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

FORM 20-F

(Mark One)

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

OR

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
for the fiscal year ended December 31, 2022

OR

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

For the transition period from ___________ to ___________

OR

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

Date of event requiring this shell company report

Commission file number: 001-36582

ALTAMIRA THERAPEUTICS 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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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 0.20 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: 1,180,053

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. ☐

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

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

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

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

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

☐ Item 17 ☐ Item 18

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

☐ Yes ☒ No

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.”, or “Altamira”, the “Company,” “we,” “our,” “ours,” “us” or similar terms refer to (i) Auris Medical Holding Ltd. a Bermuda company, or Auris Medical (Bermuda), the successor issuer to Auris Medical Holding AG (“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 (ii) to Altamira Therapeutics 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. On October 25, 2022, the Company effected a one-for-twenty reverse share split (the “2022 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 and 2022 Reverse Share Split.

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;
- our ability to timely and successfully reposition our Company around RNA delivery technology and to divest or partner our business in neurotology, rhinology and allergology;
- the COVID-19 pandemic, which continues to evolve, and which could significantly disrupt our preclinical studies and clinical trials, and therefore our receipt of necessary regulatory approvals;
- our need for substantial additional funding to continue the development of our product candidates 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 timing, scope, terms and conditions of a potential divestiture or partnering of the Company’s traditional business as well as the cash such transaction(s) may generate;
- the market acceptance and resulting sales from Bentrio® in international markets;
- our dependence on the success of OligoPhore™, SemaPhore™, AM-401 and AM-411, which are still in preclinical development, and may eventually prove to be unsuccessful;
- 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, 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.
- The Company has incurred recurring losses and negative cash flows from operations since inception and it expects to generate losses from operations for the foreseeable future primarily due to research and development costs for its potential product candidates. We expect our research and development expenses to remain significant as we advance or initiate the pre-clinical and clinical development of AM-401, AM-411 or any other product candidate. To the extent that we will be unable to generate sufficient cash proceeds from the planned divestiture or partnering of our legacy assets or other partnering activities, we will need to raise additional equity and debt financing that may not be available, if at all, at terms acceptable to the Company to fund future operations. As a result, the Company could be required to delay, scale back or abandon some or all of its development programs and other operations, which could materially harm the Company's business, prospects, financial condition and operating results. This could then result in bankruptcy, or the liquidation of the Company. These factors raise substantial doubt about the Company's ability to continue as a going concern.

- We are working to reposition our Company around RNA delivery technology and to divest or partner 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 partner our non-RNA business at attractive conditions and within a reasonable period of time.

- We have only recently 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® was cleared by the U.S. Food and Drug Administration, or the FDA, as a medical device in the U.S., but has not been commercialized in the U.S. to date. The product is marketed as an “over the counter” (OTC) 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 OligoPhore™, SemaPhore™, AM-401 and AM-411 which are still in preclinical development, respectively. If our development programs are unsuccessful or we are unable to out-license OligoPhore™, SemaPhore™, AM-401 or AM-411, 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.

- 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

Most of our products are still in the development-stage and we 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 biopharmaceutical company with most of our products still in the development stage and a 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 26.5 million, CHF 17.1 million and CHF 8.2 million for the years ended December 31, 2022, 2021 and 2020, respectively. As of December 31, 2022, we had an accumulated deficit of CHF 201.4 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, 2022, we incurred CHF 26.1 million in operating loss or CHF 13.7 million before a one-time non-cash write-off of capitalized development expenditures for our AM-125 project based on the impairment test performed under IFRS. We expect our total additional cash need in 2023 to be in the range of CHF 15 to 17 million.

To date, we have financed our operations through an initial public offering and follow-on offerings of our common shares, private placements of equity securities and short- and long-term loans.

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. 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 and/or continue our operations.

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. Such revenues to date have not been meaningful or sufficient to support our operations. 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 OligoPhore™, SemaPhore™, AM-401 and AM-411 and out-license them. Our ability to generate future revenue from product sales and out-licensing 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;
- generating data allowing to obtain Investigational New Drug ("IND") clearance from the FDA for AM-401 and AM-411 or to allow a potential licensee use OligoPhore™ or SemaPhore™ for its own IND submissions;
- developing a sustainable and scalable manufacturing process for OligoPhore™, SemaPhore™, AM-401 and AM-411 and maintaining supply and manufacturing relationships with third parties that can conduct the process and provide adequate (in amount and quality) products to support development and potential licensees' demand for our product candidates or technologies, if out-licensed;
- 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, 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 European Medicines Agency (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 out-license OligoPhore™, SemaPhore™, AM-401, AM-411 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, and there is substantial doubt about our ability to continue as a going concern. 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 as we advance or initiate the pre-clinical and clinical development of AM-401, AM-411 or any other product candidate. We expect our total additional cash need in 2023 to be in the range of CHF 15 to 17 million. As of December 31, 2022, our cash and cash equivalents were CHF 15 thousand. Our assumptions may prove to be wrong, and we may have to use our capital resources sooner than we currently expect. To the extent that we will be unable to generate sufficient cash proceeds from the planned divestiture or partnering of our legacy assets or other partnering activities, we will need substantial additional financing to meet these funding requirements. These factors raise substantial doubt about the Company’s ability to continue as a going concern. The financial statements included in this report have been prepared on a going concern basis, which contemplates the continuity of normal activities and realization of assets and settlement of liabilities in the normal course of business. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. 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, which could materially harm our business, prospects, financial condition and operating results. This could then result in bankruptcy, or the liquidation of the Company.

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 working to reposition our company around RNA delivery technology and intend to divest or partner 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 partner 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 is designed to allow for oligonucleotide delivery to extrahepatic tissues using systemic or local administration. We announced on that occasion our intention to strategically reposition the Company to focus on the development of RNA delivery technology while in the medium term evaluating opportunities to partner or divest its existing business in neurotology, rhinology and allergology within the next 12-18 months. Our 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 or partnering 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 or partnering 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 or partner 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 or out-licensing proceeds we receive in any sale or partnering transaction 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 or the out-licensing 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 or partner 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 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 further 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

The OligoPhore™ and SemaPhore™ platforms and the AM-401 and AM-411 programs are still in preclinical development. If our development programs are unsuccessful, or we are unable to out-license the platforms or programs, 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 acquisition and development of OligoPhore™, SemaPhore™ and AM-401 and AM-411, which are still in preclinical development. Our ability to generate product revenues from the out-licensing of these RNA delivery platforms and drug product candidates, will depend heavily on successful development, obtaining regulatory approval or clearance and eventual commercialization of these product candidates. The success of AM-401 or AM-411 and our other product candidates will depend on several factors, including the following:

- completing nonclinical studies that demonstrate the efficacy and safety of our product candidates;
- receiving IND or equivalent regulatory clearance from competent regulatory authorities for clinical testing;
- establishing commercial manufacturing capabilities;
- launching commercial sales, marketing and distribution operations;
- acceptance of our RNA delivery platforms and drug product candidates by by potential collaboration partners or licensees;
- competing effectively with other platform technologies or therapeutics; 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 out-license OligoPhore™ / SemaPhore™, AM-401 or AM-411, 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 impacted enrollment of patients into our “TRAVERS” phase 2 trial with AM-125. Candidates for participation in this trial underwent certain types of neurosurgery, which are elective procedures.

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.

Clinical drug and device 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 applicable current good manufacturing practices, (cGMP) for drug products, or quality system regulation (QSR) requirements for devices, 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.

We may need to generate additional clinical data should we decide to seek the approval of Bentrio® for protection against airborne viruses. In addition, we may decide to conduct a Phase 1 clinical for AM-401 or AM-411 or both prior to seeking their out-licensing.

The completion of clinical trials 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.

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 dropouts among clinical trial participants.

Our product development costs will also increase if we experience delays in testing or if we are required to conduct additional trials or other testing 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 or potential licensees of ours may have the exclusive right to commercialize our product candidates or allow competitors to bring products to market before we or our potential licensees do or shorten any periods during which we or our potential licensees have the exclusive right to commercialize our product candidates, which may harm our business and results of operations.

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 or our potential licensees 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.

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 or our potential licensees 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, or of our RNA delivery technology and could significantly harm our business, results of operations and prospects.

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 and medical devices. 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, our current development and commercial focus is limited to Bentrio®, AM-401 and AM-411 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.

We have announced our intention to reposition the Company around RNA delivery technology while exploring strategic options to either divest or partner our non-RNA traditional businesses. In particular, we have announced that we are in active discussions for the partnering of Bentrio® for North America, Europe and other key markets and have been active in the process of selling or partnering our inner ear therapeutics assets.

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 and the ability of potential licensees 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 two other product candidates, AM-401 and AM-411, in preclinical development. We or any potential potential licensee are not permitted to market or promote any of our drug product candidates before we or any potential licensee receive regulatory approval from the FDA, EMA or comparable foreign regulatory authorities, and we or any potential licensee may never receive such regulatory approval for any of our product candidates.

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 or license 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 or our potential licensees 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 U.S. for use in viral infection prevention or treatment, which is necessary before it can be commercialized for such indication in the US.

Bentrio® is a spray product designed 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. On June 24, 2022, we received 510(k) clearance.

Bentrio® was also developed for use in the reduction of the intranasal infectious viral load following inspiration of airborne viruses such as SARS-CoV-2. The FDA did not accept that this proposed intended use could proceed on the medical device pathway. The rationale provided is that it makes a drug-like claim that would require a drug approval. Feedback received from FDA in 2021, prior to the Bentrio® 510(k) clearance, suggested that the regulatory pathway for this intended use and interpretation of mechanism of action would result in the product being regulated as a drug rather than a medical device. That interpretation by FDA is arguable, especially in light of the subsequent 510(k) clearance for allergens. Additional work and engagement with FDA is needed to finalize the device vs. drug regulation pathway and associated nonclinical and clinical evidence requirements. If the device pathway is deemed appropriate, but FDA concludes there is 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® provides benefit and does not present substantial risk to the patient. This standard for granting de novo is different from the comparative 510(k) standard of being "substantially equivalent" to a predicate device that is already cleared. De novo requires an independent demonstration of a reasonable assurance safety and effectiveness, as with a high-risk PMA device, albeit in a PMA-lite, moderate risk sense. Once cleared, a de novo device creates "special controls" and becomes a 510(k) predicate for future devices. This allows subsequent devices to claim the de novo device as a new 510(k) predicate which will be cleared by FDA if the special controls are met. To grant a de novo, FDA typically requires more testing than for a 510(k) but less than for a PMA. 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, grant of a de novo, 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. On February 16, 2023, the Council of the European Union and the European Parliament Commission approved an extension of the MDR transition periods; for Class I medical devices (such as Bentrio®) an extension to May 26, 2028 was approved.

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, Bentrio® 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. We cannot assure you 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. Failure to do so in a timely manner will require us to cease marketing Bentrio® in the EU until such time, if ever, that such registration is obtained.

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 such treatments must not be marketed directly to consumers but must be presented to health care providers only. ANSM, the French National Agency for the Safety of Medicines and Health Products, requested that our indication of use for viral infections such as SARS-CoV-2 be supported by clinical data, which we initially did not have, unlike preclinical data. Therefore, in July 2022 we had to stop marketing Bentrio® for the viral infection indication in the EU and Switzerland and relaunched it in October 2022 solely for the allergic rhinitis indication. In other countries, Bentrio® is cleared for both indications. 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 with AM-125 are favorable, there is risk that they will not be acceptable to regulators or physicians.

To our knowledge, there are currently no drugs with proven efficacy for acute vestibular syndrome. 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 vestibular syndrome, 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.

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 Over-the-Counter, or 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. Indeed, continental Europe has seen a significant rate of inflation during the last twelve months.

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 drug 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® and 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. There can be no assurance that we will be able to develop the resources or outsource these activities in a sufficient or timely manner.

Risks Related to Our Reliance on Third Parties

If we fail to maintain our current strategic relationship with Washington University 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 and AM-411.

A good relationship with WU is important for our business prospects. If our relationship with WU was to deteriorate substantially or WU challenges 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. 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.

In particular, on March 4, 2022, we announced that we had entered into an exclusive licensing and distribution agreement for Bentrio® with 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 made an upfront payment of $1 million (CHF 0.9 million) and may pay to Altamira development and commercial milestones of up to $3 million and up to $19.5 million, respectively. 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 us a staggered royalty on net sales in the Territory at a high-single to low-double-digit percentage.

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 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 and AM-411 product candidates, 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 contract research organizations, or 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 EU 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 terminate, 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, or is not able to increase supply as needed, 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-401 and AM-411 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, it is not assured 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-401, AM-411 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-401 and AM-411. We currently have a relationship with one supplier each, for the supply of the peptide for AM-401 and AM-411, 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 three and five 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, AM-411, 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 2043, for AM-411 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, AM-401 and AM-411 are approved, competitors could file ANDAs for generic versions of AM-125, AM-401 and AM-411, or 505(b)(2) NDAs that reference AM-125, AM-401 and AM-411, respectively. If there are patents listed for AM-125, AM-401 and AM-411 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 and AM-411 drug product candidates 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 AM-411 or any future drug product candidates covered by the license.

In particular, we are required to use commercially reasonable efforts to meet the following development milestones: a) to file an IND application (or regulatory equivalent in foreign jurisdiction) by June 30, 2023, b) to complete a Phase 1 clinical trial 3.5 years after achieving the first milestone, and c) to complete a Phase 2 clinical trial four years after achieving the second milestone. We may elect to extend each of these milestones once by a period of twelve months, and second time by a period of an additional twelve months, by paying WU a nonrefundable fee in the amount of $50,000 for the first extension and $100,000 for the second extension.

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.

In Europe, a new unitary patent system, which takes effect on June 1, 2023, may significantly impact European patents, including those granted before the introduction of the new system. Under the new system, Applicants can, upon grant of a patent, opt for that patent to become a Unitary Patent which will be subject to the jurisdiction of a new Unitary Patent Court (UPC). Patents granted before the implementation of the new system can be opted out of UPC jurisdiction, remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC may be challenged in a single UPC-based revocation proceeding that, if successful, could invalidate the patent in all countries who are signatories to the UPC. Further, because the UPC is a new court system and there is no precedent for the court's laws, there is increased uncertainty regarding the outcome of any patent litigation. We are unable to predict what impact the new patent regime may have on our ability to exclude competitors in the European market. In addition to changes in patent laws, geopolitical dynamics, including Russia's recent incursion into Ukraine, may also impact our ability to obtain and enforce patents in particular jurisdictions. If we are unable to obtain and enforce patents as needed in particular markets, our ability to exclude competitors in those markets may be reduced.

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, Covadonga Pañeda, Chief Operating Officer for our RNA delivery activities, and Marcel Gremaud, our Chief Financial Officer, who constitute the Executive Management Committee. Since January 2023, we have received the contributions of Samuel Wickline, Trasir's founder and our Chief Scientific Adviser for RNA delivery technology on a part-time consulting basis (from June 2021 to December 2022 he served as Chief Scientific Officer).

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, senior scientists or advisors 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 our business strategy, which could have a material adverse effect on our business.

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

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and business development. 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 continue to 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 $43 in April 2022 and as low as $3.95 in December 2022. 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®;
- commencement and enrollment of and delays in clinical trials and positive or negative results of testing and clinical trials by us, strategic partners, or competitors;
- adverse regulatory decisions, including failures to receive regulatory approval for our product candidates;
- delays in executing on our plans to reposition the Company around RNA delivery technology and / or to divest or partner our business in neurotology, rhinology and allergology;
- technological innovations or commercial product introductions by us or competitors;
- changes in government regulations;
- adverse developments concerning our suppliers or manufacturers;
- 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;
- fluctuations in the value of our embedded derivative securities;
- 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, 2020 and 2022, 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 each of May 1, 2019 and October 25, 2022, 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 our common shares because they may be considered penny stocks and thus be subject to the penny stock rules.

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.

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. Additionally, as of the date of this Annual Report we have warrants outstanding, which are exercisable for an aggregate of 99,171 common shares at a weighted average exercise price of $53.45 per share, an equity commitment to sell up to $10.0 million of additional common shares to Lincoln Park Capital Fund, LLC (“LPC”) pursuant to the commitment purchase agreement we entered into on December 5, 2022 with LPC (the “2022 LPC Purchase Agreement”), less an aggregate of $854,475.00 of common shares that have been sold through April 12, 2023 under such 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 $12.9 million of additional common shares (subject to the volume limitations under Instruction I.B.5 of Form F-3). 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, including shares sold and which may be sold under the A.G.P. Sales Agreement. 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 2023 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 2023 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 2023 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, such as the potential for double taxation across jurisdictions.

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.

Management concluded that the Company's internal control over financial reporting was not effective as of December 31, 2022, due to material weaknesses identified in Item 15, "Controls and Procedures," of this Annual Report. The Company did not maintain controls to execute the criteria established in the COSO Framework for the control environment, risk assessment, control activities, information and communication, and monitoring components, which resulted in control deficiencies that constitute material weaknesses, either individually or in the aggregate, within each component of the COSO Framework. This was due to the lack of sufficient resources to execute control activities which contributed to the potential for there to have been material errors in our financial statements in addition to the material misstatement that occurred in our interim reporting for the period ended June 30, 2022.

Management is continuing to evaluate the material weaknesses and is in the process of implementing plans to remediate these material weaknesses. We expect our remediation plan to include the following, amongst others:

- Implementing an effective risk assessment process to identify and analyze risks caused by changes in our business that could impact our system of internal control, including re-designing existing controls as necessary;

- Reporting on a regular basis to the Company's Audit Committee on the effectiveness of internal controls;

- Enhancing the design of control activities to operate at a level of precision to identify all potentially material errors, and training control owners to improve required retention of documentation evidencing their execution of control activities;

- Designing and implementing controls over the generation and communication of relevant quality information to be utilized in the execution of control activities; and

- Investing in training of personnel and hiring additional resources with appropriate expertise to plan and perform more timely and thorough monitoring activities over our internal control over financial reporting.

We cannot assure you that the measures we have taken to date, and are continuing to implement, will be sufficient to remediate the material weaknesses we have identified or avoid potential future material weaknesses. The material weaknesses cannot be considered remediated until applicable controls have operated for a sufficient period and management has concluded, through testing, that these controls are operating effectively. Accordingly, we will continue to monitor and evaluate the effectiveness of our internal control over financial reporting. See Item 15. "Controls and Procedures" for more information.

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 further financial statement restatements and require us to incur the expense of remediation.

If our remedial measures are insufficient to address the material weaknesses we have identified, these will continue to be disclosed as a material weaknesses. Additionally, if there is a change in conditions, or the degree of compliance with policies or procedure deteriorates, internal review of our internal control over financial reporting or the subsequent testing by our independent registered public accounting firm may reveal other deficiencies in our internal controls over financial reporting that are deemed material weaknesses. If this occurs, our consolidated financial statements or disclosures may contain material misstatements and we could be required to restate our financial results. In addition, if we are unable to successfully remediate any of these material weaknesses, we may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting or our independent registered public accounting firm may not in future issue an unqualified opinion, each of which could lead to investors losing confidence in our reported financial information, which could have a material adverse effect on the trading price of our common shares, and we may be unable to maintain compliance with applicable stock exchange listing requirements.

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. All of our executive officers and all but one 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. We are carrying on relevant activities for the purposes of the ES Act and are required to comply with such economic substance requirements. Our compliance with the ES Act could affect the manner in which the Company operates its business or result in additional costs, which could adversely affect its business, financial condition and results of operations.

ITEM 4. INFORMATION ON THE COMPANY

A. History and development of the Company Overview

We are a clinical-and commercial-stage biopharmaceutical company developing therapeutics that address important unmet medical needs. We are currently active in two areas: the development of RNA delivery technology and therapeutics for extrahepatic targets (OligoPhore™ / SemaPhore™ platforms; AM-401 for the treatment of KRAS driven cancer, AM-411 for the treatment of rheumatoid arthritis; preclinical), and nasal sprays for protection against airborne allergens, and where approved, viruses (Bentrio®; commercial) or the treatment of vertigo (AM-125; Phase 2). We have announced our intention to reposition the Company around RNA delivery technology while exploring strategic options to either divest our non-RNA traditional businesses or partner them with one or several other companies. In particular, we have announced that we are in active discussions for the partnering of Bentrio® for North America, Europe and other key markets and have been active in the process of selling our inner ear therapeutics assets.

OligoPhore™ / SemaPhore™ platforms

Through the acquisition of Trasir in June 2021 we entered the field of RNA delivery technology. 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 is designed to allow for systemic or local delivery of RNA payloads with efficient cellular uptake and extensive 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.

AM-401

In July 2021 we announced the selection of KRAS-driven cancer as the first therapeutic indication for our OligoPhore™ oligonucleotide delivery platform. The therapeutic objective for AM-401 is to slow down KRAS driven tumor cell proliferation or to stop it altogether by delivering siRNA specifically inside tumor cells for gene knock down. The siRNA is targeting different KRAS mutations. We aim to advance the AM-401 program through preclinical studies with the objective of filing for an IND in 2024.

AM-411

In July 2022 we announced the initiation of AM-411, our second development project for an RNA therapeutic based on the OligoPhore™ delivery platform. AM-411 seeks to treat rheumatoid arthritis (RA) by targeting siRNA at p65, one of the main transcriptional regulators of the NF-kB pathway and a key checkpoint in RA inflammation. We aim to advance the AM-411 program through preclinical studies with the objective of filing for an IND in 2024.

AM-125

We have been developing AM-125 for the intranasal treatment of acute vestibular syndrome (AVS). 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 included 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 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 June 2022, we announced top-line data from our Phase 2 TRAVERS trial with AM-125 in AVS. The randomized, double-blind, placebo-controlled TRAVERS trial enrolled at more than ten study sites across Europe a total of 124 patients who suffered from acute vertigo following surgery for the removal of a tumor. Patients were randomized to receive either AM-125 at up to 20 mg or a placebo three times daily for four weeks, which was followed by a two-week treatment-free observation period. In addition, all trial participants followed a standardized course of vestibular rehabilitation therapy. Improvement in the “Tandem Romberg” test, which measures how long patients manage to maintain balance with their two feet aligned one after the other while they have their eyes closed, served as the primary efficacy outcome. For reference, the trial also included 16 patients who received ‘open label’ oral betahistine at 16 mg three times daily (the approved dose in most countries worldwide).

The TRAVERS trial demonstrated good tolerability of AM-125. Further, administration of AM-125 resulted in a dose- and time-dependent improvement in balance and signs and symptoms of vestibular dysfunction. At treatment period end, patients treated with AM-125 20 mg on average managed to maintain balance for 12.5 seconds vs. 7.5 seconds for placebo treated patients, which is a statistically significant improvement (p=0.0242; least square means in repeated-measure ANCOVA model, per protocol population). This was corroborated by higher frequency of complete spontaneous nystagmus resolution (34.5 vs. 20.0% of patients).

We have discussed the regulatory requirements for AM-125 during a pre-Investigational New Drug 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 have designed additional trials with AM-125 and in May 2023 submitted an application for an IND to the FDA. As part of our strategic repositioning, we expect to either divest the AM-125 program or out-license it and currently do not intend to continue development of the program on our own.

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, 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.

We have shown that Bentrio® can 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. 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 510(k) substantial equivalence to the marketed comparator with superior efficacy ratings by patients and clinicians, and showed good tolerability.

In May 2022, we announced the results from a clinical trial with Bentrio® in house dust mite (HDM) allergic rhinitis. The trial enrolled a total of 37 patients with a history of perennial allergic rhinitis (“PAR”) caused by HDM exposure. Study participants were randomized under an open label, three-period crossover design to receive either Bentrio® in a single or double dose, or no treatment, prior to controlled allergen exposure in an environmental exposure chamber for three hours. Bentrio® treatment reduced the increase in mean total nasal symptoms score (TNSS) by 1.1 points (-1.87 to -0.28 in the 95% confidence interval; $p<0.01$) vs. no treatment. There was no meaningful difference in outcomes between a single or double puff per nostril. Bentrio® treatment was well tolerated.

In December 2022 we completed enrollment into a randomized controlled clinical trial (the “NASAR” trial) with Bentrio® in seasonal allergic rhinitis (SAR) in Australia. NASAR enrolled 100 SAR patients that were randomized at a 1:1 ratio to either receive Bentrio® or saline spray via self-administration three times per day, or as needed, for two weeks. Saline nasal sprays are currently the most frequently used type of drug-free treatment for SAR. The primary endpoint will be the comparison of the reflective Total Nasal Symptom Score (rTNSS) under treatment with Bentrio® against saline spray. In January 2023, we announced the results of an interim analysis based on data from the first 53 participants in the NASAR trial. The interim analysis showed a decrease of the rTNSS in the Bentrio® group from 6.7 points in the pre-treatment period to 5.1 points over the 14-day treatment period, while the saline spray group showed a decrease from 7.6 to 7.1 points. The difference of 1.55 points in favor of Bentrio® was statistically significant in the ANCOVA model (LSmeans; $p = 0.015$; 95% confidence interval -2.78 to -0.32). The interim analysis further showed good tolerability both for Bentrio® and the comparator.

We believe that AM-301 could help to reduce the risks of exposure from airborne transmission of certain virus particles. 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. In January 2023 we announced top-line data from a clinical trial in acute COVID-19 (“COVAMID”). The trial enrolled a total of 160 subjects in Bulgaria and North Macedonia who were randomized within 3 days from symptom onset at a 2:1:1 ratio to receive for 10 days either Bentrio®, modified (Bentrio® (lacking one mineral component), or no treatment, followed by a 10-day observation phase. The primary efficacy endpoint was the change in PCR cycle threshold (CT). The trial showed a mean increase in the CT value from baseline to Day 11 of 15.3 for the Bentrio® group, 14.1 for the modified Bentrio® group and 13.7 for the untreated control group. The difference in the mean change of CT of the Bentrio® group vs. the untreated and the modified Bentrio® groups to Day 11 failed to reach statistical significance (LSmeans 0.8 and 0.64; $p = 0.319$ and 0.427; 95% CI -0.78 to 2.38 and -0.95 to 2.23, respectively). More Bentrio® and modified-Bentrio® treated patients achieved full resolution of COVID-19 signs and symptoms by Day 11 than untreated patients (93.7 and 92.5 vs. 85.0%) and more of them were uninfected or asymptomatic at that time point (59.5 and 65.0 vs. 45.0%). The treatment was well tolerated. The incidence of adverse events in the Bentrio® group was 2.4% (mild cases only), 9.5% in the modified-Bentrio® group, and 14.0% in the untreated group (including two cases of unwitnessed sudden death after Day 11). We believe that, based on the mode of action of Bentrio®, the product is used most effectively prophylactically.

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, 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. On June 24, 2022 we received 510(k) clearance for Bentrio®.

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.

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 partner the Keyzilen® program.

Sonsuvi®

We also have been developing Sonsuvi® for acute inner ear hearing loss. In a 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 partner 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. He stepped down as CSO, Chief Scientific Officer, by the end of 2022 and has been serving on a part-time consulting basis as Chief Scientific Adviser since January 1, 2023.

Capital expenditure and divestitures

Our actual capital expenditures for the years ended December 31, 2022, 2021 and 2020 amounted to CHF 2.1 million, CHF 6.7 million and CHF 2.3 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 delivery technology. 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 is designed to allow for systemic or local delivery of RNA payloads with efficient cellular uptake and extensive 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 two lead indications.** Based on positive results obtained with Oligophore™ delivering various siRNA payloads in more than ten different murine disease models, we have selected two therapeutic targets as the first indications in which we will seek to demonstrate early clinical proof of concept. With project AM-401 we are targeting KRAS driven cancer such as colorectal cancer or pancreatic cancer, and with project AM-411 we are targeting rheumatoid arthritis. There is a high unmet medical need for both of these indications.

- **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 the platform through collaborations with other biopharmaceutical companies and the out-licensing of technology for specific indications (including projects AM-401 and AM-411). In this way, we intend to become a delivery platform company.

- **Focus activities on RNA delivery technology by divesting or partnering our non-RNA businesses.** As we aim to expand our activities in RNA delivery technology, 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 partnering shall be applied to growing the activities in RNA delivery technology.

Delivering RNA therapeutics to extrahepatic tissues

OligoPhore™ / SemaPhore™ is a versatile platform for delivery of oligonucleotides such as siRNA (small interfering ribonucleic acid) or mRNA (messenger RNA) into target cells. 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. The polyplex readily escapes the leaky vasculature of various pathologies and is taken up avidly by cells that are capable of macropinocytosis 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 and in July 2022 the selection of rheumatoid arthritis as the second therapeutic indication for our OligoPhore™ oligonucleotide delivery platform (AM-401 and AM-411). We aim to advance the AM-401 and AM-411 programs through preclinical studies with the objective of filing for an IND in 2023 and 2024, respectively. 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 (Damase et al., 2021), 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 $4.9 billion in 2021 and is expected to grow to $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 $46.7 billion in 2021 to $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. For 2023, the market size for “over the counter” allergy medicines in the U.S. is estimated by Ibis World to reach $3.9 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 U.S. for cold and cough remedies such as antihistamines, antibiotics, decongestants, expectorants and bronchodilators are expected to exceed $10.8 billion in 2023. According to the U.S. Centers for Disease Control and Prevention (CDC), influenza resulted in 9-41 million illnesses, 140,000-710,000 hospitalizations and 12,000-52,000 deaths annually from 2010-2020. 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 the outbreak began, more than 675 million people have been reported as infected and more than 6.87 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 vestibular syndrome (AVS), which is described as sudden onset of continuous vertigo lasting days to weeks and associated with nausea, head motion intolerance, and unstable balance. 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.

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 ten 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 were almost four million emergency room visits in 2011 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 U.S. population aged 40 years and older suffered from vestibular dysfunction (i.e. failing the “Standing on Foam” test) from 2001-2004.

Also according to the NIDCD, 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 preceding 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.

As reported by Singh & Singh in a 2012 publication in the journal of Otorhinolaryngology Clinics, there are several drugs available for the treatment of vertigo, however 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, to our knowledge, there is currently no FDA or EMA approved drug therapy on the market.

Our Products and Product Candidates

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. As described by Herdeis and colleagues in a 2021 publication in the journal Current Opinion in Structural Biology, 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™ (then known as p5RHHH) 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. Our *poly*KRAS^{mut} siRNA approach allows to target different KRAS mutations and is thus polyvalent. The process of sequence selection and optimization 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.

AM-411 in rheumatoid arthritis

Rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic inflammatory condition causing joint swelling and pain which may also affect other areas, including the skin, eyes, brain, and cardiovascular system. In the US in 2014, approximately 1.3 million adults suffered from RA, as described by Hunter and colleagues in a 2017 issue of Rheumatology International. According to the World Health Organization (WHO), the autoimmune disease affects globally up to 18 million people. A study by Crowson and colleagues which was published in 2012 in the journal Arthritis and Rheumatism showed that RA affects 1 in 28 women and 1 in 59 men during their lifetime. There is no cure for RA; current treatments seek to manage RA with biologic and non-biologic immunosuppressants, corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs). While useful, drug resistance occurs in up to 50% of patients and systemic adverse reactions are frequent, including rash, hair loss, altered liver function, low blood cell counts, nausea, increased infections and neuropathy. New biologics targeting JAK/interleukins have been issued black box warnings by the FDA. According to a market research study by Allied Market Research, the global anti-rheumatics market is expected to grow from $57.9 billion in 2019 to $62.9 billion in 2027, representing the second largest therapeutic area after oncology. Adalimumab, a biologic blocking TNF which is marketed as Humira®, was #1 among RA therapeutics in 2021 and also the world’s largest selling drug outside of Pfizer’s COVID-19 vaccine.

Our solution - AM-411

AM-411 is a polyplex nanoparticle delivering siRNA to inflamed tissues to target the NF-κB signaling pathway, a critical regulator of immune and inflammatory responses. Like AM-401, the drug product is based on our OligoPhore technology which allows for delivery of RNA payloads specifically to inflamed tissues with extensive endosomal release once inside cells, generating a new class of precision medicines with potentially increased local efficacy and reduced systemic side effects. AM-411 comprises an optimized siRNA targeting p65, one of the main transcriptional regulators of the NF-kB pathway and a key checkpoint in RA inflammation that has generated high interest as a target. However, given NF-kB’s ubiquitous functions, the key challenge is to induce contextual, tissue specific effects, which is not possible with classic small molecule or biologic approaches. AM-411 reduces local inflammation without affecting the NF-κB pathway elsewhere and is less likely to generate resistance because it reduces synthesis of p65 rather than blocking the protein.

AM-411’s therapeutic potential in RA has already been demonstrated in a study using a collagen antibody–induced arthritis model in mice. As described by Zhou and colleagues in a 2014 issue of the Journal of Clinical Investigation OligoPhore nanoparticles with siRNA targeting NF-κB (p65) potently suppressed early inflammatory arthritis. The treatment effectively reduced the expression of inflammatory cytokines and cellular influx into the joints, protected against bone erosions and preserved cartilage integrity. Importantly, the treatment did not affect p65 expression in off-target organs or elicit a humoral response after serial injections.

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. The AM-411 program will benefit from extensive synergies with the AM-401 program and vice versa.

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, 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.

We have shown 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. 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.

In May 2022, we announced the results from a clinical trial with Bentrio® in house dust mite (HDM) allergic rhinitis. The trial enrolled a total of 37 patients with a history of perennial allergic rhinitis ("PAR") caused by HDM exposure. Study participants were randomized under an open label, three-period crossover design to receive either Bentrio® in a single or double dose, or no treatment, prior to controlled allergen exposure in an environmental exposure chamber for three hours. Bentrio® treatment reduced the increase in mean total nasal symptoms score (TNSS) by 1.1 points (-1.87 to -0.28 in the 95% confidence interval; $p<0.01$) vs. no treatment. There was no meaningful difference in outcomes between a single or double puff per nostril. Bentrio® treatment was well tolerated.

In December 2022 we completed enrollment into a randomized controlled clinical trial (the "NASAR" trial) with Bentrio® in seasonal allergic rhinitis (SAR) in Australia. NASAR enrolled 100 SAR patients that were randomized at a 1:1 ratio to either receive Bentrio® or saline spray via self-administration three times per day, or as needed, for two weeks. Saline nasal sprays are currently the most frequently used type of drug-free treatment for SAR. The primary endpoint will be the comparison of the reflective Total Nasal Symptom Score (rTNSS) under treatment with Bentrio® against saline spray. In January 2023, we announced the results of an interim analysis based on data from the first 53 participants in the NASAR trial. The interim analysis showed a decrease of the rTNSS in the Bentrio® group from 6.7 points in the pre-treatment period to 5.1 points over the 14-day treatment period, while the saline spray group showed a decrease from 7.6 to 7.1 points. The difference of 1.55 points in favor of Bentrio® was statistically significant in the ANCOVA model (LSmeans; $p = 0.015$; 95% confidence interval -2.78 to -0.32). The interim analysis further showed good tolerability both for Bentrio® and the comparator.

We believe that AM-301 could help to reduce the risks of exposure from airborne transmission of certain virus particles. 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.

In January 2023 we announced top-line data from a clinical trial in acute COVID-19 ("COVAMID"). The trial enrolled a total of 160 subjects in Bulgaria and North Macedonia who were randomized within 3 days from symptom onset at a 2:1:1 ratio to receive for 10 days either Bentrio®, modified (Bentrio® (lacking one mineral component), or no treatment, followed by a 10-day observation phase. The primary efficacy endpoint was the change in PCR cycle threshold (CT). The trial showed a mean increase in the CT value from baseline to Day 11 of 15.3 for the Bentrio® group, 14.1 for the modified Bentrio® group and 13.7 for the untreated control group. The difference in the mean change of CT of the Bentrio® group vs. the untreated and the modified Bentrio® groups to Day 11 failed to reach statistical significance (LSmeans 0.8 and 0.64; $p = 0.319$ and 0.427; 95% CI -0.78 to 2.38 and -0.95 to 2.23, respectively). More Bentrio® and modified-Bentrio® treated patients achieved full resolution of COVID-19 signs and symptoms by Day 11 than untreated patients (93.7 and 92.5 vs. 85.0%) and more of them were uninfected or asymptomatic at that time point (59.5 and 65.0 vs. 45.0%). The treatment was well tolerated. The incidence of adverse events in the Bentrio® group was 2.4% (mild cases only), 9.5% in the modified-Bentrio® group, and 14.0% in the untreated group (including two cases of unwitnessed sudden death after Day 11). We believe that, based on the mode of action of Bentrio®, the product is used most effectively prophylactically.

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 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. On June 24, 2022 we received 510(k) clearance for Bentrio®. In order to obtain regulatory clearance for Bentrio® in viral infection in those countries which require supportive clinical data (which includes the US and the EU, among others), additional clinical research will have to be conducted. We currently have no plans to conduct such research on our own.

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 Therapeutics, pursuant to which we have purchased various assets related to betahistine dihydrochloride in a spray formulation, which we have been 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 such as the Tandem Romberg, standing on foam or single-leg stance tests for static conditions or the tandem gait, timed "up and go" or ten meter walking tests for dynamic conditions.

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 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.

On June 13, 2022, we announced positive top-line data from our Phase 2 TRAVERS trial with AM-125 (intranasal betahistine) in acute vertigo (acute vestibular syndrome, AVS). The randomized, double-blind, placebo-controlled TRAVERS trial enrolled at more than ten study sites across Europe a total of 124 patients who suffered from acute vertigo following surgery for the removal of a tumor. Patients were randomized to receive either AM-125 at up to 20 mg or a placebo three times daily for four weeks, which was followed by a two-week treatment-free observation period. In addition, all trial participants followed a standardized course of vestibular rehabilitation therapy. Improvement in the "Tandem Romberg" test, which measures how long patients manage to maintain balance with their two feet aligned one after the other while they have their eyes closed, served as the primary efficacy outcome. For reference, the trial also included 16 patients who received 'open label' oral betahistine at 16 mg three times daily (the approved dose in most countries worldwide).

The TRAVERS trial demonstrated good tolerability of AM-125. Further, administration of AM-125 resulted in a dose- and time-dependent improvement in balance and signs and symptoms of vestibular dysfunction. At treatment period end, patients treated with AM-125 20 mg on average managed to maintain balance for 12.5 seconds vs. 7.5 seconds for placebo treated patients, which is a statistically significant improvement (p=0.0242; least square means in repeated-measure ANCOVA model, per protocol population). This was corroborated by higher frequency of complete spontaneous nystagmus resolution (34.5 vs. 20.0% of patients).

We have discussed the regulatory requirements for AM-125 during a pre-Investigational New Drug 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 have been preparing a Phase 2 clinical study with AM-125 in benign paroxysmal positional vertigo, for which we submitted an IND to the FDA in May 2023. As we aim to focus on the RNA delivery business, we do not intend to fund any further clinical trial with AM-125 on our own, but rather seek to out-license or divest the program to a partner or acquirer. We believe that, if approved, AM-125 could become the first betahistine product for the treatment of AVS in the United States.

Development of AM-201

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.

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. According to the website military.com, over 167,000 veterans were diagnosed with tinnitus in 2021 and over 2.5 million veterans are currently receiving disability benefits for it.

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 good tolerability 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 partner 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 good tolerability. 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 partner 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, AM-411 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, rheumatoid arthritis, 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.

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.

KRAS driven cancers

There are several companies marketing or developing treatments for KRAS driven cancers. Amgen and Mirati Therapeutics obtained an accelerated approval by the FDA for the KRAS G12C small molecule inhibitors sotorasib and adagrasib 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 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$^{\text{Multi}}$ (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.

Rheumatoid arthritis

The market for RA therapeutics is highly competitive and currently dominated by several large pharma companies. They are marketing primarily biologics targeting TNF-α, e.g. adalimumab (Abbvie), infliximab (Johnson & Johnson), or etanercept (Amgen), or other targets such as B cells (rituximab, Roche), T cells, (abatacept, BMS), or IL-6 (tocilizumab, Genentech). As the patent and other market access protection has lapsed for several of these biologics, biosimilars have been developed and introduced to the market by competitors. A biosimilar is a biologic that is highly similar to and has no clinically meaningful differences from an existing approved biologic. Further, large companies are marketing various small molecule JAK inhibitors such as upadacitinib (AbbVie), tofacitinib (Pfizer) or baricitinib (Lilly). In addition, there are various older drugs on the market, such as glucocorticoids, non-steroidal anti-inflammatory drugs (NSAIDs) or disease modifying antirheumatic drugs (DMARDs), including methotrexate, hydroxychloroquine and sulfasalazine.

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 Haleon, 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:

- Otolith Labs is developing a noninvasive vestibular system masking device for treatment of vestibulogenic vertigo. The headband device applies localized mechanical stimulation to the vestibular system through calibrated vibrations. It is primarily intended for use by chronic vertigo patients. The company is planning to conduct a clinical trial and obtain FDA clearance.

- 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; however, the status of such trial is unclear.

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.

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.

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 candidate that is 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. In July 2022 Sound Pharma announced the enrollment of the first patient into a Phase 3 trial in hearing loss and tinnitus in Meniere’s Disease patients.

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, 2022, we owned ten 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 four of our issued U.S. patents along with their foreign counterparts, pursuant to the terms of our co-ownership and exploitation agreement with INSERM.

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 U.S. patent filings into a non-provisional U.S. patent application relating to the formulation and use of Bentrio®. The pending patent application’s claims are directed towards aqueous compositions comprising a mucoadhesive polymer and clay particles. U.S. patent prosecution is ongoing. In addition, we filed an international Patent Cooperation Treaty (PCT) patent 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 and AM-411

We are the exclusive licensee under our agreement with Washington University 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, AM-411 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. In February 2023 we filed a provisional patent application with the USPTO describing novel nanoparticle compositions based on OligoPhore™ or derivatives thereof in combination with siRNA sequences designed to silence different types rather than one specific type of mutated KRAS (*poly*KRAS^{mut}). If granted, the new patent would be expected to expire in 2043.

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.

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 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 (WU), 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.

In particular, we are required to use commercially reasonable efforts to meet the following development milestones: a) to file an IND (or regulatory equivalent in foreign jurisdiction) June 30, 2023, b) to complete a Phase 1 clinical trial 3.5 years after achieving the first milestone, and c) to complete a Phase 2 clinical trial four years after achieving the second milestone. We may elect to extend each of these milestones once by a period of 12 months, and second time by a period of an additional 12 months, by paying WU a nonrefundable fee in the amount of $50,000 for the first extension and $100,000 for the second extension.

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. In any case, we do not view the agreement with Xigen as material to the Company and its operations.

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, AM-411 and any other drug product candidate. 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 rely primarily on distributors. In addition, we have already concluded distribution and marketing agreements with companies such as Wellesta, Nuance and Avernus for Asian and Middle Eastern countries and continue to seek further commercial partners, in particular for Europe and North America. 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 Bentrio® by consumers is unlikely to be eligible for reimbursement by health insurance plans and will therefore have to be purchased out of their own pocket. We expect the lack of reimbursement coverage to reduce the pool of potential buyers.

For our activities in RNA delivery technology, we are not seeking to commercialize any drug products on our own but rather licensing out the technology to partners in the biopharmaceutical industry.

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. The current goal is 10 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 PMA approval, after submitting a PMA. Alternatively, the device may be cleared through the de novo classification process by the FDA. Bentrio® has been considered a Class II device by FDA and cleared under the 510(k) pathway for the product'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.

Bentrio® was also developed for use in the reduction of the intranasal infectious viral load following inspiration of airborne viruses such as SARS-CoV-2. The FDA did not accept that this proposed intended use could proceed on the medical device pathway. The rationale provided is that it makes a drug-like claim that would require a drug approval. Feedback received from FDA in 2021, prior to the Bentrio® 510(k) clearance, suggested that the regulatory pathway for this intended use and interpretation of mechanism of action would result in the product being regulated as a drug rather than a medical device. That interpretation by FDA is arguable, especially in light of the subsequent 510(k) clearance for allergens. For future indications beyond the currently cleared Bentrio® intended use, additional work and engagement with FDA is needed to finalize the device vs drug regulation pathway and associated nonclinical and clinical evidence requirements. If the device pathway is deemed appropriate, we may have to submit a de novo request to the FDA since there may be no valid 510(k) predicate device available for this intended use. 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) 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 repealed and 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 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. On February 16, 2023, the Council of the European Union and the European Parliament approved an extension of the MDR transition periods; for Class I medical devices (such as Bentrio®) an extension to May 26, 2028 was approved. 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 and device 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 and QSR. 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 or device 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 or device;
- providing the FDA with updated safety and efficacy information;
- reporting on drug 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, 2022, 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 clinical-and commercial-stage biopharmaceutical company developing therapeutics that address important unmet medical needs. We are currently active in two areas: the development of RNA delivery technology and therapeutics for extrahepatic therapeutic targets (OligoPhore™ / SemaPhore™ platforms; AM-401 for the treatment of KRAS driven cancer, AM-411 for the treatment of rheumatoid arthritis; preclinical), and nasal sprays for protection against airborne allergens, and where approved, viruses (Bentrio®; commercial) or the treatment of vertigo (AM-125; Phase 2). We have announced our intention to reposition the Company around RNA delivery technology while exploring strategic options to either divest or partner our non-RNA traditional businesses.

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, 2022, we had cash and cash equivalents of CHF 15 thousand and an accumulated deficit of CHF 201.4 million. Based on our current plans, we expect to continue incurring losses as we continue our pre-clinical and clinical and development programs and build business development and alliance management activities to support the licensing out or partnering of our RNA delivery technology. We do not expect to generate licensing or 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®, and / or from out-licensing or other partnering transactions related to AM-125 or our OligoPhore™ or SemaPhore™ platforms. This situation raises substantial doubt about the Company’s ability to continue as a going concern.

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 AVS. The Otifex transaction closed in July 2017.

Financial Operations Overview

We expect our regular total additional funding requirements for operations and financial obligations in 2023 to be in the range of CHF 15 to 17 million.

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-401 for KRAS Driven Cancer. Through the acquisition of Trasir we entered the field of RNA delivery technology. In July 2021 we announced the selection of KRAS-driven cancer as the first therapeutic indication for our OligoPhore™ oligonucleotide delivery platform. The therapeutic objective for AM-401 is to slow down KRAS driven tumor cell proliferation or to stop it altogether by delivering siRNA specifically inside tumor cells for gene knock down. The siRNA is targeting different KRAS mutations. We aim to advance the AM-401 program through preclinical studies with the objective of filing for an IND in 2024. In this context, we initiated various development work relating to the peptide and siRNA components of AM-401.

- AM-411 for Rheumatoid Arthritis. In July 2022 we announced the initiation of AM-411, our second development project for an RNA therapeutic based on the OligoPhore™ delivery platform. AM-411 seeks to treat rheumatoid arthritis (RA) by targeting siRNA at p65, one of the main transcriptional regulators of the NF-kB pathway and a key checkpoint in RA inflammation. We aim to advance the AM-411 program through preclinical studies with the objective of filing for an IND in 2024.

- AM-125 for Vertigo. We have been developing AM-125 as a reformulation of betahistine for intranasal delivery. In 2019 we initiated the "TRAVERS" Phase 2 trial to evaluate the safety and efficacy of AM-125 in 124 patients suffering from acute vestibular syndrome following surgery. In June 2022 we reported top-line results from the trial showing good tolerability a dose- and time-dependent improvement in balance and signs and symptoms of vestibular dysfunction. In parallel to the clinical development, 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. We file an IND application in May 2023 which, if granted, would allow for the conduct of clinical trials in the U.S. In the context of our strategic transition to become a company focused on RNA delivery technology, we intend to out-license or sell the AM-125 program. We have impaired AM-125 as per year end 2022, which is recorded in research and development expenses.

- Bentrio® for Allergy and Viral Infection: 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 first in vitro in a series of experiments using reconstituted human nasal epithelia. Our clinical development in allergic rhinitis comprised three trials: one study each with controlled exposure to grass pollen for 4 hours and to house dust mites for 3 hours (both with 36 patients) and one study with environmental exposure to seasonal allergens for two weeks (100 patients). The two challenge studies were completed in 2021 and 2022, whereas the environmental study will complete in 2023. The studies showed good tolerability and protective effects of AM-301 for 3-4 hours. In addition, we assessed the nasal residence time of the formulation in a small study with healthy volunteers. In viral infection, we conducted a trial in patients suffering from acute COVID-19 in 2022; top-line results were presented as inconclusive in early 2023.

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, 2022 and 2021, we spent CHF 0.6 million and CHF 0.2 million on research and development expenses related to our RNA programs with AM-401 and AM-411. For the years ended December 31, 2022, 2021 and 2020, we spent CHF 2.1 million, CHF 2.8 million and CHF 2.7 million, respectively, on research and development expenses related to our intranasal betahistine program (before capitalization of expenses related to AM-125). For the years ended December 31, 2022, 2021 and 2020, we spent CHF 3.9 million, CHF 4.2 million and CHF 0.8 million on research and development expenses related to AM-301. In addition, we incurred low levels of research and development expenses related to our Keyzilen® and Sonsuvi® programs, which were mainly for maintenance and regulatory work.

In 2023, the level of research and development expenses related to our AM-401 and AM-411 programs is expected to increase as we will conduct more in vitro studies, initiate in vivo studies and expand formulation and process development work. On the other hand, the level of research and development expenses related to AM-301 and AM-125 is expected to decrease in 2023 as development projects will complete, and as we aim to divest or partner these legacy assets. 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; 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-401, AM-411 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 submission of the IND filings or if we experience significant delays in obtaining study slots with contract research organizations or sourcing appropriate animals for such studies, we could be required to expend significant additional financial resources and time on the completion of the IND enabling studies.

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 2023.

Sales and marketing expense

Our sales and marketing expense is related to Bentrio®, our sole commercial stage product, and consists principally of:

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

Sales and marketing expense decreased in 2022 over 2021 as there were fewer launch activities for sales in Europe and due to a temporary recall of Bentrio® in Europe as we had to limit the product’s labelling to the allergy indication only.

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 2022 and 2021, our interest expense consisted principally of interest due on the two convertible loans 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 500,000 (pre-merger) warrants in connection with a registered offering of 500,000 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 $ 24.00 (pre-merger). Additionally, the underwriter was granted a 30-day option to purchase up to 75,000 (pre-merger) additional common shares and/or 75,000 (pre-merger) additional warrants. On February 15, 2017, the underwriter partially exercised its option for 67,500 (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 1,986 common shares at an exercise price of $4,800.00 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 3,125 common shares, each warrant entitling its holder to purchase 0.6 common share at an exercise price of $2,000.00 per common share. As of December 31, 2021, the warrants were exercisable for an aggregate of 1,875 of our common shares (assuming we decide to round up fractional common shares to the next whole common share), at an exercise price of $2,000.00 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 15,705 common shares, and Series B warrants entitling its holder to purchase 0.25 of a common share for an aggregate of 11,218 common shares in connection with the July 2018 Registered Offering of 44,872 common shares. The original exercise price was CHF 156.00 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, 7,261 Series A warrants were exercised for an aggregate amount of CHF 1,132,762 and 7,161 Series B warrants were exercised for an aggregate amount of CHF 1,117,125.

As of December 31, 2019, 7,161 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 1,727 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 amounted to CHF 1,137 in the year ended December 31, 2022, compared to zero in the previous year.

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, 2022 and 2021

	Year Ended December 31,		
	2022	2021 1)	Change
	(in thousands of CHF)		%
Revenue	306	64	378%
Cost of goods sold	(1,444)	(2,241)	(36)%
Gross profit	**(1,138)**	**(2,177)**	**(48)%**
Other income	709	214	231%
Research and development	(19,678)	(8,361)	135%
Sales and marketing	(2,381)	(1,498)	59%
General and administrative	(3,645)	(4,947)	(26)%
Operating loss	**(26,133)**	**(16,769)**	**56%**
Interest income	1	3	(67)%
Interest expense	(912)	(190)	380%
Foreign currency exchange gain / (loss), net	56	329	(83)%
Revaluation gain / (loss) from derivative financial instruments	451	(411)	(210)%
Transaction costs	(1)	-	n/a
Loss before tax	**(26,538)**	**(17,038)**	**56%**
Income tax gain/(loss)	(10)	(21)	(148)%
Net loss attributable to owners of the Company	**(26,528)**	**(17,059)**	**56%**
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	441	265	66%
Items that are or may be reclassified to profit or loss			
Foreign currency translation differences, net of taxes of CHF 0	61	1	6,000%
Other comprehensive loss	502	266	89%
Total comprehensive loss attributable to owners of the Company	**(26,026)**	**(16,793)**	**55%**

1) Other income and research development expenses for 2021 were revised from the previously reported financial statements due to an immaterial error with regard to advance payments for research and development costs and related tax credits for the annual period. The revision resulted in a lower operating loss, loss before tax, net loss attributable to owners of the Company and Total comprehensive loss attributable to owners of the Company than previously reported for 2021. Please refer to note 33 for further information.

Revenue and cost of goods sold

Revenue includes product sales of Bentrio®. Cost of goods sold of comprised the relevant manufacturing costs for Bentrio® incurred through our contract manufacturer, expenses for storage and shipments, as well as inventory write-offs. The latter concerned products in inventory with only short remaining shelf life and amounted to CHF 0.9 million in 2022 and CHF 2.0 million in 2021. The amount of the write down was expensed to the income statement under Cost of Sales.

In the Unaudited Condensed Consolidated Interim Financial Statements of the Company as of June 30, 2022 and for the six months ended June 30, 2022 furnished with the Securities and Exchange Commission on November 30, 2022, an upfront payment of $1 million (CHF 0.9 million) related to the exclusive licensing and distribution agreement with Nuance for Bentrio® was incorrectly recorded as revenue. In the financial statements as of December 31, 2022, the upfront payment is recorded as deferred income; please refer to “Adjustment of June 30, 2022 Revenue” below.

Other income

Other income increased 231% from CHF 0.2 million in 2021 to CHF 0.7 million in 2022 primarily due to higher development tax credits related to clinical projects.

Research and development expense

	Year Ended December 31,		
	2022	2021	Change
	(in thousands of CHF)		%
Research and development expense			
Clinical projects	(3,238)	(2,380)	36%
Pre-clinical projects	(509)	(587)	(13)%
Product and process development	(473)	(1,100)	(57)%
Employee benefits	(2,585)	(1,897)	36%
Impairment intangible assets	(12,397)	(1,530)	710%
Other research and development expenses	(476)	(867)	(45)%
Total	**(19,678)**	**(8,361)**	**(135)%**

Research and development expense increased by 135% from CHF 8.4 million in 2021 to CHF 19.7 million in 2022 mainly due to the non-cash write-off (impairment) of previously capitalized internal development costs related to the AM-125 project. In general, 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 2021 and 2022 are mainly due to the following factors:

- *Capitalization of internal costs for AM-125*. In the year ended December 31, 2022, we capitalized direct costs related to our AM-125 program for a total amount of CHF 2.0 million, compared to CHF 2.8 million in the year ended December 31, 2021. As described below the capitalized internal development costs were subsequently impaired on December 31, 2022.

- *Clinical projects.* In the year ended December 31, 2022, clinical expenses increased by 36% over the previous year. We incurred lower service and milestone costs for the AM-125 program, reflecting the completion of the TRAVERS Phase 2 clinical trial in summer 2022. Spending for the clinical investigation of AM-301 increased, reflecting the conduct of several studies in allergic rhinitis (house dust mites, nasal residence time, seasonal allergic rhinitis) and in acute COVID-19.

- *Pre-clinical projects*. In the year ended December 31, 2022, pre-clinical expenses decreased by 13% principally due lower expenditures for the AM-301 program, which was partially compensated by increased expenditures for the AM-401 and AM-411 programs.

- *Product and process development*. In the year ended December 31, 2022, expenses decreased by 57% mainly due to lower expenditures on the AM-301 program, which was partially compensated by increased expenditures for the AM-401 and AM-411 programs.

- *Employee benefits*. Employee benefit costs rose in 2022 by 36% mainly due to higher headcount.

- *Impairment of intangible assets*. In accordance with the impairment test performed under IFRS, all intangible assets related to the AM-125 project were written off. In 2021 the intangible assets related to the projects AM-101, AM-111 and AM-201 were impaired.

- *Other research and development expenses*. Other research and development expenses decreased by 45% in the year ended December 31, 2022 to CHF 0.5 million.

Sales and marketing expense

	Year Ended December 31,		
	2022	2021	Change
	(in thousands of CHF)		%
Sales and marketing expense			
Marketing and sales expenses	(2,132)	(1,133)	88%
Employee benefits and expenses	(250)	(204)	22%
Product samples	-	(161)	(100)%
Total	**(2,381)**	**(1,498)**	59%

Sales and marketing expense increased by 59% in the year ended December 31, 2022 to CHF 2.4 million primarily due to increased marketing and sales activities.

General and administrative expense

	Year Ended December 31,		
	2022	2021	Change
	(in thousands of CHF)		%
General and administrative expense			
Employee benefits	(735)	(1,555)	(50)%
Business development	(16)	(967)	(98)%
Travel expenses	(96)	(76)	25%
Administration expenses	(2,669)	(2,246)	20%
Lease expenses	(6)	(52)	(88)%
Depreciation	(119)	(30)	297%
Capital tax expenses	(4)	(21)	(81)%
Total	**(3,645)**	**(4,947)**	**(26)%**

General and administrative expenses decreased by 26% from CHF 4.9 million in 2021 to CHF 3.7 million in the year ended December 31, 2022. The decrease was primarily related to lower employee benefits and business development activities related to Bentrio®, which was partly offset by higher general administrative expenses. Depreciation expenses of CHF 0.1 million relate to the leasing of office space in Basel, Switzerland.

Interest income

Interest income was minimal in both 2022 and 2021.

Interest expense

Interest expense in the year ended December 31, 2022 increased 380% to CHF 0.9 million compared to the year ended December 31, 2021 primarily due to the accrued interest on the CHF 5 million convertible loan granted by FiveT in February 2022.

Foreign currency exchange gain/(loss), net

In 2022, we recorded a foreign currency exchange gain of CHF 0.1 million compared to a loss of CHF 0.3 million in 2021.

Revaluation gain/(loss) from derivative financial instruments

Fair value measurement of derivatives embedded in the 2022 FiveT convertible loan resulted in a gain of CHF 0.5 million in 2022 compared with a loss of CHF 0.4 million in 2021 related to the 2020 FiveT convertible loan, which was converted in 2021.

On February 21, 2017, we issued 500,000 (pre-merger) warrants, each warrant entitling its holder to purchase 0.70 of a common share at an exercise price of $24.00. Additionally, the underwriter was granted a 30-day option to purchase up to 75,000 (pre-merger) additional common shares and/or 75,000 (pre-merger) additional warrants. On February 15, 2017, the underwriter partially exercised its option for 67,500 (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 1,986 common shares at an exercise price of $4,800.00 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. 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). The warrants issued in the February 2017 public offering expired on February 22, 2022, without any warrants having been exercised.

On January 30, 2018 we issued warrants in connection with a direct offering of 3,125 common shares, each warrant entitling its holder to purchase 0.6 common share at an exercise price of $2,000.00 per common share. As of December 31, 2022, the fair value of the warrants amounted to CHF 0. The revaluation gain of the derivative for the twelve months ended December 31, 2022 amounted to CHF 1,233, compared to 2021 where there was a revaluation gain of CHF 5,085. Since its initial recognition on January 30, 2018, the fair value of the warrants decreased by CHF 2,483,747 resulting in a gain in the corresponding amount (fair value as of January 30, 2018: CHF 2,483,747).

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 66% from CHF 0.3 million in 2021 to CHF 0.4 million in 2022. The gain in 2022 is primarily due to a higher discount rate which was partly compensated by a negative return on plan assets.

Foreign currency translation differences

Foreign currency translation differences increased to CHF 0.1 million in 2022 from a negligible amount in 2021.

Adjustment of June 30, 2022 Revenue

In the Unaudited Condensed Consolidated Interim Financial Statements of the Company as of June 30, 2022 and for the six months ended June 30, 2022, furnished with the Securities and Exchange Commission on November 30, 2022, an upfront payment of $1 million (CHF 0.9 million) related to the exclusive licensing and distribution agreement with Nuance for Bentrio® was incorrectly recorded as revenue. In the financial statements as of December 31, 2022, the upfront payment is recorded as deferred income. The table below reflects the impact of the adjustment on key income statement and balance sheet line items. We will reflect these adjustments in the comparatives included in the June 30, 2023 financial statements, and we will reflect the adjustments in restated financial statements as of June 30, 2022 and for the six months ended June 30, 2022 to be filed with a Form 6-K/A following the issuance of this Form 20-F.

Six months ended June 30, 2022

Adjusted consolidated Balance Sheet

	As of June 30, 2022		
	As reported	**Adjustment**	**Adjusted**
Deferred income	-	932,200	932,200
Total non-current liabilities	**1,014,188**	**932,200**	**1,946,388**
Total liabilities	**10,804,712**	**932,200**	**11,736,912**
Accumulated deficit	(182,602,921)	(932,200)	(183,535,121)
Total shareholders' equity attributable to owners of the company	**7,675,164**	**(932,200)**	**6,742,964**

Adjusted consolidated Statement of Profit or Loss and Other Comprehensive Loss

	Half-Year ended June 30, 2022		
	As reported	**Adjustment**	**Adjusted**
Revenue	1,222,998	(932,200)	290,798
Gross profit	**30,766**	**(932,200)**	**(901,434)**
Operating loss	**(7,483,561)**	**(932,200)**	**(8,415,761)**
Loss before tax	**(7,352,403)**	**(932,200)**	**(8,284,603)**
Net loss attributable of owners of the Company	**(7,306,318)**	**(932,200)**	**(8,238,518)**
Total comprehensive loss attributable to owners of the Company	**(7,160,269)**	**(932,200)**	**(8,092,469)**
Basic and diluted loss per share	**(9.43)**	**(1.20)**	**(10.63)**

Comparison of the years ended December 31, 2021 and 2020

	Year Ended December 31,		
	2021 [1)]	**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	214	174	23%
Research and development	(8,361)	(2,863)	192%
Sales and marketing	(1,498)	-	n/a
General and administrative	(4,947)	(2,594)	91%
Operating loss	**(16,769)**	**(5,283)**	**217%**
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	**(17,038)**	**(8,221)**	**107%**
Income tax gain/(loss)	(21)	21	(205)%
Net loss attributable to owners of the Company	**(17,059)**	**(8,200)**	**108%**
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	**(16,793)**	**(8,137)**	**106%**

1) Other income and research development expenses for 2021 were revised from the previously reported financial statements due to an immaterial error with regard to advance payments for research and development costs and related tax credits for the annual period. The revision resulted in a lower operating loss, loss before tax, net loss attributable to owners of the Company and Total comprehensive loss attributable to owners of the Company than previously report. Please refer to note 33 for further information.

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 23% from CHF 0.2 million in 2020 to CHF 0.2 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	(2,380)	(477)	399%
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	**(8,361)**	**(2,863)**	**192%**

Research and development expense increased by 192% from CHF 2.9 million in 2020 to CHF 8.4 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 delivery technology. 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)	-	n/a
Employee benefits and expenses	(204)	-	n/a
Product samples	(161)	-	n/a
Total	**(1,498)**	-	n/a

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 500,000 (pre-merger) warrants, each warrant entitling its holder to purchase 0.70 of a common share at an exercise price of $24.00. Additionally, the underwriter was granted a 30-day option to purchase up to 75,000 (pre-merger) additional common shares and/or 75,000 (pre-merger) additional warrants. On February 15, 2017, the underwriter partially exercised its option for 67,500 (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 1,986 common shares at an exercise price of $4,800.00 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. 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). The warrants issued in the February 2017 public offering expired on February 22, 2022, without any warrants having been exercised. As a result, no further revaluation gain or loss was recognized for the year ended December 31, 2022.

On January 30, 2018 we issued warrants in connection with a direct offering of 3,125 common shares, each warrant entitling its holder to purchase 0.6 common share at an exercise price of $2,000.00 per common share. As of December 31, 2020, the warrants were exercisable for an aggregate of 1,875 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 0. The revaluation gain of the derivative for the twelve months ended December 31, 2022 amounted to CHF 1,233, compared to 2021 where there was a revaluation gain of CHF 5,085. Since its initial recognition on January 30, 2018, the fair value of the warrants decreased by CHF 2,483,747 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 15,705 common shares, and Series B warrants entitling its holder to purchase 0.25 of a common share for an aggregate of 11,218 common shares in connection with the July 2018 Registered Offering of 44,872 common shares. The original exercise price was CHF 156.00 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 1,727 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.

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, 2022 and 2021

The table below summarizes our consolidated statement of cash flows for the years ended December 31, 2022 and 2021:

	Year Ended December 31,	
	2022	**2021**
	(in thousands of CHF)	
Net cash used in operating activities	(8,683)	(13,673)
Net cash used in investing activities	(2,142)	(3,505)
Net cash from financing activities	9,832	6,614
Net effect of currency translation on cash	24	289
Cash and cash equivalents at the beginning of the period	984	11,259
Cash and cash equivalents at the end of the period	**15**	**984**

Net cash used in operating activities decreased from CHF 13.7 million in 2021 to CHF 8.7 million in 2022 as spending on research and development and administration decreased and net working capital was lower, which was only partially compensated by higher spending on marketing and sales.

Cash used in investing activities decreased from CHF 3.5 million in 2021 to CHF 2.1 million in 2022. The decrease is primarily due to lower investments in intangible assets related to AM-125; in addition, the 2021 amount comprised the payment of the cash component of the Trasir acquisition price.

The cash inflow from financing activities increased from CHF 6.6 million in 2021 to CHF 9.8 million in 2022 as the Company obtained in February 2022 a convertible loan from FiveT in the amount of CHF 5.0 million, obtained further loans from several investors in the amount of CHF 1.05 million, and raised capital through the ATM program and equity line in the amount of CHF 3.9 million net of transaction costs.

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.

Cash and funding sources

The table below summarizes our sources of financing for the years ended December 31, 2022, 2021 and 2020.

	Equity Capital and Preference Shares	**Loans**	**Total**
		(in thousands of CHF)	
2022	3,927	6,039	9,966
2021	6,686	—	6,686
2020	15,438	1,550	16,988
Total	26,051	7,589	33,640

On December 28, 2022, the Company entered into two separate loan agreements with two private investors ("Private Lenders"), pursuant to which Private Lenders have agreed to loan to the Company an aggregate of CHF 250,000 and CHF 100,000, respectively, which loans bear interest at the rate of 5% per annum and mature as of May 30, 2023. The Company agreed to grant to the Private Lenders warrants to purchase an aggregate 33,700 and 13,480 common shares, respectively. The warrants are exercisable at an exercise price of CHF 4.4512 per share for up to five years from the date of issuance.

On December 5, 2022, we entered into a purchase agreement with Lincoln Park Capital Fund, LLC (the "2022 Commitment Purchase Agreement"). Pursuant to the purchase agreement, LPC agreed to subscribe for up to $10.0 million of our common shares over the 24-month term of the purchase agreement. As consideration for LPC's irrevocable commitment to purchase common shares upon the terms of and subject to satisfaction of the conditions set forth in the 2022 Commitment Purchase Agreement, the Company agreed to issue 50,000 common shares immediately to LPC as commitment shares. The 2022 Commitment Purchase Agreement effectively replaced the 2020 Commitment Purchase Agreement. Under the 2020 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 325,000 common shares for aggregate proceeds of $4.0 million to LPC under the 2020 Commitment Purchase Agreement. 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 29,375 common shares for aggregate proceeds of $1.8 million to LPC under the 2018 Commitment Purchase Agreement.

Under the 2022 Commitment Purchase Agreement, we have the right, from time to time at our sole discretion over the 24-month period from December 27, 2022 to require LPC to subscribe for up to 15,000 of our common shares on the applicable purchase date (a "Regular Purchase"), which maximum number of shares may be increased to certain higher amounts up to a maximum of 30,000 common shares, if the market price of our common shares at the time of the Regular Purchase equals or exceeds $10.00 (such share and dollar amounts subject to proportionate adjustments for share splits, reverse share splits, recapitalizations and other similar transactions as set forth in the Purchase Agreement), provided that LPC's purchase obligation under any single Regular Purchase shall not exceed $1,500,000. The purchase price of common shares we may elect to sell to LPC under the 2022 Commitment Purchase Agreement in a Regular Purchase, if any, will be based on prevailing market prices of our common shares immediately preceding the time of sale as set forth in the 2022 Commitment Purchase Agreement. In addition to Regular Purchases, the Company may also direct Lincoln Park to purchase other amounts of our common shares in "accelerated purchases" and in "additional accelerated purchases" under the terms set forth in the 2022 Commitment Purchase Agreement.

LPC has no right to require us to sell any common shares to LPC, but LPC is obligated to make purchases as the Company directs, subject to certain conditions. There is no maximum on the price per share that LPC must pay for our common shares that we may elect to sell to LPC pursuant to the 2022 Commitment Purchase Agreement. In all instances, the Company may not sell common shares to LPC under the 2022 Commitment Purchase Agreement to the extent that the sale of shares would result in LPC beneficially owning more than 4.99% of our common shares. As of the date of this report, we have issued a total of 140,000 of our common shares to LPC for an aggregate amount of $379,725 under the 2022 Commitment Purchase Agreement.

On September 9, 2022 the Company entered into a loan agreement with FiveT Investment Management Ltd., Dominik Lysek and Thomas Meyer (the "Lenders"), as amended, pursuant to which the Lenders have agreed to loan to the Company an aggregate of CHF 600,000.00, which loan bears interest at the rate of 5% per annum and was to mature as of March 31, 2023. The maturity date was subsequently extended to May 31, 2023. The Company agreed to grant to the Lenders warrants (the "Warrants") to purchase an aggregate 41,667 common shares. The Warrants are exercisable at an exercise price of CHF 7.20 per share for up to five years from October 1, 2022.

On February 4, 2022, the Company entered into a convertible loan agreement with FiveT Investment Management Ltd. (“FiveT IM”). The convertible loan of CHF 5.0 million, as amended (the “FiveT Loan”) carried interest at the rate of 10% per annum and was to mature on May 31, 2023. FiveT IM had the right to convert all or part of the FiveT Loan, including accrued and unpaid interest, at its option, into common shares, subject to the limitation that the Lender own no more than 4.9% of the common shares at any time. On April 13, 2023, the Company and FiveT IM entered into an amendment to the FiveT Loan (the “FiveT Loan Amendment”), which amended the conversion price of the FiveT Loan to a fixed price equal to the lower of (a) the mean daily trading volume weighted average price (“VWAP”) of the Company’s common shares on the Nasdaq Stock Market on the 20 trading days preceding the effective date of the FiveT Loan Amendment or (b) 90% of the VWAP on the effective date of the FiveT Loan Amendment. From April 13, 2023 to April 17, 2023, FiveT IM converted the entire FiveT Loan into an aggregate of 4,341,012 common shares at a conversion price of $1.4475 per share. As a result, the FiveT Loan is no longer outstanding and has been terminated.

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 $80.00 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 Medica. 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 the Company, subject to additional provisions and certain restrictions. On December 2, 2020, FiveT converted principal of CHF 895,455 into 737,000 shares of the Company 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 $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 $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 $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.

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 2022, we sold 116,843 shares under the ATM for aggregate proceeds of $1.2 million. As of the date of this Annual Report, we have sold 1,505,244 of our common shares for an aggregate offering price of $12.1 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; Going Concern

We expect that we will need additional funding. We expect our total additional cash need in 2023 to be in the range of CHF 15 to 17 million. As part of our strategic repositioning, we are aiming to divest or partner 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 99,171 common shares at a weighted average exercise price of $57.60 per share, an equity commitment to sell up to $9.1 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 $12.9 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 advance our development programs with AM-401, AM-411 and the OligoPhore™/SemaPhore™ platform up to the sale or out-licensing of these programs. If we choose not to divest or out-license one or several of these programs to partners, we expect to incur significant additional expenses for development regulatory approval and commercialization. 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, which could materially harm our business, prospects, financial condition and operating results. This could then result in bankruptcy, or the liquidation of the Company.

These factors raise substantial doubt about the Company's ability to continue as a going concern. The financial statements included in this report have been prepared on a going concern basis, which contemplates the continuity of normal activities and realization of assets and settlement of liabilities in the normal course of business. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. 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.

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 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 until the end of 2022, including certain expenses related to the patenting of intellectual property. As of December 31, 2022, the capitalized costs related to the AM-125 program were fully impaired based on the impairment analysis performed under IFRS.

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 2023 annual general meeting. All directors except Armando Anido 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	55	2003
Covadonga Pañeda	Chief Operating Officer	49	2022
Marcel Gremaud	Chief Financial Officer	65	2021
Non-Executive Directors			
Armando Anido	Director	65	2016
Mats Blom	Director	58	2017
Alain Munoz	Director	73	2018
Margrit Schwarz	Director	59	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 and has served as Chairman and CEO since that time. 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 has been the Chairman of the Board of Directors of PharmaTrail Ltd. since 2020. He holds a Ph.D. (Dr.rer.pol.) in business administration from the University of Fribourg, Switzerland.

Covadonga Pañeda, Chief Operating Officer (RNA) (from April 2022): Ms. Pañeda, Ph.D., has over 15 years of experience in drug development. From 2011 to 2018, she served as R&D Manager at Sylentis S.A., a clinical stage RNAi biopharma company, served as R&D Senior Project Leader from 2018 to 2019 at Exeltis (Insudpharma), a company focused on the development of branded pharmaceuticals, served as Director of Development from 2019 to 2020 at Canaan Research and Investment, a venture capital fund focused on biotechnology companies, and most recently, from 2020 to 2022, she served as Director of Development at Limm Therapeutics, a neuroimmune biopharma company. Dr. Pañeda obtained a Ph.D. in Biochemistry and Molecular Biology at the Faculty of Medicine at Universidad Autónoma, Madrid, Spain, and spent several years as a Post-doc at the Scripps Research Institute, La Jolla, CA. In April 2022 Ms. Pañeda joined us as Chief Development Officer and was promoted to Chief Operating Officer effective January 1, 2023.

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

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 and Director 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).

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, 2023)

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			**5**	
	Female	**Male**	**Non-Binary**	**Did Not Disclose Gender**
Part I: Gender Identity				
Directors	**1**	**4**	**0**	**0**
Part II: Demographic Background				
Underrepresented Individual in Home Country Jurisdiction			**0**	
LGBTQ+			**0**	
Did Not Disclose Demographic Background			**0**	

Other Key Service Providers

Samuel A. Wickline, Chief Scientific Adviser (Chief Scientific Officer from June 2021 to December 2022): Dr. Wickline, MD, is the founder of Trasir Therapeutics, Inc., which we acquired in 2021 and formed the basis for our activities in RNA delivery technology. 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. Dr. Wickline stepped down as CSO by the end of 2022 and serves on a part-time consulting basis as Chief Scientific Adviser since January 1, 2023.

B. Compensation

For the year ended December 31, 2022, 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 1,172,818 (2021: CHF 946,449).

For the year ended December 31, 2022, 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 49,050 (2021: CHF 29,467).

Compensation awarded to the Board of Directors in 2022

The total compensation of the members of the board of directors in 2022 is outlined below:

In CHF	Cash Compensation	Social Contributions	Stock Options (2)	Total
Thomas Meyer, PhD, Chairman (1)	—	—	—	—
Armando Anido, MBA	41.713	—	12,793	54,506
Mats Blom, MBA	41,634	—	12,793	54,427
Alain Munoz, MD	41,634	—	12,793	54,427
Margrit Schwarz, PhD	41,923	—	8,250	50,173
Total	**183,058**	—	**51,171**	**234,229**

(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.

In 2022, 2069 options were granted to each eligible member of the Board of Directors, with an exercise price of $17.20 per common share and an expiration date of May 19, 2030. 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 2022

The total compensation and the highest individual compensation to our executive officers in 2022 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	54,900	82,026	133,019	635,945
Executive Officers Total (4)	**909,469**	**122,616**	**130,490**	**172,115**	**1,334,690**

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

(2) 2022 option grants, exercise prices of $20.78 and $6.353, expiration date April 30, 2030 and October 31, 2030, 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, 2022, we had four executive officers.

Employment Agreements

We have entered into employment and/or consulting agreements with our executive officers Thomas Meyer, Covadonga Pañeda and Marcel Gremaud. We were also party to two additional employment agreements which terminated effective December 31, 2022. The employment and/or consulting agreements provide for the compensation that the executive officers 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 75,000 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. As of December 31, 2022, no common shares are available for award under the EIP.

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 Margrit Schwarz, 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 Ms. Schwarz 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 our bye-laws. 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, 2022, we had 18 employees (16.3 full time equivalents, FTEs). The breakdown by cost centers is as follows: Research & Development: 12.6 FTEs, General & Administration: 1.6 FTEs, Sales & Marketing: 1.1 FTEs, Cost of Goods Sold: 1.0 FTEs. 15.3 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."

F. Disclosure of a Registrant's Action to Recover Erroneously Awarded Compensation

Not applicable.

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major shareholders

The following table presents information relating to the beneficial ownership of our common shares as of March 15, 2023 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 April 17, 2023 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 April 17, 2023 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, 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 6,988,999 common shares issued and outstanding as of April 17, 2023. 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.

	Shares Beneficially Owned	
Shareholder	**Number**	**Percent**
5% Shareholders		
-	—	—
Executive Officers and Directors		
Thomas Meyer, Ph.D. (1)	88,603	1.27%
Armando Anido, MBA (2)	5,569	*
Mats Blom, MBA (3)	5,563	*
Alain Munoz, MD (4)	5,569	*
Margrit Schwarz (5)	2,069	*
Covadonga Pañeda, Ph.D.	—	*
Marcel Gremaud, CPA	—	*
All current directors and executive officers as a group (7 persons)	107,373	1.54%

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

(1) Consists of 51,999 common shares, warrants to purchase 18,377 common shares and options to purchase 18,227 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 3 common shares owned by Alain Munoz and 5560 options to purchase common shares under the Company’s EIP.

(5) Consists of options to purchase common shares under the Company’s EIP.

Holders

As of April 17, 2023, 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 Agreements

Ante Treuhand AG (“Ante Treuhand”) provided the services of Elmar Schärli, Chief Financial Officer to the Company until November 18, 2021. Elmar Schärli was an employee of Ante Treuhand and was not paid directly by the Company. Fees paid to Ante Treuhand for such services were CHF 231,770 in 2021. Fees paid to Ante Treuhand for other services provided during the year ended December 31, 2021 were CHF 3,025.

Gremaud GmbH has provided the Chief Financial Officer for 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 195,988 for 2022 compared to CHF 14,720 in 2021. Fees paid to Gremaud GmbH for other services provided during the year ended December 31, 2022 were CHF 0 compared to CHF 161,596 in 2021.

Loan Agreements

On September 9, 2022, the Company entered into a loan agreement with FiveT Investment Management Ltd., Dominik Lysek and Thomas Meyer, the Company’s CEO (the “Lenders”), pursuant to which the Lenders have agreed to loan to the Company an aggregate of CHF 600,000.00 (the “September 2022 Loan Agreement”), which Loan bears interest at the rate of 5% per annum and matures as of May 31, 2023. The Company issued to the Lenders warrants (the “Warrants”) to purchase an aggregate 41,666 common shares. The Warrants became exercisable immediately at an exercise price of CHF 7.20 per share, may be exercised up to five years from the date of issuance and may be exercised on a cashless basis in certain circumstances specified therein. Mr. Meyer lent CHF 200,000 of the total principal amount.

From December 8, 2022 to March 8, 2023, Mr. Meyer’s spouse provided one of the Company’s subsidiaries with a short-term loan of CHF 100,000.00, bearing interest at the rate of 5% per annum.

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 and 2022 Reverse Share Splits and the increase of authorized share capital of the Company on June 30, 2020, reduction of issued share capital on July 29, 2020, reduction of authorized share capital on September 29, 2020, increase of authorized share capital on September 29, 2022 and increase of authorized share capital on February 17, 2023, 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, 2022, our authorized share capital consisted of 5,000,000 common shares, par value CHF 0.20 per share, and 20,000,000 preference shares, par value CHF 0.02 per share, and there were 1,180,053 common shares issued and outstanding, excluding 157,730 common shares issuable upon exercise of options and 99,171 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.

Preferred 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 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 five directors. 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 contain 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 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.
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.	

Directors' fiduciary duties

Delaware Corporate Law:

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.

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.

Bermuda Corporate Law:

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 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

Delaware Corporate Law:

A Delaware corporation may, in its certificate of incorporation, eliminate the right of shareholders to act by written consent.

Bermuda Corporate Law:

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

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
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

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
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

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
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

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
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

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
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 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 Bermuda and the United States or Switzerland.

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 acquires our common shares at their original issuance and 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:

- banks, certain financial institutions and insurance companies;
- brokers, dealers or traders in securities or persons 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 and other pass through entities, and investors in such pass through entities;
- tax-exempt entities, including an "individual retirement account" or "Roth IRA";
- persons that own or are deemed to own ten percent or more of the stock by vote or value of our shares;
- 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 or other pass through entities 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 for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state therein or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- 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. 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 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 2023 taxable year or the foreseeable future. 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 with respect to the shares 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). Losses that exceed this limitation are subject to the rules generally applicable to losses provided in the Code and U.S. Treasury regulations. Amounts treated as ordinary income will not be eligible for the preferential tax rates applicable to "qualified dividend income" or long-term capital gains. 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, 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 that 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 for 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 with respect to a particular U.S. Holder, we are 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 are a PFIC for any taxable year during which a U.S. Holder holds common shares, such U.S. Holder will be required to file an annual information report with respect to the Company and any Lower-tier PFIC, generally 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.

The above description is not intended to constitute a complete analysis of all tax consequences relating to the ownership and disposition of our common shares. You should consult your tax advisor concerning the tax consequences of the ownership and disposition of our common shares in your particular situation.

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.

J. Annual Report to Security Holders

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, 2022, a 5% increase or decrease in the USD/CHF exchange rate with all other variables held constant would have resulted in a CHF 10,913 (2021: CHF 77,827) 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 82,850 (2021: CHF 117,247) 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

Our management, with the participation of our CEO and CFO, has evaluated the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934 (the "Exchange Act"), as amended, as of December 31, 2022. Based on this evaluation, our CEO and CFO concluded that our disclosure controls and procedures were not effective as of December 31, 2022, because of the material weaknesses in our internal control over financial reporting described below.

Notwithstanding the conclusion by our Chief Executive Officer and Chief Financial Officer that our disclosure controls and procedures as of December 31, 2022 were not effective, and notwithstanding the material weaknesses in our internal control over financial reporting described below, management believes that the consolidated financial statements and related financial information included in this Annual Report on Form 20-F fairly present in all material respects our financial condition, results of operations and cash flows as of and for the year ended December 31, 2022 in conformity with IFRS.

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 defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with IFRS.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements, including the possibility of human error, the circumvention or overriding of controls, or fraud. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Effective internal controls can provide only reasonable assurance with respect to the preparation and fair presentation of financial statements.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements will not be prevented or detected on a timely basis.

Management conducted an evaluation of the effectiveness of internal control over financial reporting based upon the criteria established in Internal Control-Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (the "COSO Framework"). Based on that evaluation, management concluded that the Company's internal control over financial reporting was not effective as of December 31, 2022, due to the material weaknesses identified below.

Material Weaknesses in Internal Control Over Financial Reporting

The Company did not maintain controls to execute the criteria established in the COSO Framework for the control environment, risk assessment, control activities, information and communication, and monitoring components, which resulted in control deficiencies that constitute material weaknesses, either individually or in the aggregate, within each component of the COSO Framework. This was due to the lack of sufficient resources to execute control activities which contributed to the potential for there to have been material errors in our financial statements, and therefore, resulted in the following material weaknesses:

Control Environment

The Company did not maintain a sufficient complement of personnel with appropriate levels of knowledge, experience, and training in accounting and internal control matters commensurate with the development stage nature and complexity of the Company's business. The lack of sufficient appropriately skilled and trained personnel contributed to our failure to: (i) design and implement all necessary internal controls; and (ii) consistently operate our internal controls.

The control environment material weakness contributed to other material weaknesses within our system of internal control over financial reporting in the following COSO Framework components:

Risk Assessment

The deficiencies identified in the risk assessment component of the COSO Framework constitute a material weakness, either individually or in the aggregate, relating primarily to: (i) identifying, assessing, and communicating appropriate objectives, (ii) identifying and analyzing risks to achieve such objectives, and (iii) identifying and assessing changes in the business that could impact the system of internal controls.

Control Activities

The deficiencies identified in the control activities component of the COSO Framework constitute a material weakness, either individually or in the aggregate, relating to: (i) designing controls to address relevant risks, (ii) providing evidence of control performance, (iii) providing appropriate segregation of duties, or (iv) control operation occurring at a level of precision to identify all potentially material errors.

Other income and research development expenses for 2021 were revised in the consolidated financial statements contained in this Annual Report from the previously reported financial statements due to an immaterial error with regard to advance payments for research and development costs and related tax credits for the annual period. The revision resulted in a lower operating loss, loss before tax, net loss attributable to owners of the Company and Total comprehensive loss attributable to owners of the Company than previously reported. Please refer to note 33 to the consolidated financial statements for further information on the revision. In the Unaudited Condensed Consolidated Interim Financial Statements of the Company as of June 30, 2022 and for the six months ended June 30, 2022 furnished with the Securities and Exchange Commission on November 30, 2022, an upfront payment of $1 million (CHF 0.9 million) related to the exclusive licensing and distribution agreement with Nuance for Bentrio® was incorrectly recorded as revenue. In the financial statements as of December 31, 2022, the upfront payment is recorded as deferred income. Please refer to "Adjustment of June 30, 2022 Revenue" in Item 5.A of this Annual Report for further information on this adjustment.

Information and Communication

The deficiencies identified in the information and communication component of the COSO Framework constitute a material weakness, either individually or in the aggregate, relating to communicating accurate information internally and externally, including providing information pursuant to objectives, responsibilities, and functions of internal control. The Company did not consistently operate controls for generating and using relevant quality information and did not establish communication protocols to support the functioning of internal controls based on the criteria established in the COSO Framework.

Monitoring

The deficiencies constituting a material weakness, either individually or in the aggregate, related to the monitoring component of the COSO Framework not ascertaining whether the components of internal control were present and functioning.

Remediation Plan and Status

Management is continuing to evaluate the material weaknesses discussed above and is in the process of implementing plans to remediate these material weaknesses. We expect our remediation plan to include the following, amongst others:

- Implementing an effective risk assessment process to identify and analyze risks caused by changes in our business that could impact our system of internal control, including re-designing existing controls as necessary;

- Reporting on a regular basis to the Company's Audit Committee on the effectiveness of internal controls;

- Enhancing the design of control activities to operate at a level of precision to identify all potentially material errors, and training control owners to improve required retention of documentation evidencing their execution of control activities;

- Designing and implementing controls over the generation and communication of relevant quality information to be utilized in the execution of control activities; and

- Investing in training of personnel and hiring additional resources with appropriate expertise to plan and perform more timely and thorough monitoring activities over our internal control over financial reporting.

We cannot assure you that the measures we have taken to date, and are continuing to implement, will be sufficient to remediate the material weaknesses we have identified or avoid potential future material weaknesses. The material weaknesses cannot be considered remediated until applicable controls have operated for a sufficient period and management has concluded, through testing, that these controls are operating effectively. Accordingly, we will continue to monitor and evaluate the effectiveness of our internal control over financial reporting.

C. Attestation Report of the Registered Public Accounting Firm

Not applicable.

D. Changes in Internal Control over Financial Reporting

Other than described above in this Item 15, there have been no changes in our internal control over financial reporting during the year ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our 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

	2022	2021
Audit fees	349	186
Audit-related fees	102	126
Total fees	**451**	**312**

In 2022 we were billed CHF 348,956 by Deloitte AG in connection with audit services for our annual filing as well as interim reviews, group audit, and statutory audits plus CHF 102,400 in connection with audit-related services for work in connection with our equity offerings and registration statements. In 2021 we were billed CHF 185,487, by Deloitte AG in connection with our annual filing as well as interim reviews, group audit, and statutory audits plus CHF 126,200 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 and Corporate Actions of the registrant (incorporated herein by reference to exhibit 3.1 of the Alamira Therapeutics Ltd. registration statement on Form F-1 (Registration No. 333-269823) filed with the Commission on March 7, 2023)
1.2	Bye-laws of the Registrant (incorporated herein by reference to exhibit 3.2 of the Alamira Therapeutics Ltd. registration statement on Form F-1 (Registration No. 333-269823) filed with the Commission on February 16, 2023
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)
2.16	Form of Warrant, dated as of September 9, 2022 (incorporated by reference to exhibit 4.1 of the Altamira Therapeutics Ltd. report on Form 6-K filed with the Commission on September 12, 2022)
2.17	Purchase Agreement, dated as of December 5, 2022 between Altamira Therapeutics Ltd. and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.1 of the Altamira Therapeutics Ltd. report on Form 6-K filed with the Commission on December 5, 2022)
2.18	Registration Rights Agreement, dated as of December 5, 2022 between Altamira Therapeutics Ltd. and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.2 of the Altamira Therapeutics Ltd. report on Form 6-K filed with the Commission on December 5, 2022)

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)
4.30	Loan Agreement, dated as of September 9, 2022, by and among Altamira Therapeutics Ltd. and the Lenders (incorporated by reference to exhibit 99.1 of the Altamira Therapeutics Ltd. report on Form 6-K filed with the Commission on September 12, 2022)
4.31	Share Purchase Agreement, dated October 19, 2022, by and between Altamira Therapeutics Ltd. and the purchaser party thereto (incorporated by reference to exhibit 99.1 of the Altamira Therapeutics Ltd. report on Form 6-K filed with the Commission on October 24, 2022)
4.32	Option Agreement, dated October 19, 2022, by and between Altamira Therapeutics Ltd., Zilentin AG and the other party thereto (incorporated by reference to exhibit 99.2 of the Altamira Therapeutics Ltd. report on Form 6-K filed with the Commission on October 24, 2022)
4.33	Amendment No. 1 to Convertible Loan Agreement, between 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 filed with the Commission on January 27, 2023)
4.34	Amendment No. 2 to Convertible Loan Agreement, between 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 filed with the Commission on March 9, 2023)
4.35	Amendment No. 3 to Convertible Loan Agreement, between Altamira Therapeutics Ltd. and FiveT Investment Management Ltd. (incorporated herein by reference to exhibit 10.22 of the Alamira Therapeutics Ltd. registration statement on Form F-1 (Registration No. 333-269823) filed with the Commission on March 23, 2023)
4.36	Amendment No. 4 to Convertible Loan Agreement, between Altamira Therapeutics Ltd. and FiveT Investment Management Ltd. (incorporated herein by reference to exhibit 10.23 of the Alamira Therapeutics Ltd. registration statement on Form F-1 (Registration No. 333-269823) filed with the Commission on March 27, 2023)

4.37	Amendment No. 5 to Convertible Loan Agreement, between 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 filed with the Commission on April 3, 2023)
4.38*	Amendment No. 6 to Convertible Loan Agreement, between Altamira Therapeutics Ltd. and FiveT Investment Management Ltd.
4.39	Amendment No. 7 to Convertible Loan Agreement, between 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 filed with the Commission on April 13, 2023)
4.40*	Form of Amendment No. 1 to Loan Agreement, dated December 28, 2022
4.41*	Amendment No. 2 to Loan Agreement, between Altamira Therapeutics Ltd. and the Lenders
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: May 16, 2023

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Audited Consolidated Financial Statements — Altamira Therapeutics Ltd.

As of December 31, 2022 and 2021 and for the years ended December 31, 2022, 2021, and 2020

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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, 2022 and 2021, 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, 2022, 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, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board (“IFRS”).

Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 2 to the financial statements, the Company’s present financial situation raises substantial doubt about its ability to continue as a going concern. Management’s plans in regard to this matter are also described in Note 2. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

INTANGIBLE ASSETS – IMPAIRMENT ASSESSMENT – REFER TO NOTE 2 (SECTION DEVELOPMENT EXPENDITURES), NOTE 3 (SECTION INTANGIBLE ASSETS), AND NOTE 9 (INTANGIBLE ASSETS) TO THE FINANCIAL STATEMENTS

Critical Audit Matter Description

The Company recorded an impairment loss for AM-125 in the amount of CHF 12,397,148 for the year ended December 31, 2022. The remaining carrying value of the internally developed intangible asset was nil as of December 31, 2022.

We identified the impairment assessment, specifically related to management's assumption of whether AM-125 fair value is in excess of carrying value, as a critical audit matter. Probable future cash flows are subjective because they are dependent on finding a potential buyer or securing a license agreement. Auditing this significant assumption involved a high degree of auditor judgment and an increased extent of effort.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to the likelihood of the company having future cash flows for the internally developed intangible asset, and included the following, among others:

- We assessed impairment indicators for AM-125.
- We evaluated the Company's plan not to generate probable future cash-flows from AM-125 based on the decision not to commercialize the product.
- We assessed the likelihood of the company finding a potential buyer or securing a license agreement.
- We assessed, with the assistance of our Internal Fair Value specialist, the reasonableness of the valuation model, including the discount rate and royalty rate assumptions.

Deloitte AG

/s/ Roland Mueller	/s/ Adrian Kaeppeli
Auditor in Charge	

Zurich, Switzerland
May 16, 2023

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, 2022, 2021 and 2020 (in CHF)

	Note	2022	2021 [1)]	2020
Revenue	20	**305,616**	**63,882**	**—**
Cost of Sales	21	(1,443,855)	(2,240,554)	—
Gross profit		**(1,138,239)**	**(2,176,672)**	**—**
Other operating income	19	709,449	214,217	174,475
Research and development	22	(19,677,756)	(8,360,821)	(2,862,979)
Sales and marketing	23	(2,381,384)	(1,498,218)	—
General and administrative	24	(3,644,549)	(4,946,576)	(2,594,662)
Operating loss		**(26,132,479)**	**(16,768,070)**	**(5,283,166)**
Interest income	26	969	3,219	258
Interest expense	26	(911,869)	(189,695)	(135,151)
Foreign currency exchange gain/(loss), net	26	54,645	328,641	(333,553)
Revaluation gain/(loss) from derivative financial instruments	26 31, 32	451,131	(410,918)	(2,250,222)
Transaction costs	26	(1,137)	—	(219,615)
Loss before tax		**(26,538,740)**	**(17,036,823)**	**(8,221,449)**
Income tax gain/(loss)	27	10,329	(21,620)	21,284
Net loss attributable to owners of the Company		**(26,528,411)**	**(17,058,443)**	**(8,200,165)**
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	25	441,277	264,984	(26,118)
Items that are or may be reclassified to profit or loss				
Foreign currency translation differences, net of taxes of CHF 0		61,046	772	88,862
Other comprehensive income/(loss), net of taxes of CHF 0		**502,323**	**265,756**	**62,744**
Total comprehensive loss attributable to owners of the Company		**(26,026,088)**	**(16,792,687)**	**(8,137,421)**
Basic and diluted loss per share	28	(29.13)	(25.76)	(25.27)

1) Revised, see note 33.

The accompanying notes form an integral part of these consolidated financial statements.

Consolidated Statement of Financial Position

As of December 31, 2022 and 2021

(in CHF)

	Note	December 31, 2022	December 31, 2021(1)
ASSETS			
Non-current assets			
Property and equipment	7	1	1
Right-of-use assets	8	445,827	564,714
Intangible assets	9	3,893,681	14,314,877
Other non-current financial assets		194,263	199,105
Total non-current assets		**4,533,772**	**15,078,697**
Current assets			
Inventories	10	11,644	839,221
Trade receivables		6,525	21,746
Other receivables	11	755,987	671,340
Prepayments	12	709,266	1,575,126
Derivative financial instruments	5	270,176	—
Cash and cash equivalents	13	15,395	984,191
Total current assets		**1,768,993**	**4,091,624**
Total assets		**6,302,765**	**19,170,321**
EQUITY AND LIABILITIES			
Equity			
Share capital	14	236,011	149,643
Share premium		192,622,406	188,511,476
Other reserves		258,044	62,069
Accumulated deficit		(201,431,272)	(175,686,937)
Total shareholders' (deficit)/equity attributable to owners of the Company		**(8,314,811)**	**13,036,251**
Non-current liabilities			
Derivative financial instruments	5	—	1,233
Non-current lease liabilities	8	343,629	461,485
Employee benefit liability	25	336,206	668,319
Deferred income	18	932,200	—
Deferred tax liabilities	27	125,870	142,484
Total non-current liabilities		**1,737,905**	**1,273,521**
Current liabilities			
Loan	31	5,869,797	—
Current lease liabilities	8	117,856	114,251
Trade and other payables	16	4,914,404	3,697,723
Accrued expenses	17	1,977,614	1,048,575
Total current liabilities		**12,879,671**	**4,860,549**
Total liabilities		**14,617,576**	**6,134,070**
Total equity and liabilities		**6,302,765**	**19,170,321**

1) Revised, see note 33.

The accompanying notes form an integral part of these consolidated financial statements.

Consolidated Statement of Changes in Equity
As of December 31, 2022, 2021 and 2020
(in CHF)

	Note	Share Capital	Share Premium	Loans with Warrants Equity Component	Foreign Currency Translation Reserve	Accumulated Deficit	Total Equity / (Deficit)
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		—	—	—	—	(17,058,443)	(17,058,443)
Other comprehensive income / (loss)		—	—	—	772	264,984	265,756
Total comprehensive loss		**—**	**—**	**—**	**772**	**(16,793,459)**	**(16,792,687)**
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**	**(175,686,937)**	**13,036,251**
As of January 1, 2022		**149,643**	**188,511,476**	**—**	**62,069**	**(175,686,937)**	**13,036,251**
Total comprehensive loss							
Net loss		—	—	—	—	(26,528,411)	(26,528,411)
Other comprehensive income / (loss)		—	—	—	61,046	441,277	502,323
Total comprehensive loss		**—**	**—**	**—**	**61,046**	**(26,087,134)**	**(26,026,088)**
Transactions with owners of the Company							
Capital increase		86,368	4,146,425		—	—	4,232,793
Transaction costs		—	(35,495)				(35,495)
Recognition of equity component of loans with warrants		—	—	134,929	—	—	134,929
Share based payments	15	—	—		—	342,799	342,799
Balance at December 31, 2022		**236,011**	**192,622,406**	**134,929**	**123,115**	**(201,431,272)**	**(8,314,811)**

The accompanying notes form an integral part of these consolidated financial statements.

Consolidated Statement of Cash Flows

For the Years Ended December 31, 2022, 2021, and 2020

(in CHF)

	Note	2022	2021	2020
Cash flows from operating activities				
Net loss		**(26,528,411)**	**(17,058,443)**	**(8,200,165)**
Adjustments for:				
Depreciation	7, 8, 22, 24	118,887	76,357	20,036
Impairment of intangible assets	9, 22	12,397,148	1,529,929	—
Deferred income	18	932,200	—	—
Unrealized foreign currency exchange loss/(gain), net		(46,087)	(279,329)	10,818
Net interest expense	26	891,651	174,593	127,160
Share based payments	15	342,799	1,206,303	368,793
Transaction costs	26	1,137	—	219,615
Employee benefits		109,164	65,927	80,811
Revaluation loss/(gain) derivative financial instruments	26, 31, 32	(451,131)	410,918	2,250,222
Income tax loss/(gain)	27	(10,329)	21,620	(21,284)
		(12,242,972)	**(13,852,125)**	**(5,143,994)**
Changes in:				
Inventories		827,577	(839,221)	—
Trade and other receivables		(103,601)	(340,119)	254,438
Prepayments		856,429	(1,297,537)	156,661
Trade and other payables		1,263,196	2,937,019	(175,878)
Accrued expenses		716,140	(280,755)	65,303
Net cash used in operating activities		**(8,683,231)**	**(13,672,738)**	**(4,843,470)**
Cash flows from investing activities				
Purchase of intangibles	9	(2,142,806)	(3,325,952)	(2,315,232)
Cash paid for other non-current financial assets		—	(179,104)	—
Interest received	26	969	—	258
Net cash used in investing activities		**(2,141,837)**	**(3,505,056)**	**(2,314,974)**
Cash flows from financing activities				
Proceeds from offerings and warrant exercises	14, 32	3,962,618	6,842,940	16,074,996
Transaction costs	14	(35,496)	(156,817)	(636,858)
Proceeds from loans	31	6,038,627	—	1,522,931
Repayment of loan		—	(50,000)	—
Repayment of lease liabilities		(114,251)	(18,700)	—
Interest paid	8, 26, 31	(19,503)	(3,699)	—
Net cash from financing activities		**9,831,995**	**6,613,724**	**16,961,069**
Net increase / (decrease) in cash and cash equivalents		**(993,073)**	**(10,564,070)**	**9,802,625**
Cash and cash equivalents at beginning of the period		984,191	11,258,870	1,384,720
Net effect of currency translation on cash		24,277	289,391	71,525
Cash and cash equivalents at end of the period		**15,395**	**984,191**	**11,258,870**

The accompanying notes form an integral part of these consolidated financial statements.

1. Reporting entity

Altamira Therapeutics Ltd. (the “Company”) is an exempted company incorporated under the laws of Bermuda. The Company began its operations as a corporation organized in accordance with Swiss law and domiciled in Switzerland under the name Auris Medical Holding AG (“Auris Medical (Switzerland)”). 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”). On March 18, 2019, the common shares of the Company began trading on the Nasdaq Capital Market under the trading symbol “EARS”. The Company’s registered office is located at Clarendon House, 2 Church Street, Hamilton HM 11, Bermuda. 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”. On October 25, 2022, the Company effected a one-for-twenty reverse share split (the “2022 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 2022 Reverse Share Split, as if such 2022 Reverse Share Split occurred on the first day of the periods presented.

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 $100
- Auris Medical Ltd., Dublin, Ireland (100%) with a nominal share capital of EUR 100
- Auris Medical Pty Ltd, Melbourne, Australia (100%), with a nominal share capital of AUD 100

The Company is a clinical-and commercial-stage biopharmaceutical company developing therapeutics that address important unmet medical needs. It is currently active in two areas: the development of RNA delivery technology and therapeutics for extrahepatic therapeutic targets (OligoPhore™ / SemaPhore™ platforms; AM-401 for the treatment of KRAS driven cancer, AM-411 for the treatment of rheumatoid arthritis; preclinical), and nasal sprays for protection against airborne allergens, and where approved, viruses (Bentrio®; commercial) or the treatment of vertigo (AM-125; Phase 2). The Company is working to reposition the Company around RNA delivery technology while exploring strategic options to either divest or partner its non-RNA traditional businesses.

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 May 16, 2023.

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.

Going Concern

We have incurred recurring losses and negative cash flows from operations since inception and we expect to generate losses from operations for the foreseeable future primarily due to incurring research and development costs for our potential product candidates. We expect our research and development expenses to remain significant as we advance or initiate the pre-clinical and clinical development of AM-401, AM-411 or any other product candidate. We expect our total additional cash need in 2023 to be in the range of CHF 15 to 17 million. As of December 31, 2022, our cash and cash equivalents were CHF 15 thousand. In 2023, through the issuance date of the financial statements, we have raised $5.1 million from the issuance of common shares under the A.G.P. Sales Agreement and the 2022 LPC Purchase Agreement, and CHF 2.5 million through a convertible loan provide under the 2023 FiveT Loan Agreement. In addition, we expect to receive another milestone payment of $1.0 million from Nuance upon market approval of Bentrio in China (during the 2nd quarter of 2024) as well as CHF 0.7 million in grant funding (during the 2nd and 3rd quarter of 2023). Further, the 2022 convertible loan from FiveT IM got converted into equity in April 2023.

The Board of Directors have considered the cash flow forecasts and the funding requirements of the business and continue to explore grant funding, licensing opportunities and equity investment opportunities in the Company. Apart from the inner ear therapeutic assets, the Company intends to partner or divest also its OTC consumer health products business, in order to focus on the development of its OligoPhore™/SemaPhore™ RNA delivery platform. In addition, the Company intends to raise further capital. The Board of Directors considers it feasible to generate CHF 15 to 17 million in funding within 12 months from the reporting date. At the date of issuing these financial statements, such plans have not yet been realized.

Our assumptions may prove to be wrong, and we may have to use our capital resources sooner than we currently expect. As is often the case with drug development companies, the ability of the consolidated entity to continue its development activities as a going concern is dependent upon it deriving sufficient cash from investors, from licensing and partnering activities, in particular the intended divestiture or partnering of the Company's legacy assets in the fields of inner ear therapeutics and OTC consumer health products, and from other sources of revenue such as grant funding.

To the extent that we will be unable to generate sufficient cash proceeds from the planned divestiture or partnering of our legacy assets or other partnering activities, we will need substantial additional financing to meet our funding requirements. While Management and the Board of Directors continue to apply best efforts to evaluate available options, there is no guarantee that any transaction can be realized or that such transaction would generate sufficient funds to finance operations for twelve months from the issuance of these financial statements. These factors raise substantial doubt about the Company's ability to continue as a going concern. These financial statements have been prepared on a going concern basis, which contemplates the continuity of normal activities and realization of assets and settlement of liabilities in the normal course of business. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. 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.

We expect that we will require additional funding to continue our development activities for the OligoPhore™ and SemaPhore™ platforms and AM-401 and AM-411 product candidates. Should the Company be unable to raise sufficient funding through equity or debt financings, partnerships, collaborations, or other sources, it may elect to raise additional funding under the A.G.P. Sales Agreement or the 2022 LPC Purchase Agreement. The funding capacity under this financing instruments is $12.9 million and $9.1 million, respectively. Although these agreements are binding, the ability to raise capital under these programs is subject to market and contractual conditions and the availability of registration statements filed with the SEC.

If additional capital is not available when required, the Company may need to delay or curtail its operations until such funding is received. Various internal and external factors will affect whether and when the Company's product candidates become approved for marketing and successful commercialization. The regulatory approval and market acceptance of the Company's product candidates, length of time and cost of developing and commercializing these product candidates and/or failure of them at any stage of the approval process will materially affect the Company's financial condition and future operations. Such matters are not within the control of the Company and thus all associated outcomes are uncertain.

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, which could materially harm our business, prospects, financial condition and operating results. This could then result in bankruptcy, or the liquidation of the Company.

2022 Reverse Share Split

The Company effected the 2022 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 27 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 41,430 (2021: CHF 31,879), 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 gain reflects the reassessment of deferred tax assets and liabilities booked in the 2022 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. Up to 2022, direct development expenditures for the Group’s intranasal betahistine program for the treatment of vertigo (AM-125) were capitalized as 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. All capitalized direct development expenditures were impaired as of December 31, 2022 based on the impairment test performed under IFRS.

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 important unmet medical needs. 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, 2022	December 31, 2021	December 31, 2020
CHF	Swiss Franc	Switzerland	5	1.0000	1.0000	1.0000
USD	Dollar	United States	1	0.9251	0.9110	0.8840
EUR	Euro	Europe	1	0.9901	1.0361	1.0817
AUD	Dollar	Australia	1	0.6305	0.6620	0.6822

Average exchange rates for the year for the most significant foreign currencies relative to CHF:

Currency		Geographical area	Reporting entities	2022	2021	2020
CHF	Swiss Franc	Switzerland	5	1.0000	1.0000	1.0000
USD	Dollar	United States	1	0.9550	0.9142	0.9581
EUR	Euro	Europe	1	1.0050	1.0810	1.0825
AUD	Dollar	Australia	1	0.6629	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 was the Group's assessment up to 2022 that the criteria mentioned above were met and therefore direct development expenditures were capitalized for AM-125 in 2020, 2021 and 2022, including intellectual property-related costs for the prosecution and registration of patents . As of December 31, 2022, all capitalized direct development costs related to AM-125 were impaired based on the impairment test performed under IFRS.

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) 38,219 non-registered common shares of the Company, par value CHF 0.20 per share, 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 (the "Reference Price", which amounted to $65.40 per Common Share); (ii) contingent on the occurrence of positive results from a subsequent post-closing scientific study led by Trasir ("Positive Results"), $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) $210,000 for expenses incurred by certain selling Trasir shareholders paid in $180,000 in cash and 459 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 $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 and December 31, 2022, 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 derivative in the 2022 FiveT convertible loan was initially measured at fair value by an independent consultant applying a simulation-based valuation approach. On December 31, 2022, the embedded derivative was measured based on the Black-Scholes option pricing model, resulting in a fair value of zero. 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 Company's 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

The Group recognizes revenue from the license of intellectual property and from the sale of products. To assess revenue recognition for arrangements that the Group determines are within the scope of IFRS 15, the Group performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Group satisfies a performance obligation. The Group only applies the five-step model to contracts when it is probable that the Group will collect the consideration it is entitled to in exchange for services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of IFRS 15, the Group assesses the services promised within each contract and determine those that are performance obligations and assess whether each promised service is distinct.

License of intellectual property

The Group recognizes as revenue its non-refundable license fees, milestone payments and royalties when its customer obtains control of promised services, in an amount that reflects the consideration which the Group expects to receive in exchange for those rendered services. If the license to the Group’s intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Group recognizes revenues when the license conveys a right of use, or there is a right of access to the underlying intellectual property. However, revenue for a license that provides a right to use the Company’s intellectual property before the beginning of the period during which the customer is able to use and benefit from the license is deferred. Revenue from sales-based royalty, in exchange for a license of intellectual property is recognized only when the subsequent sale occurs and the performance obligation to which the sales-based royalty has been allocated has been satisfied (in whole or in part).

Sale of products

The Group currently sells only one product, Bentrio®, a drug-free nasal spray for protection against airborne viruses and allergens. Revenue from sale of products is recognized at the point in time when control of the asset is transferred to the customer, generally on delivery of the product if no other agreement has been made. 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 up to 48.5% 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 2022, the following revised standards have been adopted:

IAS 16	Amendments to IAS 16, Proceeds before Intended Use
IAS 37	Amendments to IAS 37, Onerous contracts – Costs of Fulfilling a Contract
IFRS 3	Amendments to IFRS 3, References to the Conceptual Framework
IFRS 1, IFRS 9, IFRS 16, IAS 41	Annual improvements to IFRS Standards 2018-2020 Cycle

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, 2023, 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				
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, 2022	December 31, 2021
Financial assets		
At amortized cost		
Cash and cash equivalents	15,395	984,191
Other non-current financial assets	194,263	199,105
Trade receivables	6,525	21,746
Other receivables	—	255,187
At fair value through profit and loss		
Derivative financial instruments	270,176	—
Total financial assets	**486,359**	**1,460,229**
Financial liabilities		
At amortized cost		
Trade and other payables	4,914,404	3,697,723
Accrued expenses	1,977,614	1,048,575
Loan	5,869,797	—
Non-current lease liabilities	343,629	461,485
Current lease liabilities	117,856	114,251
At fair value through profit and loss		
Derivative financial instruments	—	1,233
Total financial liabilities	**13,223,300**	**5,323,267**

Fair values

The carrying amount of cash and cash equivalents, financial assets, trade and other receivables, trade and other payables, accrued expenses, loan and lease liabilities 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 2022 and 2021 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, 2022 and 2021. 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, 2022					
Trade and other payables	4,914,404	4,914,404	—	—	4,914,404
Accrued expenses	1,977,614	1,977,614	—	—	1,977,614
Loan and borrowings	5,869,797	5,759,877	357,192	—	6,117,069
Non-current lease liabilities	343,629	—	130,200	227,850	358,050
Current lease liabilities	117,856	32,550	97,650	—	130,200
Derivative financial instruments	—	—	—	—	—
Total	**13,223,300**	**12,684,445**	**585,042**	**227,850**	**13,497,337**

	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	—	130,200	358,050	488,250
Current lease liabilities	114,251	32,550	97,650	—	130,200
Derivative financial instruments	1,233	—	—	1,233	1,233
Total	**5,323,267**	**4,778,848**	**227,850**	**359,283**	**5,365,981**

	Fair values as at			
Financial assets / liabilities	**December 31, 2022**	**December 31, 2021**	**Fair value hierarchy**	**Valuation technique(s) and key input(s)**
Derivative fiinancial liabilities – Warrants from public offerings	Liability —	Liability 1,233	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 FiveT Convertible Loan	—	—	Level 3	Black-Scholes option pricing 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.
Derivative financial asset - Option LPC purchase agreement	Asset 270,176	Asset —	Level 3	The fair value is equal to the price paid to the counterparty for obtaining the right under the purchase agreement. The price paid corresponds to the fair value of 50,000 commitment shares issued to LPC as consideration for its commitment to purchase our common shares under the purchase agreement. Subsequent, the fair value is adjusted proportionally for the part of the right consumed.

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, 2022		Dec 31, 2021	
	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%	—	—	—
	-5%	—	—	—

Changes in liabilities arising from financing activities

			Non-cash changes		
	01.01.2022	**Financing Cash Flows [1)]**	**Fair value revaluation**	**Other changes [2)]**	**31.12.2022**
Derivative financial instrument	1,233	—	(1,233)	—	—
Loans	—	6,038,627	—	(168,830)	5,869,797
Lease liabilities	575,736	(130,200)	—	15,949	461,485
Total	576,969	5,908,427	(1,233)	(152,881)	6,331,282

			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

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, 2022 and December 31, 2021, 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, 2022	**December 31, 2021**
Financial assets		
Cash and cash equivalents	15,395	984,191
Other non-current financial assets	194,263	199,105
Trade receivables	6,525	21,746
Other receivables	—	255,187
Total	**216,183**	**1,460,229**

As of December 31, 2021 other receivables consisted of cash receivable from a capital increase implemented over the year end.

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:

	2022			2021		
in CHF	**USD**	**EUR**	**AUD**	**USD**	**EUR**	**AUD**
Cash and cash equivalents	1,791	3,462	—	388,950	539,474	—
Trade and other receivables	1,523,292	91,864	879,531	1,436,086	26,843	1,274,271
Trade and other payables	(1,086,206)	(1,452,883)	—	(104,676)	(2,615,791)	—
Accrued expenses	(220,616)	(299,435)	—	(163,823)	(295,467)	—
Net statement of financial position exposure -asset/(liability)	**218,261**	**(1,656,992)**	**879,531**	**1,556,537**	**(2,344,941)**	**1,274,271**

As of December 31, 2022, a 5% increase or decrease in the USD/CHF exchange rate with all other variables held constant would have resulted in a CHF 10,913 (2021: CHF 77,827) 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 82,850 (2021: CHF 117,247) 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 43,977 (2021: CHF 63,714) 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, 2022	**December 31, 2021**
Switzerland	4,339,509	14,734,738
Australia	—	144,854
Total	**4,339,509**	**14,879,592**

Non-current assets for geographical information exclude financial instruments and deferred tax assets.

7. Property and Equipment

	Production equipment	Office furniture and EDP	Total
At cost			
As of January 1, 2021	**353,488**	**233,706**	**587,194**
Additions	—	—	—
Disposals	—	—	—
As of December 31, 2021	**353,488**	**233,706**	**587,194**
Additions	—	—	—
Disposals	—	—	—
As of December 31, 2022	**353,488**	**233,706**	**587,194**
Accumulated depreciation			
As of January 1, 2021	**(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)**
Charge for the year	—	—	—
Disposals	—	—	—
As of December 31, 2022	**(353,488)**	**(233,705)**	**(587,193)**
Net book value			
As of December 31, 2021	—	**1**	**1**
As of December 31, 2022	—	**1**	**1**

As of December 31, 2022, and 2021 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, 2021	—	—
Additions	594,436	**594,436**
Disposals	—	—
As of December 31, 2021	**594,436**	**594,436**
Additions	—	—
Disposals	—	—
As of December 31, 2022	**594,436**	**594,436**
Accumulated depreciation		
As of January 1, 2021	—	—
Charge for the year	(29,722)	(29,722)
Disposals	—	—
As of December 31, 2021	**(29,722)**	**(29,722)**
Charge for the year	(118,887)	(118,887)
Disposals	—	—
As of December 31, 2022	**(148,609)**	**(148,609)**
Net book value		
As of December 31, 2021	**564,714**	**564,714**
As of December 31, 2022	**445,827**	**445,827**

Low value and short-term lease expenses	December 31, 2022	December 31, 2021
Expense related to short-term leases	6,001	52,280
Expense related to leases of low value assets	—	—
Total	**6,001**	**52,280**

Lease liabilities	December 31, 2022	December 31, 2021
As of January 1	575,736	—
Additions	—	594,436
Interest expense	15,949	3,000
Repayment of lease liability	(130,200)	(21,700)
As of December 31	**461,485**	**575,736**
thereof non-current	343,629	461,485
thereof current	117,856	114,251

Maturities of lease liabilities	December 31, 2022	December 31, 2021
Year 1	130,200	130,200
Year 2	130,200	130,200
Year 3	130,200	130,200
Year 4	97,650	130,200
Year 5	—	97,650
Undiscounted lease payments	**488,250**	**618,450**
Less: unearned interest	(26,765)	(42,714)
Total	**461,485**	**575,736**

9. Intangible assets

	Licenses	IP & Data rights	Patents	Internally generated	Total
At cost					
As of January 1, 2021	**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**
Exchange differences	—	—	—	168	168
Additions	—	—	275,281	1,700,503	1,975,784
As of December 31, 2022	**5,376,201**	**193,989**	**748,435**	**11,502,133**	**17,820,758**
Accumulated amortization and impairment losses					
As of January 1, 2021	—	—	—	—	—
Impairment	(1,482,520)	(47,409)	—	—	(1,529,929)
As of December 31, 2021	**(1,482,520)**	**(47,409)**	—	—	**(1,529,929)**
Impairment	—	(146,580)	(748,435)	(11,502,133)	(12,397,148)
As of December 31, 2022	**(1,482,520)**	**(193,989)**	**(748,435)**	**(11,502,133)**	**(13,927,077)**
Net book value					
As of December 31, 2021	**3,893,681**	**146,580**	**473,154**	**9,801,462**	**14,314,877**
As of December 31, 2022	**3,893,681**	—	—	—	**3,893,681**

Intangible assets comprise upfront and milestone payments related to licenses and capitalized development costs.

Commencing with the business year 2018, the Company recorded intangibles related to direct development expenditure of its AM-125 program. In 2019, a US patent on AM-125 was issued and a related EU application was allowed. As a consequence, we started to capitalize patent prosecution and registration costs and in 2022, we capitalized an amount of CHF 275,281 (2021: CHF 55,938). The additions to internally generated intangibles of CHF 1,700,503 includes an adjustment of government grants of CHF 40,653 under the Australian R&D tax incentive program. The amount of CHF 2,783,431 capitalized in 2021 was net of CHF 94,118 government grants obtained.

Based on the impairment testing performed under IFRS as of December 31, 2022, all intangible assets related to the AM-125 project were written off. Accordingly, the Company recorded an impairment of CHF 12,397,148 to its recoverable amount for AM-125 taking in consideration uncertainties regarding the realization of the cash flows in connection with the planned sale or the out-licensing of the AM-125 assets. The recoverable amount was calculated based on an out-license model of AM-125 at current development stage. The recoverable amount of the relevant intangible asset has been determined to be nil on the basis of their value in use, with consideration of fair value less costs of disposal not supporting a higher recoverable amount.

In 2021 the intangible assets related to the projects AM-101, AM-111 and AM-201 were impaired.

The remaining intangible assets are related to the acquisition of Trasir Therapeutics Inc. in 2021, 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). 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.

10. Inventories

	December 31, 2022	December 31, 2021
Finished goods	11,644	839,221
Total	**11,644**	839,221

The Company's inventory of finished goods 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, 2022 for any obsolete or slow-moving items, the Company wrote down finished good inventories in the amount of CHF 0.9 million in 2022 (2021: CHF 2.0 million). The amount of the write down was expensed to the income statement under Cost of Sales.

11. Other receivables

	December 31, 2022	December 31, 2021
R&D tax credit receivable	672,600	224,465
Receivable from share issuance	—	255,187
Value added tax receivable	78,650	168,851
Withholding tax receivable	—	7,336
Receivable from suppliers and other	4,737	15,501
Total other receivables	755,987	671,340

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, 2022 relates to the reimbursement application for compensation of R&D expenditures incurred in 2022. Other receivables were not considered impaired in the years presented herein.

12. Prepayments

	December 31, 2022	December 31, 2021
Advance payments to suppliers	659,861	1,437,708
Insurance	49,405	137,418
Total prepayments	**709,266**	**1,575,126**

13. Cash and cash equivalents

	December 31, 2022	December 31, 2021
Cash in bank accounts	15,395	984,191
Cash on hand	—	—
Total cash and cash equivalents	**15,395**	**984,191**

14. Capital and reserves

Share capital

The issued share capital of the Company at December 31 consisted of:

	December 31, 2022		December 31, 2021	
	Number	CHF	Number	CHF
Common shares with a par value of CHF 0.20 each	1,180,053	236,011	748,213	149,643
Total	**1,180,053**	**236,011**	**748,213**	**149,643**

	Common Shares (Number)	
	2022	2021
As of January 1	748,213	570,858
Exercise of warrants	—	44,872
LPC equity line	315,000	—
ATM program	116,843	59,235
Share-based payments (bonus)	—	8,731
Conversion convertible loan	—	25,841
Shares issued for Trasir acquisition	—	38,676
Fractional shares	(3)	—
Total, as of December 31	**1,180,053**	**748,213**

On December 5, 2022, the Company entered into a purchase agreement and a Registration Rights Agreement with Lincoln Park Capital Fund, LLC (the “2022 Commitment Purchase Agreement”). Pursuant to the purchase agreement, LPC agreed to subscribe for up to $10,000,000 of our common shares over the 24-month term of the purchase agreement. As consideration for LPC’s irrevocable commitment to purchase common shares upon the terms of and subject to satisfaction of the conditions set forth in the 2022 Commitment Purchase Agreement, the Company agreed to issue 50,000 common shares immediately to LPC as commitment shares. In 2022, no common shares were issued to LPC under the 2022 Commitment Purchase Agreement. The 2022 Commitment Purchase Agreement replaced the 2020 Commitment Purchase Agreement. Under the 2020 Commitment Purchase Agreement, LPC agreed to subscribe for up to $10,000,000 of our common shares over the 30-month term of the purchase agreement. Prior to its termination we had issued 325,000 common shares for aggregate proceeds of $4.0 million to LPC under the 2020 Commitment Purchase Agreement. 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 29,375 common shares for aggregate proceeds of $1.8 million to LPC under the LPC Purchase Agreement.

On June 1, 2021, the Company completed the acquisition of Trasir. The upfront acquisition price of $2.5 million was paid with 38,219 non-registered common shares at $65.40 each to the selling shareholders. In addition, 459 non-registered common shares were issued to reimburse $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 100,000 common shares at an offering price of $80.00 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 36,850 common shares at a conversion price of $27.00. On March 4, 2021 the remaining amount of CHF 604,545 plus interest of CHF 40,628 were converted into 25,841 common shares at a conversion price of $27.00.

On May 15, 2019, the Company completed a public offering of (i) 22,000 common shares with a par value of CHF 16.00 each, together with warrants to purchase 22,000 common shares, and (ii) 86,064 pre-funded warrants, with each pre-funded warrant exercisable for one common share, together with warrants to purchase 86,064 common shares, including 5,500 common shares and warrants to purchase 5,500 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 0.20 per common share and for the warrants CHF 86.80. 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, 63,192 warrants were exercised. The remaining 44,872 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 2022, we sold 116,843 shares under the ATM. As of the date of this Annual Report, we have sold 1,505,244 of our common shares for an aggregate offering price of $12.1 million pursuant to the A.G.P. Sales Agreement. The related transaction costs were charged to equity.

Authorized share capital

Our authorized share capital as of December 31, 2022 and December 31, 2021 consisted of 5,000,000 common shares, par value CHF 0.20 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"), which was amended in 2017 and 2019. In 2022, the Company granted 97,742 options (2021: 17,113 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, 2022 are as follows:

Plan	Number of options outstanding	Vesting conditions	Contractual life of options
Equity Incentive Plan Board	22,268	1 year service from grant date	6 years
Equity Incentive Plan Management & Staff	67,682	2 years' service from grant date (50%)	8 years
Equity Incentive Plan Management & Staff	67,682	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 2022	Equity Incentive Plan 2022	Equity Incentive Plan 2021	Equity Incentive Plan 2021
Fair value at grant date	USD 4.347 (2 year vesting) 1) USD 5.011 (3 year vesting) 1)	USD 6.644 (1 year vesting) 2) USD 8.760 (2 year vesting) 2) USD 10.604 (3 year vesting) 2)	USD 18.64 (2 year vesting) 1) USD 22.14 (3 year vesting) 1)	USD 24.82 (1 year vesting) 2) USD 37.00 (2 year vesting) 2) USD 43.66 (3 year vesting) 2)
Share price at grant date	USD 7.48	USD 17.8	USD 32.80	USD 70.80
Exercise price	USD 6.353	USD 20.78	USD 37.78	USD 70.220
Expected volatility	100.2%	99.1%	93.4%	101.3%
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	4.45%	2.87%	0.47%	0.06%

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 346,035 in 2022 (2021: CHF 1,206,303, 2020: CHF 368,793).

Share based compensation loss related to employee stock options amounted to CHF 346,035 in 2022 (2021: CHF 1,223,696, 2020: CHF 351,401).

The number and weighted average exercise prices (in CHF) of options under the share option programs are as follows:

	2022			2021		
	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	66,476	33.00	6.56	51,927	31.60	7.01
Expired during the year	—	—	—	—	—	—
Forfeited during the year	(6,488)	—	—	(2,565)	—	—
Exercised during the year	—	—	—	—	—	—
Granted during the year	97,742	9.40	—	17,113	45.40	—
Outstanding at December 31	**157,730**	**19.28**	**6.22**	**66,476**	**33.00**	**6.56**
Exercisable at December 31	28,796	—	—	14,419	—	—

The range of exercise prices for outstanding options was CHF 5.88 to CHF 584.66 as of December 31, 2022 and CHF 15.03 to CHF 575.80 as of December 31, 2021.

16. Trade and other payables

	December 31, 2022	December 31, 2021
Trade accounts payable - third parties	4,767,940	3,544,384
Other	146,464	153,339
Total trade and other payables	**4,914,404**	**3,697,723**

17. Accrued expenses

	December 31, 2022	December 31, 2021
Accrued research and development costs including milestone payments	741,291	557,391
Professional fees	326,365	179,461
Accrued vacation & overtime	46,868	51,218
Employee benefits incl. share based payments	362,497	196,917
Accrued interest	457,812	—
Other	42,781	63,588
Total accrued expenses	**1,977,614**	**1,048,575**

18. Deferred income

	December 31, 2022	December 31, 2021
Upfront payment	932,200	—
Total deferred income	**932,200**	—

Deferred income includes an upfront payment of $ 1 million (CHF 0.9 million) related to the exclusive licensing and distribution agreement with Nuance for Bentrio® in the defined territory. Revenue recognition for the upfront payment is deferred until transfer of production to Nuance, which will occur 4 years after Nuance obtaining the first national registration of Bentrio® in the territory or upon Nuance's cumulative orders for Bentrio® reaching a contractually defined minimum quantity of Bentrio® from the Company, whichever comes later. The upfront payment described above was incorrectly recorded as revenue in the Unaudited Condensed Consolidated Interim Financial Statements of the Company as of June 30, 2022 and for the six months ended June 30, 2022, furnished with the Securities and Exchange Commission on November 30, 2022. The foregoing information will be presented in accordance with the treatment used herein in the comparatives included in the June 30, 2023 financial statements, and we will reflect the correct treatment in restated financial statements as of June 30, 2022 and for the six months ended June 30, 2022 to be filed with a Form 6-K/A following the issuance of this Form 20-F.

19. Other operating income

	December 31, 2022	December 31, 2021	December 31, 2020
Income from R&D tax incentive (Government grants)	700,122	211,664	—
Refund of share issuance stamp duty	—	—	100,002
Other income	9,327	2,553	74,473
Total other operating income	**709,449**	**214,217**	**174,475**

20. Revenue

Set out below is the disaggregation of the Group's revenue from contracts with customers:

	December 31, 2022	December 31, 2021	December 31, 2020
Product sales	305,616	63,882	—
Total revenue	**305,616**	**63,882**	**—**

21. Cost of Sales

	December 31, 2022	December 31, 2021	December 31, 2020
Product purchases, packaging and logistics	362,584	173,758	—
Employee benefit and expenses	150,438	89,238	—
Inventory write-down	930,833	1,977,558	—
Total cost of sales	**1,443,855**	**2,240,554**	—

22. Research and development expense

	December 31, 2022	December 31, 2021	December 31, 2020
Pre-clinical projects	509,224	587,019	242,617
Clinical projects	3,237,649	2,379,536	476,972
Product and process development	473,246	1,100,453	614,744
Employee benefits and expenses	2,585,242	1,897,155	1,120,814
Lease expenses from short-term lease	—	—	34,147
Patents and trademarks	240,380	465,587	246,592
Regulatory projects	153,863	354,507	110,612
Impairment intangible assets	12,397,148	1,529,929	—
Depreciation tangible assets	81,004	46,635	16,481
Total research and development expense	**19,677,756**	**8,360,821**	**2,862,979**

Research and development expenses were capitalized in the amount of CHF 1,975,784 during 2022 compared to CHF 2,839,369 in 2021. As of December 31, 2022, all capitalized development costs related to the project AM-125 were impaired.

23. Sales and marketing expense

	December 31, 2022	December 31, 2021	December 31, 2020
Marketing and sales expenses	2,131,696	1,132,864	—
Employee benefits and expenses	249,688	204,157	—
Product samples	—	161,167	—
Total sales and marketing	**2,381,384**	**1,498,218**	—

24. General and administrative expense

	December 31, 2022	December 31, 2021	December 31, 2020
Employee benefits and expenses	735,139	1,554,778	811,373
Business development	15,727	967,046	95,663
Travel expenses	95,503	75,829	28,898
Administration expenses	2,669,460	2,245,862	1,645,530
Lease expenses from short-term lease	6,001	52,280	13,871
Depreciation of Right-of-use assets	118,887	29,722	—
Depreciation of tangible assets	—	—	3,555
Capital tax expenses	3,832	21,059	(4,228)
Total general and administrative expenses	3,644,549	4,946,576	2,594,662

25. Employee benefits

	December 31, 2022	December 31, 2021	December 31, 2020
Salaries	2,815,411	1,865,633	1,260,359
Pension costs	266,256	165,801	156,843
Other social benefits	294,017	275,258	116,290
Share based payments costs	342,799	1,223,696	351,401
Other personnel expenditures	2,024	214,940	47,295
Total employee benefits	**3,720,507**	**3,745,328**	**1,932,188**

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 342,799 in the year 2022 compared to CHF 320,879 in 2021.

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 2020, 1.00% in 2021 and 1.00% in 2022.

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

	2022	**2021**
Defined benefit obligation at January 1	4,677,632	3,529,602
Service costs	256,336	162,200
Plan participants' contribution	154,116	101,066
Interest cost	13,762	10,464
Actuarial losses	(931,636)	159,845
Plan amendments	—	(3,115)
Benefits paid through pension assets	(626,049)	717,570
Defined benefit obligation at December 31	**3,544,161**	**4,677,632**

The defined benefit obligation includes only liabilities for active employees. The weighted average modified duration of the defined benefit obligation at December 31, 2022 is 17.1 years (2021: 19.9 years).

Change in fair value of plan assets

	2022	**2021**
Fair value of plan assets at January 1	4,009,313	2,662,226
Interest income	12,187	8,586
Return on plan assets excluding interest income	(490,359)	424,829
Employer contributions	154,116	101,066
Plan participants' contributions	154,116	101,066
Benefits paid through pension assets	(626,049)	717,570
Administration expense	(5,369)	(6,030)
Fair value of plan assets at December 31	**3,207,955**	**4,009,313**

Net defined benefit liability recognized in the statement of financial position

	December 31, 2022	December 31, 2021
Present value of funded defined benefit obligation	3,544,161	4,677,632
Fair value of plan assets	(3,207,955)	(4,009,313)
Net defined benefit liability	**336,206**	**668,319**

Defined Benefit Cost

	2022	2021	2020
Service cost	256,336	159,085	151,624
Net interest expense	1,575	1,878	2,053
Administration expense	5,369	6,030	3,166
Total defined costs for the year recognized in profit or loss	**263,280**	**166,993**	**156,843**

Remeasurement of the Defined Benefit Liability

	2022	2021	2020
Actuarial loss (gain) arising from changes in financial assumptions	(876,841)	(74,284)	13,031
Actuarial loss (gain) arising from experience adjustments	(54,795)	463,238	45,881
Actuarial gain arising from demographic assumptions	—	(229,109)	—
Return on plan assets excluding interest income	490,359	(424,829)	(32,794)
Total defined benefit cost for the year recognized in the other comprehensive loss (income)	**441,277**	**(264,984)**	**26,118**

Assumptions

At December 31	2022	2021	2020
Discount rate	2.20%	0.30%	0.20%
Future salary increase	1.60%	0.85%	0.60%
Pension indexation	0.00%	0.00%	0.00%
Mortality and disability rates	BVG2020	BVG2020	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,	2022	2021
Change in assumption	0.25% increase	0.25% increase
Discount rate	(117,546)	(200,601)
Salary increase	23,058	22,961
Pension indexation	63,916	110,958
Change in assumption	+1 year	+ 1 year
Life expectancy	48,531	98,983

26. Finance income and finance expense

	2022	2021	2020
Interest income	969	3,219	258
Net foreign currency exchange gain	745,260	1,458,429	3,207,649
Revaluation gain from derivative financial instruments	451,131	5,085	—
Total finance income	**1,197,360**	**1,466,733**	**3,207,907**
Interest expense (incl. Bank charges)	911,869	189,695	135,151
Net foreign currency exchange loss	690,615	1,129,788	3,541,202
Revaluation loss from derivative financial instruments	—	416,003	2,250,222
Transaction costs	1,137	—	219,615
Total finance expense	**1,603,621**	**1,735,486**	**6,146,190**
Finance expense, net	**(406,261)**	**(268,753)**	**(2,938,283)**

In 2022, the revaluation gain from derivative financial instruments of CHF 451,131 includes CHF 449,898 related to the revaluation of the financial derivatives embedded in the 2022 FiveT convertible loan (note 31) and CHF 1,233 related to the revaluation of outstanding warrants from public offerings (note 32). In 2021, the revaluation loss from derivative financial instruments of CHF 416,003 was related to the revaluation of the financial derivatives embedded in the 2020 FiveT convertible loan at conversion. The revaluation gain of CHF 5,085 was related to the revaluation of outstanding warrants from public offerings. In 2022, finance expenses included interest paid of CHF 19,503 (2021: CHF 3,699; 2020: CHF 0).

27. Taxation

The Group's income tax expense recognized in the consolidated statement of profit or loss and other comprehensive loss was as follows:

	2022	2021	2020
Deferred income tax expense	(52,004)	(570,730)	(389,384)
Deferred income tax gain	62,332	549,110	410,668
Income tax gain/(loss)	**10,329**	**(21,620)**	**21,284**

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 13.7% in 2022 (2021: 13.5%, 2020: 12.1%) as summarized in the following table:

Reconciliation	2022	2021	2020
Loss before income tax	(26,538,740)	(17,036,823)	(8,221,449)
Income tax at statutory tax rates applicable to results in the respective countries	3,641,775	2,348,057	991,120
Effect of unrecognized temporary differences	(125,260)	(632,031)	(302,557)
Effect of unrecognized taxable losses	(3,015,088)	(1,885,486)	(184,881)
Effect of impairment of assets	—	(75,375)	—
Effect of previously unrecognized deferred tax asset	—	—	97,458
Effect of expenses not considerable for tax purposes	—	—	(47,894)
Effect of impact from application of different tax rates	(491,098)	223,215	(531,962)
Income tax gain/(loss)	**10,329**	**(21,620)**	**21,284**

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, 2022	December 31, 2021
Intangible assets	—	(51,914)
Deferred unrealized foreign exchange gains	—	—
Other receivables	(167,299)	(122,449)
Total	**(167,299)**	**(174,363)**

Deferred Tax Asset	December 31, 2022	December 31, 2021
Net operating loss (NOL)	41,429	31,879
Total	**41,429**	**31,879**
Deferred Tax, net	**(125,870)**	**(142,484)**

Deferred Tax 2022	Opening Balance	Recognized in Profit or Loss	Recognized in Equity	Exchange Differences	Closing Balance
Intangible assets	(51,914)	51,958	—	(44)	—
Other receivables	(122,449)	(52,004)	—	7,154	(167,299)
Net operating loss (NOL)	31,879	10,374	—	(825)	41,429
Total	(142,484)	10,329	—	6,285	(125,870)

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	—	—	—
Derivative financial asset	—	(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)

As of December 31, 2022, the Group had unrecognized tax loss carryforwards amounting to CHF 103.1 million (2021: CHF 109.9 million), of which CHF 101.4 million related to Auris Medical AG, Otolanum AG, Zilentin AG and Altamira Medica AG in Switzerland, CHF 1.7 million to Altamira Therapeutics Inc. in the United States (2021: CHF 108.6 million for Auris Medical AG, Otolanum AG, Zilentin AG and Altamira Medica AG and CHF 1.3 million for Auris Medical Inc.).

The Group’s unrecognized tax loss carryforwards with their expiry dates are as follows:

	December 31, 2022	December 31, 2021
Within 1 year	27,956,899	28,909,896
Between 1 and 3 years	31,668,498	50,673,943
Between 3 and 7 years	41,797,708	29,007,049
More than 7 years	1,691,572	1,264,262
Total	**103,114,677**	**109,855,150**

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, 2022	December 31, 2021
Deductible temporary differences		
Deferred income	111,025	—
Employee benefit plan	43,841	87,149
Other accounts payable	—	344,822
Total potential tax assets	**154,866**	**431,971**
Potential tax assets from loss carry-forwards not recognized	13,297,723	14,271,306
Total potential tax assets from loss carry-forwards and temporary differences not recognized	**13,452,589**	**14,703,277**

28. Loss per share

	December 31, 2022	December 31, 2021	December 31, 2020
Loss attributable to owners of the Company	(26,528,411)	(17,058,443)	(8,200,165)
Weighted average number of shares outstanding	910,723	662,314	300,707
Basic and diluted loss per share	**(29.13)**	**(25.76)**	**(27.27)**

For the years ended December 31, 2022 and 2021 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, 2022, the Company had 157,320 options outstanding under its stock option plans. The average number of options outstanding between January 1, 2022 and December 31, 2022 was 910,723 (662,314 for the period between January 1, 2021 and December 31, 2021). As of December 31, 2022, the Company had warrants to purchase up to 99,171 of its common shares issued and outstanding (as of December 31, 2021, the Company had warrants to purchase up to 12,305 common shares).

29. 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, 2022	December 31, 2021
Within one year	3,450	3,450
Between one and five years	—	—
Total	**3,450**	**3,450**

Office lease expenses of CHF 6,001, CHF 52,280 and CHF 50,260 were recorded in 2022, 2021 and 2020, respectively, in the consolidated statement of profit or loss and other comprehensive loss.

30. 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. Fees paid to Ante Treuhand for other services provided during the year ended December 31, 2021 were CHF 3,025.

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 2022 were CHF 195,988 (2021: CHF 14,720). Fees paid to Gremaud GmbH for other services provided during the year ended December 31, 2022 were CHF 0 (2021: CHF 161,596).

Thomas Meyer, the Company's CEO lent CHF 200,000 to the Company under the "September 9, 2022 Loan Agreement" with FiveT Investment Management Ltd., Dominik Lysek and Thomas Meyer for a total amount of CHF 600,000, please refer to note 30.

From December 8, 2022 to March 8, 2023, Mr. Meyer's spouse provided one of the Company's subsidiaries with a short-term loan of CHF 100,000.00, bearing interest at the rate of 5% per annum.

Compensation of the members of the Board of Directors and Management

In 2022, the compensation paid to management, excluding share bonuses and share-based payment charge, amounted to CHF 1,038,810 (2021: CHF 810,671; 2020: CHF 434,017). The fees paid to members of the Board of Directors in 2022 for their activities as board members totaled CHF 183,058 (2021: CHF 165,245; 2020: CHF 163,476).

	Executive Management			Board of Directors			Total		
	2022	2021	2020	2022	2021	2020	2022	2021	2020
Short term benefits	989,760	781,204	407,147	183,058	165,245	163,476	1,172,818	946,449	570,623
Post-employee benefits years	49,050	29,467	26,870	—	—	—	49,050	29,467	26,870
Share Bonuses	—	902,817	—	—	—	—	—	902,817	—
Share-based payment charge	172,115	192,362	204,840	51,171	48,046	57,148	223,286	240,408	261,988
Total	**1,210,925**	**1,905,850**	**638,857**	**234,229**	**213,291**	**220,624**	**1,445,154**	**2,119,141**	**859,481**

In 2022, CHF 223,286 (2021: CHF 240,408; 2020: CHF 261,988) was expensed for grants of stock options to members of the Board of Directors and management. Contributions to pension schemes amounted to CHF 49,050, CHF 29,467 and CHF 26,870 during the years 2022, 2021 and 2020, respectively. No termination benefits or other long-term benefits were paid.

Members of the Board of Directors and management held 107,110, 49,480 and 38,455 stock options as of December 31, 2022, 2021, and 2020, respectively.

31. Loans

	December 31, 2022	December 31, 2021
Convertible loan February 2022	4,898,377	—
Loans with warrants	871,420	—
Short-term loan from related party	100,000	—
Total	5,869,797	—

Convertible Loan Agreements

	December 31, 2022	December 31, 2021
As of January 1	—	**473,920**
Gross proceeds at disbursement date	5,000,000	—
Embedded derivative, separated	(449,898)	—
Transaction costs allocated to host	(10,236)	—
Carrying amount at initial recognition	**4,539,866**	**—**
Converted principal amount	—	(644,813)
Accrued interest	447,945	8,348
Amortization	358,511	162,545
Total	5,346,322	—
Accrued interest balance of December 31	447,945	—
Convertible loan balance of December 31	4,898,377	—

On December 28, 2022, the Company entered into two separate loan agreements with two private investors ("Private Lenders"), pursuant to which Private Lenders has agreed to loan to the Company an aggregate of CHF 250,000 and CHF 100,000, respectively, which loans bear interest at the rate of 5% per annum and mature as of May 30, 2023. The Company agreed to grant to Private Lenders warrants to purchase an aggregate 33,700 and 13,480 common shares. The warrants will be exercisable at an exercise price of CHF 4.4512 per share for up to five years from the date of issuance.

The loans with warrants are classified as a hybrid contract containing a host that is a financial liability and embedded derivatives (warrants) separated from the host. The embedded derivatives are classified as an equity component as they may be settled by the company exchanging a fixed amount of cash for a fixed number of its own equity instruments. The embedded derivatives are valued at initial recognition applying a Black-Scholes option pricing model. The valuation is based on input parameters, classified as Level 3. The fair value of the embedded derivative at initial recognition amounted to CHF 48,185 and was directly recognized in equity. The initial fair value of the liability component was derived by subtracting the fair value of the equity component from the nominal value of the loan. The host is subsequently carried at amortized cost, as of December 31, 2022, the carrying amount of the host amounted to CHF 305,873 and is included in the balance sheet under current liabilities.

On September 9, 2022, the Company entered into a loan agreement with FiveT Investment Management Ltd. ("FiveT IM"), Dominik Lysek and Thomas Meyer, the Company's CEO (the "Lenders"), pursuant to which the Lenders have agreed to loan to the Company an aggregate of CHF 600,000.00 (the "September 2022 Loan Agreement"), which loan bears interest at the rate of 5% per annum and matures as of March 31, 2023. The Company agreed to issue to the Lenders warrants to purchase an aggregate 41,666 common shares. Such warrants became exercisable immediately at an exercise price of CHF 7.20 per share, may be exercised up to five years from the date of issuance and may be exercised on a cashless basis in certain circumstances specified therein. Mr. Meyer lent CHF 200,000 of the total principal amount.

The loan with warrants is classified as a hybrid contract containing a host that is a financial liability and embedded derivatives (warrants) separated from the host. The embedded derivatives are classified as an equity component as they may be settled by the company exchanging a fixed amount of cash for a fixed number of its own equity instruments. The embedded derivatives are valued at initial recognition applying a Black-Scholes option pricing model. The valuation is based on input parameters, classified as Level 3. The fair value of the embedded derivative at initial recognition amounted to CHF 86,744 and was directly recognized in equity. The initial fair value of the liability component was derived by subtracting the fair value of the equity component from the nominal value of the loan. The host is subsequently carried at amortized cost, as of December 31, 2022, the carrying amount of the host amounted to CHF 561,062 and is included in the balance sheet under current liabilities.

On February 4, 2022, the Company entered into a convertible loan agreement with FiveT IM. The convertible loan of CHF 5.0 million, as amended (the "FiveT Loan") carried interest at the rate of 10% per annum and was to mature on May 31, 2023. FiveT IM had the right to convert all or part of the FiveT Loan, including accrued and unpaid interest, at its option, into common shares, subject to the limitation that the Lender own no more than 4.9% of the common shares at any time. On April 13, 2023, the Company and FiveT IM entered into an amendment to the FiveT Loan (the "FiveT Loan Amendment"), which amended the conversion price of the FiveT Loan to a fixed price equal to the lower of (a) the mean daily trading volume weighted average price ("VWAP") of the Company's common shares on the Nasdaq Stock Market on the 20 trading days preceding the effective date of the FiveT Loan Amendment or (b) 90% of the VWAP on the effective date of the FiveT Loan Amendment. From April 13, 2023 to April 17, 2023, FiveT IM converted the entire FiveT Loan into an aggregate of 4,341,012 common shares at an average conversion price of $1.4475 per share. As a result, the FiveT Loan is no longer outstanding and has been terminated.

The FiveT Loan was 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 initially valued by an independent consultant, 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 at initial recognition was 90.7%, 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.

As of December 31, 2022, the carrying amount of the host for the unconverted outstanding loan amounted to CHF 4,898,377 and is included in the balance sheet under current liabilities. The fair value of the embedded derivatives amounted to CHF 0 (at initial recognition February 8, 2022: CHF 449,898). A revaluation gain related to fair value measurement of embedded derivatives of CHF 449,898 as well as effective interest expenses and transaction costs of CHF 807,593 in total were recorded in profit or loss.

On September 7, 2020, our affiliate Altamira Medica AG ("Altamira Medica") 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 had a term of 18 months and carried interest at 8% p.a., which would not be paid in cash but added to the loan outstanding amount. At maturity, the unconverted outstanding amount of the loan including accrued interest would become payable in cash. Altamira Medica 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 Medica 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 ($27.00 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 Medica 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 Medica 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 Medica. By December 31, 2020, an amount of CHF 895,455 has been converted into 36,850 common shares of the Company (at a conversion price of $27.00).

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 Medica 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 25,841 common shares of of the Company at a conversion price of $27.00. 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.

32. Warrants from Public Offering

On February 21, 2017, the Company completed a public offering (the “February 2017 Offering”) of 500,000 (pre-merger) common shares with a nominal value of CHF 8.00 each and 500,000 (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 75,000 (pre-merger) additional common shares and/or 75,000 (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 67,500 (pre-merger) warrants.

Consequently, the Company issued warrants to purchase up to 397,250 (pre-merger) of its common shares at an exercise price of $24.00 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 1,986 common shares at an exercise price of $4,800.00. 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. The warrants issued in the February 2017 public offering expired on February 22, 2022, without any warrants having been exercised.

On January 30, 2018, the Company issued warrants in connection with a direct offering of 3,125 common shares, each warrant entitling its holder to purchase 0.6 common shares at an exercise price of $2,000.00 per common share. As of December 31, 2021, the outstanding warrants issued in such offering were exercisable for up to 1,875 common shares at an exercise price of $2,000.00 per common share. As of December 31, 2022 the fair value of the warrants amounted to CHF 0 (2021: CHF 1,233). The revaluation gain of the derivative for the twelve months ended December 31, 2022 amounted to CHF 1,233 (2021: CHF 5,085). Since its initial recognition on January 30, 2018, the fair value of the warrants has decreased by CHF 2,483,747 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 15,705 common shares, and Series B warrants entitling its holder to purchase 0.25 of a common share for an aggregate of 11,218 common shares in connection with the July 2018 Registered Offering of 44,872 common shares, each warrant entitling its holder to purchase one common share at an original exercise price of CHF 156.00 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, 7,261 Series A warrants were exercised for an aggregate amount of CHF 1,132,762 and 7,161 Series B warrants were exercised for an aggregate amount of CHF 1,117,125.

As of December 31, 2019, 7,161 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, 2022 and 2021.

33. Revision of Prior Period Financial Statements

In connection with the preparation of our consolidated financial statements, we identified an immaterial error with regard to advance payments for research and development costs and related tax credits for the annual period ended December 31, 2021. The error was mainly related to investigator float payments to a contract research organization. Due to COVID and other reasons, the scheduled services had not been provided by the end of the year and therefore the payments should have been recognized as advance payments and not as R&D expenses. We evaluated the error and determined that the related impact was not material to our financial statements for any prior periods, but that correction of the impact of the error would be significant to our results of operations for the six months ended June 30, 2022. Accordingly, we have revised previously reported financial information for such immaterial error, as previously disclosed in our Annual Report on Form 20-F for the year ended December 31, 2021. A summary of revisions to our previously reported financial statements presented herein for comparative purposes is included below.

Revised consolidated Balance Sheet

	As of December 31, 2021		
	As reported	**Adjustment**	**As revised**
Other receivables	917,833	(246,493)	671,340
Prepayments	996,910	578,216	1,575,126
Total current assets	**3,759,901**	**331,723**	**4,091,624**
Total assets	**18,838,598**	**331,723**	**19,170,321**
Accumulated deficit	(176,018,660)	331,723	(175,686,937)
Total shareholders’ equity attributable to owners of the company	**12,704,528**	**331,723**	**13,036,251**
Total equity and liabilities	**18,838,598**	**331,723**	**19,170,321**

Revised consolidated Statement of Profit or Loss and Other Comprehensive Loss

	Year ended December 31, 2021		
	As reported	**Adjustment**	**As revised**
Other income	460,710	(246,493)	214,217
Research and development	(8,939,037)	578,216	(8,360,821)
Total operating expenses	**(15,137,338)**	**331,723**	**(14,805,615)**
Operating loss	**(17,099,793)**	**331,723**	**(16,768,070)**
Loss before tax	**(17,368,546)**	**331,723**	**(17,036,823)**
Net loss attributable of owners of the Company	**(17,390,166)**	**331,723**	**(17,058,443)**
Total comprehensive loss attributable to owners of the Company	**(17,124,410)**	**331,723**	**(16,792,687)**
Basic and diluted loss per share	**(26.26)**	**0.50**	**(25.76)**

Basic and diluted loss per share as presented in the financial statements as of December 31, 2021, prior to the one-for-twenty reverse share split on October 25, 2022 was CHF 1.31, and the revised number would have been CHF 1.29.

Revised consolidated Statement of Cash Flows

We revised our consolidated statement of cash flows for the year ended December 31, 2021. There was no impact on net cash used in operating activities.

	Year ended December 31, 2021		
	As reported	**Adjustment**	**As revised**
Net loss	(17,390,166)	331,723	(17,058,443)
Changes in:			
Trade and other receivables	(586,612)	246,493	(340,119)
Prepayments	(719,321)	(578,216)	(1,297,537)
Cash used in operating activities	**(13,627,738)**	**—**	**(13,672,738)**

34. Events after the balance sheet date

On February 17, 2023 a Special General Meeting of the shareholders of the Company approved the increase of its authorized share capital from CHF 1,400,000 divided into 5,000,000 common shares of CHF 0.20 each and 20,000,000 preference shares of CHF 0.02 each to CHF 5,400,000 divided into 25,000,000 common shares of CHF 0.20 each and 20,000,000 preference shares of CHF 0.02 each, by the creation of an additional 20,000,000 common shares of CHF 0.20 each ranking pari-passu with the existing common shares of the Company.

On April 13, 2023, the Company and FiveT IM entered into an amendment to the FiveT Loan (the "FiveT Loan Amendment"), which amended the conversion price of the FiveT Loan to a fixed price equal to the lower of (a) the mean daily trading volume weighted average price ("VWAP") of the Company's common shares on the Nasdaq Stock Market on the 20 trading days preceding the effective date of the FiveT Loan Amendment or (b) 90% of the VWAP on the effective date of the FiveT Loan Amendment. From April 13, 2023 to April 17, 2023, FiveT IM converted the entire FiveT Loan into an aggregate of 4,341,012 common shares at an average conversion price of $1.4475 per share. As a result, the FiveT Loan is no longer outstanding and has been terminated.

On May 1, 2023, the Company entered into a convertible loan agreement (the "2023 FiveT Loan Agreement") with FiveT IM, pursuant to which FiveT IM has agreed to loan to the Company CHF 2,500,000, which bears interest at the rate of 10% per annum and matures 22 months from May 4, 2023. FiveT IM will have the right to convert all or part of the convertible loan, including accrued and unpaid interest, at its option, into common shares, subject to the limitation that FiveT own no more than 4.99% of the common shares at any time. The conversion price was fixed at CHF 1.42 per common share (subject to adjustment for share splits or other similar events). Further, FiveT IM received warrants to purchase an aggregate of 1,625,487 common shares at an exercise price of CHF 1.538 per common share, which may be exercised up to five years.

Commencing 60 days after May 4, 2023, but not before July 1, 2023 and subject to availability of an effective registration statement, the Company must repay at least 1/20th of the outstanding loan plus accrued interest pro rata in monthly tranches which, at the Company's discretion, may be paid at any time during the month either in: (i) cash plus 3% or (ii) common shares, or a combination of both. Such shares will be priced at the lower of (i) the mean daily trading volume weighted average price for the common shares on the 20 trading days preceding the repayment date or (ii) 90% of the daily trading volume weighted average price for common shares on the repayment date. The Company may prepay all or part of the convertible loan after three months. Until March 31, 2024, FiveT may cause the Company to redeem the convertible loan for cash in an amount of up to 20% of the cash proceeds from an out-licensing or divestiture transaction executed by the Company that results in gross cash proceeds of at least CHF 1,000,000.

On May 12, 2023, the Company and the Lenders entered into an amendment to the loan agreement concluded on September 9, 2022 (the "September 2022 Loan Amendment"), which extended the maturity date of the loan from May 31, 2023 to July 31, 2023, introduced a right for Lenders to convert the loan into common shares of the Company at CHF 1.12 per common share, which is the Swiss Franc equivalent of 120% of the mean daily trading volume weighted average price for common shares on the NASDAQ stock exchange on the 20 trading days preceding the date of the September 2022 Loan Amendment, and a right for the Company to repay the loan in common shares of the Company priced at the lower of (i) the mean daily trading volume weighted average price for the common shares on the 20 trading days preceding the repayment date or (ii) 90% of the daily trading volume weighted average price for common shares on the repayment date, and lowered the strike price for the Warrants attached to the loan to CHF 0.881 per common share, which is the Swiss Franc equivalent of the trading volume weighted average price for common shares on the NASDAQ stock exchange on trading day preceding the date of the September 2022 Loan Amendment.

On May 12, 2023, the Company and the Private Lenders entered into an amendment to the loan agreement concluded on December 28, 2022 (the December 2022 Loan Amendment"), which extended the maturity date of the loan from May 31, 2023 to July 31, 2023 and lowered the strike price for the Warrants attached to the loan to CHF 0.881 per common share, which is the Swiss Franc equivalent of the trading volume weighted average price for common shares on the NASDAQ stock exchange on trading day preceding the date of the December 2022 Loan Amendment.

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 2022 Reverse Share Split and the 2019 Reverse Share Split and the increase of authorized share capital of the Company on June 30, 2020, reduction of issued share capital on July 29, 2020, reduction of authorized share capital on September 29, 2020, increase of authorized share capital on September 29, 2022 and increase of authorized share capital on February 17, 2023 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, 2022, our authorized share capital consisted of 5,000,000 common shares, par value CHF 0.20 per share, and 20,000,000 preference shares, par value CHF 0.02 per share, and there were 1,180,053 common shares issued and outstanding, excluding 157,730 common shares issuable upon exercise of options and 99,171 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, 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 five directors. 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.

Mergers and similar arrangements

Delaware Corporate Law

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.

Bermuda Corporate Law

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.	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.
Classified boards are permitted.	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.	

Directors' fiduciary duties

Delaware Corporate Law

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.

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.

Bermuda Corporate Law

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 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

Delaware Corporate Law

A Delaware corporation may, in its certificate of incorporation, eliminate the right of shareholders to act by written consent.

Bermuda Corporate Law

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.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
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.

Variation of rights of shares

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
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

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
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

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
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 4.38

Amendment No. 6 to
Convertible Loan Agreement

April 12, 2023

FiveT Investment Management Ltd.
Suite 5B201, 2nd Floor, One Nexus Way
Camana Bay, Grand Cayman KY1-1108
Cayman Islands

Ladies and Gentlemen:

Reference is made to the Convertible Loan Agreement dated February 4, 2022, as amended on January 26, 2023, March 9, 2023, March 23, 2023, March 27, 2023, and April 3, 2023 (the "**Agreement**"), between FiveT Investment Management Ltd. (the "**Lender**") and Altamira Therapeutics Ltd. (the "**AMTL**"). The parties hereby agree that, effective as of the date hereof, the Agreement shall be amended as follows:

1. Section 14 is amended and restated in its entirety as follows:

"(a) In the event of a public or private offering by AMTL of Common Shares, other than through equity line or "at-the-market" programs (a **Qualifying Offering**), AMTL will make a partial repayment of the principal amount of the Loan and accrued and unpaid interest, comprised of (i) a USD amount equal to the accrued and unpaid interest on the principal amount of the Loan in cash and (ii) newly issued Common Shares in an amount equaling 9.9% of the total outstanding Common Shares of AMTL post-issuance and after giving effect to such offering, with such Common Shares being valued for purposes of such repayment at the effective offering price per Common Share in such offering, and with such cash repayment in (i) and offering price in (ii) being converted into Swiss Francs at the midpoint of the interbank exchange rate shown by UBS at 4:00 pm Central European Time on the Business Day immediately preceding the date of pricing or execution of the Qualifying Offering (the **Qualifying Offering Price**), with delivery of such repayment to be no later than two Business Days after the closing of such offering (the "**Repayment Date**"), it being agreed that such Common Shares shall be free of any resale restrictions under the Securities Act. Notwithstanding anything herein to the contrary, and for the avoidance of doubt, to the extent that securities of AMTL other than Common Shares ("**Other Offered Securities**") are issued and sold in a Qualifying Offering in fixed combinations accompanying the Common Shares sold in such Qualifying Offering, including, for example, as warrant coverage, Lender shall be issued the same such Other Offered Securities along with the Common Shares to be issued in (ii) above in the same proportion of Common Shares and Other Offered Securities as applies to investors purchasing securities in such Qualifying Offering.

(b) In addition, on the Repayment Date, after taking into account the repayment under Section 14(a), AMTL shall have the option to cause the Lender to convert any remaining outstanding principal amount of the Loan and accrued and unpaid Interest into a warrant, substantially in the form attached hereto as Annex 14 (the **Pre-Funded Warrant**), having an exercise price of CHF 0.01 per Common Share, and giving Lender the right to purchase from AMTL a number of Common Shares (the **Warrant Shares**) equal to (A) the total remaining outstanding principal amount of the Loan and accrued and unpaid Interest divided by (B) the Qualifying Offering Price less CHF 0.01, *provided*, *however*, that AMTL shall only be entitled to cause the Lender to convert an amount of the remaining outstanding principal amount of the Loan and accrued and unpaid Interest into a Pre-Funded Warrant to the extent that at the time of such conversion AMTL has sufficient authorized and unissued Common Shares to be issued upon the exercise thereof. Notwithstanding anything herein to the contrary, and for the avoidance of doubt, to the extent that Other Offered Securities are issued and sold in the related Qualifying Offering in fixed combinations accompanying the Common Shares sold in such Qualifying Offering, including, for example, as warrant coverage, Lender shall also be issued additional Other Offered Securities with respect to each Warrant Share in the same proportion of Common Shares and Other Offered Securities as applies to investors purchasing securities in such Qualifying Offering. Further, for the avoidance of doubt, any outstanding amount under the Loan that is not converted into the Pre-Funded Warrant will be due and payable in cash on the Maturity Date. From the date of issuance of the Pre-Funded Warrant until February 21, 2024, upon the occurrence of each and every out-licensing or divestiture transaction executed by AMTL that results in gross cash proceeds of CHF 1,000,000 or more (a **Qualifying Transaction**), the Lender, by providing written notice (a **Redemption Notice**) within five Business Days after the closing of the Qualifying Transaction, may cause AMTL to redeem for cash all or portions of the Pre-Funded Warrant, represented by the amount of Warrant Shares issuable thereunder, in an amount of up to 40% of the cash proceeds from the Qualifying Transaction, with the amount of the Pre-Funded Warrant being redeemed equal to (A) the desired redemption amount divided by (B) the Qualifying Offering Price less CHF 0.01, with delivery of such redemption amount to be no later than five Business Days after the later of (i) the receipt by AMTL of the applicable Redemption Notice and (ii) the receipt by AMTL of the cash proceeds of the Qualifying Transaction. Upon any such redemption, a proportionate number of Other Offered Securities, if any, held by Lender will also be deemed redeemed together with the applicable portion of the Pre-Funded Warrant. AMTL shall provide immediate written notification to Lender of the signing and closing of any and all Qualifying Transactions."

(c) Notwithstanding anything contained herein or in the Pre-Funded Warrant, if any, to the contrary, in the event that as a result of a Qualifying Offering there is not sufficient authorized and unissued Common Shares available to be issued upon the exercise of all or any portion of (i) the Pre-Funded Warrant and/or (ii) the Other Offered Securities, if any, issuable hereunder to Lender with respect to Warrant Shares underlying the Pre-Funded Warrant, then Lender hereby agrees to waive any requirements set forth in the Pre-Funded Warrant and such Other Offered Securities requiring AMTL to keep reserved a sufficient amount of authorized and unissued Common Shares, and Lender agrees that it will not exercise the Pre-Funded Warrant or such Other Offered Securities to the extent there are insufficient authorized and unissued Common Shares, in each case until AMTL increases its amount of authorized Common Shares at its upcoming annual meeting of its shareholders."

Except as expressly set forth herein, the Agreement remains in full force and effect. All of the amendments set forth herein shall be deemed to have been made simultaneously. This amendment shall be governed by, and construed in accordance with the substantive laws of Switzerland (to the exclusion of conflicts of laws principles and provisions). This amendment may be executed in counterparts, and delivery thereof may be made by facsimile or electronic transmission.

[*Signature Page Follows.*]

If the foregoing correctly sets forth the understanding between us, please so indicate in the space provided below for that purpose.

Very truly yours,

ALTAMIRA THERAPEUTICS LTD.

By: /s/ Thomas Meyer
Name: Thomas Meyer
Title: Chairman and CEO

ACCEPTED as of the date first above written:

FIVET INVESTMENT MANAGEMENT LTD.

By: /s/ Benjamin Kressler
Name: Benjamin Kressler
Title: Authorized Person

[*Signature Page to Amendment No. 6 to Convertible Loan Agreement*]

Exhibit 4.40

Form of Amendment No. 1 to
Loan Agreement

Dear Sir:

Reference is made to the Loan Agreement dated December 28, 2022 (the "**Agreement**"), between you (the "**Lender**") and Altamira Therapeutics Ltd. (the "**AMTL**"). The parties hereby agree that, effective as of the date hereof, the Agreement shall be amended as follows:

1. Section 4 is amended and restated in its entirety as follows:

Subject to Sections 6 (Event of Default) and 7 (Change of Control Transaction), the total outstanding principal amount under the Loan including all accrued and unpaid Interest thereon shall become due and payable in cash as of July 31, 2023 (the **Maturity Date**).

2. Section 8 is amended and restated in its entirety as follows:

8 Warrants

a. Each Loan Unit bears 6,740 Common Share purchase warrants (Warrants) which gives the Lender the right to purchase 6,740 Common Shares between December 28, 2022 and December 27, 2027 for CHF 0.881 each, pursuant to the Warrant form in Annex 8(a) (Warrant Exercise). The exercise price for each Warrant was determined based on the VWAP of the Company's share price on Nasdaq on May 11, 2023 (USD 0.985), converted at the CHF/USD rate as reported by UBS, Zurich on May 11, 2023 at 4 pm (0.8943).

b. As soon as practicable (and in any event within 30 calendar days of the Effective Date), AMTL shall file a registration statement on Form F-3 (or other appropriate form) providing for the resale by the Lender of the Common Shares issued and issuable upon any Warrant Exercise. AMTL shall use best efforts to cause such resale registration statement to be-come effective within 60 days following the Effective Date (or, in the event of a "full review" by the SEC, the 90th calendar day following the Effective Date) and to keep the registration statement effective at all times until the earlier of (1) the date as of which the Lender may sell Common Shares from the Warrant Exercise without restriction or limitation pursuant to Rule 144 (as defined below) and without the requirement to be in compliance with Rule 144(c)(1) (or any successor thereto) promulgated under the Securities Act or (2) the date on which the Lend-er no longer own any Common Shares from the Warrant Exercise.

[*Signature Page Follows.*]

If the foregoing correctly sets forth the understanding between us, please so indicate in the space provided below for that purpose.

Lender	
Place, date	
AMTL	**Altamira Therapeutics Ltd.**
Place, date	Name: Thomas Meyer Function: CEO
Place, date	Name: Marcel Gremaud Function: CFO

Amendment No. 2 to
Loan Agreement

May 12, 2023

FiveT Investment Management Ltd.
Suite 5B201, 2nd Floor, One Nexus Way
Camana Bay, Grand Cayman KY1-1108
Cayman Islands

Dominik Lysek
[***]

Thomas Meyer
[***]

Gentlemen:

Reference is made to the Loan Agreement dated September 9, 2022 (the "**Agreement**"), as amended on April 6, 2023, between FiveT Investment Management Ltd., Dominik Lysek and Thomas Meyer (the "**Lenders**") and Altamira Therapeutics Ltd. (the "**AMTL**"). The parties hereby agree that, effective as of the date hereof, the Agreement shall be amended as follows:

1. The Preamble is amended and restated in its entirety as follows:

A. AMTL is a limited company organized and existing under the laws of Bermuda with its registered office in Hamilton, Bermuda. As of the date hereof, AMTL has an authorized share capital of CHF 5,000,000 under which 6,988,999 common shares with a nominal value of CHF 0.20 each are issued and outstanding (Common Shares). The Common Shares are listed on the NASDAQ under the ticker code CYTO and the international securities identification number (ISIN) BMG0360L2099.

B. The Lenders wish to grant AMTL a loan with warrants to cover AMTL's financial needs.

C. The Lenders shall have the right to shall have the right to convert such loan into Common Shares in accordance with and subject to the terms of this Agreement.

2. Section 4 is amended and restated in its entirety as follows:

Subject to Sections 5 (Early Repayment), 6 (Event of Default), 7 (Change of Control Transaction) and 8 (Conversion; Warrants), the total outstanding principal amount under the Loan including all accrued and unpaid Interest thereon shall become due and payable in cash no later than July 31, 2023 (the **Maturity Date**).

3. Section 5 is amended and restated in its entirety as follows:

a. AMTL may elect in its sole discretion to repay in cash the total outstanding principal amount under the Loan including all accrued and unpaid Interest thereon (the Repayment Amount), at any time from the date which is three (3) months following the Effective Date by giving 1 (one) month prior written notice to the Lenders (the Repayment Notice Period).

b. The repayment shall be made within 10 (ten) calendar days following expiry of the Repayment Notice Period.

c. Subject to availability of an effective registration statement as per Section 8.1(e), AMTL may repay at its option any Loan Unit plus accrued interest in Common Shares (the Repayment Shares). Repayment Shares will be priced at the lower of (i) the mean daily trading volume weighted average price for Common Shares on the NASDAQ stock exchange on the 20 Trading Days preceding the Repayment Date or (ii) 90% of the daily trading volume weighted average price for Common Shares on the NASDAQ stock exchange on the Repayment Date (subject to adjustment for share splits, share dividends, recapitalizations, reorganizations, reclassification, combinations, reverse share splits or other similar events occurring after the Disbursement Date), but in no case lower than the nominal value of the Common Shares, converted into Swiss Francs at the midpoint of the interbank exchange rate shown by UBS on the day of receipt of the applicable notice of the payment of Repayment Shares at 4:00 pm Central European Time (the Repayment Price).

4. Section 8 is amended and restated in its entirety as follows:

8 Conversion; Warrants

8.1 Conversion

a. Any Lender has the right to request (the Conversion Right) full or partial conversion (Conversion) of the total outstanding principal amount under a Loan Unit including all accrued and unpaid Interest thereon as per the date of the Conversion Notice (the Conversion Amount), into Common Shares; the number of such Common Shares issuable or deliverable to the Lender shall be equal to the quotient obtained by dividing the Conversion Amount by the Conversion Price (such number of such Common Shares, the Conversion Shares). Any fractional Conversion Shares resulting from any Conversion shall be disregarded and the number of Conversion Shares to be issued or delivered to the Lender shall be rounded down to the next whole number without any further compensation.

b. The Lender may exercise the Conversion Right at any time from the date of effectiveness of a Registration Statement for the Conversion Shares pursuant to Section 8.1(e) until no later than the Maturity Date by giving written notice to AMTL (the Conversion Notice). The Conversion Notice shall be irrevocable and cannot be cancelled or withdrawn by the Lender.

c. The conversion price applicable for any Conversion (the Conversion Price) shall be the amount equal to 120% of the mean daily trading volume weighted average price for Common Shares on the NASDAQ stock exchange on the 20 Trading Days preceding the date of this Amendment (the Reference VWAP) (subject to adjustment for share splits, share dividends, recapitalizations, reorganizations, reclassification, combinations, reverse share splits or other similar events occurring after the date hereof), converted into Swiss Francs at the midpoint of the interbank exchange rate shown by UBS on the day preceding the date of this Amendment at 4:00 pm Central European Time.

d. AMTL shall take all actions, execute all documents and make all declarations as may be necessary or appropriate, and the Lender shall cooperate as necessary and appropriate, to give full effect to the Conversion and ensure that the Conversion Shares are duly issued or delivered to the Lender by crediting the depository account of the Lender (as designated by the Lender in the Conversion Notice) by no later than 2 (two) Trading Days following the date of receipt of the original of the Conversion Notice. AMTL shall procure that any Conversion Shares issued or delivered to the Lender under this Agreement will, no later than 2 (two) Trading Days after the date on which the Conversion Shares have been issued or delivered, be listed on the NASDAQ and become tradable without any restrictions on the NASDAQ.

e. As soon as practicable (and in any event within 15 calendar days of the Disbursement Date), AMTL shall file a registration statement on Form F-3 (or other appropriate form) providing for the resale by the Lender of the Conversion Shares issued and issuable upon any Conversion and Repayment Shares issued and issuable under Section 5(c) (the Registration Statement). Such registration statement shall cover an amount (the Initial Required Amount") of Common Shares equal to (i) the principal amount of the Loan plus accrued interest on the date of the Amendment divided by (ii) the Reference VWAP. AMTL shall use best efforts to cause such resale registration statement to become effective within 45 days following the Disbursement Date (or, in the event of a "full review" by the SEC, the 90th calendar day following the Disbursement Date) and to keep the registration statement effective at all times until (the following date, the Registration End Date) the earlier of (1) the date as of which the Lender may sell Conversion Shares and Repayment Shares without restriction or limitation pursuant to Rule 144 (as defined below) and without the requirement to be in compliance with Rule 144(c)(1) (or any successor thereto) promulgated under the Securities Act or (2) the later of (x) the date on which no principal or Interest remains outstanding under the Loan or (y) the date on which the Lender no longer owns any Conversion Shares or Repayment Shares. In addition, if at any time following the three-calendar month anniversary of the Disbursement Date but prior to the Registration End Date AMTL has issued a number of Conversion Shares and/or Repayment Shares that equals or exceeds the Initial Required Amount then AMTL shall use commercially reasonable efforts to file one or more additional resale registration statements so as to cover any additional Common Shares that may be issuable under this Agreement at such time, determined using the Reference VWAP.

8.2 Warrants

Each Loan Unit bears 6,944 Common Share purchase warrants (Warrants) which gives the Lenders the right to purchase 6,944 Common Shares between October 1, 2022 and September 30, 2027 for CHF 0.881 each, pursuant to the Warrant form in Annex 8(a) (Warrant Exercise). The exercise price for each Warrant was determined based on the VWAP of the Company's share price on Nasdaq on May 11, 2023 (USD 0.985), converted at the CHF/USD rate as reported by UBS, Zurich on May 11, 2023 (CHF/USD 0.8943).

As soon as practicable (and in any event within 21 calendar days of the Effective Date), AMTL shall file a registration statement on Form F-3 (or other appropriate form) providing for the resale by the Lenders of the Common Shares issued and issuable upon any Warrant Exercise. AMTL shall use best efforts to cause such resale registration statement to become effective within 45 days following the Effective Date (or, in the event of a "full review" by the SEC, the 90th calendar day following the Effective Date) and to keep the registration statement effective at all times until the earlier of (1) the date as of which the Lenders may sell Common Shares from the Warrant Exercise without restriction or limitation pursuant to Rule 144 (as defined below) and without the requirement to be in compliance with Rule 144(c)(1) (or any successor thereto) promulgated under the Securities Act or (2) the date on which the Lenders no longer own any Common Shares from the Warrant Exercise.

[*Signature Page Follows*.]

If the foregoing correctly sets forth the understanding between us, please so indicate in the space provided below for that purpose.

Lender	**FiveT Investment Management Ltd.**
Pfaeffikon, 12-05-2023	/s/ Benjamin Michael Kressler
Place, date	Name: Function:
Dominik Lysek	
[***], 12-05-2023	/s/ Dominik Lysek
Place, date	
Thomas Meyer	
Basel, 14-05-2023	/s/ Thomas Meyer
Place, date	
AMTL	**Altamira Therapeutics Ltd.**
Basel, 14-05-2023	/s/ Thomas Meyer
Place, date	Name: Thomas Meyer Function: CEO
Hamilton, 12-05-2023	/s/ Marcel Gremaud
Place, date	Name: Marcel Gremaud Function: CFO

[*Signature Page to Amendment No. 1 to Loan Agreement*]

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: May 16, 2023

/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: May 16, 2023

/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, 2022 (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: May 16, 2023

/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, 2022 (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: May 16, 2023

/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, 333-261127, 333-264298 and 333-267584 on Form F-3 of our report dated May 16, 2023, relating to the financial statements of Altamira Therapeutics Ltd. appearing in this Annual Report on Form 20-F for the year ended December 31, 2022.

Deloitte AG

/s/ Roland Mueller	/s/ Adrian Kaeppeli
Auditor in Charge	

Zurich, Switzerland
May 16, 2023