized when control of the goods or services is transferred to the customer, either over time or at a point in time, depending on the specific terms and conditions in the contracts.

Research and Development Costs

Research and development costs consist primarily of manufacturing costs, preclinical and clinical study costs and costs for process optimizations and improvements performed by Clinical Research Organizations ("CROs") and Contract Manufacturing Organizations ("CMOs"), salaries and other personnel costs including pension and share-based payment, the cost of facilities, professional fees, cost of obtaining and maintaining the Company's intellectual property portfolio, and depreciation of non-current assets related to research and development activities.

Research costs are incurred at the early stages of the drug development cycle from the initial drug discovery and include a variety of preclinical research activities in order to assess potential drug candidates in non-human subjects, prior to filing an Investigational New Drug Application ("IND"), or equivalent. Research costs are recognized in the consolidated statement of profit or loss when incurred.

Development activities relate to activities following an IND, or equivalent, and typically involve a single product candidate undergoing a series of studies to illustrate its safety profile and effect on human beings, prior to obtaining the necessary approval from the appropriate authorities. Development activities comprise drug candidates undergoing clinical trials starting in phase I (first time drug is administrated in a small group of humans), and further into Phase II and III, which include administration of drugs in larger patient groups. Following, and depending on clinical trial results, a Biologic License Application ("BLA") or New Drug Application ("NDA") may be submitted to the authorities, to apply for marketing approval, which, with a positive outcome will permit the Company to market and sell the products. Long-term extension trials may be ongoing following submission of a BLA or NDA.

Development costs also include product development and pre-commercial manufacturing costs related to development product candidates, and write-downs of inventories manufactured for late-stage development product candidates prior to marketing approval being obtained (pre-launch inventories).

Due to the risk related to the development of pharmaceutical products, the Company cannot estimate the future economic benefits associated with individual development activities with sufficient certainty until the development activities have been finalized and the necessary market approval of the final product has been obtained. As a consequence, all development costs are recognized in the consolidated statement of profit or loss when incurred.

Selling, General and Administrative Expenses

Selling, general and administrative expenses comprise salaries and other personnel costs including pension and share-based payment, office supplies, cost of facilities, professional fees, and depreciation of non-current assets related to selling, general and administrative activities, including pre-commercial and commercial activities. Selling, general and administrative expenses are recognized in the consolidated statement of profit or loss when incurred.

Share-based Incentive Programs

Share-based incentive programs comprise warrant programs and Restricted Stock Unit programs ("RSU-programs") and are classified as equity-settled share-based payment transactions.

The cost of equity-settled transactions is determined by the fair value at the date of grant. For warrant programs, the fair value of each warrant granted is determined using the Black-Scholes valuation model. For RSU-programs, the fair value of each RSU granted is equal to the closing share price on the date of grant of the underlying ADS.

The cost is recognized together with a corresponding increase in equity over the period in which the performance and/or service conditions are fulfilled (i.e., the vesting period). The fair value determined at the grant date of the equity-settled share-based payment is expensed on a straight-line basis over the vesting period for each tranche, based on the best estimate of the number of equity instruments that will ultimately vest. No expense is recognized for grants that do not ultimately vest.

Where an equity-settled grant is cancelled other than upon forfeiture when vesting conditions are not satisfied, the grant is treated as if it vested on the date of the cancellation, and any expense not yet recognized for the grant is recognized immediately.

Where the terms and conditions for an equity-settled grant is modified, the services measured at the grant date fair value over the vesting period are recognized, subject to performance and/or service conditions that was specified at the initial grant date(s). Additionally, at the date of modification, unvested grants are re-measured and any increase in the total fair value is recognized over the vesting period. If a new grant is substituted for the cancelled grant and designated as a replacement grant on the date that it is granted, the cancelled and new grants are treated as if they were a modification of the original grant.

Any social security contributions payable in connection with the grant or exercise of the warrants are recognized as expenses when incurred. The assumptions used for estimating the fair value of share-based payment transactions are disclosed in Note 7 "Share-based Payment".

Finance Income and Expenses

Finance income and expenses comprise interest income and expenses and realized and unrealized exchange rate gains and losses on transactions denominated in foreign currencies.

Interest income and interest expenses are stated on an accrual basis using the principal and the effective interest rate. The effective interest rate is the discount rate that is used to discount expected future cash payments or receipts through the expected life of the financial asset or financial liability to the amortized cost (the carrying amount) of such asset or liability.

Income Taxes

Tax for the year, which consists of current tax for the year and changes in deferred tax, is recognized in the consolidated statement of profit or loss by the portion attributable to the profit or loss for the year and recognized directly in equity or other comprehensive income by the portion attributable to entries directly in equity and in other comprehensive income. The current tax payable or receivable is recognized in the consolidated statement of financial position, stated as tax computed on this year's taxable income, adjusted for prepaid tax.

When computing the current tax for the year, the tax rates and tax rules enacted or substantially enacted at the reporting date are used. Current tax payable is based on taxable profit or loss for the year. Taxable profit or loss differs from net profit or loss as reported in the consolidated statements of profit or loss because it excludes items of income or expense that are taxable or deductible in prior or future years. In addition, taxable profit or loss excludes items that are never taxable or deductible.

Deferred tax is recognized according to the balance sheet liability method of all temporary differences between carrying amounts and tax-based values of assets and liabilities, apart from deferred tax on all temporary differences occurring on initial recognition of goodwill or on initial recognition of a transaction which is not a business combination, and for which the temporary difference found at the time of initial recognition neither affects profit or loss nor taxable income.

Deferred tax liabilities are recognized on all temporary differences related to investments in subsidiaries and/or associates, unless the Company is able to control when the deferred tax is realized, and it is probable that the deferred tax will not become due and payable as current tax in the foreseeable future.

Deferred tax assets, including the tax base of tax loss carry forwards, are recognized in the statement of financial position at their estimated realizable value, either as a set-off against deferred tax liabilities or as net tax assets for offset against future positive taxable income. Deferred tax assets are only offset against deferred tax liabilities if the entity has a legally enforceable right to offset, and the deferred tax assets and deferred tax liabilities relate to income taxes levied by the same tax jurisdiction. Deferred tax is calculated based on the planned use of each asset and the settlement of each liability, respectively.

Deferred tax is measured using the tax rates and tax rules in the relevant countries that, based on acts in force or acts in reality in force at the reporting date are expected to apply when the deferred tax is expected to crystallize as current tax. Changes in deferred tax resulting from changed tax rates or tax rules are recognized in the consolidated statement of profit or loss unless the deferred tax is attributable to transactions previously recognized directly in equity or other comprehensive income. In the latter case, such changes are also recognized in equity or other comprehensive income. On every reporting date, it is assessed whether sufficient taxable income is likely to arise in the future for the deferred tax asset to be utilized.

Intangible assets

Goodwill

Goodwill acquired in a business combination is initially measured at cost, being the excess of the aggregate of the consideration transferred and the amount recognized for non-controlling interests over the net identifiable assets acquired and liabilities assumed.

After initial recognition, goodwill is measured at cost less any accumulated impairment losses. Goodwill is not amortized but is subject to impairment testing at least on a yearly basis. For the purpose of impairment testing, goodwill acquired in a business combination is allocated to each of the cash-generating units, or group of cash-generating units, that are expected to benefit from the synergies of the combination. Each cash-generating unit or group of cash-generating units to which goodwill is allocated represent the lowest level within the Company at which the goodwill is monitored for internal management purposes.

Software

Software assets comprise administrative applications and serve general purposes to support the Company's operations.

Development costs that are directly attributable to the design, customization, implementation, and testing of identifiable and unique software assets controlled by the Company are recognized as intangible assets from the time that; (1) the software asset is clearly defined and identifiable; (2) technological feasibility, adequate resources to complete, and an internal use of the software asset can be demonstrated; (3) the expenditure attributable to the software asset can be measured reliably; and (4) the Company has the intention to use the software asset internally. The Company does not capitalize software with no alternative use, or where economic benefit depends on marketing approvals of drug candidates and where marketing approvals have not been obtained.

Following initial recognition of the development expenditure as an asset, the asset is carried at cost less any accumulated amortization and accumulated impairment losses. Amortization of the asset begins when the development is complete, and the asset is available for use. Software assets are amortized over the period of expected future benefits. Amortization is recognized in research and development costs, and selling, general and administrative expenses, as appropriate. Expenditures, that do not meet the criteria above are recognized as an expense as incurred.

Property, Plant and Equipment

Property, plant and equipment primarily comprises leasehold improvements, office facilities, and process equipment and tools which are located at CMOs. Property, plant and equipment also includes right-of-use assets. Refer to the separate section "Leases".

Property, plant and equipment is measured at cost less accumulated depreciation and impairment losses. Cost comprises the acquisition price, costs directly attributable to the acquisition and preparation costs of the asset until the time when it is ready to be used in operation. Subsequent costs are included in the carrying amount of the asset or recognized as a separate asset, as appropriate, only when it is probable that future economic benefits associated with the assets will flow to the Company and costs of the items can be measured reliably. All repair and maintenance costs are charged to the consolidated statement of profit or loss during the financial periods in which they are incurred.

Plant and equipment acquired for research and development activities with alternative use, which is expected to be used for more than one year, is capitalized and depreciated over the estimated useful life as research and development costs. Plant and equipment acquired for research and development activities, which has no alternative use, is recognized as research and development costs when incurred.

If the acquisition or use of the asset involves an obligation to incur costs of decommissioning or restoration of the asset, the estimated related costs are recognized as a provision and as part of the relevant asset's cost, respectively.

The basis for depreciation is cost less estimated residual value. The residual value is the estimated amount that would be earned if selling the asset today net of selling costs, assuming that the asset is of an age and a condition that is expected after the end of its useful life. Cost of a combined asset is divided into smaller components, with such significant components depreciated individually if their useful lives vary. Depreciation commences when the asset is available for use, which is when it is in the location and condition necessary for it to be capable of operating in the manner intended.

Depreciation is calculated on a straight-line basis, based on an asset's expected useful life, being within the following ranges:

Process plant and machinery	5 - 10 years
Other equipment	3 - 5 years
Leasehold improvements	3 - 11 years
Right-of-use assets	2 - 11 years

Depreciation methods, useful lives and residual amounts are reassessed at least annually.

Property, plant and equipment is written down to the lower of recoverable amount and carrying amount, as described in the "Impairment" section below. Depreciation and impairment losses of property, plant and equipment is recognized in the consolidated statement of profit or loss as cost of sales, research and development costs or as selling, general and administrative expenses, as appropriate.

Gains and losses on disposal of property, plant and equipment are recognized in the consolidated statement of profit or loss at its net proceeds, as either other operating income or other operating expenses, as appropriate.

Impairment

The recoverable amount of goodwill is estimated annually irrespective of any recorded indications of impairment. Property, plant and equipment and finite-lived intangible assets are reviewed for impairment whenever events or circumstances indicate that the carrying amount may not be recoverable.

An impairment loss is recognized for the amount by which the asset's carrying amount exceeds its recoverable amount. The recoverable amount is the higher of an asset's fair value less costs of disposal and value in use. For the purpose of assessing impairment, assets are grouped at the lowest levels for which there are largely independent cash inflows, or cash-generating units, which for goodwill represent the lowest level within the enterprise at which the goodwill is monitored for internal management purposes. Prior impairments of non-financial assets, other than goodwill, are reviewed for possible reversal at each reporting date.

Inventories

Inventories comprise raw materials, work in progress and finished goods. Work in progress and finished goods comprise service expenses incurred at CMOs, raw materials consumed, incremental storage and transportation, other direct materials, and a proportion of manufacturing overheads based on normal operation capacity.

Inventories are measured at the lower of cost incurred in bringing it to its present location and condition, and net realizable value. Net realizable value is the estimated selling price in the ordinary course of business, less estimated costs of completion and the estimated costs necessary to make the sale. Work in progress and finished goods are measured under a standard cost method that takes into account normal levels of consumption, yields, labor, efficiency and capacity utilization. Production processes are complex, where actual yields and consumptions are sensitive to a wide variety of manufacturing conditions. Standard cost variances are reviewed regularly and adjusted to ensure inventories approximate actual cost of production.

If net realizable value is lower than cost, a write-down is recognized as the excess amount by which cost exceeds net realizable value, as part of cost of sales when incurred. The amount of reversal of write-down of inventories arising from an increase in net realizable value is recognized as a reduction in cost of sales in the period in which the reversal occurs.

Manufacturing of pre-launch inventories is initiated for late-stage product candidates where manufacturing costs are recognized as inventories. However, since pre-launch inventories are not realizable prior to obtaining marketing approval, pre-launch inventories are immediately written down to zero through research and development costs. If marketing approval is obtained, prior write-downs of pre-launch inventories are reversed through research and development costs.

Cost of inventories is recognized as part of cost of sales in the period in which the related revenue is recognized.

Receivables

Receivables comprise trade receivables, income tax receivables and other receivables.

Trade receivables are classified as financial assets at amortized cost, as these are held to collect contractual cash flows and thus give rise to cash flows representing solely payments of principal and interest. Trade receivables are initially recognized at their transaction price and subsequently measured at amortized cost. Income tax receivables, and other receivables related to deposits, VAT and other indirect taxes are measured at cost less impairment. Carrying amounts of receivables usually equals their nominal value less provision for impairments.

Prepayments

Prepayments comprise advance payments relating to a future financial period. Prepayments are measured at cost.

Marketable Securities

Marketable securities may comprise government bonds, treasury bills, commercial papers, and other securities traded on established markets.

At initial recognition (trade-date), contractual terms of individual securities are analyzed to determine whether these give rise on specified dates to cash flows that are solely payments of principal and interest on the principal outstanding ("SPPI-test"). All marketable securities held at the reporting date have passed the SPPI-test.

Marketable securities are initially recognized at fair value at trade-date, and subsequently measured at amortized cost under the effective interest method. Interest income is recognized as finance income in the consolidated statement of profit or loss. Marketable securities are subject to impairment test to accommodate expected credit loss. Gains and losses are recognized as finance income or expenses in the consolidated statement of profit or loss when the specific security or portfolio of securities is derecognized, modified or impaired.

Marketable securities, having maturity profiles of three months or less after the date of acquisition are presented as cash equivalents in the consolidated statements of financial position, where securities having maturities of more than three months after the date of acquisition are presented separately as marketable securities as current (i.e., those maturing within twelve months after the reporting date) or non-current assets, as appropriate.

Cash and Cash Equivalents

Cash and cash equivalents comprise cash and on-demand deposits with financial institutions, and highly liquid marketable securities with a maturity of three months or less after the date of acquisition (trade-date). Cash and cash equivalents are measured at amortized cost.

Allowance for Expected Credit Losses on Financial Assets

Financial assets comprise receivables (excluding receivables relating to VAT, other indirect tax and income tax), marketable securities and cash and cash equivalents. Impairment of financial assets is determined on the basis of a forward-looking Expected Credit Loss (“ECL”) Model. ECLs are based on the difference between the contractual cash flows due in accordance with the contract and the cash flows expected to be received, discounted by an approximation of the original effective interest rate.

For receivables, a simplified approach in calculating ECLs is applied. Therefore, changes in credit risks are not tracked, but instead, a loss allowance based on lifetime ECL is assessed at each reporting date. Lifetime ECLs are assessed on historical credit loss experience, adjusted for forward-looking factors specific to the counterparts and the economic environment.

For cash, cash equivalents and marketable securities, ECLs are assessed for credit losses that result from default events that are possible within the next twelve months (12-month ECL). Credit risk is continuously tracked and monitored in order to identify significant deterioration. For those credit exposures for which there have been a significant increase in credit risk since initial recognition, an allowance is recognized for credit losses expected over the remaining life of the exposure, irrespective of the timing of the default.

Shareholders' Equity

The share capital comprises the nominal amount of the parent company's ordinary shares, each at a nominal value of DKK 1, or approximately €0.13. All shares are fully paid.

Share premium comprises the amounts received, attributable to shareholders' equity, in excess of the nominal amount of the shares issued at the parent company's capital increases, reduced by any expenses directly attributable to the capital increases. Under Danish legislation, share premium is an unrestricted reserve that is available to be distributed as dividends to a company's shareholders. Also, under Danish legislation, the share premium reserve can be used to offset accumulated deficits.

Treasury shares reserve comprise nominal amounts of holding of own equity instruments. No gain or loss is recognized in profit or loss on the purchase, sale, transfer or cancellation of the Company's own equity instruments. The treasury shares reserve is part of unrestricted reserves and accordingly, reduce the amount available to be distributed as dividends to the Company's shareholders.

Foreign currency translation reserve includes exchange rate adjustments relating to the translation of the results and net assets of foreign operations from their functional currencies to the presentation currency. The accumulated reserve of a foreign operation is reclassified to the consolidated statement of profit or loss at the time the Company loses control, and thus cease to consolidate such foreign operation. The foreign currency translation reserve is an unrestricted reserve that is available to be distributed as dividends to the Company's shareholders.

Retained earnings/(accumulated deficit) represents the accumulated profits or losses from the Company's operations, including corresponding entries to share-based payments recognized in the consolidated statement of profit or loss, arising from warrant programs and RSU-programs. In addition, premium from acquisition and sale of treasury shares are recognized as part of this reserve. A positive reserve is available to be distributed as dividends to the Company's shareholders.

Convertible Senior Notes and Embedded Derivative Liabilities

Convertible senior notes ("convertible notes") are separated into a financial liability and an embedded derivative component based on the terms and conditions of the contract. The embedded derivative component is accounted for separately if it is not deemed closely related to the financial liability.

The convertible notes include an embedded equity conversion option which is not deemed closely related to the financial liability, and initially recognized and measured separately at fair value as derivative liabilities based on the stated terms upon issuance of the convertible notes. The conversion option is classified as a foreign currency conversion option and thus not convertible into a fixed number of shares for a fixed amount of cash. Accordingly, the conversion option is subsequently recognized and measured as a derivative liability at fair value through profit or loss, with any subsequent remeasurement gains or losses recognized as part of finance income or expenses.

In addition, the convertible notes include a redemption option, which entitle the Company to redeem the notes at a cash amount equal to the principal amount of the convertible notes, plus accrued and unpaid interest. The redemption option is closely related to the financial liability, and not separately accounted for. The initial carrying amount of the financial liability component including the redemption option is the residual amount of the proceeds, net of transaction costs, after separating the derivative component.

Transaction costs are apportioned between the financial liability and derivative component based on the allocation of proceeds when the instrument is initially recognized. Transaction costs apportioned to the financial liability component form part of the effective interest and are amortized over the expected lifetime of the liability. Transaction costs allocated to the derivative component are expensed as incurred.

The financial liability is subsequently measured at amortized cost until it is extinguished on conversion, optional redemption or upon repayment at maturity. The financial liability is presented as part of borrowings on the statement of financial position.

Leases

Right-of-use Assets

Right-of-use assets are recognized at the lease commencement date, defined as the date the underlying asset is available for use. Right-of-use assets are measured at cost, less any accumulated depreciations and impairment losses, and adjusted for any remeasurement of lease liabilities. The cost of right-of-use assets include the amount of lease liabilities recognized, initial direct costs incurred, and lease payments made at or before the commencement date less any incentives received. In addition, right-of-use assets also include an estimate of costs to be incurred by the Company in dismantling or restoring the underlying asset to the condition if required by the terms and condition of the lease, if any.

Right-of-use assets are presented as part of property, plant and equipment, and depreciated on a straight-line basis over the shorter of the lease term and the estimated useful lives of the assets.

Lease Liabilities

At the lease commencement date, lease liabilities are recognized and measured at the present value of fixed lease payments and variable lease payments that depend on an index or a rate, whereas variable lease payments and payments related to non-lease components are excluded. Variable lease payments that do not depend on an index or a rate are recognized as expenses in the consolidated statement of profit or loss when incurred.

When interest rates implicit in the lease contracts are not readily available, the present value of lease payments are calculated by applying the incremental borrowing rate of the relevant entity holding the lease. Following the commencement date, the incremental borrowing rate is not changed unless the lease term is modified, or if the lease payments are modified and this modification results from a change in floating interest rates. From the lease commencement date and over the lease term, the carrying amount of lease liabilities is increased to reflect the accretion of interest and reduced for the lease payments made. In addition, the carrying amount of lease liabilities is remeasured if there is a modification, a change in lease term, or a change in lease payments, including changes to future payments resulting from a change in an index used to determine such lease payments.

Lease liabilities are presented as part of borrowings on the statement of financial position.

Provisions

Provisions comprise unsettled sales deductions and product returns regarding sale of commercial products where amount or timing of payment is uncertain.

Provisions for sales deductions attributed to various commercial arrangements, managed healthcare organizations, and government programs such as Medicare, Medicaid and the 340B Drug Pricing Program (“chargebacks”), and co-pay arrangements are recognized when the related sales takes place and measured using the expected value method. Payable amounts for managed healthcare organizations, government programs and chargebacks are generally settled within 90-180 days from the transaction date.

Provisions for estimated product returns are measured according to contractual sales price based on expected product returns.

Trade Payables and Accrued Expenses

Trade payables and accrued expenses are measured at amortized cost.

Other Liabilities

Other liabilities comprise payables to public authorities, short-term employee benefits, and sales rebates. Other liabilities are measured at their net-realizable values.

Contract Liabilities

Contract liabilities comprise deferred income from collaboration and license agreements, where consideration received does not match the individual deliverables with respect to amount and satisfied performance obligations.

Contract liabilities are measured at the fair value of the consideration received and is recognized as revenue in the consolidated statement of profit or loss when the relevant performance obligation, to which the deferred income relates, is satisfied.

Cash Flow Statement

The cash flow statement shows cash flows from operating, investing and financing activities as well as cash and cash equivalents at the beginning and the end of the financial year.

Cash flows from operating activities are presented using the indirect method and calculated as the profit or loss adjusted for non-cash items, working capital changes as well as finance income, finance expenses and income taxes paid.

Cash flows from investing activities include payments in connection with acquisition, development, improvement and sale, etc., of property, plant and equipment, investment in associate and marketable securities.

Cash flows from financing activities comprise payments related to the capital structure of the Company, including lease liabilities, changes in the share capital and treasury shares and issuance of convertible senior notes.

The effect of exchange rate changes on cash and cash equivalents held or due in a foreign currency is presented separately from cash flows from operating, investing and financing activities. Cash flows in currencies other than the functional currency are recognized in the cash flow statement, using the average exchange rates.

Cash and cash equivalents comprise cash and on-demand deposits with financial institutions and highly liquid marketable securities with a maturity of three months or less after the date of acquisition (trade-date).

Basic Earnings per Share

Basic Earnings per Share (“EPS”) is calculated as the consolidated net income or loss from continuing operations for the period divided by the weighted average number of ordinary shares outstanding. The weighted average number of shares takes into account the weighted average number of treasury shares during the year.

Diluted Earnings per Share

Diluted EPS is calculated as the consolidated net income or loss from continuing operations for the period divided by the weighted average number of ordinary shares outstanding adjusted for the weighted average effect of changes in treasury shares during the year, and the dilutive effect of outstanding warrants and convertible notes. If the consolidated statement of profit or loss shows a net loss, no adjustment is made for the dilutive effect, as such effect would be anti-dilutive.

New International Financial Reporting Standards Not Yet Effective

The IASB has issued a number of new or amended standards, which have not yet become effective or have not yet been adopted by the EU. Therefore, these new standards have not been incorporated in these consolidated financial statements.

Amendments to IAS 1, "Classification of Liabilities as Current or Non-current"

In January 2020, the IASB issued amendments to paragraphs 69 to 76 of IAS 1, "Presentation of Financial Statements", to specify the requirements for classifying liabilities as current or non-current. The amendments clarify:

- what is meant by a right to defer settlement;
- that a right to defer must exist at the end of the reporting period;
- that classification is unaffected by the likelihood that an entity will exercise its deferral right; and
- that only if an embedded derivative in a convertible liability is itself an equity instrument would the terms of a liability not impact its classification.

If approved by the EU, the amendments are effective for annual reporting periods beginning on or after January 1, 2024 and must be applied retrospectively. The amendments are expected to require the convertible notes (presented as part of borrowings on the statement of financial position) and derivative liabilities, presented as non-current liabilities at December 31, 2022, to be presented as current liabilities. On December 31, 2022, the carrying amount of convertible notes and derivative liabilities were €399.2 million and €158.0 million, respectively.

The consolidated financial statements are not expected to be affected by other new or amended standards.

Note 3 – Significant Accounting Judgements and Estimates

In the application of the Company's accounting policies, management is required to make judgements, estimates and assumptions about the carrying amounts of assets and liabilities that are not readily apparent from other sources. Judgements, estimates and assumptions applied are based on historical experience and other factors that are relevant, and which are available at the reporting date. Uncertainty concerning estimates and assumptions could result in outcomes, that require a material adjustment to assets and liabilities in future periods.

Estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognized prospectively. While the application of critical accounting estimates is subject to material estimation uncertainties, management's ongoing revisions of critical accounting estimates and underlying assumptions have not revealed any material impact in any of the years presented in these consolidated financial statements.

Significant Accounting Judgements

Critical accounting judgements which have a material impact on the consolidated financial statements are described in the following sections.

Internally Generated Intangible Assets

Development of Drug Candidates

IAS 38, "Intangible Assets" prescribes that intangible assets arising from development projects must be recognized in the consolidated statements of financial position if the criteria for capitalization are met. That means (1) that the development project is clearly defined and identifiable; (2) that technological feasibility, adequate resources to complete and a market for the product or an internal use of the project can be documented; (3) that the expenditure attributable to the development project can be measured reliably; and (4) that the Company has the intent to produce and market the product. Such an intangible asset shall be recognized if it can be demonstrated that the future income from the development project will exceed the aggregate cost of development, production, sale and administration of the product.

Due to the risk associated with drug development, future income from development projects related to drug candidates cannot be determined with sufficient certainty until the development activities have been completed and the necessary marketing approvals have been obtained. Accordingly, the Company does not recognize internally generated intangible assets at this time.

Significant Estimation Uncertainties

The key assumptions concerning the future and other key sources of estimation uncertainty at the reporting date, that have a risk of causing a material adjustment to the carrying amounts of assets and liabilities within the next financial year, are described below.

Revenue and Provisions

Provision for Sales Rebates and Product Returns

Sales deductions and product returns are considered variable consideration and constrained to the extent that a significant reversal in the amount of recognized revenue will not occur when the uncertainties associated with the rebate item are subsequently resolved, or for product returns, when the products are distributed to patients.

Provisions for unsettled sales deductions and product returns are estimated on the basis of a percentage of sales as defined by individual agreements and contracts, and for government rebates by individual state- and plan agreements. Further input in the calculations is based on payer channel mix, current contract prices under eligible programs, patient groups and current inventory levels in the distribution channels. Provisions are adjusted to absolute amounts and recognized as other liabilities when estimated sales rebates and returns are processed.

As of December 31, 2022, the provisions for sales rebates and product returns was €7.3 million compared to €1.2 million, as of December 31, 2021.

Share-Based Payment

Warrant Compensation Costs

IFRS 2, “Share-Based Payment” requires an entity to reflect in its consolidated statement of profit or loss and financial position, the effects of share-based payment transactions. Warrant compensation costs are recognized as cost of sales, research and development costs or selling, general and administrative expenses, as appropriate, over the vesting period, based on management’s best estimate of the number of warrants that will ultimately vest, which is subject to uncertainty.

Warrant compensation costs are measured according to the grant date fair value of the warrants granted. Estimating fair values requires the Company to apply generally accepted valuation models and apply these models consistently according to the terms and conditions of the specific warrant program. Under all warrant programs, the Black-Scholes option-pricing model has been applied to determine the fair value of warrants granted. Subjective judgements and assumptions, which are subject to estimation uncertainties, need to be exercised in determining the appropriate input to the valuation model. These inputs include expected volatility of the Company’s share price for a historic period equaling the expected lifetime of the warrants, reflecting the assumption that the historical volatility over a period similar to the life of the warrants is indicative of future trends, expected forfeitures and expected lifetime of warrants.

In 2021, the Company for the first time, in connection with determining the grant date fair value of warrants and accordingly, warrant compensation costs, applied the price of the Company’s ADSs, each representing one ordinary share of the Company, as input for expected volatility. Until December 31, 2020, the expected volatility was calculated using a simple average of daily historical data of comparable publicly traded companies, as the Company did not have sufficient data for the volatility of the Company’s own share price. Refer to Note 7 “Share-based Payment”, for additional details on the Company’s warrant program and option-pricing model input.

Warrant compensation cost recognized in the consolidated statement of profit or loss was €55.2 million, €66.1 million and €53.2 million for the years ended December 31, 2022, 2021 and 2020, respectively.

Prepayments and Accruals

Project Development Costs

Development of drug candidates requires significant resources, and establishment of long-term working relationships with CROs and CMOs. Work performed by CROs and CMOs and other suppliers often comprise deliveries for more than one reporting period, and where payment terms for contractual work do not necessarily reflect the stage of completion of the individual projects and activities. Accordingly, determination of the stage of completion for ongoing project activities include estimation uncertainties as future efforts to complete the specific activity may be difficult to predict.

On each reporting date, all significant ongoing activities are reviewed to determine the stage of completion and compared to the invoices received. Accruals are recognized for individual projects where the stage of completion exceeds costs of invoices received. Similarly, prepayments are recognized for invoiced costs in excess of the stage of completion. The Company has implemented accrual calculation models and policies, to ensure that consistent accrual procedures are applied, which includes analyzing significant project stages and payment structures, comparing project milestones to planned performance, and revisiting prior periods estimates.

As of December 31, 2022, the consolidated statement of financial position included prepaid project costs of €4.4 million and accrued project costs of €38.0 million, compared to €8.0 million and €23.5 million, respectively, as of December 31, 2021.

Valuation of Embedded Derivatives

Foreign currency conversion options embedded in the convertible notes are accounted for separately as derivative liabilities at fair value through profit or loss.

Fair value cannot be measured based on quoted prices in active markets, or other observable input, and accordingly, derivative liabilities are measured by use of valuation techniques in form of the Black-Scholes Option Pricing model. Subjective judgements and assumptions, which are subject to estimation uncertainties, need to be exercised in determining the appropriate unobservable input to the valuation model (Level 3 in the fair value hierarchy). This includes volatility of the Company's share price for a historic period, reflecting the assumption that the historical volatility is indicative of a period similar to the expected lifetime of the options.

As of December 31, 2022, the valuation of the derivative liabilities was €158.0 million compared to €142.5 million at initial recognition on March 2022. Changes in assumptions relating to these factors could affect the reported fair value of derivative liabilities. Refer to Note 15, "Financial Assets and Liabilities", for additional details.

Note 4—Revenue

Revenue from commercial sale of products relates to sale of SKYTROFA® (lonapegsomatropin-tcgd) in the U.S. market, which is sold to specialty pharmacies and specialty distributors ("commercial customers"). Customer payment terms are typically 30 days from the transaction date. SKYTROFA was approved by the U.S. Food and Drug Administration in August 2021, and the Company began shipping products to commercial customers in the fourth quarter of 2021.

Other revenue is generated primarily from three license agreements, which were entered into in 2018. The licenses grant VISEN Pharmaceuticals ("VISEN"), exclusive rights to develop and commercialize TransCon hGH, TransCon PTH and TransCon CNP in Greater China.

Revenue has been recognized in the consolidated statements of profit or loss with the following amounts:

	2022	2021	2020
		(EUR'000)	
Revenue			
Commercial sale of products	35,659	943	—
Rendering of services	4,434	751	2,140
Sale of clinical supply	8,534	3,719	2,206
Licenses	2,547	2,365	2,607
Total revenue	**51,174**	**7,778**	**6,953**
Attributable to			
Commercial customers	35,659	943	—
Collaboration partners and license agreements	15,515	6,835	6,953
Total revenue	**51,174**	**7,778**	**6,953**
Specified by timing of recognition			
Recognized over time	4,434	751	2,140
Recognized at a point in time	46,740	7,027	4,813
Total revenue	**51,174**	**7,778**	**6,953**
Specified per geographical location			
Europe	552	—	—
North America	44,156	6,856	2,679
China	6,466	922	4,274
Total revenue	**51,174**	**7,778**	**6,953**

Note 5—Segment Information

The Company is managed and operated as one business unit. No separate business areas or separate business units have been identified in relation to product candidates or geographical markets. Accordingly, except for entity wide disclosures, no information on business segments or geographical markets is disclosed. Entity wide disclosures regarding revenue are included in Note 4, "Revenue".

The Company's intangible assets and property, plant and equipment located by country are specified below, and defines the Company's non-current segment assets:

	2022	2021
	(EUR'000)	
Non-current segment assets		
Denmark (domicile country)	30,336	29,656
North America	89,439	91,755
Germany	14,148	9,910
Total non-current segment assets	**133,923**	**131,321**
Investment in associate	22,932	38,345
Marketable securities	7,492	107,561
Other receivables	1,920	1,808
Total non-current assets	**166,267**	**279,035**

Note 6—Employee costs

	2022	2021	2020
		(EUR'000)	
Employee costs			
Wages and salaries	140,420	104,583	77,374
Share-based payment	64,180	66,830	53,170
Pensions (defined contribution plans)	4,163	2,416	943
Social security costs	5,898	4,571	5,358
Total employee costs	**214,661**	**178,400**	**136,845**
Included in the profit or loss			
Cost of sales	7,239	1,380	—
Research and development costs	119,904	106,558	92,468
Selling, general and administrative expenses	87,518	70,462	44,377
Total employee costs	**214,661**	**178,400**	**136,845**
Average number of employees	719	573	410

Key Management Personnel comprises the Board of Directors, the Executive Board and Non-executive Senior Management. Compensation to Key Management Personnel comprises salaries, participation in annual bonus schemes, pensions (defined contributions plans), and share-based compensation. Share-based compensation is elaborated in further details in Note 7, "Share-based Payment".

Compensation to Key Management Personnel included within total employee costs is summarized below:

	Board of Directors [1]			Executive Board [2]			Non-executive Senior Management		
	2022	2021	2020	2022	2021	2020	2022	2021	2020
					(EUR '000)				
Compensation									
Wages and salaries	403	296	250	3,809	2,699	2,372	6,087	5,547	5,272
Share-based payment	1,273	2,032	1,913	11,392	8,770	6,359	8,872	14,906	13,912
Pensions (defined contribution plans)	—	—	—	46	23	—	118	120	89
Social security costs	—	—	—	55	49	100	89	60	122
Total compensation	**1,676**	**2,328**	**2,163**	**15,302**	**11,541**	**8,831**	**15,166**	**20,633**	**19,395**

(1) The Board of Directors comprised six to seven persons in 2022 and 2021. In 2020, the Board of Directors comprised seven persons.

(2) The Executive Board comprised four persons in 2022. For 2021 and 2020, the Executive Board comprised two to four persons and two persons respectively.

Note 7—Share-based Payment

As an incentive to employees, members of the Board of Directors and select consultants, Ascendis Pharma A/S has established warrant programs and, since December 2021, Restricted Stock Unit programs ("RSU programs"), which are equity-settled share-based payment transactions.

Restricted Stock Unit Program

Restricted Stock Units ("RSUs") are granted by the Board of Directors in accordance with authorizations given to it by the shareholders of Ascendis Pharma A/S to the Executive Board, select employees and members of the Board of Directors ("RSU-holders") in accordance with the Company's Restricted Stock Unit Program adopted in December 2021. Further, RSUs may be granted to select consultants. One RSU represents a right for the RSU-holder to receive one ADS of Ascendis Pharma A/S upon vesting if the vesting conditions are met or waived by the Board of Directors at its discretion. ADSs underlying RSUs are treasury shares that have been repurchased in the market. Upon vesting, the Company may at its sole discretion choose to make a cash settlement instead of delivering ADSs.

Vesting Conditions

RSUs granted vest over a predetermined service period, and accordingly require RSU-holders to be employed, or provide a specified period of service. RSUs vest over three years with 1/3 of the RSUs vesting on each anniversary date from the date of grant, and in the case of RSUs granted to the Company's Chief Executive Officer, subject to the achievement of performance conditions as determined by the Company's Board of Directors. RSUs generally cease to vest from the date of termination of employment, or for Board of Directors, termination of board membership, whereas unvested RSUs will lapse. In addition, vesting may be contingent upon additional vesting criteria (non-market performance conditions). The Board of Directors may at its discretion and on an individual basis decide to deviate from the vesting conditions, including, decide to accelerate vesting in the event of termination of employment or board membership, as applicable.

Adjustments

RSU-holders are entitled to an adjustment of the number of RSUs granted, applicable in the event of certain corporate changes, including among other events, increases or decreases to the share capital at a price below or above market value, the issuance of bonus shares, and changes in the nominal value of each share. In addition, The RSU program contains provisions to accelerate vesting, or compensate with grant of new equity instruments, in the event of restructuring events including change in control events.

RSU Activity

148,148 RSUs were granted for the first time in December 2021. The following table specifies the number of RSUs granted and outstanding RSUs at December 31, 2022:

	Total RSUs
Outstanding at January 1, 2022	**148,148**
Transferred during the period	(41,685)
Forfeited during the period	(23,971)
Outstanding at December 31, 2022	**82,492**
Specified by vesting date	
December 2023	41,240
December 2024	41,252
Outstanding at December 31, 2022	**82,492**

The fair value of one RSU at the date of grant was €123.46 for the year ended December 31, 2021.

Warrant program

Warrants are granted by the Board of Directors in accordance with authorizations given to it by the shareholders of Ascendis Pharma A/S to all employees, members of the Board of Directors and select consultants ("warrantholders"). Each warrant carries the right to subscribe for one ordinary share of a nominal value of DKK 1. The exercise price is equal to the fair market value of the Company's ordinary shares at the time of grant as determined by the Board of Directors. Vested warrants may be exercised in two or four annual exercise periods as described below. Apart from exercise prices, exercise periods and vesting conditions for board members, the programs are similar.

Vesting Conditions

Warrants granted vest over a predetermined service period and require warrantholders provide a specified period of service. Warrants generally cease to vest from the date of termination in the event that (i) the employee terminates the employment contract and the termination is not a result of breach of the employment terms by the Company, or (ii) in the event that the Company terminates the employment contract and the employee has given the Company good reason to do so. In relation to board members, the vesting shall cease on the termination date of the board membership regardless of the reason. In relation to consultants, the vesting shall cease on the termination date of the consultancy relationship. The warrantholder will, however, be entitled to exercise vested warrants in the first exercise period after termination.

In the event that the employment contract is terminated, and the employee has not given the Company good reason to do so, the warrantholder may keep the right to continued vesting and exercise of warrants as if the employment was still in effect. In such case, any expense not yet recognized for the outstanding warrants is recognized immediately.

Warrants granted 2012 until November 2021

Warrants granted from 2012 until November 2021, generally vest over 48 months with 1/48 of the warrants vesting per month from the date of grant. However, effective from January 2015, certain warrants granted to board members vest over 24 months with 1/24 of the warrants vesting per month from the date of grant.

Warrants granted from December 2021

For warrants granted to employees and consultants, 25% of the warrants vest one year after the date of grant, and the remaining 75% of the warrants granted vest over 36 months, with 1/36 of the warrants vesting per month, from one year after the date of grant.

For warrants granted to board members upon the board members accession, 25% of the warrants granted vest one year after the date of grant, and the remaining 75% of the warrants granted shall vest over 36 months, with 1/36 per month from one year after the date of grant. Regarding subsequent grants of warrants to board members, 50 % of the warrants vest one year after the date of grant, and the remaining 50% of the warrants vest over 12 months, with 1/12 per month from one year after the date of grant.

Exercise Periods

Vested warrants may be exercised during certain exercise periods each year, within certain periods after publication of earnings data of a fiscal quarter, interim and annual reports, as per each program's terms and conditions.

Warrants expire ten years after the grant date. Warrants not exercised by the warrantholder during the last exercise period shall become null and void without further notice or compensation or payment of any kind to the warrantholder. If the warrantholder is a consultant, advisor or board member, the exercise of warrants is conditional upon the warrantholder’s continued service to the Company at the time the warrants are exercised. If the consultant’s, advisor’s or board member’s relationship with the Company should cease without this being attributable to the warrantholder’s actions or omissions, the warrantholder shall be entitled to exercise vested warrants in the pre-defined exercise periods.

Adjustments

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, increases or decreases to the share capital at a price below or above market value, the issuance of bonus shares, changes in the nominal value of each share, and payment of dividends in excess of 10% of the Company’s equity.

Warrant Activity

The following table specifies the number and weighted average exercise prices of, and movements, in warrants during the year:

	Total Warrants	Weighted Average Exercise Price EUR
Outstanding at January 1, 2020	**5,820,211**	**46.36**
Granted during the year	1,485,931	137.57
Exercised during the year [(1)]	(905,395)	30.56
Forfeited during the year	(252,743)	64.99
Outstanding at December 31, 2020	**6,148,004**	**69.97**
Vested at the reporting date	**3,044,827**	**37.29**
Granted during the year	1,445,981	122.03
Exercised during the year [(1)]	(312,296)	38.43
Forfeited during the year	(196,616)	119.58
Outstanding at December 31, 2021	**7,085,073**	**80.30**
Vested at the reporting date	**4,022,011**	**52.63**
Granted during the year	357,092	100.40
Exercised during the year [(1)]	(214,613)	21.83
Forfeited during the year	(363,541)	123.62
Outstanding at December 31, 2022	**6,864,011**	**81.30**
Vested at the reporting date	**4,972,026**	**66.34**

(1) The weighted average share price (listed in $) at the date of exercise was €113.60, €124.62 and €128.32 for the years ended December 31, 2022, 2021 and 2020, respectively.

As of December 31, 2022, the Board of Directors was authorized to grant up to 1,959,496 additional warrants to employees, board members and select consultants without preemptive subscription rights for the shareholders of Ascendis Pharma A/S.

The following table specifies the weighted average exercise prices and weighted average remaining contractual life for outstanding warrants at December 31, 2022 per grant year.

	Number of Outstanding Warrants	Weighted Average Exercise Price EUR	Weighted Average Remaining Life (months)
Granted in 2012-2018	3,052,158	33.64	53
Granted in 2019	1,051,611	96.69	81
Granted in 2020	1,190,212	138.41	93
Granted in 2021	1,222,948	121.87	106
Granted in 2022	347,082	100.56	114
Outstanding at December 31, 2022	**6,864,011**	**81.30**	**77**

At December 31, 2022, the exercise prices of outstanding warrants under the Company's warrant programs range from €6.48 to €145.50 depending on the grant dates.

The range of exercise prices for outstanding warrants was €6.48 to €145.50 for the years ended December 31, 2021 and 2020. The weighted average remaining life for outstanding warrants was 87 months and 91 months, for the financial years ended December 31, 2021 and 2020, respectively.

Warrant Compensation Costs

Warrant compensation costs are recognized in the consolidated statements of profit or loss over the vesting period of the warrants granted.

Warrant compensation costs are determined with basis in the grant date fair value of the warrants granted and recognized over the vesting period. Fair value of the warrants is calculated at the grant dates by use of the Black-Scholes Option Pricing model with the following assumptions: (1) an exercise price equal to the estimated market price of the Company's shares at the date of grant; (2) an expected lifetime of the warrants determined as a weighted average of the time from grant date to date of becoming exercisable and from grant date to expiry of the warrants; (3) a risk-free interest rate equaling the effective interest rate on a Danish government bond with the same lifetime as the warrants; (4) no payment of dividends; and (5) an expected volatility using the Company's own share price (from 2021).

The following table summarizes the input to the Black-Scholes Option Pricing model and the calculated fair values for warrant grants in 2022, 2021 and 2020:

	2022	2021	2020
Expected volatility	48-49 %	48 – 49 %	52 – 55 %
Risk-free interest rate	(0.08) - 2.54 %	(0.54)–(0.27) %	(0.93)–(0.32) %
Expected life of warrants (years)	6.0	6.0	5.05 – 7.10
Weighted average exercise price	€ 100.40	€ 122.03	€ 137.57
Fair value of warrants granted in the year	€ 36.55 - 60.85	€ 45.91 – 64.28	€ 48.43 – 75.77

Note 8— Principal Accountant Fees and Services

The following table sets forth, for each of the years indicated, the fees billed by the Company's independent public accountants and the proportion of each of the fees out of the total amount billed by the accountants.

	2022	2021	2020
		(EUR'000)	
Principal accountant fees and services			
Audit fees	814	771	599
Tax fees	138	87	104
All other fees	—	13	22
Total principal accountant fees and services	**952**	**871**	**725**

Note 9—Tax on Profit/(Loss) for the Year and Deferred Tax

	2022	2021	2020
		(EUR'000)	
Tax on profit/(loss) for the year:			
Current tax (expense)/income	(5,377)	367	219
	(5,377)	**367**	**219**
Tax for the year can be explained as follows:			
Profit/(loss) before tax	(577,817)	(383,944)	(419,174)
Tax at the Danish corporation tax rate of 22%	**127,120**	**84,468**	**92,218**
Tax effect of:			
Non-deductible costs	(17,094)	(14,800)	(11,815)
Additional tax deductions	13,720	17,117	24,564
Impact from associate	(3,893)	3,169	(1,326)
Other effects including effect of different tax rates	(2,716)	305	2,673
Deferred tax asset, not recognized	(122,514)	(89,892)	(106,095)
Tax on profit/(loss) for the year	**(5,377)**	**367**	**219**
Effective tax rate	**0.93 %**	**(0.10)%**	**(0.05)%**

	2022	2021	2020
		(EUR'000)	
Specification of Deferred Tax Assets			
Tax deductible losses	433,174	313,011	227,234
Other temporary differences	19,961	12,856	7,726
Deferred tax asset, not recognized	(453,135)	(325,867)	(234,960)
Total Deferred Tax Assets at December 31	—	—	—

No changes to deferred tax have been recognized in the consolidated statement of profit or loss for 2022, 2021 or 2020. Deferred tax assets have not been recognized in the consolidated statements of financial position due to uncertainty relating to future utilization. Deferred tax assets can be carried forward without timing limitations.

The Company had tax losses carried forward of €1,985.0 million and €1,437.0 million at December 31, 2022 and 2021, respectively. Tax losses can be carried forward indefinitely, where certain limitations exist for amounts to be utilized each year. Under Danish tax legislation, tax losses may be partly refunded by the tax authorities to the extent such tax losses arise from research and development activities. The jointly taxed Danish entities had a negative taxable income, and accordingly were entitled to a tax refund of approximately €0.7 million for each of the years ended December 31, 2022, 2021 and 2020, respectively.

The Company is entitled to additional tax deductions, determined by annual warrants exercised by employees. For the year ended December 31, 2022, the Company was entitled to additional tax deductions with a tax value of €5.2 million, compared to €4.8 million and €16.3 million for the years ended December 31, 2021, and 2020, respectively. These future tax deductions depends on the timing and amounts of warrant exercises, and accordingly, future additional tax deductions are subject to uncertainties. Refer to Note 7, "Share-based Payment", regarding a description of warrant programs.

The parent company Ascendis Pharma A/S is jointly taxed with its Danish subsidiaries. The current Danish corporation tax is allocated between the jointly taxed Danish companies in proportion to their taxable income (full absorption with refunds for tax losses). These companies are taxed under the on-account tax scheme.

Note 10—Intangible Assets

	Goodwill	Software	Total
		(EUR'000)	
Cost			
January 1, 2021	3,495	2,222	5,717
December 31, 2021	**3,495**	**2,222**	**5,717**
December 31, 2022	**3,495**	**2,222**	**5,717**
Accumulated amortization and impairments			
Amortization charge	—	(445)	(445)
December 31, 2021	**—**	**(445)**	**(445)**
Amortization charge	—	(444)	(444)
December 31, 2022	**—**	**(889)**	**(889)**
Carrying amount			
December 31, 2021	**3,495**	**1,777**	**5,272**
December 31, 2022	**3,495**	**1,333**	**4,828**

At the reporting date, no internally generated intangible assets from development of pharmaceutical drug candidates have been recognized. Thus, all related research and development costs incurred for the years ended December 31, 2022, 2021, and 2020, were recognized in the consolidated statements of profit or loss.

Goodwill relates to the acquisition of Complex Biosystems GmbH (now Ascendis Pharma GmbH) in 2007. Goodwill was calculated as the excess amount of the purchase price to the fair value of identifiable assets acquired, and liabilities assumed at the acquisition date. Ascendis Pharma GmbH was initially a separate technology platform company but is now an integral part of the Company's research and development activities. Accordingly, it is not possible to look separately at Ascendis Pharma GmbH when considering the recoverable amount of the goodwill. Goodwill is monitored and tested for impairment on a consolidated level as the Company is considered to represent one cash-generating unit.

The recoverable amount of the cash-generating unit is determined based on an estimation of the Company's fair value less costs of disposal. The fair value of goodwill has been determined after taking into account the market value of the Company's ADSs as of the reporting date. The computation of the market value including an estimation of selling costs, significantly exceeded the carrying amount of the net assets, leaving sufficient value to cover the carrying amount of goodwill. Considering the excess value, no further assumptions are deemed relevant to be applied in determining whether goodwill is impaired.

Note 11—Property, Plant and Equipment

	Plant and Machinery	Other Equipment	Leasehold Improve-ments	Right-of-Use Assets	Total
			(EUR'000)		
Cost					
January 1, 2021	14,622	5,175	8,535	99,566	127,898
Additions	2,810	3,386	8,780	10,812	25,788
Disposals	(772)	(10)	—	(1,040)	(1,822)
Foreign exchange translation	286	271	752	6,797	8,106
December 31, 2021	**16,946**	**8,822**	**18,067**	**116,135**	**159,970**
Additions	7,787	2,487	1,284	3,245	14,803
Disposals	(32)	(395)	—	(5,480)	(5,907)
Foreign exchange translation	243	289	779	5,566	6,877
December 31, 2022	**24,944**	**11,203**	**20,130**	**119,466**	**175,743**
Accumulated depreciation					
January 1, 2021	(4,781)	(2,287)	(1,134)	(11,584)	(19,786)
Depreciation charge	(1,499)	(1,200)	(1,284)	(10,963)	(14,946)
Disposals	772	10	—	1,040	1,822
Foreign exchange translation	(19)	(70)	(70)	(852)	(1,011)
December 31, 2021	**(5,527)**	**(3,547)**	**(2,488)**	**(22,359)**	**(33,921)**
Depreciation charge	(2,039)	(1,793)	(1,942)	(11,740)	(17,514)
Disposals	25	380	—	5,480	5,885
Foreign exchange translation	(43)	(63)	(67)	(925)	(1,098)
December 31, 2022	**(7,584)**	**(5,023)**	**(4,497)**	**(29,544)**	**(46,648)**
Carrying amount					
December 31, 2021	**11,419**	**5,275**	**15,579**	**93,776**	**126,049**
December 31, 2022	**17,360**	**6,180**	**15,633**	**89,922**	**129,095**

Depreciation charges are specified below:

	2022	2021	2020
		(EUR'000)	
Depreciation charges			
Cost of sales	1,245	252	—
Research and development costs	10,892	10,102	7,311
Selling, general and administrative expenses	5,377	4,592	2,137
Total depreciation charges	**17,514**	**14,946**	**9,448**

Note 12—Investment in Associate

VISEN is a private company with business activities within development, manufacturing and commercialization of endocrinology rare disease therapies in Greater China. The Company's interest in VISEN is accounted for as an associate using the equity method in the consolidated financial statements as the Company has determined that it has significant influence but not joint control.

The Company has granted VISEN exclusive rights to develop and commercialize TransCon hGH, TransCon PTH and TransCon CNP in Greater China, and as consideration for the granting of such rights has received a 50% ownership of VISEN's issued and outstanding shares. On January 8, 2021, the Company entered into an equity investment of $12.5 million as part of VISEN's $150 million Series B financing. Following VISEN's Series B financing, the Company retained 43.93% of VISEN's issued and outstanding shares. As a result, a non-cash gain of €42.3 million was recognized in the consolidated statement of profit or loss as part of Share of profit/(loss) of associate in 2021. The Series B financing did not change the accounting treatment of VISEN.

The following table illustrates the summarized relevant financial information of VISEN:

	VISEN Pharmaceuticals	
Principal place of business	China	
	2022	**2021**
	(EUR'000)	
Statement of profit or loss		
Profit/(loss) for the year from continuing operations	**(40,283)**	**(69,283)**
Total comprehensive income	**(40,273)**	**(69,306)**
Statement of financial position		
Non-current assets	21,410	16,599
Current assets	92,204	130,825
Total assets	**113,614**	**147,424**
Equity	100,062	135,333
Non-current liabilities	180	1,545
Current liabilities	13,372	10,546
Total equity and liabilities	**113,614**	**147,424**
Company's share of equity before eliminations	**43,957**	**59,455**
Elimination of internal profit and other equity method adjustments	*(21,025)*	*(21,110)*
Company's share of equity	**22,932**	**38,345**
Investment in associate at December 31	**22,932**	**38,345**
Present ownership at December 31	43.93%	43.93%
Transactions and outstanding balances as of December 31		
Invoicing of goods and services to associate	22,327	6,472
Trade receivables from associate	3,554	1,644

Note 13—Inventories

	2022	2021
	(EUR'000)	
Inventories		
Raw materials and consumables	9,616	2,248
Work in progress	112,885	68,865
Finished goods	8,172	4,292
Total inventories	**130,673**	**75,405**

Due to production lead time, work in progress includes inventories that are not sellable before more than twelve months after the reporting date.

Note 14—Contract Liabilities

At December 31, 2022, contract liabilities comprise unsatisfied performance obligations relating to delivery of commercial supply under one of the Company's license agreements.

Revenue recognized from contract liabilities was €10.5 million, €0.4 million and €1.0 million for the years ended December 31, 2022, 2021 and 2020, respectively, and primarily related to delivery of clinical supply and research and development services under the Company's license agreements.

Note 15—Financial Assets and Liabilities

Financial assets and liabilities comprise the following:

	2022	2021
	(EUR'000)	
Financial assets by category		
Trade receivables	11,910	2,200
Other receivables (excluding income tax and indirect tax receivables)	3,884	12,276
Marketable securities	298,180	343,358
Cash and cash equivalents	444,767	446,267
Financial assets measured at amortized cost	**758,741**	**804,101**
Total financial assets	**758,741**	**804,101**
Classified in the statement of financial position		
Non-current assets	9,412	109,369
Current assets	749,329	694,732
Total financial assets	**758,741**	**804,101**
Financial liabilities by category		
Borrowings		
Convertible senior notes	399,186	—
Lease liabilities	109,191	104,961
Trade payables and accrued expenses	101,032	59,417
Financial liabilities measured at amortized cost	**609,409**	**164,378**
Derivative liabilities	157,950	—
Financial liabilities measured at fair value through profit or loss	**157,950**	**—**
Total financial liabilities	**767,359**	**164,378**
Classified in the statement of financial position		
Non-current liabilities	640,907	97,966
Current liabilities	126,452	66,412
Total financial liabilities	**767,359**	**164,378**

Finance income and expenses are specified below:

	2022	2021	2020
		(EUR'000)	
Finance income			
Interest income	7,426	692	1,812
Exchange rate gains (net)	44,755	59,026	—
Total finance income	**52,181**	**59,718**	**1,812**
Finance expenses			
Interest expenses	30,682	3,911	1,918
Fair value loss, derivatives	15,483	—	—
Other financial expenses	4,322	—	—
Exchange rate losses (net)	—	—	78,924
Total finance expenses	**50,487**	**3,911**	**80,842**

Interest income and interest expenses relate to financial assets and liabilities measured at amortized cost. Net exchange rate gains and losses primarily relate to U.S. Dollar/Euro fluctuations pertaining to the Company's cash, cash equivalents, marketable securities and convertible notes.

Borrowings

Convertible Senior Notes

In March 2022, the Company issued an aggregate principal amount of $575.0 million of fixed rate 2.25% convertible notes. The net proceeds from the offering of the convertible notes were $557.9 million (€503.3 million), after deducting the initial purchasers' discounts and commissions, and transaction costs. The convertible notes rank equally in right of payment with all future senior unsecured indebtedness. Unless earlier converted or redeemed, the convertible notes will mature on April 1, 2028.

The convertible notes accrue interest at a rate of 2.25% per annum, payable semi-annually in arrears on April 1 and October 1 of each year, beginning on October 1, 2022. At any time before the close of business on the second scheduled trading day immediately before the maturity date, noteholders may convert their convertible notes at their option into the Company's ordinary shares represented by ADSs, together, if applicable, with cash in lieu of any fractional ADS, at the then-applicable conversion rate. The initial conversion rate is 6.0118 ADSs per $1,000 principal amount of convertible notes, which represents an initial conversion price of $166.34 per ADS. The conversion rate and conversion price will be subject to customary adjustments upon the occurrence of certain events.

The convertible notes will be optionally redeemable, in whole or in part (subject to certain limitations), at the Company's option at any time, and from time to time, on or after April 7, 2025, but only if the last reported sale price per ADS exceeds 130% of the conversion price on each of (i) at least 20 trading days, whether or not consecutive, during the 30 consecutive trading days ending on, and including, the trading day immediately before the date the Company sends the related optional redemption notice; and (ii) the trading day immediately before the date the Company sends such notice.

Leases

The Company primarily leases office and laboratory facilities. Lease arrangements contain a range of different terms and conditions and are typically entered into for fixed periods. In order to improve flexibility to the Company's operations, lease arrangements may provide the Company with option to extend the lease or terminate the lease within the enforceable lease term. In the Company's current lease portfolio, extension and termination options range between six months to five years, in addition to the non-cancellable periods.

The following expenses relating to lease activities are recognized in the consolidated statements of profit or loss:

	2022	2021	2020
		(EUR'000)	
Lease expenses			
Depreciation	11,740	10,963	6,857
Short term leases and leases of low value assets	280	186	470
Lease interest	3,842	3,396	1,617
Total lease expenses	**15,862**	**14,545**	**8,944**

In February 2022, the Company entered into a facility lease in Germany with an enforceable lease term of 15 years, which is expected to commence in 2025 and comprise total lease cash-outflows of €70.3 million.

Financing Activities

Development in borrowings related to financing activities are specified below:

		Cash payments		Non-cash items				
	Beginning of period	Repayments	Proceeds	Additions/ (disposals)	Separation of embedded derivative	Accretion of interest	Foreign exchange adjustment	End of period
				(EUR'000)				
Financing activities								
December 31, 2022								
Borrowings								
Convertible senior notes	—	(6,710)	503,281	—	(142,467)	30,216	14,866	399,186
Lease liabilities	104,961	(7,995)	—	3,194	—	3,842	5,189	109,191
Total financing activities	**104,961**	**(14,705)**	**503,281**	**3,194**	**(142,467)**	**34,058**	**20,055**	**508,377**
Financing activities								
December 31, 2021								
Borrowings								
Lease liabilities	91,975	(7,755)	—	10,812	—	3,396	6,533	104,961
Total financing activities	**91,975**	**(7,755)**	**—**	**10,812**	**—**	**3,396**	**6,533**	**104,961**

For December 31, 2022, "separation of embedded derivative" on convertible senior notes relates to derivative liabilities that is separated from convertible senior notes and presented separately in the consolidated statement of financial position, please refer to following section, "Derivative Liabilities".

Derivative Liabilities

Derivative liabilities relate to the foreign currency conversion option embedded in the convertible notes. Fair value of derivative liabilities cannot be measured based on quoted prices in active markets, or other observable input, and accordingly, derivative liabilities are measured by using the Black-Scholes Option Pricing model (Level 3 in the fair value hierarchy). The fair value of the options is calculated, applying the following assumptions: (1) conversion price; (2) own share price; (3) maturity of the options; (4) a risk-free interest rate equaling the effective interest rate on a U.S. government bond with the same lifetime as the maturity of the options; (5) no payment of dividends; and (6) an expected volatility using the Company's own share price (49.24% as of December 31, 2022).

Sensitivity Analysis

Derivative liabilities were recognized in March 2022 at the initial fair value of €142.5 million.

On December 31, 2022, all other inputs and assumptions held constant, a 10% increase in volatility, will increase the fair value of derivative liabilities by approximately €15.7 million and indicates a decrease in profit or loss and equity before tax. Similarly, a 10% decrease in volatility indicates the opposite impact.

Similarly, on December 31, 2022, all other inputs and assumptions held constant, a 10% increase in the share price, will increase the fair value of derivative liabilities by approximately €27.6 million and indicates a decrease in profit or loss and equity before tax. Similarly, a 10% decrease in the share price indicates the opposite impact.

Fair Value Measurement

Derivative liabilities are measured at fair value. All other financial assets and liabilities are measured at amortized cost.

Because of the short-term maturity for cash and cash equivalents, receivables and trade payables, their fair value approximate carrying amount. Fair value of marketable securities, convertible notes and derivatives and their level in the fair value hierarchy is summarized in following table, where

Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities that the entity can access at the measurement date;

Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly; and

Level 3 inputs are unobservable inputs for the asset or liability.

	2022		2021		
	Carrying amount	Fair value	Carrying amount	Fair value	Fair value level
	(EUR'000)				(1-3)
Financial assets					
Marketable securities	298,180	295,843	343,358	342,731	1
Financial assets measured at amortized cost	**298,180**	**295,843**	**343,358**	**342,731**	
Total financial assets	**298,180**	**295,843**	**343,358**	**342,731**	
Financial liabilities					
Convertible senior notes	399,186	382,459	—	—	3
Financial liabilities measured at amortized cost	**399,186**	**382,459**	**—**	**—**	
Derivative liabilities	157,950	157,950	—	—	3
Financial liabilities measured at fair value through profit or loss	**157,950**	**157,950**	**—**	**—**	
Total financial liabilities	**157,950**	**157,950**	**—**	**—**	

Movements in level 3 fair value measurements are specified below:

	2022	2021	2020
		(EUR'000)	
Derivative liabilities			
January 1	—	—	—
Additions	142,467	—	—
Remeasurement recognized in financial income or expense	15,483	—	—
December 31	**157,950**	**—**	**—**

Note 16 – Financial Risk Management

The Company manages capital to ensure that all group enterprises will be able to continue as going concern while maximizing the return to shareholders through the optimization of debt and equity balances. The overall strategy in this regard has remained unchanged since 2012.

Capital Structure

The Company's capital structure consists of equity and external debt obtained through issuance of convertible notes. The Company is not subject to any externally imposed capital requirements or covenants. The capital structure is reviewed on an ongoing basis for the adequacy of the Company's capital compared to the resources required for carrying out ordinary activities.

Development in the Company's share capital and treasury shares reserves are described in the following sections. Other equity reserves are described in Note 2 "Summary of Significant Accounting Policies".

Share Capital

The share capital of Ascendis Pharma A/S consists of 57,152,295 fully paid shares at a nominal value of DKK 1, all in the same share class.

The number of outstanding shares of the Company are as follows:

	2022	2021	2020	2019	2018
			(Number)		
Changes in share capital					
At January 1	56,937,682	53,750,386	47,985,837	42,135,448	36,984,292
Increase through cash contributions	214,613	3,187,296	5,764,549	5,850,389	5,151,156
At December 31	**57,152,295**	**56,937,682**	**53,750,386**	**47,985,837**	**42,135,448**

Treasury Shares Reserve

The holding of treasury shares are as follows:

	Nominal value	Holding	Holding in % of total outstanding shares
	(EUR'000)	(Number)	
Treasury shares			
At January 1, 2021	—	—	—
Acquired from third parties	21	154,837	—
At December 31, 2021	**21**	**154,837**	**0.3 %**
Acquired from third parties	134	1,000,000	—
Transferred under stock incentive programs	(6)	(41,685)	—
At December 31, 2022	**149**	**1,113,152**	**2.0 %**

Financial Risk Management Objectives

The Company regularly monitors the access to domestic and international financial markets, manages the financial risks relating to its operations, and analyze exposures to risk, including market risk, such as foreign currency risk and interest rate risk, credit risk and liquidity risk.

The Company's financial risk exposure and risk management policies are described in the following sections.

Market Risk

The Company's activities expose the group enterprises to the financial risks of changes in foreign currency exchange rates and interest rates. Derivative financial instruments are not applied to manage exposure to such risks.

Foreign Currency Risk Management

The Company is exposed to foreign currency exchange risks arising from various currency exposures, primarily with respect to the U.S. Dollar ("USD").

Foreign currency exchange risks are unchanged to prior year, and primarily relate to sale and purchases in foreign currencies, and cash, cash equivalents and marketable securities, countered by convertible notes. The exposure from foreign currency exchange risks is managed by maintaining cash positions in the currencies in which the majority of future expenses are denominated, and payments are made from those reserves.

Foreign Currency Sensitivity Analysis

The following table details how a strengthening of the USD against the EUR would impact profit and loss, and equity before tax at the reporting date. A similar weakening of the USD would have the opposite effect with similar amounts. A positive number indicates an increase in profit or loss and equity before tax, while a negative number indicates the opposite. The sensitivity analysis is deemed representative of the inherent foreign currency exchange risk associated with the operations.

		Hypothetical impact on consolidated financial statements		
	Nominal positions (net)	Increase in foreign currency exchange rate	Profit and loss before tax	Equity before tax
		(EUR '000)		
USD/EUR				
December 31, 2022	60,581	10 %	6,058	6,058
December 31, 2021	549,243	10 %	54,924	54,924

Interest Rate Risk Management

Outstanding convertible notes comprise a 2.25% coupon fixed rate structure. In addition, interest rate on lease liabilities is fixed at the lease commencement date. Future indebtedness including those related to lease arrangements, if any, may be subject to higher interest rates. In addition, future interest income from interest-bearing bank deposits and marketable securities may fall short of expectations due to changes in interest rates.

Rate structure of marketable securities are specified below:

	December 31, 2022		December 31, 2021	
	Carrying amount	Fair value	Carrying amount	Fair value
	(EUR'000)			
Marketable securities specified by rate structure				
Fixed rate	205,825	203,543	323,176	322,556
Floating rate	11,787	11,773	17,975	17,968
Zero-coupon	80,568	80,527	2,207	2,207
Total marketable securities	**298,180**	**295,843**	**343,358**	**342,731**

Derivative liabilities are measured at fair value through profit or loss. Accordingly, since the fair value is exposed from the development in interest rates, the profit or loss is exposed to volatility from such development. The effects of interest rate fluctuations are not considered a material risk to the Company's financial position. Accordingly, no interest sensitivity analysis has been presented.

Credit Risk Management

The Company has adopted an investment policy with the primary purpose of preserving capital, fulfilling liquidity needs and diversifying the risks associated with cash, cash equivalents and marketable securities. This investment policy establishes minimum ratings for institutions with which the Company holds cash and cash equivalents, as well as rating and concentration limits for marketable securities held.

The exposure to credit risk primarily relates to cash, cash equivalents, and marketable securities. The credit risk on bank deposits is limited because the counterparties, holding significant deposits, are banks with minimum credit-ratings of A3/A- assigned by international credit-rating agencies. The banks are reviewed on a regular basis and deposits may be transferred during the year to mitigate credit risk. In order to mitigate the concentration of credit risks on bank deposits and to preserve capital, a portion of the bank deposits have been placed into primarily U.S. government bonds, treasury bills, corporate bonds, and agency bonds. The Company's investment policy, approved by the Board of Directors, only allows investment in marketable securities having investment grade credit-ratings, assigned by international credit-rating agencies. Accordingly, the risk from probability of default is low. On each reporting date, the risk of expected credit loss on bank deposits and marketable securities, including the hypothetical impact arising from the probability of default is considered in conjunction with the expected loss caused by default by banks or securities with similar credit-ratings and attributes. In line with previous periods, this assessment did not reveal a material impairment loss, and accordingly no provision for expected credit loss has been recognized.

Marketable securities specified by investment grade credit rating are specified below:

	December 31, 2022		December 31, 2021	
	Carrying amount	Fair value	Carrying amount	Fair value
	(EUR'000)			
Marketable securities specified by investment grade credit rating				
High grade	203,530	202,048	144,307	144,030
Upper medium grade	94,650	93,795	196,909	196,566
Lower medium grade	—	—	2,142	2,135
Total marketable securities	**298,180**	**295,843**	**343,358**	**342,731**

At the reporting dates, there are no significant overdue trade receivable balances. As a result, write-down to accommodate expected credit-losses is not deemed material.

Liquidity Risk Management

Historically, the risk of insufficient funds has been addressed through proceeds from sale of the Company's securities in private and public offerings and in 2022, through issuance of convertible notes.

Liquidity risk is managed by maintaining adequate cash reserves and banking facilities, and by matching the maturity profiles of marketable securities with cash-forecasts. The risk of shortage of funds is monitored, using a liquidity planning tool, to ensure sufficient funds are available to settle liabilities as they fall due.

Besides marketable securities and deposits, the Company's financial assets are recoverable within twelve months after the reporting date. The composition of the marketable securities portfolio and its maturity profiles are specified in the following table.

	December 31, 2022		December 31, 2021	
	Carrying amount	Fair value	Carrying amount	Fair value
	(EUR'000)			
Marketable securities specified by security type				
U.S. Treasury bills	79,086	79,043	—	—
U.S. Government bonds	99,337	98,075	95,408	95,211
Commercial papers	—	—	2,207	2,207
Corporate bonds	104,236	103,301	226,771	226,379
Agency bonds	15,521	15,424	18,972	18,934
Total marketable securities	**298,180**	**295,843**	**343,358**	**342,731**
Classified based on maturity profiles				
Non-current assets	7,492	7,201	107,561	107,175
Current assets	290,688	288,642	235,797	235,556
Total marketable securities	**298,180**	**295,843**	**343,358**	**342,731**

Marketable securities have a weighted average duration of 3.0 and 12.6 months, for current (i.e., those maturing within twelve months after the reporting date) and non-current positions, respectively. The entire portfolio of marketable securities (current and non-current) has a weighted average duration of 3.2 months.

Maturity analysis

Contractual cashflows for non-derivative financial liabilities recognized in the consolidated statements of financial position are specified below.

	< 1 year	1-5 years	>5 years	Total contractual cash-flows	Carrying amount
			(EUR'000)		
Financial liabilities					
December 31, 2022					
Borrowings					
Lease liabilities	13,996	53,821	60,946	128,763	109,191
Convertible senior notes	12,130	48,519	545,161	605,810	399,186
Total borrowings	**26,126**	**102,340**	**606,107**	**734,573**	**508,377**
Trade payables and accrued expenses	101,032	—	—	101,032	101,032
Total financial liabilities	**127,158**	**102,340**	**606,107**	**835,605**	**609,409**
Financial liabilities					
December 31, 2021					
Borrowings					
Lease liabilities	7,098	51,442	68,378	126,918	104,961
Total borrowings	**7,098**	**51,442**	**68,378**	**126,918**	**104,961**
Trade payables and accrued expenses	59,417	—	—	59,417	59,417
Total financial liabilities	**66,515**	**51,442**	**68,378**	**186,335**	**164,378**

Note 17—Commitments and Contingencies

Contractual commitments for the acquisition of property, plant and equipment were €4.4 million and €8.4 million for the years ended December 31, 2022 and 2021, respectively. Further, with certain suppliers, the Company has agreed minimum commitments related to the manufacturing of product supply, subject to continuous negotiation and adjustments according to the individual contractual terms and conditions. Cost of product supply is recognized when the Company obtains control of the goods. In addition, the Company has commitments related to short-term leases and leases of low value assets, contracts of various lengths in respect of research and development with CROs, and IT and facility related services. Costs relating to those commitments are recognized as services are received.

The Company is not aware of any significant legal claims or disputes.

Note 18—Related Party Transactions

The Board of Directors, the Executive Board and Non-executive Senior Management ("Key Management Personnel") are considered related parties as they have authorities and responsibilities with planning and directing the Company's operations. Related parties also include undertakings in which such individuals have a controlling or joint controlling interest. Additionally, all group enterprises and associates are considered related parties.

Neither the Company's related parties or major shareholders hold a controlling, joint controlling, or significant interest in the Group.

The Company has entered into employment agreements with and issued warrants and RSUs to Key Management Personnel. In addition, the Company pays fees for board tenure and board committee tenure to the independent members of the Board of Directors. For further details, refer to Note 6, "Employee Costs". Indemnification agreements have been entered with members of the Board of Directors, the Executive Board and Non-executive Senior Management.

Transactions between the parent company and group enterprises comprise management and license fees, research and development services, and clinical and commercial supplies. These transactions have been eliminated in the consolidated financial statements. Transactions and outstanding balances with the associate are disclosed in Note 12, "Investment in Associate".

In addition, the parent company Ascendis Pharma A/S is jointly taxed with its Danish subsidiaries, where the current Danish corporation tax is allocated between the jointly taxed Danish companies. For further details, refer to Note 9, "Tax on Profit/(Loss) for the Year and Deferred Tax".

Except for the information disclosed above, the Company has not undertaken any significant transactions with members of the Key Management Personnel, or undertakings in which the identified related parties have a controlling or joint controlling interest.

Note 19—Investments in Group Enterprises

Ascendis Pharma A/S's (parent company) investments in group enterprises at December 31, 2022, comprise:

Subsidiaries	Domicile	Ownership
Ascendis Pharma GmbH	Germany	100 %
Ascendis Pharma Endocrinology GmbH	Germany	100 %
Ascendis Pharma, Inc.	USA	100 %
Ascendis Pharma Endocrinology, Inc.	USA	100 %
Ascendis Pharma Ophthalmology Division A/S	Denmark	100 %
Ascendis Pharma Endocrinology Division A/S	Denmark	100 %
Ascendis Pharma Bone Diseases A/S	Denmark	100 %
Ascendis Pharma Growth Disorders A/S	Denmark	100 %
Ascendis Pharma Oncology Division A/S	Denmark	100 %

Associate	Domicile	Ownership
VISEN Pharmaceuticals	Cayman Island	43.93 %

Note 20—Ownership

The following investors, or groups of affiliated investors, are known by us to beneficially own more than 5% of the Company's outstanding ordinary shares at December 31, 2022:

- T. Rowe Price Associates, Inc., USA
- Entities affiliated with RA Capital Management, LLC, USA
- Entities affiliated with Artisan Partners Limited Partnership, USA
- Entities affiliated with FMR LLC, USA
- Baker Bros. Advisors LP, USA
- Entities affiliated with Wellington Management Group LLP, USA
- Entities affiliated with Janus Henderson Group plc, United Kingdom

The Company's American Depository Shares are held through BNY (Nominees) Limited as nominee, of The Bank of New York Mellon, UK (as registered holder of the Company's outstanding ADSs).

Note 21—Subsequent Events

No events have occurred after the reporting date that would influence the evaluation of these consolidated financial statements.

Item 19 Exhibits

The following exhibits are filed as part of this annual report:

Exhibit Number	Exhibit Description	Incorporated by Reference				Provided Herewith
		Form	Date	Number	File Number	
1.1	Articles of Association, currently in effect (English translation).	6-K	2/15/2023	1.1	001-36815	
2.1	Deposit Agreement dated January 27, 2015 among Ascendis Pharma A/S The Bank of New York Mellon and Owners and Holders of American Depositary Shares.	F-3	2/2/2016	4.2	333-209336	
2.2	Form of American Depositary Receipt (included in Exhibit 2.1).					
2.3	Description of Share Capital and American Depositary Shares.					X
4.1(a)	Rental Agreement, between Technologiepark Heidelberg II GmbH & Co. KG and Ascendis Pharma GmbH (English translation).	F-1	12/18/2014	10.3(a)	333-201050	
4.1(b)	Supplement No. 1 to Rental Agreement, between Technologiepark Heidelberg II GmbH & Co. KG and Ascendis Pharma GmbH (English translation).	F-1	12/18/2014	10.3(b)	333-201050	
4.2(a)	Reference is made to Exhibit 1.1.					
4.2(b)	Form of Warrant Certificate for Warrants issued prior to December 2015.	F-1	12/18/2014	10.4(b)	333-201050	
4.2(c)	Form of Warrant Certificate for Warrants issued since December 2015.	20-F	3/22/2017	4.4(c)	001-36815	
4.3	Form of Indemnification Agreement for board members and senior management.	F-1	1/16/2015	10.5	333-201050	
4.4	Registration Rights Agreement dated December 11, 2015 by and among Ascendis Pharma A/S, Fidelity Securities Fund: Fidelity Series Small Cap Opportunities Fund—Healthcare Sub and Fidelity Stock Selector Small Cap Fund—Health Care Sub.	6-K	12/14/2015	4.1	001-36815	
4.5	Lease Agreement dated September 7, 2015 between Ascendis Pharma A/S and Dades AS.	F-3	2/2/2016	10.1	001-36815	
4.6†	Manufacturing and Supply Agreement dated December 21, 2017, between Ascendis Pharma A/S and NOF Corporation.	20-F	3/28/2018	4.9	001-36815	
4.7†	Manufacturing and Supply Agreement dated January 12, 2017, between Ascendis Pharma A/S and Medicom Innovation Partner A/S.	20-F	3/28/2018	4.10	001-36815	

Exhibit Number	Exhibit Description	Incorporated by Reference				Provided Herewith
		Form	Date	Number	File Number	
4.8*	Supply Agreement dated January 1, 2019, between Ascendis Pharma A/S and Vetter Pharma International GMBH.	20-F	4/3/2019	4.11	001-36815	
4.9*	Manufacturing and Supply Agreement dated October 26, 2018, between Ascendis Pharma A/S and Carbogen Amcis AG.	20-F	4/3/2019	4.12	001-36815	
4.10*	Commercial Supply Agreement dated January 9, 2019, between Ascendis Pharma A/S and Fujifilm Diosynth Biotechnologies UK Limited.	20-F	4/3/2019	4.13	001-36815	
4.11*	Exclusive Licence Agreement dated November 7, 2018, between Ascendis Pharma Growth Disorders A/S and VISEN Pharmaceuticals (CNP).	20-F	4/3/2019	4.15	001-36815	
4.12*	Exclusive Licence Agreement dated November 7, 2018, between Ascendis Pharma Endocrinology Division A/S and VISEN Pharmaceuticals (hGH).	20-F	4/3/2019	4.16	001-36815	
4.13*	Exclusive Licence Agreement dated November 7, 2018, between Ascendis Pharma Bone Diseases A/S and VISEN Pharmaceuticals (PTH).	20-F	4/3/2019	4.17	001-36815	
4.14*	Tech Transfer and Manufacturing Services Agreement dated December 12, 2019 between Ascendis Pharma A/S and Lonza Ltd.	20-F	4/2/2020	4.16	001-36815	
4.15*	Packaging and Supply Agreement dated December 1, 2019 between Ascendis Pharma A/S and Sharp Corporation.	20-F	4/2/2020	4.17	001-36815	
4.16*	Manufacturing and Supply Agreement dated December 27, 2020, between Ascendis Pharma A/S and Bachem AG.	20-F	3/2/2022	4.16	001-36815	
4.17*	Manufacturing and Supply Agreement dated May 27, 2021, between Ascendis Pharma A/S and Carbogen Amcis AG.	20-F	3/2/2022	4.17	001-36815	
4.18*	Manufacturing and Supply Agreement dated August 31, 2020 between Ascendis Pharma A/S and NOF Corporation.	20-F	3/2/2022	4.18	001-36815	
4.19*	Amended and Restated Shareholders Agreement dated January 8, 2021, by and among Ascendis Pharma A/S and the parties set forth therein.	20-F	3/10/2021	4.17	001-36815	
4.20*	Amendment Letter to the Exclusive Licence Agreement dated January 4, 2021 between Ascendis Pharma Growth Disorders A/S and VISEN Pharmaceuticals (CNP).	20-F	3/10/2021	4.18	001-36815	

Exhibit Number	Exhibit Description	Incorporated by Reference				Provided Herewith
		Form	Date	Number	File Number	
4.21*	Amendment Letter to the Exclusive Licence Agreement dated January 4, 2021 between Ascendis Pharma Endocrinology Division A/S and VISEN Pharmaceuticals (hGH).	20-F	3/10/2021	4.19	001-36815	
4.22*	Amendment Letter to the Exclusive Licence Agreement dated January 4, 2021 between Ascendis Pharma Bone Diseases A/S and VISEN Pharmaceuticals (PTH).	20-F	3/10/2021	4.20	001-36815	
4.23	Ascendis Pharma A/S Restricted Stock Unit Program.	S-8	12/9/2021	99.2	333-261550	
8.1	List of Subsidiaries.					X
12.1	Certification by Principal Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
12.2	Certification by Principal Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
13.1	Certification by Principal Executive Officer Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
13.2	Certification by Principal Financial Officer Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
15.1	Consent of Independent Registered Public Accounting Firm.					X
EX-101.INS	Inline XBRL Instance Document.					X
EX-101.SCH	Inline XBRL Taxonomy Extension Schema Document.					X
EX-101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					X
EX-101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.					X
EX-101.IAB	Inline XBRL Taxonomy Extension Labels Linkbase Document.					X
EX-101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
104	Cover page interactive data file (formatted as Inline XBRL and included in Exhibit 101).					X

† Confidential treatment has been granted for certain information contained in this Exhibit. Such information has been omitted and filed separately with the SEC.

* Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Regulation S-K, Item 601(b)(10). Such excluded information is not material and is the type that the registrant treats as private or confidential.

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.

Ascendis Pharma A/S

/s/ Jan Møller Mikkelsen

By: Jan Møller Mikkelsen
President, Chief Executive Officer and Board Member (Principal Executive Officer)

Date: February 16, 2023

/s/ Scott T. Smith

By: Scott T. Smith
Executive Vice President, Chief Financial Officer (Principal Financial Officer)

Date: February 16, 2023