UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 20-F

(Mark One)

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

OR

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

for the fiscal year ended December 31, 2021

OR

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

For the transition period from _____ to _____

OR

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

Date of event requiring this shell company report

Commission file number: 001-36582

ALTAMIRA THERAPEUTICS LTD.

(formerly Auris Medical Holding Ltd.)

(Exact name of Registrant as specified in its charter)

Bermuda
(Jurisdiction of Incorporation or Organization)

Clarendon House
2 Church Street
Hamilton HM11
Bermuda
(Address of principal executive offices)

Thomas Meyer
Tel: +1 (441) 295 59 50
Clarendon House
2 Church Street
Hamilton HM11
Bermuda
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Copies to:

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1251 Avenue of the Americas
New York, NY 10020
Tel: (212) 262-6700

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Shares, par value CHF 0.01 per share	CYTO	The Nasdaq Stock Market LLC

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

None
(Title of Class)

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None
(Title of Class)

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

Common shares: 14,964,261

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

☐ Yes ☒ No

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.

☐ Yes ☒ No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

☒ Yes ☐ No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

☒ Yes ☐ No

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

Large accelerated filer ☐	Accelerated filer ☐	Non-accelerated filer ☒ Emerging Growth Company ☐

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

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

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

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

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

If "Other" has been checked in response to the previous question indicate by check mark which financial statement item the registrant has elected to follow.

☐ Item 17 ☐ Item 18

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

☐ Yes ☒ No

ALTAMIRA THERAPEUTICS LTD.

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Unless otherwise indicated or the context otherwise requires, all references in this annual report on Form 20-F (the "Annual Report") to "Altamira Therapeutics Ltd.", "Auris Medical Holding Ltd.," "Auris Medical," "Auris," the "Company," "we," "our," "ours," "us" or similar terms refer to (i) Auris Medical Holding AG (formerly Auris Medical AG), or Auris Medical (Switzerland), together with its subsidiaries, prior to our corporate reorganization by way of the merger of Auris Medical Holding AG into Auris Medical NewCo Holding AG (the "Merger"), a newly incorporated, wholly-owned Swiss subsidiary on March 13, 2018 (i.e. to the transferring entity), (ii) to Auris Medical Holding AG (formerly Auris Medical NewCo Holding AG), together with its subsidiaries after the Merger (i.e. to the surviving entity) and prior to the Redomestication (as defined below), (iii) to Auris Medical Holding Ltd., a Bermuda company, or Auris Medical (Bermuda), the successor issuer to Auris Medical (Switzerland) under Rule 12g-3(a) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), after the effective time at which Auris Medical (Switzerland) continued its corporate existence from Switzerland to Bermuda (the "Redomestication"), which occurred on March 18, 2019, and (iv) to Altamira Therapeutics Ltd. (formerly Auris Medical Holding Ltd.) after adoption of the new Company name by resolution of Special General Meeting of Shareholders held on July 21, 2021. The trademarks, trade names and service marks appearing in this report are property of their respective owners.

On May 1, 2019, the Company effected a one-for-twenty reverse share split (the "2019 Reverse Share Split") of the Company's issued and outstanding common shares. Unless indicated or the context otherwise requires, all per share amounts and numbers of common shares in this report have been retrospectively adjusted for the 2019 Reverse Share Split.

Unless indicated or the context otherwise requires, (i) all references in this report to our common shares as of any date prior to March 13, 2018 refer to the common shares of Auris Medical (Switzerland) (having a nominal value of CHF 0.40 per share (pre-2019 Reverse Share Split)) prior to the 10:1 "reverse share split" effected through the Merger, (ii) all references to our common shares as of, and after, March 13, 2018 and prior to the Redomestication refer to the common shares of Auris Medical (Switzerland) (having a nominal value of CHF 0.02 per share (pre-2019 Reverse Share Split)) after the 10:1 "reverse share split" effected through the Merger, (iii) all references to our common shares as of, and after, the Redomestication on March 18, 2019 refer to the common shares of Auris Medical (Bermuda) (having a par value of CHF 0.02 per share (pre-2019 Reverse Share Split)), (iv) the Company's common shares on or after May 1, 2019, the date of the 2019 Reverse Share Split, have a par value of CHF 0.40 and (v) the Company's common shares on or after June 30, 2020, being the date the par value of our common shares was reduced to CHF 0.01 per share. At the annual general meeting of the shareholders of the Company held on June 4, 2020, the shareholders approved the increase in the number of authorized common shares of the Company from 10,000,000 common shares to 25,000,000 common shares and the reduction the par value of the Company's common shares to CHF 0.01, with such reduction having effect on June 30, 2020.

The terms "dollar," "USD" or "$" refer to U.S. dollars and the term "Swiss Franc" and "CHF" refer to the legal currency of Switzerland.

FORWARD-LOOKING STATEMENTS

This Annual Report contains statements that constitute forward-looking statements. Many of the forward-looking statements contained in this Annual Report can be identified by the use of forward-looking words such as "anticipate," "believe," "could," "expect," "should," "plan," "intend," "will," "estimate" and "potential," among others, or the negatives thereof.

Forward-looking statements appear in a number of places in this Annual Report and include, but are not limited to, statements regarding our intent, belief or current expectations. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those identified under the section "Item 3. Key Information-D. Risk factors" in this Annual Report. These risks and uncertainties include factors relating to:

- our operation as a drug development-stage company with limited operating history and a history of operating losses;
- the COVID-19 pandemic, which continues to evolve, and which could significantly disrupt our preclinical studies and clinical trials, drug development and sales efforts;
- our need for substantial additional funding to continue the development of our product candidates and the roll-out of our first commercial product before we can expect to become profitable from sales of our products and the possibility that we may be unable to raise additional capital when needed;
- the ability of our existing distribution partners to successfully market and distribute Bentrio™ and our ability to retain such distributors and identify new ones in particular for key markets in North America and Europe;
- our capacity to supply our distributors and markets timely and with sufficient numbers of Bentrio™ nasal sprays while meeting quality requirements through subcontractors;
- our dependence on the success of AM-125 and AM-401, which are still in preclinical and clinical development, and may eventually prove to be unsuccessful;
- our ability to divest or spin-off our non-RNA businesses and to reposition our Company around RNA therapeutics;
- the success of our distributors in the commercialization of Bentrio™;
- the chance that we may become exposed to costly and damaging liability claims resulting from the testing of our product candidates in the clinic or in the commercial stage;
- the chance our clinical trials may not be completed on schedule, or at all, as a result of factors such as delayed enrollment or the identification of adverse effects;
- uncertainty surrounding whether any of our product candidates will receive regulatory approval or clearance, which is necessary before they can be commercialized;
- if our product candidates obtain regulatory approval or clearance, our product candidates being subject to expensive, ongoing obligations and continued regulatory overview;
- enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval and commercialization;
- our ability to obtain certification of Bentrio™ as a Class II medical device under the European Medical Device Regulation and to obtain regulatory approval for prophylactic or therapeutic claims related to viral infections
- dependence on governmental authorities and health insurers establishing adequate reimbursement levels and pricing policies;

- our products may not gain market acceptance, in which case we may not be able to generate product revenues;
- our reliance on our current strategic relationship with Washington University, Wellesta Holdings or Nuance Pharma and the potential success or failure of strategic relationships, joint ventures or mergers and acquisitions transactions;
- our reliance on third parties to conduct our nonclinical and clinical trials and on third-party, single-source suppliers to supply or produce our product candidates;
- our ability to obtain, maintain and protect our intellectual property rights and operate our business without infringing or otherwise violating the intellectual property rights of others;
- our ability to meet the continuing listing requirements of Nasdaq and remain listed on The Nasdaq Capital Market;
- the chance that certain intangible assets related to our product candidates will be impaired; and
- other risk factors discussed under "Item 3. Key Information-D. Risk factors".

Our actual results or performance could differ materially from those expressed in, or implied by, any forward-looking statements relating to those matters. Accordingly, no assurances can be given that any of the events anticipated by the forward-looking statements will transpire or occur, or if any of them do so, what impact they will have on our results of operations, cash flows or financial condition. Except as required by law, we are under no obligation, and expressly disclaim any obligation, to update, alter or otherwise revise any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future events or otherwise.

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

A. Directors and senior management

Not applicable.

B. Advisers

Not applicable.

C. Auditors

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

A. Offer statistics

Not applicable.

B. Method and expected timetable

Not applicable.

ITEM 3. KEY INFORMATION

A. [Reserved]

B. Capitalization and indebtedness

Not applicable.

C. Reasons for the offer and use of proceeds

Not applicable.

D. Risk factors

You should carefully consider the risks and uncertainties described below and the other information in this Annual Report. Our business, financial condition or results of operations could be materially and adversely affected if any of these risks occurs, and as a result, the market price of our common shares could decline. This Annual Report also contains forward-looking statements that involve risks and uncertainties. See "Forward-Looking Statements." Our actual results could differ materially and adversely from those anticipated in these forward-looking statements as a result of certain factors.

Summary of Risk Factors

An investment in our common shares is subject to a number of risks. The following summarizes some, but not all, of these risks. Please carefully consider all of the information discussed in "Item 3. Key Information-D. Risk Factors" in this annual report for a more thorough description of these and other risks.

- We are a drug development-stage company and have a limited operating history and a history of operating losses. We anticipate that we will continue to incur losses for the foreseeable future.

- We expect that we will need substantial additional funding before we can expect to become profitable from sales of our products. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

- We intend to reposition our Company around RNA therapeutics and to divest or spin off our business in neurotology, rhinology and allergology. We cannot give any assurance that this repositioning will be successful and that we will be able to divest or spin off our non-RNA business at attractive conditions and within a reasonable period of time.

- We have started to commercialize Bentrio™, our most advanced product, in Germany and several other European countries and by entering into distribution agreements with third parties. Bentrio™ has not received clearance as a medical device in the U.S., yet. The product is marketed as an "over the counter" consumer healthcare product. The business of selling consumer healthcare products is highly competitive and characterized by a large number of suppliers with substantially larger resources than us. We cannot give any assurance that we will be successful in commercializing Bentrio™ or with reasonable investments or within a reasonable time period.

- Apart from Bentrio™, we depend entirely on the success of AM-125 and AM-401 which are still in preclinical and clinical development, respectively. If our preclinical studies or clinical trials are unsuccessful, we do not obtain regulatory approval or we are unable to commercialize AM-125 or AM-401, or we experience significant delays in doing so, our business, financial condition and results of operations will be materially adversely affected.

- We face risks related to health epidemics and outbreaks, including the COVID-19 "coronavirus" outbreak, which could significantly disrupt our preclinical studies and clinical trials, drug development and sales efforts.

- Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results. If clinical trials of our drug product candidates are prolonged or delayed, we may be unable to obtain required regulatory approvals, and therefore be unable to commercialize our drug product candidates on a timely basis or at all.

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

- We depend on enrollment of patients in our clinical trials for our product candidates. If we are unable to enroll patients in our clinical trials, our research and development efforts could be materially adversely affected.

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

- We cannot give any assurance that any of our drug product candidates will receive regulatory approval, which is necessary before they can be commercialized.

- We cannot give any assurance that Bentrio™ will receive regulatory clearance under a 510(k) by the FDA, which is necessary before it can be commercialized in the US for its intend use in allergic rhinitis, or through a different regulatory pathway for its intended use in viral infections, or that Bentrio™ can be upclassified as a Class II medical device in the EU by 2024, which is necessary to keep the product on the market under new European medical device regulations.

- Substantial additional data may need to be generated in order to obtain marketing approval for AM-125.

- Even if our product candidates obtain regulatory approval, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

- Healthcare legislative or regulatory reform measures, including government restrictions on pricing and reimbursement, may have a negative impact on our business and results of operations.

- The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage and reimbursement levels and pricing policies.

- We may seek to form additional strategic alliances in the future with respect to our product candidates, and if we do not realize the benefits of such alliance, our business, financial condition, commercialization prospects and results of operations may be materially adversely affected.

- We rely on third parties to conduct our nonclinical and clinical trials and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

- We currently rely on third-party suppliers and other third parties for production of Bentrio™ and our product candidates and our dependence on these third parties may impair the advancement of our research and development programs and the development of our product candidates.

- If we or our licensors are unable to obtain and maintain effective patent rights for our technologies, product candidates or any future product candidates, or if the scope of the patent rights obtained is not sufficiently broad, we may not be able to compete effectively in our markets.

- Our future growth and ability to compete depends on retaining our key personnel and recruiting additional qualified personnel.

- The price of our common shares may be volatile and may fluctuate due to factors beyond our control.

Risks Related to Our Business and Industry

We are a drug development-stage company and have a limited operating history and a history of operating losses. We anticipate that we will continue to incur losses for the foreseeable future.

We are a drug development-stage biopharmaceutical company with limited operating history. Since inception, we have incurred significant operating losses. We incurred net losses (defined as net loss attributable to owners of the Company) of CHF 17.4 million, CHF 8.2 million and CHF 6.6 million for the years ended December 31, 2021, 2020 and 2019, respectively. As of December 31, 2021, we had an accumulated deficit of CHF 176.0 million.

Our losses have resulted principally from expenses incurred in research and development of our product candidates, pre-clinical research and general and administrative expenses that are required for maintaining our business infrastructure and operating as a publicly listed company. In 2021 we started to incur sales and marketing expenses as we initiated the commercialization of Bentrio™. We expect to continue to incur significant operating losses in the future as we continue our research and development efforts for our product candidates in clinical development and continue with the roll-out of Bentrio™. In our financial year ended December 31, 2021, we incurred CHF 17.1 million in operating loss and capitalized development expenditures of its AM-125 project of CHF 2.8 million, and we expect our total cash need in 2022 to be in the range of CHF 11 to 13 million.

To date, we have financed our operations through the initial public offering and a follow-on offering of our common shares, private placements of equity securities and short- and long-term loans. On July 19, 2016, we entered into a Loan and Security Agreement with Hercules Technology Growth Capital, Inc., or Hercules. The agreement provided us with a senior secured term loan facility for up to $20 million. On January 31, 2019, we made the final payment to Hercules under the facility, comprising the last amortization payment as well as an end of term charge. With the final payment, all covenants and collaterals in favor of Hercules have been lifted. On September 8, 2020, FiveT Capital Holding Ltd., or FiveT, provided a convertible loan to Altamira Medica AG, or Altamira, one of our subsidiaries. The loan had a principal amount of CHF 1.5 million, a duration of 18 months, and carried an interest rate of 8% p.a. Under the terms of the agreement, FiveT had the right to convert the loan or parts thereof including accrued interest into common shares of either Altamira or Auris Medical Holding Ltd., subject to additional provisions and certain restrictions. On December 2, 2020, FiveT converted part of the loan and on March 4, 2021 the remaining outstanding amount into common shares of Auris Medical Holding Ltd., thus retiring the loan. On February 4, 2022, FiveT Investment Management Ltd., or FiveT IM, an affiliate of FiveT, provided a convertible loan to the Company with a principal amount of CHF 5 million, a duration of 12 months, and carrying an interest rate of 10% p.a. Under the terms of the agreement, FiveT IM has the right to convert the loan or parts thereof including accrued interest into common shares of the Company, subject to additional provisions and certain restrictions.

We have only one product approved for commercialization and have generated limited revenues from product sales. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. It may be several years, if ever, before we have another product candidate approved for commercialization and begin to generate more revenues from product sales.

We have never generated meaningful revenue from product sales and may never be profitable.

We only started to generate first revenues with Bentrio™, our first commercial product, in late 2021. Our ability to generate meaningful revenue and achieve profitability depends on our ability to successfully commercialize Bentrio™ through our own efforts and through our distributors and to successfully complete the development of, and obtain the marketing approvals necessary to commercialize, one or more of our other product candidates. We do not anticipate generating revenue from sales of our other product candidates unless and until we obtain regulatory approval or clearance for, and commercialize, AM-125 and AM-401. Our ability to generate future revenue from product sales depends heavily on our success in many areas, including but not limited to:

- building customer awareness of Bentrio™ and successful conversion into sales;
- success of our distributors in commercializing Bentrio™ in their territories and contracting distributors for additional key markets in Europe and North America;
- completing research and clinical development of our drug product candidates and further clinical testing of Bentrio™;
- obtaining marketing approvals for our drug product candidates, including AM-125 or AM-401, and additional clearance or approvals for Bentrio™, for which we will have to complete development, including the conduct of clinical trials;
- developing a sustainable and scalable manufacturing process for any approved product candidates and maintaining supply and manufacturing relationships with third parties that can conduct the process and provide adequate (in amount and quality) products to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain marketing approval, either directly or with a collaborator or distributor;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

Even as we have started to commercialize Bentrio™ in Germany and several other European markets, our first product candidate cleared for commercial sale, we anticipate incurring significant costs associated with penetrating markets and building revenues. Because of the numerous risks and uncertainties with medical device and pharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses could increase beyond expectations if we are required by the FDA, the EMA, or other regulatory agencies, domestic or foreign, to change our manufacturing processes, or to perform clinical, nonclinical, or other types of trials in addition to those that we currently anticipate. In cases where we are successful in obtaining regulatory approvals to market further of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. Additionally, if we are not able to generate sufficient revenue from the sale of any approved products, we may never become profitable.

We may be unable to develop and commercialize AM-125, AM-401 or any other product candidate or we may be unable to grow revenues for Bentrio™ to meaningful levels, and, even if we do, may never achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a semiannual or annual basis. Our failure to become and remain profitable would decrease the value of the Company and could impair our ability to raise capital, expand our business or continue our operations.

We expect that we will need substantial additional funding before we can expect to become profitable from sales of our products. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our research and development expenses to remain significant in connection with our ongoing roll-out with Bentrio™ and our clinical development activities, particularly as we initiate new trials with AM-125 and Bentrio™, and advance or initiate the pre-clinical and clinical development of AM-401 or any other product candidate. We expect our total cash need in 2022 to be in the range of CHF 11 to 13 million. As of December 31, 2021, our cash and cash equivalents were CHF 1.0 million. Our assumptions may prove to be wrong, and we may have to use our capital resources sooner than we currently expect. If we are unable to raise capital when needed, we could be forced to delay, suspend, reduce or terminate our product development programs or commercialization efforts. Also, should we fail to raise sufficient funds to cover our operating expenditures for at least a 12-month period, we may no longer be considered a "going concern." The lack of a going concern assessment may negatively affect the valuation of the Company's investments in its subsidiaries and result in a revaluation of these holdings. The board of directors will need to consider the interests of our creditors and take appropriate action to restructure the business if it appears that we are insolvent or likely to become insolvent. Our future funding requirements will depend on many factors, including but not limited to:

- the amount of our investments in raising market awareness of and growing market penetration for Bentrio™;
- the success of our distributors in commercializing Bentrio™ in their territories and our ability to access additional geographies through further distributors;
- the scope, rate of progress, results and cost of our clinical trials, nonclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any products that we may develop;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing sales, marketing, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, and other arrangements that we may establish, including any required milestone and royalty payments thereunder.

We expect that we will require additional funding to continue our roll out of Bentrio™ and our ongoing clinical development activities and seek to obtain regulatory approval for, and commercialize, our product candidates. If we receive regulatory approval or clearance for any of our product candidates, and if we choose to not grant any licenses to partners, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize. We also expect to continue to incur additional costs associated with operating as a public company. Additional funds may not be available on a timely basis, on favorable terms, or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long-term business strategy. If we are not able to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Raising additional capital may cause dilution to our shareholders, restrict our operations or require us to relinquish rights to our intellectual property or future revenue streams.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, grants, and license and development agreements in connection with any collaborations. We do not have any committed external source of funds. In the event we need to seek additional funds, we may raise additional capital through the sale of equity or convertible debt securities. In such an event, our shareholders' ownership interests will be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect our shareholders' rights as holders of our common shares. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our intellectual property or future revenue streams. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We do not have a history of commercializing medical devices or pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

Our operations to date have been limited to financing and staffing the Company, developing our technology and developing our product candidates. We have not yet demonstrated an ability to successfully complete large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial scale product or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing medical devices or pharmaceutical products.

We are in the process of repositioning our Company around RNA therapeutics and intend to divest or spin off our business in neurotology, rhinology and allergology. We cannot give any assurance that this repositioning will be successful and that we will be able to divest or spin off our non-RNA business at attractive conditions and within a reasonable period of time.

In June 2021 we acquired Trasir Therapeutics Inc. ("Trasir") whose main asset is the proprietary peptide polyplex platform OligoPhore™ / SemaPhore™ that can engage any type of RNA in rapid self-assembly and allows for safe and effective oligonucleotide delivery to extrahepatic tissues using systemic administration. We announced on that occasion our intention to strategically reposition the Company to focus on the development of RNA therapeutics while in the medium term evaluating opportunities to spin off or divest its existing business in neurotology, rhinology and allergology within the next 12-18 months. This non-RNA business comprises Bentrio™ for the protection against airborne allergens and viruses, AM-125 for the treatment of vertigo, Keyzilen® (AM-101) for the treatment of acute tinnitus, Sonsuvi® (AM-111) for the treatment of acute hearing loss and certain early-stage assets such as AM-102 for the treatment of tinnitus.

Any sale process is time consuming and requires substantial management time and attention, which may have an effect on our business and results of operations.

Valuation of assets in one or several partial divestiture transactions depends on a variety of factors such as the valuation of comparable assets, interest for the type of assets and conditions on capital markets. We can provide no assurances that we will successfully sell the non-RNA business, that we will do so in accordance with our expected timeline or that we will recover the carrying value of the assets. Additionally, any decisions made regarding our deployment or use of any sales proceeds we receive in any sale involves risks and uncertainties. As a result, our decisions with respect to such proceeds may not lead to increased long-term shareholder value, or may result in a material charge to our statement of operations. If a sale of the non-RNA business at what we consider to be a reasonable price is not available, we may decide to cease efforts to sell the non-RNA business.

The purchase price and availability of certain components of Bentrio™ could be affected as a result of the Russian invasion of the Ukraine.

In the context of Russia's recent invasion of the Ukraine, oil and gas prices, which are key input factors for plastic parts such as those used for the primary packaging of Bentrio™, have increased significantly and shown high volatility. Continued escalation of political tensions, economic instability, military activity or civil hostilities in Ukraine could result in significant price increases for such components or difficulties of our component suppliers to supply such components on a timely basis. If we are unable to pass on such price increases, or if component supplies are interrupted, our business, financial condition and results of operation could be adversely affected.

Cyber-attacks or other failures in telecommunications or information technology systems could result in information theft, data corruption and significant disruption of our business operations.

We and certain of our collaborators depend on information technology and telecommunications systems for significant aspects of operations. These information technology and telecommunications systems support a variety of functions, including clinical trial management, clinical data capture and analysis, purchasing and production planning, production, logistics, quality control, customer service and support, billing, and general and administrative activities. Information technology and telecommunications systems are vulnerable to damage from a variety of sources, including telecommunications or network failures, malicious human acts and natural disasters. If we are subjected to one or more cyber-attacks or security breaches, we would suffer financial loss. Furthermore, as use of digital technologies has increased, cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication and make us even more at risk. These threats pose a risk to the security of our systems and networks, the confidentiality and the availability and integrity of our data. Any disruption or loss of information technology or telecommunications systems on which critical aspects of our operations depend could have an adverse effect on business.

Risks Related to the Development and Clinical Testing of Our Product Candidates

AM-125 and AM-401 are still in preclinical or clinical development. If our studies and trials are unsuccessful, we do not obtain regulatory approval or we are unable to commercialize AM-125 or AM-401, or we experience significant delays in doing so, our business, financial condition and results of operations will be materially adversely affected.

We have invested a significant portion of our efforts and financial resources in the development of AM-125 and AM-401, which are still in preclinical and clinical development, respectively. Our ability to generate product revenues from these drug product candidates, which we do not expect to occur for at least the next few years, if ever, will depend heavily on successful clinical development, obtaining regulatory approval or clearance and eventual commercialization of these product candidates. The success of AM-125 or AM-401 and our other product candidates will depend on several factors, including the following:

- completing clinical trials that demonstrate the efficacy and safety of our product candidates;
- receiving marketing approvals or clearance from competent regulatory authorities;
- establishing commercial manufacturing capabilities;
- launching commercial sales, marketing and distribution operations;
- acceptance of our product candidates by patients, the medical community and third-party payors;
- a continued acceptable safety profile following approval;
- competing effectively with other therapies; and
- qualifying for, maintaining, enforcing and defending our intellectual property rights and claims.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize AM-125 or AM-401, which would materially adversely affect our business, financial condition and results of operations.

We face risks related to health epidemics and outbreaks, including the COVID-19 pandemic, which could significantly disrupt our preclinical studies and clinical trials, and therefore our receipt of necessary regulatory approvals could be delayed or prevented.

In December 2019, a novel strain of coronavirus COVID-19 was reported to have surfaced in Wuhan, China. The extent to which COVID-19 may impact our preclinical and clinical trial operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration and geographic reach of the outbreak, the severity of COVID-19, and the effectiveness of actions to contain and treat COVID-19. In particular, the COVID-19 outbreak has impacted enrollment of patients into our "TRAVERS" phase 2 trial with AM-125. Candidates for participation in this trial undergo certain types of neurosurgery, which are elective procedures. In case of increasing case numbers, the COVID-19 pandemic may impact enrolment also into our planned Phase 3 trial.

The continued spread of COVID-19 globally could otherwise adversely impact our clinical trial operations, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography. Disruptions or restrictions on our ability to travel to monitor data from our clinical trials, or to conduct clinical trials, or the ability of patients enrolled in our studies to travel, or the ability of staff at study sites to travel, as well as temporary closures of our facilities or the facilities of our clinical trials partners and their contract manufacturers, would negatively impact our clinical trial activities. In addition, we rely on independent clinical investigators, contract research organizations and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our preclinical studies and clinical trials, including the collection of data from our clinical trials, and the outbreak may affect their ability to devote sufficient time and resources to our programs or to travel to sites to perform work for us. Similarly, our preclinical trials could be delayed and/or disrupted by the outbreak. As a result, the expected timeline for data readouts of our preclinical studies and clinical trials and certain regulatory filings may be negatively impacted, which would adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses and have a material adverse effect on our financial results.

On the other hand, in March 2022 we initiated the COVAMID clinical trial with Bentrio™ in patients with acute COVID-19 infection. If case numbers in the study country or countries decrease, our ability to complete the study on time may be negatively affected, additional measures and expenditures may be required to ensure enrollment, and we may experience delays in our regulatory submissions in support of obtaining a label claim for Bentrio™ also for viral infections.

Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results. If clinical trials of our drug product or device candidates are prolonged or delayed, we may be unable to obtain required regulatory approvals, and therefore be unable to commercialize our drug product candidates on a timely basis or at all.

To obtain the requisite regulatory approvals or approvals to market and sell any of our drug product or device candidates, we must demonstrate through extensive pre-clinical studies and clinical trials that our products are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of pre-clinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. For example, positive results generated to date in clinical trials for our product candidates do not ensure that later clinical trials will demonstrate similar results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through pre-clinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Our future clinical trial results may not be successful.

Clinical trials must be conducted in accordance with FDA, EMA and comparable foreign regulatory authorities' legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and Institutional Review Boards, or IRBs, at the medical institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with supplies of our product candidates produced under current good manufacturing practices, or cGMP, and other requirements. We depend on medical institutions and clinical research organizations, or CROs, to conduct our clinical trials in compliance with current good clinical practice, or cGCP, standards. To the extent the CROs fail to enroll participants for our clinical trials, fail to conduct the trials to cGCP standards or are delayed for a significant time in the execution of trials, including achieving full enrollment, we may be affected by increased costs, program delays or both, which may harm our business.

To date, we have not completed all clinical trials required for the approval of AM-125, which is currently in Phase 2 clinical development. In addition, we need to generate clinical data to support the approval of Bentrio™ for protection against airborne viruses.

The completion of clinical trials for AM-125 or Bentrio™ may be delayed, suspended or terminated as a result of many factors, including but not limited to:

- the delay or refusal of regulators or IRBs to authorize us to commence a clinical trial at a prospective trial site and changes in regulatory requirements, policies and guidelines;
- delays or failure to reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delays in patient enrollment and variability in the number and types of patients available for clinical trials;
- the inability to enroll a sufficient number of patients in trials to ensure adequate statistical power to detect statistically significant treatment effects;
- negative or inconclusive results, which may require us to conduct additional pre-clinical or clinical trials or to abandon projects that we expect to be promising;
- safety or tolerability concerns could cause us to suspend or terminate a trial if we find that the participants are being exposed to unacceptable health risks;
- regulators or IRBs requiring that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or safety concerns, among others;
- lower than anticipated retention rates of patients and volunteers in clinical trials;
- our CROs or clinical trial sites failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, deviating from the protocol or dropping out of a trial;
- delays relating to adding new clinical trial sites;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- errors in survey design, data collection and translation;
- delays in establishing the appropriate dosage levels;
- the quality or stability of the product candidate falling below acceptable standards;
- the inability to produce or obtain sufficient quantities of the product candidate to complete clinical trials; and
- exceeding budgeted costs due to difficulty in accurately predicting costs associated with clinical trials.

Any delays in completing our clinical trials will increase our costs, slow down our development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug product candidates.

Positive or timely results from pre-clinical or early-stage trials do not ensure positive or timely results in late-stage clinical trials or product approval by the FDA, the EMA or comparable foreign regulatory authorities. Product candidates that show positive pre-clinical or early clinical results may not show sufficient safety or efficacy in later stage clinical trials and therefore may fail to obtain regulatory approvals.

Also, pre-clinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. The FDA, the EMA and comparable foreign regulatory authorities have substantial discretion in the approval process and in determining when or whether regulatory approval will be obtained for any of our product candidates. Even if we believe the data collected from clinical trials of AM-125 or Bentrio™ are promising, such data may not be sufficient to support approval by the FDA, the EMA or any other regulatory authority.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants.

If we are required to conduct additional clinical trials or other testing of AM-125 or Bentrio™ or any other drug product candidate that we develop beyond the trials and testing that we currently contemplate, if we are unable to successfully complete clinical trials or other testing, if the results of these trials or tests are unfavorable or are only modestly favorable or if there are safety concerns associated with AM-125 our other drug product candidates, or Bentrio™, we may:

- be delayed in obtaining marketing approval;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- remove the product from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals or if we are required to conduct additional clinical trials or other testing of AM-125 or other drug product candidates or Bentrio™ beyond the trials and testing that we currently contemplate or conduct and we may be required to obtain additional funds to complete such additional clinical trials. We cannot assure you that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our trials after they have begun. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do or shorten any periods during which we have the exclusive right to commercialize our product candidates, which may harm our business and results of operations. In addition, some of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of regulatory approval of AM-125, any other drug product candidate, or Bentrio™ for its intended use in protection against airborne viruses.

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

If our product candidates are associated with serious adverse, undesirable or unacceptable side effects, we may need to abandon their development or limit development to certain uses or sub-populations in which such side effects are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in pre-clinical or early-stage testing have later been found to cause side effects that restricted their use and prevented further development of the compound for larger indications.

In our clinical trials of AM-125 to date, adverse events included a low number of transient and dose-dependent nasal congestion or discomfort. No treatment-related serious adverse events were observed. Occurrence of serious procedure- or treatment-related side effects could impede clinical trial enrollment and receipt of marketing approval from the FDA, the EMA and comparable foreign regulatory authorities. They could also adversely affect physician or patient acceptance of our product candidates.

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

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients; and
- our reputation and physician or patient acceptance of our products may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

We depend on enrollment of patients in our clinical trials for our product candidates. If we are unable to enroll patients in our clinical trials, our research and development efforts could be materially adversely affected.

Successful and timely completion of clinical trials will require that we enroll a sufficient number of patient candidates. Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. Patient enrollment depends on many factors, including the size and nature of the patient population, eligibility criteria for the trial, the proximity of patients to clinical sites, the design of the clinical protocol, the availability of competing clinical trials, the availability of new drugs approved for the indication the clinical trial is investigating, and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies.

The specific target population of patients and therapeutic time windows may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost-effective manner. Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

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

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of pharmaceutical products. The current and future use of product candidates by us in clinical trials, and the sale of Bentrio™ or any future-approved products, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, medical device or pharmaceutical companies or others selling such products. Any claims against us, regardless of their merit, could be difficult and costly to defend and could materially adversely affect the market for our product candidates, commercial products or any prospects for commercialization of our product candidates.

Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a drug or medical device, even after regulatory approval, may exhibit unforeseen side effects. If any of our product candidates were to cause adverse side effects during clinical trials or after approval of the product candidate, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates.

We purchase liability insurance in connection with each of our clinical trials and for commercial stage products. It is possible that our liabilities could exceed our insurance coverage. However, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

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

Due to our limited resources and access to capital, we must and have in the past decided to prioritize development of certain product candidates; these decisions may prove to have been wrong and may adversely affect our revenues.

Because we have limited resources and access to capital to fund our operations, we must decide which product candidates to pursue and the amount of resources to allocate to each. As such, we have been primarily focused on the development of AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, with our current commercial focus being limited to Bentrio™, AM-125 and AM-401 while we have deprioritized AM-201, and Keyzilen® and Sonsuvi® until we will be able to out-license or sell these programs. Our decisions concerning the allocation of research, collaboration, management and financial resources toward particular compounds, product candidates or therapeutic areas may not lead to the development of viable commercial products and may divert resources away from better opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties in respect of certain product development programs may also prove not to be optimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the market potential of our product candidates or misread trends in the biopharmaceutical industry our business, financial condition and results of operations could be materially adversely affected.

Our research and development activities could be affected or delayed as a result of possible restrictions on animal testing.

Certain laws and regulations require us to test our product candidates on animals before initiating clinical trials involving humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted, delayed or become more expensive.

Risks Related to Regulatory Approval of Our Product Candidates

We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized.

Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize one or more product candidates. We currently have one drug product candidate, AM-125, in Phase 2 clinical development and another, AM-401, in preclinical development. We are not permitted to market or promote any of our drug product candidates before we receive regulatory approval from the FDA, EMA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates.

Although certain of our employees have prior experience with submitting marketing applications to the FDA, EMA or comparable foreign regulatory authorities, we as a company have not submitted such applications for our drug product candidates. We cannot be certain that any of our product candidates will be successful in clinical trials or receive regulatory approval. Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

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

In addition, our current product candidates or any of our other future product candidates could take a significantly longer time to gain regulatory approval than expected or may never gain regulatory approval. This could delay or eliminate any potential product revenue by delaying or terminating the potential commercialization of our product candidates.

We generally plan to seek regulatory approval to commercialize our product candidates in the United States, the European Union and in additional foreign countries where we have commercial rights. To obtain regulatory approval in other countries, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical trials, commercial sales, pricing, and distribution of our product candidates. Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. Failure to obtain marketing authorization for our product candidates will result in our being unable to market and sell such products, which would materially adversely affect our business, financial conditional and results of operations. If we fail to obtain approval in any jurisdiction, the geographic market for our product candidates could be limited. Similarly, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

We cannot give any assurance that Bentrio™ will receive regulatory clearance in the US, which is necessary before it can be commercialized in the US.

Bentrio™ is a spray product for intranasal protection against airborne viruses or allergens.

Unless an exemption applies, any medical device that is to be marketed in the U.S. must first receive from the FDA either 510(k) clearance, by filing a 510(k) premarket notification, or premarket application (PMA) approval, after submitting a PMA. Alternatively, the device may be cleared through the de novo classification process by the FDA. In September 2021 we submitted a 510(k) application for premarket clearance of Bentrio™ as a Class II device for the intended use of promoting alleviation of mild allergic symptoms triggered by the inhalation of various airborne allergens. The FDA's review is currently ongoing.

To obtain 510(k) clearance, a company must submit a premarket notification demonstrating substantial equivalence between the proposed device and a legally marketed "predicate" device, which is defined as a legally marketed device, that (i) was legally marketed prior to May 28, 1976, for which the FDA has not yet called for submission of a PMA application; (ii) has been reclassified from Class III to Class II or Class I; (iii) has been cleared through the 510(k) premarket notification process; or (iv) has been previously determined to be exempt from the 510(k) process. Substantial equivalence means that the proposed device has the same intended use and the same technological characteristics as the predicate device, or, if the new device has different technological characteristics, that the device is as safe and effective as the predicate device and does not raise different questions of safety and effectiveness. We have identified two such predicate devices and have referenced them in our 510(k) submission.

Bentrio™ is also intended for use in the reduction of the intranasal infectious viral load following inspiration of airborne viruses such as SARS-CoV-2. Since there appears to be no valid predicate device available for this intended use, we may have to submit a de novo request to the FDA. Under the de novo pathway, we would have to prove that Bentrio™ does not present substantial risk to the patient (rather than just demonstrating substantial equivalence with the safety of the relevant predicate device(s)), which may require additional testing. The review by the FDA in the de novo process is longer than the 510(k) process and requires higher fees. Any device that has been classified through the de novo process may be marketed and used as predicate for future 510(k) submissions. The FDA may also, instead of accepting a 510(k) submission, require us to submit a PMA, which is typically a much more complex, lengthy, and burdensome application than a 510(k). To support a PMA, the FDA would likely require that we conduct one or more clinical studies to demonstrate that the device is safe and effective. In some cases such studies may be requested for a 510(k) as well. We may not be able to meet the requirements to obtain 510(k) clearance or PMA approval, in which case the FDA may not grant any necessary clearances or approvals. In addition, the FDA may place significant limitations upon the intended use of our products as a condition to a 510(k) clearance or PMA approval. Product applications can also be denied or withdrawn due to failure to comply with regulatory requirements or the occurrence of unforeseen problems following clearance or approval. Any delays or failure to obtain FDA clearance or approval of new products we develop, any limitations imposed by the FDA on new product use or the costs of obtaining FDA clearance or approvals could have a material adverse effect on our business, financial condition and results of operations.

The marketing and commercialization of Bentrio™ in other countries is subject to varying regulatory requirements, including in some cases also the approval of certain marketing materials and messages, which are evolving over time.

Many foreign countries in which we currently commercialize or intend to market Bentrio™ have regulatory bodies and restrictions similar to those of the FDA. International sales are subject to foreign government regulation, the requirements of which vary substantially from country to country. The time required to obtain approval by a foreign country may be longer or shorter than that required for FDA clearance and the requirements may differ.

In particular, marketing of medical devices in the European Union (EU) is subject to compliance with the Medical Devices Directive 93/92/EEC (MDD). A medical device may be placed on the market within the EU only if it conforms to certain "essential requirements" and bears the CE Mark. The most fundamental and essential requirement is that a medical device must be designed and manufactured in such a way that it will not compromise the clinical condition or safety of patients, or the safety and health of users and others. In addition, the device must achieve the essential performance(s) intended by the manufacturer and be designed, manufactured and packaged in a suitable manner.

Manufacturers must demonstrate that their devices conform to the relevant essential requirements through a conformity assessment procedure. The nature of the assessment depends upon the classification of the device. The classification rules are mainly based on three criteria: the length of time the device is in contact with the body, the degree of invasiveness and the extent to which the device affects the anatomy. Conformity assessment procedures for all but the lowest risk classification of device involve a notified body. Notified bodies are often private entities and are authorized or licensed to perform such assessments by government authorities. Manufacturers usually have some flexibility to select a notified body for the conformity assessment procedures for a particular class of device and to reflect their circumstances, e.g., the likelihood that the manufacturer will make frequent modifications to its products. Conformity assessment procedures require an assessment of available clinical evidence, literature data for the product and post-market experience in respect of similar products already marketed. Notified bodies also may review the manufacturer's quality systems. If satisfied that the product conforms to the relevant essential requirements, the notified body issues a certificate of conformity, which the manufacturer uses as a basis for its own declaration of conformity and application of the CE Mark. Application of the CE Mark allows the general commercializing of a product in the EU. The product can also be subjected to local registration requirements depending on the country. We maintain CE Marking on all of our products that require such markings as well as local registrations as required.

In May 2017, the EU adopted a new Medical Devices Regulation (EU) 2017/745 (MDR), which replaced the MDD with effect from May 26, 2021. The MDR clearly envisages, among other things, stricter controls of medical devices, including strengthening of the conformity assessment procedures, increased expectations with respect to clinical data for devices and pre-market regulatory review of high-risk devices. The MDR also envisages greater control over notified bodies and their standards, increased transparency, more robust device vigilance requirements and clarification of the rules for clinical investigations. Under transitional provisions, medical devices such as Bentrio™ with certificates of conformity issued under the MDD prior to May 26, 2021 may continue to be placed on the market for the remaining validity of the certificate, until May 27, 2024 at the latest. After the expiry of any applicable transitional period, only devices that have been CE marked under the MDR may be placed on the market in the EU.

Under the MDD, Bentrio™ is classified as a Class I device which does not require a notified body for the conformity assessment procedure. Under the MDR, AM-301 will be classified as a Class II device which will require a notified body. We expect to register Bentrio™ in the EU prior to the transition from the MDD to the MDR and plan to meet the requirements for conformity as Class II during the transition period ending May 27, 2024. With the transition from MDD to MDR, there is strong demand for the services of notified bodies, and we cannot assure you that we will be able to contract a notified body in due time, or that we will be able to meet the requirements for conformity for Bentrio™ as Class II medical device under MDR and that we will be able to maintain the current labelling of the product.

The labelling and promotion of treatments for infectious diseases such as SARS-CoV-2 is subject to special regulations in many countries. For example, in Germany we are not allowed to present or mention the potential protective effects of Bentrio™ against SARS-CoV-2 directly to consumers but must communicate them to health care providers only. ANSM, the French National Agency for the Safety of Medicines and Health Products, has requested that our indication of use for viral infections such as SARS-CoV-2 be supported by clinical data, which we currently do not have. In other countries, such as Italy, any advertisement material for medical devices must be pre-approved by the Ministry of Health, which has broad discretion over the approval process, including review timelines. As a consequence, the access to certain markets requires substantial adaptations to packaging materials, instructions for use, labelling and marketing materials, may take much longer than usual, and the sales potential for Bentrio™ may be substantially restrained.

Because we are developing therapies for which there is little clinical experience and, in some cases, using new endpoints, there is more risk that the outcome of our clinical trials will not be favorable. Even if the results of our trials are favorable, there is risk that they will not be acceptable to regulators or physicians.

There are currently no drugs with proven efficacy for acute peripheral vertigo. In addition, there has been limited historical clinical trial experience generally for the development of drugs to treat this condition. Regulatory authorities in the United States and European Union have not issued definitive guidance as to how to measure the efficacy of treatments for acute peripheral vertigo, and regulators have not yet established what is required to be demonstrated in a clinical trial in order to signify a clinically meaningful result and/or obtain marketing approval.

Whereas various balance tests and questionnaires are widely used in the diagnosis and management of vertigo, there is no universally recognized definition of the clinical meaningfulness of outcomes, and regulatory authorities have not issued guidelines for demonstrating efficacy for drug-based treatments such as AM-125. Therefore, we cannot be certain that AM-125 will be approved even if it were to show statistically significant improvements in these tests.

Substantial additional data may need to be generated in order to obtain marketing approval for AM-125.

Oral betahistine has been in clinical use for several decades and is reported to be currently marketed in 115 countries world-wide. However, in the United States oral betahistine is not approved since the FDA revoked the drug product's marketing authorization in the early 1970s over issues with unsubstantiated information about some patients in the efficacy studies upon which approval had been based. Given the absence of an approved betahistine drug product in the United States and to the extent that existing data may not be deemed sufficient, the FDA may require a full development package for AM-125.

Furthermore, additional data will be required for the specific formulation of AM-125 and the intranasal administration route. Since intranasal delivery of betahistine has the potential to result in substantially higher systemic exposures as measured by concentrations in blood plasma compared to oral delivery, existing safety assessments conducted with or for the approved drug product may not be sufficient. In addition, some of these assessments were performed a long time ago and may not be in line with current regulations and guidelines. Therefore, the scope of our development program for AM-125 may ultimately not be much smaller than one for new chemical entities.

Even if our product candidates obtain regulatory approval, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

If marketing authorization is obtained for any of our product candidates, the product will remain subject to continual regulatory review and therefore authorization could be subsequently withdrawn or restricted. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA or a comparable foreign regulatory authority approves any of our product candidates, we will be subject to ongoing regulatory obligations and oversight by regulatory authorities, including with respect to the manufacturing processes, labeling, packing, distribution, adverse event reporting, storage, advertising and marketing restrictions, and recordkeeping and, potentially, other post-marketing obligations, all of which may result in significant expense and limit our ability to commercialize such products. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs, cGDPs and cGCPs for any clinical trials that we conduct post-approval. In the European Union, the marketing authorization holder has to operate a pharmacovigilance system which conforms with and is equivalent to the respective Member State's pharmacovigilance system, requiring the holder to evaluate all information scientifically, to consider options for risk minimization and prevention and to take appropriate measures as necessary. As part of this system, we will have to, inter alia, have a qualified person responsible for pharmacovigilance, maintain a pharmacovigilance system master file, operate a risk management system for each medicinal product, monitor the outcome of risk minimization measures, and update continuously all pharmacovigilance data to update the risk assessment.

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

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

If any of these events occurs, our ability to sell such drug product may be impaired, and we may incur substantial additional expense to comply with regulatory requirements, which could materially adversely affect our business, financial condition and results of operations. The FDA's or any other regulatory authority's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Healthcare legislative or regulatory reform measures, including government restrictions on pricing and reimbursement, may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in the United States, the Patient Protection and Affordable Care Act of 2010 ("ACA") substantially changed the way healthcare is financed by both the government and private insurers, and significantly affects the pharmaceutical industry. Many provisions of the ACA impact the biopharmaceutical industry, including that in order for a biopharmaceutical product to receive federal reimbursement under the Medicare Part B and Medicaid programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the drug pricing program under the Public Health Services Act, or PHS. Since its enactment, there have been judicial and Congressional challenges and amendments to certain aspects of the ACA. There is continued uncertainty about the implementation of the ACA, including the potential for further amendments to the ACA and legal challenges to or efforts to repeal the ACA.

Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the now-departed Trump administration proposed numerous prescription drug cost control measures. Similarly, the new Biden administration has made lowering prescription drug prices one of its priorities. The Biden administration has not yet proposed any specific plans, but we expect that these will be forthcoming in the near term. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Other examples of proposed changes include, but are not limited to, expanding post-approval requirements, changing the Orphan Drug Act, and restricting sales and promotional activities for pharmaceutical products.

We cannot be sure whether additional legislative changes will be enacted, or whether government regulations, guidance or interpretations will be changed, or what the impact of such changes would be on the marketing approvals, sales, pricing, or reimbursement of our drug candidates or products, if any, may be. We expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs.

In addition, FDA regulations and guidance may be revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. Any new regulations or guidance, or revisions or reinterpretations of existing regulations or guidance, may impose additional costs or lengthen FDA review times for our product candidates. We cannot determine how changes in regulations, statutes, policies, or interpretations when and if issued, enacted or adopted, may affect our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recalls, replacements, or discontinuance of one or more of our products; and
- additional recordkeeping.

Such changes would likely require substantial time and impose significant costs or could reduce the potential commercial value of our product candidates. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any other products would harm our business, financial condition, and results of operations.

In the European Union, a new clinical trial regulation centralizes clinical trial approval, which eliminates redundancy, but in some cases this may extend timelines for clinical trial approvals due to potentially longer wait times. The regulation requires specific consents for use of data in research which, among other measures, may increase the costs and timelines for our product development efforts. The regulation also provides an obligation for clinical trial sponsors to make summaries of all trial results, accompanied by a summary understandable to laypersons, as well as the clinical trial report publicly available in a new database. Beyond this obligation, the EMA makes available to the public all clinical trials submitted with the EMA as well as raw data results ("individual patient data"). These publication requirements can conflict with legitimate secrecy interests of the sponsors and may lead to valuable clinical trial data falling into the public domain.

Austerity measures in certain European nations may also affect the prices we are able to seek if our products are approved, as discussed below.

Both in the United States and in the European Union, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We do not know whether additional legislative changes will be enacted, or whether the regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be.

Our relationships with customers and payors are subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, if violated, would expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings, among other penalties.

Healthcare providers, payors and others play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, primarily in the United States, that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable U.S. healthcare laws and regulations, include the following:

- the U.S. healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under U.S. government healthcare programs such as Medicare and Medicaid;

- the U.S. False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the U.S. Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the transparency requirements under the Health Care Reform Law require manufacturers of drugs, devices, biologics and medical supplies to report to the U.S. Department of Health and Human Services information related to payments and other transfers of value made by such manufacturers to physicians and teaching hospitals, and ownership and investment interests held by physicians or their immediate family members; and

- analogous laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

Similar laws exist in other jurisdictions.

In the European Union, there is currently no central European anti-bribery or similar legislation. However, more and more European Union member states as well as life sciences industry associations are enacting increasingly specific anti-bribery rules for the healthcare sector which are as severe and sometimes even more severe than in the United States. Germany, for example, has recently adopted new criminal provisions dealing with granting benefits to healthcare professionals. This new law has increased the legal restrictions as well as the legal scrutiny for the collaboration and contractual relationships between the pharmaceutical industry and its customers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under the U.S. federal Anti-Kickback Statute, it is possible that some of our future business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the Health Care Reform Law, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the Health Care Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business with are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Risks Related to Commercialization of Our Products and Product Candidates

The high level of competition in OTC consumer health care, much of which comes from competitors with greater resources, could adversely affect our business, financial condition and results of operations.

The business of selling brand name consumer products in the OTC Healthcare category is highly competitive. This market includes numerous manufacturers, distributors, marketers and retailers that actively compete for consumers' business both in the United States and abroad. Many of these competitors are larger and have substantially greater resources than we do, and may therefore have the ability to spend more aggressively on research and development, advertising and marketing, and to respond more effectively to changing business and economic conditions. If this were to occur, it could have a material adverse effect on our financial condition and results of operations.

We compete for consumers' attention based on a number of factors, including brand recognition, product quality, performance, value to consumers, price and product availability at the retail level. Advertising, promotion, merchandising and packaging also have a significant impact on consumer buying decisions and, as a result, on our sales. Our markets are highly sensitive to the introduction of new products, which may rapidly capture a significant share of the market. New product innovations by our competitors or our failure to develop new products or the failure of a new product launch by the Company, could have a material adverse effect on our business, financial condition and results of operations. If our advertising, marketing and promotional programs are not effective, we may be unable to grow our revenues to profitable levels or our sales may decline.

Price increases for raw materials, labor, energy, transportation costs and other manufacturer, logistics provider or distributor demands could have an adverse impact on our margins.

The costs to manufacture and distribute Bentrio™ are subject to fluctuation based on a variety of factors. Increases in commodity raw material, packaging component prices, and labor, energy and fuel costs and other input costs could have a significant impact on our financial condition and results of operations if our third party manufacturers, logistics providers or distributors pass along those costs to us. If we are unable to increase the price for our products to our customers or continue to achieve cost savings in a rising cost environment, any such cost increases would reduce our gross margins and could have a material adverse effect on our financial condition and results of operations. If we increase the price of Bentrio™ in order to maintain our current gross margins for our products, such increase may adversely affect demand for, and sales of, Bentrio™, which could have a material adverse effect on our business, financial condition and results of operations.

Product liability claims and product recalls and related negative publicity could adversely affect our sales and operating results.

We are dependent on consumers' perception of the safety and quality of Bentrio™. Negative consumer perception may arise from product liability claims and product recalls, regardless of whether such claims or recalls involve us or our product. The mere publication of information asserting concerns about the safety of our product or the ingredients used in our product could have a material adverse effect on our business and results of operations.

Product liability claims could be based on allegations that, among other things, Bentrio™ contains contaminants, include inadequate instructions or warnings regarding their use or include inadequate warnings concerning side effects and interactions with other substances. Whether or not successful, product liability claims could result in negative publicity that could adversely affect the reputation of our brand and our business, sales and operating results. Additionally, we may be required to pay for losses or injuries purportedly caused by our products. In addition, we could be required for a variety of reasons to initiate product recalls. Any product recalls could have a material adverse effect on our business, financial condition and results of operations.

In addition, although we maintain, and require our suppliers and third party manufacturers to maintain, product liability insurance coverage, potential product liability claims may exceed the amount of insurance coverage or may be excluded under the terms of the policy, which could have a material adverse effect on our financial condition. In addition, in the future we may not be able to obtain adequate insurance coverage or we may be required to pay higher premiums and accept higher deductibles in order to secure adequate insurance coverage.

We operate in highly competitive and rapidly changing industries, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.

The biopharmaceutical and pharmaceutical industries are highly competitive and subject to significant and rapid technological change. Our success is highly dependent on our ability to discover, develop and obtain marketing approval for new and innovative products on a cost-effective basis and to market them successfully. In doing so, we face and will continue to face intense competition from a variety of businesses, including large, fully integrated pharmaceutical companies, specialty pharmaceutical companies and biopharmaceutical companies, academic institutions, government agencies and other private and public research institutions in Europe, the United States and other jurisdictions. These organizations may have significantly greater resources than we do and conduct similar research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and marketing of products that compete with our product candidates.

The highly competitive nature of and rapid technological changes in the biotechnology and pharmaceutical industries could render our product candidates or our technology obsolete or non-competitive. Our competitors may, among other things:

- develop and commercialize products that are safer, more effective, less expensive, or more convenient or easier to administer;
- obtain quicker regulatory approval;
- establish superior proprietary positions;
- have access to more manufacturing capacity;
- implement more effective approaches to sales and marketing; or
- form more advantageous strategic alliances.

Should any of these occur, our business, financial condition and results of operations could be materially adversely affected.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage and reimbursement levels and pricing policies.

The successful commercialization of any of our products or product candidates will depend, in part, on the extent to which coverage and reimbursement for our products or procedures using our products will be available from government and health administration authorities, private health insurers and other third-party payors. To manage healthcare costs, many governments and third-party payors increasingly scrutinize the pricing of new technologies and require greater levels of evidence of favorable clinical outcomes and cost-effectiveness before extending coverage. In light of such challenges to prices and increasing levels of evidence of the benefits and clinical outcomes of new technologies, we cannot be sure that coverage will be available for our products or product candidates that we commercialize and, if available, that the reimbursement rates will be adequate.

Third-party payors may deny coverage and reimbursement status altogether of a given drug product, or cover the product but may also establish prices at levels that are too low to enable us to realize an appropriate return on our investment in product development. Because the rules and regulations regarding coverage and reimbursement change frequently, in some cases at short notice, even when there is favorable coverage and reimbursement, future changes may occur that adversely impact the favorable status. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States.

The unavailability or inadequacy of third-party coverage and reimbursement could have a material adverse effect on the market acceptance of our products and product candidates and the future revenues we may expect to receive from those products. In addition, we are unable to predict what additional legislation or regulation relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future, or what effect such legislation or regulation would have on our business.

Our products may not gain market acceptance, in which case we may not be able to generate product revenues, which will materially adversely affect our business, financial condition and results of operations.

Even if the FDA, the EMA or other regulatory authority clears or approves the marketing of any product candidates that we develop, physicians, healthcare providers, patients or the medical community may not accept or use them. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If Bentrio™ or our drug product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues or any profits from operations. The degree of market acceptance of Bentrio™ or any of our drug product candidates that is cleared or approved for commercial sale will depend on a variety of factors, including:

- how clinicians and potential patients perceive our novel products;
- the timing of market introduction;
- the number and clinical profile of competing products;
- our ability to provide acceptable evidence of safety and efficacy;
- the prevalence and severity of any side effects;
- relative convenience and ease of administration;
- cost-effectiveness;
- patient diagnostics and screening infrastructure in each market;
- marketing and distribution support;
- availability of coverage, reimbursement and adequate payment from health maintenance organizations and other third-party payors, both public and private; and
- other potential advantages over alternative treatment methods.

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

In addition, the potential market opportunity of Bentrio™ or our drug product candidates are difficult to precisely estimate. Our estimates of the potential market opportunity are predicated on several key assumptions such as industry knowledge and publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions could not have been assessed by an independent source in every detail. If any of the assumptions proves to be inaccurate, then the actual market for Bentrio™ or our drug product candidates could be smaller than our estimates of the potential market opportunity. If the actual market for Bentrio™ or our drug product candidates is smaller than we expect, or if the products fail to achieve an adequate level of acceptance by physicians, health care payors and patients, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

We may lack the necessary expertise, personnel and resources to successfully commercialize our products on our own or together with suitable partners.

Before Bentrio™ we have never commercialized a product candidate. To achieve commercial success for Bentrio™ and our drug product candidates, we will have to continue to develop our own sales, marketing and distribution organization or outsource these activities to third parties.

Risks Related to Our Reliance on Third Parties

If we fail to maintain our current strategic relationship with Washington University, Wellesta Holdings or Nuance Pharma, our business, commercialization prospects and financial condition may be materially adversely affected.

We have an exclusive license agreement with Washington University located in St. Louis, Missouri ("WU"). Under this agreement with WU, we are given an exclusive, worldwide, royalty-bearing license (with the right to sublicense) under certain patent rights owned or controlled by WU to research, develop, make, have made, sell, offer for sale, use and import pharmaceutical products covered under such patent rights for all fields of use. Such licensed products may include drug products formulated as nanoparticles, comprising a peptide for delivery as well as a therapeutic nucleotide, for intracellular delivery. These intellectual property rights have been the basis of our research and development of AM-401.

Good relationships with WU are important for our business prospects. If our relationship with WU were to deteriorate substantially or WU were to challenge our use of their intellectual property or our calculations of the payments we owe under our agreements, our business, financial condition, commercialization prospects and results of operations could be materially adversely affected.

We have entered into exclusive distribution and marketing agreements for Bentrio™ with a number of partners such as Wellesta Holdings ("Wellesta") for India and certain other Asian markets, Nuance Pharma ("Nuance") for China and South Korea or Avernus Pharma ("Avernus") for certain Middle East countries. Under these agreements, these distributors have the exclusive right to market and distribute Bentrio™ for a certain period of time in their territory subject to certain conditions. In order to maintain their exclusive rights, they are required to purchase certain quantities of Bentrio™. Good relationships with the distributors are important for our business prospects. If our relationships with them were to deteriorate substantially, or they fail to perform adequately, our business, financial condition, commercialization prospects and results of operations could be materially adversely affected.

We may seek to form additional strategic alliances in the future with respect to Bentrio™ or our drug product candidates, and if we do not realize the benefits of such alliance, our business, financial condition, commercialization prospects and results of operations may be materially adversely affected.

The commercialization of Bentrio™ requires substantial cash to fund expenses and access to distribution networks, which we do not currently possess. Therefore, in addition to our relationships with Wellesta, Nuance and other distributors, we may decide to enter into strategic alliances, or create joint ventures or collaborations with further OTC consumer health companies, notably in Europe and North America for the further commercialization of Bentrio™.

Our product development programs and the potential commercialization of our drug product candidates will require substantial additional cash to fund expenses and may require expertise, such as sales and marketing expertise, which we do not currently possess. Therefore, in addition to our relationship with WU for our AM-401 product candidate, for one or more of our drug product candidates, we may decide to enter into strategic alliances, or create joint ventures or collaborations with pharmaceutical or biopharmaceutical companies for the further development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Collaborations are complex and time-consuming to negotiate and document. Any delays in entering into new strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market. We may also be restricted under existing and future collaboration agreements from entering into strategic partnerships or collaboration agreements on certain terms with other potential collaborators. We may not be able to negotiate collaborations on acceptable terms, or at all, for any of our existing or future product candidates and programs because the potential partner may consider that our research and development pipeline is insufficiently developed to justify a collaborative effort, or that our product candidates and programs do not have the requisite potential to demonstrate safety and efficacy in the target population. If we are unsuccessful in establishing and maintaining a collaboration with respect to a particular product candidate, we may have to curtail the development of that product candidate, reduce the scope of or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of our sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense for which we have not budgeted. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we will not be able to bring our product candidates to market and generate product revenue. Even if we are successful in establishing a new strategic partnership or entering into a collaboration agreement, we cannot be certain that, following such a strategic transaction or license, we will be able to progress the development and commercialization of the applicable product candidates as envisaged, or that we will achieve the revenues that would justify such transaction, and we could be subject to the following risks, each of which may materially harm our business, commercialization prospects and financial condition:

- we may not be able to control the amount and timing of resources that the collaboration partner devotes to the product development program;
- the collaboration partner may experience financial difficulties;
- we may be required to relinquish important rights such as marketing, distribution and intellectual property rights;
- a collaboration partner could move forward with a competing product developed either independently or in collaboration with third parties, including our competitors; or
- business combinations or significant changes in a collaboration partner's business strategy may adversely affect our willingness to complete our obligations under any arrangement.

We rely on third parties to conduct our nonclinical and clinical trials and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

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

If any of our relationships with these third-party CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our on-going nonclinical and clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements, or for other reasons, our clinical trials may be extended, delayed, or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. CROs may also generate higher costs than anticipated. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

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

We rely on a single source for the production of Bentrio™ and may face difficulties in case of delivery problems, delays, issues with product quality or other aspects.

Bentrio™ is produced by a single third-party manufacturer. Our ability to retain our current manufacturing relationship is critical to our ability to deliver quality products to our customers in a timely manner. Without adequate supplies of quality merchandise, our sales would decrease materially and our business would suffer. In the event that our contract manufacturer is unable or unwilling to ship products to us in a timely manner, we would have to identify and qualify new manufacturing relationships. Because of the unique manufacturing requirement of Bentrio™, we may be unable to qualify new suppliers in a timely way or at the quantities, quality and price levels needed. In addition, identifying alternative manufacturers without adequate lead times may involve additional manufacturing expense, delay in production or product disadvantage in the marketplace. In general, the consequences of not securing adequate, high quality and timely supplies of merchandise would negatively impact inventory levels, which could damage our reputation and result in lost customers and sales, and could have a material adverse effect on our business, financial condition and results of operations.

We currently rely on third-party suppliers and other third parties for production of our drug product candidates and our dependence on these third parties may impair the advancement of our research and development programs and the development of our drug product candidates.

We currently rely on and expect to continue to rely on third parties, for the manufacturing and supply of chemical compounds for preclinical studies and clinical trials of our product candidates, including AM-125 and AM-401. and others for the manufacturing and supply of the drug product candidates. For the foreseeable future, we expect to continue to rely on such third parties for the manufacture of any of our drug product candidates on a clinical or commercial scale, if any of our product candidates receives regulatory approval. Reliance on third-party providers may expose us to different risks than if we were to manufacture product candidates ourselves. The facilities used by our contract manufacturers to manufacture our drug product candidates must be approved by the FDA or other regulatory authorities pursuant to inspections that will be conducted after we submit our NDA or comparable marketing application to the FDA or other regulatory authority. Although we have auditing rights with all our manufacturing counterparties, we do not have control over a supplier's or manufacturer's compliance with these laws, regulations and applicable cGMP standards and other laws and regulations, such as those related to environmental health and safety matters. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drug product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our drug product candidates, if approved. Any failure to achieve and maintain compliance with these laws, regulations and standards could subject us to the risk that we may have to suspend the manufacturing of our drug product candidates or that obtained approvals could be revoked, which would adversely affect our business and reputation. Furthermore, third-party providers may breach agreements they have with us because of factors beyond our control. They may also terminate or refuse to renew their agreements because of their own financial difficulties or business priorities, potentially at a time that is costly or otherwise inconvenient for us. If we were unable to find adequate replacement or another acceptable solution in time, our clinical trials could be delayed or our commercial activities could be harmed.

In addition, the fact that we are dependent on our suppliers and other third parties for the manufacture, storage and distribution of our drug product candidates means that we are subject to the risk that our product candidates and, if approved, commercial products may have manufacturing defects that we have limited ability to prevent or control. The sale of drug products containing such defects could result in recalls or regulatory enforcement action that could adversely affect our business, financial condition and results of operations.

Growth in the costs and expenses of components or raw materials may also adversely influence our business, financial condition and results of operations. Supply sources could be interrupted from time to time and, if interrupted, that supplies could be resumed (whether in part or in whole) within a reasonable time frame and at an acceptable cost or at all.

Our current and anticipated future dependence upon others for the manufacturing of AM-125, AM-401 and any other product candidate that we develop may adversely affect our future profit margins and our ability to commercialize any drug products that receive marketing approval on a timely and competitive basis.

Certain ingredients and the primary packaging for Bentrio™ and our drug product candidates are currently acquired from single-source suppliers. The loss of these suppliers, or their failure to supply us with the ingredients or the primary packaging, could materially and adversely affect our business.

We do not currently, and do not expect to in the future, independently conduct manufacturing activities for Bentrio™ and our drug product candidates, including AM-125 and AM-401. We currently have a relationship with one supplier each, for the supply of the drug substance of AM-125 and AM-401, the peptide for AM-401, and for the key component of Bentrio™. We do not currently have any other suppliers for the drug substance, certain other ingredients, and primary packaging of our drug product candidates and Bentrio™ and, although we believe that there are alternate sources of supply that could satisfy our clinical and commercial requirements, and we have performed some preliminary investigations to assess this availability, we cannot assure you that identifying alternate sources and establishing relationships with such sources would not result in significant delay in the development of our drug product candidates or in significant interruptions in commercial supplies of Bentrio™. Additionally, we may not be able to enter into supply arrangements with alternative suppliers on commercially reasonable terms, or at all. A delay in the development of our drug product candidates, interruption in commercial supplies of Bentrio™ or having to enter into a new agreement with a different third party on less favorable terms than we have with our current suppliers could have a material adverse impact upon on our business.

Risks Related to Intellectual Property

If we or our licensors are unable to obtain and maintain effective patent rights for our technologies, commercial products, drug product candidates or any future product candidates, or if the scope of the patent rights obtained is not sufficiently broad, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to our technologies, commercial products and drug product candidates. Our success depends in large part on our and our licensors' ability to obtain and maintain patent and other intellectual property protection in the United States and in other countries with respect to our proprietary technology and products.

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsolved. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions remain confidential for a period of time after filing, and some remain so until issued. We cannot be certain that we were the first to file any patent application related to our product candidates, or whether we were the first to make the inventions claimed in our owned patents or pending patent applications, nor can we know whether those from whom we license patents were the first to make the inventions claimed or were the first to file. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. 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, found unenforceable or invalidated, which could allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for commercial products or drug product candidates, prevent others from designing around our claims or provide us with a competitive advantage. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

We, independently or together with our licensors, have filed several patent applications covering various aspects of our commercial products, drug product candidates or technologies. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be challenged by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of our commercial products or any drug product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

We may not have sufficient patent terms to effectively protect our products and business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or otherwise provide us with a competitive advantage. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

While patent term extensions under the Hatch-Waxman Act in the United States and under supplementary protection certificates in Europe may be available to extend the patent exclusivity term for Bentrio™ and our drug product candidates, we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. In addition, upon issuance in the United States any patent term can be adjusted based on certain delays caused by the applicant(s) or the U.S. Patent and Trademark Office, or USPTO. For example, a patent term can be reduced based on certain delays caused by the patent applicant during patent prosecution.

While in the United States there is a possibility of obtaining market protection independent from any patent protection for up to 3 and 5 years from approval, and in the European Union one may obtain data exclusivity of eight years from approval with an additional two years of market exclusivity (which can potentially be extended by one year), there is no assurance that we can obtain such data exclusivity and market protection with respect to Bentrio™, AM-125, AM-401 , or any of our other drug product candidates. Our issued patents and pending patent applications are expected to expire for AM-125 in 2038, for AM-401 in 2034 and for Bentrio™ in 2040, prior to any patent term extensions to which we may be entitled under applicable laws.

If we are unable to maintain effective proprietary rights for our technologies, commercial products, drug product candidates or any future drug product candidates, we may not be able to compete effectively in our markets.

In addition to the protection afforded by patents, we rely on trade secret protection 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 product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. Moreover, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors, and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating such trade secrets. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, financial condition and results of operations.

Third-party claims of intellectual property infringement may expose us to substantial liability or prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our commercial products or drug product candidates and use our proprietary technology without alleged or actual infringement, misappropriation, or other violation of the patents and proprietary rights of third parties. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, and reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S.- and foreign-issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are marketing commercial products or developing drug product candidates. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our commercial products and drug product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture, or methods of treatment related to the use or manufacture of our commercial products or drug product candidates. Although we generally conduct certain freedom to operate search and review with respect to our product candidates, we cannot guarantee that any of our search and review is complete and thorough, nor can we be sure that we have identified each and every patent and pending application in the United States and abroad that is relevant or necessary to the commercialization of our commercial products or drug product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our commercial products or drug product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our commercial products or drug product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to continue commercialization of such commercial product or to commercialize such drug product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture, or methods of use, the holders of any such patents may be able to block our ability to continue the commercialization of our commercial products or to develop and commercialize the applicable drug product candidate unless we obtained a license or until such patent expires or is finally determined to be invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further commercialize our commercial products or develop and commercialize one or more of our drug product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

Additional competitors could enter the market with generic versions of our products, which may result in a material decline in sales of affected products.

Under the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA under section 505(b)(2) that references the FDA's prior approval of the innovator product. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. Hatch-Waxman also provides for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and reviewing) of an ANDA, or 505(b)(2) NDA. These include, subject to certain exceptions, the period during which an FDA-approved drug is subject to orphan drug exclusivity. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the "Orange Book." If there are patents listed in the Orange Book, a generic or 505(b)(2) applicant that seeks to market its product before expiration of the patents must include in the ANDA what is known as a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to protect its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if AM-125 and AM-401 are approved, competitors could file ANDAs for generic versions of AM-125 and AM-401, or 505(b)(2) NDAs that reference AM-125 and AM-401, respectively. If there are patents listed for AM-125 and AM-401 in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict whether any patents issuing from our pending patent applications will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for drug products and technologies we develop or license. Moreover, if any patents that are granted and listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected drug product could immediately face generic competition and its sales would likely decline rapidly and materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected drug product and our results of operations and cash flows could be materially and adversely affected.

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

If we fail to comply with the obligations in our Exclusive License Agreement with WU, , we could lose intellectual property rights that are important to our AM-401 drug product candidate and further potential drug product candidates.

Our Exclusive License Agreement with WU imposes various development, milestone payment, royalty, and other obligations on us. If we fail to comply with our obligations under the agreement and fail to cure such breach, or we are subject to a bankruptcy, WU has the right to terminate the agreement, in which event we would not be able to develop or market AM-401 or any future drug product candidates covered by the license.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming, and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter such infringement, we may be required to file claims against those competitors, which can be expensive and time-consuming. If we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering one of our commercial products or drug product candidates, the defendant could counterclaim that the patent covering our commercial product or drug product candidate is invalid, overbroad and/or unenforceable, or that we infringe the defendant's patents. In patent litigation in the United States, defendant counterclaims alleging invalidity, overbreadth and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. A court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop a third party from using the technology in question on the grounds that our patents do not cover that technology. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly, which could adversely affect us.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue the commercial roll-out of Bentrio™, our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our drug product candidates to market. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common shares.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

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

Our reliance on our advisors, employees and third parties requires us to share our intellectual property and trade secrets, which increases the possibility that a competitor will discover them or that our intellectual property will be misappropriated or disclosed.

Because we rely on our advisors, employees and third-party contractors and consultants to research and develop and to manufacture our commercial products and drug product candidates, we must, at times, share our intellectual property with them. We seek to protect our intellectual property and other proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of these advisors, employees and third parties to use or disclose our confidential information, including our intellectual property and trade secrets. Despite the contractual provisions employed when working with these advisors, employees and third parties, the need to share intellectual property and other confidential information increases the risk that such confidential information becomes known by our competitors, are inadvertently incorporated into the product development of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how, intellectual property and trade secrets, a competitor's discovery of our intellectual property or trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our intellectual property, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with in the future may expect to be granted rights to publish data arising out of such collaboration, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. In the future, we may also conduct joint research and development programs that may require us to share intellectual property under the terms of our research and development or similar agreements. Despite our efforts to protect our intellectual property, our competitors may discover our trade secrets or know how, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our intellectual property would impair our competitive position and have an adverse impact on our business.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our drug product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our ownership of our patents or other intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

Filing, prosecuting, and defending patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. As part of ordinary course prosecution and maintenance activities, we determine whether to seek patent protection outside the U.S. and in which countries. This also applies to patents we have acquired or in-licensed from third parties. In some cases this means that we, or our predecessors in interest or licensors of patents within our portfolio, have sought patent protection in a limited number of countries for patents covering our product candidates. Competitors may use our technologies in jurisdictions where we have not obtained or are unable to adequately enforce patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents, the reproduction of our manufacturing or other know-how or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks Related to Employee Matters and Managing Growth

Our future growth and ability to compete depends on retaining our key personnel and recruiting additional qualified personnel.

Our success depends upon the continued contributions of our key management, scientific and technical personnel, many of whom have substantial experience with or been instrumental for us and our projects. Key management includes our executive officers Thomas Meyer, our founder, Chairman and Chief Executive Officer, Samuel Wickline, Trasir's founder and our Chief Scientific Officer for RNA therapeutics, and Marcel Gremaud, Chief Financial Officer, who constitute the Executive Management Committee. Marcel Gremaud has been working as a consultant for our Company since 2013; he replaced as Chief Financial Officer Elmar Schärli, who continues to manage certain of our finance and treasury activities.

As we have been expanding our activities in the field of RNA therapeutics and started commercial operations with Bentrio™, we have been doubling our headcount through the hiring of experienced staff. The new hires include a Chief Development Officer for our activities in RNA therapeutics and a head of our newly created "OTC Consumer Health" business unit for our Bentrio™ related activities. Both of them will join our Company in 2022.

All our staff are engaged in project management or general management, and we do not have any inhouse laboratories or manufacturing facilities. During the COVID-19 pandemic, all our staff worked for several time periods remotely in accordance with Swiss public health regulations or by voluntary Company decision. Overall, the remote work did not have any significant impact on our ability to manage projects or processes effectively.

The loss of key managers and senior scientists could delay our research and development activities. Laws and regulations on executive compensation, including legislation in Switzerland, may restrict our ability to attract, motivate and retain the required level of qualified personnel. In addition, the competition for qualified personnel in the biopharmaceutical and pharmaceutical field is intense, and our future success depends upon our ability to attract, retain and motivate highly skilled scientific, technical and managerial employees. We face competition for personnel from other companies, universities, public and private research institutions and other organizations. If our recruitment and retention efforts are unsuccessful in the future, it may be difficult for us to implement business strategy, which could have a material adverse effect on our business.

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

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of sales and marketing, and to a lesser extent, drug development and regulatory affairs. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Our Common Shares

The price of our common shares may be volatile and may fluctuate due to factors beyond our control.

The share price of publicly traded emerging biopharmaceutical and drug discovery and development companies has been highly volatile and is likely to remain highly volatile in the future. For example, during the last year, our common shares have traded as high as $6.25 in March 2021 and as low as $1.21 in December 2021. The market price of our common shares may fluctuate significantly in the future due to a variety of factors, including:

- delays in the commercial roll out of Bentrio™;
- positive or negative results of testing and clinical trials by us, strategic partners, or competitors;
- delays in executing on our plans to reposition the Company around RNA therapeutics and / or to divest or spin off our business in neurotology, rhinology and allergology;
- technological innovations or commercial product introductions by us or competitors;
- changes in government regulations;
- developments concerning proprietary rights, including patents and litigation matters;
- public concern relating to the commercial value or safety of any of our product candidates;
- financing or other corporate transactions;

- publication of research reports or comments by securities or industry analysts;
- general market conditions in the pharmaceutical industry or in the economy as a whole;
- our ability to maintain the listing of our common shares on Nasdaq; or
- other events and factors beyond our control.

Additionally, these factors may affect the liquidity of our common shares, which may hurt your ability to sell our common shares in the future. In addition, the stock market in general has recently experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of individual companies. Broad market and industry factors may materially affect the market price of companies' stock, including ours, regardless of actual operating performance.

Our common shares may be involuntarily delisted from trading on The Nasdaq Capital Market if we fail to comply with the continued listing requirements. A delisting of our common shares is likely to reduce the liquidity of our common shares and may inhibit or preclude our ability to raise additional financing.

We are required to comply with certain Nasdaq continued listing requirements, including a series of financial tests relating to shareholder equity, market value of listed securities and number of market makers and shareholders. If we fail to maintain compliance with any of those requirements, our common shares could be delisted from The Nasdaq Capital Market.

In 2017, 2019 and 2020, we failed to maintain compliance with the minimum bid price requirement. To address that non-compliance, on March 13, 2018, we effected the Merger, pursuant to which we effected a "reverse share split" at a ratio of 10-for-1, and on May 1, 2019, we effected a "reverse share split" at a ratio of 20-for-1. In 2020, we regained compliance as our share price increased. Additionally, on January 11, 2018, we received a letter from Nasdaq indicating that we were not in compliance with Nasdaq's market value of listed securities requirement. As a result of the July 2018 Registered Offering, we resolved the non-compliance with the market value of listed securities requirement by complying with Nasdaq's minimum equity standard. However, there can be no assurance that we will be able to successfully maintain compliance with the several Nasdaq continued listing requirements.

If, for any reason, Nasdaq should delist our common shares from trading on its exchange and we are unable to obtain listing on another national securities exchange or take action to restore our compliance with the Nasdaq continued listing requirements, a reduction in some or all of the following may occur, each of which could have a material adverse effect on our shareholders:

- the liquidity of our common shares;
- the market price of our common shares;
- our ability to obtain financing for the continuation of our operations;
- the number of institutional and general investors that will consider investing in our common shares;
- the number of investors in general that will consider investing in our common shares;
- the number of market makers in our common shares;
- the availability of information concerning the trading prices and volume of our common shares; and
- the number of broker-dealers willing to execute trades in shares of our common shares.

Moreover, delisting may make unavailable a tax election that could affect the U.S. federal income tax treatment of holding, and disposing of, our common shares. See "Taxation—Material U.S. Federal Income Tax Considerations for U.S. Holders" below.

In the event that our common shares are delisted from Nasdaq, U.S. broker-dealers may be discouraged from effecting transactions in shares of our common shares because they may be considered penny stocks and thus be subject to the penny stock rules.

On February 6, 2019, we received a letter from Nasdaq stating that due to our continued non-compliance with the minimum $1.00 bid price requirement, our common shares were subject to delisting unless we timely requested a hearing before the Nasdaq Hearings Panel. We timely requested such a hearing on February 8, 2019, which request has stayed any delisting or suspension action by Nasdaq pending the hearing and the expiration of any additional extension period granted following the hearing. On May 20, 2019, we announced that the Nasdaq Hearings Panel notified us in a letter that we had regained compliance with the minimum bid price requirement under Nasdaq Listing Rule 5550(a)(2). The Nasdaq Hearings Panel further determined that we were in compliance with all applicable Nasdaq listing standards.

The SEC has adopted a number of rules to regulate "penny stock" that restrict transactions involving stock which is deemed to be penny stock. Such rules include Rules 3a51-1, 15g-1, 15g-2, 15g-3, 15g-4, 15g-5, 15g-6, 15g-7, and 15g-9 under the Securities Exchange Act of 1934 (the "Exchange Act"). These rules may have the effect of reducing the liquidity of penny stocks. "Penny stocks" generally are equity securities with a price of less than $5.00 per share (other than securities registered on certain national securities exchanges or quoted on the Nasdaq Stock Market if current price and volume information with respect to transactions in such securities is provided by the exchange or system). Our common shares have in the past constituted, and may again in the future constitute, "penny stock" within the meaning of the rules. The additional sales practice and disclosure requirements imposed upon U.S. broker-dealers may discourage such broker-dealers from effecting transactions in our common shares, which could severely limit the market liquidity of such common shares and impede their sale in the secondary market.

A U.S. broker-dealer selling penny stock to anyone other than an established customer or "accredited investor" (generally, an individual with net worth in excess of $1,000,000 or an annual income exceeding $200,000, or $300,000 together with his or her spouse) must make a special suitability determination for the purchaser and must receive the purchaser's written consent to the transaction prior to sale, unless the broker-dealer or the transaction is otherwise exempt. In addition, the "penny stock" regulations require the U.S. broker-dealer to deliver, prior to any transaction involving a "penny stock", a disclosure schedule prepared in accordance with SEC standards relating to the "penny stock" market, unless the broker-dealer or the transaction is otherwise exempt. A U.S. broker-dealer is also required to disclose commissions payable to the U.S. broker-dealer and the registered representative and current quotations for the securities. Finally, a U.S. broker-dealer is required to submit monthly statements disclosing recent price information with respect to the "penny stock" held in a customer's account and information with respect to the limited market in "penny stocks."

Shareholders should be aware that, according to the SEC, the market for "penny stocks" has suffered in recent years from patterns of fraud and abuse. Such patterns include (i) control of the market for the security by one or a few broker-dealers that are often related to the promoter or issuer; (ii) manipulation of prices through prearranged matching of purchases and sales and false and misleading press releases; (iii) "boiler room" practices involving high-pressure sales tactics and unrealistic price projections by inexperienced sales persons; (iv) excessive and undisclosed bid-ask differentials and markups by selling broker-dealers; and (v) the wholesale dumping of the same securities by promoters and broker-dealers after prices have been manipulated to a desired level, resulting in investor losses. Our management is aware of the abuses that have occurred historically in the penny stock market. Although we do not expect to be in a position to dictate the behavior of the market or of broker-dealers who participate in the market, management will strive within the confines of practical limitations to prevent the described patterns from being established with respect to our securities.

Certain principal shareholders and members of our executive team and board of directors own a significant portion of our common shares and as a result will be able to exercise significant control over us, and your interests may conflict with the interests of such shareholders.

Certain principal shareholders and their affiliated entities as well as members of our executive team and board of directors own approximately 9.5% of our common shares. Depending on the level of attendance at our general meetings of shareholders, these shareholders may be in a position to determine the outcome of decisions taken at any such general meeting. Any shareholder or group of shareholders controlling more than 50% of the shares represented at our general meetings of shareholders may control any shareholder resolution requiring an absolute majority of the shares represented, including the election of members to the board of directors of the Company, certain decisions relating to our capital structure, the approval of certain significant corporate transactions and certain amendments to our bye-laws (the "Bye-laws"). To the extent that the interests of these shareholders may differ from the interests of the Company's other shareholders, the latter may be disadvantaged by any action that these shareholders may seek to pursue. Among other consequences, this concentration of ownership may have the effect of delaying or preventing a change in control and might therefore negatively affect the market price of our common shares.

Future sales, or the possibility of future sales, of a substantial number of our common shares could adversely affect the price of our common shares.

Future sales of a substantial number of our common shares, or the perception that such sales will occur, could cause a decline in the market price of our common shares. Approximately 11.4% of our common shares issued and outstanding are held by affiliates. If these shareholders sell substantial amounts of common shares in the public market, or the market perceives that such sales may occur, the market price of our common shares and our ability to raise capital through an issue of equity securities could be adversely affected. Additionally, as of the date of this Annual Report we have warrants outstanding, which are exercisable for an aggregate of 246,102 common shares at a weighted average exercise price of $59.85 per share, an equity commitment to sell up to $8.5 million of additional common shares to Lincoln Park Capital Fund, LLC ("LPC") pursuant to the commitment purchase agreement we entered into on April 23, 2020 with LPC (the "LPC Purchase Agreement") and an at-the-market offering program pursuant to the sales agreement we entered into with A.G.P./Alliance Global Partners ("A.G.P.") on November 30, 2018, as amended on April 5, 2019 (the "A.G.P. Sales Agreement") for sales of up to $18.3 million of additional common shares. We have also filed registration statements to register the resale of the common shares underlying the warrants that we have offered and sold in unregistered transactions, the common shares that are sold to LPC and the common shares and other equity securities that we have issued under our prior equity incentive plans or may issue under our new omnibus equity compensation plan. These common shares may be freely sold in the public market upon issuance, subject to certain limitations applicable to affiliates. In addition, we have filed a registration statement covering the issuance and sale by us of up to $79 million of common shares, debt securities, warrants, purchase contracts, units and common shares. We may issue such securities, including our common shares and warrants to purchase common shares, at any time and from time to time subject to the limitations set forth in General Instruction I.B.5 of Form F-3. If a large number of our common shares and/or warrants to purchase common shares are sold in the public market, the sales could reduce the trading price of our common shares and impede our ability to raise future capital.

We do not expect to pay dividends in the foreseeable future.

We have not paid any dividends since our incorporation. Even if future operations lead to significant levels of distributable profits, we currently intend that any earnings will be reinvested in our business and that dividends will not be paid until we have an established revenue stream to support continuing dividends. The proposal to pay future dividends to shareholders will in addition effectively be at the discretion of our board of directors after taking into account various factors including our business prospects, cash requirements, financial performance and new product development. In addition, payment of future dividends is subject to certain limitations pursuant to Bermuda law or by our Bye-laws. We are subject to Bermuda law restrictions on the payment of dividends including that no dividends may be declared by our board of directors or paid by the Company if there are reasonable grounds for believing that: (i) we are, or would after the payment be, unable to pay our liabilities as they become due; or (ii) that the realizable value of our assets would thereby be less than our liabilities. Accordingly, investors cannot rely on dividend income from our common shares and any returns on an investment in our common shares will likely depend entirely upon any future appreciation in the price of our common shares.

If we are or become classified as a passive foreign investment company ("PFIC"), our U.S. shareholders may suffer adverse tax consequences as a result.

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

Based upon our current and projected income and assets, and projections as to the value of our assets, we do not anticipate that we will be a PFIC for the 2022 taxable year or the foreseeable future. However, no assurance can be given in this regard because the determination of whether we will be or become a PFIC is a factual determination made annually that will depend, in part, upon the composition of our income and assets, and we have not and will not obtain an opinion of counsel regarding our classification as a PFIC. Fluctuations in the market price of our common shares may cause us to be classified as a PFIC in any taxable year because the value of our assets for purposes of the asset test, including the value of our goodwill and unbooked intangibles, may be determined by reference to the market price of our common shares from time to time (which may be volatile). If our market capitalization subsequently declines, we may be or become classified as a PFIC for the 2022 taxable year or future taxable years. Furthermore, the composition of our income and assets may also be affected by how, and how quickly, we use our liquid assets and any future fundraising activity. Under circumstances where our revenues from activities that produce passive income significantly increases relative to our revenues from activities that produce non-passive income, or where we determine not to deploy significant amounts of cash for active purposes, our risk of becoming classified as a PFIC may substantially increase. It is also possible that the Internal Revenue Service (the "IRS") may challenge the classification or valuation of our Company's assets, including its goodwill and other unbooked intangibles, or the classification of certain amounts received by our Company, which may result in our Company being, or becoming classified as, a PFIC for the 2022 taxable year or future taxable years. Accordingly, there can be no assurance that we will not be a PFIC in the current or for any future taxable year and U.S. investors should invest in our common shares only if they are willing to bear the U.S. federal income tax consequences associated with investments in PFICs.

If we were a PFIC for any taxable year during which a U.S. investor held our common shares, certain adverse U.S. federal income tax consequences could apply to the U.S. Holder. See "Taxation—Material U.S. Federal Income Tax Considerations for U.S. Holders."

We are a holding company with no material direct operations.

We are a holding company with no material direct operations. As a result, we would be dependent on dividends, other payments or loans from our subsidiaries in order to pay a dividend. Our subsidiaries are subject to legal requirements of their respective jurisdictions of organization that may restrict their paying dividends or other payments, or making loans, to us.

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

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

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

We are a foreign private issuer. As a result, in accordance with Nasdaq Listing Rule 5615(a)(3), we comply with home country governance requirements and certain exemptions thereunder rather than complying with certain of the corporate governance requirements of Nasdaq.

Bermuda law does not require that a majority of our board of directors consists of independent directors. Our board of directors therefore may include fewer independent directors than would be required if we were subject to Nasdaq Listing Rule 5605(b)(1). In addition, we are not subject to Nasdaq Listing Rule 5605(b)(2), which requires that independent directors regularly have scheduled meetings at which only independent directors are present.

Bermuda law does not require that we disclose information regarding third-party compensation of our directors or director nominee. As a result, our practice varies from the third-party compensation disclosure requirements of Nasdaq Listing Rule 5250(b)(3). We follow the requirements of Bermuda law with respect to our compensation committee, disclosure of compensation of our directors and executive officers and information regarding third-party compensation of our directors or director nominee, each of which differ from the requirements of the Nasdaq Listing Rules.

In addition, as permitted by Bermuda law, we have opted not to implement a standalone nominating committee. To this extent, our practice varies from the independent director oversight of director nominations requirements of Nasdaq Listing Rule 5605(e).

The quorum for a general meeting of shareholders is as set out in our Bye-laws, which provides for a quorum of two or more persons present at the start of the meeting and representing in person or by proxy issued and outstanding voting shares in the company. Our practice thus varies from the requirement of Nasdaq Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting stock. We must provide shareholders with an agenda and other relevant documents for the general meeting of shareholders. However, Bermuda law has no regulatory regime for the solicitation of proxies, thus our practice varies from the requirement of Nasdaq Listing Rule 5620(b), which sets forth certain requirements regarding the solicitation of proxies. In addition, we have opted out of shareholder approval requirements for the issuance of securities in connection with certain events such as the acquisition of stock or assets of another company, the establishment of or amendments to equity-based compensation plans for employees, a change of control of us and certain private placements. To this extent, our practice varies from the requirements of Nasdaq Listing Rule 5635, which generally requires an issuer to obtain shareholder approval for the issuance of securities in connection with such events.

As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

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

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

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

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act of 2002, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also subject us to regulatory scrutiny and sanctions, impair our ability to raise revenue and cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common shares.

We are required to disclose changes made in our internal controls and procedures, and our management is required to assess the effectiveness of these controls annually. However, for as long as we are a "non-accelerated filer" under Securities and Exchange Commission rules, our independent registered public accounting firm is not required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. An independent assessment of the effectiveness of our internal controls could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, the price of our common shares and our trading volume could decline.

The trading market for our common shares depends in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. We cannot assure you that analysts will cover us or provide favorable coverage. If one or more of the analysts who cover us downgrade our common shares or publish inaccurate or unfavorable research about our business, the price of our common shares would likely decline. If one or more of these analysts cease coverage of the Company or fail to publish reports on us regularly, demand for our common shares could decrease, which might cause the price of our common shares and trading volume to decline.

As a Bermuda company, it may be difficult for you to enforce judgments against us or our directors and executive officers.

We are a Bermuda exempted company. As a result, the rights of holders of our common shares are governed by Bermuda law and our memorandum of continuance (the "Memorandum of Continuance") and Bye-laws. The rights of shareholders under Bermuda law may differ from the rights of shareholders of companies incorporated in other jurisdictions. Many of our directors referred to in this Annual Report are not residents of the United States, and a substantial portion of our assets are located outside the United States. As a result, it may be difficult for investors to effect service of process on those persons in the United States or to enforce in the United States judgments obtained in U.S. courts against us or those persons based on the civil liability provisions of the U.S. securities laws. It is doubtful whether courts in Bermuda will enforce judgments obtained in other jurisdictions, including the United States, against us or our directors or officers under the securities laws of those jurisdictions or entertain actions in Bermuda against us or our directors or officers under the securities laws of other jurisdictions.

Bermuda law differs from the laws in effect in the United States and may afford less protection to holders of our common shares.

We are subject to the laws of Bermuda. As a result, our corporate affairs are governed by the Companies Act 1981 of Bermuda (the "Companies Act"), which differs in some material respects from laws typically applicable to U.S. corporations and shareholders, including the provisions relating to interested directors, amalgamations, mergers and acquisitions, takeovers, shareholder lawsuits and indemnification of directors. Generally, the duties of directors and officers of a Bermuda company are owed to the company only. Shareholders of Bermuda companies typically do not have rights to take action against directors or officers of the company and may only do so in limited circumstances. Class actions are not available under Bermuda law. The circumstances in which derivative actions may be available under Bermuda law are substantially more proscribed and less clear than they would be to shareholders of U.S. corporations. The Bermuda courts, however, would ordinarily be expected to permit a shareholder to commence an action in the name of a company to remedy a wrong to the company where the act complained of is alleged to be beyond the corporate power of the company or illegal, or would result in the violation of the company's memorandum of association (or memorandum of continuance) or bye-laws. Furthermore, consideration would be given by a Bermuda court to acts that are alleged to constitute a fraud against the minority shareholders or, for instance, where an act requires the approval of a greater percentage of the company's shareholders than that which actually approved it.

When the affairs of a company are being conducted in a manner that is oppressive or prejudicial to the interests of some shareholders, one or more shareholders may apply to the Supreme Court of Bermuda, which may make such order as it sees fit, including an order regulating the conduct of the company's affairs in the future or ordering the purchase of the shares of any shareholders by other shareholders or by the company. Additionally, under our Bye-laws and as permitted by Bermuda law, each shareholder has waived any claim or right of action against our directors or officers for any action taken by directors or officers in the performance of their duties, except for actions involving fraud or dishonesty. In addition, the rights of holders of our common shares and the fiduciary responsibilities of our directors under Bermuda law are not as clearly established as under statutes or judicial precedent in existence in jurisdictions in the United States, particularly the State of Delaware. Therefore, holders of our common shares may have more difficulty protecting their interests than would shareholders of a corporation incorporated in a jurisdiction within the United States.

Our Bye-laws restrict shareholders from bringing legal action against our officers and directors.

Our Bye-laws contain a broad waiver by our shareholders of any claim or right of action, both individually and on our behalf, against any of our officers or directors. The waiver applies to any action taken by an officer or director, or the failure of an officer or director to take any action, in the performance of his or her duties, except with respect to any matter involving any fraud or dishonesty on the part of the officer or director. This waiver limits the right of shareholders to assert claims against our officers and directors unless the act or failure to act involves fraud or dishonesty.

We have anti-takeover provisions in our Bye-laws that may discourage a change of control.

Our Bye-laws contain provisions that could make it more difficult for a third party to acquire us without the consent of our board of directors. These provisions provide for:

- directors only to be removed for cause;
- restrictions on the time period in which directors may be nominated;
- our board of directors to determine the powers, preferences and rights of our preference shares and to issue the preference shares without shareholder approval; and
- an affirmative vote of 66 2/3% of our voting shares for certain "business combination" transactions which have not been approved by our board of directors.

These provisions could make it more difficult for a third party to acquire us, even if the third party's offer may be considered beneficial by many shareholders. As a result, shareholders may be limited in their ability to obtain a premium for their shares.

Legislation enacted in Bermuda as to economic substance may affect our operations.

Pursuant to the Economic Substance Act 2018 (as amended) of Bermuda (the "ES Act") that came into force on January 1, 2019, a registered entity other than an entity which is resident for tax purposes in certain jurisdictions outside Bermuda ("non-resident entity") that carries on as a business any one or more of the "relevant activities" referred to in the ES Act must comply with economic substance requirements. The ES Act may require in-scope Bermuda entities which are engaged in such "relevant activities" to be directed and managed in Bermuda, have an adequate level of qualified employees in Bermuda, incur an adequate level of annual expenditure in Bermuda, maintain physical offices and premises in Bermuda or perform core income-generating activities in Bermuda. The list of "relevant activities" includes carrying on any one or more of the following activities: banking, insurance, fund management, financing, leasing, headquarters, shipping, distribution and service center, intellectual property and holding entities. The ES Act could affect the manner in which Altamira Therapeutics operates its business, which could adversely affect its business, financial condition and results of operations.

Although it is presently anticipated that the ES Act will have no material impact on Altamira Therapeutics or its operations, as the legislation is new and remains subject to further clarification and interpretation, it is not currently possible to ascertain the precise impact of the ES Act on Altamira Therapeutics.

ITEM 4. INFORMATION ON THE COMPANY

A. History and development of the Company

Overview

We are a biopharmaceutical company dedicated to developing therapeutics that address important unmet medical needs. For the most part since the formation of our Company, we have been focusing on the development of therapeutics for inner ear disorders: (i) Keyzilen® (AM-101) in acute inner ear tinnitus, (ii) Sonsuvi® (AM-111) in acute inner ear hearing loss and (iii) AM-125 in acute peripheral vertigo. We advanced Keyzilen® and Sonsuvi® to Phase 3 clinical trials, and we are currently in Phase 2 clinical development with AM-125. In 2021 we launched Bentrio™, a drug free medical device for protection against airborne allergens and viruses in selected European markets. Further, through the acquisition of Trasir Therapeutics ("Trasir") in 2021, we entered the field of RNA delivery. In this context, we announced our intention to reposition the Company around RNA therapeutics with AM-401 for the treatment of KRAS driven cancers being our first project, and to divest or spin off our non-RNA businesses, which are our assets in neurotology, rhinology and allergology, including Bentrio™, AM-125, Keyzilen®, Sonsuvi® and certain early-stage drug product candidates.

AM-125

We are developing AM-125 for the intranasal treatment of acute peripheral vertigo. In February 2017 we entered into an asset purchase agreement with Otifex, pursuant to which we have purchased various assets related to betahistine dihydrochloride in a spray formulation. The assets include preclinical and clinical data as well as certain intellectual property rights. In a Phase 1 clinical trial conducted by Otifex in 40 healthy volunteers intranasal betahistine showed good tolerability and significantly higher betahistine concentrations in blood plasma than reported for oral betahistine administration.

In 2018, we conducted a second Phase 1 clinical trial with AM-125 in 72 healthy volunteers. The randomized double blind placebo controlled trial demonstrated superior bioavailability over a range of four intranasal betahistine doses compared to oral betahistine, with plasma exposure being 5 to 29 times higher (unadjusted for dose; p-value between 0.056 and $p < 0.0001$). Further, it confirmed the favorable safety profile of intranasal betahistine and showed that the treatment was well tolerated when administered three times daily for three days. Single doses were escalated up to 60 mg, and repeated doses up to 40 mg. For the latter, the maximum tolerated dose based on local tolerability was determined at 40 mg.

In July 2019, we started enrollment into a randomized placebo-controlled Phase 2 clinical study with AM-125. The "TRAVERS" Phase 2 trial is expected to enroll 118 patients suffering from acute vertigo following neurosurgery (for surgical removal of a vestibular schwannoma, a tumor growing behind the inner ear, resection of the vestibular nerve, which is called vestibular neurectomy, or surgical removal of parts of the inner ear, which is called labyrinthectomy). Starting three days after neurosurgery, trial participants self-administer AM-125 or placebo 3 x daily for four weeks; they are then followed for a further two weeks. The trial is being conducted in several countries ex US.

In September 2020 we announced the results of an interim analysis from Part A of the trial, which comprised a dose escalation – 1, 10 or 20 mg or placebo – in 33 patients. The interim analysis showed a dose-dependent improvement in balance as well as good safety and tolerability of ascending doses of AM-125. At the highest dose of 20 mg (3 x daily), AM-125-treated patients improved their performance of the "Tandem Romberg" and the "Standing on Foam" balance tests from baseline to 14 days post-surgery (primary endpoint) on average 1.9 to 2.4 times more than placebo-treated patients (6.0 vs. 3.1 and 10.5 vs. 4.3 seconds, respectively). In contrast to placebo, the improvement from baseline was statistically significant for AM-125 20 mg and for all active dose groups, respectively ($p<0.02$ and $p<0.01$ to $p<0.05$, respectively). These positive results were supported by similar improvements in additional efficacy measures, including additional objective as well as clinician- and patient-reported outcomes.

Based on the results from the interim analysis, we selected the two highest doses, 10 and 20 mg, for testing against placebo in 72 patients in Part B of the trial. As we remained blinded to treatment allocation during the interim analysis, the corresponding data from Part A will be pooled with those from Part B. Prior to starting Part B of the trial in October 2020, we tested oral betahistine (48 mg) open label for reference purposes.

Enrollment into TRAVERS has been impacted by the COVID-19 pandemic, as the type of neurosurgery required for participation in the trial is classified as an elective procedure and hence was postponed and as many participating sites temporarily reduced or suspended clinical research activities. The effect was particularly felt in the spring of 2020 and then again in early 2021. In February 2022 we announced the completion of enrollment into TRAVERS. We expect to obtain top-line results in the second quarter of 2022.

We have discussed the regulatory requirements for AM-125 during a pre-Investigational New Drug ("IND") meeting with the FDA and in the context of scientific advice meetings with the EMA and two European national health authorities to further define the development program. We expect to have further exchanges with regulatory agencies following conclusion of the TRAVERS trial, upon which we aim to obtain an IND. We expect to initiate a Phase 3 clinical trial with AM-125 in acute peripheral vertigo in late 2022. We believe that, if approved, AM-125 could become the first betahistine product for the treatment of acute peripheral vertigo in the United States. We are currently evaluating the feasibility of a clinical study with AM-125 in central vertigo, which may lead to the initiation of a Phase 2 trial later in 2022.

Under product code AM-201, we evaluated intranasal betahistine also for its potential use in the prevention of antipsychotic induced weight gain and drowsiness. In 2019, we initiated a Phase 1b trial in Europe to evaluate AM-201's safety and therapeutic effects in this indication. Participants received either AM-201 (1, 2.5, 5, 10, 20 or 30 mg) or placebo in parallel with oral olanzapine (10 mg) once a day for four weeks. In May 2020, we announced that at AM-201 30 mg, the mean weight gain from baseline to the end of the treatment period was 2.8 kg compared against 3.7 kg in control subjects; the primary efficacy endpoint of mean reduction in weight gain was 0.9 kg and statistically significant ($p<0.02$; n=81 with pre-specified Bayesian augmented controls). In the context of our strategic repositioning, we have decided to deprioritize project AM-201 and suspended all development work.

Bentrio™ (AM-301)

In September 2020 we announced the launch of the development of Bentrio™ (AM-301), a drug-free nasal spray for protection against airborne viruses and allergens through a newly created subsidiary, Altamira Medica Ltd. Bentrio™, which is now being commercialized in Germany and other European countries under the CE mark as an "over the counter" product under the brand name Bentrio™, is a gel emulsion which works by forming a protective layer on the nasal mucosa that acts as a mechanical barrier against airborne viruses allergens. The barrier consists of two elements: (1) a mucoadhesive film lining the nasal cavity and preventing contact of airborne viruses or allergens with the nasal mucosa to reduce the risk of viral infection or allergic reactions; (2) the trapping / binding of such viruses or allergens through electrostatic effects, allowing for their removal e.g. through mucociliary clearance. In addition, the product helps to humidify and thus maintain the nasal mucosa's function in clearing viruses and allergens from the nasal cavity. The key component of Bentrio™ is bentonite, a naturally occurring clay.

Following formulation development, we tested Bentrio™ *in vitro* in a series of experiments using reconstituted human nasal epithelia infected with SARS-CoV-2 or H1N1 influenza virus. Daily treatment with AM-301, beginning right before inoculation or 24-30 hours thereafter showed significant reductions of the viral titer compared to saline treated controls. In case of SARS-CoV-2, a protective effect was observed with the original virus, the Delta variant as well as the Omicron variant.

Based on these *in vitro* results, we believe that AM-301 could help to reduce the risks of exposure from airborne transmission of SARS-CoV-2. It is estimated that about 90% of air is inhaled via the nose, and it has been established that infection with SARS-CoV-2 via the nose is a major transmission pathway for COVID-19. In 2021 we prepared a randomized placebo-controlled clinical trial in acute COVID-19 ("COVAMID") for further confirmation of the protective effects of Bentrio™; due to the largely unpredictable waves of infection on one hand and varying regulatory timelines and requirements, the trial could start enrollment only in March 2022.

In 2021 we conducted an open-label randomized cross-over study with AM-301 that enrolled 36 patients with allergic rhinitis caused by grass pollen. Study participants were administered a single dose of Bentrio™ nasal spray or hydroxypropylmethylcellulose, a comparator product, prior to controlled pollen exposure for four hours in an allergen challenge chamber. The challenge was repeated with the alternate treatment following a wash-out period. The study demonstrated a rapid onset and long durability of Bentrio's protective effect, established substantial equivalence to the marketed comparator with superior efficacy ratings by patients and clinicians, and showed good tolerability.

We believe that Bentrio™ could provide help to people suffering from allergic rhinitis by reducing their exposure to airborne allergen particles e.g. from pollens, house dust or animal hair. For further clinical data, in December 2021 we initiated a randomized open-label trial with Bentrio™ and saline nasal spray as control in seasonal allergic rhinitis (SAR) and an open-label clinical trial with AM-301 in perennial allergic rhinitis (PAR) with controlled house dust mite exposure. We expect the PAR trial to read out in the second quarter of 2022 and the SAR trial in late 2022.

Since Bentrio™ does not contain any active substance, it is regulated and marketed as an "over-the-counter" medical device. In May 2021 we completed the conformity assessment procedure for marketing the product in the member states of the European Union (EU), and in September 2021 we filed a 510(k) premarket notification with the FDA, which is currently under review for the intended use of promoting alleviation of mild allergic symptoms triggered by the inhalation of various airborne allergens.

We intend to market Bentrio™ primarily through third parties. We already have entered into marketing and distribution agreements with several collaboration partners in Asia and Europe and intend to cover further markets in particular in Europe and North America.

AM-401

Through the acquisition of Trasir in June 2021 we entered the field of RNA therapeutics. Trasir's core technology is the proprietary peptide polyplex platform OligoPhore™ and its equivalent SemaPhore™ that can engage any type of short interfering RNA (siRNA) or messenger RNA (mRNA), respectively, in rapid self-assembly. The technology allows for safe and effective systemic delivery of RNA payloads with efficient cellular uptake and full endosomal release. Importantly, it enables delivery to target tissues outside the liver, creating the potential for developing RNA-based therapies for a range of indications with substantial unmet need.

In various murine models of disease, OligoPhore™ and SemaPhore™ have been shown to protect the RNA payload (siRNA and/or mRNA) from degradation in the circulation, while enabling pH-dependent nucleotide endosomal escape and cytoplasmic delivery. Proof-of-concept for efficient delivery and target knockdown has been demonstrated for targets in the NF-kB family, various members of the ETS transcription factor family, and targets in the JNK and TAM pathways, enabling a preclinical development pathway for several oncology indications, rare diseases, as well as rheumatoid and osteoarthritis and inflammatory pathologies such as atherosclerosis.

In July 2021 we announced the selection of KRAS-driven cancer as the first therapeutic indication for our OligoPhore™ oligonucleotide delivery platform. We aim to advance the AM-401 program through preclinical studies with the objective of filing for an NDA in 2023. In parallel, we will seek to leverage the OligoPhore™ / SemaPhore™ platform through collaborations with other biopharmaceutical companies and the out-licensing of technology for specific indications.

Keyzilen®

We have been developing Keyzilen®, Esketamine gel for injection, for the treatment of acute inner ear tinnitus. Esketamine is a potent, small molecule non-competitive NMDA receptor antagonist. Keyzilen® is formulated in a biocompatible gel and delivered via intratympanic injection. It demonstrated a favorable safety profile and positive effect on PROs associated with tinnitus in two Phase 2 clinical trials. In two Phase 3 clinical trials (TACTT2 and TACTT3), we were unable to confirm the efficacy of Keyzilen™ as both of them did not meet their primary efficacy endpoints. We believe we have identified two principal sources for the negative outcomes from the TACTT trials: (i) the high frequency of tinnitus loudness ratings over an extended period of time and (ii) an unexpectedly high level of variability in outcomes among study sites. A survey among a number of TACTT3 participants revealed that the daily capture of tinnitus loudness and annoyance caused a number of patients to excessively focus on their tinnitus symptoms. In addition, it was observed that a non-negligible number of study participants presumably became tired of the daily ratings after some time and stopped providing actual values. With respect to variability, our analysis subsequent to the unblinding of the trial data has shown positive outcomes at numerous sites, including many of the high enrolling study centers, but inconclusive or contradictory outcomes at other sites.

In April 2019, we announced that we had completed the design of a pivotal Phase 2/3 trial for Keyzilen®. The trial shall, in two stages, reaffirm the compound's efficacy in the treatment of acute tinnitus and provide confirmatory efficacy data to support a filing for marketing authorization. In September 2019, we announced that we have obtained advice on the development plan and regulatory pathway from the U.S. Food and Drug Administration ("FDA") in the context of a Type C meeting and from the European Medicines Agency ("EMA") in the context of a Scientific Advice procedure for Keyzilen®. In the context of our strategic repositioning, we aim to divest or spin off the Keyzilen® program.

Sonsuvi®

We also have been developing Sonsuvi® for acute inner ear hearing loss. In our Phase 2 clinical trial, AM-111 showed a favorable safety profile. Furthermore, in patients with severe to profound ASNHL, we observed a clinically relevant improvement in hearing threshold, speech discrimination and a higher rate of complete tinnitus remission compared with placebo. In November 2017, we announced that the HEALOS Phase 3 clinical trial that investigated Sonsuvi® in the treatment of acute inner ear hearing loss did not meet the primary efficacy endpoint. However, a post-hoc analysis of the subpopulation with profound acute hearing loss (PTA ≥ 90 dB at baseline in accordance with a commonly used classification of hearing loss severity) revealed a clinically meaningful and nominally significant improvement in the Sonsuvi® 0.4 mg/mL treatment group.

Based on the HEALOS results, we submitted the design of a new pivotal trial with AM-111 0.4 mg/mL in patients suffering from acute profound hearing loss to the EMA and subsequently also to the FDA for review. Through a Protocol Assistance procedure the EMA endorsed the proposed trial design, choice of efficacy and safety endpoints, as well as the statistical methodology. In a Type C meeting with written responses, the proposed choice of primary and secondary efficacy endpoints, the safety endpoints, as well as the planned sample size and statistical methodology were also endorsed by the FDA. In the context of our strategic repositioning, we aim to divest or spin off the Sonsuvi® program.

Trasir Acquisition

On June 1, 2021, the Company, Auris Medical Inc., an Illinois corporation and wholly owned subsidiary of the Company ("Subco"), Trasir Therapeutics, Inc., a Delaware corporation ("Trasir"), and each of the stockholders of Trasir (the "Trasir Stockholders") entered into an Agreement and Plan of Merger (the "Merger Agreement"). Pursuant to the Merger Agreement, the Company acquired Trasir through the merger of Subco with and into Trasir (the "Merger"), with Trasir surviving the merger as the surviving entity (the "Surviving Corporation"). The Merger closed on June 1, 2021. As a result of the Merger, the shares of common stock of Trasir immediately prior to the effective time of the Merger converted into the right to receive: (i) the applicable pro rata share of an aggregate of 764,370 common shares, calculated based on a value of $2,500,000 divided by the average closing price of the common shares on the 15 trading days preceding the closing date; (ii) contingent on the occurrence of positive results from a subsequent post-closing scientific study led by Trasir ("Positive Results"), the applicable pro rata share of $1,500,000 of common shares, to be calculated based on the average closing price of the common shares on the 15 trading days preceding the occurrence of Positive Results; and (iii) $210,000 for expenses (the "Trasir Stockholder Expenses") incurred in connection with the execution, delivery and performance of the Merger Agreement by certain Trasir Stockholders, paid partially in cash and partially in common shares based on the average closing price of the common shares on the 15 trading days preceding the closing date. In connection with the Merger, the Company also entered into an employment agreement with Dr. Samuel Wickline. Effective June 1, 2021, Dr. Wickline became the Chief Scientific Officer of the Company.

Capital expenditure and divestitures

Our actual capital expenditures for the years ended December 31, 2021, 2020 and 2019 amounted to CHF 6.7 million, CHF 2.3 million and CHF 3.2 million, respectively. Our capital expenditures primarily consist of intangible assets (capitalized expenditures) related to AM-125 (mainly in Switzerland and Australia) and the upfront and milestone payments related to the acquisition of Trasir.

Corporate information

We are an exempted company organized under the laws of Bermuda. We began our current operations in 2003. On April 22, 2014, we changed our name from Auris Medical AG to Auris Medical Holding AG and transferred our operational business to our newly incorporated subsidiary Auris Medical AG, which is now our main operating subsidiary. On March 13, 2018, we effected a corporate reorganization through the Merger into a newly formed holding company for the purpose of effecting the equivalent of a 10-1 "reverse share split." Following shareholder approval at an extraordinary general meeting of shareholders held on March 8, 2019 and upon the issuance of a certificate of continuance by the Registrar of Companies in Bermuda on March 18, 2019, the Company discontinued as a Swiss company and, pursuant to Article 163 of the Swiss Federal Act on Private International Law and pursuant to Section 132C of the Companies Act 1981 of Bermuda (the "Companies Act"), continued existence under the Companies Act as a Bermuda company with the name "Auris Medical Holding Ltd." (the "Redomestication"). By resolution of a Special General Meeting of Shareholders held on July 21, 2021 we adopted the new company name Altamira Therapeutics Ltd. Our registered office is located at Clarendon House, 2 Church Street, Hamilton HM11, Bermuda, telephone number +1 (441) 295 5950. We maintain a website at www.altamiratherapeutics.com where general information about us is available. Investors can obtain copies of our filings with the SEC from this site free of charge, as well as from the SEC website at www.sec.gov. We are not incorporating the contents of our website into this Annual Report.

B. Business overview

Strategy

Our goal is to become a leading biomedical company focused on developing and commercializing RNA therapeutics. We believe that the use of RNA therapeutics – be it siRNA, mRNA or other types – to control the expression of disease-relevant genes holds great promise. By engaging targets that are otherwise 'undruggable' by small molecules and proteins, whole new avenues are expected to open up with RNA therapeutics for treating intractable diseases. However, delivering RNA therapeutics into the right cell of the right tissue has been one of the key challenges preventing their more widespread adoption so far.

So far, most RNA therapeutics have been directed at the liver using delivery platforms based on lipid nanoparticles or GalNAc, an amino sugar derivative of galactose. In contrast, delivery to non-liver (that is extrahepatic) tissues has been largely elusive so far. Our proprietary peptide polyplex platform OligoPhore™ and its equivalent SemaPhore™ can engage any type of short interfering RNA (siRNA) or messenger RNA (mRNA), respectively, in rapid self-assembly. The technology allows for safe and effective systemic delivery of RNA payloads with efficient cellular uptake and full endosomal release. Importantly, it enables delivery to target tissues outside the liver, creating the potential for developing RNA-based therapies for a range of indications with substantial unmet need.

The key elements of our strategy are:

- **Demonstrate preclinical and clinical proof of concept with OligoPhore™ in KRAS driven cancer as first indication.** Based on positive results obtained with Oligophore™ delivering various siRNA payloads in more than ten different murine disease models, we have selected KRAS driven cancer as the first indication in which we will seek to demonstrate clinical proof of concept.

- **Leverage OligoPhore™ / SemaPhore™ platform through partnering.** Considering the suitability of our peptide polyplex platform for multiple therapeutic indications especially in oncology and immune diseases but also elsewhere, and for various types of therapeutics nucleotides, we aim to leverage it through collaborations with other biopharmaceutical companies and the out-licensing of technology for specific indications. In this way, we intend to become a delivery platform company.

- **Focus activities on RNA therapeutics by divesting or spinning off our non-RNA businesses.** As we aim to expand our activities in RNA therapeutics, we intend to dedicate our full resources and management focus on them. Although we continue to believe that our businesses in neurotology, rhinology and allergology hold great promise, we consider that the related assets should be rather developed outside our Company. Any proceeds from their divestiture or spin-off shall be applied to growing the activities in RNA therapeutics.

Delivering RNA therapeutics to extrahepatic tissues

OligoPhore™ / SemaPhore™ is a versatile platform for safe and effective delivery of oligonucleotides such as siRNA (small interfering ribonucleic acid) or mRNA (messenger RNA) into target cells, using systemic or local administration. Using the same technology, OligoPhore™ designates the platform for oligonucleotides, whereas SemaPhore™ designates the platform for mRNA. It is based on a proprietary 21 amino acid peptide that can engage any type of RNA in rapid self-assembly into a polyplex. The polyplex has a size, charge, and other physical features that allow it to escape hepatic clearance and thus to reach other target tissues than the liver. OligoPhore™ / SemaPhore™ protects the RNA payload from degradation in the circulation and allows for rapid cellular uptake, while enabling pH-dependent nucleotide full endosomal escape and cytoplasmic delivery.

Effective delivery and positive treatment outcomes have been demonstrated with OligoPhore™ in more than 10 diverse murine models of disease for cancer, cardiovascular, and rheumatological targets in the NF-κB family, various members of the ETS transcription factor family, and targets in the JNK and TAM pathways. With SemaPhore™, positive results have been demonstrated so far in three different murine disease models in osteoarthritis, atherosclerosis and aortic aneurysm with WNT 16, $p27^{Kip1}$ and SOD2 as targets. All of these results have been published in peer-reviewed journals.

The preparation of the polyplex formulations is relatively straightforward. The peptide carrier rapidly condenses nucleotides within minutes by mixing at a pre-defined ratio. The interaction between RNA sequence and peptide is initially electrostatic, but importantly an exothermic process of strong hydrogen bonding takes place between the histidines and nucleic acids to markedly stabilize the polyplex. A thin coating of albumin or hyaluronic acid is used to further stabilize the system. Once the polyplex is formed it can be injected intravenously or intraperitoneally, or by any other route that reaches the circulation. It readily escapes the leaky vasculature of various pathologies and is taken up avidly by cells that are capable of macropinocytosis ("big drinking") such as cancer cells or macrophages. However, we also have transfected endothelium, smooth muscle, and other cell types. Once in the endosome, the natural process of acidification breaks strong bonds between the RNA and the peptide to disassemble the polyplex. The released peptide interacts with the endosomal membrane to permeabilize it and release the RNA into the cytoplasm. The peptide is then diluted quickly and broken down, causing no unintended damage to the cell membrane itself.

In July 2021 we announced the selection of KRAS-driven cancer as the first therapeutic indication for our OligoPhore™ oligonucleotide delivery platform. We aim to advance the AM-401 program through preclinical studies with the objective of filing for an NDA in 2023. In parallel, we will seek to leverage the OligoPhore™ / SemaPhore™ through collaborations with other biopharmaceutical companies and the out-licensing of technology for specific indications.

Market for RNA therapeutics

RNA therapeutics is a rapidly emerging field of human medicine that has the potential to change the standard of care for many diseases and target previously undruggable pathways. Traditional small molecule drugs target active sites of proteins so as to inhibit or alter their function; however, only ~1.5% of the human genome encodes proteins (Ezkurdia et al., 2014), and only 10–14% of proteins have active binding sites that are "druggable" targets for small molecules (Hopkins and Groom, 2002). Thus the "druggable" targets for small molecule therapies is limited. This limitation was addressed in part by recombinant protein technology which has become a significant share of the pharmaceutical market (Damase et al., 2021). However, recombinant proteins have limitations as drugs, particularly due to size and stability issues. By contrast, nucleic-acid based strategies avoid many of these limitations as they make use of the translational machinery of the human cell.

RNA therapeutics comprise four broad categories: aptamers, antisense oligonucleotides (ASOs), RNA interference (RNAi) and messenger RNA (mRNA). Aptamers are oligonucleotide or peptide molecules that bind to a specific target molecule to inhibit signal transduction. ASOs bind to mRNA, rendering it inactive, whereas RNAi (short interfering RNA or siRNA and micro RNA or miRNA) promote the degradation of specific mRNA molecules. Rather than silencing defective genes as ASOs and RNAi do, mRNA promotes protein expression to compensate for a defective gene/protein. Regardless of the type of RNA therapeutic, delivery into target cells and tissues has proved to be a major challenge as RNA is inherently unstable and tends to show poor cellular uptake. Various delivery technologies have been developed to address these challenges, including the use of nanocarriers or bioconjugates for targeted delivery. While there has been substantial progress with delivery of RNA therapeutics to the liver, other target tissues and organs have remained difficult to reach.

In 2016 the FDA approved the first two ASO based therapeutics and in 2018 the first siRNA therapeutic. Further approvals have followed, and there is a growing number of RNA therapeutics in clinical development. With the rapid development of vaccines against COVID-19, which use mRNA to instruct muscle cells to produce the non-infectious SARS-CoV-2 spike protein to induce specific neutralizing antibodies, some key advantages of RNA-based therapeutics such as rapid design and scale-up in manufacturing have been highlighted. According to a recent report published by Allied Market Research the global market for RNA therapeutics (RNAi and ASOs) reached USD 4.9 billion in 2021 and is expected to grow to USD 25.1 billion in 2030. In another recent report by Research and Markets, it is estimated that the global market for mRNA therapeutics should grow from USD 46.7 billion in 2021 to USD 101.3 billion by 2026.

Protection against airborne viruses and allergens

With our Bentrio™ nasal spray, we are aiming to provide protection against airborne viruses and allergens. The nose is the first organ of the respiratory system. Its main function is breathing, bringing warm humidified air into the lungs. Filtering of the air by nasal hair in the nostrils prevents large particles from entering the lungs. The interior of the nose, which is called the nasal cavity, is lined by the nasal mucosa, one of the anatomical structures which form the physical barriers of the body's immune system. These barriers provide mechanical protection from the invasion of infectious and allergenic pathogens. Sneezing is a reflex to expel unwanted particles from the nose that irritate the mucosal lining.

Through the intake of air, the nasal cavity and nasal mucosa are exposed to a variety of airborne pathogens such as viruses and bacteria and allergens such as pollen, house dust mites or animal hair. Unless they are neutralized by the immune system, these pathogens may cause infections. In case of allergens, the body may develop sensitivity to them, resulting in an inflammatory reaction including the release of certain chemicals such as histamine affecting the nasal mucosa. This inflammatory condition is called allergic rhinitis. Its main symptoms include nasal itching and sneezing, runny nose, and nasal congestion.

Market for allergic rhinitis and viral infection treatments

Allergic rhinitis is a very frequent condition. According to results from the National Health Interview Survey published in 2010 by Schiller and colleagues, roughly 7.8% of people 18 and over in the U.S. have hay fever. In 2010, 11.1 million visits to physician offices resulted with a primary diagnosis of allergic rhinitis, as shown by the National Ambulatory Medical Care Survey. Besides de-sensitization (allergen-specific immunotherapy), there is no cure for allergic rhinitis. In most cases treatment aims to relieve symptoms. Antihistamines relieve symptoms of allergic rhinitis by blocking or reducing the action of histamines, which the body releases when under attack from allergens. However, antihistamines can sometimes cause drowsiness. The most effective and safest way to prevent or decrease the allergic symptoms is to avoid, remove, or protect against exposure to airborne allergens. In 2020, the market size for "over the counter" allergy medicines in the US was estimated at USD 4 billion.

Infections from airborne viruses are very common. Viruses known to spread by airborne transmission (and also other routes) include rhinoviruses (cause common cold symptoms), influenza viruses (type A, type B, H1N1), varicella viruses (cause chickenpox), measles virus, mumps virus, enterovirus, norovirus, coronaviruses among others. Worldwide and nearly year-round, human rhinovirus (HRV) is the most common cause of upper respiratory tract infection and is responsible for more than one-half of cold-like illnesses. The treatment of HRV infection remains primarily supportive, including over-the-counter products aimed at symptom relief. Revenues in the US for cold and cough remedies such as antihistamines, antibiotics, decongestants, expectorants and bronchodilators are expected to exceed USD 12 billion in 2021. According to the US Centers for Disease Control and Prevention (CDC), influenza has resulted in 9-45 million illnesses, 140,000-810,000 hospitalizations and 12,000- 61,000 deaths annually since 2010. Protection against influenza may be achieved by seasonal vaccination ("flu shots"); in case of infection, there are a number of approved antiviral drugs available such as oseltamivir, zanamivir, peramivir or baloxavir marboxil.

The current COVID-19 pandemic has highlighted the large impact that viral infections can have on health, quality of life and economic activity. Since outbreak, more than 480 million people have been reported as infected and more than 6.1 million deaths have been counted globally. Thanks to massive and urgent efforts by public and private entities, vaccines could be developed in record time; in addition, the first oral antiviral treatments were approved, and dozens of other potential treatments have been under development. Although most of the population has been vaccinated in industrialized countries, a substantial number of people remain unvaccinated with even lower vaccination rates in most developing countries. It is uncertain at this point when and to what extent the COVID-19 pandemic can be ended or significantly mitigated in its effects as vaccine roll-outs take time and mutations of SARS-CoV-2 have developed which appear to reduce the protective effects of the newly developed vaccines.

Treatment of neurotologic conditions

The three most frequent neurotologic disorders are vertigo / dizziness, hearing loss and tinnitus. With AM-125, we are aiming to treat acute peripheral vertigo, which is a disorder of the vestibular system. The vestibular system is responsible for the sensations of balance and motion. For this, the brain receives, integrates, and analyzes information it receives from the left and right inner ear on the altitude, rotation, and linear motion of the head, visual input from the eyes and input from joint and muscle receptors (the propriosensory system). When vestibular input from each inner ear is equal, the system is in balance, and there is no sense of movement. When inputs are unequal, the brain interprets this as movement. As a result, compensatory eye movements and postural adjustments occur to maintain balance. However, when some pathology (e.g., inflammation or trauma) disrupts signaling unilaterally, the result is an imbalance in vestibular input that can lead to vertigo.

Betahistine, the active substance of AM-125, has been used for decades for the treatment of vertigo. However, when administered orally, only small quantities of the drug actually reach the blood stream and can be distributed to the inner ear and the brain due to rapid and pronounced first pass metabolism. As a consequence of the low bioavailability, there has been significant variability in therapeutic outcomes. With AM-125, we are using intranasal delivery of betahistine.

The nasal cavity is highly vascularized and provides a large surface area for drug absorption. In addition, the nasal route allows for avoiding hepatic first-pass metabolism and degradation of a drug in the gastrointestinal tract when taken orally since the active substance will be absorbed directly into the blood circulation. Further, intranasal delivery is convenient, non-invasive and suitable for self-administration.

For our projects Keyzilen® (AM-101) and Sonsuvi® (AM-111), we are targeting specifically the cochlea, which together with the vestibule and the semicircular canals of the peripheral vestibular system forms the inner ear. The snail-shaped cochlea is the sensory organ at the periphery of the auditory system, which transmits sound along the auditory pathway up to the brain for hearing. Acute insults to the cochlea from a variety of sources – for example, loud noise, infection or insufficient blood supply – may lead to excessive levels of glutamate, the principal neurotransmitter in the cochlea as well as other pathological processes. This in turn may damage cochlear hair cells, which tune and amplify sound inside the cochlea or convert mechanical movement into neural signals, as well as cochlear neurons. Such damage may result in the symptoms of inner ear hearing loss and/or inner ear tinnitus that can be transitory as natural repair mechanisms set in or that become permanent when hair cells or neurons die or are permanently injured.

Because the cochlea is located deep inside the head and because it is separated from the middle ear by a combination of bone and membranes, the interior of the cochlea is a challenging location for drug delivery. We have chosen to deliver certain of our products via intratympanic injection across the ear drum (also known as the tympanic membrane) into the middle ear cavity. By formulating our products with biocompatible gels, we facilitate the diffusion of active substances across the round window membrane into the cochlea at clinically meaningful concentrations.

The vestibular system communicates with the cochlea and consists of three semi-circular canals and the vestibule. It is responsible for the sensations of balance and motion. The vestibular system uses the same kinds of fluids and detection cells (hair cells) as the cochlea and sends information to the brain regarding the altitude, rotation, and linear motion of the head. The vestibular system works with the visual system to keep objects in view when the head is moved. Joint and muscle receptors are also important in maintaining balance. The brain receives, interprets, and processes the information from all these systems to create the sensation of balance.

When vestibular input from each ear is equal, the system is in balance, and there is no sense of movement. When inputs are unequal, the brain interprets this as movement. As a result, compensatory eye movements and postural adjustments occur to maintain balance. However, when some pathology (e.g., inflammation or trauma) disrupts signaling unilaterally, the result is an imbalance in vestibular input that can lead to vertigo.

Market for neurotologic treatments

Inner ear disorders, including hearing loss, tinnitus, and vertigo, are common and often inter-related conditions. Chronic inner ear disorders such as tinnitus and hearing loss are highly prevalent. According to the National Institute on Deafness and Other Communication Disorders, or NIDCD, more than four out of 10 Americans, at some point in their lives, experience an episode of dizziness significant enough to see a doctor. According to research by Saber Tehrani and colleagues published in the journal Academic Emergency Medicine in 2013 there are almost 4 million emergency room visits per year in the U.S. for problems of dizziness or vertigo. According to data from the National Health and Nutrition Examination Survey published by Agrawal and colleagues in the journal Archives of Internal Medicine in 2013, 35.4% of the US population aged 40 years and older is suffering from vestibular dysfunction (i.e. failing the “Standing on Foam” test).

Also according to the NICDC, approximately 10% of the U.S. adult population, or about 25 million Americans, have experienced tinnitus lasting at least five minutes in the past year. Additionally, according to a 2016 publication by Bhatt et al. in the journal JAMA Otolaryngology—Head and Neck Surgery, 21.4 million (9.6%) U.S. adults experienced tinnitus in the past 12 months. The NIDCD also reports that 37.5 million Americans, or 15% of the adult U.S. population, report having some trouble hearing. Epidemiological studies reveal comparable prevalence rates for Europe. Additionally, according to a 2016 publication by Hoffman et al. in the journal JAMA Otolaryngology—Head and Neck Surgery, the annual prevalence of speech-frequency hearing loss among adults aged 20 to 69 years was 14.1% (27.7 million) in the 2011-2012 period.

Although there are several drugs available for the treatment of vertigo, they were all introduced several decades ago and have only limited clinical utility. In the US, diphenhydramine, meclizine, promethazine and benzodiazepines are frequently used as vestibular suppressants; they act centrally and have a sedating effect which may impose a serious limitation when the activities of the subject require alertness. Outside the US, betahistine is frequently used as a non-sedating treatment for vertigo; it was also introduced several decades ago. As for the treatment of tinnitus or hearing loss, there is currently no FDA or EMA approved drug therapy on the market.

Our Products and Product Candidates

Bentrio™ (AM-301) in the protection against airborne allergens and viruses

Allergic rhinitis and upper respiratory airway infections

Through the intake of air, the mucosa-lined nasal cavity as the uppermost part of the respiratory system is exposed to a variety of airborne pathogens such as viruses and bacteria. Unless they are neutralized by the immune system, these pathogens may cause infections. Viruses known to spread by airborne transmission (and also other routes) include rhinoviruses (cause common cold symptoms), influenza viruses (type A, type B, H1N1), varicella viruses (cause chickenpox), measles virus, mumps virus, enterovirus, norovirus, coronaviruses among others.

Further, the nasal cavity is exposed to allergens such as pollen, house dust mites or animal hair. The body may develop sensitivity to such allergens, resulting in an inflammatory reaction (allergic rhinitis), including the release of certain chemicals such as histamine which affect the nasal mucosa. The main symptoms of allergic rhinitis include nasal itching and sneezing, runny nose, and nasal congestion.

The nasal mucosa is one of the anatomical structures which form the physical barriers of the body's immune system. The mucosal lining of the nasal cavity represents the outer surface of the body to the ambient air and its contents and is prepared for it as the first line of defense. These barriers provide mechanical protection from the invasion of infectious and allergenic pathogens. Nasal mucociliary clearance provides another defense mechanism: mucus secreted by the nasal mucosa traps inhaled allergens, pathogens and other particles and is then transported with the trapped matter by the ciliated cells of the respiratory epithelium to the pharynx, where it is swallowed.

Proper humidification helps to maintain the nasal mucosa's function in clearing viruses and allergens from the nasal cavity. Further protection may be achieved by wearing face masks or avoidance of exposure to potential sources of infection or allergens.

Our solution – Bentrio™

In September 2020 we announced the launch of the development of AM-301, a drug-free nasal spray for protection against airborne viruses and allergens through a newly created subsidiary, Altamira Medica Ltd. AM-301 is a gel emulsion which works by forming a protective layer on the nasal mucosa that acts as a mechanical barrier against airborne viruses allergens. The barrier consists of two elements: (1) a mucoadhesive film lining the nasal cavity and preventing contact of airborne viruses or allergens with the nasal mucosa to reduce the risk of viral infection or allergic reactions; (2) the trapping / binding of such viruses or allergens through electrostatic effects, allowing for their removal e.g. through mucociliary clearance. In addition, the product helps to humidify and thus maintain the nasal mucosa's function in clearing viruses and allergens from the nasal cavity.

The key component of AM-301 is bentonite, a naturally occurring clay. Following formulation development, we tested Bentrio™ *in vitro* in a series of experiments using reconstituted human nasal epithelia infected with SARS-CoV-2 or H1N1 influenza virus. Daily treatment with AM-301, beginning right before inoculation or 24-30 hours thereafter showed significant reductions of the viral titer compared to saline treated controls. In case of SARS-CoV-2, a protective effect was observed with the original virus, the Delta variant as well as the Omicron variant.

Based on these *in vitro* results, we believe that AM-301 could help to reduce the risks of exposure from airborne transmission of SARS-CoV-2. It is estimated that about 90% of air is inhaled via the nose, and it has been established that infection with SARS-CoV-2 via the nose is a major transmission pathway for COVID-19. In 2021 we prepared a randomized placebo-controlled clinical trial in acute COVID-19 ("COVAMID") for further confirmation of the protective effects of Bentrio™; due to the largely unpredictable waves of infection on one hand and varying regulatory timelines and requirements, the trial could start enrollment only in March 2022.

In 2021 we conducted an open-label randomized cross-over study with AM-301 that enrolled 36 patients with allergic rhinitis caused by grass pollen. Study participants were administered a single dose of Bentrio™ nasal spray or hydroxypropylmethylcellulose, a comparator product, prior to controlled pollen exposure for four hours in an allergen challenge chamber. The challenge was repeated with the alternate treatment following a wash-out period. The study demonstrated a rapid onset and long durability of Bentrio's protective effect, established substantial equivalence to the marketed comparator with superior efficacy ratings by patients and clinicians, and showed good tolerability.

We believe that Bentrio™ could provide help to people suffering from allergic rhinitis by reducing their exposure to airborne allergen particles e.g. from pollens, house dust or animal hair. For further clinical data, in December 2021 we initiated a randomized open-label trial with Bentrio™ and saline nasal spray as control in seasonal allergic rhinitis (SAR) and an open-label clinical trial with AM-301 in perennial allergic rhinitis (PAR) with controlled house dust mite exposure. We expect the PAR trial to read out in the second quarter of 2022 and the SAR trial in late 2022.

Since Bentrio™ does not contain any active substance, it is regulated and marketed as an "over-the-counter" medical device. In May 2021 we completed the conformity assessment procedure for marketing the product in the member states of the European Union (EU), and in September 2021 we filed a 510(k) premarket notification with the FDA, which is currently under review for the intended use of promoting alleviation of mild allergic symptoms triggered by the inhalation of various airborne allergens.

AM-125 in Vestibular Disorders

Vestibular Disorders

Balance disorders are medical conditions that evoke the sensation of unsteadiness, dizziness or vertigo. Patients suffering from balance disorders are often profoundly impacted in their daily activities. Balance problems can be caused by many different health conditions, medications or anything that affects certain areas of the brain or the inner ear labyrinth. Balance disorders originating from the inner ear labyrinth include benign paroxysmal positional vertigo, or positional vertigo, labyrinthitis, vestibular neuronitis and Meniere's disease, a chronic condition characterized by severe episodic vertigo, tinnitus, and fluctuating hearing loss.

In case of vertigo, patients experience a false sensation of movement of oneself or the environment. This can be a spinning or wheeling sensation, or they simply feel pulled to one side. This may lead to imbalance, nausea or vomiting. The cause of vertigo can be an imbalance between the left and right vestibular systems in signaling position and acceleration to the brain. The symptom of vertigo may partially or fully resolve thanks to spontaneous recovery of the peripheral vestibular function and / or through compensation of the imbalance at the brain level, which is known as vestibular compensation.

The imbalance between the left and right vestibular systems and thus the sensation of vertigo may be reduced by dampening the vestibular function in the unaffected, opposite inner ear through pharmacotherapy. This minimizes the extent of the imbalance falsely interpreted as movement. Most existing therapies rely on this strategy to minimize vertigo symptoms, but also have unintended sedative effects. Examples include meclizine, benzodiazepines, dimenhydrinate or amitriptyline.

Betahistine is widely used around the world for the treatment of vestibular disorders, notably Meniere's disease and vertigo. Its development goes back to the use of intravenous histamine, which provided symptomatic relief for these disorders. Betahistine is a structural analog of histamine. It acts as a partial histamine H1-receptor agonist and, more powerfully, as a histamine H3-receptor antagonist. Betahistine has been shown to increase cochlear, vestibular and cerebral blood flow, facilitate vestibular compensation and inhibit neuronal firing in the vestibular nuclei. Unlike other drugs, it has no sedating effect. Betahistine is typically taken orally with a recommended daily dose of 24 to 48 mg, divided in 2 or 3 single doses.

Betahistine is generally recognized as a safe drug and there exists a large body of data on the pharmacology, pharmacokinetics and toxicology of the compound. It is approved in about 115 countries world-wide for the treatment of Meniere's disease and vestibular vertigo, but not in the United States. In 1970, the Commissioner of FDA withdrew approval of the NDA after the discovery that the submission contained unsubstantiated information about some patients in the efficacy studies upon which approval was based. Today, betahistine is available in the United States only from compounding pharmacies or through importation. Despite limited availability, a survey by Clyde and colleagues published in Otology & Neurotology in 2017 revealed that 56% of U.S. neurotologists and 16% of generalists use betahistine and 20-30% of neurotologists use it often or always when treating patients with Meniere's disease.

Various studies and meta-analyses have demonstrated therapeutic benefits of betahistine in both the treatment of vertigo as well as in supporting vestibular rehabilitation. However, the evidence for therapeutic benefits is variable, and it has been suggested that efficacy could be increased with higher doses and / or longer treatment periods. It is well known that orally administered betahistine is rapidly and almost completely metabolized into 2-pyridylacetic acid, also known as 2-PAA, which lacks pharmacological activity. As a consequence, the bioavailability of oral betahistine is estimated to be very low.

Our Solution—AM-125

In February 2017 we entered into an asset purchase agreement with Otifex, pursuant to which we have purchased various assets related to betahistine dihydrochloride in a spray formulation, which we are developing for intranasal treatment of vertigo under the product code AM-125. The assets include preclinical and clinical data as well as certain intellectual property rights. In a Phase 1 clinical trial conducted by Otifex in 40 healthy volunteers intranasal betahistine showed good tolerability and significantly higher betahistine concentrations in blood plasma than reported for oral betahistine administration.

Therapeutic rationale for AM-125 in vertigo

We are aiming to address the currently limited therapeutic utility of betahistine arising from its low oral bioavailability by avoiding first pass metabolism by monoamine oxidase. Intranasal administration of betahistine provides substantially higher bioavailability than oral administration as there is only very little monoamine oxidase activity known to occur in the nose, allowing higher quantities of betahistine to be absorbed into the blood stream and reach target histamine receptors in the inner ear and brain. As preclinical and clinical data suggest that betahistine's therapeutic effects increase with higher systemic exposure, we expect AM-125's higher bioavailability to translate into more pronounced therapeutic benefits.

Vertigo endpoints

Vertigo cannot be measured directly. Therapy typically aims to a) reduce the symptoms of vestibular dysfunction underlying vertigo and / or b) accelerate vestibular compensation and recovery. Status and therapeutic outcomes are usually assessed by a battery of tests, addressing static and dynamic deficits, balance impairment, functional performance and disability, using both objective and subjective measures.

Loss of postural control affects essentially all patients suffering from acute vertigo and has a substantial impact on day-to-day functioning. It is assessed relatively easily through a number of widely used balance and functional tests:

- Static conditions: Romberg test, standing on foam, single-leg stance
- Dynamic conditions: tandem gait, timed "up and go", 10 meter walking or other tests

Other outcome measures target the interaction between inner ear and ocular sensory input. Nystagmography measures the velocity and direction of involuntary eye movements (nystagmus) triggered by vestibular imbalance and the head-impulse test measures to which extent the reflex is disturbed that triggers eye movement as a response to a movement of the head. Further, there are clinician or patient reported clinical outcomes that subjectively capture the illusion of movement, the duration of the illusion, motion intolerance, neurovegetative signs, and instability. Examples include the Dizziness Handicap Inventory (DHI) questionnaire, the Vestibular Rehabilitation Benefits Questionnaire (VRBQ) or the European Evaluation of Vertigo (EEV) questionnaire.

Clinical development of AM-125

In 2018, we conducted a second Phase 1 clinical trial with AM-125 in 72 healthy volunteers. The randomized double blind placebo controlled trial demonstrated superior bioavailability over a range of four intranasal betahistine doses compared to oral betahistine, with plasma exposure being 5 to 29 times higher (unadjusted for dose; p-value between 0.056 and $p < 0.0001$). Further, it confirmed the favorable safety profile of intranasal betahistine and showed that the treatment was well tolerated when administered three times daily for three days. Single doses were escalated up to 60 mg, and repeated doses up to 40 mg. For the latter, the maximum tolerated dose based on local tolerability was determined at 40 mg.

In July 2019, we started enrollment into a randomized placebo-controlled Phase 2 clinical study with AM-125. The "TRAVERS" Phase 2 trial is expected to enroll 118 patients suffering from acute vertigo following surgical removal of a vestibular schwannoma, a tumor growing behind the inner ear, resection of the vestibular nerve (vestibular neurectomy) or surgical removal of parts of the inner ear (labyrinthectomy). Starting three days after neurosurgery, trial participants self-administer AM-125 or placebo 3 x daily for four weeks; they are then followed for a further two weeks. The trial is being conducted in several countries ex US.

In September 2020 we announced the results of an interim analysis from Part A of the trial, which comprised a dose escalation – 1, 10 or 20 mg or placebo – in 33 patients. The interim analysis showed a dose-dependent improvement in balance as well as good safety and tolerability of ascending doses of AM-125. At the highest dose of 20 mg (3 x daily), AM-125-treated patients improved their performance of the "Tandem Romberg" and the "Standing on Foam" balance tests from baseline to 14 days post-surgery (primary endpoint) on average 1.9 to 2.4 times more than placebo-treated patients (6.0 vs. 3.1 and 10.5 vs. 4.3 seconds, respectively). In contrast to placebo, the improvement from baseline was statistically significant for AM-125 20 mg and for all active dose groups, respectively ($p<0.02$ and $p<0.01$ to $p<0.05$, respectively). These positive results were supported by similar improvements in additional efficacy measures, including additional objective as well as clinician- and patient-reported outcomes.

Based on the results from the interim analysis, we selected the two highest doses, 10 and 20 mg, for testing against placebo in 72 patients in Part B of the trial. As we remained blinded to treatment allocation during the interim analysis, the corresponding data from Part A will be pooled with those from Part B. Prior to starting Part B of the trial in October 2020, we tested oral betahistine (48 mg) open label for reference purposes.

Enrollment into TRAVERS has been impacted by the COVID-19 pandemic, as the type of neurosurgery required for participation in the trial is classified as an elective procedure and hence was postponed and as many participating sites temporarily reduced or suspended clinical research activities. The effect was particularly felt in the spring of 2020 and then again in early 2021. In February 2022 we announced the completion of enrollment into TRAVERS. We expect to obtain top-line results in the second quarter of 2022.

We have discussed the regulatory requirements for AM-125 during a pre-Investigational New Drug ("IND") meeting with the FDA and in the context of scientific advice meetings with the EMA and two European national health authorities to further define the development program. We expect to have further exchanges with regulatory agencies following conclusion of the TRAVERS trial, upon which we aim to obtain an IND. We expect to initiate a Phase 3 clinical trial with AM-125 in acute peripheral vertigo in late 2022. We believe that, if approved, AM-125 could become the first betahistine product for the treatment of acute peripheral vertigo in the United States. We are currently evaluating the feasibility of a clinical study with AM-125 in central vertigo, which may lead to the initiation of a Phase 2 trial later in 2022.

In May 2018, we initiated project AM-201 to evaluate intranasal betahistine also for the prevention of antipsychotic-induced weight gain and somnolence. Betahistine is thought to counteract the effects of antipsychotics such as olanzapine and to relieve the inhibitory effect on the H1 receptor by binding to and activating the H1 receptor to normalize/reduce the food take and consequently lead to reduced weight gain and somnolence. We believe the weight-attenuating effect is intensified by betahistine's property as antagonist at the H3 receptor.

In 2019, we initiated a Phase 1b trial in Europe to evaluate AM-201's safety and therapeutic effects in this indication. Participants received either AM-201 (1, 2.5, 5, 10, 20 or 30 mg) or placebo in parallel with oral olanzapine (10 mg) once a day for four weeks. In May 2020, we announced that at AM-201 30 mg, the mean weight gain from baseline to the end of the treatment period was 2.8 kg compared against 3.7 kg in control subjects; the primary efficacy endpoint of mean reduction in weight gain was 0.9 kg and statistically significant ($p<0.02$; $n=81$ with pre-specified Bayesian augmented controls). As expected, intranasal delivery of betahistine allowed for substantially higher concentrations in blood plasma compared with levels previously reported for oral betahistine. In the context of our strategic repositioning, we have decided to deprioritize project AM-201 and suspended all development work.

AM-401 in KRAS driven cancers

KRAS driven cancers

The KRAS gene encodes the Ras protein which controls - like an "on / off switch" – cell growth, cell maturation, and cell death. Through mutations, the Ras proteins can be rendered persistently active, causing cancer cells to grow and spread in the body. Mutations of KRAS are associated with poor prognosis in several cancers, and there is a substantial body of evidence supporting the role of KRAS in the initiation and maintenance of cancer. Mutated forms of KRAS are found in one-fifth of all human cancers, including 32% of non-small-cell lung cancers (NSCLCs), 40% of colorectal cancers (CRCs) and 85–90% of pancreatic cancers. According to the American Cancer Society, overall, almost 150,000 new cases of KRAS mutated tumors are diagnosed in the United States alone across these three tumor types each year. It has been estimated that mutations in KRAS alone account for approximately one million deaths per year worldwide (Simanshu et al., 2017).

Since the original discovery of KRAS as an oncogene in 1982, there have been intense efforts to develop a targeted therapeutic for KRAS mutant cancers. Although the role of KRAS mutations in cancer has been known for decades, they have remained a challenging target for therapeutic interventions. KRAS was long considered undruggable, in part because its surface lacked obvious binding sites. Only recently did the FDA approve with sotorasib the first ever treatment for KRAS driven cancer. Sotorasib, a small molecule, received accelerated approval as second-line treatment for KRAS G12C-mutated NSCLC.

Our solution – AM-401

We are applying our OligoPhore™ technology to KRAS driven cancers for first clinical proof of concept. Our unique approach utilizes a custom-designed 21 amino acid peptide that rapidly condenses peptide and nucleotide components into a polyplex with a size, charge, and other physical features that allow it to escape hepatic clearance. The technology has the following features:

- Stability: siRNA is complexed in nanoparticle polyplex format, and is only released inside of cells after endosomal uptake and not in the circulation
- Extrahepatic delivery: the nanoparticle is not sequestered in liver, but will readily permeate inflamed pathological tissues
- Endosomal escape: we have co-opted the natural cellular process of endosomal acidification to disassemble the polyplex, which is followed by full release of siRNA into the cytoplasm
- Selectivity: the polyplex silences molecular targets in diseased tissues only
- Safety: no cellular or adaptive immune responsivity to nanoparticle components or siRNA after multiple serial doses, and no organ toxicities observed in mice after serial dosing

The therapeutic objective for AM-401 is to slow down KRAS driven tumor cell growth and proliferation or to stop it altogether by delivering siRNA specifically inside tumor cells for gene knock down. As described by Strand and colleagues in a 2019 issue of the scientific journal Oncotarget, *in vitro* and *in vivo* experiments demonstrated efficient uptake of OligoPhore™ nanoparticles with KRAS-targeted siRNA in colorectal and pancreatic cancer cells, strong inhibition of KRAS expression, reduced viability of tumor cells and significant reduction in tumor growth and volume. Importantly, a murine model demonstrated the capacity of the OligoPhore™ platform to drive targeted delivery of the nanoparticles specifically to tumor cells.

Based on these outcomes, we started *in silico* and *in vitro* work to screen and select the most effective siRNA sequences and to optimize their properties. This will be followed by further *in vivo* testing. Meanwhile, we have been working on the scale up in the synthesis of the peptide base of OligoPhore™ and process development for the manufacture of the nanoparticles. We intend to review and discuss our plans for IND-enabling preclinical studies with the FDA in the context of a Pre-IND meeting. Subject to the opening of an IND (or equivalent clearance by another regulatory agency), we expect to conduct a Phase 1 clinical trial in patients with KRAS driven cancer.

Keyzilen® in Tinnitus

Tinnitus, frequently perceived as a ringing in the ears, is the perception of sound when no external sound is present. Similar to pain, it is an unwanted, unpleasant and thus distressing sensation. Tinnitus may result in further symptoms such as inability to concentrate, irritability, anxiety, insomnia, and clinical depression. In many cases, tinnitus significantly impairs quality of life and affects normal day-to-day activities. According to the American Tinnitus Association, approximately 16 million persons in the United States have tinnitus symptoms severe enough to seek medical attention and about two million persons cannot function on a normal day-to-day basis. In addition, tinnitus is now the number one service-connected disability for all veterans, before hearing loss. In 2012, 9.7% of all veterans received service-related disability compensation for the condition.

Acoustic trauma and other insults to the inner ear may trigger increased levels of extra-cellular glutamate, which in turn cause excessive activation of cochlear NMDA receptors. This process results in damage or killing of sensory cells and is thought to be responsible for abnormal spontaneous “firing” of auditory nerve fibers, which may be perceived as tinnitus. Under normal circumstances, the NMDA receptors are thought to play no role in the auditory nerve’s transmission of nerve pulses that carry sound information. In case of a trauma such as excessive sound exposure these receptors may become pathologically active, and thus tinnitus is triggered.

We have been developing Keyzilen®, Esketamine gel for injection, for the treatment of acute inner ear tinnitus. Esketamine is a potent, small molecule non-competitive NMDA receptor antagonist. Keyzilen® is formulated in a biocompatible gel and delivered via intratympanic injection. It demonstrated a favorable safety profile and positive effect on PROs associated with tinnitus in two Phase 2 clinical trials. In two Phase 3 clinical trials (TACTT2 and TACTT3), we were unable to confirm the efficacy of Keyzilen™ as both of them did not meet their primary efficacy endpoints. We believe we have identified two principal sources for the negative outcomes from the TACTT trials: (i) the high frequency of tinnitus loudness ratings over an extended period of time and (ii) an unexpectedly high level of variability in outcomes among study sites. A survey among a number of TACTT3 participants revealed that the daily capture of tinnitus loudness and annoyance caused a number of patients to excessively focus on their tinnitus symptoms. In addition, it was observed that a non-negligible number of study participants presumably became tired of the daily ratings after some time and stopped providing actual values. With respect to variability, our analysis subsequent to the unblinding of the trial data has shown positive outcomes at numerous sites, including many of the high enrolling study centers, but inconclusive or contradictory outcomes at other sites.

In April 2019, we announced that we had completed the design of a pivotal Phase 2/3 trial for Keyzilen®. The trial shall, in two stages, reaffirm the compound’s efficacy in the treatment of acute tinnitus and provide confirmatory efficacy data to support a filing for marketing authorization. In September 2019, we announced that we have obtained advice on the development plan and regulatory pathway from the U.S. Food and Drug Administration (“FDA”) in the context of a Type C meeting and from the European Medicines Agency (“EMA”) in the context of a Scientific Advice procedure for Keyzilen®. In the context of our strategic repositioning, we aim to divest or spin off the Keyzilen® program.

Sonsuvi® (AM-111) in Hearing Loss

Sonsuvi® is being developed for the treatment of acute sensorineural hearing loss (ASNHL), where there is damage to the sensory cells of the inner ear. ASNHL may be triggered by a variety of insults, such as exposure to excessively loud sound, infection, inflammation or certain ototoxic drugs. These insults may also result in tinnitus. According to an article by Alexander and Harris published in Otology & Neurotology in 2013, the average annual incidence of sudden deafness is 66,954 new cases among the U.S. insured population. There are no currently approved treatments for this patient population.

Sonsuvi® contains a synthetic D-form peptide (Brimapitide or D-JNKI-1) that protects sensorineural structures in the inner ear from stress-induced damage. Sonsuvi® has been granted orphan drug status by both EMA and FDA and has been granted fast track designation by the FDA for the treatment of sudden sensorineural hearing loss.

We have been developing Sonsuvi® for acute inner ear hearing loss. In our Phase 2 clinical trial, AM-111 showed a favorable safety profile. Furthermore, in patients with severe to profound ASNHL, we observed a clinically relevant improvement in hearing threshold, speech discrimination and a higher rate of complete tinnitus remission compared with placebo. In November 2017, we announced that the HEALOS Phase 3 clinical trial that investigated Sonsuvi® in the treatment of acute inner ear hearing loss did not meet the primary efficacy endpoint. However, a post-hoc analysis of the subpopulation with profound acute hearing loss (PTA $\geq$ 90 dB at baseline in accordance with a commonly used classification of hearing loss severity) revealed a clinically meaningful and nominally significant improvement in the Sonsuvi® 0.4 mg/mL treatment group.

Based on the HEALOS results, we submitted the design of a new pivotal trial with AM-111 0.4 mg/mL in patients suffering from acute profound hearing loss to the EMA and subsequently also to the FDA for review. Through a Protocol Assistance procedure the EMA endorsed the proposed trial design, choice of efficacy and safety endpoints, as well as the statistical methodology. In a Type C meeting with written responses, the proposed choice of primary and secondary efficacy endpoints, the safety endpoints, as well as the planned sample size and statistical methodology were also endorsed by the FDA. In the context of our strategic repositioning, we aim to divest or spin off the Sonsuvi® program.

Competition

We face or may face competition from different sources with respect to our commercial product Bentrio™ and our drug product candidates AM-125, AM-401 and our other pipeline products or any product candidates that we may seek to develop or commercialize in the future. Any product candidates that we successfully develop and commercialize will compete with existing therapies, even if they are not licensed specifically for use in our target therapeutic indications or if they lack clear proof of efficacy.

Possible competitors may be biotechnology, pharmaceutical and medical device companies as well as academic institutions, government agencies and private and public research institutions, which may in the future develop products to treat KRAS driven cancer, vertigo, allergic rhinitis or viral infections. Bentrio™ and any drug product candidates that we successfully develop and commercialize will compete with new therapies that may become available in the future. We believe that the key competitive factors affecting the success of our product candidates, if approved, are likely to be efficacy, safety, convenience, price, tolerability and the availability of reimbursement from government and other third-party payors.

Allergic rhinitis and upper respiratory airway infections

We believe that our main competitors for Bentrio™ are Marinomed Biotech AG or Marinomed, SaNOtize Research and Development Corp. or Sanotize, Nasaleze Ltd. or Nasaleze, Nasus Pharma Ltd. or Nasus Pharma, and larger companies such as GSK, Bayer, Sanofi, Procter & Gamble, Reckitt Benckiser, and Johnson & Johnson. These companies already market a variety of OTC drug or drug-free products for the management of allergic rhinitis and/or protection against certain viruses. E.g. Nasaleze and Nasus Pharma market nasal sprays based on hydroxypropylmethylcellulose (HPMC) powder which serves to establish a barrier on the nasal mucosa. Marinomed is marketing through various licensees a nasal spray based on carrageenan, a sulfated polymer from red seaweed, for protection against certain respiratory viral infections. Sanotize is marketing a nasal spray drug that uses nitric oxide to kill viruses. Other marketed products include nasal sprays, tablets or lozenges (e.g. based on corticosteroids or antihistamines). Some of the aforementioned drugs or medicinal products are marketed globally, whereas others are marketed only regionally. We believe that we will be able to differentiate AM-301 against competing products based on its triple mode of action devoid of any active substance, its extended nasal residence time, and utility in protecting against deleterious effects of both airborne allergens and viruses.

Vestibular Disorders

There are a number of product candidates in clinical development by third parties that aim to prevent or treat vertigo. Based on publicly available information, we have identified the following drug product candidates that are currently in clinical development:

- Otonomy is developing a polymer-based formulation for the steroid dexamethasone (Otividex; OTO-104) for patients with Meniere's disease. In August 2017 Otonomy announced that a Phase 3 clinical trial conducted in the United States had failed to show a treatment effect of OTO-104 against placebo and that a European Phase 3 clinical trial was terminated early. In November 2017 the company announced that the European study showed a statistically significant reduction in the count of definitive vertigo days. In February 2021 the company announced that a new Phase 3 trial with OTO-104 had failed to reach its primary efficacy endpoint.

- Sound Pharma has a product candidate (SPI-1005, ebselen), that mimics and prompts production of the enzyme glutathione peroxidase and is designed for oral administration. In June 2019 Sound Pharmaceuticals announced top-line results from a Phase 2 clinical trial with SP-1005 with Meniere's disease. The company reported a significant improvement in hearing; however, no information was provided with regard to any potential treatment effects on vertigo. In 2020, Sound Pharmaceuticals announced its intention to move SPI-1005 into Phase 3 development.

The aforementioned developments have the potential to compete with AM-125. Likewise, AM-125, if approved, will compete with products that are licensed or used off-label for the treatment of vestibular disorders and Meniere's disease, including steroids, diuretics, anti-emetics or anti-nausea medications as well as oral betahistine, the standard of care for treatment of Meniere's disease and vestibular vertigo in many countries outside the United States. Although we expect that AM-125 will offer benefits over oral betahistine due to the ability to bypass the strong first-pass metabolism associated with oral intake and provide for a higher bioavailability and avoid gastric side effects, it may take time to change prescribing and usage patterns in favor of the newer product.

KRAS driven cancers

There are several companies developing treatments for KRAS driven cancers. Amgen obtained an accelerated approval by the FDA for the KRAS G12C small molecule inhibitor sotorasib as second-line treatment in NSCLC with G12C mutated KRAS (that is a glycine-to-cysteine substitution at codon 12 of KRAS). G12C mutations are also the targets for small molecule inhibitors under development by Mirati Therapeutics (adagrasib), Novartis (IDQ443), Genentech (GDC-6036), Eli Lilly (LY3537982), and Boehringer Ingelheim (BI 1823911) with target indications in NSCLC, colorectal cancer (CRC), pancreatic cancer and other solid tumors carrying the KRAS G12C mutation. Merck and Moderna are in early stage clinical development with a patient-specific mRNA-based vaccine encoding KRAS neoantigens (mRNA-5671). Revolution Medicines has several small molecule inhibitors under development, which target G12C (RMC-6291), G12D (RMC-9805), G13C (RMC-8839) or all RAS cancer mutations (RAS^{Multi} (On)). There are also programs using RNAi such as NBF-006 by Nitto Denko, which seeks to inhibit the expression of glutathione-S-transferase P and uses lipid nanoparticles for delivery, or siG12D LODER by Silenseed Ltd., which releases siRNA targeting the KRAS G12D mutation from in implanted biodegradable bio polymeric matrix.

The aforementioned developments have the potential to compete with AM-401. In addition, there exist various treatment paradigms for key targets such as NSCLC, CRC and pancreatic cancers, including resection, chemotherapy, treatment with biologics and combinations thereof, and various lines of therapy. The relative positioning within current or future lines of therapy and thus the most relevant competition to AM-401 are uncertain at this point of development.

RNA delivery technologies

There are several companies offering commercial- or developmental-stage technologies for delivering RNA payloads to hepatic or extrahepatic cells. These include Acuitas Therapeutics Inc., Dicerna Pharmaceuticals, Inc., Genevant Sciences Corp., Entrada Therapeutics Inc., Sirnaomics Ltd., Ovensa Inc., or Feldan Bio Inc. Although we consider that our OligoPhore™ / SemaPhore™ platform offers unique advantages over current delivery approaches such as lipid nanoparticles, GalNAc or vector conjugates through the ability to use of systemic administration, delivery to extrahepatic tissues, efficient cellular uptake and high levels of endosomal release, it may take time to raise awareness and interest among potential customers within the biopharmaceutical industry, resulting in its successful adoption.

Acute inner ear tinnitus

There are a number of products in pre-clinical research and clinical development by third parties to treat tinnitus in the broader sense. Most of them are aiming to provide symptomatic relief (without treating the underlying cause) and targeting chronic rather than acute tinnitus. Examples include TRT or tinnitus maskers as well as more recent approaches like transcranial magnetic stimulation, vagus nerve stimulation, or customized sound therapy. Otonomy Inc. is developing OTO-313, an NMDA receptor antagonist like Keyzilen®. In February 2022 Otonomy announced the completion of enrollment into a Phase 2 trial with the compound.

Acute inner ear hearing loss

There are a number of product candidates in pre-clinical research and clinical development by third parties that aim to prevent or treat acute inner ear hearing loss. Based on publicly available information, we have identified the following drug product candidates that are currently in clinical development:

- Sound Pharma has a product candidate (SPI-1005, ebselen), that mimics and prompts production of the enzyme glutathione peroxidase and is designed for oral administration. In a Phase 2 clinical trial SP-1005 was tested for the prevention of noise-induced hearing loss in young adults. The study showed a reduction in the temporary hearing threshold that in one dose was better by 2.75 dB than in the placebo group.

- Sensorion, a French company, is developing SENS-401 (R-azasetron besylate) for the treatment of sudden sensorineural hearing loss by way of oral administration. In January 2022, the company reported that a Phase 2 trial failed to reach its primary endpoint.

- Frequency Therapeutics is developing FX-322, a small molecule for the regeneration cochlear hair cells through activation of progenitor cells already present in the cochlea. In March 2021 the company reported that four dose regimens of FX-322 did not do better than placebo in a Phase 2 trial.

We believe that Sonsuvi® is the only product candidate administered after an incidence of acute hearing loss that so far has demonstrated in a randomized, placebo controlled clinical trial a clinically relevant and significant improvement in hearing. To the extent that other drug developers demonstrate clinical efficacy for their product candidates in the prevention and treatment of permanent hearing loss from ASNHL, our competitive position may be weakened, and the market exclusivity under the orphan drug designation may be circumvented.

Intellectual Property

Patents

We seek regulatory approval for our products in disease areas with high unmet medical need, great market potential and where we have a proprietary position through patents covering various aspects of our products, e.g., composition, dosage, formulation, and use, etc. Our success depends on an intellectual property portfolio that supports our future revenue streams as well as erects barriers to our competitors. For example, we have broad disclosures in our patent applications and can pursue patent claims directed to our own leading product candidates as well as claims directed to certain potentially competing products. In addition, our earlier filed patent applications are prior art to others including certain of our competitors who filed their patent applications later than ours. We are maintaining and building our patent portfolio through: filing new patent applications; prosecuting existing applications and licensing and acquiring new patents and patent applications.

Despite these measures, any of our intellectual property and proprietary rights could be challenged, invalidated, circumvented, infringed or misappropriated, or such intellectual property and proprietary rights may not be sufficient to permit us to take advantage of current market trends or otherwise to provide competitive advantages.

As of December 31, 2021, we own eleven issued U.S. patents and five pending U.S. patent applications along with foreign counterparts of particular patents and applications in various jurisdictions. We co-own three of our issued U.S. patents, and one of our pending patent applications with INSERM, along with their foreign counterparts, pursuant to the terms of our co-ownership and exploitation agreement.

In addition, as of December 31, 2021, we have exclusively licensed from Xigen seven issued U.S. patents , along with their foreign counterparts in various jurisdictions that cover the composition of matter or method of use of JNK ligand peptides in a limited field including the intratympanic treatment of ASNHL.

With respect to our issued patents in the United States, we may also be entitled to obtain a patent term extension to extend the patent expiration date. For example, in the United States, we can apply for a patent term extension of up to 5 years for one of the patents covering a product once the product is approved by the FDA. The exact duration of the extension depends on the time we spend in clinical trials as well as getting a new drug application approval from the FDA.

Bentrio™

In September 2021, we converted four provisional US patent filings into a non-provisional US patent application relating to the formulation and use of Bentrio™. The patent application's key claim is directed towards aqueous compositions comprising a mucoadhesive polymer and clay particles. In addition, we filed an international PCT application.

Intranasal Betahistine

We have acquired from Otifex a patent application on the composition and use of intranasal betahistine, which issued on October 29, 2019, as a US patent covering the composition and use of intranasal betahistine. Further, we acquired in 2018 two U.S. patents relating to the use of betahistine for the prevention and treatment of olanzapine induced weight gain, and we acquired in 2019 two U.S. patents relating to the use of betahistine for the treatment of attention deficit/hyperactivity disorder and atypical depression.

AM-401

We are the exclusive licensee under our agreement with WU of a portfolio of patents and patent applications that relate to peptide based polyplexes for RNA delivery. The portfolio includes two issued US patents along with their foreign counterparts in various jurisdictions that cover the composition of matter or method of use of the peptide based polyplexes. These licensed patents and patent applications relating to AM-401 and potential further applications of the technology are expected to expire between 2034 and 2037, prior to any patent term extensions to which we may be entitled under applicable laws.

Keyzilen®

We are the owner or co-owner of patents and patent applications relating to Ketamine or its use in inner ear tinnitus. In particular, we have an agreement entitled "Co-Ownership/Exploitation Agreement" with INSERM with respect to its Ketamine patent portfolio. We have rights to four issued U.S. patents and corresponding patents and applications in other jurisdictions covering formulation and use of Ketamine. Our issued patents relating to Keyzilen® are expected to expire between 2024 and 2028, prior to any patent term extensions to which we may be entitled under applicable laws.

Sonsuvi®

We are the exclusive licensee under our agreement with Xigen of a portfolio of patents that relate, among other things, to JNK ligand peptides or their use in hearing loss. This portfolio includes seven issued U.S. patents along with their foreign counterparts in various jurisdictions that cover the composition of matter or method of use of the JNK ligand peptides. These licensed patents and patent applications relating to Sonsuvi® are expected to expire between 2023 and 2027, prior to any patent term extensions to which we may be entitled under applicable laws.

Proprietary Rights

In addition to patent protection, we intend to use other means to protect our proprietary rights. We may pursue marketing exclusivity periods that are available under regulatory provisions in certain countries, including the US, Europe and Japan. For example, if we are the first to obtain market approval of a small molecule product in the United States, we would expect to receive at least 5 years of market exclusivity in the U.S.

Furthermore, orphan drug exclusivity has been or may be sought where available. Such exclusivity has a term of 7 years in the United States and 10 years in Europe. We have obtained orphan drug designation for Sonsuvi® for the treatment of ASNHL in the United States and Europe. Orphan drug protection has been or may be sought where available if such protection also grants 7 years of market exclusivity. In addition, we have acquired a U.S. orphan drug designation for betahistine for the treatment of obesity associated with Prader-Willi syndrome.

We have obtained U.S. trademark registrations for Altamira, Auris Medical Cochlear Therapies (and Design), Keyzilen® and Sonsuvi®. Further, we have obtained several U.S. trademark registrations for betahistine.

In addition, we rely upon unpatented trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position. We seek to protect our ownership of know-how and trade secrets through an active program of legal mechanism including assignments, confidentiality agreements, material transfer agreements, research collaborations and licenses.

Collaboration and License Agreements

Washington University

On December 11, 2020, we entered into an Exclusive License Agreement with Washington University, which Exclusive License Agreement was subsequently amended and restated in June 2021 (as so amended and restated, the "Agreement"), with effect as of December 11, 2020. Pursuant to the Agreement, WU granted us an exclusive, worldwide, royalty-bearing license (with the right to sublicense) during the term of the Agreement under certain patent rights owned or controlled by WU to research, develop, make, have made, sell, offer for sale, use and import pharmaceutical products covered under such patent rights for all fields of use. Such licensed products may include "silencing RNA" (siRNAs) pharmaceutical preparations formulated in combination with our proprietary delivery technologies. In consideration for such worldwide, exclusive license, we will be obligated to pay WU: annual license maintenance fees in the low five figures through first commercial sale; pre-clinical and clinical regulatory milestones; sales milestones; and a low single digit royalty based on annual net sales of licensed products worldwide for at least the applicable patent term or period of marketing exclusivity, whichever is longer, but in no case less than a minimum royalty term of 12 years; and a percentage share (in the double digits) of sublicensing revenues received by the Company in connection with licensed products. Such regulatory and sales milestones may total up to an aggregate of $4,375,000. In the event the Company fails to meet certain regulatory diligence milestones, WU will have the right to terminate the license.

INSERM

In 2006, we entered into a co-ownership/exploitation agreement with the INSERM, a publicly funded government science and technology agency in France. Pursuant to the terms of the agreement, we were granted the exclusive right to exploit any products derived from patents that resulted from our joint research program with INSERM that was conducted in 2003 to 2005 and led to the development of Keyzilen®. Pursuant to the terms of the co-ownership/exploitation agreement, we are given the exclusive right to exploit the patents issuing from the filed patent applications for all claimed applications, including the treatment of tinnitus, in order to develop, promote, manufacture, cause to be manufactured, use, sell and distribute any products, processes or services deriving from such patents, including Keyzilen®, in any country in which these patent applications have been filed during the term of the agreement. INSERM is entitled to use the inventions covered by the patents and applications for its own research purposes, free of charge, but may not generate any direct or indirect profits from such use. Pursuant to the terms of our agreement with INSERM, we are required to finance research and development work towards achieving certain specified marketing authorizations, and to use best efforts in so far as commercially and financially feasible to develop, market, and obtain regulatory authorization for products covered by such patents.

As consideration for the exclusive rights granted to us under the agreement, we have agreed to pay INSERM a two tiered low single digit royalty (where the higher rate is due on any net sales above a certain threshold) on the net sales of any product covered by the patents (including the use of Keyzilen® in the treatment of tinnitus triggered by cochlear glutamate excitotoxicity) earned in each country in which these patent applications have been filed during the term of the agreement. We have also agreed to pay INSERM a low double digit fee on any sums of any nature (except royalties and certain costs) collected by us in respect of the granting of licenses to third parties.

The agreement will remain in force until the last of the patents covered by the agreement expires or becomes invalid. The patent covered by the agreement with the latest expiration date expires in 2028. The agreement will be terminated if we cease operations or are liquidated, may be terminated by either party in case of non-performance by the other party and may be terminated by INSERM in the absence of sales of a product deriving from the patents for a period from when it first marketed and if such a product is not marketed for a period from the date when marketing authorization is obtained.

Xigen

In October 2003, we entered into a collaboration and license agreement with Xigen, pursuant to which Xigen granted us an exclusive worldwide license to use specified compounds to develop, manufacture and commercialize “pharmaceutical products as well as drug delivery devices and formulations for local administration of therapeutic substances to the inner ear for the treatment of ear disorders” (the Area). We also have a right of first refusal to license certain additional compounds developed by Xigen which may be used for the Area, specifically any cell permeable inhibitors to effectively block certain signal pathways in apoptotic processes.

Under this agreement, we made an upfront payment to Xigen of CHF 200,000 and we are obligated to make development milestone payments on an indication-by-indication basis of up to CHF 1.5 million and regulatory milestone payments on a product-by-product basis of up to CHF 2.5 million, subject to a mid-twenties percentage reduction for smaller indications, e.g., those qualifying for orphan drug status. To date, we have paid CHF 1.325 million to Xigen under the agreement. We will be required to pay Xigen a mid-single digit percentage royalty on net sales of each licensed product that uses a compound licensed under the agreement, which royalty for a given indication shall be partially offset by milestone payments we have paid for such indication, until the later of 10 years after the first commercial sale of any licensed product using such licensed compound in any country, and the first expiration of a patent owned by or exclusively licensed to Xigen that covers the use of such licensed compound in any country, subject to our obligation to enter into good faith negotiations with Xigen, upon expiration of the relevant patent on a licensed compound, about the conditions of our further use of such licensed compound.

Under this agreement we and Xigen grant each other access to non-clinical or clinical data relating to the compounds licensed under the agreement free of charge for use in the other party’s proprietary development programs. We have also agreed, upon Xigen’s request, to offer third parties access to our non-clinical and clinical data relating to compounds licensed under the agreement for use outside the field of our license, provided that with respect to third party access, we are compensated for a portion of our costs in obtaining such data.

Xigen is responsible for maintaining the patents licensed to us under our agreement. New patents filed by us for specific inner ear indications or formulations of compounds licensed under our agreement are jointly owned by us and Xigen, and exclusively licensed to us in our field. We retain all know-how and other results from our development of compounds licensed under the agreement.

Our agreement with Xigen remains in effect until terminated. In August 2019 Xigen was acquired by Kuste Biopharma SAS, or Kuste, a French company. In February 2021, we were notified by Kuste of its decision to terminate the agreement effective May 10, 2021 due to the alleged lack of any development work since August 2018. We consider that the purported termination is without effect and that the agreement continues to be in full force and effect in accordance with its terms. We have retained legal counsel and intend to defend our interests, as appropriate and necessary.

Manufacturing

We currently rely on and expect to continue to rely on third parties for the manufacture of Bentrio™ and the supply of raw materials and to manufacture supplies for clinical trials of our drug product candidates, including AM-125, AM-401 and any other drug product candidate, Keyzilen® and Sonsuvi®. For the foreseeable future, we expect to continue to rely on such third parties for the manufacture of any of our products or drug product candidates on a clinical or commercial scale. Reliance on third-party providers may expose us to more risk than if we were to manufacture product candidates ourselves. The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA or other regulatory authorities pursuant to inspections that will be conducted after we submit our NDA or comparable marketing application to the FDA or other regulatory authority. We do not have control over a supplier's or manufacturer's compliance with these laws, regulations and applicable cGMP standards and other laws and regulations, such as those related to environmental health and safety matters. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our products or drug product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products or drug product candidates, if approved. Any failure to achieve and maintain compliance with these laws, regulations and standards could subject us to the risk that we may have to suspend the manufacturing of our products or drug product candidates or that obtained approvals could be revoked, which would adversely affect our business and reputation. Furthermore, third-party providers may breach agreements they have with us because of factors beyond our control. They may also terminate or refuse to renew their agreements because of their own financial difficulties or business priorities, potentially at a time that is costly or otherwise inconvenient for us. If we were unable to find adequate replacement or another acceptable solution in time, our clinical trials could be delayed or our commercial activities could be harmed.

In addition, the fact that we are dependent on our suppliers and other third parties for the manufacture, storage and distribution of our products and drug product candidates means that we are subject to the risk that the products may have manufacturing defects that we have limited ability to prevent or control. The sale of products containing such defects could result in recalls or regulatory enforcement action that could adversely affect our business, financial condition and results of operations.

Growth in the costs and expenses of components or raw materials may also adversely influence our business, financial condition and results of operations. Supply sources could be interrupted from time to time and, if interrupted, it is not assured that supplies could be resumed (whether in part or in whole) within a reasonable timeframe and at an acceptable cost or at all.

Commercialization Strategy

Given our current stage of product development, we currently have only a limited commercialization infrastructure. For the commercialization of Bentrio™, which we initiated in July 2021 in selected European countries, we plan to rely primarily on distributors. In this context, we have already concluded distribution and marketing agreements with companies such as Wellesta, Nuance and Avernus and continue to seek further commercial partners. However, we may be unable to secure appropriate or timely support and as a result experience a delay of the product launch or product sales below our expectations. Further, as an "OTC" product, the purchase of AM-301 by consumers is unlikely to be eligible for reimbursement by health insurance plans and will therefore have to be purchased out of their own pockets. We expect the lack of reimbursement coverage to reduce the pool of potential buyers.

If any of our drug product candidates is granted marketing approval, we intend to focus our initial commercial efforts in the United States and select European markets, which we believe represent the largest market opportunities for us. In those markets, we expect our commercial operations to include our own specialty sales force that we will specifically develop to target ENTs and specialists in neurotology and neurology, both in hospitals and in private practice. For these and other markets, we expect to seek partnerships that would maximize our products' commercial potential.

For the commercialization of our AM-301 nasal spray device, which we intend to initiate in 2021 subject to regulatory clearance and approvals, respectively, we plan to rely on commercial partners with presence in "over-the-counter" markets and / or providers of "go to market" services. We may be unable to secure appropriate or timely support and as a result experience a delay of the product launch or product sales below our expectations.

Government Regulation

Product Approval Process

The clinical testing, manufacturing, labeling, storage, distribution, record keeping, advertising, promotion, import, export and marketing, among other things, of our product candidates are subject to extensive regulation by governmental authorities in the United States and other countries. The FDA, under the Federal Food, Drug, and Cosmetic Act, regulates pharmaceutical products and medical devices in the United States.

The steps required before a drug may be approved for marketing in the United States generally include:

- the completion of pre-clinical laboratory tests and animal tests conducted under GLP regulations;
- the submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials commence;
- the performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication and conducted in accordance with cGCP;
- the submission to the FDA of an NDA;
- the FDA's acceptance of the NDA;
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the product is made to assess compliance with cGMPs; and
- the FDA's review and approval of an NDA prior to any commercial marketing or sale of the drug in the United States.

The testing and approval process requires substantial time, effort and financial resources, and the receipt and timing of any approval is uncertain.

Pre-clinical studies include laboratory evaluations of the product candidate, as well as animal studies to assess the potential safety and efficacy of the product candidate. The results of the pre-clinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of the IND, which must become effective before clinical trials may be commenced. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concerns or questions about the conduct of the trials as outlined in the IND prior to that time. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed.

Clinical trials involve the administration of the drug product candidates to healthy volunteers or patients with the disease to be treated under the supervision of a qualified principal investigator. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent Institutional Review Board, or IRB, either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries. The FDA, the IRB or the clinical trial sponsor may suspend or terminate clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the study. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

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

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

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

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

Phase 4 clinical trials are conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations, or when otherwise requested by the FDA in the form of post-market requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in withdrawal of approval.

The results of pre-clinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information on the manufacture, composition and quality of the product, are submitted to the FDA in the form of an NDA requesting approval to market the product. The NDA must be accompanied by a significant user fee payment. The FDA has substantial discretion in the approval process and may refuse to accept any application or decide that the data is insufficient for approval and require additional pre-clinical, clinical or other studies.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted. However, if only one indication for a product has orphan designation, a pediatric assessment may still be required for any applications to market that same product for the non-orphan indication(s).

Once the NDA submission has been submitted, the FDA has 60 days after submission of the NDA to conduct an initial review to determine whether it is sufficient to accept for filing. Under the Prescription Drug User Fee Act, the FDA sets a goal date by which it plans to complete its review. This is typically 12 months from the date of submission of the NDA application. The review process is often extended by FDA requests for additional information or clarification. Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with cGMPs and may also inspect clinical trial sites for integrity of data supporting safety and efficacy. The FDA may also convene an advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical trial data. The FDA is not bound by the recommendations of an advisory committee, but generally follows such recommendations in making its decisions. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information. The FDA may require post-marketing testing and surveillance to monitor safety or efficacy of a product.

After the FDA evaluates the NDA and conducts inspections of manufacturing facilities where the drug product and/or its API will be produced, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, pre-clinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

Device Approval Process

Unless an exemption applies, any medical device that is to be marketed in the U.S. must first receive from the FDA either 510(k) clearance, by filing a 510(k) premarket notification, or premarket application (PMA) approval, after submitting a PMA. Alternatively, the device may be cleared through the de novo classification process by the FDA. Based on advice from regulatory consultants and our own research, we expect AM-301 to be considered a Class II device by FDA and that the 510(k) pathway applies to AM-301's intended use of promoting alleviation of mild allergic symptoms triggered by the inhalation of various airborne allergens.

To obtain 510(k) clearance, a company must submit a premarket notification demonstrating substantial equivalence between the proposed device and a legally marketed "predicate" device, which is defined as a legally marketed device, that (i) was legally marketed prior to May 28, 1976, for which the FDA has not yet called for submission of a PMA application; (ii) has been reclassified from Class III to Class II or Class I; (iii) has been cleared through the 510(k) premarket notification process; or (iv) has been previously determined to be exempt from the 510(k) process. Substantial equivalence means that the proposed device has the same intended use and the same technological characteristics as the predicate device, or, if the new device has different technological characteristics, that the device is as safe and effective as the predicate device and does not raise different questions of safety and effectiveness. We have identified two such predicate devices and plan to reference them in our planned 510(k) submission for Bentrio™.

Bentrio™ is also intended for use in the reduction of the intranasal infectious viral load following inspiration of airborne viruses such as SARS-CoV-2. Since there may be no valid predicate device available for this intended use, we may have to submit a de novo request to the FDA. Under the de novo pathway, we would have to prove that AM-301 does not present substantial risk to the patient rather than just demonstrating substantial equivalence with the safety of the relevant predicate device(s), which may require additional testing. The review by the FDA in the de novo process is longer than the review process for 510(k) submissions and requires higher fees. Any device that has been classified through the de novo process may be marketed and used as predicate for future 510(k) submissions.

Many foreign countries in which we intend to market Bentrio™ have regulatory bodies and restrictions similar to those of the FDA. International sales are subject to foreign government regulation, the requirements of which vary substantially from country to country. The time required to obtain approval by a foreign country may be longer or shorter than that required for FDA clearance and the requirements may differ.

In particular, Bentrio™ may be marketed in the European Union (EU) is subject to compliance with the Medical Devices Directive 93/92/EEC (MDD), pursuant to which a medical device may be placed on the market within the EU only if it conforms to certain "essential requirements" and bears the CE Mark. The most fundamental and essential requirement is that a medical device must be designed and manufactured in such a way that it will not compromise the clinical condition or safety of patients, or the safety and health of users and others. In addition, the device must achieve the essential performance(s) intended by the manufacturer and be designed, manufactured and packaged in a suitable manner. In May 2017, the EU adopted a new Medical Devices Regulation (EU) 2017/745 (MDR), which will repeal and replace the MDD with effect from May 26, 2021. The MDR clearly envisages, among other things, stricter controls of medical devices, including strengthening of the conformity assessment procedures, increased expectations with respect to clinical data for devices and pre-market regulatory review of high-risk devices. The MDR also envisages greater control over notified bodies and their standards, increased transparency, more robust device vigilance requirements and clarification of the rules for clinical investigations. Under transitional provisions, medical devices with notified body certificates issued under the MDD prior to May 26, 2021 may continue to be placed on the market for the remaining validity of the certificate, until May 27, 2024 at the latest. After the expiry of any applicable transitional period, only devices that have been CE marked under the MDR may be placed on the market in the EU.

Manufacturers must demonstrate that their devices conform to the relevant essential requirements through a conformity assessment procedure. The nature of the assessment depends upon the classification of the device. The classification rules are mainly based on three criteria: the length of time the device is in contact with the body, the degree of invasiveness and the extent to which the device affects the anatomy. Conformity assessment procedures for all but the lowest risk classification of device involve a notified body. Notified bodies are often private entities and are authorized or licensed to perform such assessments by government authorities. Manufacturers usually have some flexibility to select a notified body for the conformity assessment procedures for a particular class of device and to reflect their circumstances, e.g., the likelihood that the manufacturer will make frequent modifications to its products. Conformity assessment procedures require an assessment of available clinical evidence, literature data for the product and post-market experience in respect of similar products already marketed. Notified bodies also may review the manufacturer's quality systems. If satisfied that the product conforms to the relevant essential requirements, the notified body issues a certificate of conformity, which the manufacturer uses as a basis for its own declaration of conformity and application of the CE Mark. Application of the CE Mark allows the general commercializing of a product in the EU. The product can also be subjected to local registration requirements depending on the country. We maintain CE Marking on all of our products that require such markings as well as local registrations as required.

Pharmaceutical Coverage, Pricing and Reimbursement

In both domestic and foreign markets, our sales of any approved drug products will depend in part on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products, if approved, unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of our products will therefore depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by third-party payors. These third-party payors are increasingly focused on containing healthcare costs by challenging the price and examining the cost-effectiveness of medical products and services.

In addition, significant uncertainty exists as to the coverage and reimbursement status of newly approved healthcare product candidates. The market for our product candidates for which we may receive regulatory approval will depend significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or another alternative is available. Furthermore, third-party payor reimbursement to providers for our product candidates may be subject to a bundled payment that also includes the procedure administering our products. To the extent there is no separate payment for our product candidates, there may be further uncertainty as to the adequacy of reimbursement amounts.

Because each third-party payor individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming, costly and sometimes unpredictable process. We may be required to provide scientific and clinical support for the use of any product to each third-party payor separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. This process could delay the market acceptance of any product and could have a negative effect on our future revenues and operating results. We cannot be certain that our product candidates will be considered cost-effective. Because coverage and reimbursement determinations are made on a payor-by-payor basis, obtaining acceptable coverage and reimbursement from one payor does not guarantee the Company will obtain similar acceptable coverage or reimbursement from another payor. If we are unable to obtain coverage of, and adequate reimbursement and payment levels for, our product candidates from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition and future success.

Furthermore, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the Company placing the medicinal product on the market. We may face competition for our product candidates from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

Healthcare Reform

In the United States and foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations as we begin to directly commercialize our products.

In particular, there have been and continue to be a number of initiatives at the U.S. federal and state level that seek to reduce healthcare costs. Initiatives to reduce the federal deficit and to reform healthcare delivery are increasing cost-containment efforts. We anticipate that Congress, state legislatures and the private sector will continue to review and assess alternative benefits, controls on healthcare spending through limitations on the growth of private health insurance premiums and Medicare and Medicaid spending, the creation of large insurance purchasing groups, price controls on pharmaceuticals and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit or eliminate our spending on development projects and affect our ultimate profitability.

In the future, there may continue to be additional proposals relating to the reform of the United States healthcare system, some of which could further limit the prices we are able to charge for our products candidates, or the amounts of reimbursement available for our product candidates. If future legislation were to impose direct governmental price controls and access restrictions, it could have a significant adverse impact on our business. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts. Some states have implemented, and other states are considering, price controls or patient access constraints under the Medicaid program, and some states are considering price-control regimes that would apply to broader segments of their populations that are not Medicaid-eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payor or policy actions, which may include cost containment and healthcare reform measures. Such policy actions could have a material adverse impact on our profitability.

The federal Drug Supply Chain Security Act imposes obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Manufacturers will be required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. Further, under this new legislation, manufacturers will have drug product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Other Regulatory Requirements

Maintaining substantial compliance with appropriate federal, state and local statutes and regulations requires the expenditure of substantial time and financial resources. Drug manufacturers are required to register their establishments with the FDA and certain state agencies, and after approval, the FDA and these state agencies conduct periodic unannounced inspections to ensure continued compliance with ongoing regulatory requirements, including cGMPs. In addition, after approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval.

The FDA may require post-approval testing and surveillance programs to monitor safety and the effectiveness of approved products that have been commercialized. Any drug products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including:

- record-keeping requirements;
- reporting of adverse experiences with the drug;
- providing the FDA with updated safety and efficacy information;
- reporting on advertisements and promotional labeling;
- drug sampling and distribution requirements; and
- complying with electronic record and signature requirements.

In addition, the FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. There are numerous regulations and policies that govern various means for disseminating information to health-care professionals as well as consumers, including to industry sponsored scientific and educational activities, information provided to the media and information provided over the Internet. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label.

The FDA has very broad enforcement authority and the failure to comply with applicable regulatory requirements can result in administrative or judicial sanctions being imposed on us or on the manufacturers and distributors of our approved products, including warning letters, refusals of government contracts, clinical holds, civil penalties, injunctions, restitution and disgorgement of profits, recall or seizure of products, total or partial suspension of production or distribution, withdrawal of approvals, refusal to approve pending applications, and criminal prosecution resulting in fines and incarceration. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. In addition, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market.

Other Healthcare Laws

Because of our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors, we will also be subject to healthcare regulation and enforcement by the federal government and the states and foreign governments in which we will conduct our business, including our clinical research, proposed sales, marketing and educational programs. Failure to comply with these laws, where applicable, can result in the imposition of significant civil penalties, criminal penalties, or both. The U.S. laws that may affect our ability to operate, among others, include: the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information; certain state laws governing the privacy and security of health information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts; the federal healthcare programs' Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs; federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent; federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters; the Physician Payments Sunshine Act, which requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members; and state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers.

In addition, many states have similar laws and regulations, such as anti-kickback and false claims laws that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, to the extent that our products are sold in a foreign country, we may be subject to similar foreign laws.

C. Organizational structure

The registrant corporation, Altamira Therapeutics Ltd., had seven wholly-owned subsidiaries as of December 31, 2021, which are each listed in Exhibit 8.1 filed hereto. We primarily operate our business out of our operating subsidiary Auris Medical AG.

D. Property, plants and equipment

Our registered office is in Hamilton, Bermuda. We also lease approximately 4,700 square feet of office space in Basel, Switzerland. This property serves as the corporate headquarters of our principal operating subsidiary.

ITEM 4A. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

You should read the following discussion and analysis of our financial condition and results of operations together with our audited consolidated financial statements, including the notes thereto, included in this Annual Report. The following discussion is based on our financial information prepared in accordance with IFRS as issued by the IASB, which might differ in material respects from generally accepted accounting principles in other jurisdictions. The following discussion includes forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including but not limited to those described under "Item 3. Key Information—D. Risk factors" and elsewhere in this Annual Report.

A. Operating results

Overview

We are a company dedicated to developing therapeutics that address important unmet medical needs. We are currently active in three areas: the development of RNA therapeutics for delivery to extrahepatic targets (with AM-401 targeting KRAS driven cancers as first project, preclinical stage), the development of intranasal betahistine for the treatment of vertigo (AM-125, in Phase 2). Through our affiliate Altamira Medica, we are commercializing a nasal spray for protection against airborne viruses and allergens (Bentrio™ / AM-301).

To date, we have financed our operations through public offerings of our common shares, private placements of equity securities, and short- and long-term loans. As of December 31, 2021, we had cash and cash equivalents of CHF 1.0 million and an accumulated deficit of CHF 176.0 million. In 2021, we started to commercialize our first product, Bentrio™. Based on our current plans, we expect to continue incurring losses as we continue our clinical and pre-clinical development programs, apply for marketing approval for our product candidates and build a sales and marketing force. We do not expect to generate royalty or product revenues sufficient to fund our operations unless and until we achieve substantially higher royalty or product revenues from the commercialization of Bentrio™, complete the development of AM-125 and successfully commercialize the product, and / or from out-licensing or other partnering transactions.

Collaboration and License Agreements

Washington University

In 2020, we entered into an Exclusive License Agreement with Washington University located in St. Louis, Missouri ("WU"), which Exclusive License Agreement was subsequently amended and restated in June 2021, with effect as of December 11, 2020. Pursuant to the agreement, WU granted us an exclusive, worldwide, royalty-bearing license (with the right to sublicense) during the term of the agreement under certain patent rights owned or controlled by WU to research, develop, make, have made, sell, offer for sale, use and import pharmaceutical products covered under such patent rights for all fields of use. Such licensed products may include drug products formulated as nanoparticles, comprising a peptide for delivery as well as a therapeutic nucleotide, for intracellular delivery. In consideration for such worldwide, exclusive license, we will be obligated to pay WU: annual license maintenance fees in the low five figures through first commercial sale; pre-clinical and clinical regulatory milestones; sales milestones; and a low single digit royalty based on annual net sales of licensed products worldwide for at least the applicable patent term or period of marketing exclusivity, whichever is longer, but in no case less than a minimum royalty term of 12 years; and a percentage share (in the double digits) of sublicensing revenues received by us in connection with licensed products. Such regulatory and sales milestones may total up to an aggregate of $4,375,000. In the event we fail to meet certain regulatory diligence milestones, WU will have the right to terminate the license.

INSERM

In 2006, we entered into a co-ownership/exploitation agreement with the INSERM, a publicly funded government science and technology agency in France. Pursuant to the terms of the agreement, we were granted the exclusive right to exploit any products derived from patents that resulted from our joint research program with INSERM that was conducted in 2003 to 2005 and led to the development of Keyzilen®. Pursuant to the terms of the co-ownership/exploitation agreement, we were given the exclusive right to exploit the patents issuing from the filed patent applications for all claimed applications, including the treatment of tinnitus, in order to develop, promote, manufacture, cause to be manufactured, use, sell and distribute any products, processes or services deriving from such patents, including Keyzilen®, in any country in which these patent applications have been filed during the term of the agreement.

As consideration for the exclusive rights granted to us under the agreement, we agreed to pay INSERM a two tiered low single digit percentage royalty (where the higher rate is due on any net sales above a certain threshold) on the net sales of any product covered by the patents (including the use of Keyzilen® in the treatment of tinnitus triggered by cochlear glutamate excitotoxicity) earned in each country in which these patent applications have been filed during the term of the agreement. We have also agreed to pay INSERM a low double-digit fee on any sums of any nature (except royalties and certain costs) collected by us in respect of the granting of licenses to third parties.

Xigen

In October 2003, we entered into a collaboration and license agreement with Xigen, pursuant to which Xigen granted us an exclusive worldwide license to use specified compounds to develop, manufacture and commercialize "pharmaceutical products as well as drug delivery devices and formulations for local administration of therapeutic substances to the inner ear for the treatment of ear disorders" (the Area). We also have a right of first refusal to license certain additional compounds developed by Xigen which may be used for the Area, specifically any cell permeable inhibitors to effectively block certain signal pathways in apoptotic processes.

Under this agreement, we made an upfront payment to Xigen of CHF 200,000 and we are obligated to make development milestone payments on an indication-by-indication basis of up to CHF 1.5 million and regulatory milestone payments on a product-by-product basis of up to CHF 2.5 million, subject to a mid-twenties percentage reduction for smaller indications, e.g., those qualifying for orphan drug status. To date, we have paid CHF 1.325 million to Xigen under the agreement. We will be required to pay Xigen a mid-single digit percentage royalty on net sales of each licensed product that uses a compound licensed under the agreement, which royalty for a given indication shall be partially offset by milestone payments we have paid for such indication, until the later of 10 years after the first commercial sale of any licensed product using such licensed compound in any country, and the first expiration of a patent owned by or exclusively licensed to Xigen that covers the use of such licensed compound in any country, subject to our obligation to enter into good faith negotiations with Xigen, upon expiration of the relevant patent on a licensed compound, about the conditions of our further use of such licensed compound.

Otifex

On February 2, 2017, we entered into an asset purchase agreement with Otifex Therapeutics Pty Ltd ("Otifex"), pursuant to which we agreed to purchase and Otifex agreed to sell us certain pre-clinical and clinical assets related to a formulation for the intranasal application of betahistine, which we refer to as AM-125, as well as associated intellectual property rights. We are developing the formulation for the treatment of vertigo. The Otifex transaction closed in July 2017.

Financial Operations Overview

We expect our regular total cash need in 2022 to be in the range of CHF 11 to 13 million. Further cash needs may arise in 2022 related to the AM-125 and AM-401 programs as a function of their advancement and subject to additional funding.

Research and development expense

Research and development expense consists principally of:

- salaries for research and development staff and related expenses, including employee benefits;
- costs for production of pre-clinical compounds, drug substances and drug products by contract manufacturers;
- fees and other costs paid to contract research organizations in connection with additional pre-clinical testing and the performance of clinical trials;
- costs of related facilities, materials and equipment;
- costs associated with obtaining and maintaining patents;
- costs related to the preparation of regulatory filings and fees; and
- depreciation, amortization and impairment of tangible and intangible fixed assets used to develop our product candidates.

Our research and development expense mainly relates to the following key programs:

- AM-125 for Vertigo. We are evaluating the safety and efficacy of AM-125 in the "TRAVERS" Phase 2 trial, which started in the third quarter of 2019 and is conducted in several European countries. The trial is enrolling a total of 118 patients suffering from acute vertigo following neurosurgery. In September 2020 we announced the results of an interim analysis from Part A of the trial, which comprised a dose escalation – 1, 10 or 20 mg or placebo – in 33 patients. The interim analysis showed a dose-dependent improvement in balance as well as good safety and tolerability of ascending doses of AM-125. Based on the results from the interim analysis, we selected the two highest doses, 10 and 20 mg, for testing against placebo in 72 patients in Part B of the trial. Prior to starting Part B of the trial in October 2020, we tested oral betahistine (48 mg) open label for reference purposes. Enrollment into TRAVERS has been impacted by the COVID-19 pandemic, as the type of neurosurgery required for participation in the trial is classified as an elective procedure and hence was postponed and as many participating sites temporarily reduced or suspended clinical research activities. We completed enrollment in February 2022. Apart from the clinical evaluation, we have been conducting various preclinical studies with AM-125 and working on the analytical and process development for the manufacturing of the drug product.

- AM-201 for Antipsychotic-Induced Weight Gain. We conducted a Phase 1b trial in Europe with AM-201 in antipsychotic-induced weight gain. Participants received either AM-201 (1, 2.5, 5, 10, 20 or 30 mg) or placebo in parallel with oral olanzapine (10 mg) once a day for four weeks. In May 2020, we announced that at AM-201 30 mg, the mean weight gain from baseline to the end of the treatment period was 2.8 kg compared against 3.7 kg in control subjects; the primary efficacy endpoint of mean reduction in weight gain was 0.9 kg and statistically significant ($p<0.02$; n=81 with pre-specified Bayesian augmented controls). There were no activities in 2021 related to the AM-201 program.

- Bentrio™ for Protection Against Airborne Allergens and Viruses: In September 2020 we announced the launch of the development of AM-301, a drug-free nasal spray for protection against airborne viruses and allergens. Following formulation development, we tested AM-301 in vitro in a series of experiments using reconstituted human nasal epithelia infected with SARS-CoV-2 or H1N1 influenza virus. Daily treatment with AM-301, beginning right before inoculation or 24-30 hours thereafter showed significant reductions of the viral titer compared to saline treated controls. In 2021 we conducted an open-label randomized cross-over study with AM-301 that enrolled 36 patients with allergic rhinitis caused by grass pollen. Study participants were administered a single dose of Bentrio™ nasal spray or hydroxypropylmethylcellulose, a comparator product, prior to controlled pollen exposure for four hours in an allergen challenge chamber. The challenge was repeated with the alternate treatment following a wash-out period. The study demonstrated a rapid onset and long durability of Bentrio's protective effect, established substantial equivalence to the marketed comparator with superior efficacy ratings by patients and clinicians, and showed good tolerability. Further, we prepared a randomized placebo-controlled clinical trial with AM-301 in COVID-19, and in December 2021 we initiated enrollment into a randomized open-label trial with AM-301 and saline nasal spray as control in seasonal allergic rhinitis and into an open-label clinical trial with AM-301 in perennial allergic rhinitis (PAR) with controlled house dust mite exposure.

- *AM-401* for KRAS Driven Cancer. Through the acquisition of Trasir we entered the field of RNA therapeutics. In July 2021 we announced the selection of KRAS-driven cancer as the first therapeutic indication for our OligoPhore™ oligonucleotide delivery platform and our intention to develop an RNA therapeutic under the development code of AM-401. In this context, we initiated various development work relating to the peptide and siRNA components of AM-401.

Other research and development expenses mainly relate to the maintenance of our late-stage projects Sonsuvi® (AM-111) and Keyzilen® (AM-101) and pre-clinical studies of AM-102 (second generation tinnitus treatment).

For the years ended December 31, 2021, 2020 and 2019, we spent CHF 2.8 million, CHF 2.7 million and CHF 4.3 million, respectively, on research and development expenses related to our intranasal betahistine program (before capitalization of expenses related to AM-125). For the year ended December 31, 2021 and 2020, we spent CHF 4.8 million and 0.8 million on research and development expenses related to AM-301. For the same time periods, we spent CHF 0.1 million, CHF 0.1 million, and CHF 0.5 million, respectively, on research and development expenses related to Keyzilen®. For the same time periods, we spent CHF 0.1 million, CHF 0.1 million, and CHF 0.1 million, respectively, on research and development expenses related to Sonsuvi®. In addition, we incurred research and development expenses related to our earlier stage products.

The level of research and development expenses related to AM-301 is expected to decrease in 2022 as development projects will complete, and further in 2023. On the other hand, research and development expenses related to AM-125 are expected to increase from 2022 onward as we expect to initiate another Phase 2 clinical trial and move also into Phase 3 clinical development. At this time, we cannot reasonably estimate the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, or the period, if any, in which material net cash inflows may commence from any of our product candidates. This is due to numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress, results and cost of our clinical trials, nonclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any products that we may develop;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals and payer discussions;
- the cost and timing of establishing sales, marketing, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, and other arrangements that we may establish, including any required milestone and royalty payments thereunder.

A change in the outcome of any of these variables with respect to the development of AM-125, AM-301, AM-401, or any other product candidate that we may develop could mean a significant change in the costs and timing associated with the development of such product candidate. For example, if the FDA or other regulatory authority were to require us to conduct pre-clinical and clinical studies beyond those which we currently anticipate will be required for the completion of clinical development or if we experience significant delays in enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of the clinical development.

In the context of our strategic repositioning, we have decided to deprioritize the development of Sonsuvi® (AM-111), Keyzilen® (AM-101) and AM-201 and to seek their divestiture. We therefore do not expect to incur any or any meaningful research and development expenses for these programs in 2022.

Sales and marketing expense

In 2021, we incurred for the first time ever sales and marketing expenses as we prepared for and carried out the market launch of Bentrio™ in selected European countries. The expenses amounted to CHF 1.5 million and consisted principally of:

- Fees for advertising and public relations agencies and consultants;
- Costs for advertisements on TV, in printed media and online media;
- Product samplings;
- Salaries for marketing and sales staff and related expenses, including employee benefits; and
- Listing fees.

General and administrative expense

Our general and administrative expense consists principally of:

- salaries for general and administrative staff and related expenses, including employee benefits;
- business development expenses, including travel expenses;
- administration expenses including professional fees for auditors and other consulting expenses not related to research and development activities, professional fees for lawyers not related to the protection and maintenance of our intellectual property and IT expenses;
- cost of facilities, communication and office expenses; and
- depreciation and amortization of tangible and intangible fixed assets not related to research and development activities.

Interest income

Our policy is to invest funds in low risk investments including interest bearing deposits. Saving and deposit accounts generate a small amount of interest income.

Interest expense

In 2021 and 2020, our interest expense consisted principally of interest due on the convertible loan provided by FiveT.

Revaluation loss/gain from derivative financial instruments

Expenses related to fair value measurement of derivatives embedded in the FiveT convertible loan of CHF 416,003 were recorded as financial expenses in profit or loss.

On February 21, 2017, we issued 10,000,000 (pre-merger) warrants in connection with a registered offering of 10,000,000 common shares (the "February 2017 Registered Offering"), each warrant entitling its holder to purchase 0.70 of a common share at an exercise price von $ 1.20 (pre-merger). Additionally, the underwriter was granted a 30-day option to purchase up to 1,500,000 (pre-merger) additional common shares and/or 1,500,000 (pre-merger) additional warrants. On February 15, 2017, the underwriter partially exercised its option for 1,350,000 (pre-merger) warrants. Revaluation gain/(loss) show the changes in fair value of the warrant issued in connection with this offering. As of December 31, 2021, the outstanding warrants issued in the February 2017 offering were exercisable for up to 39,725 common shares at an exercise price of $240.00 per common share. As of December 31, 2021, the fair value of the warrants amounted to CHF 0. The revaluation loss of the derivative for the twelve months ended December 31, 2021 amounted to CHF 0 (2020: CHF 0). Since its initial recognition on February 21, 2017, the fair value decreased by CHF 5,091,817, resulting in a gain in the corresponding amount (fair value as of February 21, 2017: CHF 5,091,817).

On January 30, 2018 we issued warrants in connection with a direct offering of 62,499 common shares, each warrant entitling its holder to purchase 0.6 common share at an exercise price of $100.00 per common share. As of December 31, 2021, the warrants were exercisable for an aggregate of 37,501 of our common shares (assuming we decide to round up fractional common shares to the next whole common share), at an exercise price of $100.00 per common share. Revaluation gain/(loss) show the changes in fair value of the warrant issued in connection with this offering. As of December 31, 2021, the fair value of the warrants amounted CHF 1,233. The revaluation gain of the derivative for the twelve months ended December 31, 2021 amounted to CHF 5,085, compared to 2020 where there was a revaluation loss of CHF 1,965. Since its initial recognition on January 30, 2018, the fair value of the warrants has decreased by CHF 2,482,514 resulting in a gain in the corresponding amount (fair value as of January 30, 2018: CHF 2,483,747).

On July 17, 2018, the Company issued Series A warrants each entitling its holder to purchase 0.35 of a common share for an aggregate of 314,102 common shares, and Series B warrants entitling its holder to purchase 0.25 of a common share for an aggregate of 224,358 common shares in connection with the July 2018 Registered Offering of 897,435 common shares. The original exercise price was CHF 7.80 per common share. Revaluation gain/(loss) show the changes in fair value of the outstanding Series B warrant issued in connection with this offering. As of December 31, 2019, 145,226 Series A warrants were exercised for an aggregate amount of CHF 1,132,762 and 143,221 Series B warrants were exercised for an aggregate amount of CHF 1,117,125.

As of December 31, 2019, 143,221 Series B exercised warrants were subject to revaluation at the time that they were exercised and the fair value amounted to CHF 3,005,348 (2018: CHF 3,005,348). Since its initial recognition on July 17, 2018 the fair value of the warrants has increased by CHF 2,433,099, resulting in a loss in the corresponding amounts (fair value as of July 17, 2018: CHF 572,249).

As of December 31, 2019, the number of Series B warrants outstanding subject to revaluation were 34,535 and the fair value amounted to CHF 0.00. On June 18, 2020, the outstanding warrants expired without further warrants being exercised. As a result, no further revaluation gain or loss was recognized for the year ended December 31, 2020 (fair value as of July 17, 2018: CHF 137,987).

Foreign currency exchange gain/(loss), net

Our foreign currency exchange gain/(loss), net, consists primarily of unrealized gains or losses on our USD and EUR denominated cash and cash equivalents. We do not hedge our investments by currency borrowings or other hedging instruments.

Transaction costs

Transaction costs are shown as costs if they are not directly attributable to the equity transaction. Transaction costs decreased by CHF 219,615 to zero in the year ended December 31, 2021 compared to the previous year. In 2020, the costs related to the write-off of the remaining capitalized derivate financial instrument related to a commitment purchase agreement with LPC dated May 2, 2018 (the "2018 Commitment Purchase Agreement").

Other comprehensive loss

Remeasurements of the net defined benefit liability, which comprise actuarial gains and losses, the return on plan assets (excluding interest) and the effect of the asset ceiling (if any, excluding interest), are recognized in other comprehensive loss.

Assets and liabilities of our subsidiaries with functional currency other than CHF are included in our consolidated financial statements by translating the assets and liabilities into CHF at the exchange rates applicable at the end of the reporting period. Income and expenses for each consolidated statement of profit or loss and other comprehensive income are translated at average exchange rates (unless this average is not a reasonable approximation of the cumulative effect of the rates prevailing on the transaction dates, in which case income and expenses are translated at the dates of the transaction).

Foreign currency differences arising from translating the financial statements of our subsidiaries from currencies other than CHF are recognized in other comprehensive income and presented in the foreign currency translation reserve under equity in the statement of financial position. When a foreign operation is disposed of such that control, significant influence or joint control is lost, the cumulative amount in the translation reserve related to that foreign operation is reclassified to profit or loss as part of the gain or loss on disposal.

Results of Operations

The numbers below have been derived from our consolidated financial statements included elsewhere herein. The discussion below should be read along with these consolidated financial statements and it is qualified in its entirety by reference to them.

Comparison of the years ended December 31, 2021 and 2020

	Year Ended December 31,		
	2021	2020	Change
	(in thousands of CHF)		%
Revenue	64	-	n/a
Cost of goods sold	(2,241)	-	n/a
Gross profit	**(2,177)**	**-**	**n/a**
Other income	461	174	165%
Research and development	(8,939)	(2,863)	212%
Sales and marketing	(1,498)	-	n/a
General and administrative	(4,947)	(2,594)	91%
Operating loss	**(17,100)**	**(5,283)**	**224%**
Interest income	3	0	100%
Interest expense	(190)	(135)	41%
Foreign currency exchange gain / (loss), net	329	(333)	(199)%
Revaluation gain / (loss) from derivative financial instruments	(411)	(2,250)	(82)%
Transaction costs	-	(220)	(100)%
Loss before tax	**(17,369)**	**(8,221)**	**111%**
Income tax gain/(loss)	(21)	21	(205)%
Net loss attributable to owners of the Company	**(17,390)**	**(8,200)**	**112%**
Other comprehensive loss:			
Items that will never be reclassified to profit or loss			
Re-measurements of defined benefits liability, net of taxes of CHF 0	265	(26)	(1,119)%
Items that are or may be reclassified to profit or loss			
Foreign currency translation differences, net of taxes of CHF 0	1	89	(99)%
Other comprehensive loss	266	63	322%
Total comprehensive loss attributable to owners of the Company	**(17,124)**	**(8,137)**	**110%**

Revenue and cost of goods sold

In 2021, we recorded our first revenues of CHF 0.1 million as we launched Bentrio™ starting in the summer through online pharmacies in Germany and Austria and, based upon additional stability data which allowed to extend the product's shelf life to a suitable range, from December also through stationary pharmacies in Germany. Cost of goods sold of CHF 2.2 million comprised the relevant manufacturing costs for Bentrio™ incurred through our contract manufacturer, expenses for storage and shipments, including set-up costs for our third-party central warehouse in Europe, as well as inventory write-offs. The latter concerned products in inventory at December 31, 2021 with only short remaining shelf life and / or in labelling and packaging configurations (stock keeping units, "SKUs") for certain European countries where approval of certain marketing materials and messages was still pending.

Other income

Other income increased 165% from CHF 0.2 million in 2020 to CHF 0.5 million in 2021 as we booked for the first-time research and development tax credits related to clinical projects.

Research and development expense

	Year Ended December 31,		
	2021	2020	Change
	(in thousands of CHF)		%
Research and development expense			
Clinical projects	(2,958)	(477)	520%
Pre-clinical projects	(587)	(243)	142%
Product and process development	(1,100)	(615)	79%
Employee benefits	(1,897)	(1,121)	69%
Other research and development expenses	(2,397)	(407)	489%
Total	**(8,939)**	**(2,863)**	**212%**

Research and development expense increased by 212% from CHF 2.9 million in 2020 to CHF 8.9 million in 2021. Our research and development expense is dependent on the development phases of our research projects and may therefore fluctuate significantly from year to year. The variances in expense between 2020 and 2021 are mainly due to the following factors:

- *Capitalization of internal costs for AM-125*. In the year ended December 31, 2021, we capitalized direct costs related to our AM-125 program for a total amount of CHF 2.8 million, compared to CHF 2.3 million in the year ended December 31, 2020.

- *Clinical projects*. In the year ended December 31, 2021, we incurred higher service and milestone costs due to our clinical development with AM-301, reflecting the completion of a clinical investigation in allergic rhinitis (pollen, single dose), the preparation of a study in COVID-19 patients as well as the initiation of studies in seasonal allergic rhinitis (pollen, repeated dosing) and perennial allergic rhinitis (house dust mite, repeated dosing). In 2020, expenses for clinical projects were related to the completion of a clinical trial with AM-201 in antipsychotic-induced weight gain and preparations for the allergic rhinitis study with AM-301.

- *Pre-clinical projects*. In the year ended December 31, 2021, pre-clinical expenses increased by 142% principally due to the conduct of in vitro and in vivo studies with AM-301.

- *Product and process development*. In the year ended December 31, 2021, expenses increased by 79% mainly due to the scale-up and validation of the manufacturing process for AM-301 as well as analytical development for AM-301. In 2021 they also included for the first-time expenses related to the development of AM-401.

- *Employee benefits*. Employee benefit costs rose in 2021 due to higher headcount and increases in recruiting fees and share-based bonus payments.

- *Other research and development expenses*. Other research and development expenses increased by CHF 2.0 million in the year ended December 31, 2021 compared to the year ended December 31, 2020 primarily due to impairment costs related to our AM-101, AM-111 and AM-201 programs of CHF 1.5 million related to our strategic decision to reposition the Company around RNA therapeutics. In addition, we incurred higher expenses for patents and regulatory affairs as we filed intellectual property around AM-301 and compiled the technical dossier for the declaration of conformity for AM-301 in the EU and submitted a 510(k) application for premarket clearance for AM-301 to the FDA.

Sales and marketing expense

	Year Ended December 31,		
	2021	2020	Change
	(in thousands of CHF)		%
Sales and marketing expense			
Marketing and sales expenses	(1,133)	-	-%
Employee benefits and expenses	(204)	-	-%
Product samples	(161)	-	-%
Total	**(1,498)**	-	-%

In 2021, we incurred sales and marketing expenses of CHF 1.5 million, which were primarily related to costs for the creation and production of advertisement and other marketing materials, online campaigns, employee benefits, consulting and product samplings.

General and administrative expense

	Year Ended December 31,		
	2021	2020	Change
	(in thousands of CHF)		%
General and administrative expense			
Employee benefits	(1,555)	(811)	92%
Business development	(967)	(96)	907%
Travel expenses	(76)	(29)	162%
Administration expenses	(2,246)	(1,646)	36%
Lease expenses	(52)	(14)	271%
Depreciation tangible assets	(30)	(4)	650%
Capital tax expenses	(21)	6	300%
Total	**(4,947)**	**(2,594)**	**91%**

General and administrative expenses increased by 91% from CHF 2.6 million in 2020 to CHF 4.9 million in the year ended December 31, 2021. The increase was primarily related to higher headcount and share-based bonus payments, business development activities related to Bentrio™ and higher consulting expenses.

Interest income

Interest income increased in the year ended December 31, 2021 compared to year the ended December 31, 2020 due to higher balances on interest-bearing short-term deposits.

Interest expense

Interest expense in the year ended December 31, 2021 as well as in December 31, 2020 included mainly the interest accrued on the convertible loan provided by FiveT Capital.

Foreign currency exchange gain/(loss), net

In 2021, we recorded a foreign currency exchange gain of CHF 0.3 million compared to a loss of CHF 0.3 million in 2020 as the Swiss Franc depreciated against some of the major currencies.

Revaluation gain/(loss) from derivative financial instruments

Expenses related to fair value measurement of derivatives embedded in the FiveT convertible loan of CHF 416,003 were recorded as financial expenses in profit or loss for the financial year 2021 compared to CHF 2.3 million in 2020.

On February 21, 2017, we issued 10,000,000 (pre-merger) warrants, each warrant entitling its holder to purchase 0.70 of a common share at an exercise price of $1.20. Additionally, the underwriter was granted a 30-day option to purchase up to 1,500,000 (pre-merger) additional common shares and/or 1,500,000 (pre-merger) additional warrants. On February 15, 2017, the underwriter partially exercised its option for 1,350,000 (pre-merger) warrants. Revaluation gain/(loss) shows the changes in fair value of the warrants issued in connection with this offering. As of December 31, 2021, the outstanding warrants issued in the February 2017 offering were exercisable for up to 39,725 common shares at an exercise price of $240.00 per common share. As of December 31, 2021, the fair value of the warrants amounted to CHF 0. The revaluation loss of the derivative for the twelve months ended December 31, 2021 amounted to CHF 0 (2020: CHF 0). Since its initial recognition as of February 21, 2017, the fair value decreased by CHF 5,091,817 resulting in a gain in the corresponding amount (fair value as of February 21, 2017: CHF 5,091,817).

On January 30, 2018 we issued warrants in connection with a direct offering of 62,499 common shares, each warrant entitling its holder to purchase 0.6 common share at an exercise price of $100.00 per common share. As of December 31, 2020, the warrants were exercisable for an aggregate of 37,501 of our common shares (assuming we decide to round up fractional common shares to the next whole common share). Revaluation gain/(loss) shows the changes in fair value of the warrants issued in connection with this offering. As of December 31, 2021, the fair value of the warrants amounted to CHF 1,233. The revaluation gain of the derivative for the twelve months ended December 31, 2021 amounted to CHF 5,085, compared to 2020 where there was a revaluation loss of CHF 1,965. Since its initial recognition on January 30, 2018, the fair value of the warrants decreased by CHF 2,482,514 resulting in a gain in the corresponding amount (fair value as of January 30, 2018: CHF 2,483,747).

On July 17, 2018, the Company issued Series A warrants each entitling its holder to purchase 0.35 of a common share for an aggregate of 314,102 common shares, and Series B warrants entitling its holder to purchase 0.25 of a common share for an aggregate of 224,358 common shares in connection with the July 2018 Registered Offering of 897,435 common shares. The original exercise price was CHF 7.80 per common share. Revaluation gain/(loss) shows the changes in fair value of the outstanding Series B warrants issued in connection with this offering.

On June 18, 2020, the remaining 34,535 outstanding Series B warrants expired without further warrants being exercised. As a result, no further revaluation gain or loss was recognized for the year ended December 31, 2020 (fair value as of July 17, 2018: CHF 137,987).

Income tax gain/(loss)

Income tax gain/(loss) reflects the assessment of deferred tax assets and liabilities.

Remeasurements of defined benefits liability

Remeasurements of the net defined benefits liability, which comprise actuarial gains and losses, the return on plan assets (excluding interest) and the effect of the asset ceiling (if any, excluding interest), increased 1,119% from a negative adjustment in the amount of CHF 26,000 in 2020 to a positive adjustment of CHF 0.3 million in 2021. The gain in 2021 is primarily due to a change in demographic and financial assumptions, and a higher return on plan assets.

Foreign currency translation differences

Foreign currency translation differences decreased by 99% from CHF 0.1 million in 2020 to a negligible amount in 2021. The decrease was primarily related to changes in the opening and closing balance of the group's currency translation differences.

Comparison of the years ended December 31, 2020 and 2019

	Year Ended December 31,		
	2020	**2019**	**Change**
	(in thousands of CHF)		**%**
Other operating income	174	—	100%
Research and development	(2,863)	(3,325)	(14)%
General and administrative	(2,594)	(3,934)	(34)%
Operating loss	**(5,283)**	**(7,259)**	**(27)%**
Interest income	0	18	(100)%
Interest expense	(135)	(29)	366%
Foreign currency exchange loss, net	(333)	(219)	52%
Revaluation gain / (loss) from derivative financial instruments	(2,250)	664	(439)%
Transaction Costs	(220)	—	(100)%
Loss before tax	**(8,221)**	**(6,825)**	**20%**
Income tax gain/(loss)	21	194	(89)%
Net loss attributable to owners of the Company	**(8,200)**	**(6,631)**	**24%**
Other comprehensive loss:			
Items that will never be reclassified to profit or loss			
Re-measurements of defined benefits liability, net of taxes of CHF 0	(26)	(72)	(64)%
Items that are or may be reclassified to profit or loss			
Foreign currency translation differences, net of taxes of CHF 0	89	16	456%
Other comprehensive loss	63	(56)	(213)%
Total comprehensive loss attributable to owners of the Company	**(8,137)**	**(6,687)**	**22%**

Research and development expense

	Year Ended December 31,		
	2020	2019	Change
	(in thousands of CHF)		%
Research and development expense			
Clinical projects	(477)	(993)	(52)%
Pre-clinical projects	(243)	(182)	34%
Drug manufacture and substance	(615)	(481)	28%
Employee benefits	(1,121)	(1,374)	(18)%
Other research and development expenses	(407)	(295)	38%
Total	**(2,863)**	**(3,325)**	**(14)%**

Research and development expense decreased by 14% from CHF 3.3 million in 2019 to CHF 2.9 million in 2020. Our research and development expense is dependent on the development phases of our research projects and may therefore fluctuate significantly from year to year. The variances in expense between 2019 and 2020 are mainly due to the following factors:

- Capitalization of internal costs for AM-125. In the year ended December 31, 2020, we capitalized direct costs related to our AM-125 program for a total amount of CHF 2.3 million, compared to CHF 3.2 million in the year ended December 31, 2019.

- Clinical projects. In the year ended December 31, 2020, we incurred lower service and milestone costs for our studies with intranasal betahistine, mainly reflecting the completion of Phase 1b trial with AM-201.

- Pre-clinical projects. In the year ended December 31, 2020, pre-clinical expenses increased by 33% principally due to the initiation of our AM-301 project activities.

- Drug manufacture and substance. In the year ended December 31, 2020, drug manufacture and substance expenses increased by 28% mainly due to AM-301 project activities.

- Employee benefits. Employee benefit costs decreased in 2020 due to lower headcount and lower recruiting fees. In addition, we received reimbursements under the Swiss short-time work scheme, which was used for three months in connection with a temporary reduction in project activities due to the COVID-19 pandemic.

- Other research and development expenses. Other research and development expenses increased by CHF 0.1 million in the year ended December 31, 2020 compared to the year ended December 31, 2019 primarily due to AM-301 regulatory costs.

General and administrative expense

	Year Ended December 31,		
	2020	2019	Change
	(in thousands of CHF)		%
General and administrative expense			
Employee benefits	(811)	(1,011)	(20)%
Business development	(96)	(114)	(16)%
Travel expenses	(29)	(103)	(72)%
Administration expenses	(1,646)	(2,653)	(38)%
Lease expenses	(14)	(27)	(48)%
Depreciation tangible assets	(4)	(11)	(64)%
Capital tax expenses	6	(15)	(133)%
Total	**(2,594)**	**(3,934)**	**(34)%**

General and administrative expenses decreased by 34% from CHF 3.9 million in 2019 to CHF 2.6 million in the year ended December 31, 2020. The decrease is related to lower employee benefits due to lower headcount and reimbursements under the Swiss short-time work scheme, which was used for three months in connection with a temporary reduction in company activities due to the COVID-19 pandemic. Administration costs decreased mainly due to lower consultancy costs (redomestication in the previous period) and lower headcount.

Interest income

Interest income decreased in the year ended December 31, 2020 compared to year the ended December 31, 2019 due to no interest earned in the year ended December 31, 2020 on short-term deposits.

Interest expense

Interest expense in 2020 includes interest related to the convertible loan agreement with FiveT Capital. This compares to CHF 0.03 million in the year ended December 31, 2019 which was related to the Hercules loan.

Foreign currency exchange gain/(loss), net

Foreign currency exchange loss increased in 2020 mainly due to the depreciation of the USD and EUR against the Swiss Franc.

Revaluation gain/(loss) from derivative financial instruments

Expenses related to fair value measurement of derivatives embedded in the FiveT convertible loan of CHF 2,250,222 were recorded as financial expenses in profit or loss for the financial year 2020.

On January 31, 2019, we made the final payment to Hercules under the facility, comprising the last amortization payment as well as an end of term charge. With the final payment, all covenants and collaterals in favor of Hercules have been lifted. In addition, Hercules agreed to return the warrant held by Hercules exercisable for 783 common shares at an exercise price of $788 per common share for no consideration to us in exchange for our payment to Hercules.

On February 21, 2017, we issued 10,000,000 (pre-merger) warrants, each warrant entitling its holder to purchase 0.70 of a common share at an exercise price of $1.20. Additionally, the underwriter was granted a 30-day option to purchase up to 1,500,000 (pre-merger) additional common shares and/or 1,500,000 (pre-merger) additional warrants. On February 15, 2017, the underwriter partially exercised its option for 1,350,000 (pre-merger) warrants. Revaluation gain/(loss) show the changes in fair value of the warrant issued in connection with this offering. As of December 31, 2020, the outstanding warrants issued in the February 2017 offering were exercisable for up to 39,725 common shares at an exercise price of $240.00 per common share. As of December 31, 2020, the fair value of the warrants amounted to CHF 0. The revaluation loss of the derivative for the twelve months ended December 31, 2020 amounted to CHF 0, compared to 2019 where there was a revaluation gain of CHF 166,301. Since its initial recognition as of February 21, 2017, the fair value decreased by CHF 5,091,817, resulting in a gain in the corresponding amount (fair value as of February 21, 2017: CHF 5,091,817).

On January 30, 2018 we issued warrants in connection with a direct offering of 62,499 common shares, each warrant entitling its holder to purchase 0.6 common share at an exercise price of $100.00 per common share. As of December 31, 2020, the warrants became exercisable for an aggregate of 37,501 of our common shares (assuming we decide to round up fractional common shares to the next whole common share), at an exercise price of $100.00 per common share. Revaluation gain/(loss) show the changes in fair value of the warrant issued in connection with this offering. As of December 31, 2020, the fair value of the warrants amounted CHF 6,318. The revaluation loss of the derivative for the twelve months ended December 31, 2020 amounted to CHF 1,965, compared to 2019 where there was a revaluation gain of CHF 285,298. Since its initial recognition on January 30, 2018, the fair value of the warrants has decreased by CHF 2,477,429 resulting in a gain in the corresponding amount (fair value as of January 30, 2018: CHF 2,483,747).

On July 17, 2018, the Company issued Series A warrants each entitling its holder to purchase 0.35 of a common share for an aggregate of 314,102 common shares, and Series B warrants entitling its holder to purchase 0.25 of a common share for an aggregate of 224,358 common shares in connection with the July 2018 Registered Offering of 897,435 common shares. The original exercise price was CHF 7.80 per common share. Revaluation gain/(loss) shows the changes in fair value of the outstanding Series B warrants issued in connection with this offering.

As of December 31, 2019, 145,226 Series A warrants were exercised for an aggregate amount of CHF 1,132,762 and 143,221 Series B warrants were exercised for an aggregate amount of CHF 1,117,125.

As of December 31, 2019, 143,221 Series B exercised warrants were subject to revaluation at the time that they were exercised and the fair value amounts to CHF 3,005,348 (2018: CHF 3,005,348). Since its initial recognition on July 17, 2018 the fair value of the warrants has increased by CHF 2,433,099, resulting in a loss in the corresponding amounts (fair value as of July 17, 2018: CHF 572,249).

As of December 31, 2019, the number of Series B warrants outstanding subject to revaluation were 34,535 and the fair value amounted to CHF 0.00. On June 18, 2020, the outstanding warrants expired without further warrants being exercised. As a result, no further revaluation gain or loss was recognized for the year ended December 31, 2020 (fair value as of July 17, 2018: CHF 137,987).

Income tax expense

Income tax expense reflects the assessment of deferred tax assets and liabilities.

Remeasurements of defined benefits liability

Remeasurements of the net defined benefits liability, which comprise actuarial gains and losses, the return on plan assets (excluding interest) and the effect of the asset ceiling (if any, excluding interest), decreased 64% from 2019 to 2020. The loss in 2020 is primarily due to an actuarial loss arising from experience adjustment.

Foreign currency translation differences

Foreign currency translation differences increased by 456% from 2019 to 2020. The increase was primarily related to changes in the opening and closing balance of the group's currency translation differences.

B. Liquidity and capital resources

Since inception, we have incurred significant operating losses. Only in 2021 we started to generate revenue. We have financed our operations through the public offerings of our common shares, private placements of equity securities and short-term loans.

Cash flow

Comparison of the years ended December 31, 2021 and 2020

The table below summarizes our consolidated statement of cash flows for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	**2020**
	(in thousands of CHF)	
Net cash used in operating activities	(13,673)	(4,844)
Net cash used in investing activities	(3,505)	(2,315)
Net cash from financing activities	6,614	16,961
Net effect of currency translation on cash	289	72
Cash and cash equivalents at the beginning of the period	11,259	1,385
Cash and cash equivalents at the end of the period	**984**	**11,259**

The increase in cash used in operating activities from CHF 4.8 million in 2020 to CHF 13.7 million in 2021 primarily reflects the increase in research and development activities, the increase in headcount, the market launch of Bentrio™ as well as the related increase in net working capital.

Cash used in investing activities increased from CHF 2.3 million in 2020 to CHF 3.5 million in 2021. The increase is primarily due to higher purchases of intangible assets related to AM-125 as well as the payment of the cash component of the Trasir acquisition price.

The cash inflow from financing activities decreased from CHF 17.0 million in 2020 to CHF 6.6 million in 2021 due to lower proceeds from equity issues and the exercise of warrants. Also, in 2020 we had obtained CHF 1.5 million through the provision of the FiveT convertible loan.

Comparison of the years ended December 31, 2020 and 2019

The table below summarizes our consolidated statement of cash flows for the years ended December 31, 2020 and 2019:

	Year Ended December 31,	
	2020	**2019**
	(in thousands of CHF)	
Net cash used in operating activities	(4,844)	(8,393)
Net cash used in investing activities	(2,315)	(3,001)
Net cash from financing activities	16,961	7,378
Net effect of currency translation on cash	72	8
Cash and cash equivalents at the beginning of the period	1,385	5,393
Cash and cash equivalents at the end of the period	**11,259**	**1,385**

The decrease in cash used in operating activities from CHF 8.4 million in 2019 to CHF 4.8 million in 2020 reflects the impact of lower operating expenses primarily driven by lower project activities as the COVID-19 pandemic weighed on enrollment rates for the TRAVERS trial with AM-125, the conclusion of the Phase 1b trial with AM-201 and lower consultancy costs.

Cash used in investing activities decreased from CHF 3.0 million in 2019 to CHF 2.3 million in 2020. The decrease is due to lower investments in intangible assets in 2020.

The cash inflow from financing activities increased from CHF 7.4 million to CHF 17.0 million due to higher proceeds from equity issues, the exercise of warrants as well the provision of the FiveT convertible loan.

Cash and funding sources

The table below summarizes our sources of financing for the years ended December 31, 2021, 2020 and 2019.

	Equity Capital and Preference Shares	**Loans**	**Total**
	(in thousands of CHF)		
2021	6,686	—	6,686
2020	15,438	1,550	16,988
2019	8,845	—	8,845
Total	30,969	1,550	32,519

On February 4, 2022, the Company entered into a convertible loan agreement (the "Loan Agreement") with FiveT Investment Management Ltd. (the "Lender"), pursuant to which the Lender has agreed to loan to the Company CHF 5,000,000 (the "Loan"), which Loan bears interest at the rate of 10% per annum and matures 12 months from the date (the "Disbursement Date") the Loan proceeds were disbursed to the Company, which occurred on February 8, 2022. The Company may prepay all or part of the Loan after six months after the Disbursement Date; provided that the Company will pay an amount equal to 130% of the desired prepayment amount. The Lender has the right to convert all or part of the Loan, including accrued and unpaid interest, at its option, into common shares, subject to the limitation that the Lender own no more than 9.99% of the common shares at any time. The conversion price of the Loan into common shares is USD 1.9458, which corresponds to 150% of USD 1.2972 (the trading volume weighted average price, the "VWAP", per common share on the NASDAQ stock exchange on the Disbursement Date), converted into Swiss Francs at the midpoint of the interbank exchange rate shown by UBS on the day of receipt of the conversion notice at 4:00 pm Central European Time. The conversion price shall be lowered in the event that the Company raises equity before the maturity date of the Loan through a public or private offering of common shares at an issue price that is at least 10 (ten) % below the VWAP (the "New Issue"), according to the formula set forth in the Loan Agreement (the "Adjustment"). Sales of common shares through equity line or at-the-market programs are not considered New Issues triggering the Adjustment.

On December 3, 2020, the Company entered into securities purchase agreements with several institutional investors for the purchase and sale of 2,000,000 common shares at an offering price of $4.00 per share, pursuant to a registered direct offering. The net proceeds of the offering were approximately $7.3 million.

On September 8, 2020, FiveT provided a convertible loan to our subsidiary Altamira. The loan had a principal amount of CHF 1.5 million, a duration of 18 months, and carried an interest rate of 8% p.a. Under the terms of the agreement, FiveT had the right to convert the loan or parts thereof including accrued interest into common shares of either Altamira or Auris Medical Holding Ltd., subject to additional provisions and certain restrictions. On December 2, 2020, FiveT converted principal of CHF 895,455 into 737,000 shares of Auris Medical Holding Ltd. at the pre-defined maximum conversion price of $1.35 per share. At December 31, 2020, the remaining principal amount outstanding together with accrued interest was CHF 636,465. Under the terms and conditions of the convertible loan, we had the right to repay the convertible loan and accrued interest at 130% after the first six months at the earliest On March 4, 2021, FiveT converted the remaining outstanding amount under the loan, thus retiring the loan.

Due to the COVID-19 pandemic, in 2020 Swiss banks granted special loans under certain conditions with a guarantee by the Swiss Government. Our Company was eligible for a loan of CHF 50,000, which was granted on March 26, 2020. The loan is interest-free and may be repaid at any time with a maximum term of five years. The company repaid the loan on June 18, 2021.

On April 23, 2020, the Company entered into a purchase agreement and a Registration Rights Agreement with Lincoln Park Capital Fund, LLC (the "2020 Commitment Purchase Agreement"). Pursuant to the purchase agreement, LPC agreed to subscribe for up to USD 10,000,000 of our common shares over the 30-month term of the purchase agreement. In 2020, we issued 1,200,000 of our common shares to LPC for an aggregate amount of USD 1.1 million. At the date of this annual report, we have sold 1,500,000 of our common shares to LPC for a total amount of USD 1.6 million. The 2020 Commitment Purchase Agreement effectively replaced the 2018 Commitment Purchase Agreement. Under the 2018 Commitment Purchase Agreement LPC agreed to purchase common shares for up to $10,000,000 over the 30-month term of the Purchase Agreement. Prior to its termination we had issued 587,500 common shares for aggregate proceeds of $1.8 million to LPC under the 2018 Commitment Purchase Agreement. The 2018 Commitment Purchase Agreement replaced the Purchase Agreement that we entered into with LPC on October 10, 2017 (the "2017 Commitment Purchase Agreement"), which was terminated as a result of the Merger. Under the 2017 Commitment Purchase Agreement, LPC agreed to subscribe for up to $13,500,000 of our common shares, and prior to its termination, we had issued an aggregate of 2,600,000 (pre-merger) common shares for aggregate proceeds of $1.8 million to LPC under the 2017 Commitment Purchase Agreement.

Under the 2020 Commitment Purchase Agreement, we have the right, from time to time at our sole discretion over the 30-month period from and after May 12, 2020, to require LPC to subscribe for up to 150,000 of our common shares, subject to adjustments as set forth below (such maximum number of shares, as may be adjusted from time to time, the "Regular Purchase Share Limit"; each such purchase, a "Regular Purchase"); provided, however, that (i) the Regular Purchase Share Limit shall be increased to 300,000 of our common shares if the total number of outstanding common shares on the purchase date exceeds 10,000,000, (ii) the Regular Purchase Share Limit shall be increased to 350,000 of our common shares if the closing sale price of our common shares is not below $1.00 on the purchase date and the total number of outstanding common shares on the purchase date exceeds 12,500,000 and (iii) the Regular Purchase Share Limit shall be increased to 400,000 of our common shares if the closing sale price of our common shares is not below $1.00 on the purchase date and the total number of outstanding common shares on the purchase date exceeds 15,000,000. The Regular Purchase Share Limit is subject to proportionate adjustment in the event of a reorganization, recapitalization, non-cash dividend, stock split or other similar transaction; provided, that if after giving effect to such full proportionate adjustment, the adjusted Regular Purchase Share Limit would preclude us from requiring LPC to subscribe for common shares at an aggregate purchase price equal to or greater than $150,000 in any single Regular Purchase (which dollar threshold shall not be adjusted for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction), then the Regular Purchase Share Limit for such Regular Purchase will not be fully adjusted, but rather the Regular Purchase Share Limit for such Regular Purchase shall be adjusted as specified in the 2020 Commitment Purchase Agreement, such that, after giving effect to such adjustment, the Regular Purchase Share Limit will be equal to (or as close as can be derived from such adjustment without exceeding) $150,000. We may not require LPC to purchase in any single Regular Purchase common shares having an aggregate purchase price greater than $1,000,000 (which dollar threshold shall not be adjusted for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction). We may not issue any of our common shares as a Regular Purchase on a date in which the closing sale price of our common shares is below the sum of (x) the U.S. Dollar equivalent of the then applicable par value per common share and (y) $0.01 (which dollar amount shall not be subject to adjustment for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction). The purchase price for Regular Purchases shall be equal to the lesser of (i) the lowest sale price of our common shares on the applicable purchase date and (ii) the average of the three lowest closing sale prices of our common shares during the 10 business days immediately prior to the applicable purchase date, as reported on the Nasdaq Capital Market.

In addition to Regular Purchases described above, we may also direct LPC to purchase "accelerated amounts" and/or "additional accelerated amounts" on any business day on which we have properly submitted a Regular Purchase Notice, and/or an Accelerated Purchase (as defined elsewhere in this prospectus) has been completed and all of the shares to be purchased thereunder have been properly delivered to LPC in accordance with the 2020 Commitment Purchase Agreement prior to such time on such business day, and provided that the closing price of our common shares on such business day is not less than $1.00 per share. In all instances, we may not issue common shares to LPC under the 2020 Commitment Purchase Agreement if it would result in LPC beneficially owning more than 4.99% of our outstanding common shares. The net proceeds under the 2020 Commitment Purchase Agreement will depend on the frequency and prices at which we issue our common shares to LPC.

On May 15, 2019, the Company completed a public offering of (i) 440,000 common shares with a par value of CHF 0.40 each, together with warrants to purchase 440,000 common shares, and (ii) 1,721,280 pre-funded warrants, with each pre-funded warrant exercisable for one common share, together with warrants to purchase 1,721,280 common shares, including 110,000 common shares and warrants to purchase 110,000 common shares sold pursuant to a partial exercise by the underwriters of the underwriters' over-allotment option (the "May 2019 Registered Offering"). The exercise price for the pre-funded warrants was CHF 0.01 per common share and for the warrants CHF 4.34. In December 2020, 1,263,845 warrants were exercised at a total exercise price of CHF 5.5 million; at December 31, 2020 a total of 897,435 warrants were still outstanding. In March 2021, the remaining warrants were exercised for CHF 3.9 million.

On November 30, 2018, we entered into the A.G.P. Sales Agreement with A.G.P. Pursuant to the terms of the A.G.P. Sales Agreement, as amended on April 5, 2019, we may offer and sell our common shares, from time to time through A.G.P. by any method deemed to be an "at-the-market" offering as defined in Rule 415(a)(4) promulgated under the Securities Act. Pursuant to the A.G.P. Sales Agreement, we may sell common shares up to a maximum aggregate offering price of $25.0 million. In 2021, we sold 1,184,700 shares under the ATM for aggregate proceeds of $3.5 million. As of the date of this Annual Report, we have sold 2,943,318 of our common shares for an aggregate offering price of $6.7 million pursuant to the A.G.P. Sales Agreement.

We have no other ongoing material financial commitments, such as lines of credit or guarantees that are expected to affect our liquidity over the next five years, other than leases.

Funding requirements

We expect that we will need additional funding. We expect our total cash need in 2022 to be in the range of CHF 11 to 13 million. As part of our strategic repositioning, we are aiming to spin off or divest our traditional development projects in neurotology, rhinology and allergology, which may provide us with additional sources of funding.

As of the date of this Annual Report we have warrants outstanding, which are exercisable for an aggregate of 246,102 common shares at a weighted average exercise price of $59.85 per share, an equity commitment to sell up to $8.4 million of additional common shares to LPC pursuant to the LPC Purchase Agreement and an at-the-market offering program pursuant to the A.G.P. Sales Agreement for sales of up to $18.3 million of additional common shares.

We have based our estimate of funding requirements on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future funding requirements will depend on many factors, including but not limited to:

- the scope, rate of progress, results and cost of our clinical trials, nonclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any product that we may develop;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing sales, marketing, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, and other arrangements that we may establish, including any required milestone and royalty payments thereunder.

We expect that we will require additional funding to complete our development programs with AM-125, AM-AM-301, and AM-401, obtain regulatory approval for them and to commercialize our product candidates AM-125 AM-401 or any other product candidate and to further advance the market roll-out of Bentrio™. If we receive regulatory approval for AM-125 or AM-401, and if we choose not to grant any licenses to partners, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize. Additional funds may not be available on a timely basis, on favorable terms, or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long-term business strategy. If we are not able to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We may raise additional capital through the sale of equity or convertible debt securities. In such an event, your ownership interest will be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect your rights as a holder of our common shares.

For more information as to the risks associated with our future funding needs, see “Item 3. Key Information—D. Risk factors.”

Significant accounting policies and use of estimates and judgment

Our management’s discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with IFRS. The preparation of these financial statements requires us to make judgments, estimates and assumptions that affect the application of accounting policies and the reported amounts of assets, liabilities, income and expenses. Actual results may differ from these estimates.

While our significant accounting policies are more fully described in the notes to our audited consolidated financial statements appearing elsewhere in this Annual Report, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Intangible assets

Research and development

The project stage forms the basis for the decision as to whether costs incurred for the Company's development projects can be capitalized. For the AM-125 program, given the current stage of the development project, the nature of the development approach and the fact that there is an existing market for oral betahistine, direct development expenditures have been capitalized, including certain expenses related to the patenting of intellectual property.

Intellectual property-related costs for patents are part of the expenditure for the research and development projects. Therefore, registration costs for patents are expensed when incurred as long as the research and development project concerned does not meet the criteria for capitalization.

Licenses, Intellectual Property and Data rights

Intellectual property rights that are acquired by the Company are capitalized as intangible assets if they are controlled by the Company, are separately identifiable and are expected to generate future economic benefits, even if uncertainty exists as to whether the research and development will ultimately result in a marketable product. Consequently, upfront and milestone payments to third parties for the exclusive use of pharmaceutical compounds in specified areas of treatment are recognized as intangible assets.

Measurement

Intangible assets acquired that have finite useful lives are measured at cost less accumulated amortization and any accumulated impairment losses.

Subsequent expenditure

Subsequent expenditure is capitalized only when it increases the future economic benefits embodied in the specific asset to which it relates. All other expenditure, including expenditure on internally generated goodwill and brands, is recognized in profit or loss as incurred.

Amortization

All licenses of the Company have finite lives. Amortization will start once the Company's intangible assets are available for use. Amortization of licenses is calculated on a straight-line basis over the period of the expected benefit or until the license expires. The estimated useful life of the Company's licenses is 10 years from the date first available for use or the remaining term of patent protection. The Company assesses at each balance sheet date whether intangible assets which are not yet ready for use are impaired.

Income tax

Income tax expense comprises current and deferred tax. It is recognized in profit or loss except to the extent that it relates to a business combination, or items recognized directly in equity or in other comprehensive income/loss, or OCI.

Current tax

Current tax comprises the expected tax payable or receivable on the taxable income or loss for the year and any adjustment to tax payable or receivable in respect of previous years. It is measured using tax rates enacted or substantively enacted at the reporting date. Taxable profit differs from "loss before tax" as reported in the consolidated statement of profit or loss and other comprehensive loss because of items of income or expense that are taxable or deductible in other years and items that are never taxable or deductible.

Deferred tax

Deferred income tax is recognized, using the balance sheet liability method, on temporary differences arising between the tax bases of assets and liabilities and their carrying amounts in the consolidated financial statements. Deferred tax is not recognized for:

- temporary differences on the initial recognition of assets or liabilities in a transaction that is not a business combination and that affects neither accounting nor taxable profit or loss;
- temporary differences related to investments in subsidiaries to the extent that the Company is able to control the timing of the reversal of the temporary differences and it is probable that they will not reverse in the foreseeable future; and
- taxable temporary differences arising on the initial recognition of goodwill.

Deferred income tax is determined using tax rates and laws that have been enacted or substantively enacted by the balance sheet date and are expected to apply when the related deferred income tax asset is realized or the deferred income tax liability is settled.

Deferred income tax assets are recognized to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilized. Deferred tax assets are reviewed at each reporting date and are reduced to the extent that it is no longer probable that the related tax benefit will be realized.

Deferred tax assets and liabilities are offset when there is a legally enforceable right to set off tax assets against tax liabilities and when they relate to income taxes levied by the same taxation authority and the Company intends to settle its tax assets and liabilities on a net basis.

Employee benefits

The Company maintains a pension plan for all employees employed in Switzerland through payments to an independent collective foundation. Under IFRS, the pension plan qualifies as a defined benefit plan. There are no pension plans for the subsidiaries in Ireland, Australia and the United States.

The Company's net obligation in respect of defined benefit plans is calculated by estimating the amount of future benefit that employees have earned in return for their service in the current and prior periods, discounting that amount and deducting the fair value of any plan assets.

The recognized asset is limited to the present value of economic benefits available in the form of any future refunds from the plan or reductions in future contributions to the plan. In order to calculate the present value of economic benefits, consideration is given to any minimum funding requirements.

Remeasurements of the net defined benefit liability, which comprise actuarial gains and losses, the return on plan assets (excluding interest) and the effect of the asset ceiling (if any, excluding interest), are recognized immediately in OCI. The Company determines the net interest expense (income) on the net defined benefit liability (asset) for the period by applying the discount rate used to measure the defined benefit obligation at the beginning of the annual period to the then-net defined benefit liability (asset), taking into account any changes in the net defined benefit liability (asset) during the period as a result of contributions and benefit payments. Net interest expense and other expenses related to defined benefit plans are recognized in profit or loss.

Share-based compensation

Stock Options

The Company maintains a share-based payment plan in the form of a stock option plan for its employees, members of the Board of Directors as well as key service providers. Stock options are granted at the Board's discretion without any contractual or recurring obligations.

The share-based compensation plan qualifies as an equity settled plan. The grant-date fair value of share-based payment awards granted to employees is recognized as an expense, with a corresponding increase in equity, over the period that the employees become unconditionally entitled to the awards. Under the Company's equity incentive plan (the "Equity Incentive Plan" or "EIP") adopted in August 2014 and amended in April 2017 and June 2019, 50% of granted share options granted to employees vest after a period of service of two years from the grant date and the remaining 50% vest after a period of service of three years from the grant date. Share options granted to members of the Board of Directors from 2016 onwards vest after a period of one year after the grant date.

The amount recognized as an expense is adjusted to reflect the number of awards for which the related service and non-market performance conditions are expected to be met, such that the amount ultimately recognized as an expense is based on the number of awards that meet the related service and non-market performance conditions at the vesting date. Share-based payments that are not subject to any further conditions are expensed immediately at grant date. In the year the options are exercised the proceeds received net of any directly attributable transaction costs are credited to share capital (par value) and share premium.

Valuation of stock options

The fair value of our stock options is determined by our Management and our Board of Directors and takes into account numerous factors to determine a best estimate of the fair value of our share options as of each grant date.

Option pricing and values are determined based on the Black Scholes option pricing model, and assumptions are made for inputs such as volatility of our stock and the risk-free rate.

Recent accounting pronouncements

See Note 4 to our audited financial statements included elsewhere in this Annual Report for a full description of recent accounting pronouncements, including the expected dates of adoption and effects on the Company's financial condition, results of operations and cash flows.

C. Research and development, patents and licenses, etc.

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

D. Trend information

See "Item 5. Operating and Financial Review and Prospects."

E. Critical Accounting Estimates

Not applicable.

F. Safe harbor

See "Forward-Looking Statements."

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and senior management

Our directors have been elected for a one-year term and, accordingly, the term will expire at the time of our 2022 annual general meeting. All directors except Calvin W. Roberts will stand for re-election.

The following table presents information about our executive officers and directors.

Name	Position	Age	Initial Year of Appointment
Executive Officers			
Thomas Meyer	Chairman, Director and Chief Executive Officer	54	2003
Samuel A. Wickline	Chief Scientific Officer	69	2021
Marcel Gremaud	Chief Financial Officer	64	2021
Non-Executive Directors			
Armando Anido	Director	64	2016
Mats Blom	Director	57	2017
Alain Munoz	Director	72	2018
Calvin W. Roberts	Director	69	2015
Margrit Schwarz	Director	58	2021

Unless otherwise indicated, the current business addresses for our executive officers and directors is Altamira Therapeutics Ltd., Clarendon House, 2 Church Street, Hamilton HM 11, Bermuda.

Executive Officers

Thomas Meyer, Founder, Chairman of the Board of Directors and Chief Executive Officer: Mr. Meyer founded Auris Medical in April 2003. Prior to founding us, he was the Chief Executive Officer of Disetronic Group, a leading Swiss supplier of precision infusion and injection systems. He worked for Disetronic in various functions starting in 1988, becoming member of the Board of Directors in 1996, Deputy Chief Executive Officer in 1999 and Chief Executive Officer in early 2000. Prior to joining Disetronic, he advised several Swiss companies in strategy, marketing and corporate finance. He is currently the Chairman of the Board of Directors of PharmaTrail Ltd. He holds a Ph.D. (Dr.rer.pol.) in business administration from the University of Fribourg, Switzerland.

Samuel A. Wickline, Chief Scientific Officer: Mr. Wickline, MD, is the founder of Trasir Therapeutics, Inc., which we acquired in 2021 and formed the basis for our activities in RNA therapeutics. Before joining Altamira Therapeutics, he was the Director of the USF Health Heart Institute, Associate Dean and Chair in Cardiovascular Medicine, Professor of Cardiovascular Sciences, Molecular Physiology and Pharmacology, and Medical Engineering at the University of South Florida (USF). Previously, he was Professor of Medicine, Physics, Biomedical Engineering, and Cell Biology and Physiology at Washington University, St. Louis.

Marcel Gremaud, Chief Financial Officer: Mr. Gremaud, CPA, has been Altamira Therapeutics' Chief Financial Officer since November 2021. Mr. Gremaud has acquired more than 30 years' experience in controlling and accounting in international pharma companies and start-ups. In 2001 he founded Gremaud GmbH, an audit and accounting company supporting companies in financial consolidation and accounting in accordance with IFRS or Swiss GAAP FER.

Non-Executive Directors

Armando Anido, Director, Chairman of the Compensation Committee: Mr. Anido has been a member of our Board of Directors since April 2016. Mr. Anido has more than 30 years of executive, operational and commercial leadership experience in the biopharmaceutical industry. He has served as Chairman and Chief Executive Officer of Zynerba Pharmaceuticals, Inc., since October 2014. Prior to Zynerba, Mr. Anido served as Chief Executive Officer of NuPathe, Inc., and Auxilium Pharmaceuticals, Inc. Prior to Auxilium, Mr. Anido held commercial leadership roles at MedImmune, Glaxo Wellcome and Lederle Labs. He is currently a member of the Board of Directors of SCYNEXIS, Inc. (SCYX), and he was a member of the Board of Directors of Aviragen Therapeutics, Inc. until it merged with Vaxart Inc. (VXRT) and Adolor Corporation until it was sold to Cubist Pharmaceuticals. Mr. Anido earned a BS in Pharmacy and an MBA from West Virginia University.

Mats Blom, Director: Mr. Blom has been a member of our Board of Directors since April 2017. Mr. Blom is Chief Financial Officer (CFO) of NorthSea Therapeutics B.V., a biotechnology company focused on oral, structurally engineered lipid therapeutics. Prior to joining NorthSea, he served as CFO of Modus Therapeutics A/B, a biotechnology company developing therapeutics to restore healthy blood flow for patients with debilitating diseases, Zealand Pharma A/B, a biotechnology company focused on the discovery, design and development of innovative peptide-based medicines, and Swedish Orphan International, an orphan drug company acquired by BioVitrum in 2009. In addition, Mr. Blom has extensive managerial experience and has held CFO positions at Active Biotech AB and Anoto Group AB. Previously, he served as a management consultant at Gemini Consulting and Ernst & Young. He is currently a member of the Board of Directors of Hansa Biopharma AB (HNSA), Egetis Therapeutics AB (EGTX) and Pephexia Therapeutics ApS. Mats Blom holds a BA in Business Administration and Economics from the University of Lund and an MBA from IESE University of Navarra, Barcelona.

Alain Munoz, Director: Mr. Munoz, MD, has been a member of our Board of Directors since March 2018 and previously served on our Board of Directors between 2007 and 2015. Mr. Munoz is an entrepreneur and independent management consultant in the pharmaceutical and biotechnology industry. From 1990 to 2000, Dr. Munoz worked with the Fournier Group, as Research and Development Director and then Senior Vice President of the Pharmaceutical Division. He joined Fournier from Sanofi Research, where he started as Director in the cardiovascular and anti-thrombotic products department and then as Vice President international development. Dr. Munoz is qualified in cardiology and anesthesiology from the University Hospital of Montpellier, France where he was head of the clinical cardiology department. He has been a member of the Scientific Committee of the French drug agency. He serves on the Board of Zealand Pharma A/S (ZEAL.CO) and Amryt Pharma Plc (AMYT.L). He is Chairman of the Board of Acticor Biotech (ALACT.PA and a member of the Scientific Advisory Board of Valneva (VLA.PA).

Calvin W. Roberts, Director: Mr. Roberts, MD, has been a member of our Board of Directors since April 2015. Mr. Roberts is President and CEO of Lighthouse Guild International, a not for profit provider of services to the blind and visually impaired. Previously, he was Senior Vice President and Chief Medical Officer, Eye Care at Bausch Health Companies Inc. (NYSE: BHC). Dr. Roberts is a specialist in cataract and refractive surgery and has been a pioneer in the use of ophthalmic non-steroidals. Since 1982 he has been a Clinical Professor of Ophthalmology at Weill Medical College of Cornell University. In addition, he had a private ophthalmology practice in New York City between 1998 and 2008 and is the author of over 50 peer-reviewed articles. Dr. Roberts was a member of the Board of Directors and the Audit Committee of Alimera Sciences, Inc. (NASDAQ: ALIM) from its founding in 2003 until 2019, and of Iveric Bio Corporation (NASDAQ: ISEE) since 2019.

Margrit Schwarz, Director: Ms. Schwarz has been a member of our Board of Directors since July 2021. She currently serves as Chief Business Officer of HepareGeniX, a clinical-stage biotechnology company in the liver regeneration space. Prior executive positions include Chief Operating Officer of Draupnir Bio, and Chief Scientific Officer and Head of R&D at Genevant Sciences, where she was responsible for developing a portfolio of RNAi and mRNA drug candidates in the liver and rare disease space. Dr Schwarz has also served as VP & Global Head External Innovation at Roche, VP & Therapeutic Area Head Cardiorenal at Boehringer Ingelheim, and Director Research at Amgen. She has led preclinical R&D and IND-enabling phases for multiple development candidates, including the anti-PCSK9 therapeutic antibody Repatha, launched in 2015. She is an Entrepreneur-in-Residence at Novo Seeds and has been a member of the Board of Directors of the KERN Conference since 2009. She holds a PhD in biochemistry from the University of Cologne, Germany, and an MBA from Columbia University, NY.

Board Diversity Matrix (As of March 31, 2022)				
To be completed by Foreign Issuers (with principal executive offices outside of the U.S.) and Foreign Private Issuers				
Country of Principal Executive Offices:	Bermuda			
Foreign Private Issuer	**Yes**			
Disclosure Prohibited Under Home Country Law	**No**			
Total Number of Directors	**6**			
	Female	**Male**	**Non-Binary**	**Did Not Disclose Gender**
Part I: Gender Identity				
Directors	**1**	**5**	**0**	**0**
Part II: Demographic Background				
Underrepresented Individual in Home Country Jurisdiction	**0**			
LGBTQ+	**0**			
Did Not Disclose Demographic Background	**0**			

B. Compensation

For the year ended December 31, 2021, the aggregate compensation accrued or paid to the members of our board of directors and our executive officers for services in all capacities was CHF 946,449 (2020: CHF 947,701).

For the year ended December 31, 2021, the amount set aside or accrued by us to provide pension, retirement or similar benefits to members of our board of directors or executive officers amounted to a total of CHF 29,467 (2020: CHF 26,870).

Compensation awarded to the Board of Directors in 2021

The total compensation of the members of the board of directors in 2021 is outlined below:

In CHF	Cash Compensation	Social Contributions	Stock Options(2)	Total
Thomas Meyer, PhD, Chairman(1)	—	—	—	—
Armando Anido, MBA	41.311	—	12,012	53,323
Mats Blom, MBA	41,311	—	12,012	53.323
Alain Munoz, MD	41,311	—	12,012	53,323
Calvin W. Roberts, MD	41,311	—	12,012	53,323
Margrit Schwarz, PhD	18,491	—	—	18,491
Total	**183,735**	—	**48,048**	**231,783**

(1) Disclosed under "Compensation Awarded to Our Executive Officers" below. The Chief Executive Officer does not receive any additional compensation for the exercise of the office of the Chairman.

(2) In 2021, 10,672 options were granted to each eligible member of the Board of Directors, with an exercise price of USD 3.20 per common share and an expiration date of May 17, 2029. The fair value calculation of the options was based on the Black-Scholes option pricing model. Assumptions were made regarding inputs such as volatility and the risk-free rate in order to determine the fair value of the options.

Compensation Awarded to our Executive Officers in 2021

The total compensation and the highest individual compensation to our executive officers in 2021 are outlined below

in CHF	Fixed Cash Compensation	Variable Compensation (1)	Social contributions and fringe benefits	Stock Options(2)	Total
Thomas Meyer, PhD, Chief Executive Officer(3)	366,000	542,705	109,086	152,665	1,170,456
Executive Officers Total(4)	**523,230**	**542,705**	**144,536**	**192,362**	**1,402,833**

(1) The variable compensation is paid in shares of the company.

(2) 2021 option grants, exercise prices of $3.511 and $1.889, expiration date April 30, 2029 and October 31, 2029, respectively. The fair value calculation of the options was based on the Black-Scholes option pricing model. Assumptions were made regarding inputs such as volatility and the risk-free rate in order to determine the fair value of the options.

(3) Highest paid executive.

(4) On December 31, 2021, we had two executive officers.

Employment Agreements

We have entered into employment and/or consulting agreements with our executive officers Thomas Meyer, Samuel A. Wickline and Marcel Gremaud. The employment and/or consulting agreements provide for the compensation that Messrs. Meyer, Wickline and Gremaud are entitled to receive, including certain equity grants, and the employment agreement of Mr. Meyer contains a termination notice period of six months. The Company will have title to the intellectual property rights developed in connection with the executive officer's employment, if any.

None of our directors has entered into service agreements with the Company. However, we may in the future enter into employment or services agreements with such individuals, the terms of which may provide for, among other things, cash or equity-based compensation and benefits.

Equity Incentive Plans

Equity Incentive Plan

In August 2014, as amended and restated in June 2019, we established the EIP with the purpose of motivating and rewarding those employees and other individuals who are expected to contribute significantly to our success, and advancing the interests of our shareholders by enhancing our ability to attract, retain and motivate individuals. Since January 15, 2021, the maximum number of shares available for issuance under the EIP is 1,500,000 common shares. The option exercise price for options under the EIP is determined by the compensation committee at the time of grant but shall not be less than the par value of a common share on the grant date.

Plan administration. The EIP is administered by our compensation committee. Approval of the committee is required for all grants of awards under the EIP. The committee may delegate to one or more officers the authority to grant options and stock appreciation rights, and the committee may delegate to another committee (which may consist of solely one director) the authority to grant all types of awards.

Eligibility. Any director, employee, consultant or any other individual who provides services to us or any of our affiliates is eligible to be selected to receive an award under the EIP.

Awards. Awards include options, stock appreciation rights, restricted stock, restricted stock units, performance awards and other stock-based awards.

Vesting period. The committee determines the time or times at which an option becomes vested and exercisable, provided that the minimum vesting period is 12 months. The committee may specify in an award agreement that an "in-the-money" option be automatically exercised on its expiration date. For restricted stock and restricted stock units, the award agreement will specify the vesting schedule and, with respect to restricted stock units, the delivery schedule.

Accelerated vesting. Subject to any additional vesting conditions that may be specified in an individual award agreement, the EIP provides that upon a change of control of the Company (as defined in the EIP) the committee may cause options and stock appreciation rights to be cancelled in consideration of full acceleration of the award or a substitute award with equal intrinsic value (as defined in the EIP). It also provides that the committee may decide, or include in any award agreement, the circumstances in which, and the extent to which, an award may be exercised, settled, vested, paid or forfeited in the event of a participant's termination of service prior to exercise or settlement of an award.

Amendment. Our board of directors has the authority to amend the EIP subject, in certain circumstances, to required shareholder approval or the consent of an affected participant.

Indemnification

Section 98 of the Companies Act provides generally that a Bermuda company may indemnify its directors, officers and auditors against any liability which by virtue of any rule of law would otherwise be imposed on them in respect of any negligence, default, breach of duty or breach of trust, except in cases where such liability arises from fraud or dishonesty of which such director, officer or auditor may be guilty in relation to the company. Section 98 further provides that a Bermuda company may indemnify its directors, officers and auditors against any liability incurred by them in defending any proceedings, whether civil or criminal, in which judgment is awarded in their favor or in which they are acquitted or granted relief by the Supreme Court of Bermuda pursuant to section 281 of the Companies Act.

Our Bye-laws provide that we shall indemnify our officers and directors in respect of their actions and omissions, except in respect of their fraud or dishonesty. Our Bye-laws provide that the shareholders waive all claims or rights of action that they might have, individually or in right of the company, against any of the company's directors or officers for any act or failure to act in the performance of such director's or officer's duties, except in respect of any fraud or dishonesty of such director or officer. Section 98A of the Companies Act permits us to purchase and maintain insurance for the benefit of any officer or director in respect of any loss or liability attaching to him in respect of any negligence, default, breach of duty or breach of trust, whether or not we may otherwise indemnify such officer or director. We have purchased and maintain a directors' and officers' liability policy for such a purpose.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, may be permitted to directors, officers and controlling persons of the Company, the Company has been advised that, in the opinion of the Securities and Exchange Commission, such indemnification is against public policy as expressed in the Securities Act of 1933, as amended, and is, therefore, unenforceable.

C. Board practices

Board Composition and Election of Directors

Our board of directors is currently composed of six members, see "Item 6. Directors, Senior Management and Employees—A. Directors and senior management." Each director is elected for a one-year term.

Our Bye-laws provide that directors may be elected at either the annual general meeting or a special general meeting. Unless shareholders determine otherwise, under our Bye-laws directors hold office until the next annual general meeting or until their successors are elected or appointed or their office is otherwise vacated.

We are a foreign private issuer. As a result, in accordance with the Nasdaq stock exchange listing requirements, we comply with home country governance requirements and certain exemptions thereunder rather than the Nasdaq stock exchange corporate governance requirements. For an overview of our corporate governance principles, see "Item 16G. Corporate governance."

Committees of the Board of Directors

Audit Committee

The audit committee, which consists of Mats Blom, Alain Munoz and Calvin W. Roberts, assists our board of directors in overseeing our accounting and financial reporting processes and the audits of our financial statements. In addition, the audit committee is directly responsible for the appointment, compensation, retention and oversight of the work of our independent registered public accounting firm. Mr. Blom serves as chairman of the committee. The audit committee consists exclusively of members of our board of directors who are financially literate, and Mr. Blom is considered an "audit committee financial expert" as defined by the SEC. Our board of directors has determined that Mr. Blom, Mr. Munoz and Mr. Roberts satisfy the "independence" requirements set forth in Rule 10A-3 under the Exchange Act.

The audit committee is governed by a charter that complies with Nasdaq rules. The audit committee is responsible for, among other things:

- the appointment, compensation, retention and oversight of any auditor or accounting firm engaged for the purpose of preparing or issuing an audit report or performing other audit, review or attest services;
- pre-approving the audit services and non-audit services to be provided by our independent auditor before the auditor is engaged to render such services;
- reviewing and discussing with the independent auditor its responsibilities under generally accepted auditing standards, the planned scope and timing of the independent auditor's annual audit plan(s) and significant findings from the audit;
- obtaining and reviewing a report from the independent auditor describing all relationships between the independent auditor and the Company consistent with the applicable PCAOB requirements regarding the independent auditor's communications with the audit committee concerning independence;
- confirming and evaluating the rotation of the audit partners on the audit engagement team as required by law;
- reviewing with management and the independent auditor, in separate meetings whenever the Audit Committee deems appropriate, any analyses or other written communications prepared by the Management and/or the independent auditor setting forth significant financial reporting issues and judgments made in connection with the preparation of the financial statements, including analyses of the effects of alternative IFRS methods on the financial statements; and other critical accounting policies and practices of the Company;
- reviewing, in conjunction with the Chief Executive Officer and Chief Financial Officer of the Company, the Company's disclosure controls and procedures and internal control over financial reporting;
- establishing procedures for the receipt, retention and treatment of complaints received by the Company regarding accounting, internal accounting controls or auditing matters, and the confidential, anonymous submission by employees of the Company of concerns regarding questionable accounting or auditing matters;

- approving or ratifying any related person transaction (as defined in our related person transaction policy) in accordance with our related person transaction policy.

The audit committee meets at least four times per year.

Compensation Committee

The compensation committee, which consists of Armando Anido and Alain Munoz, assists our board of directors in overseeing our cash compensation and equity award recommendations for our executive officers along with the rationale for such recommendations, as well as summary information regarding the aggregate compensation provided to our directors and executive officers. While Bermuda law does not require that we adopt a compensation committee, we have established a compensation committee in accordance with Bermuda law. As a result, our practice varies from the requirements of Nasdaq Listing Rule 5605(d), which sets forth certain requirements as to the responsibilities, composition and independence of compensation committees.

D. Employees

As of December 31, 2021, we had 17 employees (14.5 full time equivalents, FTEs). The breakdown by cost centers is as follows: Research & Development: 10 FTEs, General & Administration: 2.9 FTEs, Sales & Marketing: 1.1 FTEs, Cost of Goods Sold: 0.5 FTEs. 13.5 FTEs were located in Switzerland and 1 FTE in the U.S. None of our employees is subject to a collective bargaining agreement or represented by a trade or labor union. We consider our relations with our employees to be good.

E. Share ownership

See "Item 7. Major Shareholders and Related Party Transactions—A. Major shareholders."

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major shareholders

The following table presents information relating to the beneficial ownership of our common shares as of March 15, 2022 by:

- each person, or group of affiliated persons, known by us to own beneficially 5% or more of our outstanding common shares;
- each of our executive officers and directors; and
- all executive officers and directors as a group.

The number of common shares beneficially owned by each entity, person, executive officer or director is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any common shares over which the individual has sole or shared voting power or investment power as well as any common shares that the individual has the right to acquire within 60 days of March 15, 2022 through the exercise of any option, warrant or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all common shares held by that person.

Common shares that a person has the right to acquire within 60 days of March 28, 2022 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all executive officers and directors as a group. Unless otherwise indicated below, the address for each beneficial owner is Altamira Therapeutics Ltd., Clarendon House, 2 Church Street, Hamilton HM 11, Bermuda.

The percentage of common shares beneficially owned is based on 15,264,261 common shares issued and outstanding as of March 28, 2022. Each common share confers the right on the holder to cast one vote at a general meeting of shareholders and no shareholder has different voting rights.

Shareholder	Shares Beneficially Owned	
	Number	Percent
5% Shareholders		
-	—	—
Executive Officers and Directors		
Thomas Meyer, PhD (1)	1,088,070	7.13%
Armando Anido, MBA (2)	69,990	*
Mats Blom, MBA (3)	69,869	*
Alain Munoz, MD (4)	69,869	*
Calvin W. Roberts, MD (5)	69,974	*
Margrit Schwarz	—	*
Samuel A. Wickline, MD (6)	620,669	4.07%
Marcel Gremaud, CPA	—	*
All current directors and executive officers as a group (8 persons)	1,988,750	13.03%

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

(1) Consists of 836,431 common shares, warrants to purchase 89,744 common shares and options to purchase 161,895 common shares under the EIP.

(2) Consists of options to purchase common shares under the Company's EIP.

(3) Consists of options to purchase common shares under the Company's EIP.

(4) Consists of 62 common shares owned by Alain Munoz and options to purchase common shares under the Company's EIP.

(5) Consists of 76 common shares jointly owned by Calvin W. Roberts and Andrea Colvin Roberts. Also, consists of 100 common shares held by Calvin W. Roberts, MD PC Pension Plan. Calvin Roberts is a trustee for Calvin W. Roberts, MD PC Pension Plan. Also consists of options to purchase common shares under the Company's EIP.

(6) Consists of 620,669 common shares.

Holders

As of March 28, 2022, we had six shareholders of record of our common shares.

Significant Changes in Ownership by Major Shareholders

None

B. Related party transactions

Related Person Transaction Policy

Prior to our initial public offering, we entered into a new related person transaction policy under which any such transaction must be approved or ratified by the audit committee or the board of directors.

Indemnification Agreements

We have entered into indemnification agreements with our directors and executive officers. The indemnification agreements and our Bye-laws require us to indemnify our directors and executive officers to the fullest extent permitted by law.

Employment Agreements

Certain of our executive officers have entered into employment agreements with the Company, certain of which provide for notice of termination periods and include restrictive covenants. None of our directors have entered into service agreements with the Company. See "Item 6. Directors, Senior Management and Employees—B. Compensation—Employment Agreements."

Mandate Agreement

Ante Treuhand AG ("Ante Treuhand") provided the Chief Financial Officer to the Company until November 18, 2021. The Chief Financial Officer is an employee of Ante Treuhand and is not paid directly by the Company. Fees paid to Ante Treuhand for CFO services were CHF 231,770 in 2021 compared to CHF 173,030 in 2020. Fees paid to Ante Treuhand for other services provided during the year ended December 31, 2021 were CHF 18,020 compared to CHF 3,025 in 2020.

Gremaud GmbH provides the Chief Financial Officer to the company since November 18, 2021. The Chief Financial Officer is an employee of Gremaud GmbH and is not paid directly by the Company. Fees paid to Gremaud GmbH for CFO services were CHF 14,720 for 2021. Fees paid to Gremaud GmbH for other services provided during the year ended December 31, 2021 were CHF 161,596 compared to CHF 27,625 in 2020.

C. Interests of experts and counsel

Not applicable.

ITEM 8. FINANCIAL INFORMATION

A. Consolidated statements and other financial information

Financial Statements

See "Item 18. Financial Statements," which contains our financial statements prepared in accordance with IFRS.

Legal Proceedings

From time to time we may become involved in legal proceedings that arise in the ordinary course of business. During the period covered by the financial statements contained herein, we have not been a party to or paid any damages in connection with litigation that has had a material adverse effect on our financial position.

No assurance can be given that future litigation will not have a material adverse effect on our financial position. See "Item 3. Key Information—D. Risk factors."

Dividends and Dividend Policy

We have never paid or declared any cash dividends on our shares, and we do not anticipate paying any cash dividends on our common shares in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and any payment of dividends will, amongst other requirements, be subject to legal restrictions.

B. Significant changes

A discussion of the significant changes in our business can be found under "Item 4. Information on the Company—A. History and development of the Company" and "Item 4. Information on the Company—B. Business Overview."

ITEM 9. THE OFFER AND LISTING

A. Offering and listing details

Not applicable.

B. Plan of distribution

Not applicable.

C. Markets

Our common shares began trading on the Nasdaq Global Market on August 11, 2014 under the symbol "EARS". On September 28, 2017, we transferred our common shares from the Nasdaq Global Market to the Nasdaq Capital Market under the same symbol ("EARS"). On March 14, 2018, our post-Merger common shares began trading on the Nasdaq Capital Market. Following approval of our shareholders at a Special General Meeting of Shareholders held on July 21, 2021 we changed our name from Auris Medical Holding Ltd. to Altamira Therapeutics Ltd., and our shares started trading under the new name and the new ticker symbol "CYTO" on the Nasdaq Capital Market on July 26, 2021.

There can be no assurance that our common shares will remain listed on the Nasdaq Capital Market. See "Item 3. Key Information—D. Risk Factors—Risks Related to Our Common Shares—Our common shares may be involuntarily delisted from trading on The Nasdaq Capital Market if we fail to comply with the continued listing requirements. A delisting of our common shares is likely to reduce the liquidity of our common shares and may inhibit or preclude our ability to raise additional financing."

D. Selling shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the issue

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. Share capital

Not applicable.

B. Memorandum of Continuance and Bye-laws

We are an exempted company incorporated under the laws of Bermuda. On January 24, 2019, our board of directors determined that it would be in our best interest to change our legal seat and jurisdiction of incorporation, respectively, from Switzerland to Bermuda pursuant to the Redomestication. Our shareholders approved the Redomestication and adopted the Memorandum of Continuance and the Bye-laws at an extraordinary meeting of shareholders held on March 8, 2019. Upon the issuance of a certificate of continuance by the Registrar of Companies in Bermuda on March 18, 2019, the Company discontinued as a Swiss company and, pursuant to Article 163 of the Swiss Federal Act on Private International Law and pursuant to Section 132C of the Companies Act continued existence under the Companies Act as a Bermuda company with the name "Auris Medical Holding Ltd."

At a Special General Meeting of Shareholders held on July 21, 2021, the Company adopted the new name "Altamira Therapeutics Ltd." which was registered with the Bermuda Registrar of Companies and a Certificate of Change of Name was issued by the Bermuda Registrar of Companies.

Set forth below is a description of our share capital, Memorandum of Continuance and Bye-laws. Additionally, set forth below is a comparison of select provisions of the corporate laws of Delaware and Bermuda showing the default positions in each jurisdiction that govern shareholder rights.

Bermuda Description of Share Capital

The following description of our share capital summarizes certain provisions of our Memorandum of Continuance (which is equivalent for these purposes to a memorandum of association under Bermuda law) and our Bye-laws. Such summaries do not purport to be complete and are subject to, and are qualified in their entirety by reference to, all of the provisions of our Memorandum of Continuance and Bye-laws in effect from the continuance of the Company. We urge you to read the forms of our Memorandum of Continuance and Bye-laws, included as exhibits to this Annual Report.

General

We are an exempted company incorporated under the laws of Bermuda. We began our current operations in 2003 as a corporation organized in accordance with Swiss law and domiciled in Switzerland under the name Auris Medical AG, and our name was changed to Auris Medical Holding AG on April 22, 2014. Following the Merger on March 13, 2018, the surviving entity was named Auris Medical Holding AG. Upon the issuance of a certificate of continuance by the Registrar of Companies in Bermuda on March 18, 2019, the Redomestication was effected and we continued in Bermuda pursuant to Section 132C of the Companies Act as a Bermuda company, subject to the Companies Act and other laws of Bermuda, with the name "Auris Medical Holding Ltd". At a Special General Meeting of Shareholders held on July 21, 2021, the Company adopted the new name "Altamira Therapeutics Ltd.". Our registered office is located at Clarendon House, 2 Church Street, Hamilton HM 11, Bermuda.

The Memorandum of Continuance provides that the objects of our business are unrestricted, and we have the capacity, rights, powers and privileges of a natural person.

Since the Redomestication, other than the 2019 Reverse Share Split and as otherwise described herein, including the change of the company name to Altamira Therapeutics Ltd. on 21 July 2021, there have been no material changes to our share capital, mergers, amalgamations or consolidations of us or any of our subsidiaries, no material changes in the mode of conducting our business, no material changes in the types of products produced or services rendered and no name changes. There have been no bankruptcy, receivership or similar proceedings with respect to us or our subsidiaries.

There have been no public takeover offers by third parties for our shares nor any public takeover offers by us for the shares of another company which have occurred during the last or current financial years.

Share Capital

As of December 31, 2021, our authorized share capital consisted of 25,000,000 common shares, par value CHF 0.01 per share, and 20,000,000 preference shares, par value CHF 0.02 per share, and there were 14,964,261 common shares issued and outstanding, excluding 1,329,510 common shares issuable upon exercise of options and 246,102 common shares issuable upon exercise of warrants, and no preference shares issued and outstanding. All the Company's issued and outstanding shares are fully paid in.

Pursuant to our Bye-laws, subject to any resolution of the shareholders to the contrary, our board of directors is authorized to issue any of our authorized but unissued shares. There are no limitations on the right of non-Bermudians or non-residents of Bermuda to hold or vote our shares.

Common Shares

Holders of common shares have no pre-emptive, redemption, conversion or sinking fund rights. Holders of common shares are entitled to one vote per share on all matters submitted to a vote of holders of common shares. Unless a different majority is required by law or by our Bye-laws, resolutions to be approved by holders of common shares require approval by a simple majority of votes cast at a general meeting at which a quorum is present.

In the event of our liquidation, dissolution or winding up, the holders of common shares are entitled to share equally and ratably in our assets, if any, remaining after the payment of all of our debts and liabilities, subject to any liquidation preference on any issued and outstanding preference shares.

Preference Shares

Pursuant to Bermuda law and our Bye-laws, our board of directors by resolution may establish one or more series of preference shares having such number of shares, designations, dividend rates, relative voting rights, conversion or exchange rights, redemption rights, liquidation rights and other relative participation, optional or other special rights, qualifications, limitations or restrictions as may be fixed by the board without any further shareholder approval. Such rights, preferences, powers and limitations as may be established could have the effect of discouraging an attempt to obtain control of us.

Dividend Rights

Under Bermuda law, the board of directors may declare a dividend without shareholder approval, but a company may not declare or pay dividends if there are reasonable grounds for believing that: (i) the company is, or would after the payment be, unable to pay its liabilities as they become due; or (ii) the realizable value of its assets would thereby be less than its liabilities. Under our Bye-laws, each common share is entitled to dividends if, as and when dividends are declared by our board of directors, subject to any preferred dividend right of the holders of any preference shares.

Variation of Rights

If at any time we have more than one class of shares, the rights attaching to any class, unless otherwise provided for by the terms of issue of the relevant class, may be varied either: (i) with the consent in writing of the holders of 75% of the issued shares of that class; or (ii) with the sanction of a resolution passed by a majority of the votes cast at a general meeting of the relevant class of shareholders at which a quorum consisting of at least two or more persons holding or representing issued and outstanding shares of the relevant class is present. Our Bye-laws specify that the creation or issue of shares ranking equally with existing shares will not, unless expressly provided by the terms of issue of existing shares, vary the rights attached to existing shares. In addition, the creation or issue of preference shares ranking prior to common shares will not be deemed to vary the rights attached to common shares or, subject to the terms of any other series of preference shares, to vary the rights attached to any other series of preference shares.

Transfer of Shares

Our board of directors may in its absolute discretion and without assigning any reason refuse to register the transfer of a share that it is not fully paid. Our board of directors may also refuse to recognize an instrument of transfer of a share unless it is accompanied by the relevant share certificate and such other evidence of the transferor's right to make the transfer as our board of directors shall reasonably require. Subject to these restrictions, a holder of common shares may transfer the title to all or any of his common shares by completing a form of transfer in the form set out in our Bye-laws (or as near thereto as circumstances admit) or in such other common form as the board may accept. The instrument of transfer must be signed by the transferor and transferee, although in the case of a fully paid share our board of directors may accept the instrument signed only by the transferor.

Share Split and Reverse Share Split effected by consolidating our common shares

Our board of directors may in its absolute discretion and without further approval of shareholders divide, consolidate or sub-divide our share capital in any manner permitted by the Companies Act, including approving a reverse share split by consolidating our common shares (together with a corresponding increase in the par value thereof) in a ratio determined by the board of directors. Our Bye-laws also provide that upon an alteration or reduction of share capital where fractions of shares or some other difficulty would arise, our board of directors may deal with or resolve the same in any manner as it thinks fit.

Meeting of Shareholders

Under Bermuda law, a company is required to convene at least one general meeting of shareholders each calendar year (the "annual general meeting"). However, the members may by resolution waive this requirement, either for a specific year or period of time, or indefinitely. When the requirement has been so waived, any member may, on notice to the company, terminate the waiver, in which case an annual general meeting must be called.

Bermuda law provides that a special general meeting of shareholders may be called by the board of directors of a company and must be called upon the request of shareholders holding not less than 10% of the paid-up capital of the company carrying the right to vote at general meetings. Bermuda law also requires that shareholders be given at least five days' advance notice of a general meeting, but the accidental omission to give notice to any person does not invalidate the proceedings at a meeting. Our Bye-laws provide that the board of directors may convene an annual general meeting or a special general meeting. Under our Bye-laws, at least 14 days' notice of an annual general meeting or a special general meeting must be given to each shareholder entitled to vote at such meeting. This notice requirement is subject to the ability to hold such meetings on shorter notice if such notice is agreed: (i) in the case of an annual general meeting by all of the shareholders entitled to attend and vote at such meeting; or (ii) in the case of a special general meeting by a majority in number of the shareholders entitled to attend and vote at the meeting holding not less than 95% in nominal value of the shares entitled to vote at such meeting. The quorum required for a general meeting of shareholders is two or more persons present in person at the start of the meeting and representing in person or by proxy issued and outstanding common shares.

Access to Books and Records and Dissemination of Information

Members of the general public have a right to inspect the public documents of a company available at the office of the Registrar of Companies in Bermuda. These documents include the company's memorandum of association (or memorandum of continuance), including its objects and powers, and certain alterations to the memorandum of association (or memorandum of continuance). The shareholders have the additional right to inspect the bye-laws of the company, minutes of general meetings and the company's audited financial statements, which must be presented to the annual general meeting. The register of members of a company is also open to inspection by shareholders and by members of the general public without charge. The register of members is required to be open for inspection for not less than two hours in any business day (subject to the ability of a company to close the register of members for not more than thirty days in a year). A company is required to maintain its share register in Bermuda but may, subject to the provisions of the Companies Act, establish a branch register outside of Bermuda. A company is required to keep at its registered office a register of directors and officers that is open for inspection for not less than two hours in any business day by members of the public without charge. A company is also required to file with the Registrar of Companies in Bermuda a list of its directors to be maintained on a register, which register will be available for public inspection subject to such conditions as the Registrar may impose and on payment of such fee as may be prescribed. Bermuda law does not, however, provide a general right for shareholders to inspect or obtain copies of any other corporate records.

Election and Removal of Directors

Our Bye-laws provide that our board shall consist of three directors or such greater number as the board may determine. Our board of directors currently consists of six directors, but it is anticipated that our board will consist of five directors following the holding of our annual general meeting in 2022. Each director shall hold office for such term as the shareholders may determine or, in their absence of such determination, until the next annual general meeting or until their successors are elected or appointed or their office is otherwise vacated.

Any shareholder or shareholders holding or representing not less than 5% of the total voting rights wishing to propose for election as a director someone who is not an existing director or is not proposed by our board must give notice of the intention to propose the person for election. Where a director is to be elected at an annual general meeting, that notice must be given not less than 90 days nor more than 120 days before the anniversary of the last annual general meeting prior to the giving of the notice or, in the event the annual general meeting is called for a date that is not 30 days before or after such anniversary the notice must be given not later than 10 days following the earlier of the date on which notice of the annual general meeting was posted to members or the date on which public disclosure of the date of the annual general meeting was made. Where a director is to be elected at a special general meeting, that notice must be given not later than 10 days following the earlier of the date on which notice of the special general meeting was posted to members or the date on which public disclosure of the date of the special general meeting was made.

A director may be removed, with cause, by the shareholders, provided notice of the shareholders meeting convened to remove the director is given to the director. The notice must contain a statement of the intention to remove the director and must be served on the director not less than fourteen days before the meeting. The director is entitled to attend the meeting and be heard on the motion for his removal.

Proceedings of Board of Directors

Our Bye-laws provide that our business is to be managed and conducted by our board of directors. Bermuda law permits individual and corporate directors and there is no requirement in our Bye-laws or Bermuda law that directors hold any of our shares. There is also no requirement in our Bye-laws or Bermuda law that our directors must retire at a certain age.

The remuneration of our directors is determined by our board of directors, and there is no requirement that a specified number or percentage of "independent" directors must approve any such determination. Our directors may also be paid all travel, hotel and other expenses properly incurred by them in connection with our business or their duties as directors.

Provided a director discloses a direct or indirect interest in any contract or arrangement with us as required by Bermuda law, such director is entitled to vote in respect of any such contract or arrangement in which he or she is interested unless he or she is disqualified from voting by the chairman of the relevant board meeting.

Indemnification of Directors and Officers

Section 98 of the Companies Act provides generally that a Bermuda company may indemnify its directors, officers and auditors against any liability which by virtue of any rule of law would otherwise be imposed on them in respect of any negligence, default, breach of duty or breach of trust, except in cases where such liability arises from fraud or dishonesty of which such director, officer or auditor may be guilty in relation to the company. Section 98 further provides that a Bermuda company may indemnify its directors, officers and auditors against any liability incurred by them in defending any proceedings, whether civil or criminal, in which judgment is awarded in their favor or in which they are acquitted or granted relief by the Supreme Court of Bermuda pursuant to section 281 of the Companies Act.

Our Bye-laws provide that we shall indemnify our officers and directors in respect of their actions and omissions, except in respect of their fraud or dishonesty. Our Bye-laws provide that the shareholders waive all claims or rights of action that they might have, individually or in right of the company, against any of the company's directors or officers for any act or failure to act in the performance of such director's or officer's duties, except in respect of any fraud or dishonesty of such director or officer. Section 98A of the Companies Act permits us to purchase and maintain insurance for the benefit of any officer or director in respect of any loss or liability attaching to him in respect of any negligence, default, breach of duty or breach of trust, whether or not we may otherwise indemnify such officer or director. We have purchased and maintain a directors' and officers' liability policy for such a purpose. See "Comparison of Corporate Law—Indemnification of directors and executive management and limitation of liability."

Amendment of Memorandum of Continuance and Bye-laws

Bermuda law provides that the memorandum of association (or memorandum of continuance) of a company may be amended by a resolution passed at a general meeting of shareholders. Our Bye-laws provide that no bye-law shall be rescinded, altered or amended, and no new bye-law shall be made, unless it shall have been approved by a resolution of our board of directors and by a resolution of our shareholders. In the case of certain bye-laws, such as the Bye-laws relating to election and removal of directors, approval of business combinations and amendment of bye-law provisions, the required resolutions must include the affirmative vote of at least 66 2⁄3% of our directors then in office and of at least 66 2⁄3% percent of the votes attaching to all shares in issue.

Under Bermuda law, the holders of an aggregate of not less than 20% in par value of a company's issued share capital or any class thereof have the right to apply to the Supreme Court of Bermuda for an annulment of any amendment of the memorandum of association (or memorandum of continuance) adopted by shareholders at any general meeting, other than an amendment which alters or reduces a company's share capital as provided in the Companies Act. Where such an application is made, the amendment becomes effective only to the extent that it is confirmed by the Bermuda court. An application for an annulment of an amendment of the memorandum of association (or memorandum of continuance) must be made within twenty-one days after the date on which the resolution altering the company's memorandum of association (or memorandum of continuance) is passed and may be made on behalf of persons entitled to make the application by one or more of their number as they may appoint in writing for the purpose. No application may be made by shareholders voting in favor of the amendment.

Amalgamations, Mergers and Business Combinations

The amalgamation or merger of a Bermuda company with another company or corporation (other than certain affiliated companies) requires an amalgamation or merger agreement that is approved by the company's board of directors and by its shareholders. Unless the company's bye-laws provide otherwise, the approval of 75% of the shareholders voting at such meeting is required to approve the amalgamation or merger agreement, and the quorum for such meeting must be two persons holding or representing more than one-third of the issued shares of the company. Our Bye-laws provide that an amalgamation or a merger (other than with a wholly owned subsidiary or as described below) that has been approved by the board must only be approved by a majority of the votes cast at a general meeting of the shareholders at which the quorum shall be two or more persons present in person and representing in person or by proxy issued and outstanding common voting shares. Any amalgamation or merger or other business combination (as defined in the Bye-laws) not approved by our board of directors must be approved by the holders of not less than 66 2⁄3% of all votes attaching to all shares then in issue entitling the holder to attend and vote on the resolution.

Under Bermuda law, in the event of an amalgamation or merger of a Bermuda company with another company or corporation, a shareholder of the Bermuda company who did not vote in favor of the amalgamation or merger and who is not satisfied that fair value has been offered for such shareholder's shares may, within one month of notice of the shareholders meeting, apply to the Supreme Court of Bermuda to appraise the fair value of those shares.

Our Bye-laws contain provisions regarding "business combinations" with "interested shareholders". Pursuant to the Bye-laws, in addition to any other approval that may be required by applicable law, any business combination with an interested shareholder within a period of three years after the date of the transaction in which the person became an interested shareholder must be approved by our board and authorized at an annual or special general meeting by the affirmative vote of at least 66 2⁄3% of our issued and outstanding voting shares that are not owned by the interested shareholder, unless: (i) prior to the time that the shareholder becoming an interested shareholder, our board of directors approved either the business combination or the transaction that resulted in the shareholder becoming an interested shareholder; or (ii) upon consummation of the transaction that resulted in the shareholder becoming an interested shareholder, the interested shareholder owned at least 85% of our issued and outstanding voting shares at the time the transaction commenced. For purposes of these provisions, "business combinations" include mergers, amalgamations, consolidations and certain sales, leases, exchanges, mortgages, pledges, transfers and other dispositions of assets, issuances and transfers of shares and other transactions resulting in a financial benefit to an interested shareholder. An "interested shareholder" is a person that beneficially owns 15% or more of our issued and outstanding voting shares and any person affiliated or associated with us that owned 15% or more of our issued and outstanding voting shares at any time three years prior to the relevant time.

Compulsory Acquisition of Shares Held by Minority Holders

An acquiring party is generally able to acquire compulsorily the common shares of minority holders in the following ways:

(1) By a procedure under the Companies Act known as a "scheme of arrangement." A scheme of arrangement could be effected by obtaining the agreement of the company and of holders of its shares (or any class of shares), representing in the aggregate a majority in number and at least 75% in value of the shares or class of shares present and voting at a court ordered meeting held to consider the scheme or arrangement. The scheme of arrangement must then be sanctioned by the Bermuda Supreme Court. If a scheme of arrangement receives all necessary agreements and sanctions, upon the filing of the court order with the Registrar of Companies in Bermuda, all holders of common shares could be compelled to sell their shares under the terms of the scheme or arrangement.

(2) If the acquiring party is a company it may compulsorily acquire all the shares of the target company, by acquiring pursuant to a tender offer 90% of the shares or class of shares not already owned by, or by a nominee for, the acquiring party (the offeror), or any of its subsidiaries. If an offeror has, within four months after the making of an offer for all the shares or class of shares not owned by, or by a nominee for, the offeror, or any of its subsidiaries, obtained the approval of the holders of 90% or more of all the shares to which the offer relates, the offeror may, at any time within two months beginning with the date on which the approval was obtained, require by notice any nontendering shareholder to transfer its shares on the same terms as the original offer. In those circumstances, nontendering shareholders will be compelled to sell their shares unless the Supreme Court of Bermuda (on application made within a one-month period from the date of the offeror's notice of its intention to acquire such shares) orders otherwise.

(3) Where one or more parties holds not less than 95% of the shares or a class of shares of a company, such holder(s) may, pursuant to a notice given to the remaining shareholders or class of shareholders, acquire the shares of such remaining shareholders or class of shareholders. When this notice is given, the acquiring party is entitled and bound to acquire the shares of the remaining shareholders on the terms set out in the notice, unless a remaining shareholder, within one month of receiving such notice, applies to the Supreme Court of Bermuda for an appraisal of the value of its shares. This provision only applies where the acquiring party offers the same terms to all holders of shares whose shares are being acquired.

Anti-Takeover Provisions

Two-thirds supermajority shareholder voting requirement: Our Bye-laws provide that, except to the extent that a proposal has received the prior approval of the board, the approval of an amalgamation, merger or consolidation with or into any other person shall require the affirmative vote of not less than 66 2⁄3% of all votes attaching to all shares then in issue entitling the holder to attend and vote on the resolution (except for certain "business combinations" with "interested shareholders" as set forth in *Amalgamations, Mergers and Business Combinations* above).

Amendments to the Bye-laws: Our Bye-laws provide that no bye-law may be rescinded, altered or amended and no new bye-law may be made until the same has been approved by a resolution of the board and by a resolution of the shareholders. In the case of certain bye-laws, such as the Bye-laws relating to election and removal of directors, approval of business combinations and amendment of bye-law provisions, the required resolutions must include the affirmative vote of at least 66 2⁄3% of our directors then in office and of at least 66 2⁄3% percent of the votes attaching to all issued and outstanding shares.

Limitations on the election of directors: Our Bye-laws provide that a person may be proposed for election or appointment as a director at a general meeting either by the board or by one or more shareholders holding our shares which in the aggregate carry not less than 5% of the voting rights in respect of the election of directors. In addition, unless a person is proposed for election or appointment as a director by the board, when a person is proposed for appointment or election as a director, written notice of the proposal must be given to us as follows. Where a director is to be appointed or elected: (1) at an annual general meeting, such notice must be given not less than 90 days nor more than 120 days before the anniversary of the last annual general meeting prior to the giving of the notice or, in the event the annual general meeting is called for a date that is not 30 days before or after such anniversary the notice must be given not later than 10 days following the earlier of the date on which notice of the annual general meeting was posted to shareholders or the date on which public disclosure of the date of the annual general meeting was made; and (2) at a special general meeting, such notice must be given not later than 10 days following the earlier of the date on which notice of the special general meeting was posted to shareholders or the date on which public disclosure of the date of the special general meeting was made.

Shareholder Suits

Class actions and derivative actions are generally not available to shareholders under Bermuda law. The Bermuda courts, however, would ordinarily be expected to permit a shareholder to commence an action in the name of a company to remedy a wrong to the company where the act complained of is alleged to be beyond the corporate power of the company or illegal, or would result in the violation of the company's memorandum of association (or memorandum of continuance) or bye-laws. Furthermore, consideration would be given by a Bermuda court to acts that are alleged to constitute a fraud against the minority shareholders or, for instance, where an act requires the approval of a greater percentage of the company's shareholders than that which actually approved it.

When the affairs of a company are being conducted in a manner which is oppressive or prejudicial to the interests of some part of the shareholders, one or more shareholders may apply to the Supreme Court of Bermuda, which may make such order as it sees fit, including an order regulating the conduct of the company's affairs in the future or ordering the purchase of the shares of any shareholders by other shareholders or by the company.

Our Bye-laws contain a provision by virtue of which our shareholders waive any claim or right of action that they have, both individually and on our behalf, against any director or officer in relation to any action or failure to take action by such director or officer, except in respect of any fraud or dishonesty of such director or officer. The SEC has advised that the operation of this provision as a waiver of the right to sue for violations of federal securities laws would likely be unenforceable in U.S. courts.

Capitalization of Profits and Reserves

Pursuant to our Bye-laws, our board of directors may (i) capitalize any part of the amount of our share premium or other reserve accounts or any amount credited to our profit and loss account or otherwise available for distribution by applying such sum in paying up unissued shares to be allotted as fully paid bonus shares pro-rata (except in connection with the conversion of shares) to the shareholders; or (ii) capitalize any sum standing to the credit of a reserve account or sums otherwise available for dividend or distribution by paying up in full, partly paid or nil paid shares of those shareholders who would have been entitled to such sums if they were distributed by way of dividend or distribution.

Exchange controls

We have received consent under the Exchange Control Act 1972 from the Bermuda Monetary Authority for the issue and transfer of the common shares to and between non-residents of Bermuda for exchange control purposes provided our shares remain listed on an appointed stock exchange, which includes the Nasdaq Capital Market. In granting such consent the Bermuda Monetary Authority accepts no responsibility for our financial soundness or the correctness of any of the statements made or opinions expressed in this Annual Report.

Registrar or Transfer Agent

A register of holders of the common shares is maintained by Conyers Corporate Services (Bermuda) Limited in Bermuda, and a branch register is maintained in the United States by American Stock Transfer & Trust Company, LLC, who serves as branch registrar and transfer agent.

Untraced Shareholders

Our Bye-laws provide that our board of directors may forfeit any dividend or other monies payable in respect of any shares which remain unclaimed for six years from the date when such monies became due for payment. In addition, we are entitled to cease sending dividend warrants and checks by post or otherwise to a shareholder if such instruments have been returned undelivered to, or left uncashed by, such shareholder on at least two consecutive occasions or, following one such occasion, reasonable enquires have failed to establish the shareholder's new address. This entitlement ceases if the shareholder claims a dividend or cashes a dividend check or a warrant.

Certain Provisions of Bermuda Law

We have been designated by the Bermuda Monetary Authority as a non-resident for Bermuda exchange control purposes. This designation allows us to engage in transactions in currencies other than the Bermuda dollar, and there are no restrictions on our ability to transfer funds (other than funds denominated in Bermuda dollars) in and out of Bermuda or to pay dividends to United States residents who are holders of our common shares.

We have received consent from the Bermuda Monetary Authority for the issue and free transferability of all of our common shares to and between non-residents of Bermuda for exchange control purposes, provided our shares remain listed on an appointed stock exchange, which includes the Nasdaq Capital Market. Approvals or permissions given by the Bermuda Monetary Authority do not constitute a guarantee by the Bermuda Monetary Authority as to our performance or creditworthiness. Accordingly, in giving such consent or permissions, the Bermuda Monetary Authority shall not be liable for the financial soundness, performance or default of our business or for the correctness of any opinions or statements expressed in this Annual Report. Certain issues and transfers of common shares involving persons deemed resident in Bermuda for exchange control purposes require the specific consent of the Bermuda Monetary Authority.

In accordance with Bermuda law, share certificates are only issued in the names of companies, partnerships or individuals. In the case of a shareholder acting in a special capacity (for example as a trustee), certificates may, at the request of the shareholder, record the capacity in which the shareholder is acting. Notwithstanding such recording of any special capacity, we will not be bound to investigate or see to the execution of any such trust. We will take no notice of any trust applicable to any of our shares, whether or not we have been notified of such trust.

Comparison of Corporate Law

Set forth below is a comparison of select provisions of the corporate laws of Delaware and Bermuda showing the default positions in each jurisdiction that govern shareholder rights.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Mergers and similar arrangements	
Under the Delaware General Corporation Law, with certain exceptions, a merger, consolidation, sale, lease or transfer of all or substantially all of the assets of a corporation must be approved by the board of directors and a majority of the outstanding shares entitled to vote thereon. A shareholder of a Delaware corporation participating in certain major corporate transactions may, under certain circumstances, be entitled to appraisal rights pursuant to which such shareholder may receive cash in the amount of the fair value of the shares held by such shareholder (as determined by a court) in lieu of the consideration such shareholder would otherwise receive in the transaction. The Delaware General Corporation Law also provides that a parent corporation, by resolution of its board of directors, may merge with any subsidiary, of which it owns at least 90.0% of each class of capital stock without a vote by the shareholders of such subsidiary. Upon any such merger, dissenting shareholders of the subsidiary would have appraisal rights.	The amalgamation or merger of a Bermuda company with another company or corporation (other than certain affiliated companies) requires the amalgamation or merger agreement to be approved by the company's board of directors and by its shareholders. Unless the company's bye-laws provide otherwise, the approval of 75% of the shareholders voting at a general meeting is required to approve the amalgamation or merger agreement, and the quorum for such meeting must be two persons holding or representing more than one-third of the issued shares of the company. The Bye-laws provide that a merger or an amalgamation (other than with a wholly owned subsidiary or as described below) that has been approved by the board must only be approved by a majority of the votes cast at a general meeting of the shareholders at which the quorum shall be two or more persons present in person and representing in person or by proxy issued and outstanding voting shares. The Bye-laws contain provisions regarding "business combinations" with "interested shareholders". Pursuant to our Bye-laws, in addition to any other approval that may be required by applicable law, any business combination with an interested shareholder within a period of three years after the date of the transaction in which the person became an interested shareholder must be approved by Auris Medical's board and authorized at an annual or special general meeting by the affirmative vote of at least 66 and 2/3rds% of Auris Medical's issued and outstanding voting shares that are not owned by the interested shareholder, unless: (i) prior to the time that the shareholder becoming an interested shareholder, our board of directors approved either the business combination or the transaction that resulted in the shareholder becoming an interested shareholder; or (ii) upon consummation of the transaction that resulted in the shareholder becoming an interested shareholder, the interested shareholder owned at least 85% of our issued and outstanding voting shares at the time the transaction commenced. For purposes of these provisions, "business combinations" include mergers, amalgamations, consolidations and certain sales, leases, exchanges, mortgages, pledges, transfers and other dispositions of assets, issuances and transfers of shares and other transactions resulting in a financial benefit to an interested shareholder. An "interested shareholder" is a person that beneficially owns 15% or more of our issued and outstanding voting shares and any person affiliated or associated with us that owned 15% or more of our issued and outstanding voting shares at any time three years prior to the relevant time. Under Bermuda law, in the event of an amalgamation or merger of a Bermuda company with another company or corporation, a shareholder of the Bermuda company who did not vote in favor of the amalgamation or merger and who is not satisfied that fair value has been offered for such shareholder's shares may, within one month of notice of the shareholders meeting, apply to the Supreme Court of Bermuda to appraise the fair value of those shares. Note that each share of an amalgamating or merging company carries the right to vote in respect of an amalgamation or merger whether or not is otherwise carries the right to vote.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Shareholders' suits	
Class actions and derivative actions generally are available to shareholders of a Delaware corporation for, among other things, breach of fiduciary duty, corporate waste and actions not taken in accordance with applicable law. In such actions, the court has discretion to permit the winning party to recover attorneys' fees incurred in connection with such action.	Class actions and derivative actions are generally not available to shareholders under Bermuda law. The Bermuda courts, however, would ordinarily be expected to permit a shareholder to commence an action in the name of a company to remedy a wrong to the company where the act complained of is alleged to be beyond the corporate power of the company or illegal, or would result in the violation of the company's memorandum of association or bye-laws. Furthermore, consideration would be given by a Bermuda court to acts that are alleged to constitute a fraud against the minority shareholders or, for instance, where an act requires the approval of a greater percentage of the company's shareholders than that which actually approved it. When the affairs of a company are being conducted in a manner which is oppressive or prejudicial to the interests of some part of the shareholders, one or more shareholders may apply to the Supreme Court of Bermuda, which may make such order as it sees fit, including an order regulating the conduct of the company's affairs in the future or ordering the purchase of the shares of any shareholders by other shareholders or by the company. The Bye-laws contain a provision by virtue of which Auris Medical's shareholders waive any claim or right of action that they have, both individually and on Auris Medical's behalf, against any director or officer in relation to any action or failure to take action by such director or officer, except in respect of any fraud or dishonesty of such director or officer.
Shareholder vote on board and management compensation	
Under the Delaware General Corporation Law, the board of directors has the authority to fix the compensation of directors, unless otherwise restricted by the certificate of incorporation or bylaws.	The Bye-laws contains a provision that the board of directors has the power to determine the remuneration, if any, of the directors.
Annual vote on board renewal	
Unless directors are elected by written consent in lieu of an annual meeting, directors are elected in an annual meeting of stockholders on a date and at a time designated by or in the manner provided in the bylaws. Re-election is possible. Classified boards are permitted.	The Bye-laws provide that the directors shall hold office for such term as the shareholders may determine or, in their absence of such determination, until the next annual general meeting, or until their successors are elected or appointed or their office is otherwise vacated. Re-election is possible. Provision for staggered boards of directors may be included in a company's bye-laws.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Indemnification of directors and executive management and limitation of liability	
The Delaware General Corporation Law provides that a certificate of incorporation may contain a provision eliminating or limiting the personal liability of directors (but not other controlling persons) of the corporation for monetary damages for breach of a fiduciary duty as a director, except no provision in the certificate of incorporation may eliminate or limit the liability of a director for: any breach of a director's duty of loyalty to the corporation or its shareholders; acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law; statutory liability for unlawful payment of dividends or unlawful stock purchase or redemption; or any transaction from which the director derived an improper personal benefit.	Section 98 of the Companies Act provides generally that a Bermuda company may indemnify its directors, officers and auditors against any liability which by virtue of any rule of law would otherwise be imposed on them in respect of any negligence, default, breach of duty or breach of trust, except in cases where such liability arises from fraud or dishonesty of which such director, officer or auditor may be guilty in relation to the company. Section 98 further provides that a Bermuda company may indemnify its directors, officers and auditors against any liability incurred by them in defending any proceedings, whether civil or criminal, in which judgment is awarded in their favor or in which they are acquitted or granted relief by the Supreme Court of Bermuda pursuant to section 281 of the Companies Act.
A Delaware corporation may indemnify any person who was or is a party or is threatened to be made a party to any proceeding, other than an action by or on behalf of the corporation, because the person is or was a director or officer, against liability incurred in connection with the proceeding if the director or officer acted in good faith and in a manner reasonably believed to be in, or not opposed to, the best interests of the corporation; and the director or officer, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful.	The Bye-laws contain provisions that provide that Auris Medical shall indemnify its officers and directors in respect of their actions and omissions, except in respect of their fraud or dishonesty. Our bye-laws provide that the shareholders waive all claims or rights of action that they might have, individually or in right of the company, against any of the company's directors or officers for any act or failure to act in the performance of such director's or officer's duties, except in respect of any fraud or dishonesty of such director or officer. Section 98A of the Companies Act permits Auris Medical to purchase and maintain insurance for the benefit of any officer or director in respect of any loss or liability attaching to him in respect of any negligence, default, breach of duty or breach of trust, whether or not we may otherwise indemnify such officer or director. We have purchased and maintain a directors' and officers' liability policy for such a purpose.
Unless ordered by a court, any foregoing indemnification is subject to a determination that the director or officer has met the applicable standard of conduct: by a majority vote of the directors who are not parties to the proceeding, even though less than a quorum; by a committee of directors designated by a majority vote of the eligible directors, even though less than a quorum; by independent legal counsel in a written opinion if there are no eligible directors, or if the eligible directors so direct; or by the shareholders.	
Moreover, a Delaware corporation may not indemnify a director or officer in connection with any proceeding in which the director or officer has been adjudged to be liable to the corporation unless and only to the extent that the court determines that, despite the adjudication of liability but in view of all the circumstances of the case, the director or officer is fairly and reasonably entitled to indemnity for those expenses which the court deems proper.	

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Directors' fiduciary duties	
A director of a Delaware corporation has a fiduciary duty to the corporation and its shareholders. This duty has two components: the duty of care; and the duty of loyalty.	At common law, members of a board of directors owe a fiduciary duty to the company to act in good faith in their dealings with or on behalf of the company and exercise their powers and fulfill the duties of their office honestly. This duty includes the following elements: (i) a duty to act in good faith in the best interests of the company; (ii) a duty not to make a personal profit from opportunities that arise from the office of director; (iii) a duty to avoid conflicts of interest; and (iv) a duty to exercise powers for the purpose for which such powers were intended.
The duty of care requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of, and disclose to shareholders, all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. This duty prohibits self-dealing by a director and mandates that the best interest of the corporation and its shareholders take precedence over any interest possessed by a director, officer or controlling shareholder and not shared by the shareholders generally. In general, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence a breach of one of the fiduciary duties. Should such evidence be presented concerning a transaction by a director, a director must prove the procedural fairness of the transaction, and that the transaction was of fair value to the corporation.	The Companies Act also imposes a duty on directors and officers of a Bermuda company to: (i) act honestly and in good faith with a view to the best interests of the company; and (ii) exercise the care, diligence and skill that a reasonably prudent person would exercise in comparable circumstances. In addition, the Companies Act imposes various duties on directors and officers of a company with respect to certain matters of management and administration of the company.
Shareholder action by written consent	
A Delaware corporation may, in its certificate of incorporation, eliminate the right of shareholders to act by written consent.	The Companies Act provides that shareholders may take action by written consent, except in respect of the removal of an auditor from office before the expiry of his term or in respect of a resolution passed for the purpose of removing a director before the expiration of his term of office. A resolution in writing is passed when it is signed by the members of the company who at the date of the notice of the resolution represent such majority of votes as would be required if the resolution had been voted on at a meeting or when it is signed by all the members of the company or such other majority of members as may be provided by the bye-laws of the company.

Shareholder proposals

A shareholder of a Delaware corporation has the right to put any proposal before the annual meeting of shareholders, provided it complies with the notice provisions in the governing documents. A special meeting may be called by the board of directors or any other person authorized to do so in the governing documents, but shareholders may be precluded from calling special meetings.

Shareholder(s) may, as set forth below and at their own expense (unless the company otherwise resolves), require the company to: (i) give notice to all shareholders entitled to receive notice of the annual general meeting of any resolution that the shareholder(s) may properly move at the next annual general meeting; and/or (ii) circulate to all shareholders entitled to receive notice of any general meeting a statement in respect of any matter referred to in the proposed resolution or any business to be conducted at such general meeting. The number of shareholders necessary for such a requisition is either: (i) any number of shareholders representing not less than 5% of the total voting rights of all shareholders entitled to vote at the meeting to which the requisition relates; or (ii) not less than 100 shareholders.

Pursuant to the Bye-laws, any shareholder or shareholders holding or representing not less than 5% of the total voting rights wishing to propose for election as a director someone who is not an existing director or is not proposed by Auris Medical's board must give notice of the intention to propose the person for election in accordance with the Bye-laws.

Cumulative voting

Under the Delaware General Corporation Law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation provides for it.

Under Bermuda law, the voting rights of shareholders are regulated by the company's bye-laws and, in certain circumstances, by the Companies Act. The Bye-laws provide for a plurality of voting for elections of directors, and cumulative voting for elections of directors is not permitted.

Removal of directors

A Delaware corporation with a classified board may be removed only for cause with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise.

Under the Bye-laws, a director may be removed, with cause, by the shareholders, provided notice of the shareholders meeting convened to remove the director is given to the director. The notice must contain a statement of the intention to remove the director and must be served on the director not less than fourteen days before the meeting. The director is entitled to attend the meeting and be heard on the motion for his removal.

Transactions with interested shareholders

The Delaware General Corporation Law generally prohibits a Delaware corporation from engaging in certain business combinations with an "interested shareholder" for three years following the date that such person becomes an interested shareholder. An interested shareholder generally is a person or group who or which owns or owned 15.0% or more of the corporation's outstanding voting stock within the past three years.

There is no similar law in Bermuda.

The Bye-laws contain provisions regarding "business combinations" with "interested shareholders" which are described above under "mergers and similar arrangements."

Dissolution; Winding up

Unless the board of directors of a Delaware corporation approves the proposal to dissolve, dissolution must be approved by shareholders holding 100.0% of the total voting power of the corporation. Only if the dissolution is initiated by the board of directors may it be approved by a simple majority of the corporation's outstanding shares. Delaware law allows a Delaware corporation to include in its certificate of incorporation a supermajority voting requirement in connection with dissolutions initiated by the board.

A Bermuda company may be wound up by the Bermuda court on application presented by the company itself, its creditors (including contingent or prospective creditors) or its contributories. The Bermuda court has authority to order winding up in a number of specified circumstances including where it is, in the opinion of the Bermuda court, just and equitable to do so.

A Bermuda company limited by shares may be wound up voluntarily when the shareholders so resolve in general meeting. In the case of a voluntary winding up, the company shall, from the commencement of the winding up, cease to carry on its business, except so far as may be required for the beneficial winding up thereof.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Variation of rights of shares	
A Delaware corporation may vary the rights of a class of shares with the approval of a majority of the outstanding shares of such class, unless the certificate of incorporation provides otherwise.	Under the Bye-laws, if at any time we have more than one class of shares, the rights attaching to any class, unless otherwise provided for by the terms of issue of the relevant class, may be varied either: (i) with the consent in writing of the holders of 75% of the issued shares of that class; or (ii) with the sanction of a resolution passed by a majority of the votes cast at a general meeting of the relevant class of shareholders at which a quorum consisting of at least two persons holding or representing issued shares of the relevant class is present. The Bye-laws specify that the creation or issue of shares ranking equally with existing shares will not, unless expressly provided by the terms of issue of existing shares, vary the rights attached to existing shares. In addition, the creation or issue of preference shares ranking prior to common shares will not be deemed to vary the rights attached to common shares or, subject to the terms of any other series of preference shares, to vary the rights attached to any other series of preference shares.
Amendment of governing documents	
A Delaware corporation's governing documents may be amended with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise.	A Bermuda company's memorandum of association and bye-laws may be amended by resolutions of the board of directors and the shareholders, subject to the company's bye-laws.
Inspection of Books and Records	
Shareholders of a Delaware corporation, upon written demand under oath stating the purpose thereof, have the right during the usual hours for business to inspect for any proper purpose, and to obtain copies of list(s) of shareholders and other books and records of the corporation and its subsidiaries, if any, to the extent the books and records of such subsidiaries are available to the corporation.	Members of the general public have a right to inspect the public documents of a company available at the office of the Registrar of Companies in Bermuda. These documents include the company's memorandum of association/continuance, including its objects and powers, and certain alterations to the memorandum of association/continuance. The shareholders have the additional right to inspect the bye-laws of the company, minutes of general meetings and the company's audited financial statements, which must be presented to the annual general meeting. The register of members of a company is also open to inspection by shareholders without charge, and by members of the general public on payment of a fee. The register of members is required to be open for inspection for not less than two hours in any business day (subject to the ability of a company to close the register of members for not more than thirty days in a year). A company is required to maintain its share register in Bermuda but may, subject to the provisions of the Companies Act, establish a branch register outside of Bermuda. A company is required to keep at its registered office a register of directors and officers that is open for inspection for not less than two hours in any business day by members of the public without charge. Bermuda law does not, however, provide a general right for shareholders to inspect or obtain copies of any other corporate records.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Payment of dividends	
The board of directors may approve a dividend without shareholder approval. Subject to any restrictions contained in its certificate of incorporation, the board may declare and pay dividends upon the shares of its capital stock either: out of its surplus, or in case there is no such surplus, out of its net profits for the fiscal year in which the dividend is declared and/or the preceding fiscal year. Stockholder approval is required to authorize capital stock in excess of that provided in the charter. Directors may issue authorized shares without stockholder approval.	Under Bermuda law, the board of directors may declare a dividend without shareholder approval, but a company may not declare or pay dividends if there are reasonable grounds for believing that: (i) the company is, or would after the payment be, unable to pay its liabilities as they become due; or (ii) that the realizable value of its assets would thereby be less than its liabilities. Under the Bye-laws, each common share is entitled to dividends if, as and when dividends are declared by our board of directors, subject to any preferred dividend right of the holders of any preference shares.
Creation and issuance of new shares	
All creation of shares requires the board of directors to adopt a resolution or resolutions, pursuant to authority expressly vested in the board of directors by the provisions of the company's certificate of incorporation.	The authorized share capital of a Bermuda company is determined by the company's shareholders.

C. Material contracts

Except as otherwise disclosed in this Annual Report (including the Exhibits), we are not currently, and have not been in the last two years, party to any material contract, other than contracts entered into in the ordinary course of business.

D. Exchange controls

We have been designated by the Bermuda Monetary Authority as a non-resident for Bermuda exchange control purposes. This designation allows us to engage in transactions in currencies other than the Bermuda dollar, and there are no restrictions on our ability to transfer funds (other than funds denominated in Bermuda dollars) in and out of Bermuda or to pay dividends to United States residents who are holders of our common shares.

We have received consent from the Bermuda Monetary Authority for the issue and free transferability of all of our common shares to and between non-residents of Bermuda for exchange control purposes, provided our shares remain listed on an appointed stock exchange, which includes the Nasdaq Capital Market. Approvals or permissions given by the Bermuda Monetary Authority do not constitute a guarantee by the Bermuda Monetary Authority as to our performance or creditworthiness. Accordingly, in giving such consent or permissions, the Bermuda Monetary Authority shall not be liable for the financial soundness, performance or default of our business or for the correctness of any opinions or statements expressed in this Annual Report. Certain issues and transfers of common shares involving persons deemed resident in Bermuda for exchange control purposes require the specific consent of the Bermuda Monetary Authority.

E. Taxation

The following summary contains a description of the material Bermuda, Swiss and U.S. federal income tax consequences of the acquisition, ownership and disposition of common shares, but it does not purport to be a comprehensive description of all the tax considerations that may be relevant to a decision to purchase common shares. The summary is based upon the tax laws of Bermuda and regulations thereunder, of Switzerland and regulations thereunder and on the tax laws of the United States and regulations thereunder as of the date hereof, which may be subject to change.

Bermuda Tax Considerations

At the present time, there is no Bermuda income or profits tax, withholding tax, capital gains tax, capital transfer tax, estate duty or inheritance tax payable by us or by our shareholders in respect of our shares. We have received an assurance from the Minister of Finance of Bermuda under the Exempted Undertakings Tax Protection Act 1966 that, in the event that any legislation is enacted in Bermuda imposing any tax computed on profits or income, or computed on any capital asset, gain or appreciation or any tax in the nature of estate duty or inheritance tax, such tax shall not, until March 31, 2035, be applicable to us or to any of our operations or to our shares, debentures or other obligations except insofar as such tax applies to persons ordinarily resident in Bermuda or is payable by us in respect of real property owned or leased by us in Bermuda. There is no double taxation treaty between Bermudas and the United States or Switzerland.

Swiss Tax Considerations

With the deletion of Auris Medical Holding AG from the Swiss Commercial Register as of December 9, 2020, we consider that our taxability in Switzerland has ceased.

Material U.S. Federal Income Tax Considerations for U.S. Holders

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders (defined below) of owning and disposing of common shares, but it does not purport to be a comprehensive description of all tax considerations that may be relevant to a particular person's decision to hold the common shares. This discussion applies only to a U.S. Holder that holds common shares as capital assets for U.S. federal income tax purposes. In addition, it does not describe all of the tax consequences that may be relevant in light of the U.S. Holder's particular circumstances, including alternative minimum tax consequences, the potential application of the provisions of the Internal Revenue Code of 1986, as amended (the "Code"), known as the Medicare contribution tax and tax consequences applicable to U.S. Holders subject to special rules, such as:

- certain financial institutions;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons holding common shares as part of a straddle, wash sale, conversion transaction or persons entering into a constructive sale with respect to the common shares;
- persons whose functional currency for U.S. federal income tax purposes is not the U.S. dollar;
- entities classified as partnerships for U.S. federal income tax purposes;
- tax-exempt entities, including an "individual retirement account" or "Roth IRA";
- persons that own or are deemed to own ten percent or more of our stock by vote or value;
- persons who acquired our common shares pursuant to the exercise of an employee stock option or otherwise as compensation; or
- persons holding shares in connection with a trade or business conducted outside of the United States.

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

This discussion is based on the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury regulations, all as of the date hereof, any of which is subject to change, possibly with retroactive effect.

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

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the United States, any state therein or the District of Columbia; or
- an estate the income of which is subject to U.S. federal income taxation regardless of its source.
- a trust with respect to which a U.S. court is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of its substantial decisions, or that has a valid election in effect to be treated as a U.S. person under applicable U.S. Treasury Regulations.

U.S. Holders should consult their tax advisers concerning the U.S. federal, state, local and non-U.S. tax consequences of owning and disposing of common shares in their particular circumstances.

Passive Foreign Investment Company Rules

Special U.S. tax rules apply to U.S. Holders of stock in a company that are considered to be a PFIC. However, our actual PFIC status for the current or any future taxable year is uncertain and cannot be determined until after the end of such taxable year. In addition, we may, directly or indirectly, hold equity interests in other PFICs, or Lower-tier PFICs. In general, a non-U.S. corporation will be considered a PFIC for any taxable year in which (i) 75% or more of its gross income consists of passive income or (ii) 50% or more of the average quarterly value of its assets consists of assets that produce, or are held for the production of, passive income. For purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as if it held its proportionate share of the assets of the other corporation and received directly its proportionate share of the income of the other corporation. Passive income generally includes dividends, interest, rents, royalties and capital gains. Cash is a passive asset for PFIC purposes. Goodwill (the value of which may be determined by reference to the company's market capitalization) is generally treated as an active asset to the extent attributable to activities intended to produce active income.

Based on our gross income, the average value of our assets, including goodwill, and the nature of the current stage of our business, we do not believe we were a PFIC for the year ended December 31, 2021. There can be no assurance that the IRS will agree with our conclusion and that the IRS would not successfully challenge our position. Furthermore, there can be no assurance regarding our PFIC status for the current year or any particular year in the future because PFIC status is factual in nature, depends upon factors not wholly within our control, generally cannot be determined until the close of the taxable year in question and is determined annually. Our status as a PFIC will depend on the nature and composition of our income and the nature, composition and value of our assets (which may be determined based on the fair market value of each asset, with the value of goodwill and going concern value being determined in large part by reference to the market value of our common shares, which may be volatile). Our status may also depend, in part, on how quickly we utilize the cash proceeds from our fundraising activities in our business. Accordingly, there can be no assurance that we will not be a PFIC in the current or for any future taxable year. Therefore, U.S. Holders should invest in our common shares only if they are willing to bear the U.S. federal income tax consequences associated with investments in PFICs.

If we are a PFIC for any taxable year and any of our non-U.S. subsidiaries or other companies in which we own equity interests were also a PFIC (any such entity, a "Lower-tier PFIC"), under attribution rules, U.S. Holders will be deemed to own their proportionate shares of Lower-tier PFICs and will be subject to U.S. federal income tax according to the rules described in the following paragraphs on (i) certain distributions by a Lower-tier PFIC and (ii) a disposition of shares of a Lower-tier PFIC, in each case as if the U.S. Holder held such shares directly, even if the U.S. Holder has not received the proceeds of those distributions or dispositions.

Generally, if we are a PFIC for any taxable year during which a U.S. Holder holds our shares, the U.S. Holder may be subject to certain adverse tax consequences. Unless a U.S. Holder makes a timely "mark to market" election or "qualified electing fund" election, each as discussed below, gain recognized on a disposition (including, under certain circumstances, a pledge) of common shares by the U.S. Holder, or on an indirect disposition of shares of a Lower-tier PFIC, will be allocated ratably over the U.S. Holder's holding period for the shares. The amounts allocated to the taxable year of disposition and to years before we became a PFIC, if any, will be taxed as ordinary income. The amounts allocated to each other taxable year will be subject to tax at the highest rate in effect for that taxable year for individuals or corporations, as appropriate, and an interest charge will be imposed on the tax attributable to the allocated amounts. Further, to the extent that any distribution received by a U.S. Holder on our common shares (or a distribution by a Lower-tier PFIC to its shareholder that is deemed to be received by a U.S. Holder) exceeds 125% of the average of the annual distributions on the shares received during the preceding three years or the U.S. Holder's holding period, whichever is shorter, the distribution will be subject to taxation in the same manner as gain, described immediately above.

If we are a PFIC for any year during which a U.S. Holder holds common shares, we generally will continue to be treated as a PFIC with respect to the U.S. Holder for all succeeding years during which the U.S. Holder holds common shares, even if we cease to meet the threshold requirements for PFIC status. U.S. Holders should consult their tax advisers regarding the potential availability of a "deemed sale" election that would allow them to eliminate this continuing PFIC status under certain circumstances.

If we are a PFIC and our common shares are "regularly traded" on a "qualified exchange," a U.S. Holder may make a mark-to-market election that would result in tax treatment different from the general tax treatment for PFICs described above. Our common shares will be treated as "regularly traded" in any calendar year in which more than a de minimis quantity of the common shares is traded on a qualified exchange on at least 15 days during each calendar quarter. Nasdaq, on which the common shares are currently listed, is a qualified exchange for this purpose. U.S. Holders should consult their tax advisers regarding the availability and advisability of making a mark-to-market election in their particular circumstances and the consequences to them if the common shares are delisted from Nasdaq (see "Item 3. Key Information—D. Risk Factors—Risks Related to Our Business and Industry—Our common shares may be involuntarily delisted from trading on The Nasdaq Capital Market if we fail to comply with the continued listing requirements. A delisting of our common shares is likely to reduce the liquidity of our common shares and may inhibit or preclude our ability to raise additional financing" above). In particular, U.S. Holders should consider carefully the impact of a mark-to-market election with respect to their common shares given that we may have Lower-tier PFICs for which a mark-to-market election may not be available.

If we are a PFIC and a U.S. Holder makes the mark-to-market election, the U.S. Holder generally will recognize as ordinary income any excess of the fair market value of the common shares at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the common shares over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. Holder makes the election, the U.S. Holder's tax basis in the common shares will be adjusted to reflect the income or loss amounts recognized. Any gain recognized on a sale or other disposition of common shares in a year in which we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark to-market election). Distributions paid on common shares will be treated as discussed below under "*Taxation of Distributions*." Once made, the election cannot be revoked without the consent of the IRS unless the common shares cease to be marketable.

Alternatively, if we are a PFIC and a U.S. Holder can make an election, if we provide the necessary information, to treat us and each Lower-tier PFIC as a qualified electing fund (a "QEF Election") in the first taxable year that we (and each Lower-tier PFIC) are treated as a PFIC with respect to the U.S. Holder. A U.S. Holder must make the QEF Election for each PFIC by attaching a separate properly completed IRS Form 8621 (Information Return by a Shareholder of a Passive Foreign Investment Company or Qualified Electing Fund) for each PFIC to its timely filed U.S. federal income tax return. Upon request of a U.S. Holder, we intend to provide the information necessary for a U.S. Holder to make a QEF Election with respect to us for any other taxable year for which we determine that we were a PFIC and will use commercially reasonable efforts to cause each Lower-tier PFIC which we control to provide such information with respect to such Lower-tier PFIC. However, no assurance can be given that such QEF Election information will be available for any Lower-tier PFIC and we cannot guarantee that we will continue to provide such determination or information in future years.

If a U.S. Holder makes a QEF Election with respect to a PFIC, the U.S. Holder will be currently taxable on its *pro rata* share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is classified as a PFIC. If a U.S. Holder makes a QEF Election with respect to us, any distributions paid by us out of our earnings and profits that were previously included in the U.S. Holder's income under the QEF Election will not be taxable to the U.S. Holder. A U.S. Holder will increase its tax basis in its common shares by an amount equal to any income included under the QEF Election and will decrease its tax basis by any amount distributed on the common shares that is not included in its income. In addition, a U.S. Holder will recognize capital gain or loss on the disposition of common shares in an amount equal to the difference between the amount realized and its adjusted tax basis in the common shares. A U.S. Holder will not be taxed on the ordinary income and net capital gain under the QEF rules for any year that we are not a PFIC. U.S. Holders should note that if we are a PFIC and they make QEF Elections with respect to us and Lower-tier PFICs, they may be required to pay U.S. federal income tax with respect to their common shares for any taxable year significantly in excess of any cash distributions received on the shares for such taxable year. U.S. Holders should consult their tax advisers regarding making QEF Elections in their particular circumstances.

Furthermore, if we were a PFIC or, with respect to a particular U.S. Holder, were treated as a PFIC for the taxable year in which we paid a dividend or the prior taxable year, the preferential dividend rate with respect to dividends paid to certain non-corporate U.S. Holders will not apply.

If we were a PFIC for any taxable year during which a U.S. Holder held common shares, such U.S. Holder would be required to file an annual information report with such U.S. Holder's U.S. Federal income tax return on IRS Form 8621.

U.S. Holders should consult their tax advisers concerning our PFIC status and the tax considerations relevant to an investment in a PFIC.

Taxation of Distributions

As discussed above under "Item 8. Financial Information—Dividends and Dividend Policy," we do not currently expect to make distributions on our common shares. In the event that we do make distributions of cash or other property, subject to the PFIC rules described above, distributions paid on common shares, other than certain *pro rata* distributions of common shares, will be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we may not calculate our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. The U.S. dollar amount of any dividend will be treated as foreign-source dividend income to U.S. Holders and will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will be included in a U.S. Holder's income on the date of the U.S. Holder's receipt of the dividend.

Sale or Other Disposition of Common Shares

Subject to the PFIC rules described above, for U.S. federal income tax purposes, gain or loss realized on the sale or other disposition of common shares will be capital gain or loss, and will be long-term capital gain or loss if the U.S. Holder held the common shares for more than one year. The amount of the gain or loss will equal the difference between the U.S. Holder's tax basis in the common shares disposed of and the amount realized on the disposition, in each case as determined in U.S. dollars. This gain or loss will generally be U.S.-source gain or loss for foreign tax credit purposes. The deductibility of capital losses is subject to limitations. U.S. Holders should consult their tax advisers regarding the proper treatment of gain or loss, the availability of a foreign tax credit, and for U.S. Holders that sell common shares for an amount denominated in a currency other than the U.S. dollar should consult their tax advisers regarding any potential foreign currency gain or loss that may have to be recognized.

Information Reporting and Backup Withholding

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

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

Information Reporting with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals and certain entities may be required to report information relating to an interest in our common shares, subject to certain exceptions (including an exception for common shares held in accounts maintained by certain U.S. financial institutions). U.S. Holders should consult their tax advisers regarding whether or not they are obligated to report information relating to their ownership and disposition of the common shares.

F. Dividends and paying agents

Not applicable.

G. Statement by experts

Not applicable.

H. Documents on display

We are subject to the informational requirements of the Exchange Act. Accordingly, we are required to file reports and other information with the SEC, including annual reports on Form 20-F and reports on Form 6-K. The SEC maintains an Internet website that contains reports and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

Under Bermuda law shareholders have the right to inspect the bye-laws of the company, minutes of general meetings and the company's audited financial statements, which must be presented to the annual general meeting. The register of members of a company is also open to inspection by shareholders and by members of the general public without charge. The register of members is required to be open for inspection for not less than two hours in any business day (subject to the ability of a company to close the register of members for not more than thirty days in a year).

As a foreign private issuer, we are exempt under the Exchange Act from, among other things, the rules prescribing the furnishing and content of proxy statements, and our executive officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we will not be required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act.

I. Subsidiary information

Not applicable.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Credit Risk

We manage credit risk on a group basis. Credit risk arises from cash and cash equivalents and deposits with banks, as well as from other receivables. Our policy is to invest funds in low risk investments including interest bearing deposits. Only independent banks and financial institutions are used and banks with which we currently hold term deposits have a minimum S&P rating of "A". Receivables are not past due and not impaired and include only well-known counterparties.

We hold cash and cash equivalents in our principal operating currencies (CHF, USD, EUR and AUD).

Market Risk

In the ordinary course of our business activities, we are exposed to various market risks that are beyond our control, including fluctuations in foreign exchange rates, and which may have an adverse effect on the value of our financial assets and liabilities, future cash flows and profit. As a result of these market risks, we could suffer a loss due to adverse changes in foreign exchange rates. Our policy with respect to these market risks is to assess the potential of experiencing losses and the consolidated impact thereof, and to mitigate these market risks.

Currency Risk

We operate internationally and are exposed to foreign exchange risk arising from various exposures, primarily with respect to the US Dollar and Euro. Foreign exchange risk arises from future commercial transactions, recognized assets and liabilities and net investments in foreign operations. To manage foreign exchange risk we maintain foreign currency cash balances to cover anticipated future purchases of materials and services in foreign currencies. We do not hedge our foreign exchange risk.

As of December 31, 2021, a 5% increase or decrease in the USD/CHF exchange rate with all other variables held constant would have resulted in a CHF 77,827 (2020: CHF 455,241) increase or decrease in the net result. Also, a 5% increase or decrease in the EUR/CHF exchange rate with all other variables held constant would have resulted in a CHF 117,247 (2020: CHF 13,648) increase or decrease in the net annual result.

We have subsidiaries in the United States, Ireland and Australia, whose net assets are exposed to foreign currency translation risk. Due to the small size of these subsidiaries the translation risk is not significant.

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt securities

Not applicable.

B. Warrants and rights

Not applicable.

C. Other securities

Not applicable.

D. American Depositary Shares

Not applicable.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

A. Defaults

No matters to report.

B. Arrears and delinquencies

No matters to report.

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

E. Use of Proceeds

Not applicable.

ITEM 15. CONTROLS AND PROCEDURES

A. Disclosure Controls and Procedures

As of the end of the period covered by this Annual Report, an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act) was performed under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, our principal executive officer and principal financial officer, respectively. There are inherent limitations to the effectiveness of any system of disclosure controls and procedures, including the possibility of human error and the circumvention or overriding of the controls and procedures. Accordingly, even effective disclosure controls and procedures can only provide reasonable assurance of achieving their control objectives.

Based on the evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective, as of the end of the period covered by this Annual Report, in providing a reasonable level of assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods in SEC rules and forms, including providing a reasonable level of assurance that information required to be disclosed by us in such reports is accumulated and communicated to our management, including our principal executive officer and our principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

B. Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) of the Exchange Act. Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based upon criteria established in *Internal Control – Integrated Framework* (2013) by the Committee of Sponsoring Organizations of the Treadway Commission. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our internal control over financial reporting was effective as of December 31, 2021.

C. Attestation Report of the Registered Public Accounting Firm

Not applicable.

D. Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) that occurred during the period covered by this Annual Report that has materially affected, or is reasonably likely to materially affect, internal control over financial reporting.

ITEM 16. [RESERVED]

ITEM 16A. Audit committee financial expert

Our board of directors has determined that Mats Blom is the audit committee financial expert, as that term is defined by the SEC, and is independent for the purposes of SEC and Nasdaq rules.

ITEM 16B. Code of ethics

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics which covers a broad range of matters including the handling of conflicts of interest, compliance issues and other corporate policies such as insider trading and equal opportunity and non-discrimination standards. Our Code of Business Conduct applies to all of our directors, executive officers and employees. We have published our Code of Business Conduct and Ethics on our website, *www.altamiratherapeutics.com*. The information contained on our website is not a part of this Annual Report.

ITEM 16C. Principal Accountant Fees and Services

	2021	2020
Audit fees	186	252
Audit-related fees	126	99
Total fees	**312**	**351**

In 2021 we were billed CHF 185,487 by Deloitte AG in connection with audit services for our annual filing as well as interim reviews, group audit, and statutory audits plus CHF 126,200 in connection with audit-related services for work in connection with our equity offerings and registration statements. In 2020 we were billed CHF 252,100, by Deloitte AG in connection with our annual filing as well as interim reviews, group audit, and statutory audits plus CHF 98,900 in connection with audit related services in the context of registration statement fillings and issuance of shares and other statutory required audit reports.

Pre-Approval Policies and Procedures

To ensure the independence and objectivity of the Company's external auditors, the provision of all non-audit services by the external auditors are pre-approved by the Audit Committee.

ITEM 16D. Exemptions from the listing standards for audit committees

Not applicable.

ITEM 16E. Purchases of equity securities by the issuer and affiliated purchasers

In 2021, no purchases of our equity securities were made by or on behalf of Altamira Therapeutics Ltd. or any affiliated purchaser.

ITEM 16F. Change in registrant's certifying accountant

Not applicable.

ITEM 16G. Corporate governance

Summary of Significant Corporate Governance Differences From Nasdaq Listing Standards

Our common shares are listed on the Nasdaq Capital Market, or Nasdaq. We are therefore required to comply with certain of the Nasdaq's corporate governance listing standards, or the Nasdaq Standards. As a foreign private issuer, we may follow our home country's corporate governance practices in lieu of certain of the Nasdaq Standards. Our corporate governance practices differ in certain respects from those that U.S. companies must adopt in order to maintain a Nasdaq listing. A brief, general summary of those differences is provided as follows.

Independent Directors

Bermuda law does not require that a majority of our board of directors consist of independent directors. Our board of directors therefore may include fewer independent directors than would be required if we were subject to Nasdaq Listing Rule 5605(b)(1). In addition, we are not be subject to Nasdaq Listing Rule 5605(b)(2), which requires that independent directors must regularly have scheduled meetings at which only independent directors are present.

Audit Committee

We relied on the phase-in rules of the SEC and Nasdaq with respect to the independence of our audit committee. These rules require all members of our audit committee must meet the independence standard for audit committee members within one year of our initial public offering. All current members of our audit committee meet the independence requirements.

Compensation Committee

While Bermuda law does not require that we have a compensation committee, we have established a compensation committee in accordance with Bermuda law. As a result, our practice varies from the requirements of Nasdaq Listing Rule 5605(d), which sets forth certain requirements as to the responsibilities, composition and independence of compensation committees.

Nominating and Corporate Governance Committee

As permitted by the listing requirements of Nasdaq, we have also opted out of the requirements of Nasdaq Listing Rule 5605(e), which requires an issuer to have independent director oversight of director nominations.

Quorum requirements

Under Bermuda law we are required to specify a quorum in our Bye-laws. Our Bye-laws provide for a quorum of two or more persons present at the start of the meeting and representing in person or by proxy issued and outstanding voting shares in the company. Our practice thus varies from the requirement of Nasdaq Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting stock.

Solicitation of proxies

Our Bye-laws provide that our shareholders may appoint a proxy holder, and we must provide shareholders with an agenda and other relevant documents for the general meeting of shareholders. However, Bermuda law has no regulatory regime for the solicitation of proxies and thus our practice varies from the requirement of Nasdaq Listing Rule 5620(b), which sets forth certain requirements regarding the solicitation of proxies.

Shareholder approval

We have opted out of shareholder approval requirements for the issuance of securities in connection with certain events such as the acquisition of stock or assets of another company, the establishment of or amendments to equity-based compensation plans for employees, a change of control of us and certain private placements. To this extent, our practice varies from the requirements of Nasdaq Listing Rule 5635, which generally requires an issuer to obtain shareholder approval for the issuance of securities in connection with such events.

Third Party Compensation

Bermuda law does not require that we disclose information regarding third party compensation of our directors or director nominees. As a result, our practice varies from the third-party compensation disclosure requirements of Nasdaq Listing Rule 5250(b)(3).

Diversity disclosure

Bermuda law does not require that we disclose information regarding board diversity. As a result, our practice varies from the requirements of Nasdaq Listing Rule 5606.

ITEM 16H. Mine safety disclosure

Not applicable.

ITEM 16I. Disclosure Regarding Foreign Jurisdictions that Prevent Inspection

Not applicable.

PART III

ITEM 17. Financial statements

We have responded to Item 18 in lieu of this item.

ITEM 18. Financial statements

Financial Statements are filed as part of this Annual Report, see page F-1.

ITEM 19. Exhibits

(a) The following documents are filed as part of this registration statement:

1.1	Memorandum of Continuance of the registrant (incorporated herein by reference to exhibit 1.2 of the Auris Medical Holding Ltd. Annual Report on Form 20-F filed with the Commission on March 14, 2019)
1.2	Bye-laws of the Registrant (incorporated herein by reference to exhibit 1.3 of the Auris Medical Holding Ltd. Annual Report on Form 20-F filed with the Commission on March 14, 2019)
2.1	Form of Registration Rights Agreement between Auris Medical Holding AG and the shareholders listed therein (incorporated by reference to exhibit 4.1 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-197105) filed with the Commission on July 21, 2014)
2.2	Warrant Agreement, dated as of March 13, 2018, between Auris Medical Holding AG and Hercules Capital, Inc. (incorporated by reference to exhibit 2.2 of the Auris Medical Holding AG Annual Report on Form 20-F filed with the Commission on March 22, 2018)
2.3	Registration Rights Agreement, dated as of October 10, 2017 between Auris Medical Holding AG and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.3 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on October 11, 2017)
2.4	Purchase Agreement, dated as of May 2, 2018 between Auris Medical Holding AG and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on May 2, 2018)
2.5	Registration Rights Agreement, dated as of May 2, 2018 between Auris Medical Holding AG and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.2 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on May 2, 2018)
2.6	Form of Pre-Funded Warrant (incorporated by reference to exhibit 4.6 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-225676) filed with the Commission on July 12, 2018)
2.7	Form of Series A Warrant (incorporated by reference to exhibit 4.7 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-225676) filed with the Commission on July 12, 2018)
2.8	Form of Series B Warrant (incorporated by reference to exhibit 4.8 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-225676) filed with the Commission on July 12, 2018)
2.9	Form of Common Warrant (incorporated by reference to exhibit 4.1 of the Auris Medical Holding Ltd. report on Form 6-K filed with the commission on May 16, 2019)
2.10	Form of Pre-Funded Warrant (incorporated by reference to exhibit 4.2 of the Auris Medical Holding Ltd. report on Form 6-K filed with the commission on May 16, 2019)
2.11	Form of Common Warrant Agent Agreement (incorporated by reference to exhibit 4.3 of the Auris Medical Holding Ltd. report on Form 6-K filed with the commission on May 16, 2019)
2.12	Form of Pre-Funded Warrant Agent Agreement (incorporated by reference to exhibit 4.4 of the Auris Medical Holding Ltd. report on Form 6-K filed with the commission on May 16, 2019)
2.13*	Description of Securities Registered under Section 12 of the Exchange Act
2.14	Purchase Agreement, dated as of April 23, 2020 between Auris Medical Holding Ltd. and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.1 of the Auris Medical Holding Ltd. report on Form 6-K furnished with the Commission on April 23, 2020)
2.15	Registration Rights Agreement, dated as of April 23, 2020 between Auris Medical Holding Ltd. and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.2 of the Auris Medical Holding Ltd. report on Form 6-K furnished with the Commission on April 23, 2020)

4.1†	Collaboration and License Agreement, dated October 21, 2003, between Auris Medical AG and Xigen SA (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-197105) filed with the Commission on June 27, 2014)
4.2†	Co-Ownership and Exploitation Agreement, dated September 29, 2003, between Auris Medical AG and INSERM (incorporated by reference to exhibit 10.2 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-197105) filed with the Commission on June 27, 2014)
4.3	Form of Indemnification Agreement (incorporated by reference to exhibit 99.4 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on May 11, 2016)
4.4	Stock Option Plan A (incorporated by reference to exhibit 10.11 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-197105) filed with the Commission on June 27, 2014)
4.5	Stock Option Plan C (incorporated by reference to exhibit 10.12 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-197105) filed with the Commission on June 27, 2014)
4.6	Equity Incentive Plan, as amended (incorporated by reference to exhibit 99.1 to the Auris Medical Holding AG registration statement on Form S-8 (Registration no. 333-217306) filed with the Commission on April 14, 2017)
4.7	English language translation of Lease Agreement between Auris Medical AG and PSP Management AG (incorporated by reference to exhibit 4.8 of the Auris Medical Holding AG Annual Report on Form 20-F filed with the Commission on March 14, 2017)
4.8	Controlled Equity OfferingSM Sales Agreement, dated as of June 1, 2016, between Auris Medical Holding AG and Cantor Fitzgerald & Co. (incorporated by reference to exhibit 1.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on June 1, 2016)
4.9	Share Lending Agreement, dated as of June 1, 2016, between Thomas Meyer and Cantor Fitzgerald & Co. (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on June 1, 2016)
4.10	Loan and Security Agreement, dated as of July 19, 2016, between Auris Medical Holding AG, the several banks and other financial institutions or entities from time to time parties to the agreement and Hercules Capital, Inc. (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on July 19, 2016)
4.11	Consent and Waiver, dated as of March 8, 2018, between Auris Medical Holding AG, the several banks and other financial institutions or entities from time to time parties to the agreement and Hercules Capital, Inc. (incorporated by reference to exhibit 4.12 of the Auris Medical Holding AG Annual Report on Form 20-F filed with the Commission on March 22, 2018)
4.12	Joinder Agreement dated as of March 13, 2018 to the Loan and Security Agreement, dated as of July 19, 2016, between Auris Medical Holding AG, the several banks and other financial institutions or entities from time to time parties to the agreement and Hercules Capital, Inc. (incorporated by reference to exhibit 4.13 of the Auris Medical Holding AG Annual Report on Form 20-F filed with the Commission on March 22, 2018)
4.13	Share Pledge Agreement, dated July 19, 2016, between Auris Medical Holding AG and Hercules Capital, Inc. (incorporated by reference to exhibit 10.3 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on July 19, 2016)
4.14	Claims Security Assignment Agreement, dated July 19, 2016, between Auris Medical Holding AG and Hercules Capital, Inc. (incorporated by reference to exhibit 10.4 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on July 19, 2016)
4.15	Bank Account Claims Security Assignment Agreement, dated July 19, 2016, between Auris Medical Holding AG and Hercules Capital, Inc. (incorporated by reference to exhibit 10.5 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on July 19, 2016)
4.16	Purchase Agreement, dated as of October 10, 2017 between Auris Medical Holding AG and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on October 11, 2017)
4.17	Purchase Agreement, dated as of October 10, 2017 between Auris Medical Holding AG and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.2 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on October 11, 2017)
4.18	Placement Agency Agreement, dated as of January 28, 2018, between Auris Medical Holding AG and Ladenburg Thalmann & Co. Inc. (incorporated by reference to exhibit 1.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on January 30, 2018)
4.19	Securities Purchase Agreement, dated as of January 26, 2018 by and among Auris Medical Holding AG and the investors named therein (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on January 30, 2018)

4.20	Agreement and Plan of Merger, dated as of February 9, 2018 by and among Auris Medical Holding AG and Auris Medical NewCo Holding AG (incorporated by reference to exhibit 99.3 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on February 9, 2018)
4.21	Share Transfer Agreement, dated as of February 9, 2018 by and between Thomas Meyer and Auris Medical Holding AG (incorporated by reference to exhibit 4.22 of the Auris Medical Holding AG Annual Report on Form 20-F filed with the Commission on March 22, 2018)
4.22	Sales Agreement, dated as of November 30, 2018, between Auris Medical Holding AG and A.G.P./Alliance Global Partners (incorporated by reference to exhibit 1.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on November 30, 2018)
4.23	Form of Indemnification Agreement (incorporated by reference to exhibit 10.23 of the Auris Medical Holding Ltd. registration statement on Form F-1 (Registration no. 333-229465) filed with the Commission on March 20, 2019)
4.24	Amendment No. 1 to Sales Agreement, dated as of April 5, 2019, between Auris Medical Holding Ltd. and A.G.P./Alliance Global Partners (incorporated by reference to exhibit 1.1 of the Auris Medical Holding Ltd. report on Form 6-K filed with the Commission on April 5, 2019)
4.25	Convertible Loan Agreement, dated as of September 7, 2020, by and among Auris Medical Holding Ltd., Altamira Medica AG and FiveT Capital Holding AG (incorporated by reference to exhibit 99.1 of the Auris Medical Holding Ltd. report on Form 6-K furnished with the Commission on September 8, 2020)
4.26†	Agreement and Plan of Merger, dated June 1, 2021, by and among Auris Medical Holding Ltd., Auris Medical Inc., Trasir Therapeutics, Inc., and each of the stockholders of Trasir Therapeutics, Inc. (incorporated by reference to exhibit 2.1 of the Auris Medical Holding Ltd. report on Form 6-K furnished with the Commission on June 3, 2021)
4.27†	Exclusive License Agreement, dated December 11, 2020, by and between Washington University and Trasir Therapeutics, Inc. (incorporated by reference to exhibit 10.1 of the Auris Medical Holding Ltd. report on Form 6-K furnished with the Commission on June 3, 2021)
4.28	Convertible Loan Agreement, dated as of February 4, 2022, by and among Altamira Therapeutics Ltd. and FiveT Investment Management Ltd. (incorporated by reference to exhibit 99.1 of the Altamira Therapeutics Ltd. report on Form 6-K furnished with the Commission on February 8, 2022)
4.29†	Licensing & Distribution Agreement, dated February 28, 2022, by and between Altamira Medica Ltd. and Nuance Pharma Limited. (incorporated by reference to exhibit 10.1 of the Altamira Therapeutics Ltd. report on Form 6-K furnished with the Commission on March 4, 2022)
8.1*	List of subsidiaries
12.1*	Certification of Thomas Meyer pursuant to 17 CFR 240.13a-14(a)
12.2*	Certification of Elmar Schaerli pursuant to 17 CFR 240.13a-14(a)
13.1*	Certification of Thomas Meyer pursuant to 17 CFR 240.13a-14(b) and 18 U.S.C.1350
13.2*	Certification of Elmar Schaerli pursuant to 17 CFR 240.13a-14(b) and 18 U.S.C. 1350
15.1*	Consent of Deloitte AG
101.INS*	Inline XBRL Instance Document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
104*	Cover Page Interactive Data File formatted as Inline XBRL and contained in Exhibit 101

* Filed herewith

† Portions of this exhibit have been redacted pursuant to Item 4 of the "Instructions As To Exhibits" of Form 20-F because the Company customarily and actually treats the redacted information as private or confidential and the omitted information is not material. The Company hereby agrees to furnish an unredacted copy of the exhibit to the Commission upon request.

(b) Financial Statement Schedules

None.

Signatures

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

ALTAMIRA THERAPEUTICS LTD.

By: /s/ Thomas Meyer
Name: Thomas Meyer
Title: Chief Executive Officer

Date: April 12, 2022

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Audited Consolidated Financial Statements — Altamira Therapeutics Ltd.

As of December 31, 2021 and 2020 and for the years ended December 31, 2021, 2020, and 2019

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Altamira Therapeutics Ltd.

Opinion on the Financial Statements

We have audited the accompanying consolidated statements of financial position of Altamira Therapeutics Ltd. and subsidiaries (the "Company") as of December 31, 2021 and 2020, the related consolidated statements of profit or loss and other comprehensive income / (loss), changes in equity, and cash flows, for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board ("IFRS").

Basis for Opinion

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

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

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

INTANGIBLE ASSETS – CAPITALIZED DEVELOPMENT EXPENDITURE – refer to note 2 (section development expenditures), note 3 (section intangible assets – research and development), and note 9 (intangible assets) to the financial statements

Critical Audit Matter Description

The Company capitalized development expenditure for AM-125, a product candidate for the treatment of vertigo, in the amount of CHF 2,783,431 for the year ended December 31, 2021. The total carrying value of internally developed intangible assets was CHF 9,801,462 as of December 31, 2021.

We identified the Company's accounting treatment of capitalized development expenditure as a critical audit matter. This required a high degree of auditor judgment and an increased extent of effort when performing audit procedures to evaluate the reasonableness of management's judgments of technical feasibility, intention and ability to complete the development of AM-125 and to generate future economic profits from the intangible asset.

How the Critical Audit Matter Was Addressed in the Audit

We performed the following audit procedures amongst others, to address this critical audit matter:

- We assessed, with the assistance of our IFRS specialist, whether the Company's accounting policy and treatment is in line with IFRS and the underlying nature of the development of AM-125;
- We evaluated whether the technical feasibility criteria is met through assessment of the nature of the development approach of AM-125 and the results from ongoing studies;
- We evaluated new or contradictory evidence that would affect the intention and ability to complete the development of AM-125 or to generate profits in the future, including review of minutes of meetings of the board of directors and inquiries with management and project managers throughout the year, and;
- We tested a sample of capitalized research and development costs to evaluate if they fulfil the criteria of being directly attributable to the development of AM-125 and evaluate whether amounts agree to supporting documentation and the confirmations received from clinical research organisations (CRO) to determine whether only costs related to the development of AM-125 are capitalized.

Deloitte AG

/s/ Roland Mueller

/s/ Adrian Kaeppeli

Auditor in Charge

Zurich, Switzerland
April 12, 2022

We have served as the Company's auditor since 2014.

Consolidated Statement of Profit or Loss and Other Comprehensive Income/(Loss)
For the Years Ended December 31, 2021, 2020 and 2019
(in CHF)

	Note	2021	2020	2019
Revenue		**63,882**	**—**	**—**
Cost of Sales	19	(2,240,554)	—	—
Gross profit		**(2,176,672)**	**—**	**—**
Other operating income	18	460,710	174,475	—
Research and development	20	(8,939,037)	(2,862,979)	(3,325,281)
Sales and marketing	21	(1,498,218)	—	—
General and administrative	22	(4,946,576)	(2,594,662)	(3,933,863)
Operating loss		**(17,099,793)**	**(5,283,166)**	**(7,259,144)**
Interest income	24	3,219	258	17,882
Interest expense	24	(189,695)	(135,151)	(28,628)
Foreign currency exchange gain/(loss), net	24	328,641	(333,553)	(219,573)
Revaluation gain/(loss) from derivative financial instruments	24 29, 30	(410,918)	(2,250,222)	663,725
Transaction costs	24	—	(219,615)	—
Loss before tax		**(17,368,546)**	**(8,221,449)**	**(6,825,738)**
Income tax gain/(loss)	25	(21,620)	21,284	193,837
Net loss attributable to owners of the Company		**(17,390,166)**	**(8,200,165)**	**(6,631,901)**
Other comprehensive income/(loss):				
Items that will never be reclassified to profit or loss				
Remeasurements of defined benefit liability, net of taxes of CHF 0	23	264,984	(26,118)	(72,010)
Items that are or may be reclassified to profit or loss				
Foreign currency translation differences, net of taxes of CHF 0		772	88,862	16,446
Other comprehensive income/(loss), net of taxes of CHF 0		**265,756**	**62,744**	**(55,564)**
Total comprehensive loss attributable to owners of the Company		**(17,124,410)**	**(8,137,421)**	**(6,687,465)**
Basic and diluted loss per share	26	(1.31)	(1.36)	(2.28)

The accompanying notes form an integral part of these consolidated financial statements.

Consolidated Statement of Financial Position
As of December 31, 2021 and 2020
(in CHF)

	Note	December 31, 2021	December 31, 2020
ASSETS			
Non-current assets			
Property and equipment	7	1	46,636
Right-of-use assets	8	564,714	—
Intangible assets	9	14,314,877	9,115,410
Other non-current financial assets		199,105	20,001
Total non-current assets		**15,078,697**	**9,182,047**
Current assets			
Inventories	10	839,221	—
Trade receivables		21,746	—
Other receivables	11	917,833	80,861
Prepayments	12	996,910	277,589
Cash and cash equivalents	13	984,191	11,258,870
Total current assets		**3,759,901**	**11,617,320**
Total assets		**18,838,598**	**20,799,367**
EQUITY AND LIABILITIES			
Equity			
Share capital	14	149,643	114,172
Share premium		188,511,476	177,230,300
Foreign currency translation reserve		62,069	61,297
Accumulated deficit		(176,018,660)	(160,635,879)
Total shareholders' (deficit)/equity attributable to owners of the Company		**12,704,528**	**16,769,890**
Non-current liabilities			
Derivative financial instruments	5	1,233	6,318
Non-current lease liabilities	8	461,485	—
Employee benefit liability	23	668,319	867,376
Deferred tax liabilities	25	142,484	125,865
Total non-current liabilities		**1,273,521**	**999,559**
Current liabilities			
Loan	29	—	523,920
Derivative financial instruments	29	—	310,439
Current lease liabilities	8	114,251	—
Trade and other payables	16	3,697,723	762,453
Accrued expenses	17	1,048,575	1,433,106
Total current liabilities		**4,860,549**	**3,029,918**
Total liabilities		**6,134,070**	**4,029,477**
Total equity and liabilities		**18,838,598**	**20,799,367**

The accompanying notes form an integral part of these consolidated financial statements.

Consolidated Statement of Changes in Equity
As of December 31, 2021, 2020 and 2019
(in CHF)

	Note	Share Capital	Share Premium	Foreign Currency Translation Reserve	Accumulated Deficit	Total Equity / (Deficit)
As of January 1, 2019		**710,336**	**149,286,723**	**(44,011)**	**(146,303,398)**	**3,649,650**
Total comprehensive loss						
Net loss		—	—	—	(6,631,901)	(6,631,901)
Other comprehensive income / (loss)		—	—	16,446	(72,010)	(55,564)
Total comprehensive loss		**—**	**—**	**16,446**	**(6,703,911)**	**(6,687,465)**
Transactions with owners of the Company						
Capital increase / Exercise of warrants		940,044	8,853,599	—	—	9,793,643
Transaction costs		—	(948,615)	—	—	(948,615)
Share based payments	15	—	—	—	228,920	228,920
Balance at December 31, 2019		**1,650,380**	**157,191,707**	**(27,565)**	**(152,778,389)**	**6,036,133**
As of January 1, 2020		**1,650,380**	**157,191,707**	**(27,565)**	**(152,778,389)**	**6,036,133**
Total comprehensive loss						
Net loss		—	—	—	(8,200,165)	(8,200,165)
Other comprehensive income / (loss)		—	—	88,862	(26,118)	62,744
Total comprehensive loss		**—**	**—**	**88,862**	**(8,226,283)**	**(8,137,421)**
Transactions with owners of the Company						
Reduction par value		(1,973,044)	1,973,044	—	—	—
Capital increase / Exercise of warrants		429,466	15,645,530	—	—	16,074,996
Transaction costs		—	(636,858)	—	—	(636,858)
Conversion of loan		7,370	3,056,877	—	—	3,064,247
Share based payments	15	—	—	—	368,793	368,793
Balance at December 31, 2020		**114,172**	**177,230,300**	**61,297**	**(160,635,879)**	**16,769,890**
As of January 1, 2021		**114,172**	**177,230,300**	**61,297**	**(160,635,879)**	**16,769,890**
Total comprehensive loss						
Net loss		—	—	—	(17,390,166)	(17,390,166)
Other comprehensive income / (loss)		—	—	772	264,984	265,756
Total comprehensive loss		—	—	**772**	**(17,125,182)**	**(17,124,410)**
Transactions with owners of the Company						
Capital increase / Exercise of warrants		20,822	7,083,869	—	—	7,104,691
Transaction costs		—	(156,817)			(156,817)
Conversion of loan		5,168	1,366,087	—	—	1,371,255
Share based/Asset purchase		7,735	2,447,081	—	1,078,800	3,533,616
Share based payments	15	1,746	540,956	—	663,601	1,206,303
Balance at December 31, 2021		**149,643**	**188,511,476**	**62,069**	**(176,018,660)**	**12,704,528**

The accompanying notes form an integral part of these consolidated financial statements.

Consolidated Statement of Cash Flows
For the Years Ended December 31, 2021, 2020, and 2019
(in CHF)

	Note	2021	2020	2019
Cash flows from operating activities				
Net loss		**(17,390,166)**	**(8,200,165)**	**(6,631,901)**
Adjustments for:				
Depreciation	7, 8, 20, 22	76,357	20,036	30,823
Impairment of intangible assets	9, 20	1,529,929	—	—
Unrealized foreign currency exchange loss, net		(279,329)	10,818	21,290
Net interest expense	24	174,593	127,160	1,205
Share based payments	15	1,206,303	368,793	226,601
Transaction costs	24	—	219,615	—
Employee benefits		65,927	80,811	40,150
Revaluation loss/(gain) derivative financial instruments	24, 29, 30	410,918	2,250,222	(663,725)
Income tax loss/(gain)	25	21,620	(21,284)	(193,837)
		(14,183,848)	**(5,143,994)**	**(7,169,394)**
Changes in:				
Inventories		(839,221)	—	—
Trade and other receivables		(586,612)	254,438	(18,925)
Prepayments		(719,321)	156,661	(82,948)
Trade and other payables		2,937,019	(175,878)	(898,088)
Accrued expenses		(280,755)	65,303	(224,077)
Net cash used in operating activities		**(13,672,738)**	**(4,843,470)**	**(8,393,432)**
Cash flows from investing activities				
Purchase of property and equipment	7	—	—	(63,600)
Purchase of intangibles	9	(3,325,952)	(2,315,232)	(2,955,036)
Cash paid for other non-current financial assets		(179,104)	—	—
Interest received	24	—	258	17,882
Net cash used in investing activities		**(3,505,056)**	**(2,314,974)**	**(3,000,754)**
Cash flows from financing activities				
Proceeds from offerings and warrant exercises	14, 30	6,842,940	16,074,996	9,793,643
Transaction costs	14	(156,817)	(636,858)	(948,615)
Proceeds from loans	29	—	1,522,931	—
Repayment of loan		(50,000)	—	(1,463,328)
Repayment of lease liabilities		(18,700)	-	-
Interest paid	8, 24, 29	(3,699)	—	(3,745)
Net cash from financing activities		**6,613,724**	**16,961,069**	**7,377,955**
Net increase / (decrease) in cash and cash equivalents		**(10,564,070)**	**9,802,625**	**(4,016,231)**
Cash and cash equivalents at beginning of the period		11,258,870	1,384,720	5,393,207
Net effect of currency translation on cash		289,391	71,525	7,744
Cash and cash equivalents at end of the period		**984,191**	**11,258,870**	**1,384,720**

The accompanying notes form an integral part of these consolidated financial statements.

1. Reporting entity

Altamira Therapeutics Ltd. (formerly Auris Medical Holding Ltd.) (the "Company") is an exempted company incorporated in Bermuda and is subject to Bermuda law. The Company's registered address is Clarendon House, 2 Church Street, Hamilton HM11, Bermuda. These consolidated financial statements comprise the Company and its subsidiaries (together referred to as the "Group" and individually as "Group entities"). The Company is the ultimate parent of the following Group entities:

- Auris Medical AG, Basel, Switzerland (100%) with a nominal share capital of CHF 2,500,000
- Otolanum AG, Zug, Switzerland (100%) with a nominal share capital of CHF 100,000
- Zilentin AG, Zug, Switzerland (100%), with a nominal share capital of CHF 100,000
- Altamira Medica AG, Zug, Switzerland (100%), with a nominal share capital of CHF 3,000,000
- Altamira Therapeutics, Inc., Dover, Delaware, United States (100%) with a nominal share capital of USD 100
- Auris Medical Ltd., Dublin, Ireland (100%) with a nominal share capital of EUR 100
- Auris Medical Pty Ltd, Collingwood, Australia (100%), with a nominal share capital of AUD 100

On March 13, 2018, the former Auris Medical Holding Ltd. merged (the "Merger") into Auris Medical NewCo Holding AG ("Auris NewCo"), a newly incorporated, wholly-owned Swiss subsidiary following shareholder approval at an extraordinary general meeting of shareholders held on March 12, 2018. Following the Merger, Auris NewCo, the surviving company, had a share capital of CHF 122,347.76, divided into 6,117,388 (pre-2019 Reverse Share Split) common shares with a nominal value of CHF 0.02 (pre-2019 Reverse Share Split) each. Pursuant to the Merger, the Company's shareholders received one common share with a nominal value of CHF 0.02 (pre-2019 Reverse Share Split) of Auris NewCo for every 10 of the Company's common shares held prior to the Merger, effectively resulting in a "reverse stock split" at a ratio of 10-for-1. Auris NewCo changed its name to "Auris Medical Holding AG" following consummation of the Merger. Following shareholder approval at an extraordinary general meeting of shareholders held on March 8, 2019 and upon the issuance of a certificate of continuance by the Registrar of Companies in Bermuda on March 18, 2019, the Company discontinued as a Swiss company and, pursuant to Article 163 of the Swiss Federal Act on Private International Law and pursuant to Section 132C of the Companies Act 1981 of Bermuda (the "Companies Act"), continued existence under the Companies Act as a Bermuda company with the name "Auris Medical Holding Ltd." (the "Redomestication"). The common shares of Auris Medical Holding Ltd. traded on the Nasdaq Capital Market under the trading symbol "EARS." On July 21, 2021, the Company changed its name to Altamira Therapeutics Ltd. Since July 26, 2021, the Company's common shares are traded under the trading symbol "CYTO".

The Company is primarily involved in the development of therapeutics that address important unmet medical needs. The Company is currently active in three areas: the development of RNA therapeutics for delivery to extrahepatic targets (with AM-401 targeting KRAS driven cancers as first project, preclinical stage), the development of intranasal betahistine for the treatment of vertigo (AM-125, in Phase 2). Through its affiliate Altamira Medica, the Company is commercializing a nasal spray for protection against airborne viruses and allergens (AM-301).

2. Basis of preparation

Statement of compliance

These consolidated financial statements have been prepared in accordance with International Financial Reporting Standards as issued by the International Accounting Standards Board ("IFRS").

These consolidated financial statements were approved by the Board of Directors and the Audit Committee of the Company on April 7, 2022.

Basis of measurement

The consolidated financial statements are prepared on the historical cost basis, except for the revaluation to fair value of certain financial liabilities. Historical cost is generally based on the fair value of the consideration given in exchange for goods and services. The principal accounting policies adopted are set out below.

In addition, for financial reporting purposes, fair value measurements are categorized into Level 1, 2 or 3 based on the degree to which the inputs to the fair value measurements are observable and the significance of the inputs to the fair value measurement in its entirety, which are described as follows:

- Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities that the entity can access at the measurement date
- Level 2 inputs are inputs, other than quoted prices included within Level 1, that are observable for the asset or liability, either directly or indirectly; and
- Level 3 inputs are unobservable inputs for the asset or liability.

Functional and reporting currency

These consolidated financial statements are presented in Swiss Francs ("CHF"), which is the Company's functional ("functional currency") and the Group's reporting currency.

Redomestication

The Redomestication of the Company from Switzerland to Bermuda is a continuance of its business. Therefore, the consolidated financial statements present the operation of Auris Medical Holding AG for the time before the Redomestication and of Auris Medical Holding Ltd for the time following the Redomestication.

2019 Reverse Share Split

The Company effected the 2019 Reverse Share Split of its common shares at a ratio of 1-for-20. No fractional common shares were issued as fractional common shares were settled in cash. Impacted amounts and share information included in the consolidated financial statements and notes thereto have been adjusted for the reverse share split as if such reverse share split occurred on the first day of the periods presented. Certain amounts in the notes to the consolidated financial statements may be slightly different than previously reported due to rounding of fractional shares as a result of the reverse share split.

Use of estimates and judgments

The preparation of financial statements in conformity with IFRS requires management to make judgments, estimates and assumptions that affect the application of accounting policies and the reported amounts of assets, liabilities, income and expenses. Actual results may differ from these estimates.

Estimates and underlying assumptions are reviewed on an ongoing basis. Revisions of accounting estimates are recognized in the period in which the estimates are revised and in any future periods affected.

Information about judgments made in applying accounting policies that have the most significant effects on the amounts recognized in the consolidated financial statements are described below.

Income taxes

As disclosed in Note 25 the Group has significant tax losses in Switzerland. These tax losses represent potential value to the Group to the extent that the Group is able to create taxable profits in Switzerland prior to expiry of such losses. Tax losses may be used within 7 years from the year the losses arose.

The Group also has tax losses in the United States which may be used within 20 years of the end of the year in which losses arose, or for a shorter time period in accordance with prevailing state law.

Other than a tax asset in the amount of CHF 31,879 (31.12.2020: CHF 476,363), the Group has not recorded any deferred tax assets in relation to these tax losses. Deferred tax assets on tax losses were only considered to the extent that they offset taxable temporary differences within the same entity. The key factors which have influenced management in arriving at this evaluation are the fact that the business is still in a development phase and the Group has not yet a history of making profits. Should management's assessment of the likelihood of future taxable profits change, a deferred tax asset will be recorded. Income tax loss reflects the reassessment of deferred tax assets and liabilities booked in the 2021 fiscal year.

Development expenditures

The project stage forms the basis for the decision as to whether costs incurred for the Group's development projects can be capitalized. We do not capitalize clinical development expenditures until the Group obtains regulatory approval (i.e. approval to commercially use the product), as this is considered to be essentially the first point in time where it becomes probable that future revenues can be generated. For the Group's intranasal betahistine program for the treatment of vertigo (AM-125), however, the development is primarily focused on the delivery route and formulation and not the drug itself (already an approved generic) and aims to demonstrate higher bioavailability through intranasal delivery. Given the nature of the development approach and the fact that there is an existing market in which oral betahistine for the treatment of vertigo has been approved, direct development expenditures have been capitalized.

As of each reporting date, the Group estimates the level of service performed by the vendors and the associated costs incurred for the services performed. As part of the process of preparing the Group's financial statements, the Group is required to estimate its accrued expenses. This process involves reviewing contracts, identifying services that have been performed on the Group's behalf and estimating the level of service performed and the associated cost incurred for the service when it has not yet been invoiced or otherwise notified of the actual cost.

Employee benefits

The Group maintains a pension plan for all employees in Switzerland through payments to a legally independent collective foundation. This pension plan qualifies under IFRS as defined benefit pension plan.

The Group's net obligation in respect of defined benefit plans is calculated by estimating the amount of future benefit that employees have earned in return for their service in the current and prior periods, discounting that amount and deducting the fair value of any plan assets. The Company makes relevant actuarial assumptions with regard to the discount rate, future salary increases and life expectancy.

Research and Development and Accrued Expenses

The Company records the costs associated with research, nonclinical and clinical trials, and manufacturing process development as incurred. These costs are a significant component of the Company's research and development expenses, with a substantial portion of the Company's on-going research and development activities being conducted by third party service providers, including contract research and manufacturing organizations.

The Company accrues for expenses resulting from obligations under agreements with contract research organizations ("CROs"), contract manufacturing organizations ("CMOs"), and other outside service providers for which payment flows do not match the periods over which materials or services are provided to the Company. Accrued expenses are recorded based on estimates of services received and efforts expended pursuant to agreements established with CROs, CMOs, and other outside service providers. These estimates are typically based on contracted amounts applied to the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the services. The Company makes significant judgments and estimates in determining the accrued expense balance in each reporting period. In the event advance payments are made to a CRO, CMO, or outside service provider, the payments will be recorded as prepayments which will be expensed as the contracted services are performed. Inputs, such as the services performed, the number of patients enrolled, or the trial duration, may vary from the Company's estimates. As actual costs become known, the Company adjusts its prepayments and accrued expenses.

3. Significant accounting policies

The accounting policies set out below have been applied consistently to all periods presented in these consolidated financial statements, unless otherwise indicated.

Basis of consolidation

Subsidiaries

Subsidiaries are entities controlled by the Group. The Group controls an entity when it is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. The financial statements of subsidiaries are included in the consolidated financial statements from the date on which control commences until the date on which control ceases.

Transactions eliminated on consolidation

All inter-company balances, transactions and unrealized gains on transactions have been eliminated in consolidation. Unrealized losses are also eliminated unless the transaction provides evidence of an impairment of the asset transferred.

Segment reporting

A segment is a distinguishable component of the Group that engages in business activities from which it may earn revenues and incur expenses, including revenues and expenses that relate to transactions with any of the Group's other components.

The Chief Executive Officer is determined to be the Group's Chief Operating Decision Maker ("CODM"). The CODM assesses the performance and allocates the resources of the Group as a whole, as all of the Group's activities are focusing on the development of therapeutics for the treatment and prevention of ear, nose, throat and related disorders. Financial information is only available for the Group as a whole. Therefore, management considers there is only one operating segment under the requirements of IFRS 8, Operating Segments.

Foreign currency

Foreign currency transactions

Items included in the financial statements of Group entities are measured using the currency of the primary economic environment in which the entity operates. Foreign currency transactions are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of such transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognized in profit or loss. Non-monetary items that are measured based on historical cost in a foreign currency are not re-translated.

Foreign operations

Assets and liabilities of Group entities whose functional currency is other than CHF are included in the consolidation by translating the assets and liabilities into the reporting currency at the exchange rates applicable at the end of the reporting period. Income and expenses are translated at average exchange rates (unless this average is not a reasonable approximation of the cumulative effect of the rates prevailing on the transaction dates, in which case income and expenses are translated at the dates of the transaction).

These foreign currency translation differences are recognized in Other Comprehensive income/(loss) and presented in the foreign currency translation reserve in equity. When a foreign operation is disposed of such that control is lost, the cumulative amount in the translation reserve related to that foreign operation is reclassified to profit or loss as part of the gain or loss on disposal.

Closing rates for the most significant foreign currencies relative to CHF:

Currency		Geographical area	Reporting entities	December 31, 2021	December 31, 2020	December 31, 2019
CHF	Swiss Franc	Switzerland	5	1.0000	1.0000	1.0000
USD	Dollar	United States	1	0.9110	0.8840	0.9674
EUR	Euro	Europe	1	1.0361	1.0817	1.0855
AUD	Dollar	Australia	1	0.6620	0.6822	—

Average exchange rates for the year for the most significant foreign currencies relative to CHF:

Currency		Geographical area	Reporting entities	2021	2020	2019
CHF	Swiss Franc	Switzerland	5	1.0000	1.0000	1.0000
USD	Dollar	United States	1	0.9142	0.9581	0.9938
EUR	Euro	Europe	1	1.0810	1.0825	1.1128
AUD	Dollar	Australia	1	0.6866	0.6546	—

Property and equipment

Property and equipment is measured at historical costs less accumulated depreciation and any accumulated impairment losses. Historical costs include expenditures that are directly attributable to the acquisition of the items. When parts of an item of tangible assets have different useful lives, they are accounted for as separate tangible asset items (major components). Depreciation is calculated on a straight-line basis over the expected useful life of the individual asset. The applicable estimated useful lives are as follows:

Production equipment	5 years
Office furniture and electronic data processing equipment (“EDP”)	3 years

Subsequent costs are included in the asset’s carrying amount or recognized as a separate asset, as appropriate, only when it is probable that future economic benefits associated with the item will flow to the Group and the cost of the item can be measured reliably. The carrying amount of the replaced part is derecognized. All other repairs and maintenance are charged to profit or loss during the financial period in which they are incurred.

Depreciation methods, useful lives and residual values are reviewed at each reporting date and adjusted if appropriate. When an asset is reviewed for impairment, the asset’s carrying amount may be written down immediately to its recoverable amount, provided the asset’s carrying amount is greater than its estimated recoverable amount. Management assesses the recoverable amount by assessing the higher of its fair value less costs to sell or its value in use.

Cost and accumulated depreciation related to assets retired or otherwise disposed are removed from the accounts at the time of retirement or disposal and any resulting gain or loss is included in profit or loss in the period of disposition.

Intangible assets

Research and development

Expenditures on the Group's research programs are not capitalized, they are expensed when incurred.

Expenditures on the Group's development programs are generally not capitalized except if development costs can be measured reliably, the product or process is technically and commercially feasible, future economic benefits are probable, and the Group intends to and has sufficient resources to complete development and to use or sell the asset. For the development projects of the Group, these criteria are generally only met when regulatory approval for commercialization is obtained. For the AM-125 program for the treatment of vertigo it is the Group's assessment that the criteria mentioned above are met and therefore direct development expenditures have been capitalized for AM-125 in 2019, 2020 and 2021. Intellectual property-related costs for patents are part of the expenditure for research and development projects. Therefore, the costs for the prosecution and registration of patents are expensed when incurred as long as the research and development project concerned does not meet the criteria for capitalization. In case of AM-125, where in 2019 a US patent was issued and a related EU application was allowed, prosecution and registration costs have been capitalized as the criteria have been met.

Licenses, intellectual property and data rights

Intellectual property rights that are acquired by the Group are capitalized as intangible assets if they are controlled by the Group, are separately identifiable and are expected to generate future economic benefits, even if uncertainty exists as to whether the research and development will ultimately result in a marketable product. Consequently, upfront and milestone payments to third parties for the exclusive use of pharmaceutical compounds in specified areas of treatment are recognized as intangible assets.

Measurement

Intangible assets acquired that have finite useful lives are measured at cost less accumulated amortization and any accumulated impairment losses.

Subsequent expenditure

Subsequent expenditure is capitalized only when it increases the future economic benefits embodied in the specific asset to which it relates. All other expenditure, including expenditure on internally generated goodwill and brands, is recognized in profit or loss as incurred.

Amortization

All licenses of the Group have finite lives. Amortization will commence once the Group's intangible assets are available for use which will be the case after regulatory approvals are obtained and the related products are available for use. Amortization of licenses is calculated on a straight-line basis over the period of the expected benefit or until the license expires, whichever is shorter. The estimated useful life is 10 years or the remaining term of patent protection. The Group assesses at each statement of financial position date whether intangible assets which are not yet ready for use are impaired.

Impairment of non-financial assets

Property and equipment and intangible assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. For the purpose of assessing impairment, assets are grouped at the lowest levels for which there are separately identifiable cash flows (cash-generating units). An impairment loss is recognized as the amount by which the asset's carrying amount exceeds its recoverable amount. The recoverable amount is the higher of an asset's fair value less costs to sell or value in use. Impairment losses are recognized in profit or loss. Assets that were previously impaired are reviewed for possible reversal of the impairment at each reporting date. Any increase in the carrying amount of an asset will be based on the depreciated historical costs had the initial impairment not been recognized.

Asset purchase

On June 1, 2021, we acquired 100% of the share capital of privately held Trasir Therapeutics Inc. ("Trasir") through the merger of our subsidiary Auris Medical Inc. with and into Trasir (the "Merger"), with Trasir surviving the merger as the surviving entity. Trasir was subsequently renamed Altamira Therapeutics, Inc. and redomiciled in Dover, Delaware. Founded in 2014, Trasir has been a pioneer in the development of nanoparticles for extrahepatic oligonucleotide delivery.

The purchase price for Trasir comprised: (i) 764,370 non-registered common shares of the Company, par value CHF 0.01 per share, calculated based on a value of USD 2,500,000 divided by the average closing price of the Common Shares on the 15 trading days preceding the closing date (the "Reference Price", which amounted to USD 3.27 per Common Share); (ii) contingent on the occurrence of positive results from a subsequent post-closing scientific study led by Trasir ("Positive Results"), USD 1,500,000 of common shares of the Company to be calculated based on the average closing price of the common shares on the 15 trading days preceding the occurrence of Positive Results; and (iii) USD 210,000 for expenses incurred by certain selling Trasir shareholders paid in USD 180,000 in cash and 9,173 non-registered common shares based on the Reference Price.

Trasir's main asset is an exclusive license agreement (the "License Agreement") with Washington University located in St. Louis, Missouri ("WU"). Pursuant to the License Agreement, WU granted Trasir an exclusive, worldwide, royalty-bearing license (with the right to sublicense) during the term of the License Agreement under certain patent rights owned or controlled by WU to research, develop, make, have made, sell, offer for sale, use and import pharmaceutical products covered under such patent rights for all fields of use. Such licensed products may include "silencing RNA" (siRNAs) pharmaceutical preparations formulated in combination with Trasir's proprietary delivery technologies. In consideration for such worldwide, exclusive license, the Company (through its acquisition of Trasir, described above) will be obligated to pay WU: annual license maintenance fees in the low five figures through first commercial sale; pre-clinical and clinical regulatory milestones; sales milestones; and a low single digit royalty based on annual net sales of licensed products worldwide for at least the applicable patent term or period of marketing exclusivity, whichever is longer, but in no case less than a minimum royalty term of 12 years; and a percentage share (in the double digits) of sublicensing revenues received by the Company in connection with licensed products. Such regulatory and sales milestones may total up to an aggregate of USD 4,375,000. In the event the Company fails to meet certain regulatory diligence milestones, WU will have the right to terminate the license.

The acquisition of Trasir was treated as an asset acquisition because substantially all the fair value is concentrated in a single identifiable asset, the License Agreement with WU. The acquisition of the license is settled to a large extent in exchange for a variable number of the Company's publicly listed shares. IFRS 2 "Share-based payments" was applied. With regards to the contingent part of the purchase price as mentioned under (ii) above, a downward adjustment of CHF 269,700 to the estimated fair value was made to reflect the possibility of not meeting the condition of Positive Results. As of December 31, 2021, the total carrying amount of the license acquired amounted to CHF 3,893,681, including directly attributable transaction costs of CHF 198,246.

Leases

The Group assesses at contract inception whether a contract is, or contains, a lease. That is, if the contract conveys the right to control the use of an identified asset for a period of time in exchange for consideration. The Group applies a single recognition and measurement approach for all leases, except for short-term leases and leases of low-value assets. The Group recognizes lease liabilities to make lease payments and right-of-use assets representing the right to use the underlying assets.

Right-of-use assets

The Group recognizes right-of-use assets at the commencement date of the lease. Right-of-use assets are measured at cost, less any accumulated depreciation and impairment losses, and adjusted for any remeasurements of lease liabilities. The cost of right-of-use assets includes the amount of lease liabilities recognized, initial direct costs incurred, and lease payments made at or before the commencement date. Unless the Group is reasonably certain to obtain ownership of the leased asset at the end of the lease term, the recognized right-of-use assets are depreciated on a straight-line basis over the shorter of its estimated useful life and the lease term. Right-of-use assets are subject to impairment.

Lease liabilities

At the commencement date of the lease, the Group recognizes lease liabilities measured at the present value of lease payments to be made over the lease term. The lease payments include fixed payments less any lease incentives receivable, variable lease payments that depend on an index or a rate, and amounts expected to be paid under residual value guarantees. The lease payments also include the exercise price of a purchase option reasonably certain to be exercised by the Group and payments of penalties for terminating a lease, if the lease term reflects the Group exercising the option to terminate. The variable lease payments that do not depend on an index or a rate are recognized as expense in the period during which the event or condition that triggers the payment occurs. In calculating the present value of lease payments, the Group uses the incremental borrowing rate at the lease commencement date if the interest rate implicit in the lease is not readily determinable. After the commencement date, the amount of lease liabilities is increased to reflect the accumulation of interest and reduced by the lease payments made. In addition, the carrying amount of lease liabilities is remeasured if there is a modification, a change in the lease term, a change in the in-substance fixed lease payments or a change in the assessment to purchase the underlying asset.

Short-term leases and leases of low-value assets

The Group applies the short-term lease recognition exemption to its short-term leases. It also applies the lease of low-value assets recognition exemption to leases that are considered of low value (i.e. below CHF 5,000). Lease payments on short-term leases and leases of low-value assets are recognized as expense over the lease term.

Inventories

Inventories are stated at the lower of cost and net realizable value. Cost comprises direct materials and, where applicable, direct labor costs and those overheads that have been incurred in bringing the inventories to their present location and condition. Cost is calculated using the first-in, first-out method. Net realizable value represents the estimated selling price less all estimated costs of completion and costs to be incurred in marketing, selling and distribution.

Financial instruments

The Group classifies its financial assets in the following categories: loans and receivables based on the expected loss model. The classification depends on the nature and purpose of the financial assets and is determined at the time of initial recognition.

Recognition and derecognition of non-derivative financial assets and liabilities

The Group initially recognizes loans and receivables and debt securities issued on the date when they are originated. All other financial assets and financial liabilities are initially recognized on the trade date.

The Group derecognizes a financial asset when the contractual rights to the cash flows from the asset expire, or it transfers the rights to receive the contractual cash flows in a transaction in which substantially all of the risks and rewards of ownership of the financial asset are transferred, or it neither transfers nor retains substantially all of the risks and rewards of ownership and does not retain control over the transferred asset. Any interest in such derecognized financial assets that is created or retained by the Group is recognized as a separate asset or liability.

The Group derecognizes a financial liability when its contractual obligations are discharged, cancelled, or expired.

Financial assets and financial liabilities are offset and the net amount presented in the statement of financial position when, and only when, the Group has a legal right to offset the amounts and intends either to settle them on a net basis or to realize the asset and settle the liability simultaneously.

Non-derivative financial assets and liabilities—measurement

Loans and receivable

These are non-derivative financial assets with fixed or determinable payments that are not quoted in an active market. Loans and receivables are initially recognized at fair value plus any directly attributable transaction costs. Subsequent to initial recognition, they are measured at amortized cost using the effective interest method, less expected losses.

Cash and cash equivalents

The Group considers all short-term, highly liquid investments that are readily convertible into known amounts of cash and which are subject to an insignificant risk of changes in value with original maturities of three months or less at the date of the purchase to be cash equivalents.

Non-derivative financial liabilities—measurement

Non-derivative financial liabilities are initially recognized at fair value less any directly attributable transaction costs. Subsequent to initial recognition, these liabilities are measured at amortized cost using the effective interest method.

Convertible loans

In a convertible loan classified as a hybrid contract containing a host and a separated embedded derivative, both classified as liability, the carrying amount of the host contract at initial recognition is the difference between the carrying amount of the hybrid contract and the fair value of the embedded derivative. Transaction costs that relate to the issue of the convertible loan are allocated to the host and embedded derivative in proportion to the allocation of the gross proceeds. Transaction costs relating to the embedded derivative are immediately recognized in profit and loss. Transaction costs relating to the host contract are included in the carrying amount of the liability. The host contract is then subsequently measured at amortized cost, using the effective interest method.

Share capital

All shares of the Company are registered shares and classified as part of shareholders' equity. Incremental costs directly attributable to the issue of the Company's shares, net of any tax effects, are recognized as a deduction from equity. The warrants are classified as a financial liability at fair value through profit or loss and the cost allocated to the liability component will be immediately expensed to the income statement.

The Company has not paid any dividends since its inception and does not anticipate paying dividends in the foreseeable future.

Repurchase and reissue of ordinary shares (treasury shares)

When shares recognized as equity are repurchased, the amount of the consideration paid, which includes directly attributable costs, net of any tax effects, is recognized as a deduction from equity. Repurchased shares are classified as treasury shares and are presented in the treasury share reserve. When treasury shares are sold or reissued subsequently, the amount received is recognized as an increase in equity and the resulting surplus or deficit (calculated as the difference between initial cost and fair value) on the transaction is presented within share premium.

Impairment of non-derivative financial assets

Financial assets are assessed at each reporting date to determine whether there is objective evidence of impairment.

Objective evidence that financial assets are impaired includes:

- default or delinquency by a debtor;
- indications that a debtor or issuer will enter bankruptcy;
- adverse changes in the payment status of borrowers or issuers;
- the disappearance of an active market for a security; or
- observable data indicating that there is measurable decrease in expected cash flows from a group of financial assets.

Financial assets measured at amortized cost

The Group considers evidence of impairment for these assets at an individual asset level. An impairment loss is calculated as the difference between an asset's carrying amount and the present value of the estimated future cash flows discounted at the asset's original effective interest rate. Losses are recognized in profit or loss and reflected in an allowance account. When the Group considers that there are no realistic prospects of recovery of the asset, the relevant amounts are written off. If the amount of impairment loss subsequently decreases and the decrease can be related objectively to an event occurring after the impairment was recognized, then the previously recognized impairment loss is reversed through profit or loss.

Derivative Financial Instruments

Derivative financial instruments (assets) are accounted as the cost to obtain the rights from a third party to issue shares under the purchase agreement and changes in fair value are shown as profit or loss. The fair value calculation of the derivative financial instrument (asset) is adjusted on the utilization of the asset based on total dollar amount of the purchase agreement.

Derivative financial instruments (liabilities) are accounted at fair value and changes in fair value are shown as profit or loss. The fair value calculation of the derivative financial instruments is based on the Black-Scholes option pricing model. Assumptions are made for volatility and the risk-free rate in order to estimate the fair value of the instrument. Transaction cost related to derivative financial instruments are recorded through profit and loss.

Embedded Derivatives

Derivatives may be embedded in another contractual arrangement. The Group accounts for an embedded derivative separately from the host contract when:

- The host contract is not an asset in the scope of IFRS 9
- The host contract is not itself carried at fair value through profit and loss (FVPL)
- The terms of the Embedded Derivative would meet the definition of a derivative if they were contained in a separate contract
- The economic characteristics and risks of the embedded derivative are not closely related to the economic characteristics and risks of the host

The separated embedded derivatives were measured at fair value by an independent consultant applying a simulation-based valuation approach. Assumptions are made for volatility, risk free rate and other features of the instrument. All changes in the fair value of embedded derivatives were recognized in profit and loss.

Income tax

Income tax expense comprises current and deferred tax. It is recognized in profit or loss except to the extent that it relates to a business combination, or items recognized directly in equity or in Other Comprehensive Income.

Current tax

Current tax comprises the expected tax payable or receivable on the taxable income or loss for the year and any adjustment to tax payable or receivable in respect of previous years. It is measured using tax rates enacted or substantively enacted at the reporting date.

Deferred tax

Deferred income tax is recognized, using the balance sheet liability method, on temporary differences arising between the tax bases of assets and liabilities and their carrying amounts in the consolidated financial statements. Deferred tax is not recognized for:

- temporary differences on the initial recognition of assets or liabilities in a transaction that is not a business combination and that affects neither accounting nor taxable profit or loss;
- temporary differences related to investments in subsidiaries to the extent that the Group is able to control the timing of the reversal of the temporary differences and it is probable that they will not reverse in the foreseeable future; and
- taxable temporary differences arising on the initial recognition of goodwill.

Deferred income tax is determined using tax rates and laws that have been enacted or substantively enacted by the reporting date and are expected to apply when the related deferred income tax asset is realized or the deferred income tax liability is settled.

Deferred income tax assets are recognized to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilized. Deferred tax assets are reviewed at each reporting date and are reduced to the extent that it is no longer probable that the related tax benefit will be realized.

Deferred tax assets and liabilities are offset when there is a legally enforceable right to set off tax assets against tax liabilities and when they relate to income taxes levied by the same taxation authority and the Group intends to settle its tax assets and liabilities on a net basis.

Employee benefits

The Group maintains a pension plan for all employees in Switzerland through payments to a legally independent collective foundation. This pension plan qualifies under IFRS as defined benefit pension plan. There are no pension plans for the subsidiaries in Ireland, Australia and the United States.

The Group's net obligation in respect of defined benefit plans is calculated by estimating the amount of future benefit that employees have earned in return for their service in the current and prior periods, discounting that amount and deducting the fair value of any plan assets.

The recognized asset is limited to the present value of economic benefits available in the form of any future refunds from the plan or reductions in future contributions to the plan. In order to calculate the present value of economic benefits, consideration is given to any minimum funding requirements.

Remeasurements of the net defined benefit liability, which comprise actuarial gains and losses, the return on plan assets (excluding interest) and the effect of the asset ceiling (if any, excluding interest), are recognized immediately in Other Comprehensive Income. Past service costs, including curtailment gains or losses, are recognized immediately in general and administrative expenses within the operating results. Settlement gains or losses are recognized in general and administrative expenses within the operating results. The Group determines the net interest expense (income) on the net defined benefit liability (asset) for the period by applying the discount rate used to measure the defined benefit obligation at the beginning of the annual period or in case of any significant events between measurement dates to the then-net defined benefit liability (asset), taking into account any changes in the net defined benefit liability (asset) during the period as a result of contributions and benefit payments. Net interest expense and other expenses related to defined benefit plans are recognized in profit or loss.

Share-based compensation

The Company maintains a share-based payment plan in the form of a stock option plan for its employees, members of the Board of Directors as well as key service providers. Stock options are granted at the Board's discretion without any contractual or recurring obligations.

The share-based compensation plans qualify as equity settled plans. The grant-date fair value of share-based payment awards granted to employees is recognized as an expense, with a corresponding increase in equity, over the period that the employees become unconditionally entitled to the awards. Under the Auris Medical Holding Ltd. Long Term Equity Incentive Plan (the "Equity Incentive Plan" or "EIP"), 50% of granted share options granted to employees vest after a period of service of two years from the grant date and the remaining 50% vest after a period of service of three years from the grant date. Share options granted to members of the Board of Directors granted from 2016 onwards vest after a period of one year after the grant date.

The amount recognized as an expense is adjusted to reflect the number of awards for which the related service and non-market performance conditions are expected to be met, such that the amount ultimately recognized as an expense is based on the number of awards that meet the related service and non-market performance conditions at the vesting date. Share-based payments that are not subject to any further conditions are expensed immediately at grant date. In the year the options are exercised the proceeds received net of any directly attributable transaction costs are credited to share capital (par value) and share premium.

Valuation of share options

Option pricing and values are determined based on the Black Scholes option pricing model and assumptions are made for inputs such as volatility of the Company's stock and the risk-free rate.

Provisions

Provisions are recognized when the Group has a present obligation (legal or constructive) as a result of a past event, where it is more likely than not that an outflow of resources will be required to settle the obligation, and where a reliable estimate can be made of the amount of the obligation. Provisions are not recognized for future operating losses. Provisions are measured at the present value of the expenditures expected to be required to settle the obligation using a pre-tax rate that reflects current market assessments of the time value of money and the risks specific to the liability.

Revenue recognition

Revenue from contracts with customers is recognized at an amount that reflects the consideration to which the Company expects to be entitled in exchange for transferring goods or services to a customer. Revenue from the sale of products is recognized at the point in time when the customer obtains control of those products which is generally upon delivery at the customer. Revenue is net of value-added tax, rebates, discounts and returns.

Government grants

Government grants are not recognized until there is reasonable assurance that the Group will comply with the conditions attaching to them and that the grants will be received. Government grants are recognized in profit or loss on a systematic basis over the periods in which the Company recognizes as expenses the related research and development costs for which the grants are intended to compensate. Government grants that are receivable as compensation for expenses already incurred are recognized in profit or loss in the period in which they become receivable.

The company obtains credits under the Australian R&D Tax Incentive program (R&DITC). The program provides a tax offset of 43.5% of eligible R&D expenditures. If the tax offset exceeds the Company's tax liability, the balance is paid in cash after submission of a valid claim. Based on the specific features of the program, IAS 20 Government Grants is applied for the accounting treatment of the Australian R&DITC. The reimbursement application is made by the Company annually, once the fiscal year is closed, based on the financial statements. The income from grants related to R&D expenditures are presented separately under the heading of 'other operating income'. Grants that relate to the acquisition of an asset are recognized in profit or loss as the asset is depreciated or amortized. These grants are recognized as a reduction in the cost of the asset.

Earnings/(loss) per share

Basic earnings/(loss) per share are calculated by dividing the net profit/(loss) attributable to owners of the Company by the weighted average number of shares outstanding during the period. Diluted earnings/(loss) per share are calculated by dividing the net profit/(loss) attributable to the owners of the Company by the weighted average number of shares outstanding during the period adjusted for the conversion of all dilutive potential ordinary shares.

4. New standards, amendments and interpretations adopted by the Group

In 2021, the following revised standards have been adopted:

IFRS 9/IAS 39/IFRS 7/IFRS 4/IFRS 16	Amendments to IFRS 9/IAS 39/IFRS 7/IFRS 4/IFRS 16, Interest Rate Benchmark Reform – Phase 2
IFRS 16	COVID-19-Related Rent Concessions beyond 30 June 2021

Adoption has not had a material impact on the amounts reported in these financial statements but may impact the accounting for future transactions and arrangements.

A number of new standards, amendments to standards and interpretations are effective for annual periods beginning after January 1, 2022, and have not been applied in preparing these consolidated financial statements.

Standard/Interpretation		Impact	Effective date	Planned application by the Group
New standards, interpretations or amendments				
IAS 16	Amendments to IAS 16, Proceeds before Intended Use	1)	January 1,2022	FY 2022
IAS 37	Amendments to IAS 37, Onerous contracts – Costs of Fulfilling a Contract	1)	January 1, 2022	FY 2022
IFRS 3	Amendments to IFRS 3, References to the Conceptual Framework	1)	January 1, 2022	FY 2022
IFRS 1, IFRS 9, IFRS 16, IAS 41	Annual improvements to IFRS Standards 2018-2020 Cycle	1)	January 1, 2022	FY 2022
IFRS 17	Insurance contracts	1)	January 1, 2023	FY 2023
IAS 1	Amendments to IAS 1, Classification of Liabilities as Current or Non-current	1)	January 1, 2023	FY 2023
IAS 1	Amendments to IAS 1 and IFRS practice Statement 2, Disclosure of Accounting Policies	1)	January 1, 2023	FY 2023
IAS 8	Amendments to IAS 8, Definition of Accounting Estimates	1)	January 1, 2023	FY 2023
IAS 12	Amendments to IAS 12, Deferred tax related to Assets and Liabilities arising from a Single Transaction	1)	January 1, 2023	FY 2023
IFRS 10, IAS 28	Amendments to IFRS 10 and IAS 28, Sale or Contribution of Assets between an Investor and its Associate or Joint Venture	1)	To be set	To be set

1) No material impact on the Group is expected from these standards and amendments issued but not effective.

5. Financial instruments and risk management

The following table shows the carrying amounts of financial assets and financial liabilities:

	December 31, 2021	December 31, 2020
Financial assets		
Cash and cash equivalents	984,191	11,258,870
Loans and receivables		
Other non-current financial assets	199,105	20,001
Other receivables	255,187	10,040
Total financial assets	**1,438,483**	**11,288,911**
Financial liabilities		
At amortized cost		
Trade and other payables	3,697,723	762,453
Accrued expenses	1,048,575	1,433,106
Loan	—	523,920
Non-current lease liabilities	461,485	—
Current lease liabilities	114,251	—
At fair value through profit and loss		
Derivative financial instruments	1,233	316,757
Total financial liabilities	**5,323,267**	**3,036,236**

Fair values

The carrying amount of cash and cash equivalents, other receivables, trade and other payables, accrued expenses and loan is a reasonable approximation of their fair value due to the short-term nature of these instruments.

Financial risk factors

The Group's activities expose it to a variety of financial risks: market risk, credit risk, interest rate and liquidity risk. The Group's overall risk management program focuses on the unpredictability of financial markets and seeks to minimize potential adverse effects on the Group's financial performance. Management identifies, evaluates and controls financial risks. No financial derivatives have been used in 2021 and 2020 to hedge risk exposures. The Group invests its available cash in instruments with the main objectives of preserving principal, meeting liquidity needs and minimizing foreign exchange risks. The Group allocates its liquid assets to first tier Swiss or international banks.

Liquidity risk

The Group's principal source of liquidity is its cash reserves which are mainly obtained through the issuance of new shares. The Group has succeeded in raising capital to fund its development activities to date and has raised funds that will allow it to meet short-term development expenditures. The Company will require regular capital injections to continue its development work, which may be dependent on meeting development milestones, technical results and/or commercial success. Management monitors rolling forecasts of the Group's liquidity requirements to ensure it has sufficient cash to meet operational needs. The ability of the Group to maintain adequate cash reserves to sustain its activities in the medium term is highly dependent on the Group's ability to raise further funds. Consequently, the Group is exposed to continued liquidity risk.

The table below analysis the remaining contractual maturities of financial liabilities, including estimated interest payments as of December 31, 2021 and 2020. The amounts disclosed in the table are the undiscounted cash flows:

	Carrying amount	Less than 3 months	Between 3 months and 2 years	2 years and later	Total
December 31, 2021					
Trade and other payables	3,697,723	3,697,723	—	—	3,697,723
Accrued expenses	1,048,575	1,048,575	—	—	1,048,575
Loan and borrowings	—	—	—	—	—
Non-current lease liabilities	461,485	—	117,856	343,629	461,485
Current lease liabilities	114,251	28,231	86,020	—	114,251
Derivative financial instruments	1,233	—	—	1,233	1,233
Total	**5,323,267**	**4,774,529**	**203,876**	**344,862**	**5,323,267**

	Carrying amount	Less than 3 months	Between 3 months and 2 years	2 years and later	Total
December 31, 2020					
Trade and other payables	762,453	762,453	—	—	762,453
Accrued expenses	1,433,106	1,433,106	—	—	1,433,106
Loan and borrowings	523,920	473,920	50,000		523,920
Derivative financial instruments	316,757	310,439	—	6,318	316,757
Total	**3,036,236**	**2,979,918**	**50,000**	**6,318**	**3,036,236**

Fair value measurement

	Fair values as at		Fair value	
Financial assets / liabilities	**December 31, 2021**	**December 31, 2020**	**hierarchy**	**Valuation technique(s) and key input(s)**
Derivative financial liabilities – Warrants from public offerings	Liability 1,233	Liability 6,318	Level 2	Black-Scholes option pricing model The share price is determined by Company's NASDAQ quoted-price. The strike price and maturity are defined by the contract. The volatility assumption is driven by Company's historic quoted share price and the risk free rate is estimated based on observable yield curves at the end of each reporting period.
Derivative financial liabilities – Embedded derivatives	—	310,439	Level 3	Monte Carlo simulation model The valuation is based on input parameters classified as level 3. Input parameters include the historical volatility of AMHL shares, risk-free rate, expected remaining life, expected exercise date and share prices of AMHL at valuation dates.

For level 3 financial liability, the sensitivity analysis below represents the potential absolute change in fair value. The favorable and unfavorable effects on the result before taxes, resulting from using reasonably alternative assumptions for the valuation of the option component of the Convertible Loan (FiveT) has been calculated by recalibrating the modes using unobservable inputs based on an average change in volatility of 5%.

	Dec 31, 2021		Dec 31, 2020	
	Increase/Decrease in volatility assumption	Effect on result before taxes on CHF	Increase/Decrease in volatility assumption	Effect on result before taxes on CHF
Change in volatility	—	—	+5%	2,770
	—	—	-5%	-5,475

Changes in liabilities arising from financing activities

			Non-cash changes		
	01.01.2021	Financing Cash Flows [1)]	Fair value revaluation	Other changes [2)]	31.12.2021
Derivative financial instrument	316,757	—	410,918	(726,442)	1,233
Loans	523,920	(50,000)	—	(473,920)	—
Lease liabilities	—	(21,700)	—	597,436	575,736
Total	840,677	(71,700)	410,918	(602,926)	576,969

			Non-cash changes		
	01.01.2020	Financing Cash Flows [1)]	Fair value revaluation	Other changes [2)]	31.12.2020
Derivative financial instrument	4,353	—	219,315	93,089	316,757
Loans	—	1,522,931	—	(999,011)	523,920
Total	4,353	1,522,931	219,315	(905,922)	840,677

1) The financing cash flows are from loan borrowings or loan and lease repayments.
2) Other non-cash changes include conversion of convertible loan including de-recognition of embedded derivative and initial recognition of lease liability.

Credit risk

Credit risk is managed on a Group basis. Credit risk arises from cash and cash equivalents and deposits with banks, as well as from trade and other receivables. The Company's policy is to invest funds in low risk investments including interest bearing deposits. Trade and other receivables were current as of December 31, 2021 and December 31, 2020, not impaired and included only well-known counterparties.

The Group has been holding cash and cash equivalents in the Group's principal operating currencies (CHF, USD, EUR and AUD) with international banks of high credit rating.

The Group's maximum exposure to credit risk is represented by the carrying amount of each financial asset in the consolidated statement of financial position:

	December 31, 2021	December 31, 2020
Financial assets		
Cash and cash equivalents	984,191	11,258,870
Trade receivables	21,746	—
Other receivables	255,187	10,040
Total	**1,261,124**	**11,268,910**

As of December 31, 2021 other receivables consisted of cash receivable from a capital increase implemented over the year end and on December 31, 2020 of a bank deposit for guaranteeing credit card liabilities.

Market risk

Currency risk

The Group operates internationally and is exposed to foreign exchange risk arising from various exposures, primarily with respect to US Dollar, Euro and Australian Dollar. Foreign exchange risk arises from future commercial transactions, recognized assets and liabilities and net investments in foreign operations. The summary of quantitative data about the exposure of the Group's financial assets and liabilities to currency risk was as follows:

	2021			2020	
in CHF	**USD**	**EUR**	**AUD**	**USD**	**EUR**
Cash and cash equivalents	388,950	539,474	—	9,214,709	694,287
Trade and other receivables	1,436,086	26,843	1,274,271	479	—
Trade and other payables	(104,676)	(2,615,791)	—	(75,712)	(397,853)
Accrued expenses	(163,823)	(295,467)	—	(34,648)	(569,400)
Net statement of financial position exposure - asset/(liability)	**1,556,537**	**(2,344,941)**	**1,274,271**	**9,104,828**	**(272,966)**

As of December 31, 2021, a 5% increase or decrease in the USD/CHF exchange rate with all other variables held constant would have resulted in a CHF 77,827 (2020: CHF 455,241) increase or decrease in the net result. A 5% increase or decrease in the EUR/CHF exchange rate with all other variables held constant would have resulted in a CHF 117,247 (2020: CHF 13,648) increase or decrease in the net result. Also, a 5% increase or decrease in the AUD/CHF exchange rate with all other variables held constant would have resulted in a CHF 63,714 (2020: CHF 0) increase or decrease in the net result.

The Company has subsidiaries in the United States, Australia and Ireland, whose net assets are exposed to foreign currency translation risk. Due to the small size of the subsidiaries the translation risk is not significant.

Capital risk management

The Company and its subsidiaries are subject to capital maintenance requirements under local law in the country in which it operates. To ensure that statutory capital requirements are met, the Company monitors capital, at the entity level, on an interim basis as well as annually. From time to time the Company may take appropriate measures or propose capital increases to ensure the necessary capital remains intact.

6. Segment information

Geographical information

The Group's non-current assets by the Company's country of domicile were as follows:

	December 31, 2021	**December 31, 2020**
Switzerland	14,734,738	9,030,778
Australia	144,854	151,269
Total	**14,879,592**	**9,182,047**

Non-current assets exclude financial instruments.

7. Property and Equipment

	Production equipment	Office furniture and EDP	Total
At cost			
As of January 1, 2020	**353,488**	**233,706**	**587,194**
Additions	—	—	—
Disposals	—	—	—
As of December 31, 2020	**353,488**	**233,706**	**587,194**
Additions	—	—	—
Disposals	—	—	—
As of December 31, 2021	**353,488**	**233,706**	**587,194**
Accumulated depreciation			
As of January 1, 2020	**(290,491)**	**(230,031)**	**(520,522)**
Charge for the year	(16,481)	(3,555)	(20,036)
Disposals	—	—	—
As of December 31, 2020	**(306,972)**	**(233,586)**	**(540,558)**
Charge for the year	(46,516)	(119)	(46,635)
Disposals	—	—	—
As of December 31, 2021	(353,488)	(233,705)	(587,193)
Net book value			
As of December 31, 2020	**46,516**	**120**	**46,636**
As of December 31, 2021	—	**1**	**1**

As of December 31, 2021, and 2020 no items of property and equipment were pledged.

8. Right-of-use assets and lease liabilities

Right-of-use assets	Office building	Total
At cost		
As of January 1, 2020	**—**	**—**
As of December 31, 2020	—	—
Additions	594,436	**594,436**
Disposals	—	—
As of December 31, 2021	**594,436**	**594,436**
Accumulated depreciation		
As of January 1, 2020	—	—
As of December 31, 2020	**—**	**—**
Charge for the year	(29,722)	(29,722)
Disposals	—	—
As of December 31, 2021	**(29,722)**	**(29,722)**
Net book value		
As of December 31, 2020	**—**	**—**
As of December 31, 2021	**564,714**	**564,714**

Low value and short-term lease expenses	December 31, 2021	December 31, 2020
Expense related to short-term leases	52,280	61,509
Expense related to leases of low value assets	—	—
Total	**52,280**	**61,509**

Lease liabilities	December 31, 2021	December 31, 2020
As of January 1	—	—
Additions	594,436	—
Interest expenses	3,000	—
Repayment of lease liability	(21,700)	—
As of December 31	575,736	—
thereof non-current	461,485	—
thereof current	114,251	

Maturities of lease liabilities	December 31, 2021	December 31, 2020
Year 1	130,200	—
Year 2	130,200	—
Year 3	130,200	—
Year 4	130,200	—
Year 5	97,650	—
Undiscounted lease payments	**618,450**	**—**
Less: unearned interest	(42,714)	—
Total	**575,736**	**—**

9. Intangible assets

	Licenses	IP & Data rights	Patents	Internally generated	Total
At cost					
As of January 1, 2020	1,482,520	**193,989**	**239,593**	**4,849,511**	**6,765,613**
Exchange differences				6,120	6,120
Additions	—	—	177,623	2,166,054	2,343,677
As of December 31, 2020	**1,482,520**	**193,989**	**417,216**	**7,021,685**	**9,115,410**
Exchange differences	—	—	—	(3,654)	(3,654)
Additions	3,893,681	—	55,938	2,783,431	6,733,050
As of December 31, 2021	**5,376,201**	**193,989**	**473,154**	**9,801,462**	**15,844,806**
Accumulated amortization and impairment losses					
As of December 31, 2020	—	—	—	—	—
Impairment	(1,482,520)	(47,409)	—	—	(1,529,929)
As of December 31, 2021	**(1,482,520)**	**(47,409)**	—	—	**(1,529,929)**
Net book value					
As of December 31, 2020	**1,482,520**	**193,989**	**417,216**	**7,021,685**	**9,115,410**
As of December 31, 2021	**3,893,681**	**146,580**	**473,154**	**9,801,462**	**14,314,877**

Intangible assets comprise upfront and milestone payments related to licenses. The increase in 2021 was related to the acquisition of Trasir Therapeutics Inc., which was treated as an asset acquisition because substantially all the fair value of Trasir was concentrated in a worldwide exclusive license agreement with Washington University (Note 3). Further, in 2021 all intangible assets related to the projects AM-101, AM-111 and AM-201 were impaired, taking into account the future repositioning of the company. Amortization will commence once the intangible assets are available for use, which will be the case after regulatory approvals are obtained and the related products are available for use.

In 2019, a US patent on AM-125 was issued and a related EU application was allowed. As a consequence, we started to capitalize prosecution and registration costs. In 2021, we capitalized CHF 55,938 (2020: CHF 177,623).

Commencing with the business year 2018, the Company recorded intangibles related to direct development expenditure of its AM-125 program. The capitalized amount for the year ended December 31, 2021 was CHF 2,839,369 (2020: CHF 2,343,677). The additions to internally generated intangibles of CHF 2,783,431 are net of CHF 94,118 government grants obtained under the Australian R&D tax incentive program (2020: CHF 0).

10. Inventories

	December 31, 2021	December 31, 2020
Finished goods	839,221	—
Total	**839,221**	**—**

As of December 31, 2021, the Company' s inventory consisted of the product Bentrio, a drug-free nasal spray for protection against airborne viruses and allergens. Bentrio has a limited shelf life, which may affect the salability of the product, and is packaged in various configurations (stock keeping units, "SKUs") for different markets and in different languages to address specific requirements under national rules and regulations or by trade channels. During product launch, shelf life is still relatively short since data from supporting stability studies are still limited; this tends to restrict salability through certain trade channels. In addition, there is only limited visibility on product take-up across different markets due to the lack of a sales history, and national rules and regulations may require prior approval of certain marketing materials and messages. Based on a management review of the inventory as at December 31, 2021 for any obsolete or slow-moving items, the Company wrote down finished good inventories in the amount of CHF 2.0 million in 2021. The amount of the write down was expensed to the income statement under Cost of Sales.

11. Other receivables

	December 31, 2021	December 31, 2020
R&D tax credit receivable	470,958	—
Receivable from share issuance	255,187	—
Advance payments to suppliers	—	479
Value added tax receivable	168,851	38,337
Withholding tax receivable	7,336	6,087
Deposit credit cards	—	10,040
Other	15,501	25,918
Total other receivables	**917,833**	**80,861**

As described in note 3 Significant accounting policies, the Company obtains government grants under the Australian R&D Tax Incentive program. The R&D tax credit receivable as of December 31, 2021 relates to the reimbursement application for compensation of R&D expenditures incurred in 2021. Other receivables were not considered impaired in the years under review.

12. Prepayments

	December 31, 2021	December 31, 2020
Advance payments to suppliers	859,492	5,020
Clinical projects and related activities	—	164,916
Insurance	137,418	104,590
Other	—	3,063
Total prepayments	**996,910**	**277,589**

13. Cash and cash equivalents

	December 31, 2021	December 31, 2020
Cash in bank accounts	984,191	11,258,870
Cash on hand	—	—
Total cash and cash equivalents	**984,191**	**11,258,870**

14. Capital and reserves

Share capital

The issued share capital of the Company at December 31 consisted of:

	December 31, 2021		December 31, 2020	
	Number	**CHF**	**Number**	**CHF**
Common shares with a par value of CHF 0.01 each	14,964,261	149,643	11,417,159	114,172
Total	**14,964,261**	**149,643**	**11,417,159**	**114,172**

	Common Shares (Number)	
	2021	**2020**
As of January 1	11,417,159	4,125,949
Exercise of warrants	897,435	1,263,845
LPC equity line	—	1,610,120
ATM program	1,184,700	1,628,827
Share-based payments (bonus)	174,610	51,418
Conversion convertible loan	516,814	737,000
Shares issued for Trasir acquisition	773,543	—
Registered direct offering	—	2,000,000
Total, as of December 31	**14,964,261**	**11,417,159**

On June 1, 2021, the Company completed the acquisition of Trasir. The upfront acquisition price of USD 2.5 million was paid with 764,370 non-registered common shares at USD 3.27 each to the selling shareholders. In addition, 9,173 non-registered common shares were issued to reimburse USD 30,000 in expenses incurred by certain selling Trasir shareholders.

On December 3, 2020, the Company entered into securities purchase agreements with several institutional investors for the purchase and sale of 2,000,000 common shares at an offering price of $4.00 per share, pursuant to a registered direct offering. The net proceeds of the offering were approximately $7.3 million.

On December 1, 2020, a tranche of the convertible loan provided by FiveT in the amount of CHF 895,455 was converted into 737,000 common shares at a conversion price of $1.35. On March 4, 2021 the remaining amount of CHF 604,545 plus interest of CHF 40,628 were converted into 516,814 common shares at a conversion price of $1.35.

On April 23, 2020, the Company entered into a purchase agreement and a Registration Rights Agreement with Lincoln Park Capital Fund, LLC (the "2020 Commitment Purchase Agreement"). Pursuant to the purchase agreement, LPC agreed to subscribe for up to USD 10,000,000 of our common shares over the 30-month term of the purchase agreement. In 2020, we issued 1,200,000 of our common shares to LPC for an aggregate amount of USD 1.1 million. The 2020 Commitment Purchase Agreement replaced the 2018 Commitment Purchase Agreement. Under the 2018 Commitment Purchase Agreement agreed to purchase common shares for up to $10,000,000 over the 30-month term of the Purchase Agreement. Prior to its termination we had issued 587,500 common shares for aggregate proceeds of $1.8 million to LPC under the LPC Purchase Agreement. The Purchase Agreement replaced the Purchase Agreement that we entered into with LPC on October 10, 2017 (the "2017 Commitment Purchase Agreement"), which was terminated as a result of the Merger. Under the 2017 Commitment Purchase Agreement, LPC agreed to subscribe for up to $13,500,000 of our common shares, and prior to its termination, we had issued an aggregate of 2,600,000 (pre-merger) common shares for aggregate proceeds of $1.8 million to LPC under the 2017 Commitment Purchase Agreement.

On May 15, 2019, the Company completed a public offering of (i) 440,000 common shares with a par value of CHF 0.40 each, together with warrants to purchase 440,000 common shares, and (ii) 1,721,280 pre-funded warrants, with each pre-funded warrant exercisable for one common share, together with warrants to purchase 1,721,280 common shares, including 110,000 common shares and warrants to purchase 110,000 common shares sold pursuant to a partial exercise by the underwriters of the underwriters' over-allotment option (the "May 2019 Registered Offering"). The exercise price for the pre-funded warrants was CHF 0.01 per common share and for the warrants CHF 4.34. The net proceeds to us from the May 2019 Registered Offering were approximately $7.7 million, after deducting underwriting discounts and other offering expenses payable by us. All pre-funded warrants were exercised in 2019. In December 2020, 1,263,845 warrants were exercised. The remaining 897,435 warrants were exercised in March 2021.

On November 30, 2018, we entered into the A.G.P. Sales Agreement with A.G.P. Pursuant to the terms of the A.G.P. Sales Agreement, as amended on April 5, 2019, we may offer and sell our common shares, from time to time through A.G.P. by any method deemed to be an "at-the-market" offering as defined in Rule 415(a)(4) promulgated under the Securities Act. Pursuant to the A.G.P. Sales Agreement, we may sell common shares up to a maximum aggregate offering price of $25.0 million. In 2021, we sold 1,184,700 shares under the ATM. As of the date of this Annual Report, we have sold 1,943,318 of our common shares for an aggregate offering price of $5.4 million pursuant to the A.G.P. Sales Agreement. The related transaction costs of CHF 71,161 were charged to equity.

Authorized share capital

On January 24, 2019, our board of directors determined that it would be in our best interest to change our legal seat and jurisdiction of incorporation, respectively, from Switzerland to Bermuda (the "Redomestication"). The Company's Memorandum of Continuance and the Bye-laws that were adopted at an extraordinary meeting of shareholders held on March 8, 2019 provided for an authorized share capital of 200,000,000 common shares and 20,000,000 preference shares. Following a reverse share split at a ratio of 20-for-1 on May 1, 2019, a decision by the annual general meeting of shareholders on June 4, 2020 to increase the authorized share capital and the reduction of the par value of June 30, 2020, our authorized share capital consists of 25,000,000 common shares, par value CHF 0.01 per share, and 20,000,000 preference shares, par value CHF 0.02 per share.

15. Share-based compensation

Description

In 2014, the Group introduced an equity incentive plan (the ("EIP") as amended in 2017 and 2019. In September 2019, all employees and directors of the Company opted-in to forfeit all option grants received prior to 2019 in exchange for new options (the "September 2019 Conversion Grant"). The number of new options was calculated on a value neutral basis using the Black-Scholes model. Including the September 2019 Conversion Grant, the Company granted 390,620 options in 2019 under the EIP. Plan C was terminated in 2019. The last outstanding options under Plan C were replaced by the September 2019 Conversion Grant. In 2021, the Company granted 342,263 options (2020: 726,637 options) under the EIP.

Holders of vested options are entitled to purchase common shares of the Company. Under the Equity Incentive Plan, the Board of Directors defined the exercise price as the average daily closing price of the Company's shares during the 30 days preceding the date of grant. All options are to be settled by the physical delivery of shares. The key terms and conditions related to the grants under these programs at December 31, 2021 are as follows:

Plan	Number of options outstanding	Vesting conditions	Contractual life of options
Equity Incentive Plan Board	279,771	1 year service from grant date	6 years
Equity Incentive Plan Management & Staff	523,881	2 years' service from grant date (50%)	8 years
Equity Incentive Plan Management & Staff	523,881	3 years' service from grant date (50%)	8 years

Measurement of fair values

The fair value of the options was measured based on the Black-Scholes formula.

	Stock Option Plan			
	Equity Incentive Plan 2021	**Equity Incentive Plan 2021**	**Equity Incentive Plan 2020**	**Equity Incentive Plan 2020**
Fair value at grant date	USD 0.932 (2 year vesting) [1)] USD 1.107 (3 year vesting) [1)]	USD 1.241 (1 year vesting) [2)] USD 1.850 (2 year vesting) [2)] USD 2.183 (3 year vesting) [2)]	USD 0.325 (2 year vesting) [1)] USD 0.391 (3 year vesting) [1)]	USD 0.258 (1 year vesting) [2)] USD 0.514 (2 year vesting) [2)] USD 0.578 (3 year vesting) [2)]
Share price at grant date	USD 1.64	USD 3.54	USD 0.79	USD 0.92
Exercise price	USD 1.889	USD 3.511	USD 0.878	USD 0.825
Expected volatility	93.4%	101.3%	84.96%	72.72%
Expected life	2 and 3 years	1, 2 and 3 years	2 and 3 years	1, 2 and 3 years
Expected dividends	—	—	—	—
Risk-free interest rate	0.47%	0.06%	0.82%	0.61%

1) October grants for the respective year
2) April grants for the respective year

The Company uses its own historic volatility to calculate expected volatility. The expected life of all options is assumed to correspond to the vesting period.

The total expense recognized for equity-settled share-based payment transactions were CHF 1,206,303 in 2021 (2020: CHF 368,793, 2019: CHF 228,920).

Share based compensation loss related to employee stock options amounted to CHF 1,223,696 in 2021 (2020: CHF 351,401, 2019: CHF 226,601).

Share based compensation expense of CHF 0 related to the purchase of intangibles was capitalized for the year ended December 31, 2021 (2020: CHF 0, 2019: 2,319).

The number and weighted average exercise prices (in CHF) of options under the share option programs are as follows:

	2021			2020		
	Number of options	Weighted average exercise price	Weighted average remaining term	Number of options	Weighted average exercise price	Weighted average remaining term
Outstanding at January 1	1,038,537	1.58	7.01	324,053	3.01	7.60
Expired during the year	—	—	—	—	—	—
Forfeited during the year	(51,290)	—	—	—	—	—
Exercised during the year	—	—	—	—	—	—
Granted during the year	342,263	2.27	—	714,484	0.87	—
Outstanding at December 31	**1,329,510**	**1.65**	**6.56**	**1,038,537**	**1.58**	**7.01**
Exercisable at December 31	288,446	—	—	37,576	—	—

The range of exercise prices for outstanding options was CHF 0.75 to CHF 28.79 as of December 31, 2021 and CHF 0.73 to CHF 27.93 as of December 31, 2020.

16. Trade and other payables

	December 31, 2021	December 31, 2020
Trade accounts payable - third parties	3,544,384	722,272
Other	153,339	40,181
Total trade and other payables	**3,697,723**	**762,453**

17. Accrued expenses

	December 31, 2021	December 31, 2020
Accrued research and development costs including milestone payments	557,391	1,105,089
Professional fees	179,461	172,273
Accrued vacation & overtime	51,218	44,466
Employee benefits incl. share based payments	196,917	101,821
Other	63,588	9,457
Total accrued expenses	**1,048,575**	**1,433,106**

18. Other operating income

	December 31, 2021	December 31, 2020	December 31, 2019
Income from R&D tax incentive (Government grants)	458,157	—	—
Refund of share issuance stamp duty	—	100,002	—
Other income	2,553	74,473	—
Total other operating income	**460,710**	174,475	—

19. Cost of Sales

	December 31, 2021	December 31, 2020	December 31, 2019
Product purchases, packaging and logistics	173,758	—	—
Employee benefit and expenses	89,238	—	—
Inventory write-down	1,977,558	—	—
Total cost of sales	**2,240,554**	—	—

20. Research and development expense

	December 31, 2021	December 31, 2020	December 31, 2019
Pre-clinical projects	587,019	242,617	182,346
Clinical projects	2,957,752	476,972	993,085
Product and process development	1,100,453	614,744	481,453
Employee benefits and expenses	1,897,155	1,120,814	1,373,543
Lease expenses from short-term lease	—	34,147	26,057
Patents and trademarks	465,587	246,592	168,367
Regulatory projects	354,507	110,612	80,347
Impairment intangible assets	1,529,929	—	—
Depreciation tangible assets	46,635	16,481	20,083
Total research and development expense	**8,939,037**	**2,862,979**	**3,325,281**

Research and development expenses were capitalized in the amount of CHF 2,839,369 during 2021 compared to CHF 2,343,677 in 2020.

21. Sales and marketing expense

	December 31, 2021	December 31, 2020	December 31, 2019
Marketing and sales expenses	1,132,864	—	—
Employee benefits and expenses	204,157	—	—
Product samples	161,167	—	—
Total sales and marketing	**1,498,218**	—	—

22. General and administrative expense

	December 31, 2021	December 31, 2020	December 31, 2019
Employee benefits and expenses	1,554,778	811,373	1,010,708
Business development	967,046	95,663	113,959
Travel expenses	75,829	28,898	102,679
Administration expenses	2,245,862	1,645,530	2,653,914
Lease expenses from short-term lease	52,280	13,871	27,362
Depreciation Right-of-use assets	29,722	—	—
Depreciation tangible assets	—	3,555	10,740
Capital tax expenses	21,059	(4,228)	14,501
Total general and administrative expenses	4,946,576	2,594,662	3,933,863

23. Employee benefits

	December 31, 2021	December 31, 2020	December 31, 2019
Salaries	1,865,633	1,260,359	1,832,382
Pension costs	165,801	156,843	130,792
Other social benefits	275,258	116,290	217,448
Share based payments costs	1,223,696	351,401	226,601
Other personnel expenditures	214,940	47,295	(22,973)
Total employee benefits	**3,745,328**	**1,932,188**	**2,384,250**

In 2021 share based compensation expense included CHF 902,817 for one regular and one extraordinary share bonus grant related to the strategic repositioning of the Company. The latter, which amounts to CHF 810,252, including CHF 360,112 for a future share grant contingent on achieving the Positive Results related to the Trasir transaction. Share based compensation included expense related to employee stock options of CHF 320,879 in the year 2021 compared to CHF 351,401 in 2020. On the other hand, expenses for salaries in the previous year had benefited from reimbursements of CHF 63,208 under the Swiss short-time work scheme, which had been used for three months in connection with a temporary reduction in project activities due to the COVID-19 pandemic.

Benefit plans

The Company participates in a retirement plan (the "Plan") organized as an independent collective foundation, that covers all of its employees in Switzerland, including management. The collective foundation is governed by a foundation board. The board is made up of an equal number of employee and employer representatives of the affiliated companies. The Company has no direct influence on the investment strategy of the collective foundation. Moreover, certain elements of the employee benefits are defined in the same way for all affiliated companies. This is mainly related to the annuity factors at retirement and to interest allocated on retirement savings. The employer itself cannot determine the benefits or how they are financed directly. The foundation board of the collective foundation is responsible for the determination of the investment strategy, for making changes to the pension fund regulations and in particular, also for defining the financing of the pension benefits.

The old age benefits are based on retirement savings for each employee, coupled with annual retirement credits and interest (there is no possibility to credit negative interest). At retirement age, the insured members can choose whether to take a pension for life, which includes a spouse's pension, or a lump sum. In addition to retirement benefits, the plan benefits also include disability and death benefits. Insured members may also buy into the scheme to improve their pension provision up to the maximum amount permitted under the rules of the plan and may withdraw funds early for the purchase of a residential property for their own use subject to limitations under Swiss law. On leaving the Company, retirement savings are transferred to the pension institution of the new employer or to a vested benefits institution. This type of benefit may result in pension payments varying considerably between individual years. In defining the benefits, the minimum requirements of the Swiss Law on Occupational Retirement, Survivors and Disability Pension Plans (BVG) and its implementing provisions must be observed. The BVG defines the minimum pensionable salary and the minimum retirement credits. In Switzerland, the minimum interest rate applicable to these minimum retirement savings is set by the Swiss Federal Council at least once every two years. The rate was 1.00% in 2019, 1.00% in 2020 and 1.00% in 2021.

The assets are invested by the collective foundation to which many companies contribute, in a diversified portfolio that respects the requirements of the Swiss BVG. Therefore, disaggregation of the pension assets and presentation of plan assets in classes that distinguish the nature and risks of those assets is not possible. Under the Plan, both the Company and the employee share the costs equally. The structure of the plan and the legal provisions of the BVG mean that the employer is exposed to actuarial risks. The main risks are investment risk, interest risk, disability risk and the risk of longevity. Through the affiliation to a collective foundation, the Company has minimized these risks, since they are shared between a much greater number of participants.

For accounting purposes under IFRS, the plan is treated as a defined benefit plan.

The following tables present information about the net defined benefit liability and its components:

Change in defined benefit obligation

	2021	2020
Defined benefit obligation at January 1	3,529,602	3,087,947
Service costs	162,200	151,624
Plan participants' contribution	101,066	76,032
Interest cost	10,464	9,482
Actuarial losses	159,845	58,912
Plan amendments	(3,115)	—
Transfer-out amounts	(142,951)	(201,310)
Transfer-in amounts of new employees	860,521	346,915
Defined benefit obligation at December 31	**4,677,632**	**3,529,602**

The defined benefit obligation includes only liabilities for active employees. The weighted average modified duration of the defined benefit obligation at December 31, 2021 is 19.9 years (2020: 21.9 years).

Change in fair value of plan assets

	2021	2020
Fair value of plan assets at January 1	2,662,226	2,327,500
Interest income	8,586	7,429
Return on plan assets excluding interest income	424,829	32,794
Employer contributions	101,066	76,032
Plan participants' contributions	101,066	76,032
Transfer-out amounts	(142,951)	(201,310)
Transfer-in amounts of new employees	860,521	346,915
Administration expense	(6,030)	(3,166)
Fair value of plan assets at December 31	**4,009,313**	**2,662,226**

Net defined benefit liability recognized in the statement of financial position

	December 31, 2021	December 31, 2020
Present value of funded defined benefit obligation	4,677,632	3,529,602
Fair value of plan assets	(4,009,313)	(2,662,226)
Net defined benefit liability	**668,319**	**867,376**

Defined Benefit Cost

	2021	2020	2019
Service cost	159,085	151,624	138,580
Net interest expense	1,878	2,053	5,137
Administration expense	6,030	3,166	4,051
Total defined costs for the year recognized in profit or loss	**166,993**	**156,843**	**147,768**

Remeasurement of the Defined Benefit Liability

	2021	2020	2019
Actuarial loss (gain) arising from changes in financial assumptions	(74,284)	13,031	360,541
Actuarial loss (gain) arising from experience adjustments	463,238	45,881	(215,156)
Actuarial gain arising from demographic assumptions	(229,109)	—	—
Return on plan assets excluding interest income	(424,829)	(32,794)	(73,375)
Total defined benefit cost for the year recognized in the other comprehensive loss (income)	**(264,984)**	**26,118**	**72,010**

Assumptions

At December 31	2021	2020	2019
Discount rate	0.30%	0.20%	0.30%
Future salary increase	0.85%	0.60%	1.10%
Pension indexation	0.00%	0.00%	0.00%
Mortality and disability rates	BVG2015G	BVG2015G	BVG2015G

Sensitivity analysis

Reasonably possible changes at the reporting date to one of the relevant actuarial assumptions, holding other assumptions constant, would have affected the defined benefit obligation by the amounts shown below.

December 31,	2021	2020
Change in assumption	0.25% increase	0.25% increase
Discount rate	(200,601)	(166,228)
Salary increase	22,961	13,602
Pension indexation	110,958	88,460
Change in assumption	+ 1 year	+ 1 year
Life expectancy	98,983	88,215

24. Finance income and finance expense

	2021	2020	2019
Interest income	3,219	258	17,882
Net foreign currency exchange gain	1,458,429	3,207,649	1,343,153
Revaluation gain from derivative financial instruments	5,085	—	663,725
Total finance income	**1,466,733**	**3,207,907**	**2,024,760**
Interest expense (incl. Bank charges)	189,695	135,151	28,628
Net foreign currency exchange loss	1,129,788	3,541,202	1,562,725
Revaluation loss from derivative financial instruments	416,003	2,250,222	—
Transaction costs	—	219,615	—
Total finance expense	**1,735,486**	**6,146,190**	**1,591,353**
Finance (expense)/income, net	**(268,753)**	**(2,938,283**	**433,407**

In 2021, the revaluation loss from derivative financial instruments of CHF 416,003 is related to the revaluation of the financial derivatives embedded in the FiveT convertible loan (note 29), at conversion. The revaluation gain of CHF 5,085 is related to the revaluation of outstanding warrants from public offerings (note 30). In 2020 there was a revaluation loss from derivative financial instruments of CHF 2,250,222 and in 2019 a revaluation gain of CHF 663,725. In 2021, net foreign currency exchange gains contain translation gains of CHF 289,961 (2020: CHF 71,525; 2019: CHF 7,744) which arose on the Company's USD and EUR denominated cash and cash equivalents. In 2021, finance expenses included interest paid of CHF 3,700 (2020: CHF 0; 2019: CHF 3,745).

25. Taxation

The Group's income tax expense recognized in the consolidated statement of profit or loss and other comprehensive loss was as follows:

	2021	2020	2019
Deferred income tax expense	(570,730)	(389,384)	(213,355)
Deferred income tax gain	549,110	410,668	407,192
	(21,620)	**21,284**	**193,837**

The Group's effective income tax expense differed from the expected theoretical amount computed by applying the Group's applicable weighted average tax rate of 13.5% in 2021 (2020: 12.1%, 2019: 12.5%) as summarized in the following table:

Reconciliation	2021	2020	2019
Loss before income tax	(17,368,546)	(8,221,449)	(6,825,738)
Income tax at statutory tax rates applicable to results in the respective countries	2,348,057	991,120	854,636
Effect of unrecognized temporary differences	(632,031)	(302,557	89,974
Effect of unrecognized taxable losses	(1,885,486)	(184,881)	(913,309)
Effect of utilization of previously unrecognized taxable losses	—	—	193,155
Effect of impairment of deferred tax assets	(75,375)	—	(131,055)
Effect of previously unrecognized deferred tax asset	—	97,458	20,977
Effect of expenses not considerable for tax purposes	—	(47,894)	(29,549
Effect of changes in local tax legislation and/or local tax rates	—	—	110,758
Effect of impact from application of different tax rates	223,215	(531,962)	(1,750)
Income tax gain/(loss)	(21,620)	21,284	193,837

The tax effect of taxable temporary differences that give rise to deferred income tax liabilities or to deferred income tax assets as of December 31 is presented below:

Deferred Tax Liabilities	December 31, 2021	December 31, 2020
Intangible assets	(51,914)	(252,174)
Deferred unrealized foreign exchange gains	—	(350,054)
Other receivables	(122,449)	—
Total	**(174,363)**	**(602,228)**

Deferred Tax Asset	December 31, 2021	December 31, 2020
Net operating loss (NOL)	31,879	476,363
Total	**31,879**	**476,363**
Deferred Tax, net	**(142,484)**	**(125,865)**

Deferred Tax 2021	Opening Balance	Recognized in Profit or Loss	Recognized in Equity	Exchange Differences	Closing Balance
Intangible assets	(252,174)	199,056	—	1,204	(51,914)
Deferred unrealized foreign exchange gains	(350,054)	350,054	—	—	—
Other receivables	—	(127,000)	—	4,551	(122,449)
Net operating loss (NOL)	476,363	(443,730)	—	(754)	31,879
Total	(125,865)	(21,620)	—	5,001	(142,484)

Deferred Tax 2020	Opening Balance	Recognized in Profit or Loss	Recognized in Equity	Closing Balance
Intangible assets	(212,844)	(39,330)	—	(252,174)
Deferred unrealized foreign exchange gains	—	(350,054)	—	(350,054)
Derivative financial asset	(26,156)	26,156	—	—
Net operating loss (NOL)	91,851	384,512	—	476,363
Total	**(147,149)**	**21,284**	**—**	**(125,865)**

As of December 31, 2021, the Group had unrecognized tax loss carryforwards amounting to CHF 109.9 million (2020: CHF 114.0 million), of which CHF 108.6 million related to Auris Medical AG, Otolanum AG, Zilentin AG and Altamira Medica AG in Switzerland, CHF 1.3 million to Altamira Therapeutics Inc. in the United States (2020: CHF 113.0 million for Auris Medical AG, Otolanum AG, Zilentin AG and Altamira Medica AG and CHF 1.0 million for Auris Medical Inc.).

The Group's unrecognized tax loss carryforwards with their expiry dates are as follows:

	December 31, 2021	December 31, 2020
Within 1 year	28,909,896	19,575,171
Between 1 and 3 years	50,673,943	56,866,795
Between 3 and 7 years	29,007,049	36,701,692
More than 7 years	1,264,262	870,200
Total	**109,855,150**	**114,013,858**

Due to the uncertainty surrounding the future results of operations and the uncertainty as to whether the Group can use the loss carryforwards for tax purposes, deferred tax assets on tax loss carryforwards were only considered to the extent that they offset taxable temporary differences within the same taxable entity. No deferred tax assets are calculated on temporary differences related to pension obligations from IAS 19.

The tax effect of the major unrecognized temporary differences and loss carryforwards is presented in the table below:

	December 31, 2021	December 31, 2020
Deductible temporary differences		
Employee benefit plan	87,149	113,106
Derivative financial instruments	—	36,973
Other accounts payable	344,822	258,303
Stock option plans	—	—
Total potential tax assets	**431,971**	**408,382**
Taxable unrecognized temporary differences		
Convertible loan	—	19,359
Total unrecognized potential tax liabilities	—	19,359
Offsetting potential tax liabilities with potential tax assets	—	(19,359)
Net potential tax assets from temporary differences not recognized	431,971	389,023
Potential tax assets from loss carry-forwards not recognized	14,271,306	14,896,367
Total potential tax assets from loss carry-forwards and temporary differences not recognized	**14,703,277**	**15,285,390**

26. Loss per share

	December 31, 2021	December 31, 2020	December 31, 2019
Loss attributable to owners of the Company	(17,390,166)	(8,200,165)	(6,631,901)
Weighted average number of shares outstanding	13,246,281	6,014,146	2,909,056
Basic and diluted loss per share	**(1.31)**	**(1.36)**	**(2.28)**

For the years ended December 31, 2021 and 2020 basic and diluted loss per share is based on the weighted average number of shares issued and outstanding and excludes shares to be issued under the Stock Option Plans (Note 15) as they would be anti-dilutive. As of December 31, 2021, the Company had 1,329,510 options outstanding under its stock option plans. The average number of options outstanding between January 1, 2021 and December 31, 2021 was 1,149,761 (633,314 for the period between January 1, 2020 and December 31, 2020). As of December 31, 2021, the Company had warrants to purchase up to 246,102 of its common shares issued and outstanding (as of December 31, 2020, the Company had warrants to purchase up to 1,143,537 common shares).

27. Commitments and contingencies

Lease commitments

The future minimum lease payments under non-cancellable lease term that are not accounted for in the statement of financial position were as follows:

	December 31, 2021	December 31, 2020
Within one year	3,450	25,580
Between one and five years	—	—
Total	**3,450**	**25,580**

Office lease expenses of CHF 52,280, CHF 50,260 and CHF 49,314 were recorded in 2021, 2020 and 2019, respectively, in the consolidated statement of profit or loss and other comprehensive loss.

28. Related party transactions

For purposes of these consolidated financial statements, parties are considered to be related if one party has the ability to control the other party or exercise significant influence over the other party in making financial or operational decisions. Also, parties under common control of the Group are considered to be related. Key management personnel are also related parties. In considering each possible related party relationship, attention is directed to the substance of the relationship, and not merely the legal form.

Ante Treuhand AG ("Ante Treuhand") provided the Chief Financial Officer to the Company until November 18, 2021. The Chief Financial Officer is an employee of Ante Treuhand and is not paid directly by the Company. Fees paid to Ante Treuhand for CFO services in 2021 were CHF 231,770 (CHF 2020: 173,030). Fees paid to Ante Treuhand for other services provided during the year ended December 31, 2021 were CHF 3,025 (2020: CHF 18,020).

Gremaud GmbH provides the Chief Financial Officer to the Company since November 19, 2021. The Chief Financial Officer is an employee of Gremaud GmbH and is not paid directly by the Company. Fees paid to Gremaud GmbH for CFO services in 2021 were CHF 14,720. Fees paid to Gremaud GmbH for other services provided during the year ended December 31, 2021 were CHF 161,596 (2020 CHF 27,625).

Compensation of the members of the Board of Directors and Management

In 2021, the total compensation paid to management amounted to CHF 1,210,472 (2020: CHF 522,237; 2019: CHF 934,179). The fees paid to members of the Board of Directors in 2021 for their activities as board members totaled CHF 165,245 (2020: CHF 163,476; 2019: CHF 170,755).

	Executive Management			Board of Directors			Total		
	2021	2020	2019	2021	2020	2019	2021	2020	2019
Short term benefits	781,204	407,147	717,905	165,245	163,476	170,755	946,449	570,623	888,660
Post-employee benefits years	29,467	26,870	42,560	—	—	—	29,467	26,870	42,560
Share Bonuses	902,817	—	—	—	—	—	902,817	—	—
Share-based payment charge	192,362	204,840	109,912	48,046	57,148	49,323	240,408	261,988	159,235
Total	**1,905,850**	**638,857**	**870,377**	**213,291**	**220,624**	**220,078**	**2,119,141**	**859,481**	**1,090,455**

In 2021, CHF 240,408 (2020: CHF 261,988; 2019: CHF 159,235) was expensed for grants of stock options to members of the Board of Directors and management. The 2021 share based payment charge shown above excludes adjustments for instruments forfeited in 2021 due to termination of service. In 2021 one regular and one extraordinary bonus were granted in shares. Contributions to pension schemes amounted to CHF 29,467, CHF 26,870 and CHF 42,560 during the years 2021, 2020 and 2019, respectively. No termination benefits or other long-term benefits were paid.

Members of the Board of Directors and management held 989,606, 769,101 and 271,999 stock options as of December 31, 2021, 2020, and 2019, respectively.

29. Loan

	December 31, 2021	December 31, 2020
Loan guaranteed by Swiss government (COVID-19)	—	50,000
Convertible loan	—	473,920
Total	—	**523,920**

Convertible Loan Agreement

	December 31, 2021	December 31, 2020
As of January 1	**473,920**	—
Gross proceeds at disbursement date	—	1,500,000
Embedded derivative, separated	—	(230,974)
Transaction costs allocated to host	—	(22,495)
Carrying amount at initial recognition	—	**1,246,531**
Converted principal amount	(644,813)	(895,455)
Accrued interest at 8%	8,348	31,920
Amortization	162,545	90,924
As of December 31	—	**473,920**

On September 7, 2020, our affiliate Altamira Medica AG ("Altamira") and Auris Medical Holding Ltd. ("the Company") entered into a convertible loan agreement with FiveT Capital Holding AG ("FiveT") to raise CHF 1,500,000 to fund the initial development of AM-301. The loan has a term of 18 months and carries interest at 8% p.a., which shall not be paid in cash but added to the loan outstanding amount. At maturity, the unconverted outstanding amount of the loan including accrued interest shall become payable in cash. Altamira may choose to repay the total outstanding amount including the accrued interest at 130%, first time after 6 months with a prior written notice of 1 month. Prior to the expiry of the repayment notice period, the lender may convert the repayment amount.

Under the convertible loan agreement FiveT has the right to convert the outstanding principal amount including interest into the Company's common shares or alternatively into Altamira shares. The pricing of a conversion into our common shares is at the lower of 150% of the share price at close of the disbursement date ($1.35 fixed on September 8, 2020) and 95% of the average price of our common share at close of the 5 trading dates preceding the date of the conversion notice. However, the conversion price shall not be less than the higher of the par value and the backward-looking 3-month floor price of 75% of the average closing price of our common shares. The pricing of a conversion into Altamira shares is at the lower of CHF 3.00 and the issue price of a qualified financing round, meaning that a third-party investor will hold at least 10% of Altamira shares after completion of such financing round. The convertible loan agreement further contains a limitation on the conversion rights in the sense that they may not result in an ownership interest of more than 9.99% in the Company or 49.99% in Altamira. By December 31, 2020, an amount of CHF 895,455 has been converted into 737,000 common shares of the Company (at a conversion price of $1.35).

The convertible loan is classified as a hybrid contract containing a host that is a financial liability and embedded derivatives separated from the host and measured at fair value with all changes in fair value recognized in profit or loss. The embedded financial derivatives are valued by an independent consultant initially and at period end at fair value, applying a simulation-based valuation approach. The valuation of the embedded financial derivatives is based on input parameters, classified as Level 3. One of the significant inputs is the historical volatility of the Company's common shares. The underlying share price development has been simulated based on a Geometric Brownian Motion (GBM). In accordance with the GBM definition, a normalized, sustainable level of volatility was applied. The normalized volatility used as per December 31, 2020 was 90.9%, over a lookback period of 12 months. Other significant assumptions relate to the expected exercise date, the expected execution date, the calculation of the repayment amount, as well as assumptions with regards to the early repayment trigger and to the conversion option in Altamira shares. The embedded derivatives of the convertible loan are closely related to each other and are therefore accounted for as a single instrument (i.e., a compound derivative). Due to the conversion based on market share price, the conversion right may result in a variable number of conversion shares and the embedded derivatives are therefore classified as a financial liability.

The carrying amount of the host contract at initial recognition is the difference between the carrying amount of the hybrid contract and the fair value of the embedded derivatives. The host is then subsequently measured at amortized cost, using the effective interest rate method. As of December 31, 2020, the carrying amount (including accrued interest) of the host for the unconverted outstanding loan amounted to CHF 473,920 and is included in the balance sheet under current liabilities. On March 4, 2021, the remaining amount of CHF 644,813 including amortization and interest was converted into 516,814 common shares of Altamira at a conversion price of USD 1.35. As a result, the carrying amount of the convertible loan as of December 31, 2021 is CHF 0.

The fair value of the embedded derivatives of the outstanding loan units amounted to CHF 0 (31.12.2020: CHF 310,439 included in current derivative financial instruments). Expenses related to fair value measurement of embedded derivatives of CHF 416,003 (2020: CHF 2,248,257) as well as effective interest and transaction costs of CHF 170,893 (2020: CHF 127,418) were recorded as financial expenses in profit or loss.

30. Warrants from Public Offering

On February 21, 2017, the Company completed a public offering (the "February 2017 Offering") of 10,000,000 (pre-merger) common shares with a nominal value of CHF 0.40 each and 10,000,000 (pre-merger) warrants, each warrant entitling its holder to purchase 0.70 of a common share. The net proceeds to the Company from the February 2017 Offering were approximately CHF 9.1 million ($ 9.1 million), after deducting underwriting discounts and other estimated offering expenses payable by us. The Company had transaction costs amounting to CHF 903,919. The transactions costs were recorded as CHF 397,685 in equity for the issuance of the common shares and CHF 506,234 to finance expense in the statement of profit or loss and comprehensive loss for the issuance of the warrants.

The underwriter was granted a 30-day option to purchase up to 1,500,000 (pre-merger) additional common shares and/or 1,500,000 (pre-merger) additional warrants. On February 15, 2017, the underwriter partially exercised its 30-day option to purchase additional common shares and/or warrants in the amount of 1,350,000 (pre-merger) warrants.

Consequently, the Company issued warrants to purchase up to 7,945,000 (pre-merger) of its common shares at an exercise price of $ 1.20 per share. The warrants are exercisable during a five-year period beginning on date of issuance. The fair value calculation of the warrants is based on the Black-Scholes option price model. Assumptions are made regarding inputs such as volatility and the risk-free rate in order to determine the fair value of the warrant. If a warrant is exercised, the Company will receive variable proceeds because the Company's functional currency is CHF and the exercise price is in USD, which results in the warrants being considered liability instruments. Therefore, the warrants were assigned fair values using the Black-Scholes model. The residual value was assigned to the common share sold along with each warrant in accordance with IAS 32 Financial instruments. The gross proceeds from the February 2017 offering were CHF 9,998,305 of which CHF 5,091,817 (fair value as of February 21, 2017) was assigned to the warrants and CHF 4,906,488 was assigned to equity.

As of December 31, 2021, the outstanding warrants issued in the 2017 February Offering are exercisable for up to 39,725 common shares at an exercise price of $240.00. As of December 31, 2021, the fair value of the warrants amounted to CHF 0.00 (2020: CHF 0.00). As the fair value remained unchanged, no revaluation gain or loss resulted for the year ended December 31, 2021.

On January 30, 2018, the Company issued warrants in connection with a direct offering of 62,499 common shares, each warrant entitling its holder to purchase 0.6 common shares at an exercise price of $100.00 per common share. As of December 31, 2021, the outstanding warrants issued in such offering were exercisable for up to 37,501 common shares at an exercise price of $100.00 per common share. As of December 31, 2021 the fair value of the warrants amounted to CHF 1,233 (2020: CHF 6,318). The revaluation gain of the derivative for the twelve months ended December 31, 2021 amounted to CHF 5,085 (2020: revaluation loss of CHF 1,965). Since its initial recognition on January 30, 2018, the fair value of the warrants has decreased by CHF 2,482,514 resulting in a gain in the corresponding amount (fair value as of January 30, 2018: CHF 2,483,747).

On July 17, 2018, the Company issued Series A warrants each entitling its holder to purchase 0.35 of a common share for an aggregate of 314,102 common shares, and Series B warrants entitling its holder to purchase 0.25 of a common share for an aggregate of 224,358 common shares in connection with the July 2018 Registered Offering of 897,435 common shares, each warrant entitling its holder to purchase one common share at an original exercise price of CHF 7.80 per common share. Revaluation gain/(loss) show the changes in fair value of the outstanding Series B warrant issued in connection with this offering.

As of December 31, 2019, 145,226 Series A warrants were exercised for an aggregate amount of CHF 1,132,762 and 143,221 Series B warrants were exercised for an aggregate amount of CHF 1,117,125.

As of December 31, 2019, 143,221 Series B exercised warrants were subject to revaluation at the time that they were exercised and the fair value amounted to CHF 3,005,348. Since its initial recognition on July 17, 2018 the fair value of the warrants has increased by CHF 2,433,099, resulting in a loss in the corresponding amounts (fair value as of July 17, 2018: CHF 572,249). On June 18, 2020, the Series B warrants expired without further warrants being exercised.

Due to the expiry on June 18, 2020, no Series B warrants were outstanding and subject to revaluation on December 31, 2021 and 2020. Accordingly, there was no revaluation gain or loss on these warrants for the year ended December 31, 2021 and 2020.

31. Events after the balance sheet date

On February 4, 2022, the Company entered into a convertible loan agreement (the “Loan Agreement”) with FiveT Investment Management Ltd. (the “Lender”), pursuant to which the Lender has agreed to loan to the Company CHF 5,000,000 (the “Loan”), which Loan bears interest at the rate of 10% per annum and matures 12 months from the date (the “Disbursement Date”) the Loan proceeds were disbursed to the Company, which occurred on February 8, 2022. The Company may prepay all or part of the Loan after six months after the Disbursement Date; provided that the Company will pay an amount equal to 130% of the desired prepayment amount. The Lender has the right to convert all or part of the Loan, including accrued and unpaid interest, at its option, into common shares, subject to the limitation that the Lender own no more than 9.99% of the common shares at any time. The conversion price of the Loan into common shares is USD 1.9458, which corresponds to 150% of USD 1.2972 (the trading volume weighted average price, the “VWAP”, per common share on the NASDAQ stock exchange on the Disbursement Date), converted into Swiss Francs at the midpoint of the interbank exchange rate shown by UBS on the day of receipt of the conversion notice at 4:00 pm Central European Time. The conversion price shall be lowered in the event that the Company raises equity before the maturity date of the Loan through a public or private offering of common shares at an issue price that is at least 10 (ten) % below the VWAP (the “New Issue”), according to the formula set forth in the Loan Agreement (the “Adjustment”). Sales of common shares through equity line or at-the-market programs are not considered New Issues triggering the Adjustment.

On March 4, 2022 we announced that we had entered into an exclusive licensing and distribution agreement for Bentrio™ with Nuance Pharma Ltd. ("Nuance") in Chinese Mainland, Hong Kong, Macau and South Korea (the "Territory"). Under the terms of the Agreement, we will initially supply Bentrio™ to Nuance. Nuance will make an upfront payment of $1 million and pay to Altamira development and commercial milestones of up to $3 million and up to $19.5 million, respectively. Nuance will have the right to register and commercialize Bentrio™ in the Territory. In a second stage, Nuance will assume local production of the product for the Territory upon certain milestones. Once Nuance assumes local production of Bentrio™, it will pay to Altamira a staggered royalty on net sales in the Territory at a high-single to low-double-digit percentage.

Exhibit 2.13

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

The following description sets forth certain material terms and provisions of the securities of Altamira Therapeutics Ltd. ("Altamira," the "Company," "we," "us," and "our") that are registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). This description also summarizes relevant provisions of Bermuda law, including the Companies Act 1981 of Bermuda (the "Companies Act"). The following summary does not purport to be complete and is subject to, and is qualified in its entirety by reference to, the applicable provisions of Bermdua law and our Memorandum of Continuance and Bye-laws, copies of which are incorporated by reference as exhibits to the Annual Report on 20-F of which this Exhibit is a part. We encourage you to read our Memorandum of Continuance and Bye-laws and the applicable provisions of Bermuda law for additional information. Capitalized terms used and not otherwise defined in this Exhibit shall have the respective meanings ascribed to them in the Annual Report on 20-F of which this Exhibit is a part.

General

We are an exempted company incorporated under the laws of Bermuda. On January 24, 2019, our board of directors determined that it would be in our best interest to change our legal seat and jurisdiction of incorporation, respectively, from Switzerland to Bermuda pursuant to the Redomestication. Our shareholders approved the Redomestication and adopted the Memorandum of Continuance and the Bye-laws at an extraordinary meeting of shareholders held on March 8, 2019. Upon the issuance of a certificate of continuance by the Registrar of Companies in Bermuda on March 18, 2019, the Company discontinued as a Swiss company and, pursuant to Article 163 of the Swiss Federal Act on Private International Law and pursuant to Section 132C of the Companies Act continued existence under the Companies Act as a Bermuda company with the name "Auris Medical Holding Ltd."

At a Special General Meeting of Shareholders held on July 21, 2021, the Company adopted the new name "Altamira Therapeutics Ltd." which was registered with the Bermuda Registrar of Companies and a Certificate of Change of Name was issued by the Bermuda Registrar of Companies.

Set forth below is a description of our share capital, Memorandum of Continuance and Bye-laws. Additionally, set forth below is a comparison of select provisions of the corporate laws of Delaware and Bermuda showing the default positions in each jurisdiction that govern shareholder rights.

Bermuda Description of Share Capital

The following description of our share capital summarizes certain provisions of our Memorandum of Continuance (which is equivalent for these purposes to a memorandum of association under Bermuda law) and our Bye-laws. Such summaries do not purport to be complete and are subject to, and are qualified in their entirety by reference to, all of the provisions of our Memorandum of Continuance and Bye-laws in effect from the continuance of the Company. We urge you to read the forms of our Memorandum of Continuance and Bye-laws, included as exhibits to this Annual Report.

General

We are an exempted company incorporated under the laws of Bermuda. We began our current operations in 2003 as a corporation organized in accordance with Swiss law and domiciled in Switzerland under the name Auris Medical AG, and our name was changed to Auris Medical Holding AG on April 22, 2014. Following the Merger on March 13, 2018, the surviving entity was named Auris Medical Holding AG. Upon the issuance of a certificate of continuance by the Registrar of Companies in Bermuda on March 18, 2019, the Redomestication was effected and we continued in Bermuda pursuant to Section 132C of the Companies Act as a Bermuda company, subject to the Companies Act and other laws of Bermuda, with the name "Auris Medical Holding Ltd". At a Special General Meeting of Shareholders held on July 21, 2021, the Company adopted the new name "Altamira Therapeutics Ltd.". Our registered office is located at Clarendon House, 2 Church Street, Hamilton HM 11, Bermuda.

The Memorandum of Continuance provides that the objects of our business are unrestricted, and we have the capacity, rights, powers and privileges of a natural person.

Since the Redomestication, other than the 2019 Reverse Share Split and as otherwise described herein, including the change of the company name to Altamira Therapeutics Ltd. on 21 July 2021, there have been no material changes to our share capital, mergers, amalgamations or consolidations of us or any of our subsidiaries, no material changes in the mode of conducting our business, no material changes in the types of products produced or services rendered and no name changes. There have been no bankruptcy, receivership or similar proceedings with respect to us or our subsidiaries.

There have been no public takeover offers by third parties for our shares nor any public takeover offers by us for the shares of another company which have occurred during the last or current financial years.

Share Capital

As of December 31, 2021, our authorized share capital consisted of 25,000,000 common shares, par value CHF 0.01 per share, and 20,000,000 preference shares, par value CHF 0.02 per share, and there were 14,964,261 common shares issued and outstanding, excluding 1,329,510 common shares issuable upon exercise of options and 246,102 common shares issuable upon exercise of warrants, and no preference shares issued and outstanding. All the Company's issued and outstanding shares are fully paid in.

Pursuant to our Bye-laws, subject to any resolution of the shareholders to the contrary, our board of directors is authorized to issue any of our authorized but unissued shares. There are no limitations on the right of non-Bermudians or non-residents of Bermuda to hold or vote our shares.

Common Shares

Holders of common shares have no pre-emptive, redemption, conversion or sinking fund rights. Holders of common shares are entitled to one vote per share on all matters submitted to a vote of holders of common shares. Unless a different majority is required by law or by our Bye-laws, resolutions to be approved by holders of common shares require approval by a simple majority of votes cast at a general meeting at which a quorum is present.

In the event of our liquidation, dissolution or winding up, the holders of common shares are entitled to share equally and ratably in our assets, if any, remaining after the payment of all of our debts and liabilities, subject to any liquidation preference on any issued and outstanding preference shares.

Preference Shares

Pursuant to Bermuda law and our Bye-laws, our board of directors by resolution may establish one or more series of preference shares having such number of shares, designations, dividend rates, relative voting rights, conversion or exchange rights, redemption rights, liquidation rights and other relative participation, optional or other special rights, qualifications, limitations or restrictions as may be fixed by the board without any further shareholder approval. Such rights, preferences, powers and limitations as may be established could have the effect of discouraging an attempt to obtain control of us.

Dividend Rights

Under Bermuda law, the board of directors may declare a dividend without shareholder approval, but a company may not declare or pay dividends if there are reasonable grounds for believing that: (i) the company is, or would after the payment be, unable to pay its liabilities as they become due; or (ii) the realizable value of its assets would thereby be less than its liabilities. Under our Bye-laws, each common share is entitled to dividends if, as and when dividends are declared by our board of directors, subject to any preferred dividend right of the holders of any preference shares.

Variation of Rights

If at any time we have more than one class of shares, the rights attaching to any class, unless otherwise provided for by the terms of issue of the relevant class, may be varied either: (i) with the consent in writing of the holders of 75% of the issued shares of that class; or (ii) with the sanction of a resolution passed by a majority of the votes cast at a general meeting of the relevant class of shareholders at which a quorum consisting of at least two or more persons holding or representing issued and outstanding shares of the relevant class is present. Our Bye-laws specify that the creation or issue of shares ranking equally with existing shares will not, unless expressly provided by the terms of issue of existing shares, vary the rights attached to existing shares. In addition, the creation or issue of preference shares ranking prior to common shares will not be deemed to vary the rights attached to common shares or, subject to the terms of any other series of preference shares, to vary the rights attached to any other series of preference shares.

Transfer of Shares

Our board of directors may in its absolute discretion and without assigning any reason refuse to register the transfer of a share that it is not fully paid. Our board of directors may also refuse to recognize an instrument of transfer of a share unless it is accompanied by the relevant share certificate and such other evidence of the transferor's right to make the transfer as our board of directors shall reasonably require. Subject to these restrictions, a holder of common shares may transfer the title to all or any of his common shares by completing a form of transfer in the form set out in our Bye-laws (or as near thereto as circumstances admit) or in such other common form as the board may accept. The instrument of transfer must be signed by the transferor and transferee, although in the case of a fully paid share our board of directors may accept the instrument signed only by the transferor.

Share Split and Reverse Share Split effected by consolidating our common shares

Our board of directors may in its absolute discretion and without further approval of shareholders divide, consolidate or sub-divide our share capital in any manner permitted by the Companies Act, including approving a reverse share split by consolidating our common shares (together with a corresponding increase in the par value thereof) in a ratio determined by the board of directors. Our Bye-laws also provide that upon an alteration or reduction of share capital where fractions of shares or some other difficulty would arise, our board of directors may deal with or resolve the same in any manner as it thinks fit.

Meeting of Shareholders

Under Bermuda law, a company is required to convene at least one general meeting of shareholders each calendar year (the "annual general meeting"). However, the members may by resolution waive this requirement, either for a specific year or period of time, or indefinitely. When the requirement has been so waived, any member may, on notice to the company, terminate the waiver, in which case an annual general meeting must be called.

Bermuda law provides that a special general meeting of shareholders may be called by the board of directors of a company and must be called upon the request of shareholders holding not less than 10% of the paid-up capital of the company carrying the right to vote at general meetings. Bermuda law also requires that shareholders be given at least five days' advance notice of a general meeting, but the accidental omission to give notice to any person does not invalidate the proceedings at a meeting. Our Bye-laws provide that the board of directors may convene an annual general meeting or a special general meeting. Under our Bye-laws, at least 14 days' notice of an annual general meeting or a special general meeting must be given to each shareholder entitled to vote at such meeting. This notice requirement is subject to the ability to hold such meetings on shorter notice if such notice is agreed: (i) in the case of an annual general meeting by all of the shareholders entitled to attend and vote at such meeting; or (ii) in the case of a special general meeting by a majority in number of the shareholders entitled to attend and vote at the meeting holding not less than 95% in nominal value of the shares entitled to vote at such meeting. The quorum required for a general meeting of shareholders is two or more persons present in person at the start of the meeting and representing in person or by proxy issued and outstanding common shares.

Access to Books and Records and Dissemination of Information

Members of the general public have a right to inspect the public documents of a company available at the office of the Registrar of Companies in Bermuda. These documents include the company's memorandum of association (or memorandum of continuance), including its objects and powers, and certain alterations to the memorandum of association (or memorandum of continuance). The shareholders have the additional right to inspect the bye-laws of the company, minutes of general meetings and the company's audited financial statements, which must be presented to the annual general meeting. The register of members of a company is also open to inspection by shareholders and by members of the general public without charge. The register of members is required to be open for inspection for not less than two hours in any business day (subject to the ability of a company to close the register of members for not more than thirty days in a year). A company is required to maintain its share register in Bermuda but may, subject to the provisions of the Companies Act, establish a branch register outside of Bermuda. A company is required to keep at its registered office a register of directors and officers that is open for inspection for not less than two hours in any business day by members of the public without charge. A company is also required to file with the Registrar of Companies in Bermuda a list of its directors to be maintained on a register, which register will be available for public inspection subject to such conditions as the Registrar may impose and on payment of such fee as may be prescribed. Bermuda law does not, however, provide a general right for shareholders to inspect or obtain copies of any other corporate records.

Election and Removal of Directors

Our Bye-laws provide that our board shall consist of three directors or such greater number as the board may determine. Our board of directors currently consists of six directors, but it is anticipated that our board will consist of five directors following the holding of our annual general meeting in 2022. Each director shall hold office for such term as the shareholders may determine or, in their absence of such determination, until the next annual general meeting or until their successors are elected or appointed or their office is otherwise vacated.

Any shareholder or shareholders holding or representing not less than 5% of the total voting rights wishing to propose for election as a director someone who is not an existing director or is not proposed by our board must give notice of the intention to propose the person for election. Where a director is to be elected at an annual general meeting, that notice must be given not less than 90 days nor more than 120 days before the anniversary of the last annual general meeting prior to the giving of the notice or, in the event the annual general meeting is called for a date that is not 30 days before or after such anniversary the notice must be given not later than 10 days following the earlier of the date on which notice of the annual general meeting was posted to members or the date on which public disclosure of the date of the annual general meeting was made. Where a director is to be elected at a special general meeting, that notice must be given not later than 10 days following the earlier of the date on which notice of the special general meeting was posted to members or the date on which public disclosure of the date of the special general meeting was made.

A director may be removed, with cause, by the shareholders, provided notice of the shareholders meeting convened to remove the director is given to the director. The notice must contain a statement of the intention to remove the director and must be served on the director not less than fourteen days before the meeting. The director is entitled to attend the meeting and be heard on the motion for his removal.

Proceedings of Board of Directors

Our Bye-laws provide that our business is to be managed and conducted by our board of directors. Bermuda law permits individual and corporate directors and there is no requirement in our Bye-laws or Bermuda law that directors hold any of our shares. There is also no requirement in our Bye-laws or Bermuda law that our directors must retire at a certain age.

The remuneration of our directors is determined by our board of directors, and there is no requirement that a specified number or percentage of "independent" directors must approve any such determination. Our directors may also be paid all travel, hotel and other expenses properly incurred by them in connection with our business or their duties as directors.

Provided a director discloses a direct or indirect interest in any contract or arrangement with us as required by Bermuda law, such director is entitled to vote in respect of any such contract or arrangement in which he or she is interested unless he or she is disqualified from voting by the chairman of the relevant board meeting.

Indemnification of Directors and Officers

Section 98 of the Companies Act provides generally that a Bermuda company may indemnify its directors, officers and auditors against any liability which by virtue of any rule of law would otherwise be imposed on them in respect of any negligence, default, breach of duty or breach of trust, except in cases where such liability arises from fraud or dishonesty of which such director, officer or auditor may be guilty in relation to the company. Section 98 further provides that a Bermuda company may indemnify its directors, officers and auditors against any liability incurred by them in defending any proceedings, whether civil or criminal, in which judgment is awarded in their favor or in which they are acquitted or granted relief by the Supreme Court of Bermuda pursuant to section 281 of the Companies Act.

Our Bye-laws provide that we shall indemnify our officers and directors in respect of their actions and omissions, except in respect of their fraud or dishonesty. Our Bye-laws provide that the shareholders waive all claims or rights of action that they might have, individually or in right of the company, against any of the company's directors or officers for any act or failure to act in the performance of such director's or officer's duties, except in respect of any fraud or dishonesty of such director or officer. Section 98A of the Companies Act permits us to purchase and maintain insurance for the benefit of any officer or director in respect of any loss or liability attaching to him in respect of any negligence, default, breach of duty or breach of trust, whether or not we may otherwise indemnify such officer or director. We have purchased and maintain a directors' and officers' liability policy for such a purpose. See "Comparison of Corporate Law—Indemnification of directors and executive management and limitation of liability."

Amendment of Memorandum of Continuance and Bye-laws

Bermuda law provides that the memorandum of association (or memorandum of continuance) of a company may be amended by a resolution passed at a general meeting of shareholders. Our Bye-laws provide that no bye-law shall be rescinded, altered or amended, and no new bye-law shall be made, unless it shall have been approved by a resolution of our board of directors and by a resolution of our shareholders. In the case of certain bye-laws, such as the Bye-laws relating to election and removal of directors, approval of business combinations and amendment of bye-law provisions, the required resolutions must include the affirmative vote of at least 66 2⁄3% of our directors then in office and of at least 66 2⁄3% percent of the votes attaching to all shares in issue.

Under Bermuda law, the holders of an aggregate of not less than 20% in par value of a company's issued share capital or any class thereof have the right to apply to the Supreme Court of Bermuda for an annulment of any amendment of the memorandum of association (or memorandum of continuance) adopted by shareholders at any general meeting, other than an amendment which alters or reduces a company's share capital as provided in the Companies Act. Where such an application is made, the amendment becomes effective only to the extent that it is confirmed by the Bermuda court. An application for an annulment of an amendment of the memorandum of association (or memorandum of continuance) must be made within twenty-one days after the date on which the resolution altering the company's memorandum of association (or memorandum of continuance) is passed and may be made on behalf of persons entitled to make the application by one or more of their number as they may appoint in writing for the purpose. No application may be made by shareholders voting in favor of the amendment.

Amalgamations, Mergers and Business Combinations

The amalgamation or merger of a Bermuda company with another company or corporation (other than certain affiliated companies) requires an amalgamation or merger agreement that is approved by the company's board of directors and by its shareholders. Unless the company's bye-laws provide otherwise, the approval of 75% of the shareholders voting at such meeting is required to approve the amalgamation or merger agreement, and the quorum for such meeting must be two persons holding or representing more than one-third of the issued shares of the company. Our Bye-laws provide that an amalgamation or a merger (other than with a wholly owned subsidiary or as described below) that has been approved by the board must only be approved by a majority of the votes cast at a general meeting of the shareholders at which the quorum shall be two or more persons present in person and representing in person or by proxy issued and outstanding common voting shares. Any amalgamation or merger or other business combination (as defined in the Bye-laws) not approved by our board of directors must be approved by the holders of not less than 66 2⁄3% of all votes attaching to all shares then in issue entitling the holder to attend and vote on the resolution.

Under Bermuda law, in the event of an amalgamation or merger of a Bermuda company with another company or corporation, a shareholder of the Bermuda company who did not vote in favor of the amalgamation or merger and who is not satisfied that fair value has been offered for such shareholder's shares may, within one month of notice of the shareholders meeting, apply to the Supreme Court of Bermuda to appraise the fair value of those shares.

Our Bye-laws contain provisions regarding "business combinations" with "interested shareholders". Pursuant to the Bye-laws, in addition to any other approval that may be required by applicable law, any business combination with an interested shareholder within a period of three years after the date of the transaction in which the person became an interested shareholder must be approved by our board and authorized at an annual or special general meeting by the affirmative vote of at least 66 2⁄3% of our issued and outstanding voting shares that are not owned by the interested shareholder, unless: (i) prior to the time that the shareholder becoming an interested shareholder, our board of directors approved either the business combination or the transaction that resulted in the shareholder becoming an interested shareholder; or (ii) upon consummation of the transaction that resulted in the shareholder becoming an interested shareholder, the interested shareholder owned at least 85% of our issued and outstanding voting shares at the time the transaction commenced. For purposes of these provisions, "business combinations" include mergers, amalgamations, consolidations and certain sales, leases, exchanges, mortgages, pledges, transfers and other dispositions of assets, issuances and transfers of shares and other transactions resulting in a financial benefit to an interested shareholder. An "interested shareholder" is a person that beneficially owns 15% or more of our issued and outstanding voting shares and any person affiliated or associated with us that owned 15% or more of our issued and outstanding voting shares at any time three years prior to the relevant time.

Compulsory Acquisition of Shares Held by Minority Holders

An acquiring party is generally able to acquire compulsorily the common shares of minority holders in the following ways:

(1) By a procedure under the Companies Act known as a "scheme of arrangement." A scheme of arrangement could be effected by obtaining the agreement of the company and of holders of its shares (or any class of shares), representing in the aggregate a majority in number and at least 75% in value of the shares or class of shares present and voting at a court ordered meeting held to consider the scheme or arrangement. The scheme of arrangement must then be sanctioned by the Bermuda Supreme Court. If a scheme of arrangement receives all necessary agreements and sanctions, upon the filing of the court order with the Registrar of Companies in Bermuda, all holders of common shares could be compelled to sell their shares under the terms of the scheme or arrangement.

(2) If the acquiring party is a company it may compulsorily acquire all the shares of the target company, by acquiring pursuant to a tender offer 90% of the shares or class of shares not already owned by, or by a nominee for, the acquiring party (the offeror), or any of its subsidiaries. If an offeror has, within four months after the making of an offer for all the shares or class of shares not owned by, or by a nominee for, the offeror, or any of its subsidiaries, obtained the approval of the holders of 90% or more of all the shares to which the offer relates, the offeror may, at any time within two months beginning with the date on which the approval was obtained, require by notice any nontendering shareholder to transfer its shares on the same terms as the original offer. In those circumstances, nontendering shareholders will be compelled to sell their shares unless the Supreme Court of Bermuda (on application made within a one-month period from the date of the offeror's notice of its intention to acquire such shares) orders otherwise.

(3) Where one or more parties holds not less than 95% of the shares or a class of shares of a company, such holder(s) may, pursuant to a notice given to the remaining shareholders or class of shareholders, acquire the shares of such remaining shareholders or class of shareholders. When this notice is given, the acquiring party is entitled and bound to acquire the shares of the remaining shareholders on the terms set out in the notice, unless a remaining shareholder, within one month of receiving such notice, applies to the Supreme Court of Bermuda for an appraisal of the value of its shares. This provision only applies where the acquiring party offers the same terms to all holders of shares whose shares are being acquired.

Anti-Takeover Provisions

Two-thirds supermajority shareholder voting requirement: Our Bye-laws provide that, except to the extent that a proposal has received the prior approval of the board, the approval of an amalgamation, merger or consolidation with or into any other person shall require the affirmative vote of not less than 66 2⁄3% of all votes attaching to all shares then in issue entitling the holder to attend and vote on the resolution (except for certain "business combinations" with "interested shareholders" as set forth in *Amalgamations, Mergers and Business Combinations* above).

Amendments to the Bye-laws: Our Bye-laws provide that no bye-law may be rescinded, altered or amended and no new bye-law may be made until the same has been approved by a resolution of the board and by a resolution of the shareholders. In the case of certain bye-laws, such as the Bye-laws relating to election and removal of directors, approval of business combinations and amendment of bye-law provisions, the required resolutions must include the affirmative vote of at least 66 2⁄3% of our directors then in office and of at least 66 2⁄3% percent of the votes attaching to all issued and outstanding shares.

Limitations on the election of directors: Our Bye-laws provide that a person may be proposed for election or appointment as a director at a general meeting either by the board or by one or more shareholders holding our shares which in the aggregate carry not less than 5% of the voting rights in respect of the election of directors. In addition, unless a person is proposed for election or appointment as a director by the board, when a person is proposed for appointment or election as a director, written notice of the proposal must be given to us as follows. Where a director is to be appointed or elected: (1) at an annual general meeting, such notice must be given not less than 90 days nor more than 120 days before the anniversary of the last annual general meeting prior to the giving of the notice or, in the event the annual general meeting is called for a date that is not 30 days before or after such anniversary the notice must be given not later than 10 days following the earlier of the date on which notice of the annual general meeting was posted to shareholders or the date on which public disclosure of the date of the annual general meeting was made; and (2) at a special general meeting, such notice must be given not later than 10 days following the earlier of the date on which notice of the special general meeting was posted to shareholders or the date on which public disclosure of the date of the special general meeting was made.

Shareholder Suits

Class actions and derivative actions are generally not available to shareholders under Bermuda law. The Bermuda courts, however, would ordinarily be expected to permit a shareholder to commence an action in the name of a company to remedy a wrong to the company where the act complained of is alleged to be beyond the corporate power of the company or illegal, or would result in the violation of the company's memorandum of association (or memorandum of continuance) or bye-laws. Furthermore, consideration would be given by a Bermuda court to acts that are alleged to constitute a fraud against the minority shareholders or, for instance, where an act requires the approval of a greater percentage of the company's shareholders than that which actually approved it.

When the affairs of a company are being conducted in a manner which is oppressive or prejudicial to the interests of some part of the shareholders, one or more shareholders may apply to the Supreme Court of Bermuda, which may make such order as it sees fit, including an order regulating the conduct of the company's affairs in the future or ordering the purchase of the shares of any shareholders by other shareholders or by the company.

Our Bye-laws contain a provision by virtue of which our shareholders waive any claim or right of action that they have, both individually and on our behalf, against any director or officer in relation to any action or failure to take action by such director or officer, except in respect of any fraud or dishonesty of such director or officer. The SEC has advised that the operation of this provision as a waiver of the right to sue for violations of federal securities laws would likely be unenforceable in U.S. courts.

Capitalization of Profits and Reserves

Pursuant to our Bye-laws, our board of directors may (i) capitalize any part of the amount of our share premium or other reserve accounts or any amount credited to our profit and loss account or otherwise available for distribution by applying such sum in paying up unissued shares to be allotted as fully paid bonus shares pro-rata (except in connection with the conversion of shares) to the shareholders; or (ii) capitalize any sum standing to the credit of a reserve account or sums otherwise available for dividend or distribution by paying up in full, partly paid or nil paid shares of those shareholders who would have been entitled to such sums if they were distributed by way of dividend or distribution.

Exchange controls

We have received consent under the Exchange Control Act 1972 from the Bermuda Monetary Authority for the issue and transfer of the common shares to and between non-residents of Bermuda for exchange control purposes provided our shares remain listed on an appointed stock exchange, which includes the Nasdaq Capital Market. In granting such consent the Bermuda Monetary Authority accepts no responsibility for our financial soundness or the correctness of any of the statements made or opinions expressed in this Annual Report.

Registrar or Transfer Agent

A register of holders of the common shares is maintained by Conyers Corporate Services (Bermuda) Limited in Bermuda, and a branch register is maintained in the United States by American Stock Transfer & Trust Company, LLC, who serves as branch registrar and transfer agent.

Untraced Shareholders

Our Bye-laws provide that our board of directors may forfeit any dividend or other monies payable in respect of any shares which remain unclaimed for six years from the date when such monies became due for payment. In addition, we are entitled to cease sending dividend warrants and checks by post or otherwise to a shareholder if such instruments have been returned undelivered to, or left uncashed by, such shareholder on at least two consecutive occasions or, following one such occasion, reasonable enquires have failed to establish the shareholder's new address. This entitlement ceases if the shareholder claims a dividend or cashes a dividend check or a warrant.

Certain Provisions of Bermuda Law

We have been designated by the Bermuda Monetary Authority as a non-resident for Bermuda exchange control purposes. This designation allows us to engage in transactions in currencies other than the Bermuda dollar, and there are no restrictions on our ability to transfer funds (other than funds denominated in Bermuda dollars) in and out of Bermuda or to pay dividends to United States residents who are holders of our common shares.

We have received consent from the Bermuda Monetary Authority for the issue and free transferability of all of our common shares to and between non-residents of Bermuda for exchange control purposes, provided our shares remain listed on an appointed stock exchange, which includes the Nasdaq Capital Market. Approvals or permissions given by the Bermuda Monetary Authority do not constitute a guarantee by the Bermuda Monetary Authority as to our performance or creditworthiness. Accordingly, in giving such consent or permissions, the Bermuda Monetary Authority shall not be liable for the financial soundness, performance or default of our business or for the correctness of any opinions or statements expressed in this Annual Report. Certain issues and transfers of common shares involving persons deemed resident in Bermuda for exchange control purposes require the specific consent of the Bermuda Monetary Authority.

In accordance with Bermuda law, share certificates are only issued in the names of companies, partnerships or individuals. In the case of a shareholder acting in a special capacity (for example as a trustee), certificates may, at the request of the shareholder, record the capacity in which the shareholder is acting. Notwithstanding such recording of any special capacity, we will not be bound to investigate or see to the execution of any such trust. We will take no notice of any trust applicable to any of our shares, whether or not we have been notified of such trust.

Comparison of Corporate Law

Set forth below is a comparison of select provisions of the corporate laws of Delaware and Bermuda showing the default positions in each jurisdiction that govern shareholder rights.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Mergers and similar arrangements	
Under the Delaware General Corporation Law, with certain exceptions, a merger, consolidation, sale, lease or transfer of all or substantially all of the assets of a corporation must be approved by the board of directors and a majority of the outstanding shares entitled to vote thereon. A shareholder of a Delaware corporation participating in certain major corporate transactions may, under certain circumstances, be entitled to appraisal rights pursuant to which such shareholder may receive cash in the amount of the fair value of the shares held by such shareholder (as determined by a court) in lieu of the consideration such shareholder would otherwise receive in the transaction. The Delaware General Corporation Law also provides that a parent corporation, by resolution of its board of directors, may merge with any subsidiary, of which it owns at least 90.0% of each class of capital stock without a vote by the shareholders of such subsidiary. Upon any such merger, dissenting shareholders of the subsidiary would have appraisal rights.	The amalgamation or merger of a Bermuda company with another company or corporation (other than certain affiliated companies) requires the amalgamation or merger agreement to be approved by the company's board of directors and by its shareholders. Unless the company's bye-laws provide otherwise, the approval of 75% of the shareholders voting at a general meeting is required to approve the amalgamation or merger agreement, and the quorum for such meeting must be two persons holding or representing more than one-third of the issued shares of the company. The Bye-laws provide that a merger or an amalgamation (other than with a wholly owned subsidiary or as described below) that has been approved by the board must only be approved by a majority of the votes cast at a general meeting of the shareholders at which the quorum shall be two or more persons present in person and representing in person or by proxy issued and outstanding voting shares. The Bye-laws contain provisions regarding "business combinations" with "interested shareholders". Pursuant to our Bye-laws, in addition to any other approval that may be required by applicable law, any business combination with an interested shareholder within a period of three years after the date of the transaction in which the person became an interested shareholder must be approved by our board and authorized at an annual or special general meeting by the affirmative vote of at least 66 and 2/3rds% of our issued and outstanding voting shares that are not owned by the interested shareholder, unless: (i) prior to the time that the shareholder becoming an interested shareholder, our board of directors approved either the business combination or the transaction that resulted in the shareholder becoming an interested shareholder; or (ii) upon consummation of the transaction that resulted in the shareholder becoming an interested shareholder, the interested shareholder owned at least 85% of our issued and outstanding voting shares at the time the transaction commenced. For purposes of these provisions, "business combinations" include mergers, amalgamations, consolidations and certain sales, leases, exchanges, mortgages, pledges, transfers and other dispositions of assets, issuances and transfers of shares and other transactions resulting in a financial benefit to an interested shareholder. An "interested shareholder" is a person that beneficially owns 15% or more of our issued and outstanding voting shares and any person affiliated or associated with us that owned 15% or more of our issued and outstanding voting shares at any time three years prior to the relevant time. Under Bermuda law, in the event of an amalgamation or merger of a Bermuda company with another company or corporation, a shareholder of the Bermuda company who did not vote in favor of the amalgamation or merger and who is not satisfied that fair value has been offered for such shareholder's shares may, within one month of notice of the shareholders meeting, apply to the Supreme Court of Bermuda to appraise the fair value of those shares. Note that each share of an amalgamating or merging company carries the right to vote in respect of an amalgamation or merger whether or not is otherwise carries the right to vote.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Shareholders' suits	
Class actions and derivative actions generally are available to shareholders of a Delaware corporation for, among other things, breach of fiduciary duty, corporate waste and actions not taken in accordance with applicable law. In such actions, the court has discretion to permit the winning party to recover attorneys' fees incurred in connection with such action.	Class actions and derivative actions are generally not available to shareholders under Bermuda law. The Bermuda courts, however, would ordinarily be expected to permit a shareholder to commence an action in the name of a company to remedy a wrong to the company where the act complained of is alleged to be beyond the corporate power of the company or illegal, or would result in the violation of the company's memorandum of association or bye-laws. Furthermore, consideration would be given by a Bermuda court to acts that are alleged to constitute a fraud against the minority shareholders or, for instance, where an act requires the approval of a greater percentage of the company's shareholders than that which actually approved it. When the affairs of a company are being conducted in a manner which is oppressive or prejudicial to the interests of some part of the shareholders, one or more shareholders may apply to the Supreme Court of Bermuda, which may make such order as it sees fit, including an order regulating the conduct of the company's affairs in the future or ordering the purchase of the shares of any shareholders by other shareholders or by the company. The Bye-laws contain a provision by virtue of which our shareholders waive any claim or right of action that they have, both individually and on our behalf, against any director or officer in relation to any action or failure to take action by such director or officer, except in respect of any fraud or dishonesty of such director or officer.
Shareholder vote on board and management compensation	
Under the Delaware General Corporation Law, the board of directors has the authority to fix the compensation of directors, unless otherwise restricted by the certificate of incorporation or bylaws.	The Bye-laws contains a provision that the board of directors has the power to determine the remuneration, if any, of the directors.
Annual vote on board renewal	
Unless directors are elected by written consent in lieu of an annual meeting, directors are elected in an annual meeting of stockholders on a date and at a time designated by or in the manner provided in the bylaws. Re-election is possible. Classified boards are permitted.	The Bye-laws provide that the directors shall hold office for such term as the shareholders may determine or, in their absence of such determination, until the next annual general meeting, or until their successors are elected or appointed or their office is otherwise vacated. Re-election is possible. Provision for staggered boards of directors may be included in a company's bye-laws.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Indemnification of directors and executive management and limitation of liability	
The Delaware General Corporation Law provides that a certificate of incorporation may contain a provision eliminating or limiting the personal liability of directors (but not other controlling persons) of the corporation for monetary damages for breach of a fiduciary duty as a director, except no provision in the certificate of incorporation may eliminate or limit the liability of a director for: any breach of a director's duty of loyalty to the corporation or its shareholders; acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law; statutory liability for unlawful payment of dividends or unlawful stock purchase or redemption; or any transaction from which the director derived an improper personal benefit.	Section 98 of the Companies Act provides generally that a Bermuda company may indemnify its directors, officers and auditors against any liability which by virtue of any rule of law would otherwise be imposed on them in respect of any negligence, default, breach of duty or breach of trust, except in cases where such liability arises from fraud or dishonesty of which such director, officer or auditor may be guilty in relation to the company. Section 98 further provides that a Bermuda company may indemnify its directors, officers and auditors against any liability incurred by them in defending any proceedings, whether civil or criminal, in which judgment is awarded in their favor or in which they are acquitted or granted relief by the Supreme Court of Bermuda pursuant to section 281 of the Companies Act.
A Delaware corporation may indemnify any person who was or is a party or is threatened to be made a party to any proceeding, other than an action by or on behalf of the corporation, because the person is or was a director or officer, against liability incurred in connection with the proceeding if the director or officer acted in good faith and in a manner reasonably believed to be in, or not opposed to, the best interests of the corporation; and the director or officer, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful.	The Bye-laws contain provisions that provide that we shall indemnify its officers and directors in respect of their actions and omissions, except in respect of their fraud or dishonesty. Our bye-laws provide that the shareholders waive all claims or rights of action that they might have, individually or in right of the company, against any of the company's directors or officers for any act or failure to act in the performance of such director's or officer's duties, except in respect of any fraud or dishonesty of such director or officer. Section 98A of the Companies Act permits us to purchase and maintain insurance for the benefit of any officer or director in respect of any loss or liability attaching to him in respect of any negligence, default, breach of duty or breach of trust, whether or not we may otherwise indemnify such officer or director. We have purchased and maintain a directors' and officers' liability policy for such a purpose.
Unless ordered by a court, any foregoing indemnification is subject to a determination that the director or officer has met the applicable standard of conduct: by a majority vote of the directors who are not parties to the proceeding, even though less than a quorum; by a committee of directors designated by a majority vote of the eligible directors, even though less than a quorum; by independent legal counsel in a written opinion if there are no eligible directors, or if the eligible directors so direct; or by the shareholders.	
Moreover, a Delaware corporation may not indemnify a director or officer in connection with any proceeding in which the director or officer has been adjudged to be liable to the corporation unless and only to the extent that the court determines that, despite the adjudication of liability but in view of all the circumstances of the case, the director or officer is fairly and reasonably entitled to indemnity for those expenses which the court deems proper.	

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Directors' fiduciary duties	
A director of a Delaware corporation has a fiduciary duty to the corporation and its shareholders. This duty has two components: the duty of care; and the duty of loyalty.	At common law, members of a board of directors owe a fiduciary duty to the company to act in good faith in their dealings with or on behalf of the company and exercise their powers and fulfill the duties of their office honestly. This duty includes the following elements: (i) a duty to act in good faith in the best interests of the company; (ii) a duty not to make a personal profit from opportunities that arise from the office of director; (iii) a duty to avoid conflicts of interest; and (iv) a duty to exercise powers for the purpose for which such powers were intended.
The duty of care requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of, and disclose to shareholders, all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. This duty prohibits self-dealing by a director and mandates that the best interest of the corporation and its shareholders take precedence over any interest possessed by a director, officer or controlling shareholder and not shared by the shareholders generally. In general, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence a breach of one of the fiduciary duties. Should such evidence be presented concerning a transaction by a director, a director must prove the procedural fairness of the transaction, and that the transaction was of fair value to the corporation.	The Companies Act also imposes a duty on directors and officers of a Bermuda company to: (i) act honestly and in good faith with a view to the best interests of the company; and (ii) exercise the care, diligence and skill that a reasonably prudent person would exercise in comparable circumstances. In addition, the Companies Act imposes various duties on directors and officers of a company with respect to certain matters of management and administration of the company.
Shareholder action by written consent	
A Delaware corporation may, in its certificate of incorporation, eliminate the right of shareholders to act by written consent.	The Companies Act provides that shareholders may take action by written consent, except in respect of the removal of an auditor from office before the expiry of his term or in respect of a resolution passed for the purpose of removing a director before the expiration of his term of office. A resolution in writing is passed when it is signed by the members of the company who at the date of the notice of the resolution represent such majority of votes as would be required if the resolution had been voted on at a meeting or when it is signed by all the members of the company or such other majority of members as may be provided by the bye-laws of the company.

Shareholder proposals

A shareholder of a Delaware corporation has the right to put any proposal before the annual meeting of shareholders, provided it complies with the notice provisions in the governing documents. A special meeting may be called by the board of directors or any other person authorized to do so in the governing documents, but shareholders may be precluded from calling special meetings.

Shareholder(s) may, as set forth below and at their own expense (unless the company otherwise resolves), require the company to: (i) give notice to all shareholders entitled to receive notice of the annual general meeting of any resolution that the shareholder(s) may properly move at the next annual general meeting; and/or (ii) circulate to all shareholders entitled to receive notice of any general meeting a statement in respect of any matter referred to in the proposed resolution or any business to be conducted at such general meeting. The number of shareholders necessary for such a requisition is either: (i) any number of shareholders representing not less than 5% of the total voting rights of all shareholders entitled to vote at the meeting to which the requisition relates; or (ii) not less than 100 shareholders.

Pursuant to the Bye-laws, any shareholder or shareholders holding or representing not less than 5% of the total voting rights wishing to propose for election as a director someone who is not an existing director or is not proposed by our board must give notice of the intention to propose the person for election in accordance with the Bye-laws.

Cumulative voting

Under the Delaware General Corporation Law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation provides for it.

Under Bermuda law, the voting rights of shareholders are regulated by the company's bye-laws and, in certain circumstances, by the Companies Act. The Bye-laws provide for a plurality of voting for elections of directors, and cumulative voting for elections of directors is not permitted.

Removal of directors

A Delaware corporation with a classified board may be removed only for cause with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise.

Under the Bye-laws, a director may be removed, with cause, by the shareholders, provided notice of the shareholders meeting convened to remove the director is given to the director. The notice must contain a statement of the intention to remove the director and must be served on the director not less than fourteen days before the meeting. The director is entitled to attend the meeting and be heard on the motion for his removal.

Transactions with interested shareholders

The Delaware General Corporation Law generally prohibits a Delaware corporation from engaging in certain business combinations with an "interested shareholder" for three years following the date that such person becomes an interested shareholder. An interested shareholder generally is a person or group who or which owns or owned 15.0% or more of the corporation's outstanding voting stock within the past three years.

There is no similar law in Bermuda.

The Bye-laws contain provisions regarding "business combinations" with "interested shareholders" which are described above under "mergers and similar arrangements."

Dissolution; Winding up

Unless the board of directors of a Delaware corporation approves the proposal to dissolve, dissolution must be approved by shareholders holding 100.0% of the total voting power of the corporation. Only if the dissolution is initiated by the board of directors may it be approved by a simple majority of the corporation's outstanding shares. Delaware law allows a Delaware corporation to include in its certificate of incorporation a supermajority voting requirement in connection with dissolutions initiated by the board.

A Bermuda company may be wound up by the Bermuda court on application presented by the company itself, its creditors (including contingent or prospective creditors) or its contributories. The Bermuda court has authority to order winding up in a number of specified circumstances including where it is, in the opinion of the Bermuda court, just and equitable to do so.

A Bermuda company limited by shares may be wound up voluntarily when the shareholders so resolve in general meeting. In the case of a voluntary winding up, the company shall, from the commencement of the winding up, cease to carry on its business, except so far as may be required for the beneficial winding up thereof.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Variation of rights of shares	
A Delaware corporation may vary the rights of a class of shares with the approval of a majority of the outstanding shares of such class, unless the certificate of incorporation provides otherwise.	Under the Bye-laws, if at any time we have more than one class of shares, the rights attaching to any class, unless otherwise provided for by the terms of issue of the relevant class, may be varied either: (i) with the consent in writing of the holders of 75% of the issued shares of that class; or (ii) with the sanction of a resolution passed by a majority of the votes cast at a general meeting of the relevant class of shareholders at which a quorum consisting of at least two persons holding or representing issued shares of the relevant class is present. The Bye-laws specify that the creation or issue of shares ranking equally with existing shares will not, unless expressly provided by the terms of issue of existing shares, vary the rights attached to existing shares. In addition, the creation or issue of preference shares ranking prior to common shares will not be deemed to vary the rights attached to common shares or, subject to the terms of any other series of preference shares, to vary the rights attached to any other series of preference shares.
Amendment of governing documents	
A Delaware corporation's governing documents may be amended with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise.	A Bermuda company's memorandum of association and bye-laws may be amended by resolutions of the board of directors and the shareholders, subject to the company's bye-laws.
Inspection of Books and Records	
Shareholders of a Delaware corporation, upon written demand under oath stating the purpose thereof, have the right during the usual hours for business to inspect for any proper purpose, and to obtain copies of list(s) of shareholders and other books and records of the corporation and its subsidiaries, if any, to the extent the books and records of such subsidiaries are available to the corporation.	Members of the general public have a right to inspect the public documents of a company available at the office of the Registrar of Companies in Bermuda. These documents include the company's memorandum of association/continuance, including its objects and powers, and certain alterations to the memorandum of association/continuance. The shareholders have the additional right to inspect the bye-laws of the company, minutes of general meetings and the company's audited financial statements, which must be presented to the annual general meeting. The register of members of a company is also open to inspection by shareholders without charge, and by members of the general public on payment of a fee. The register of members is required to be open for inspection for not less than two hours in any business day (subject to the ability of a company to close the register of members for not more than thirty days in a year). A company is required to maintain its share register in Bermuda but may, subject to the provisions of the Companies Act, establish a branch register outside of Bermuda. A company is required to keep at its registered office a register of directors and officers that is open for inspection for not less than two hours in any business day by members of the public without charge. Bermuda law does not, however, provide a general right for shareholders to inspect or obtain copies of any other corporate records.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Payment of dividends	
The board of directors may approve a dividend without shareholder approval. Subject to any restrictions contained in its certificate of incorporation, the board may declare and pay dividends upon the shares of its capital stock either: out of its surplus, or in case there is no such surplus, out of its net profits for the fiscal year in which the dividend is declared and/or the preceding fiscal year. Stockholder approval is required to authorize capital stock in excess of that provided in the charter. Directors may issue authorized shares without stockholder approval.	Under Bermuda law, the board of directors may declare a dividend without shareholder approval, but a company may not declare or pay dividends if there are reasonable grounds for believing that: (i) the company is, or would after the payment be, unable to pay its liabilities as they become due; or (ii) that the realizable value of its assets would thereby be less than its liabilities. Under the Bye-laws, each common share is entitled to dividends if, as and when dividends are declared by our board of directors, subject to any preferred dividend right of the holders of any preference shares.
Creation and issuance of new shares	
All creation of shares requires the board of directors to adopt a resolution or resolutions, pursuant to authority expressly vested in the board of directors by the provisions of the company's certificate of incorporation.	The authorized share capital of a Bermuda company is determined by the company's shareholders.

Exhibit 8.1

SUBSIDIARIES OF THE REGISTRANT

Name of Subsidiary	Jurisdiction of Incorporation or Organization
Auris Medical AG	Switzerland
Otolanum AG	Switzerland
Zilentin AG	Switzerland
Altamira Medica AG	Switzerland
Altamira Therapeutics, Inc.	Delaware
Auris Medical Ltd.	Ireland
Auris Medial Pty Ltd	Australia

Exhibit 12.1

CERTIFICATION

I, Thomas Meyer, certify that:

1. I have reviewed this annual report on Form 20-F of Altamira Therapeutics Ltd.;

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

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

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

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

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

   (d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and

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

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

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

Date: April 12, 2022

/s/ Thomas Meyer

Thomas Meyer
Chief Executive Officer

Exhibit 12.2

CERTIFICATION

I, Marcel Gremaud, certify that:

1. I have reviewed this annual report on Form 20-F of Altamira Therapeutics Ltd.;

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

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

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

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

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

   (d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and

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

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

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

Date: April 12, 2022

/s/ Marcel Gremaud

Marcel Gremaud
Chief Financial Officer

Exhibit 13.1

CERTIFICATION

The certification set forth below is being submitted in connection with Altamira Therapeutics AG's annual report on Form 20-F for the year ended December 31, 2021 (the "Report") for the purpose of complying with Rule 13a-14(b) or Rule 15d-14(b) of the Securities Exchange Act of 1934 (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code.

Thomas Meyer, the Chief Executive Officer of Altamira Therapeutics Ltd., certifies that, to the best of his knowledge:

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

2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of Altamira Therapeutics Ltd.

Date: April 12, 2022

/s/ Thomas Meyer

Name: Thomas Meyer
Chief Executive Officer

Exhibit 13.2

CERTIFICATION

The certification set forth below is being submitted in connection with Altamira Therapeutics AG's annual report on Form 20-F for the year ended December 31, 2021 (the "Report") for the purpose of complying with Rule 13a-14(b) or Rule 15d-14(b) of the Securities Exchange Act of 1934 (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code.

Marcel Gremaud, the Chief Financial Officer of Altamira Therapeutics Ltd., certifies that, to the best of his knowledge:

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

2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of Altamira Therapeutics Ltd.

Date: April 12, 2022

/s/ Marcel Gremaud

Name: Marcel Gremaud
Chief Financial Officer

Exhibit 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-232735 and 333-252141 on Form S-8 and Registration Statement Nos. 333-228121, 333-249347 and 333-261127 on Form F-3 of our report dated April 12, 2022, relating to the financial statements of Altamira Therapeutics Ltd. appearing in this Annual Report on Form 20-F for the year ended December 31, 2021.

Deloitte AG

/s/ Roland Mueller

/s/ Adrian Kaeppeli

Auditor in Charge

Zurich, Switzerland
April 12, 2022