I. RISK FACTORS

An investment in Santhera shares ("**Shares**") involves a high degree of risk. Prospective investors should carefully consider the risks related to any investment in the Shares before making a decision to invest in the Shares. The risks described below are not the only ones applicable to Santhera Pharmaceuticals Holding AG (the "**Company**") and/or its subsidiaries (together with the Company, the "Group", "Santhera", "we" or "us"). Additional risks not presently known or currently deemed immaterial may also impair the Group's business, results of operations, financial condition or prospects. The realization of one or more of these risks individually or together with other circumstances may have a material adverse effect on the Group's business, results of operations, financial condition or prospects. In addition, each of the risks set out below could adversely affect the trading price of the Shares, and investors in Shares may lose all or a part of their investment.

The order in which the risks are presented below is not intended to indicate the probability of their occurrence or the materiality of the risk.

By issuing these risk factors, we do not promote or solicit any investment in the Shares or related securities.

Date: February 18, 2020

A. Risks related to our business and financial situation

1. Risks related to our financial position, capital needs and transactions

Our ability to continue as a going concern depends on our ability to obtain funding by way of equity and/or debt financings in the immediate short term. A material uncertainty exists as to whether the Company's current funding is sufficient to support its going concern for another twelve months. We may not be able to obtain future financing or only obtain it on terms that significantly dilute the Company's shareholders and/or restrict our flexibility to operate. Also, our cash-preserving measures may adversely impact our operations and prospects.

As at December 31, 2019, we had cash and cash equivalents of CHF 31.4 million. We incurred a net loss of CHF 51.5 million in 2017, of CHF 54.2 million in 2018 and of CHF 26.9 million in the six months ended June 30, 2019.

Our operations have used substantial amounts of cash since our inception and we continue to require significant amounts of cash for operating our business and to satisfy our obligations. We also expect our expenses to increase further in connection with our ongoing development activities as well as the ramping up of our commercialization activities relating to Puldysa®. Also, if we choose to exercise our option from Idorsia to obtain an exclusive sub-license from Idorsia to commercialize ReveraGen's vamorolone, which we currently anticipate to be able to do in the fourth quarter of 2020 according to the current development plan, we would need to make a cash payment to Idorsia of USD 30 million. Further, our CHF 60 million Senior Unsecured Convertible Bonds 2017-2022 (the "**Bonds**") will become due for redemption in February 2022, and our interest payment obligation with respect to the aggregate principal amount of the Bonds amounts to CHF 3 million *per annum*. We currently expect that we will need to raise funds by way of equity and/or debt financing in the immediate short term in order to continue as a going concern and to continue our operations as planned. Without such funds, there will be material uncertainty as to whether we will be able to continue as a going concern for another twelve months.

Pursuant to note 2 to the interim condensed consolidated financial statements for the six-month period ended June 30, 2019, a material uncertainty exists as to whether the Company's current funding is sufficient to support its going concern for another twelve months. We plan to include an analogous note in our audited consolidated financial statements for the year ended December 31, 2019. The inclusion of a going concern qualification or emphasis of matter paragraph in any audit opinion related to our financial statements in the future may materially adversely affect our trading and our ability to raise new capital that we need to fund our operations.

We currently expect that we will continue to depend significantly on equity and debt financing, in addition to cash flows from potential milestone payments. Such financing may not be available to us on acceptable terms, or at all, in particular in the short term. Also, the Bonds prohibit us from issuing any secured marketable debt instruments or incurring any secured financial debt (including bank debt) exceeding CHF 10 million in the aggregate (subject to exceptions) unless the Bonds are secured equally and rateably, or the Paying and Conversion Agent under the Bonds consents, which could adversely impact our ability to raise additional debt financing. If we fail to obtain additional funds on acceptable terms when needed, we may have to delay, reduce or terminate our product development programs and/or the ramping up of our commercialization activities relating to Puldysa®, and we may not be able to meet the cash requirements for operating our business, for exercising our option with respect to vamorolone (if we choose to do so), and for making payments with respect to our financial obligations, including interest and principal payments on our Bonds, and we may be required to file for bankruptcy.

If we are able to raise additional equity or issue equity-linked instruments, the Company's shareholders could be significantly diluted. If we incur additional debt, the terms of such debt may subject us to restrictive covenants or security obligations that limit our flexibility in conducting future business activities, such as incurring additional debt or acquiring or licensing intellectual property rights.

Further, we have taken measures to reduce our cash outflow and we anticipate to take further cash-preserving measures in the immediate short term. Such measures may adversely impact our operations and our medium- to long-term prospects.

We have outlicensed our only commercial product, Raxone®, to Chiesi Group in August 2019 and we do not expect to generate significant revenue from the sale of Raxone® by ourselves going forward. We may not receive any of the milestone payments of up to EUR 49 million agreed with Chiesi Group, which would have a negative impact on our timeline towards profitability.

In August 2019, we outlicensed our rights in our only product, Raxone®, which is approved for commercial sale for the treatment of Leber's hereditary optic neuropathy ("**LHON**") in the European Union (the "**EU**"), the United Kingdom (the "**UK**") and certain other jurisdictions, to Chiesi Group. Under the agreement, Chiesi Group made an initial payment of EUR 44 million and we have the right to receive up to EUR 49 million in staggered milestone payments if and when Chiesi Group meets certain sales thresholds. It is uncertain whether and when Chiesi Group will meet any of these sales thresholds. Consequently, we may not receive any of these milestone payments or may receive only partial milestone payments, each of which would have a negative impact on our timeline towards profitability. Also, our transaction with Chiesi Group was met with concern from certain investors. In any case, even if we receive the milestone payments from Chiesi Group in full, we will still require additional funds to reach profitability.

Following the outlicensing of Raxone® to Chiesi Group, our revenue from the sale of Raxone® by ourselves and our distributors has been significantly reduced. Until our transaction with Chiesi Group, our sales of Raxone® in France constituted a significant part of our overall sales. Under a transitory regime agreed with Chiesi Group, we continue to sell Raxone® in France. However, as the French Ministry for Solidarity and Health has finally refused to register Raxone® on the lists of reimbursed products in France, we do not expect any further sales of Raxone® in France unless a broader agreement with the French authorities can be reached. As of the date hereof, Raxone® is still listed for reimbursement and the Company continues to sell Raxone® in France to hospitals.

We have not received marketing authorization for any of our current product candidates for any country. We have incurred significant losses since our inception and expect to incur substantial losses and negative operating cash flows for the foreseeable future and may never achieve or maintain profitability.

Other than Raxone®, which we have outlicensed to Chiesi Group, we currently have no products approved for commercial sale. Our most advanced product candidate is Puldysa®, whose active ingredient is idebenone and which we develop for the treatment of Duchenne muscular dystrophy ("**DMD**"), and we have acquired an option to receive a sublicense to ReveraGen's product candidate vamorolone in DMD and in other indications. We have not received marketing authorization for our product candidates for any country

(whereby references herein to "our" product candidates include vamorolone as well as in-licensed product candidates such as POL6014, unless otherwise stated or the context requires otherwise).

We have incurred consistent cash-outflow and significant losses since our inception, including a net loss of CHF 35.4 million in 2016, of CHF 51.5 million in 2017, of CHF 54.2 million in 2018 and of CHF 26.9 million in the six months ended June 30, 2019. We expect to continue to incur significant operating losses for the foreseeable future, as we continue our development and commercialization efforts and make investments. We expect our expenses to increase substantially over the coming years, primarily due to higher operating expenses in connection with our ongoing development activities as well as the ramping up of our commercialization activities relating to Puldysa®. To become and remain profitable, we must successfully complete the development of our product candidates, obtain marketing authorizations and pricing and reimbursement approvals for them, expand our development pipeline, maintain and manage our manufacturing arrangements with third parties, maintain and build up an effective internal sales and marketing organization, establish and maintain sales and marketing arrangements with third parties and raise sufficient funds to finance our activities. We may never succeed in these activities, and even if we do, we may never generate sales that are significant enough to achieve profitability.

Our future profitability, if any, will depend on us being able to obtain marketing authorization and, thereafter, pricing and reimbursement approvals for our product candidates, in particular Puldysa® and vamorolone in DMD.

Our future success and profitability (if any) will depend on our ability to obtain marketing authorization and, thereafter, pricing and reimbursement approvals for Puldysa® in the EU and in the United States of America (the "**U.S.**"), as well as on other factors. We may never receive a marketing authorization for Puldysa® (see next risk factor). Even if we eventually obtain such marketing authorization for the EU, we may not receive it on terms acceptable to us, or our product may not be commercially viable. Moreover, pricing and reimbursement decisions in the EU remain a competence of each Member State and therefore may vary significantly from one country to another. For a summary of risks related to pricing and reimbursement see the risk factor "*The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain coverage and adequate reimbursement for our marketed product (which is outlicensed to Chiesi Group) or any product for which we receive marketing authorization in the future and price controls could limit our ability to market those products and decrease our ability to generate sales.*"

In the EU, we have applied with the European Medicines Agency ("**EMA**") to obtain a conditional marketing authorization ("**CMA**") for Puldysa® for the treatment of respiratory dysfunction in patients with DMD who are not using steroids, and have not yet sought marketing authorization for Puldysa® in DMD patients who are using steroids, and our phase III clinical trial ("**SIDEROS**") for Puldysa® in this subgroup of DMD patients is still ongoing and its outcome is uncertain. In the U.S., we have not filed a New Drug Application ("**NDA**") for Puldysa®. If the SIDEROS trial, where we currently expect the last patient visit to occur in the fourth quarter of 2021, has a favorable outcome, we plan to submit an NDA for Puldysa® to treat respiratory dysfunction in DMD patients irrespective of their steroid use. If we are unsuccessful or significantly delayed in obtaining marketing authorization for Puldysa® or its subsequent commercialization, we would have to rely on the further development of vamorolone in DMD, for which we have acquired an option to in-license, and on our early stage pipeline that comprises POL6014 in cystic fibrosis ("**CF**") (currently in phase I multiple ascending dose trial), omigapil in congenital muscular dystrophy ("**CMD**") (phase I clinical trial completed) and our pre-clinical collaboration with the University of Basel's Center for Molecular Life Sciences (*Biozentrum*) regarding a potential gene therapy for laminin-alpha 2 (LAMA2)-deficient congenital muscular dystrophy (LAMA2-MD). Given the uncertainties around the development and commercialization of pharmaceuticals, we may not be able to develop and commercialize any such product candidates in a timely manner or at all.

Our past application for marketing authorization with respect to our most advanced product candidate, Puldysa® (formerly under the trademark Raxone®), has been unsuccessful. We may never receive a marketing authorization for Puldysa®.

The EMA's Committee for Medicinal Products for Human Use ("**CHMP**") had issued a negative opinion on our initial marketing authorization application ("**MAA**") with respect to idebenone – filed in 2016 under the trademark Raxone® – for the treatment of respiratory dysfunction in DMD patients with declining respiratory function who are not using steroids in September 2017. In January 2018 the CHMP maintained such negative opinion following a re-examination procedure that we requested despite an updated proposal for post-authorization measures and a clarification of the wording of the indication that we had proposed. In May 2019, we applied with the EMA to obtain a CMA with respect to Puldysa® for the treatment of respiratory dysfunction in DMD patients who are not using steroids. The CHMP may issue a negative opinion on our application. Should this occur, regulators elsewhere, in particular the FDA, if and when we file an NDA for Puldysa® in the U.S., may be more reluctant to grant us marketing authorization for Puldysa®. If we do not receive a marketing authorization for Puldysa® in the EU and if our ongoing SIDEROS trial for Puldysa® in certain DMD patients who are using steroids does not have a favorable outcome, we may have or elect to abandon our activities with regard to Puldysa® entirely.

News on our development and commercialization efforts that we expect to receive in 2020 and in the longer term may have a significant and potentially adverse effect on the value of the Group and, as a consequence, the market price of the Shares.

The value of the Group strongly depends on the results of our clinical trials and on the decisions by regulatory authorities. We expect to receive material new information on such matters in 2020 and in the longer term. In particular, we currently expect an opinion from the CHMP on our application for CMA with regard to Puldysa® in the second quarter of 2020, and six-month top line data of ReveraGen's ongoing pivotal Phase IIb clinical trial of vamorolone in DMD (VISION-DMD) in the fourth quarter of 2020, on the basis of which we will decide whether we exercise our option to obtain an exclusive sub-license to commercialize vamorolone. Any negative outcomes or delays of these events may have a significant adverse effect on the value of the Group and may adversely affect its business and prospects. As a consequence, the market price of the Shares is expected to be very volatile. Should any such news be unfavorable, the market price of the Shares may significantly decline and, potentially, not recover.

We may be required to refund to the French Social Security part of our revenue generated from the sale of Raxone® in France since January 1, 2016. If we are required to make such a refund in cash, our financial situation, results of operations and prospects may be materially adversely affected.

In France, Raxone® has been financed by the French Social Security under the so-called post-*autorisation temporaire d'utilisation*, or post-ATU, financing scheme (*dispositif pérenne*) since the product was launched. As a result of the refusal of the French Ministry for Solidarity and Health to register Raxone® on the lists of reimbursed products in France for patients and hospitals (see risk factor "*We have outlicensed our only commercial product, Raxone®, to Chiesi Group in August 2019 and we do not expect to generate significant revenue from the sale of Raxone® by ourselves going forward. We may not receive any of the milestone payments of up to EUR 49 million agreed with Chiesi Group, which would have a negative impact on our timeline towards profitability.*"), applicable rules require that we as the holder of the ATU refund to the French Social Security the difference between the price at which we sold Raxone® under the ATU and a reference price to be set by the *Comité économique des produits de santé* (CEPS). Therefore, the CEPS could require us to refund part of our revenue generated from the sale of Raxone® in LHON in France since January 1, 2016. In the assessment of our French legal counsels, it is impossible as of the date of this Listing Prospectus to assess the amount of a potential refund because the reference price to be set by the CEPS is unknown. Also, the process of establishing a potential refund and its modalities could be protracted. Considering the legal background, the fact that there is to our knowledge no established practice regarding the application of the relevant rules, the high unmet medical need for a treatment of LHON in France and other factors, our French legal counsels estimate that the chances that the authorities will require a refund from us without discussion are less than 50%. Should the authorities agree to discuss the matter with us, our French legal counsels estimate that it is more likely than not that the CEPS will accept an alternative way of compensation by way of discounts on future sales to be determined with the CEPS. For the latter scenario,

which management deems to be the most likely one, we currently estimate the cost of goods and supply for the products to be provided under such refund scheme to be less than CHF 0.6 million *per annum*. However, should we be required to make a cash payment, our financial situation, results of operations and prospects may be materially adversely affected.

We may not realize the benefits of our in-licensing of POL6014 from Polyphor, of our option to in-license vamorolone from Idorsia, of any other product candidates or compounds that we may in-license or acquire, of any strategic alliances that we may form, joint ventures that we may create, or strategic transactions that we may enter into in the future.

We have acquired, in-licensed or acquired an option to in-license all of our current product candidates, typically against payment of upfront consideration and milestone and royalty payments. In February 2018, we in-licensed the compound POL6014 from Polyphor against an initial consideration (paid in Shares) of CHF 6.5 million, and we agreed to cash payments of up to CHF 121 million contingent on future development, regulatory and particularly sales milestones. In November 2018, we acquired an option to obtain from Idorsia an exclusive sub-license to commercialize ReveraGen's vamorolone in all indications. We paid an equity consideration of 1,000,000 Shares and a cash consideration of USD 20 million to Idorsia for the option. If we exercise such option, which we can only do if we have the required funds, Idorsia will be entitled to receive a cash payment from us of USD 30 million upon exercise of the option, as well as commercial milestone payments of up to USD 80 million in the DMD indication and four one-time sales milestone payments of up to USD 130 million in aggregate. Regulatory milestone payments payable by us to Idorsia for three additional indications amount to up to USD 205 million in aggregate. Upon commercialization of vamorolone, we have committed to pay to Idorsia tiered royalties ranging from a single-digit to low double-digit percentage on the annual net sales of vamorolone.

We may not be able to realize the benefit of our past or future acquisitions or in-licensing transactions, or they may turn out to have been made at too high a price. Likewise, any strategic alliances, joint ventures or strategic transactions that we may enter into in the future may fail to achieve the expected results and may divert capital resources and management time. It is unclear whether and when any product candidates may generate revenues for the Company.

2. Risks related to the development of our product candidates

Any setbacks impacting the compound idebenone (the active ingredient in Puldysa® and Raxone®) may adversely affect our outlicensed product and our most advanced product candidate simultaneously.

We rely on the compound idebenone for use in Raxone®, our product outlicensed to Chiesi Group, and our most advanced product candidate, Puldysa®. Any adverse effects resulting from the use of idebenone in the human body, or any difficulty in the manufacture, or problem with the supply, of idebenone, or any measures taken by regulators in relation to idebenone, could adversely affect Raxone® and our most advanced product candidate Puldysa® simultaneously.

Our product candidates must prove their efficacy and safety in rigorous clinical testing. Drug development involves a lengthy and expensive process, with an uncertain outcome. Failure may occur at any stage of clinical development.

Before we may seek marketing authorization for any product candidate, we must conduct extensive clinical trials to demonstrate its safety and efficacy in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to its outcome. A failure of one or more clinical trials can occur at any stage of testing. Promising results in preclinical studies of a product candidate may not be predictive of similar results in humans during clinical trials, and successful results from early clinical trials may not be replicated in later and larger clinical trials or in clinical trials for different indications or different patient populations. For example, the results of our phase III clinical trial (DELOS) of idebenone, the active ingredient in Puldysa®, in certain DMD patients are not predictive of the results of our ongoing phase III clinical trial (SIDEROS) of idebenone in a different DMD patient population.

The conduct of clinical trials may be prevented, delayed, or even futile, and delays in the commencement, enrollment or completion of clinical trials for any of our product candidates could result in increased costs, or prevent us from commercializing our product candidates on a timely basis, or at all.

Before a clinical trial may begin, we or our partners must obtain approval from the competent regulatory authority and/or the competent ethics committee. We or our partners may not obtain authorization for further testing of our product candidates. Clinical trials of our product candidates may not be conducted as planned, and commencement, enrollment or completion may not occur on our planned schedule, if at all, for many reasons, which could result in increased costs and could negatively affect our or our partners' ability to complete the clinical trial. We have experienced delays in clinical trials and cost overruns in the past and may do so again in the future. If we or our partners are not able to successfully design, operate, complete and correctly evaluate the results of the clinical trials for our product candidates, we will not be able to seek marketing authorization or commercialize them.

If we or our partners experience delays or difficulties in the enrollment of patients in clinical trials, the conduct and completion of clinical trials may be delayed or prevented. Also, the availability of idebenone from inexpensive sources may adversely affect patient enrollment or the results of our clinical trials with respect to Puldysa®.

Initiation and successful and timely completion of clinical trials requires us to enroll a sufficient number of eligible patients in these trials. Given our focus on orphan drugs, our clinical trials look to enroll patients with characteristics that are found in a small number of patients and are likely to compete with other clinical trials for product candidates targeting treatment of patients with the same characteristics. As the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which reduces the number of patients available for our clinical trials at these clinical trial sites.

As idebenone can be purchased over the internet and via other inexpensive sources, patients may be reluctant to enroll in our clinical trials where they do not know whether they will receive idebenone or a placebo. Also, the parallel use of idebenone by patients in the placebo arm of a trial may adversely affect the results of our clinical trials.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our clinical trials, which could prevent their completion. We are, for example, in the process of enrolling patients for a phase III clinical trial (SIDEROS) for idebenone in certain DMD patients. Enrollment is still ongoing and has been slower than anticipated. Based on our current estimates, we expect the last patient visit to occur in the fourth quarter of 2021. Should there be any further delays in patient enrollment or if we are unable to recruit enough patients, the SIDEROS trial (and, consequently, the availability of any data) could be significantly delayed or even prevented.

We may not be successful in our efforts to build up our development pipeline or to spend our limited resources on the most promising product candidates.

We may not be able to develop our existing product candidates or to identify and develop further product candidates that are safe and effective despite spending substantial technical, financial, and personnel resources thereon. Because we have limited resources, we may forgo or delay pursuit of opportunities with certain product candidates or indications that later prove to have a greater potential than the product candidates or indications on which we have chosen to focus. Even if we are successful in continuing to build our development pipeline, the product candidates that we identify 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 authorization and achieve market acceptance.

We rely and will in the future rely on third parties to conduct clinical trials for our product candidates, and if these third parties do not properly and successfully perform their obligations, we may not be able to successfully complete the respective development of our product candidates.

We rely on Clinical Research Organizations ("**CROs**") and other third parties to assist in managing, monitoring and otherwise carrying out clinical trials for our product candidates. Together with the salaries paid to our employees in the product development department, the fees and expenses of these CROs account for most of our development expenses. We compete with many other companies for the resources of these third parties. These third parties generally may terminate their engagements with us at any time.

If the quality or accuracy of the data that these third parties obtain is compromised due to the failure on the part of these parties to adhere to clinical trial protocols or to regulatory requirements, or if these third parties otherwise fail to comply with clinical trial protocols or meet expected deadlines, the clinical trials of our product candidates may not meet regulatory requirements. In one case, we had to terminate our relationship with a CRO for cause in 2016 and had to engage another CRO to complete the clinical trial conducted by the former CRO. If clinical trials do not meet regulatory requirements or if these third parties need to be replaced for any reason, the development of our product candidates may be delayed or suspended, may be more expensive than planned or may ultimately fail.

Although we rely extensively on third parties to conduct our product development work, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with its general investigational plan, protocol, legal and regulatory requirements and scientific standards. We may incur financial liabilities or suffer negative regulatory consequences as a result of any shortcoming in meeting such responsibilities irrespective of whether we have delegated such responsibility to a CRO or other third party.

We may not be successful in maintaining existing or establishing and maintaining additional collaborations, and we may not fulfil our obligations vis-à-vis our collaboration partners.

We have entered into a number of collaborations and licensing arrangements, for example with other pharmaceutical companies, clinical research centers and other research institutions. These existing collaborations are, and any future collaborations or partnerships may be, important to our business. Generally, such collaborations allow us to share the development costs with our collaboration partners, thereby significantly reducing our own costs, and to utilize the expertise and know-how of our development partners.

In collaboration agreements, we often undertake to take certain specified efforts to develop a product candidate. If we are unable to fulfil, or otherwise do not fulfil, these obligations, we may be in breach of our obligations vis-à-vis the respective collaboration partner, which may result in a termination of the collaboration or in our liability vis-à-vis the collaboration partner.

Generally, we may not be able to maintain our current or any future collaborations or partnerships, including for reasons beyond our control. In the event of termination of a collaboration, we may be unable to progress the relevant product candidate on our own or may be unable to successfully find a new partner with which to do so on terms favorable to us or at all. Also, any termination of a collaboration by our partner could make it difficult for us to attract new strategic partners or adversely affect how we are perceived in scientific and financial communities.

We will face significant competition in seeking partners for future product development collaborations. In order for us to successfully partner our product candidates, potential partners must view us and the respective product candidate as attractive, also in light of the terms that we are seeking. Even if we successfully establish new collaborations, their terms may not be favorable to us.

If we fail to establish or maintain a collaboration related to a particular product candidate, we will bear all of the related development cost and risk and may be unable to develop that product candidate on our own for lack of resources or other reasons.

If serious adverse events or undesirable or unacceptable side effects are identified during the development of any of our product candidates or after commercialization of any product or any future products,

we may need to abandon the development of the product candidates or withdraw the product from the market.

If any of our product candidates cause undesirable or unacceptable side effects in clinical trials or have characteristics that are unexpected, we may decide or be required to interrupt, delay or abandon the relevant product candidate's development or may choose to limit its development to more narrow uses or patient subpopulations in which such side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Serious procedure- or treatment-related side effects may occur at any stage of product development and even after commercialization. Any such side effects may cause us to abandon or limit the development of the relevant product candidate or we may decide or be required to withdraw the relevant product from the market, which may result in a sudden and sharp drop of our net sales and/or significant impairment charges. These risks are amplified by the fact that idebenone is the active ingredient of both Raxone®, our product outlicensed to Chiesi Group, and of our most advanced product candidate, Puldysa®.

3. Risks related to marketing approval of our product candidates and legal compliance matters

Following clinical development, our product candidates will require marketing authorization. If we are not able to obtain marketing authorization for a particular product candidate in a timely manner, on terms acceptable to us or at all, we will not be able to commercialize it, and our ability to generate sales will be materially impaired.

Our product candidates require marketing authorizations from the FDA in the U.S., from the European Commission in the EU and from comparable regulatory authorities in other relevant jurisdictions (such as Swissmedic in Switzerland), prior to commercialization. In most jurisdictions, the process of obtaining marketing authorization for a product candidate is expensive and may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Failure to obtain marketing authorization for a product candidate will prevent us from commercializing the product candidate.

Our experience in filing and supporting the applications necessary to gain marketing authorization for a product candidate is limited and some of our marketing applications were not successful. So far, we have received marketing authorizations only for one product, Raxone®, which we have outlicensed to Chiesi Group. The CHMP had issued a negative opinion on our initial MAA for idebenone – filed in 2016 under the trademark Raxone® – in certain DMD patients in September 2017 and maintained its negative opinion in January 2018. We have never filed an NDA with, or obtained marketing authorization from, the FDA in the U.S., which is a significant pharmaceutical market. We have started (but may fail) to build up our in-house capacity for purposes of obtaining marketing authorization for Puldysa® in the U.S., and we continue to rely on external advisors to assist us with the marketing authorization process in the U.S.

Regulatory authorities have substantial discretion in the timing and substance of the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. For example, the CHMP, when it maintained its negative opinion on our initial MAA for idebenone in certain DMD patients in the EU, considered that the effect of idebenone on patients' respiratory function observed in our phase III clinical trial with idebenone in certain DMD patients with declining respiratory function who were not receiving steroids (DELOS) would or may have been considered to be clinically relevant if it were maintained over several years, rather than the 52 weeks observed in the DELOS trial. Moreover, it is possible that the FDA may not consider the SIDEROS trial, or any additional studies for Puldysa® performed and completed that it may request, sufficient to approve any NDA for Puldysa® that we may submit. If our clinical data are found insufficient, we may be forced to abandon seeking marketing authorization in the EU or the U.S. for Puldysa®.

Regulatory authorities may also narrow the uses or patient subpopulations for which the product is approved or require extensive warnings on the label, thereby limiting the potential market for or interest in the product.

If we experience delays in obtaining or fail to obtain marketing authorizations for any of our product candidates in any key jurisdiction, especially in the U.S. and the EU, their commercial prospects may be harmed or they may no longer be commercially viable. As a result, our ability to generate sales will be materially impaired.

Fast track, breakthrough therapy and similar designations for some of our product candidates may not lead to a faster development or regulatory review or approval process, will not increase the likelihood of receiving marketing authorization and may be revoked.

We have received fast track designation and rare pediatric disease designation from the FDA in particular for idebenone in DMD, and ReveraGen has received orphan drug designation for vamorolone from both the FDA and the EMA, as well as fast track designation from the FDA. We may seek fast track or similar designations for POL6014 in CF and/or any future product candidates. Further, the UK's Medicines and Healthcare Products Regulatory Agency (the "**MHRA**") has given certain DMD patients access to idebenone under the Early Access to Medicines Scheme ("**EAMS**") following its designation as Promising Innovative Medicine ("**PIM**") by the MHRA. We may seek, but may not necessarily receive designations comparable to breakthrough therapy designations or PIM in other jurisdictions and for other products or product candidates.

Regulatory authorities typically have broad discretion in granting fast track, break through therapy, PIM and similar designations and may rescind or revoke such designations. Even if such designation is granted, such designation is not predictive of future clinical trial results, does not necessarily (and in the case of certain designations will not) result in a faster development process, review or marketing approval compared to conventional approval procedures and does not increase the likelihood that a product candidate will receive marketing authorization. Many drugs that have received such designations have failed to obtain marketing authorization. If we fail to obtain any such designation for a product candidate that we think meets the criteria or any existing designations is revoked, further development of that product candidate and, ultimately, its commercialization could be materially adversely affected.

Raxone® is, and any product candidate for which we may obtain marketing authorization will be, subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions, post-marketing studies or withdrawal from the market, and we may be subject to penalties if we or the third parties with which we collaborate fail to comply with regulatory requirements or experience unanticipated problems with that product.

The commercialization activities by Chiesi Group with respect to Raxone® under our outlicensing agreement are, and our own commercialization activities with respect to any product candidates for which we may receive marketing authorization will be, subject to comprehensive regulation by regulatory authorities in each jurisdiction in which it is authorized. This regulation includes requirements regarding the testing, manufacture, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution of the relevant product. For example, we need to with respect to Raxone®, and we will need to for any product for which we may receive marketing authorization in the future, submit safety and other post-marketing information and reports, ensure that our contract manufacturers observe current Good Manufacturing Practice ("**cGMP**") requirements and comply with requirements regarding safety monitoring and pharmacovigilance.

Regulatory authorities may also impose requirements for expensive post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. For example, under the European Commission's marketing authorization that was granted for Raxone® "under exceptional circumstances" because the European Commission found that comprehensive efficacy and safety data cannot be obtained, we are required to conduct several post-authorization measures. We have a contractual obligation to Chiesi Group to conduct the post-authorization measures with regard to Raxone® that are required under our marketing authorization for the EU at our own cost.

In May 2019, we applied with the EMA to obtain a CMA with respect to Puldysa® for the treatment of respiratory dysfunction in certain patients with DMD. Even if the CHMP recommends that the European Commission grant marketing authorization, such marketing authorization would very likely be subject to

the condition that we conduct a post-authorization safety study ("**PASS**") and an externally controlled long-term open label study as post-authorization measures. Any such requirements for Puldysa® or for any other products for which we may receive marketing authorization in the future may adversely affect our profit and cash flow generated from the relevant products, and such additional clinical trials involve the risks associated with any clinical trials. For example, if our phase IV clinical trial of Raxone® does not establish the product's long-term efficacy, this may adversely impact its commercial success and thus the likelihood that our rights to milestone payments are triggered, as well as the timing thereof, under our agreement with Chiesi Group. Also, later discovery of previously unknown adverse effects or other problems with our products, manufacturers or manufacturing processes, or non-compliance with regulatory requirements may have serious consequences for us, including legal or regulatory actions such as warning letters, suspension of manufacturing, seizure of product, injunctions, withdrawal of the relevant product from the market and sanctions.

Our relationships with customers and third-party payers and our general business operations are and will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm or diminished earnings, among other penalties.

Healthcare providers and third-party payers play a primary role in the recommendation and prescription of Raxone® and any product candidates for which we may obtain marketing authorizations. The arrangements with healthcare professionals, third-party payers and customers that we or our distributors have entered or will enter into may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we or our distributors market, sell and distribute our products (for which we receive marketing authorization). Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. If authorities conclude that our or our distributors' business practices do not comply with applicable laws and regulations, we or our employees or distributors may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government-funded healthcare programs such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, or the curtailment or restructuring of our operations.

If we or our third-party contractors or employees fail to comply with environmental, health and safety laws, we could become subject to civil or criminal penalties, other remedial measures or incur costs that could harm our business.

We are subject to a variety of environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of biological materials and hazardous materials and wastes. The operations of our third-party manufacturers and suppliers involve the use of hazardous and flammable materials, including chemicals and biological materials, and also produce hazardous waste products. We cannot eliminate the risk of contamination or injury from these materials or wastes. In the event of such contamination or injury, we could be held liable for any resulting damages, and any liability could exceed our insurance coverage and our own resources. Non-compliance by us or our third-party contractors or employees with environmental, health and safety laws and regulations may result in substantial fines, civil or criminal penalties or other sanctions. In addition, we may incur substantial costs in order to comply with such laws and regulations.

4. Risks related to the commercialization of our product candidates and marketing and sale of our products

Our product, Raxone®, outlicensed to Chiesi Group, and any of our product candidates (to the extent we receive marketing authorization for them) may fail to achieve the degree of market acceptance by physicians, patients, third-party payers and others in the medical community necessary for commercial success despite having received marketing authorization.

Raxone®, our product outlicensed to Chiesi Group, and any product candidates, if any, for which we receive marketing authorization in the future, may fail to gain sufficient market acceptance by physicians, patients,

third-party payers and others in the medical community despite having received marketing authorization. For example, other novel products may be preferred to our product. If any such products do not achieve an adequate level of acceptance, we may not generate significant product sales and we may not become profitable.

Off-label and unlicensed uses of currently available forms of idebenone may adversely affect the sales of Raxone® and, if and when it is approved, of Puldysa®.

Physicians may prescribe available products containing idebenone (the active ingredient in Raxone® and Puldysa®) for uses for which they are not approved, such as the treatment of LHON or DMD, if they view such products as a less expensive treatment or a better alternative to Raxone® or Puldysa® (if and when approved). A considerable number of physicians in Europe, and to a lesser degree in the U.S. and other countries, have been prescribing or recommending products containing idebenone to their patients on an off-label basis. The off-label product is either acquired from internet sources or in countries where it is approved and marketed for a different indication. By way of example, and without any claim to completeness:

- Takeda's Mnesis®, 45mg tablets containing idebenone, is registered in Italy for the treatment of "cognitive-behavioral deficits resulting from cerebral pathologies whether from vascular or degenerative origin" and is used off-label and prescribed as an unlicensed medicine for the treatment of other (non-approved) indications in Italy and in certain other countries.
- Sweden's Medical Products Agency ("**MPA**") has granted several licenses to individual patients for the prescription and reimbursement of Mnesis® for the treatment of LHON and so far we have not been able to successfully challenge these decisions.
- Because the tablets labeled Raxone®, which are marketed by Chiesi Group for the treatment of LHON, and the tablets labeled Puldysa® are identical, it is conceivable that pricing and reimbursement decisions with respect to Puldysa®, if and when we have obtained marketing authorization, will take into consideration the pricing of Raxone®. As a consequence, we may not obtain the price that we believe is adequate for a drug to treat respiratory dysfunction in DMD patients.
- Pharmacies have been compounding idebenone. See risk factor "*Pharmacies have been compounding idebenone. Future compounding may adversely affect sales by Chiesi Group of Raxone® and our potential future sales of Puldysa®.*"

Any off-label or unlicensed use of idebenone, especially from inexpensive sources, and any reimbursement for such use granted by third-party payers may reduce our revenue from the sale of Raxone® by Chiesi Group (and, to the limited extent we still sell it, by us) and our potential sales of Puldysa®.

We have only started to develop our marketing and sales organization, have limited experience in marketing products and do not expect to have significant marketing synergies between our current product candidates, if and when approved. If we are unable to establish and expand our marketing and sales capabilities or enter into distribution agreements with third parties, we may not be able to generate product sales.

We have limited experience in marketing products in Europe and have no experience in marketing products in the U.S. and elsewhere. Our internal sales and marketing force that we built up from January 2015 is small and is currently preparing for the launch of Puldysa® in the EU. In the U.S., our team currently manages our patient advocacy interactions, prepares for market entry in the U.S. and is the source of our U.S. regulatory and medical affairs expertise, whereas commercialization will only be possible if we file an NDA with, and receive marketing authorization from, the FDA regarding Puldysa®.

In connection with the contemplated launch of Puldysa® in the EU (if and when we receive marketing authorization), and as a result of the ramp up of our activities in the U.S., we will need to develop further in-house marketing, sales and distribution capabilities. All of these activities are associated with an increase in the headcount of our marketing and sales personnel and of the related overhead and higher overall fixed costs, and will also require significant management resources and time. At the same time, we may engage additional third-party distributors to perform marketing, sale and/or distribution services. Any income that

we receive or may receive from our current or future third-party distributors will depend upon the efforts of such distributors, over which we may have little or no control. We may not be able to develop and expand in-house marketing, sales and distribution capabilities or establish or maintain relationships with third-party collaborators to successfully commercialize Puldysa® upon its approval in key markets and for particular indications, which would adversely impact our ability to generate product sales.

Puldysa® and our product candidates (if approved) will have different prescriber bases: primarily neurologists in the case of Puldysa® and vamorolone in DMD, and primarily pulmonologists in the case of POL6014 in CF. As a result, we expect to have somewhat limited marketing synergies between our products and may have to build separate sales channels for each of our products, which is expensive and may result in our products suffering from low profit margins or a lack of profitability.

We face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than we do, as well as reducing the price at which we are able to sell our products.

The development and commercialization of new products is highly competitive. For instance, we believe that companies that are currently developing new products for the treatment of LHON (which may compete with Raxone®) may be granted marketing authorization during the next several years, which would reduce sales by Chiesi Group of Raxone® and thereby the likelihood that our rights to milestone payments are triggered, as well as the timing thereof, under our agreement with Chiesi Group. Also, to our knowledge, three treatments for DMD developed by third parties that are not based on steroids have been approved to date, and there are a number of late-stage clinical trials of drugs targeting muscle weakness in DMD. . The fact that neither idebenone (the active ingredient in Raxone® and Puldysa®) nor vamorolone enjoys composition of matter patent protection lowers entry barriers for competitors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive or are better marketed than Raxone®, Puldysa® or any other product candidates for which we receive marketing authorization. Our competitors may obtain marketing authorizations for their products more rapidly than we do, which could result in them establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected by third-party payers seeking to encourage the use of products that are less expensive than ours.

Should we or our distributors be found to have improperly promoted off-label uses, we may become subject to significant liability.

Given that the tablets labeled Raxone®, which are marketed by Chiesi Group for the treatment of LHON, and the tablets labeled Puldysa® are identical, it is conceivable that, if and when we have obtained marketing authorization for Puldysa®, physicians prescribe Raxone® to their DMD patients in a manner that is inconsistent with our marketing authorizations in the EU and elsewhere. This would adversely affect our sales of Puldysa®. Also, if we cannot successfully manage the marketing of our products by restricting off-label promotion or if we or our current or future distributors promote our products beyond their approved indications, we could become subject to enforcement action for off-label promotion and significant liability.

The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain coverage and adequate reimbursement for our marketed product (which is out-licensed to Chiesi Group) or any product for which we receive marketing authorization in the future and price controls could limit our ability to market those products and decrease our ability to generate sales.

The availability and extent of coverage and reimbursement by governmental and private third-party payers is essential for most patients to be able to afford expensive treatments. Sales of Raxone® (with respect to which we have a right to milestone payments under our agreement with Chiesi Group if and when Chiesi Group meets certain sales thresholds) and potential sales of Puldysa® (if and when we have obtained marketing approval) and any other products for which we receive marketing authorization in the future will depend substantially on the extent to which the costs will be paid by third-party payers. Also, we may rely

on the efforts of third-party distributors to obtain pricing and reimbursement approvals in certain countries. We may have little or no control over the efforts of such third parties.

Seeking third-party reimbursement is a time-consuming and expensive process, which typically requires us to provide scientific and clinical support and pharmaco-economic arguments for the use of the relevant product to each third-party payer separately. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, and third-party payers may nonetheless refuse reimbursement. Also, one third-party payer's decision to provide coverage for a product does not assure that other payers will also provide coverage, and pricing negotiations may continue after reimbursement has been obtained. Third-party payers may reject our requests for pricing and reimbursement of any future product and we may have to initiate legal proceedings in relation to such decisions. Even where reimbursement may be approved in the future, we may have to grant a significant discount on the list price and may have to reduce the price further in the future. Irrespective of the level of initial pricing, we expect the prices of our current and any future products to erode substantially during any market exclusivity period. We expect such price erosion to be accelerated after we have lost any such market exclusivity.

If reimbursement is not available or only to limited levels, we may not succeed in commercializing a product even if marketing authorization has been obtained. Even if coverage is provided, the approved reimbursement amount may not allow us to realize a sufficient return on our investment. All of this also applies to sales of Raxone®, *mutatis mutandis*, with respect to which we have a right to milestone payments under our agreement with Chiesi Group if and when Chiesi Group meets certain sales thresholds.

Recently enacted and future healthcare reform legislation involves a high degree of uncertainty and may adversely affect our business.

We operate in a highly regulated industry. New laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could adversely affect pricing, reimbursement, marketing or sales of our marketed product (which is outlicensed to Chiesi Group) or any product candidates for which we may receive marketing authorization in the future. In the United States and other jurisdictions, there have been a number of legislative and regulatory changes, proposed changes and statements by the current President of the United States regarding the pharmaceutical industry and the healthcare system that could prevent or delay marketing authorization and pricing and reimbursement approvals of our product candidates or make them more expensive, or their terms less attractive, or restrict or regulate post-approval activities. In particular, we may face uncertainties as a result of U.S. federal legislative and administrative efforts to repeal, substantially modify or invalidate some or all of the provisions of the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act (collectively, the "**PPACA**"). A repeal or replacement of the PPACA, if it occurs, may adversely affect our business and financial results. All of these enacted or future measures may prevent us from generating sales, attain profitability, commercialize or market our products.

Pharmacies have been compounding idebenone. Future compounding may adversely affect sales by Chiesi Group of Raxone® and our potential future sales of Puldysa®.

Compounding (also called pharmacy or magistral preparation) is a practice in which a licensed pharmacist prepares medicines in a pharmacy by combining, mixing, or altering pharmaceutical ingredients. Under certain conditions, the sale of compounded idebenone (the active ingredient of Raxone® and Puldysa®) is legal. In the EU, such compounding exemption is based on Article 3 of the EU Directive 2001/83. We are aware of pharmacies in Germany and the Netherlands that advertised compounded idebenone on the internet for the treatment of LHON, DMD and other indications at considerably lower prices than we previously charged, and Chiesi Group currently charges, for Raxone®, sometimes making reference to the clinical trials that we have conducted.

In the past, compounding of idebenone has also resulted in litigation: a pharmacist in Germany filled capsules with generic idebenone purchased from a third party and advertised their sale on his website. In Au-

gust 2017, the *Landgericht Hamburg* prohibited the pharmacist's advertising and sale of idebenone capsules, holding among other things that the portioning of the active pharmaceutical ingredient and filling of capsules are not covered by the compounding privilege. An appeal by the pharmacist is pending.

Compounding of idebenone still continues and, consequently, reduces sales by Chiesi Group of Raxone® and thereby the likelihood that our rights to milestone payments are triggered, as well as the timing thereof, under our agreement with Chiesi Group and, eventually, if we receive marketing authorization, our sales of Puldysa®.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of our marketed product (which is outlicensed to Chiesi Group) or any product candidates for which we receive marketing authorization in the future.

We face an inherent risk of product liability exposure related to the commercialization of Raxone® by Chiesi Group and any product candidate for which we receive marketing authorization in the future, as well as to the use of our product candidates in humans in clinical trials. If we cannot successfully defend ourselves against claims that our products or product candidates caused injuries, we may incur substantial liabilities. In addition, if our product liability risk in relation to Raxone® materializes, we may also be contractually liable to Chiesi Group.

We currently have product liability insurance for Raxone® and insurance for human clinical trials covering all clinical trials conducted by us. However, our current product liability coverage may not be adequate in scope to protect us in the event of a successful product liability claim, nor does it cover any contractual liability to Chiesi Group we may incur in connection with product liability matters. Further, we may not be able to maintain our current insurance or obtain product liability insurance for any products for which we may receive marketing authorization in the future on reasonable terms and at acceptable cost, and our insurance may in any event provide insufficient coverage against potential liabilities. As a result, we may have to bear substantial uninsured losses.

Our future profitability may be adversely affected if our estimates regarding the size of the market for our product candidates are inaccurate.

To evaluate the commercial potential of our product candidates, we have to estimate the size of the market for these product candidates. We base these estimates on the frequency of the respective condition, on our evaluation of market conditions and on other factors, using publicly available information. In formulating these estimates, we have to make certain assumptions, which have not been verified by third parties. If our assumptions are incorrect, there is a risk that our estimates could be wrong and our future profitability may be adversely affected.

5. Risks related to market exclusivity rights and intellectual property

Our business model relies on orphan drug exclusivity for our product candidate, Puldysa®, and most of our other current or future clinical product candidates. Orphan drug designation can be difficult to obtain and maintain, and it provides only limited protection from competition.

It is our strategy to develop and commercialize product candidates in indications qualifying for orphan drug designation in order to obtain marketing exclusivity. The market exclusivity period of an orphan drug designation is generally shorter than a patent protection period. In the U.S., for instance, such period is seven years, and in the EU, it is 10 years (reduced to six years if the relevant drug no longer meets the criteria or is sufficiently profitable) after receipt of marketing authorization. Also, orphan drug exclusivity may be lost if the applicable regulatory authority determines that the request for designation was materially defective, if the manufacturer is unable to assure sufficient quantity of the drug to meet patient needs, or for other reasons.

To date, we have obtained orphan drug designations (a) for our marketed product, Raxone® (which is outlicensed to Chiesi Group), in the EU (maximum duration until fall 2025), the U.S. and South Korea; (b) for our product candidate Puldysa®, in the EU and the U.S.; (c) for our product candidate omigapil in CMD, in

the EU and the U.S.; and (d) for POL6014 in alpha-1 antitrypsin deficiency, primary ciliary dyskinesia and cystic fibrosis ("**CF**") in the EU. ReveraGen has received orphan drug designation for vamorolone in the U.S. and in the EU. We have not filed for orphan drug designation in all national and regional jurisdictions where such protection may be available; instead, we have sought such protections only with respect to jurisdictions that we currently anticipate being key to our business.

Obtaining an orphan drug designation can be difficult, and we may not be successful in obtaining or maintaining orphan drug designations for our marketed product (which is outlicensed to Chiesi Group) or any of our product candidates. The procedure for obtaining orphan drug designation is an independent procedure in each jurisdiction, and applications might be denied in some jurisdictions, but granted in others. Further, orphan drug designation may be obtained for the same product in the same indication by several parties, and only the first such party to obtain marketing approval will receive marketing exclusivity for the relevant product in the relevant indication. Consequently, despite us having obtained an orphan drug designation for a product candidate in a particular indication, if a third party were to obtain orphan drug designation and marketing authorization and the correspondence market exclusivity for the same product in the same indication, we would be excluded from marketing such product in such indication during the applicable exclusivity period.

If we lose orphan drug designation or fail to maintain that designation for the duration of the applicable exclusivity period in relation to our marketed product (with respect to which we have a right to milestone payments under our outlicensing arrangement with Chiesi Group if and when Chiesi Group meets certain sales thresholds) or, after receipt of marketing authorization (if any), any of our product candidates, we may be unable to generate sufficient sales to become profitable.

Our marketed product, Raxone® (which is outlicensed to Chiesi Group), is not patent protected, and we hold only limited method of use patents for Puldysa®. Even granted patents may not be enforceable, and we may be subject to ownership disputes over patents or other intellectual property.

As the composition of matter patent for idebenone (the active ingredient in Raxone® and Puldysa®) has expired, we can only seek method of use patent protection, as we have done for the use of idebenone in DMD. Likewise, there are to our knowledge no composition of matter patents or patent applications with respect to vamorolone, with respect to which we have an option to obtain an exclucive sub-license from Idorsia. Typically, the protection derived from method of use patents is not as strong as the protection derived from composition of matter patents. Method of use patents do not prevent a third party from using, applying or manufacturing the same compound for other indications and may not prevent a third party from finding a way to circumvent the patent. For these reasons, a third party may be able to use idebenone in different or comparable formulas, applications or indications. Further, method of use patents are, in general, more susceptible to invalidity attacks by third parties than composition of matter patents.

Raxone® (which is outlicensed to Chiesi Group and with respect to which we have a right to milestone payments if and when Chiesi Group meets certain sales thresholds), is not patent protected. Our method of use patents for the use of idebenone in DMD are due to expire in March 2026 in the EU, Japan, and the U.S. Most composition of matter patents for omigapil, including those in the U.S. and the EU, with regard to which we have an exclusive license from Novartis, have expired. Our method of use patents for the use of omigapil in CMD in the U.S., the EU and other jurisdictions are due to expire in 2026 or 2027, as applicable. The composition of matter patents with respect to POL6014 held by Polyphor and certain other parties and exclusively licensed or sublicensed, as applicable, to us, are due to expire in 2025, subject to potential extended market protection. ReveraGen holds method of use patents for the use of vamorolone in DMD and other indications in the U.S., the EU, China and other jurisdictions. The main patents relating thereto are due to expire in 2029. Further, we may not be able to rely on patent protection for any of our future product candidates.

The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates in certain countries. There is no assurance that all potentially relevant prior art relating to such patents and patent applications has been identified. We may be unaware of prior art that could be used to invalidate an issued patent or prevent pending patent applications from issuing as patents. Even if patents do successfully issue and even if such patents cover our product candidates, third parties may

challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated. Without extensive patent protection, we will only be able to rely upon the limited market exclusivity, if any, resulting from any orphan drug designation, which may be revoked, will only apply for a limited time period and will be subject to other conditions and limitations (see risk factor "*Our business model relies on orphan drug exclusivity for our product candidate, Puldysa® in DMD, and most of our current or future clinical product candidates. Orphan drug designation can be difficult to obtain and maintain, and it provides only limited protection from competition*."). If we are unable to obtain, or if we or our licensors or sublicensors lose, patent protection with respect to any of our products or product candidates, we may be unable to prevent competitors from entering the market with a product that is similar to or the same as our product or product candidate. Further, we may be subject to ownership disputes over patents or other intellectual property with licensors, sublicensors, former employees, collaborators or other third parties.

We have in-licensed our early stage pipeline and other intellectual property, and have acquired an option to in-license vamorolone, from third parties. We could lose our rights to use the licensed intellectual property or our option to in-license intellectual property in the event of termination of or dispute relating to the relevant agreement or if such intellectual property is unenforceable for any reason. In addition, enforcement of in-licensed intellectual property and defending against third-party claims in relation thereto are more complex than in the case of our owned intellectual property.

We have acquired an exclusive option to obtain from Idorsia an exclusive sub-license to commercialize ReveraGen's vamorolone. We will have the right to exercise this option against payment of USD 30 million at the latest when results from ReveraGen's ongoing Phase IIb clinical trial (VISION-DMD) are available . In addition, we have in-licensed omigapil from Novartis and POL6014 from Polyphor, in each case on an exclusive world-wide basis.

The same risks that apply to the intellectual property rights we own generally apply with respect to protection of intellectual property that we license. If we or our licensors fail to prosecute, maintain and enforce such intellectual property or if such intellectual property is unenforceable or if a licensor would enter bankruptcy or similar distressed status, we could lose our rights to use such intellectual property or our exclusivity with respect to those rights. The same may be the case if the agreements by which we have in-licensed or under which we have the option to in-license intellectual property are terminated or if a dispute arises between us and our licensing partners in relation to our rights or obligations under the license or option agreements, including any such conflict, dispute or disagreement arising from our failure to satisfy payment obligations under any such agreements. In addition, the enforcement of in-licensed intellectual property in case of violations or misappropriation by third parties and defending against third-party claims in relation to in-licensed intellectual property are more complex than in the case of owned intellectual property. Such proceedings may require coordination with the licensor, and licensors typically have rights to intervene or veto rights. As a result of these factors, our ability to develop and commercialize the affected product candidates may be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products.

Third-party claims of intellectual property infringement or misappropriation may prevent or delay our product development and commercialization efforts.

There is a substantial amount of litigation involving patent and other intellectual property rights in the pharmaceutical and biotechnology industries, including patent infringement lawsuits, interferences, oppositions and *inter partes* reexamination proceedings before the government patent offices. Numerous patents and pending patent applications owned by third parties exist in the fields in which we are active. Third parties may assert that we infringe their intellectual property, and patent applications covering our product candidates could have been filed by others without our knowledge. We may also face a claim of misappropriation if a third party believes that we inappropriately obtained and used trade secrets of such third party. Parties making claims against us may obtain injunctive or other equitable relief that could effectively prevent us from further developing or commercializing our product candidates or marketing our product or any future products. We have not conducted a freedom-to-operate search or analysis for our own or in-licensed products (including vamorolone). Thus, we may not be aware of third parties' intellectual property that our products, or our sale or commercialization thereof, may infringe or that, if issued, would block us from selling or otherwise commercializing our products. If any third-party patents were held by a court of

competent jurisdiction to cover aspects of our materials, formulations, methods of manufacture or methods of treatment, the holder of any such patents would be able to block our ability to develop and commercialize the applicable product candidate until such patent expired or unless we or our partners obtain a license. These licenses may not be available on acceptable terms, if at all. Even if we or our partners were able to obtain a license, the rights may be non-exclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product candidate, or be forced to cease some aspect of our business operations, if as a result of actual or threatened patent infringement claims, we or our partners are unable to enter into licenses on acceptable terms. Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time-consuming, regardless of the outcome, and result in significant demands on the time and attention of the management teams. In the event of a successful claim of infringement, we may be required to pay substantial damages, royalties or other financial remedies and incur other significant costs, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible, or require substantial time and monetary expenditure, or incur other significant costs and lose the patent protection to which we thought we were entitled.

During the course of any patent or other intellectual property litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If potential and current partners or collaborators or securities analysts or investors regard these announcements as negative, the perceived value of our technology, product candidates and products, development programs or intellectual property could be diminished.

Furthermore, the U.S. government has reserved certain rights to vamorolone. As a consequence, ReveraGen is required to comply with certain formalities, including in particular the filing of certain information with governmental databases. Whether or not ReveraGen complies with this requirement is beyond our control. Should ReveraGen be found to be, or have at any point been, in breach of such filing or other obligations in connection with vamorolone, this could result in the retransfer of intellectual property rights in connection with vamorolone to the U.S. Army Medical Research and Materiel Command (USAMRMC) or any successor or other governmental entity or authority and/or in any of ReveraGen, Idorsia and/or ourselves being involved in a litigation relating to intellectual property rights in connection with vamorolone, each of which could have a materially adverse effect on our business, results of operations, financial position and cash flows and potentially damage our reputation.

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

We and our licensors have not filed for patent protection in all national and regional jurisdictions where such protection may be available; instead, we have sought such protection only with respect to jurisdictions that we currently anticipate being key to our business, in particular the U.S. and the EU. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant proceeding of each patent in each jurisdiction is an independent proceeding, and applications might in some jurisdictions be refused, while granted in others, which may ultimately limit our ability to rely on jurisdictional exclusivity, if any, for our marketed product (which is outlicensed to Chiesi Group) or our product candidates in certain jurisdictions. Depending on the jurisdiction, the scope of patent protection may vary for the same product candidate or technology.

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

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license

to third parties with respect to any patents relevant to our business, our competitive position may be impaired and our business and results of operation may be adversely affected.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

We rely on trade secrets and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our technology and development processes that involve proprietary know-how, information or technology that is not covered by patents. In addition, we rely on our employees, advisors, third party contractors such as CROs, consultants and collaboration partners to develop and manufacture our product and product candidates, which is why we must, at times, share our intellectual property and trade secrets with them.

Trade secrets can be difficult to protect. We seek to protect our proprietary and in-licensed technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, and outside scientific advisors, contractors and collaborators, but our employees, consultants, outside scientific advisors, contractors and collaborators may intentionally or inadvertently disclose our trade secret information to competitors. In addition, our competitors may gain access to our trade secrets through legal or illegal means or independently develop substantially equivalent information and techniques. We may not be able to protect trade secrets effectively and we may not have adequate remedies against misappropriation of trade secrets. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming and the outcome is unpredictable. In addition, courts outside the U.S. sometimes are less willing than U.S. courts to protect trade secrets. Misappropriation, unauthorized disclosure or a competitor's discovery of our trade secrets could materially impair our competitive position or our business.

Many of our employees were previously employed at universities or other pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that we or our employees have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of our employees' former employers or other third parties. We may also be subject to ownership disputes in respect of intellectual property created by these employees during the course of their employment with us. Any of such claims could result in our competitive position being impaired and our business and results of operation may be adversely affected.

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

Competitors may infringe our intellectual property, the intellectual property of our licensors, or the market exclusivity resulting from orphan drug designations that we have achieved. To counter or defend against such claims can be expensive and time-consuming. In an infringement proceeding, a court may decide that a patent owned or in-licensed by us is invalid or unenforceable and/or may refuse to stop the other party from using the technology at issue. An adverse result in any litigation over exclusivity rights could put one or more of our or our licensors' patents at risk of being invalidated or interpreted narrowly or an orphan drug designation of being revoked. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation in many jurisdictions, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in the patents or other intellectual property we own or license-in. We may be subject to ownership disputes in the future arising from, for example, conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we or our licensors 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 employees.

6. Risks related to manufacturing, employment matters, operations, managing growth, corporate structure and financial reporting

We have no manufacturing capabilities or capacity of our own and rely on third parties for production of our compounds and finished drug products.

We have no manufacturing capabilities or capacity of our own and have outsourced the entire manufacture, formulation, packaging, storage and distribution of Raxone®, Puldysa® and our other compounds to third parties. Under our outlicensing arrangement with Chiesi Group, we have undertaken to supply Raxone® to Chiesi Group in the necessary quantities.

For the production of Raxone®/Puldysa® we rely on a drug substance supplier, with whom we have agreed on a seven-year exclusivity period (subject to exceptions) starting with the first launch of our product in the EU and the U.S., respectively. In the EU, such exclusivity period will lapse in October 2022. We currently have one finished drug product supplier of Raxone®/Puldysa®. If any of our manufacturing agreements is terminated or not renewed by the third-party provider, we may not be able to timely negotiate a new agreement with that or another third-party provider on acceptable terms or at all. Furthermore, switching a supplier of the drug substance or the finished drug product is an expensive and time-consuming process.

We rely on our licensor, Novartis, to provide omigapil. We source the active pharmaceutical ingredient of POL6014 from a third party and we rely on PARI Pharma GmbH, Gräfelfing, Germany, as the manufacturer of the nebulizer called eFlow® with which POL6014 is administered. We currently have no plans to build up or acquire manufacturing capacity and the related know-how of our own in relation to omigapil and POL6014. If we choose to exercise our option from Idorsia to obtain an exclusive sub-license to commercialize vamorolone in DMD, we would have vamorolone manufactured by third parties as well.

The facilities used by our suppliers to manufacture our compounds and the finished products containing such compounds are subject to approval and inspections by regulatory authorities. We do not have full control over our suppliers' quality control or compliance with laws, regulations or cGMP standards, and any non-compliance could result in sanctions being imposed also on us, including fines, injunctions, civil penalties, delays, suspension, withdrawal or non-grant of market of approvals, seizures or recalls of products, operating restrictions and criminal prosecutions.

The compounds we use are complex and difficult to manufacture. Only a handful of manufacturers are able to manufacture these compounds, and our manufacturers may experience production problems.

The manufacturing of our compounds necessitates compliance with regulatory requirements, such as cGMP, and is complex, time-consuming and expensive. In particular, only a handful of manufacturers are able to manufacture idebenone in compliance with all regulatory requirements. Manufacturing idebenone involves heavy metal catalysts, the incomplete removal of which in the manufacturing process would result in toxic amounts of these impurities remaining in the drug substance, and non-cGMP synthesis of idebenone may result in other toxic or cancerogenic by-products. Problems with the manufacturing process, even minor deviations from the normal process, could result in contamination, product defects or manufacturing failures that could result in harm to patients, lot failures, product recalls, product liability claims, or insufficient inventory. Regulatory authorities may require us to submit samples of any lot or may require that we do not distribute a lot until the agency authorizes its release. Our contract manufacturers may be unable to achieve adequate quantities and quality of clinical-grade materials, and their supply chain could be interrupted from time to time. Any such problems could materially harm our business, financial condition, results of operations, and prospects.

If we lose the services of any member of our top management or other key members of our management, scientific or commercial staff, or if we fail to attract and retain key scientific or other personnel, we may be unable to successfully develop and commercialize our product candidates or any future products for which we obtain marketing authorization.

We are highly dependent on the performance and expertise of members of our top management, especially our newly appointed CEO, and other key members of our management, scientific and commercial staff. We

are a small company with many key functions being carried out by one person only. The loss of the services of any of our key personnel for any reason or our inability to attract new highly qualified and experienced employees could harm our business. Furthermore, we do not currently maintain "key person" insurance for any of our executives or other employees.

A limited number of people have experience and know-how in neuromuscular and pulmonary diseases and the product and product candidates developed by us. To foster retention, we have established employee participation plans, but there is intense competition for skilled personnel. If our product candidates are granted marketing authorizations or if we expand our development activities, we would need to hire additional personnel, which may be difficult to recruit and retain on acceptable terms given such competition.

We will need to grow the size and capabilities of our organization, and we may experience difficulties in managing this growth.

As of December 31, 2019, we had 117 employees (112.9 full-time equivalent) and we expect our headcount to increase in the near future in connection with the preparations for the contemplated launch of Puldysa® (if and when approved) in the EU, as a result of the ramp up of our activities in the U.S. and our planned clinical development of POL6014, as well as in connection with the commercialization of vamorolone in DMD if we choose to exercise our option from Idorsia to obtain an exclusive sub-license to commercialize this product candidate. Our future financial performance will depend, in part, on our ability to effectively manage any future growth. We will need to expand and effectively manage our organization, personnel, operations and facilities in order to successfully develop and commercialize our product candidates. We will only be able to organize operations efficiently and avoid a misallocation of resources if we continue to improve our operational, financial and management controls, reporting systems and procedures. Our management may have to divert a disproportionate amount of its attention away from day-to-day activities in order to manage these growth activities. If we are unable to effectively expand our organization, we may not achieve our development and commercialization goals and our operational efficiency may be materially adversely affected.

Our and our partners' computer systems may fail or suffer security breaches, which could result in a material disruption of our product development programs and our business operations.

Despite the implementation of security measures, our computer systems and those of our current and any future suppliers, CROs and other contractors, consultants and collaborators are vulnerable to damage from computer viruses, ransomware, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs and our business operations, whether due to a loss of our trade secrets or other disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs due to efforts to recover or reproduce the data. To the extent that any disruption or security breach were to result in data loss or inappropriate disclosure of confidential or proprietary information or personal data of patients or other persons, we may be exposed to liability and suffer reputational damage.

7. Risks related to general economic and financial market conditions

Changes in the macro-economic environment and political developments in Europe, the United States and elsewhere may have a material adverse effect on the Group and may reduce the value of our Shares.

Over the past years, there has been a series of political and economic events such as the past global economic financial crisis, sovereign debt and financial crises in several EU countries, the UK leaving the EU (commonly known as "Brexit"), increased trade disputes and increased tensions in the Middle East. These events have impacted the global economy at large, the economies and financial situation of governments in many of our current and potential future markets, as well as exchange rates (in particular the euro/Swiss franc rate) and have been associated with, among other things, instability of financial institutions, high market volatility, liquidity problems, limited availability of financing and legal uncertainty. Recession or rising inflation and other effects may also be a consequence of these events. This uncertain macro-economic

environment may have a material adverse effect on our business, results of operations, financial condition, prospects, or the market price of our securities, including our Shares.

We are exposed to currency fluctuation risks and other financial risks.

While we incur costs mainly in Swiss francs, a significant proportion of our costs are required to be paid in euros and in the future in USD. To the limited extent we generate sales, we receive payments primarily in euros. If and as our business grows, we expect that a significant part of our sales and a significant part of our expenses will be denominated in euros. Our reporting currency is the Swiss franc and, as a result, financial line items are converted into Swiss francs at applicable foreign exchange rates. Further, we are subject to interest rate risks. Unfavorable developments in the value of the Swiss franc as compared to the euro, in interest rates and in the capital markets could have a material adverse effect our financial condition and results. For a discussion of our foreign exchange rate, interest rate, credit and liquidity risks please also refer to Note 29 to the consolidated financial statements for the year ended December 31, 2018.

B. Risks related to the Shares

Shareholders may suffer dilution as a result of further issuance of equity, conversions of our Bonds or further issuances of other securities convertible into equity.

Whenever we issue further equity securities, the existing shareholders of the Company may incur substantial dilution. We will need to raise additional equity or equity-linked financing in the future in order to continue our operations as planned.

In addition, holders of our Bonds have the right to convert the Bonds before their maturity in 2022 into an aggregate of up to 925,926 Shares at a conversion price of CHF 64.80 per Share. Based on the current market price of our Shares, we currently believe that it is rather unlikely that the Bonds will be converted into Shares. We may contemplate to convene a bondholders' meeting at some point in time to propose a significant reduction of the Conversion Price. The Company's currently available conditional capital for financings, mergers and acquisitions of CHF 2,500,000 would allow a reduction of the conversion price to as low as CHF 24 per Share and result in a corresponding dilution for the shareholders.

Also, the Company has issued, and may issue in the future, other rights to acquire Shares.

If and whenever a capital increase is implemented, our then-existing shareholders will incur substantial dilution. Additional dilution may occur to the then-existing shareholders if and to the extent that the Bonds will be converted and such rights to acquire Shares will ultimately be exercised and settled in Shares. Moreover, to the extent that the Company issues additional shares or equity-linked instruments (*e.g.*, for financing purposes or for employee participations), investors' ownership interest will be further diluted, and the terms of such issued shares may include liquidation or other preferences that adversely affect investors' rights as a shareholder.

The Share price has been and is expected to be volatile, and investors may not be able to resell their Shares at or above the price at which they have acquired their Shares.

The market price of the Shares has historically been subject to substantial fluctuations. We expect the market price of the Shares to continue to be highly volatile. Such volatility may depend upon many factors within and beyond our control, including the risk factors listed herein, our or our competitors' financial and business performance, general market conditions and the volatility in financial and other markets (*i.e.*, the degree to which prices fluctuate over a particular period in a particular market, regardless of market levels) in general. In some cases, the markets have produced downward pressure on share prices for certain issuers seemingly without regard to those issuers' underlying financial strength. As a result, the Shares may trade at prices significantly below the price at which any Shares have been or will have been acquired.

The trading market for the Shares is not liquid and shareholders may not trade or sell their Shares easily or at all.

The volume of the trading market for the Shares on the SIX Swiss Exchange has been low and is expected to be low in the future. Therefore, the trading market may not provide enough liquidity to allow shareholders to trade or sell their Shares easily or at all. The Company is not obliged to provide a bid or offer price for the Shares. Further, the Company's market making arrangement with Kepler Cheuvreux SA may be terminated at any time, and even while this arrangement is in place, there is no assurance that shareholders will be able to trade or sell their Shares easily or at all.

Future sales of a substantial number of Shares or derivative instruments by us or our investors could adversely affect the market price of the Shares.

Sales, or the possibility or perceived possibility of sales, of a substantial number of Shares in the market could have a material adverse effect on the market price of the Shares. Within the framework of the option agreement entered into by the Company and Idorsia in November 2018, Idorsia has entered into a lock-up undertaking with the Company with respect to the 1,000,000 Shares that Idorsia had acquired under such option agreement. Such lock-up undertaking will terminate with the Company's consent or (ii) when we obtain FDA approval for sale of vamorolone in DMD in the U.S. Other than that, investors may sell some or all of their Shares in the open market or otherwise at any time. Also, holders of Bonds have the right to convert the Bonds into Shares at any time before the maturity of the Bonds in 2022 and will be able to sell some or all of the Shares issued by the Company upon such conversion in the open market or otherwise at any time. In addition, the Company may issue additional Shares out of its existing authorized share capital or may propose to its shareholders to approve additional capital increases, in each case excluding shareholders' preemptive rights. As a result of the respective issuances or sales of Shares, or if such issuances or sales are anticipated by investors, the market price of the Shares could fall substantially.

The Company does not expect to pay dividends in the foreseeable future.

Since its inception, the Company has never paid any dividends and it does not anticipate paying dividends in the foreseeable future. Investors cannot rely on dividend income from the Shares, and any returns on an investment in the Shares will likely depend entirely upon any future appreciation in the price of the Shares and the ability of investors to sell Shares in the market.

Shareholders outside Switzerland may not be able to exercise preemptive rights in future issuances of equity or other securities that are convertible into equity.

Under Swiss law, shareholders may have certain preemptive rights to subscribe on a pro rata basis for issuances of newly issued equity or other securities that are convertible into equity. Due to laws and regulations in their respective jurisdictions, non-Swiss shareholders may not be able to exercise such rights unless we take action to register or otherwise qualify the particular rights offering under the laws of that jurisdiction. There can be no assurance that we would take any such action, and we will have the full discretion to decide not to take such action in one or more jurisdictions, including the EU, the UK and the U.S. If shareholders in such jurisdictions are unable to exercise their subscription rights, their ownership interest in the Company would be diluted.

Shareholders may face additional investment risk from currency exchange rate fluctuations in connection with their holding of Shares.

The Shares are and will be quoted in Swiss francs only, and future dividends, if any, will be denominated in Swiss francs. If the Swiss franc depreciates against a foreign currency that is the main currency of a shareholder, the value of the Shares or of any dividend, expressed in such foreign currency, will decrease accordingly. Prospective investors should be aware that exchange rates between currencies are highly volatile. Foreign exchange fluctuations between a shareholder's main currency and the Swiss franc may adversely affect shareholders who intend to convert the proceeds from the sale of the Shares or future dividends, if any, into their main currency and may potentially cause a partial or total loss of a shareholder's initial investment.

If securities or industry analysts do not publish research at all or publish inaccurate or unfavorable research about the Group's business, the market price and/or the trading volume of the Shares could decline.

The trading market for the Shares depends in part on the research and reports that securities or industry analysts publish about the Group or its business. If no or few securities or industry analysts cover the Company, the market price for the Shares could be adversely affected. If one or more of the analysts who cover the Group downgrades a recommendation with regard to the Shares, publishes inaccurate or unfavorable research about the Group's business, ceases to cover the Group or fails to publish reports on it regularly, the market price and/or the trading volume of the Shares would likely decline.

Our largest shareholders are able to exert influence over the Company, and their interests may not necessarily be the same as those of other shareholders.

As of the date hereof, the Company's largest shareholder is Idorsia, who owns 1,333,333 Shares, corresponding to 11.9% of the voting rights in the Company. Idorsia and our other investors who to our knowledge hold more than 3% of the voting rights in the Company together own an aggregate of 18.7% of the voting rights in the Company. Any of our investors may start acting in concert or may acquire significant ownership interests in the Company in the future. Such shareholders or groups of shareholders may be able to exert influence over, and potentially block, certain matters that must be decided by the Company's general meeting of shareholders, in particular those matters that require the consent of two-thirds of voting rights represented. The influence of significant shareholders or groups of shareholders is accentuated by the low historic rates of participation at the Company's past three annual general meetings of shareholders, which were 36.8% in 2019, 33.3% in 2018 and 49.3% in 2017. The interests of influential shareholders may not be the same as the interests of the Company's other shareholders, and respective corporate decisions may materially adversely affect the interests of the other investors in the Company.