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, 2020

OR

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

For the transition period from _____ to _____

OR

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

Date of event requiring this shell company report

Commission file number: 001-36582

AURIS MEDICAL HOLDING LTD.

(Exact name of Registrant as specified in its charter)

Bermuda
(Jurisdiction of incorporation)

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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Lowenstein Sandler LLP
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New York, NY 10020
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Securities registered or to be registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Shares, par value CHF 0.01 per share	EARS	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: 11,417,159

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 during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

☒ Yes ☐ No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act. (Check one):

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

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

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

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

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

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

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

☐ Item 17 ☐ Item 18

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

☐ Yes ☒ No

AURIS MEDICAL HOLDING LTD.

TABLE OF CONTENTS

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

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

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

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

FORWARD-LOOKING STATEMENTS

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

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

- our operation as a development-stage company with limited operating history and a history of operating losses;
- the COVID-19 “coronavirus” outbreak, 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 outcome of our review of strategic options and of any action that we may pursue as a result of such review;
- our dependence on the success of AM-125, AM-201, AM-301, Keyzilen® (AM-101) and Sonsuvi® (AM-111), which are still in clinical development, 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, which is necessary before they can be commercialized;
- if our product candidates obtain regulatory approval, 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;
- the chance that we do not obtain orphan drug exclusivity for Sonsuvi®, which would allow our competitors to sell products that treat the same conditions;
- 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 relationships with INSERM or Xigen 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. Selected Financial Data

The following tables summarize our consolidated financial data as of the dates and for the periods indicated. The consolidated financial statement data as of December 31, 2020 and 2019 and for each of the years in the three-year period ended December 31, 2020 has been derived from our consolidated financial statements presented elsewhere in this Annual Report, which have been prepared in accordance with International Financial Reporting Standards as issued by the International Accounting Standards Board ("IFRS"). The consolidated financial data for the years ended December 31, 2017 and 2016 has been derived from our audited consolidated financial statements which have been prepared in accordance with IFRS and which have not been included herein.

This financial information should be read in conjunction with "Item 5-Operating and Financial Review and Prospects" and our consolidated audited financial statements, including the notes thereto, included in this Annual Report.

	For the years ended December 31,				
	2020	2019	2018	2017	2016
	(in thousands of CHF except for share and per share data)				
Profit or Loss and Other Comprehensive Loss:					
Other income	174	—	—	—	—
Research and development	(2,863)	(3,325)	(6,690)	(19,211)	(24,777)
General and administrative	(2,594)	(3,934)	(4,264)	(5,150)	(5,447)
Operating loss	**(5,283)**	**(7,259)**	**(10,954)**	**(24,361)**	**(30,224)**
Interest income	—	18	—	54	68
Interest expense	(135)	(29)	(1,070)	(1,640)	(829)
Foreign currency exchange gain/(loss), net	(333)	(219)	(140)	(825)	(100)
Revaluation gain from derivative financial instruments	(2,250)	664	1,350	3,372	291
Transaction costs	(220)	—	(520)	(1,027)	—
Loss before tax	**(8,221)**	**(6,825)**	**(11,334)**	**(24,427)**	**(30,794)**
Income tax gain/(loss)	21	194	(162)	18	131
Income tax expense	—	—	—	—	—
Net loss attributable to owners of the Company	**(8,200)**	**(6,631)**	**(11,496)**	**(24,409)**	**(30,663)**
Other comprehensive loss:					
Items that will never be reclassified to profit or loss:					
Remeasurements of defined benefits liability	(26)	(72)	1,277	272	(394)
Items that are or may be reclassified to profit or loss:					
Foreign currency translation differences	89	16	(11)	50	(20)
Other comprehensive income/(loss)	**63**	**(56)**	**1,266**	**322**	**(414)**
Total comprehensive loss attributable to owners of the Company	**(8,137)**	**(6,687)**	**(10,230)**	**(24,087)**	**(31,077)**
Net loss per share					
Net loss per share, basic and diluted(1)	(1.36)	(2.28)	(14.46)	(111.61)	(178.60)
Weighted-average number of shares used to compute net loss per common share, basic and diluted	6,014,146	2,909,056	795,043	218,709	171,646

(1) Basic net loss per common share and diluted net loss per common share are the same. See Note 21 to our audited consolidated financial statements included elsewhere in this Annual Report.

	As of December 31,				
	2020	2019	2018	2017	2016
	(in thousands of CHF)				
Statement of Financial Position Data:					
Cash and cash equivalents	11,259	1,385	5,393	14,973	32,442
Total assets	20,799	9,226	9,877	17,826	35,658
Total liabilities	4,029	3,190	6,227	19,888	21,515
Share capital	114	1,650	710	19,350	13,732
Total shareholders' (deficit)/equity attributable to owners of the Company	16,770	6,036	3,650	(2,162)	14,143

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 ordinary 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 development-stage company and have a limited operating history and a history of operating losses. We anticipate that we will continue to incur losses for the foreseeable future.
- We expect that we will need substantial additional funding before we can expect to become profitable from sales of our products. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- We are in the process of evaluating potential next steps in the development of our late-stage product candidates Keyzilen® and Sonsuvi®. We cannot give any assurance that these candidates will continue to be developed, receive regulatory approval or be successfully commercialized or partnered.
- We depend entirely on the success of AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, which are still in clinical development. If our clinical trials are unsuccessful, we do not obtain regulatory approval or we are unable to commercialize AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, 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, and therefore our receipt of necessary regulatory approvals could be delayed or prevented.
- Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results. If clinical trials of our drug product candidates are prolonged or delayed, we may be unable to obtain required regulatory approvals, and therefore be unable to commercialize our drug product candidates on a timely basis or at all.
- If serious adverse, undesirable or unacceptable side effects are identified during the development of our product candidates or following approval, if any, we may need to abandon our development of such product candidates, the commercial profile of any approved label may be limited, or we may be subject to other significant negative consequences following marketing approval, if any.
- We depend on enrollment of patients in our clinical trials for our product candidates. If we are unable to enroll patients in our clinical trials, our research and development efforts could be materially adversely affected.
- We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or at the commercial stage; and our product liability insurance may not cover all damages from such claims.
- We cannot give any assurance that any of our drug product candidates will receive regulatory approval, which is necessary before they can be commercialized.
- We cannot give any assurance that our medical device candidate AM-301 will receive regulatory clearance, which is necessary before it can be commercialized.
- Substantial additional data may need to be generated in order to obtain marketing approval for AM-125.

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

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

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

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

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

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

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

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

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

Risks Related to Our Business and Industry

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

We are a development-stage biopharmaceutical company with limited operating history. Since inception, we have incurred significant operating losses. We incurred net losses (defined as net loss attributable to owners of the Company) of CHF 8.2 million, CHF 6.6 million and CHF 11.5 million for the years ended December 31, 2020, 2019 and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of CHF 160.6 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. 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. In our financial year ended December 31, 2020, we incurred CHF 5.3 million in operating loss and capitalized development expenditures of its AM-125 project of CHF 2.3 million, and we expect our total cash need in 2021 to be in the range of CHF 11.5 to 13 million for our expected total operating expenses of CHF 7 to 7.5 million and our expected capitalized research and development costs of CHF 4.5 to 5.5 million. Further cash needs may arise in 2021 related to the manufacture of AM-301 as well as marketing and sale activities as we intend to commercialize the product in selected markets; these cash needs may initially not be covered by cash flows from product revenues.

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

We have no products approved for commercialization and have never generated any 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 a product candidate approved for commercialization and begin to generate revenues from product sales.

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

We have no products approved for commercialization and have never generated any revenue. Our ability to generate revenue and achieve profitability depends on our ability to successfully complete the development of, and obtain the marketing approvals necessary to commercialize, one or more of our product candidates. We do not anticipate generating revenue from product sales unless and until we obtain regulatory approval or clearance for, and commercialize, AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®. Our ability to generate future revenue from product sales depends heavily on our success in many areas, including but not limited to:

- completing research and clinical development of our product candidates;
- obtaining marketing approvals for our product candidates, including AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, for which we will have to complete clinical trials;
- developing a sustainable and scalable manufacturing process for any approved product candidates and maintaining supply and manufacturing relationships with third parties that can conduct the process and provide adequate (in amount and quality) products to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain marketing approval, either directly or with a collaborator or distributor;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

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

We may be unable to develop and commercialize AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®AM-201 or any other product candidate and, even if we do, may never achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a semiannual or annual basis. Our failure to become and remain profitable would decrease the value of the Company and could impair our ability to raise capital, expand our business or continue our operations.

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

We expect our research and development expenses to remain significant in connection with our ongoing clinical development activities, particularly as we initiate new trials with AM-125, AM-201 and AM-301, may initiate new trials of Keyzilen® and Sonsuvi® and may initiate pre-clinical and clinical development of other product candidates. We expect our total cash need in 2021 to be in the range of CHF 11.5 to 13.0 million for our expected total operating expenses of CHF 7 to 7.5 million and our expected capitalized research and development costs of CHF 4.5 to 5.5 million. As of December 31, 2020, our cash and cash equivalents were CHF 11.3 million. Our assumptions may prove to be wrong, and we may have to use our capital resources sooner than we currently expect. If we are unable to raise capital when needed, we could be forced to delay, suspend, reduce or terminate our product development programs or commercialization efforts. Also, should we fail to raise sufficient funds to cover our operating expenditures for at least a 12 month period, we may no longer be considered a "going concern." The lack of a going concern assessment may negatively affect the valuation of the Company's investments in its subsidiaries and result in a revaluation of these holdings. The board of directors will need to consider the interests of our creditors and take appropriate action to restructure the business if it appears that we are insolvent or likely to become insolvent. Our future funding requirements will depend on many factors, including but not limited to:

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

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

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

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

We do not have a history of commercializing 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 pharmaceutical products.

We are in the process of evaluating potential next steps in the development of our late-stage product candidates Keyzilen® and Sonsuvi®. We cannot give any assurance that these candidates will continue to be developed, receive regulatory approval or be successfully commercialized or partnered.

We do not have any products that have gained regulatory approval. We have two late-stage clinical product candidates, (i) Keyzilen® (AM-101), which is being developed for the treatment of acute inner ear tinnitus and (ii) Sonsuvi® (AM-111), which is being developed for the treatment of acute inner ear hearing loss. On March 13, 2018, we announced that the TACTT3 Phase 3 clinical trial with Keyzilen® did not meet its primary efficacy endpoint of a statistically significant improvement in the Tinnitus Functional Index, or TFI, score from baseline to Day 84 in the active treated group compared to placebo either in the overall population or in the otitis media subpopulation. This followed our announcement in August 2016 that, TACTT2, the previously conducted Phase 3 sister trial with Keyzilen®, did not meet its two co-primary efficacy endpoints of statistically significant changes in tinnitus loudness and tinnitus burden compared to placebo.

On April 25, 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 following traumatic cochlear injury and provide confirmatory efficacy data to support a filing for marketing authorization. On September 13, 2019, we announced that we had 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®. If we continue development of Keyzilen® with a pivotal Phase 2/3 trial in order to pursue regulatory approval, which may require additional studies and trials in the future, we would need to obtain additional funds for any such additional study or studies, and we may be unable to do so. We currently aim to implement the further development of Keyzilen® with non-dilutive funding, which may include strategic partnering, special purpose vehicle financing, grant funding or a combination thereof. If we are not able to obtain additional funds, we will not be able to complete the development, testing and commercialization of Keyzilen®.

On November 28, 2017, we announced that the HEALOS Phase 3 clinical trial that investigated our other late-stage product candidate, Sonsuvi®, in the treatment of acute inner ear hearing loss did not meet the primary efficacy endpoint of a statistically significant improvement in hearing from baseline to Day 28 compared to placebo for either active treatment groups in the overall study population. However, in post-hoc analyses, a clinically meaningful and nominally significant improvement in hearing was observed in the subpopulation of patients with acute profound hearing loss at baseline. Based on these 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 European Medicines Agency, or EMA, and subsequently also to the U.S. Food and Drug Administration, or 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. We currently aim to implement the further development of Sonsuvi® through strategic partnering, special purpose vehicle financing, grant funding or a combination thereof. If we are not able to obtain additional funds, we will not be able to complete the development, testing and commercialization of Sonsuvi®.

On December 30, 2019, we announced the formation of a new subsidiary, Zilentin Ltd., to bundle our development projects for the treatment of tinnitus and hearing loss in a separate entity. Upon completion of the transfers from other Group companies, Zilentin Ltd. is expected to own all tangible and intangible assets related to the development of tinnitus therapeutics, including Keyzilen®, and hearing loss therapeutics (Sonsuvi®).

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

We depend entirely on the success of AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, which are still in clinical development. If our clinical trials are unsuccessful, we do not obtain regulatory approval or we are unable to commercialize AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, or we experience significant delays in doing so, our business, financial condition and results of operations will be materially adversely affected.

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, which are still in clinical development. Our ability to generate product revenues, which we do not expect to occur for at least the next few years, if ever, will depend heavily on successful clinical development, obtaining regulatory approval or clearance and eventual commercialization of these product candidates. We currently generate no revenues from sales of any products, and we may never be able to develop or commercialize a marketable product. The success of AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi® and our other product candidates will depend on several factors, including the following:

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

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, 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 "coronavirus" outbreak, which could significantly disrupt our preclinical studies and clinical trials, and therefore our receipt of necessary regulatory approvals could be delayed or prevented.

In December 2019, a novel strain of coronavirus COVID-19 was reported to have surfaced in Wuhan, China. The extent to which COVID-19 may impact our preclinical and clinical trial operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration and geographic reach of the outbreak, the severity of COVID-19, and the effectiveness of actions to contain and treat COVID-19. In particular, the COVID-19 outbreak has impacted enrollment of patients into our "TRAVERS" phase 2 trial with AM-125. Candidates for participation in this trial undergo certain types of neurosurgery, which are elective procedures. Due to the COVID-19 outbreak, the sites participating in the "TRAVERS" trial have postponed elective procedures and temporarily reduced or suspended clinical research activities. This temporarily happened in spring 2020 and again in early 2021. We expect to complete enrollment in the third quarter of 2021, at the earliest.

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 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.

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

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

To date, we have not completed all clinical trials required for the approval of any of our drug product candidates. Keyzilen®and Sonsuvi® are in Phase 3 clinical development, subject to our ability to find non-dilutive partnering for such programs, and AM-125 and AM-201 are in Phase 2 and Phase 1 clinical development, respectively.

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

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

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

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

If we are required to conduct additional clinical trials or other testing of AM-125, AM-201, Keyzilen® or Sonsuvi® or any other product candidate that we develop beyond the trials and testing that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are unfavorable or are only modestly favorable or if there are safety concerns associated with AM-125, AM-201, Keyzilen® or Sonsuvi® or our other drug product candidates, we may:

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

Our product development costs will also increase if we experience delays in testing or marketing approvals or if we are required to conduct additional clinical trials or other testing of AM-125, AM-201, Keyzilen® or Sonsuvi® beyond the trials and testing that we currently contemplate and we may be required to obtain additional funds to complete such additional clinical trials. We cannot assure you that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our trials after they have begun. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do or shorten any periods during which we have the exclusive right to commercialize our product candidates, which may harm our business and results of operations. In addition, some of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of regulatory approval of AM-125, AM-201, Keyzilen® or Sonsuvi® or any other drug product candidate.

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

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

In our clinical trial of AM-125 and AM-201 to date, adverse events included a low number of transient and dose-dependent nasal congestion or discomfort. No treatment-related serious adverse events were observed. In our clinical trials of Keyzilen® and Sonsuvi® to date, adverse events have included procedure-related transient changes in tinnitus loudness, muffled hearing, ear discomfort or pain, incision site complications and middle ear infections. A limited number of serious adverse events were observed (in 1.2 to 2.5% of patients enrolled in the Keyzilen® trials and in 2.7 to 4.5% of patients in the Sonsuvi® trials); all (Keyzilen®) or most (Sonsuvi®) were considered unrelated or unlikely related to the treatment. Occurrence of serious procedure- or treatment-related side effects could impede clinical trial enrollment and receipt of marketing approval from the FDA, the EMA and comparable foreign regulatory authorities. They could also adversely affect physician or patient acceptance of our product candidates.

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

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

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

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

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

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

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

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of pharmaceutical products. Currently, we have no products that have been approved for commercial sale; however, the current and future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, 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 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, 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. It is possible that our liabilities could exceed our insurance coverage. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for any of our product candidates. However, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

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

We have obtained orphan drug designation for Sonsuvi® for the treatment of ASNHL from the FDA and the EMA, and we may rely on obtaining and maintaining orphan drug exclusivity for Sonsuvi®, if approved. Orphan drug designation may not ensure that we will enjoy market exclusivity in a particular market, and if we fail to obtain or maintain orphan drug exclusivity for Sonsuvi®, we may be subject to earlier competition and our potential revenue will be reduced.

Sonsuvi® has been granted orphan drug designation for the treatment of ASNHL by the FDA and EMA. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the EMA's Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Even though we have obtained orphan drug designation for Sonsuvi® for the treatment of ASNHL in the United States and Europe, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug designation for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Moreover, the FDA can waive orphan drug exclusivity if we are unable to manufacture sufficient supplies of Sonsuvi® if the FDA finds that a subsequent applicant demonstrates clinical superiority to Sonsuvi®. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

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

Because we have limited resources and access to capital to fund our operations, we must decide which product candidates to pursue and the amount of resources to allocate to each. As such, we have been primarily focused on the development of AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, with our current commercial focus being limited to AM-125, AM-201 and AM-301 while we search for non-dilutive or strategic transactions with respect to Keyzilen® and Sonsuvi®. 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, in particular for inner ear disorders, our business, financial condition and results of operations could be materially adversely affected.

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

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

Risks Related to Regulatory Approval of Our Product Candidates

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

Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize one or more product candidates. We currently have one drug product candidate, AM-125, in Phase II clinical development, and another, AM-201, in Phase I clinical development. Additionally, we have two late-stage drug product candidates, (i) Keyzilen® (AM-101), which is being developed for the treatment of acute inner ear tinnitus and (ii) Sonsuvi® (AM-111), being developed for the treatment of acute inner ear hearing loss. We are not permitted to market or promote any of our drug product candidates before we receive regulatory approval from the FDA, EMA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates.

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

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

In addition, no product for the treatment of acute inner ear tinnitus, acute inner ear hearing loss or antipsychotic-induced weight gain has been approved by the FDA or the EMA. Accordingly, our current product candidates or any of our other future product candidates could take a significantly longer time to gain regulatory approval than expected or may never gain regulatory approval. This could delay or eliminate any potential product revenue by delaying or terminating the potential commercialization of our product candidates.

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

We cannot give any assurance that our medical device candidate AM-301 will receive regulatory clearance, which is necessary before it can be commercialized.

Under project code AM-301, we are developing a spray product for intranasal protection against airborne viruses or allergens. AM-301 is formulated as a gel emulsion and – unlike drug products – does not contain any active pharmaceutical ingredient. The formulation is neither absorbed nor metabolized and does not have any pharmacological or immunological interaction with the human body. Its effects – trapping of virus or allergen particles, coating of nasal mucosa tissues and humidification of such tissues – are purely of physical-mechanical nature. We therefore consider AM-301 to be a medical device rather than a drug product and that different regulatory requirements apply.

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

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

AM-301 is also intended for use in the reduction of the intranasal infectious viral load following inspiration of airborne viruses such as SARS-CoV-2. Since there may be no valid predicate device available for this intended use, we may have to submit a de novo request to the FDA. Under the de novo pathway, we would have to prove that AM-301 does not present substantial risk to the patient (rather than just demonstrating substantial equivalence with the safety of the relevant predicate device(s)), which may require additional testing. The review by the FDA would take a minimum of 150 days in the de novo process compared to a minimum of 90 days in the 510(k) process and requires higher fees. Any device that has been classified through the de novo process may be marketed and used as predicate for future 510(k) submissions. The FDA may also, instead of accepting a 510(k) submission, require us to submit a PMA, which is typically a much more complex, lengthy and burdensome application than a 510(k). To support a PMA, the FDA would likely require that we conduct one or more clinical studies to demonstrate that the device is safe and effective. In some cases such studies may be requested for a 510(k) as well. We may not be able to meet the requirements to obtain 510(k) clearance or PMA approval, in which case the FDA may not grant any necessary clearances or approvals. In addition, the FDA may place significant limitations upon the intended use of our products as a condition to a 510(k) clearance or PMA approval. Product applications can also be denied or withdrawn due to failure to comply with regulatory requirements or the occurrence of unforeseen problems following clearance or approval. Any delays or failure to obtain FDA clearance or approval of new products we develop, any limitations imposed by the FDA on new product use or the costs of obtaining FDA clearance or approvals could have a material adverse effect on our business, financial condition and results of operations.

During public health emergencies, FDA can use emergency authorities, including Emergency Use Authorizations (EUAs), to help make medical products available as quickly as possible by allowing unapproved medical products to reach patients in need when there are no adequate, FDA-approved and available alternatives. In addition to COVID-19 tests, the FDA has issued EUAs for other devices, such as ventilators, respirators, face shields, and decontamination systems to treat COVID-19 patients and to protect healthcare workers. Since AM-301 has been shown to significantly reduce the viral infectious load following inoculation of reconstituted human nasal epithelia and based on its favorable safety and tolerability profile, we believe that the device may be eligible for and made available under the EUA procedure. However, the FDA has broad discretion over the grant of EUAs, and there is no guarantee that AM-301 will become available to the general public earlier than through the regular regulatory pathway.

Following a preliminary review of our pre-submission for AM-301 by the FDA's Center for Devices and Radiological Health (CDRH), we were notified by the Agency that the Center for Drug Evaluation and Research (CDER) would be responsible for the review of our product and that our pre-submission request for EUA was transferred to CDER. Based on additional feedback from the FDA, we decided to update the pre-submission request for the 510(k) pathway by restricting the intended use to promoting alleviation of mild allergic symptoms triggered by the inhalation of various airborne allergens given available precedence. In addition, we filed a pre-submission Request for Designation (RFD) to the Agency's Office of Combination Products (OCP) for the second intended use of reducing the intranasal infectious viral load following inspiration of airborne viruses in order to determine the Agency component that will have jurisdiction for AM-301. We believe that the product meets the FDA's requirements for classification as a medical device also for this second intended use and will therefore be reviewed by CDRH rather than CDER, however, there can be no guarantee that the FDA will agree with our analysis.

Many foreign countries in which we intend to market AM-301 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 will repeal and replace the MDD with effect from May 26, 2021. The MDR clearly envisages, among other things, stricter controls of medical devices, including strengthening of the conformity assessment procedures, increased expectations with respect to clinical data for devices and pre-market regulatory review of high-risk devices. The MDR also envisages greater control over notified bodies and their standards, increased transparency, more robust device vigilance requirements and clarification of the rules for clinical investigations. Under transitional provisions, medical devices with notified body certificates issued under the MDD prior to May 26, 2021 may continue to be placed on the market for the remaining validity of the certificate, until May 27, 2024 at the latest. After the expiry of any applicable transitional period, only devices that have been CE marked under the MDR may be placed on the market in the EU.

Under the MDD, AM-301 is classified as a Class I device which does not require a notified body for the conformity assessment procedure. Under the MDR, AM-301 will be classified as a Class II device which will require a notified body. We expect to register AM-301 in the EU prior to the transition from the MDD to the MDR and plan to meet the requirements for conformity as Class II during the transition period ending May 27, 2024.

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

There are currently no drugs with proven efficacy for acute inner ear tinnitus, acute inner ear hearing loss or acute peripheral vertigo. In addition, there has been limited historical clinical trial experience generally for the development of drugs to treat these conditions. 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 inner ear tinnitus, acute inner ear hearing loss or acute peripheral vertigo, and regulators have not yet established what is required to be demonstrated in a clinical trial in order to signify a clinically meaningful result and/or obtain marketing approval.

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

We designed our Phase 3 trials for Keyzilen® and Sonsuvi® to include endpoints that we believe are clinically justified and meaningful. Specifically, with regard to Keyzilen®, the FDA and EMA supported the use of the Tinnitus Functional Index (TFI) questionnaire as the primary efficacy outcome measure. The TFI captures the impact of tinnitus on the patient's day-to-day functioning. Furthermore, the two agencies agreed on a weekly collection of patient-reported tinnitus loudness. The FDA considers the improvement in tinnitus loudness as a co-primary efficacy endpoint, whereas the EMA endorsed it as a secondary efficacy endpoint.

With regard to Sonsuvi®, the FDA and EMA have indicated that a 10 dB improvement in hearing thresholds compared to placebo is clinically significant, in line with clinical practice. However, no product has been approved for marketing based upon such guidance and we cannot be certain that Sonsuvi® will be approved even if it were to demonstrate such result in further Phase 3 trials.

For the clinical investigation of AM-301 for the intended use of alleviation of allergic rhinitis symptoms, we are using the Total Nasal Symptom Score (TNSS) questionnaire, which is routinely used in allergic rhinitis studies. To date, we did not have any interaction with the FDA regarding its use in the context of the allergen challenge chamber that we are conducting to support the substantial equivalence of AM-301 to one of the designated predicate devices. Also, we have received no regulatory guidance so far regarding the use of acceptable endpoints for determining the efficacy of AM-301 for its intended use in the alleviation of intranasal viral load. If we do not accurately predict which endpoints demonstrate the efficacy of AM-301, or if we fail to meet them, our development efforts for AM-301 may be materially curtailed.

Some of our conclusions regarding the potential efficacy of Sonsuvi® in our completed HEALOS clinical trial for the treatment of ASNHL in the subgroup of patients with profound acute hearing loss is based on retrospective analyses of the results, which are generally considered less reliable indicators of efficacy than pre-specified analyses.

After determining that we did not achieve the primary efficacy endpoint in our completed HEALOS clinical trial of Sonsuvi®for the treatment of ASNHL, we performed retrospective analyses that we believe show treatment effects on the magnitude of hearing recovery in favor of Sonsuvi® in cases of profound hearing loss at baseline. Although we believe that these additional analyses were warranted, a retrospective analysis performed after unblinding trial results can result in the introduction of bias if the analysis is inappropriately tailored or influenced by knowledge of the data and actual results. In particular, the analysis that resulted in a clinically meaningful effect being observed in active-treated patients who suffered from profound acute hearing loss poses greater risk of bias as such subgroup was not pre-specified in the trial design, notwithstanding that we applied a commonly used definition of profound hearing loss.

Because of these limitations, regulatory authorities typically give greatest weight to results from pre-specified analyses and less weight to results from post-hoc, retrospective analyses. According to discussions with the EMA and FDA, the therapeutic benefits that were observed in the HEALOS subgroup of profound acute hearing loss will need to be confirmed prospectively in one or more additional Phase 3 trials in order to gain regulatory market approval. However, there is no guarantee that we will ever receive such regulatory approval.

Safety issues with isomers of our product candidates or with approved products of third parties that are similar to our product candidates, could delay or prevent the regulatory approval process or result in restrictions on labeling.

Discovery of previously unknown problems, or increased focus on a known problem, with an approved product may result in restrictions on its permissible uses, including withdrawal of the medicine from the market. Esketamine and betahistine, the active pharmaceutical ingredients, or APIs, of Keyzilen® and AM-125, may be affected by the safety of the drugs related to them. Although both APIs have been used successfully in patients for many years, newly observed toxicities or worsening of known toxicities, in pre-clinical studies of, or in patients receiving, Esketamine, the racemate Ketamine or betahistine, or reconsideration of known toxicities of these APIs in the setting of new indications, could result in increased regulatory scrutiny of Keyzilen®or AM-125. For example, Ketamine is regulated by the Drug Enforcement Administration, or DEA, under the Controlled Substances Act, or CSA, as a Schedule III drug. DEA scheduling is a separate process that can delay when a drug may become available to patients beyond a NDA approval date, and the timing and outcome of such DEA process is uncertain. Although we have observed no abuse liability associated with Keyzilen® to date, if Keyzilen® were to be scheduled under the CSA, such scheduling could negatively impact the ability or willingness of physicians to prescribe Keyzilen® and our ability to commercialize it.

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

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

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

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

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

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

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

If any of these events occurs, our ability to sell such 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 adopted a new “Agency policy on publication of clinical data” (in force since January 1, 2015) based on which 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 may be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, if violated, could 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 Product Candidates

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 AM-125, AM-201, Keyzilen® or Sonsuvi® or our other 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 AM-125, AM-201, Keyzilen® or Sonsuvi® or any other product candidate that we commercialize and, if available, that the reimbursement rates will be adequate.

Our customers, including hospitals, physicians and other healthcare providers that purchase certain injectable drugs administered during a procedure, such as our product candidates, generally rely on third-party payors to pay for all or part of the costs and fees associated with the drug and the procedures administering the drug. These third-party payors may pay separately for the drug or may bundle or otherwise include the costs of the drug in the payment for the procedure. We are unable to predict at this time whether our product candidates, if approved, will be eligible for such separate payments. Nor can we predict at this time the adequacy of payments, whether made separately for the drug and procedure or with a bundled or otherwise aggregate payment amount for the drug and procedure. In addition, obtaining and maintaining adequate coverage and reimbursement status is time-consuming and costly.

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 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 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 AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi® or any other product candidate that we develop does 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 AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi® or any of our product candidates that is 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, particularly as Keyzilen® and Sonsuvi® have to be administered by an ear, nose, throat physician, and in case of Keyzilen® the procedure has to be repeated for a total of three times;
- cost-effectiveness;
- patient diagnostics and screening infrastructure in each market, particularly as Keyzilen®, Sonsuvi® and AM-125, are being developed for the treatment of acute inner ear disorders and are thus dependent on a relatively rapid diagnosis and dosing process;
- 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 AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi® 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 AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi® could be smaller than our estimates of the potential market opportunity. If the actual market for AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi® 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 have never commercialized a product candidate before and may lack the necessary expertise, personnel and resources to successfully commercialize our products on our own or together with suitable partners.

We have never commercialized a product candidate, and we currently have no sales force, marketing or distribution capabilities. To achieve commercial success for AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi® and our other product candidates, we will have to develop our own sales, marketing and supply organization or outsource these activities to a third party.

Factors that may affect our ability to commercialize our product candidates on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, obtaining access to or persuading adequate numbers of physicians to prescribe our drug candidates and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization requires significant investment, is time-consuming and could delay the launch of our product candidates. We may not be able to build an effective sales and marketing organization. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may not generate revenues from them or be able to reach or sustain profitability.

Risks Related to Our Reliance on Third Parties

If we fail to maintain our current strategic relationships with INSERM and Xigen, our business, commercialization prospects and financial condition may be materially adversely affected.

We have a co-ownership/exploitation agreement with the *Institut National de la Santé et de la Recherche Médicale*, or INSERM, governing the exploitation of any products derived from patents that resulted from our joint research program with INSERM that was conducted in 2003 to 2005. Under this agreement with INSERM, 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. We alone are entitled to grant manufacturing or sales licenses for any patents to our subsidiaries and/or third parties. 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. We have agreed to finance any additional research and development work necessary to obtain marketing authorizations for inventions covered by these patents and applications. If we fail to use reasonable efforts in carrying out this additional research, then INSERM may revoke the exclusivity of exploitation granted to us under this agreement. Additionally, we have an exclusive worldwide license from Xigen for the application of Xigen's novel intracellular peptide therapeutics in the area of ear disorders. These intellectual property rights have been the basis of our research and development of Keyzilen® and Sonsuvi®.

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

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 license agreement under which we are developing Sonsuvi® 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 license agreement continues to be in full force and effect in accordance with its terms. Either we or Xigen may terminate the agreement for the other party's material breach or bankruptcy, in the event of force majeure, or after a specified period following the initial date of the agreement, if we were not progressing any activities with respect to the licensed compound. Such period has passed for Sonsuvi® and we progressed the licensed compound sufficiently during the period. We have retained legal counsel and intend to defend our interests, as appropriate and necessary.

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.

Our product development programs and the potential commercialization of our 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 relationships with INSERM and Xigen, for our Keyzilen®and Sonsuvi® product candidates respectively, for one or more of our product candidates, we may decide to enter into strategic alliances, or create joint ventures or collaborations with pharmaceutical or biopharmaceutical companies for the further development and potential commercialization of those product candidates.

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

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

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

We have relied upon and plan to continue to rely upon third-party CROs to monitor and manage data for our ongoing nonclinical and clinical programs, including the clinical trials of AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®. We rely on these parties for execution of our nonclinical and clinical studies and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with cGMP, cGCP, and Good Laboratory Practice, or GLP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Union and comparable foreign regulatory authorities for all of our product candidates in nonclinical and clinical development. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, trial sites and other contractors. If we or any of our CROs or vendors fail to comply with applicable regulations, the data generated in our nonclinical and clinical trials may be deemed unreliable and the EMA, FDA, other regulatory authorities may require us to perform additional nonclinical and clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that all of our clinical trials comply with cGCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

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

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

We currently rely on third-party suppliers and other third parties for production of 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.

We currently rely on and expect to continue to rely on third parties, for the manufacturing and supply of chemical compounds for the clinical trials of our product candidates, including AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, and others for the manufacturing and supply of pre-filled syringes and spray pumps. For the foreseeable future, we expect to continue to rely on such third parties for the manufacture of any of our 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 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 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 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 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 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 products containing such defects could result in recalls or regulatory enforcement action that could adversely affect our business, financial condition and results of operations.

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

Our current and anticipated future dependence upon others for the manufacturing of AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi® and any other product candidate that we develop may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

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

We do not currently, and do not expect to in the future, independently conduct manufacturing activities for our product candidates, including AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®. We currently have a relationship with one supplier each, for the supply of the API of Keyzilen®, Sonsuvi®, AM-125 and AM-201 and for the key component of AM-301. We are reliant upon single source third-party contract manufacturing organizations to manufacture and supply the drug substance, certain other ingredients, primary packaging and final product for each of AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®. We do not currently have any other suppliers for the drug substance, certain other ingredients, primary packaging and final product of our product candidates 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 product candidates. Additionally, we may not be able to enter into supply arrangements with alternative suppliers on commercially reasonable terms, or at all. A delay in the development of our product candidates or having to enter into a new agreement with a different third party on less favorable terms than we have with our current suppliers could have a material adverse impact upon on our business.

Risks Related to Intellectual Property

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.

We rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to our technologies and 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 our 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 product candidates. 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 any 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 AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. In addition, upon issuance in the United States any patent term can be adjusted based on certain delays caused by the applicant(s) or the U.S. Patent and Trademark Office, or USPTO. For example, a patent term can be reduced based on certain delays caused by the patent applicant during patent prosecution.

While in the United States there is a possibility of obtaining market protection independent from any patent protection for up to 3 and 5 years from approval, and in the European Union one may obtain data exclusivity of eight years from approval with an additional two years of market exclusivity (which can potentially be extended by one year), there is no assurance that we can obtain such data exclusivity and market protection with respect to AM-125, AM-201, AM-301, Keyzilen® or Sonsuvi®, or any of our other product candidates. Our issued patents and pending patent applications are expected to expire for Keyzilen® between 2024 and 2028, for Sonsuvi® between 2020 and 2027, and for AM-125 and AM-201 in 2038, prior to any patent term extensions to which we may be entitled under applicable laws.

Patent policy and rule changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Assuming the other requirements for patentability are met, in the United States prior to March 15, 2013, the first to invent the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act, or the Leahy-Smith Act, enacted on September 16, 2011, the United States has moved to a first to file system. The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and may also affect patent litigation. Certain aspects of the Leahy-Smith Act are currently unclear as the courts address the USPTO's implementing regulations. In general, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition In addition, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

If we are unable to maintain effective proprietary rights for our technologies, product candidates or any future 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 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 developing 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 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 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 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 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 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 commercialize such 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 develop and commercialize the applicable 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 develop and commercialize one or more of our 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 Keyzilen®, Sonsuvi®, AM-125 and AM-201 are approved, competitors could file ANDAs for generic versions of Keyzilen®, Sonsuvi®, AM-125 and AM-201, or 505(b)(2) NDAs that reference Keyzilen®, AM-111, AM-125 and AM-201, respectively. If there are patents listed for Keyzilen®, Sonsuvi®, AM-125 and AM-201 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 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 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 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.

The patent protection and patent prosecution for some of our product candidates is dependent on third parties.

While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to our product candidates, there may be times when the filing and prosecution activities for patents relating to our product candidates are controlled by our licensors. This is the case under our agreement with Xigen, where Xigen is entirely responsible for the prosecution and maintenance of the licensed patents and patent applications directed to Sonsuvi®. Xigen has no obligation to provide us any information with respect to such prosecution and we will not have access to any patent prosecution or maintenance information that is not publicly available. Although we monitor Xigen's ongoing prosecution and maintenance of the licensed patents, if Xigen or any of our future licensing partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering Sonsuvi® or any of our product candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products. Specifically, Xigen is concurrently developing another indication for brimapitide (XG-102), the active substance of Sonsuvi®. This may cause a conflict of interest and adversely affect Xigen's ability to prosecute the patent portfolio licensed to us in the best interest of our business. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed from third parties including with respect to the patents and applications licensed to us under our co-ownership and exploitation agreement with INSERM for Keyzilen®, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution. We are required to consult and cooperate with INSERM regarding the prosecution, maintenance, and enforcement of, and in certain instances INSERM has the right to independently enforce, the relevant patents, which may place those patients at risk or hinder our ability to develop and commercialize those product candidates or protect our patent rights.

If we fail to comply with the obligations in our intellectual property agreements, including those under which we license intellectual property and other rights from third parties, or otherwise experience disruptions to our business relationships with our licensors and partners, we could lose intellectual property rights that are important to our business.

We are a party to a number of intellectual property license and co-ownership agreements that are important to our business and expect to enter into additional such agreements in the future. Our existing agreements impose, and we expect that future agreements will impose, various diligence, commercialization, milestone payment, royalty, and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, we may be required to make certain payments to the licensor, we may lose the exclusivity of our license, or the licensor may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license. Moreover, if we fail to comply with our obligations under our co-ownership and exploitation agreement with INSERM for Keyzilen®, including certain commercialization requirements, or we are subject to a bankruptcy, INSERM may terminate the agreement and we may lose our rights to exclusively exploit and commercialize the applicable patents. In such event we would not be able to prevent INSERM from exploiting or licensing to the third parties the rights to exploit the applicable patents, which would have a material adverse effect on our ability to successfully commercialize the affected product candidates. Under our co-ownership agreement with INSERM we may be required to assign our rights in the relevant patents to INSERM if we choose not to or fail to continue to prosecute maintain or patents or patent applications in a given country or countries, in which event we would not be able to develop or market products covered by the applicable patents.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding intellectual property subject to a licensing or co-ownership agreement, including:

- the scope of rights granted under the agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor or partner that is not subject to the agreement;
- the sublicensing of patent and other rights;
- our diligence and commercialization obligations under the agreement and what activities satisfy those obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors or partners and us and our collaborators; and
- the priority of invention of patented technology.

If disputes over intellectual property and other rights that we have licensed or co-own prevent or impair our ability to maintain our current licensing or exclusivity arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license, maintain or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities.

For example, we sometimes collaborate with U.S. and foreign academic institutions to accelerate our pre-clinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our applicable product candidate or program.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain a license to third-party intellectual property rights necessary for the development of a product candidate or program, we may have to abandon development of that product candidate or program and our business and financial condition could suffer.

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

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

Risks Related to Employee Matters and Managing Growth

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

Our success depends upon the continued contributions of our key management, scientific and technical personnel, many of whom have substantial experience with or been instrumental for us and our projects. Key management includes our executive officers Thomas Meyer, our founder, Chairman and Chief Executive Officer and Elmar Schaerli, Chief Financial Officer.

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

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

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

Risks Related to Our Common Shares

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

The share price of publicly traded emerging biopharmaceutical and drug discovery and development companies has been highly volatile and is likely to remain highly volatile in the future. For example, during the last year, our common shares have traded as high as $6.60 in December 2020 and as low as $0.65 in March 2020. The market price of our common shares may fluctuate significantly in the future due to a variety of factors, including:

- positive or negative results of testing and clinical trials by us, strategic partners, or competitors;
- delays in entering into strategic relationships with respect to development and/or commercialization of our product candidates or entry into strategic relationships on terms that are not deemed to be favorable to us;
- technological innovations or commercial product introductions by us or competitors;

- changes in government regulations;
- developments concerning proprietary rights, including patents and litigation matters;
- public concern relating to the commercial value or safety of any of our product candidates;
- financing or other corporate transactions;
- publication of research reports or comments by securities or industry analysts;
- general market conditions in the pharmaceutical industry or in the economy as a whole;
- our ability to maintain the listing of our common shares on Nasdaq; or
- other events and factors beyond our control.

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

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

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

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

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

- the liquidity of our common shares;
- the market price of our common shares;
- our ability to obtain financing for the continuation of our operations;
- the number of institutional and general investors that will consider investing in our common shares;
- the number of investors in general that will consider investing in our common shares;
- the number of market makers in our common shares;

- the availability of information concerning the trading prices and volume of our common shares; and

- the number of broker-dealers willing to execute trades in shares of our common shares.

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

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

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

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

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

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

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

Certain principal shareholders and their affiliated entities as well as members of our executive team and board of directors own approximately 5.0% of our common shares. Depending on the level of attendance at our general meetings of shareholders, these shareholders may be in a position to determine the outcome of decisions taken at any such general meeting. Any shareholder or group of shareholders controlling more than 50% of the shares represented at our general meetings of shareholders may control any shareholder resolution requiring an absolute majority of the shares represented, including the election of members to the board of directors of the Company, certain decisions relating to our capital structure, the approval of certain significant corporate transactions and certain amendments to our bye-laws (the "Bye-Laws"). To the extent that the interests of these shareholders may differ from the interests of the Company's other shareholders, the latter may be disadvantaged by any action that these shareholders may seek to pursue. Among other consequences, this concentration of ownership may have the effect of delaying or preventing a change in control and might therefore negatively affect the market price of our common shares.

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

Future sales of a substantial number of our common shares, or the perception that such sales will occur, could cause a decline in the market price of our common shares. Approximately 5.0% of our common shares issued and outstanding are held by affiliates. If these shareholders sell substantial amounts of common shares in the public market, or the market perceives that such sales may occur, the market price of our common shares and our ability to raise capital through an issue of equity securities could be adversely affected. Additionally, as of the date of this Annual Report we have warrants outstanding, which are exercisable for an aggregate of 246,102 common shares at a weighted average exercise price of $60.03 per share, an equity commitment to sell up to $8.9 million of additional common shares to Lincoln Park Capital Fund, LLC ("LPC") pursuant to the commitment purchase agreement we entered into on April 23, 2020 with LPC (the "LPC Purchase Agreement") and an at-the-market offering program pursuant to the sales agreement we entered into with A.G.P./Alliance Global Partners ("A.G.P.") on November 30, 2018, as amended on April 5, 2019 (the "A.G.P. Sales Agreement") for sales of up to $21.8 million of additional common shares. We have also filed registration statements to register the resale of the common shares underlying the warrants that we have offered and sold in unregistered transactions, the common shares that are sold to LPC and the common shares and other equity securities that we have issued under our prior equity incentive plans or may issue under our new omnibus equity compensation plan. These common shares may be freely sold in the public market upon issuance, subject to certain limitations applicable to affiliates. In addition, we have filed a registration statement covering the issuance and sale by us of up to $100 million of common shares, debt securities, warrants, purchase contracts, units and common shares. We may issue such securities, including our common shares and warrants to purchase common shares, at any time and from time to time subject to the limitations set forth in General Instruction I.B.5 of Form F-3. If a large number of our common shares and/or warrants to purchase common shares are sold in the public market, the sales could reduce the trading price of our common shares and impede our ability to raise future capital.

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

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

We are a holding company with no material direct operations.

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

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

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

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

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

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

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

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

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

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

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

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

We believe that we were a "passive foreign investment company," or PFIC, for U.S. federal income tax purposes for our 2020 taxable year, and we expect to be a PFIC for our current year and for the foreseeable future.

We believe that we were a "passive foreign investment company," or PFIC, for U.S. federal income tax purposes for our 2020 taxable year, and we expect to be a PFIC for our current year and for the foreseeable future. However, our actual PFIC status for the current or any future taxable year is uncertain and cannot be determined until after the end of such taxable year. In addition, we may, directly or indirectly, hold equity interests in other PFICs. Under the Internal Revenue Code of 1986, as amended, we will be a PFIC for any taxable year in which (i) 75% or more of our gross income consists of passive income or (ii) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, passive income. 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.

If we are a PFIC for any taxable year during which a U.S. investor holds our shares, the U.S. investor may be subject to adverse tax consequences, including (i) the treatment of all or a portion of any gain on disposition as ordinary income, (ii) the application of a deferred interest charge on such gain and the receipt of certain dividends and (iii) compliance with certain reporting requirements.

For further discussion of the adverse U.S. federal income tax consequences of our classification as a PFIC, see "Material U.S. Federal Income Tax Considerations for U.S. Holders."

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

ITEM 4. INFORMATION ON THE COMPANY

A. History and development of the Company

Overview

We are a clinical-stage biopharmaceutical company dedicated to developing therapeutics that address important unmet medical needs in neurotology, rhinology and allergy and CNS disorders. We are focusing on the development of intranasal betahistine for the treatment of vertigo (AM-125, in Phase 2) and for the prevention of antipsychotic-induced weight gain and somnolence (AM-201, post Phase 1b). Through our affiliate Altamira Medica, we are developing a nasal spray for protection against airborne viruses and allergens (AM-301). In addition, we have two Phase 3 programs under development, subject to our ability to obtain non-dilutive funding or partnering: (i) Keyzilen® (AM-101), which is being developed for the treatment of acute inner ear tinnitus and (ii) Sonsuvi® (AM-111), which is being developed for the treatment of acute inner ear hearing loss. Sonsuvi® has been granted orphan drug status by the FDA and the EMA and has been granted fast track designation by the FDA.

Our product candidates AM-125, AM-201 and AM-301 are administered with a metered spray into the nose. In case of AM-125 and AM-201, intranasal application allows for the active substance to reach the blood stream rapidly while avoiding the substantial “first-pass” metabolism associated with the current standard oral intake of betahistine. In case of AM-301, the spray delivers the formulation directly to the site of action within the nasal cavity.

Our product candidates Keyzilen® and Sonsuvi® are injected under local anesthesia into the middle ear by a technique called intratympanic injection. Once injected into the middle ear, the active substance, which is formulated in a biocompatible gel, diffuses into the inner ear. The procedure is short, safe, has a long history of use and allows for highly targeted drug delivery with minimal systemic exposure. It is performed by an ear, nose and throat, or ENT, specialist on an outpatient basis over one or more visits.

AM-125

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

In 2018, we conducted a second Phase 1 clinical trial with AM-125 in 72 healthy volunteers. The randomized double blind placebo controlled trial demonstrated superior bioavailability over a range of four intranasal betahistine doses compared to oral betahistine, with plasma exposure being 5 to 29 times higher (unadjusted for dose; p-value between 0.056 and $p < 0.0001$). Further, it confirmed the favorable safety profile of intranasal betahistine and showed that the treatment was well tolerated when administered three times daily for three days. One group of study participants received a single dose of intranasal betahistine or placebo and, following a wash-out period, three doses 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. The other group of study participants received oral betahistine or placebo for reference. Pharmacokinetic parameters in blood plasma were determined for betahistine and its metabolites, and relative bioavailability for intranasal betahistine was calculated compared to oral betahistine 48 mg, which is the maximum approved daily dose as marketed worldwide (ex U.S.).

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

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

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

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

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

AM-201

Intranasal betahistine could have many other therapeutic uses beyond the treatment of acute peripheral vertigo. Under the product code AM-201, we are developing intranasal betahistine for 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 October 2019, we announced interim results from the first 50 participants in the trial. The study demonstrated good safety and tolerability of AM-201 and revealed relevant reductions in olanzapine-induced weight gain and daytime sleepiness. The trial then proceeded to the next higher and final dose level of 30 mg tested in an additional 30 healthy volunteers. 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. We expect to file for an IND in alignment with the IND filing for AM-125.

AM-301

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

The key component of AM-301 is a naturally occurring substance. Through a specialized testing laboratory, we performed an experiment with SARS-CoV-2, where the key component was added in various concentrations to a suspension of the virus for various time periods. Unbound virus particles were then collected from the suspension and transferred onto cell cultures for incubation, allowing for viral replication. The experiment showed that after only 5 minutes of contact between AM-301's key component and the virus suspension the viral infectious load was reduced by up to 99%.

Following formulation development, we tested AM-301 for its capability to prevent or mitigate SARS-CoV-2 infection of nasal epithelial cells, which are part of the nasal mucosa and the first barrier against continuously inhaled substances such as pathogens and allergens. The experiment was performed over four days on reconstituted human nasal epithelia, which are frequently used to study the effects of human respiratory viruses. In saline-treated control cultures, SARS-CoV-2 replicated efficiently, resulting in a rapid increase in viral titer (as measured by the Median Tissue Culture Infectious Dose, TCID50). In contrast, daily treatment with AM-301, beginning right before inoculation, showed effective protection against viral infection. 48 hours post-infection, average virus titers were 90.0% lower than those observed in controls ($p<0.01$). 72 hours and 96 hours post-infection, average virus titers were 99.2 and 99.4% lower, respectively ($p<0.001$). Even when unbound virus was not removed daily through apical washing, allowing the virus to accumulate in the culture for 4 days, the reduction in viral titer was 92.4% compared to saline-treated controls ($p<0.001$).

Based on these *in vitro* results, we believe that AM-301 could help to reduce the risks of exposure from airborne transmission of SARS-CoV-2. It is estimated that about 90% of air is inhaled via the nose, and it has been established that infection with SARS-CoV-2 via the nose is a major transmission pathway for Covid-19. We are currently conducting and planning additional studies to evaluate further AM-301's effects against SARS-CoV-2 as well as other types of viruses.

In January 2021 we announced the initiation of a clinical investigation of AM-301 in allergic rhinitis. The clinical investigation is an open-label randomized cross-over study that will enroll 36 patients with allergic rhinitis to grass pollen. Study participants will be administered a single dose of AM-301 nasal spray or a comparator product (one puff into each nostril) prior to controlled pollen exposure for four hours in an allergen challenge chamber. The challenge will be repeated with the alternate treatment following a wash-out period. The difference in the Total Nasal Symptom Score (TNSS) between the two treatments over the 4-hour exposure will serve as the primary efficacy endpoint; the investigation shall aim to demonstrate clinical non-inferiority of AM-301 to the comparator product.

We believe that AM-301 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. We are currently conducting and planning additional studies to evaluate further AM-301's preventative effects for allergy management.

Since AM-301 does not contain any active substance, we believe that it will be regulated and marketed as an "over-the-counter" medical device. Following the conduct of further studies in safety and efficacy, the Company is targeting submission of regulatory applications to the U.S. Food and Drug Administration ("FDA") and regulatory authorities in other jurisdictions in 2021.

Keyzilen®

We are 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 has demonstrated a favorable safety profile and positive effect on PROs associated with tinnitus in two Phase 2 clinical trials. The Phase 3 clinical development program so far comprised two pivotal clinical trials with highly similar design, one in North America (TACTT2) and one in Europe, which we refer to as TACTT3.

Tinnitus is categorized as acute during the three months after onset and chronic when it persists for more than three months. Approximately 25% of American adults (50 million people) have experienced tinnitus with nearly 8% of American adults (16 million people) having frequent occurrences. Epidemiological studies reveal comparable prevalence rates for Europe. Among the tinnitus patients seen by general practitioners and ENT specialists in the United States and the top five European markets who reported seeing at least one tinnitus patient in the previous three months, approximately 36% of patients sought medical treatment during the first three months following tinnitus onset.

Possible causes of acute inner ear tinnitus include traumatic insult such as exposure to excessive noise, or middle ear infection (otitis media, or OM). We have conducted Phase 2 trials in this specific tinnitus population with Keyzilen®, which demonstrated a favorable safety profile. Furthermore, in our Phase 2 clinical trials, Keyzilen® showed a dose dependent, persistent and clinically relevant improvement, as compared to the placebo, in subjective tinnitus loudness as well as other patient reported outcomes, such as tinnitus annoyance, tinnitus severity, sleep difficulties and general tinnitus impact. In August 2016, we announced that the trial Efficacy and Safety of Keyzilen® (AM-101) in the Treatment of Acute Peripheral Tinnitus 2, or TACTT2, the first of two pivotal Phase 3 clinical trials with Keyzilen®, did not meet the two co-primary endpoints of statistically significant changes in tinnitus loudness and tinnitus burden as measured by the TFI compared to placebo. However, the TACTT2 trial data showed treatment effects on TFI in favor of Keyzilen® for certain subgroups and supported the positive safety profile established in the Phase 2 trials.

In the second quarter of 2017 we announced results from AMPACT1 and AMPACT2 (AM-101 in the Post-Acute Treatment of Peripheral Tinnitus 1 and 2), two open-label extension studies of the Phase 3 TACTT2 and TACTT3 clinical trials, respectively. The AMPACT studies were conducted at the request of the US Food and Drug Administration (FDA) to generate safety data from chronic intermittent use of Keyzilen® for up to 12 months. Both AMPACT1 and AMPACT2 confirmed the good safety profile of Keyzilen®.

Based on the outcomes from the TACTT2 trial, we amended our protocol for the TACTT3 Phase 3 clinical trial of Keyzilen® in two steps. Under the final, amended trial protocol, the change in TFI score was elevated from a key secondary endpoint to a primary efficacy endpoint, the trial size was increased to enhance statistical sensitivity to the effects of treatment, and the subgroup of patients with otitis media-related tinnitus was included in confirmatory statistical testing along with the overall study population. The change in tinnitus loudness was downgraded from a primary to a secondary efficacy endpoint. As in TACTT2, tinnitus loudness was initially rated on a daily basis; however, the rating frequency was subsequently reduced in between study visits in order to lighten the burden of patients and reduce the potential impact of the frequent measures. Enrollment into the TACTT3 trial was resumed in early 2017 and completed in September 2017.

In March 2018, we announced that the TACTT3 trial did not meet its primary efficacy endpoint of a statistically significant improvement in the Tinnitus Functional Score from baseline to Day 84 in the active treated group compared to placebo either in the overall population or in the otitis media subpopulation. This outcome was confirmed by further analyses. We consider that additional studies with Keyzilen® will be necessary to move the program forward, and that the way how outcomes are measured Keyzilen® will need to be improved in order to provide more robust efficacy data. 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 following traumatic cochlear injury 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®. We intend to fund further development of Keyzilen® either through partnerships or research grants. See "Item 4. Information on the Company—B. Business overview—Keyzilen® Phase 3 Clinical Program."

Sonsuvi®

We are also developing Sonsuvi® for acute inner ear hearing loss. In our Phase 2 clinical trial, AM-111 showed a favorable safety profile. Furthermore, in patients with severe to profound ASNHL, we observed a clinically relevant improvement in hearing threshold, speech discrimination and a higher rate of complete tinnitus remission compared with placebo. In November 2017, we announced that the HEALOS Phase 3 clinical trial that investigated Sonsuvi® in the treatment of acute inner ear hearing loss did not meet the primary efficacy endpoint of a statistically significant improvement in hearing from baseline to Day 28 compared to placebo for either active treatment groups in the overall study population. 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. Further, patients treated with Sonsuvi® 0.4 mg/mL showed a nominally significantly lower incidence of no hearing improvement compared to placebo by Day 91 as well as a superior improvement in word recognition score. Outcomes with Sonsuvi® 0.8 mg/mL tended to be somewhat less pronounced than those observed for Sonsuvi® 0.4 mg/mL. Sonsuvi® was well tolerated and the primary safety endpoint was met.

Together with the outcomes of the HEALOS trial, we announced that ASSENT, the second Phase 3 clinical trial investigating Sonsuvi®, was terminated early in order to avoid the need for substantial protocol changes and interruptions of enrollment pending feedback from health authorities on the regulatory pathway. ASSENT was planned to enroll a total of 300 patients in the US, Canada and South Korea. In contrast to HEALOS and the Phase 2 trial, where patients with insufficient hearing recovery had the option of receiving a course of oral corticosteroids as reserve therapy, all patients in ASSENT would receive oral corticosteroids as a background therapy. At the time of early termination, the ASSENT trial had recruited 56 patients.

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. We intend to fund further development of Sonsuvi® through partnerships.

In December 2019 we announced the formation of a new subsidiary, Zilentin Ltd., to bundle our development projects for the treatment of tinnitus and hearing loss in a separate entity. Upon completion of the transfers from other Group companies, Zilentin Ltd. shall own all tangible and intangible assets related to the development of tinnitus therapeutics, including Keyzilen®, and hearing loss therapeutics (Sonsuvi®).

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"). 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.aurismedical.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 novel therapeutics and medical devices to address unmet medical needs in neurotology, rhinology and allergy and CNS disorders. The key elements of our strategy to achieve this goal are:

- **Target disorders that have a defined pathophysiology and that are amenable to treatment or prevention.** We are focusing on disorders for which the pathophysiology is defined, can be effectively targeted and where affected patients or patients at risk seek medical attention proactively.

- **Use delivery techniques and proprietary formulations for effective, safe and rapid targeted administration.** All our product candidates are designed for targeted drug delivery. Where the target is inside the inner ear, such as in case of acute inner ear hearing loss or tinnitus, we employ intratympanic injections into the middle ear. Where the target is localized not only in the inner ear, but also in the brain, as in the case of vertigo, we are using a spray formulation for intranasal drug delivery to reach it more effectively than with oral administration. When the target are the mucosal membranes inside the nose as for protection against airborne viruses and allergens, we are using a spray formulation as well.

- **Leverage products into additional therapeutic indications.** We consider our intranasal betahistine program as a platform on which various indications can be developed. The program started with project AM-125 for the treatment of acute vertigo and has been expanded with project AM-201 to address also the prevention of antipsychotic-induced weight gain. We see additional opportunities in other indications and seek to explore those for further indication expansions. Also, we have leveraged our experience in nasal spray products into the development of AM-301 for protection against airborne viruses and allergens.

Targeting the nose and the inner ear

We have focused our development efforts on targeting the nose and the inner ear. The nose is the first organ of the respiratory system and is also the principal organ in the olfactory system. The main function of the nose 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.

The nose is an interesting site for the delivery of therapeutics both for drugs acting locally and acting systemically, i.e. those drugs intended to be distributed within the whole body. 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.

The inner ear is comprised of the cochlea, the organ of hearing, and the vestibular system, the organ of balance. The snail-shaped cochlea is the sensory organ at the periphery of the auditory system, which transmits sound along the auditory pathway up to the brain for hearing. Acute insults to the cochlea from a variety of sources—for example, loud noise, infection or insufficient blood supply—may lead to excessive levels of glutamate, the principal neurotransmitter in the cochlea as well as other pathological processes. This in turn may damage cochlear hair cells, which tune and amplify sound inside the cochlea or convert mechanical movement into neural signals, as well as cochlear neurons. Such damage may result in the symptoms of inner ear hearing loss and/or inner ear tinnitus that can be transitory as natural repair mechanisms set in or that become permanent when hair cells or neurons die or are permanently injured.

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

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

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

Market

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

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

The current COVID-19 pandemic has highlighted the large impact that viral infections can have on health, quality of life and economic activity. Since outbreak, more than 110 million people have been reported as infected and more than 2.5 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, dozens of potential treatments have been under development. However, 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.

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

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

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

According to a 2011 publication by Hall et al. in the journal BMC Health Services Research, among the tinnitus patients seen by physicians who reported seeing at least one tinnitus patient in the previous three months, approximately 36% of patients sought medical treatment during the first three months following the onset of the disorder.

The market for ear disorders is underserved. There are three main reasons for this:

- **Inner ear physiology.** It has been extremely challenging for pharmaceutical companies to deliver drugs at effective concentrations to the inner ear. Like the eye, the inner ear is a protected space. Systemically administered drugs such as intravenous or oral formulations in doses high enough to reach effective inner-ear concentrations often bring unacceptable systemic toxicity.

- **Heterogeneity of inner ear disorders.** Hearing loss, tinnitus and vertigo are symptoms of many different underlying etiologies, and they manifest themselves in many different ways. For example, tinnitus may be provoked by such different proximal causes as whiplash injury, excessive noise exposure, the flu or even certain dental problems. In some cases, the tinnitus originates inside the cochlea, but then becomes “centralized,” that is, the phantom sound persists even long after the initial source of the sensation has been removed. In case of vertigo, possible triggers include infection, inflammation, surgical trauma, disturbances of inner ear fluid balance or debris inside the inner ear. There has been a dearth of knowledge about the pathophysiology of tinnitus, hearing loss and vertigo, which has hindered the pharmaceutical industry in pursuing therapeutics in this area.

- **Lack of clinical trial paradigms.** Historically, there have been challenges regarding the clinical endpoints used in measuring changes in tinnitus. Since tinnitus usually is perceived only by the patient affected by it, so far there has been no direct way of measuring it. Like pain, tinnitus assessments have to rely on subjective endpoints. Tinnitus assessments consist either of psychoacoustic measures, performed by audiologists and other hearing specialists and sometimes considered as “semi-objective,” or they are based on PROs. Unlike in pain, there has been a lack of guidelines and validation work on these PROs, and the relevance and reliability of psychoacoustic measures as efficacy outcome variables have been questioned.

- **Challenges with bioavailability.** Betahistine, the active substance of AM-125 and also AM-201, 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.

For these reasons, the industry's discovery and development of novel therapies for inner ear disorders has lagged far behind efforts in other therapeutic areas.

We are addressing each of these issues with our approach to developing therapeutics targeting the inner ear. Using targeted drug delivery to the inner ear reduces systemic exposure to our product candidates. We target specific types of tinnitus, hearing loss and vertigo that are addressable with drug-based therapies. We have worked with regulatory agencies to develop and validate acceptable clinical trial paradigms.

Our Product Candidates

AM-125 in Vestibular Disorders

Vestibular Disorders

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

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

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

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

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

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

Our Solution—AM-125

In February 2017 we entered into an asset purchase agreement with Otifex, pursuant to which we have purchased various assets related to betahistine dihydrochloride in a spray formulation, which we are developing for intranasal treatment of vertigo under the product code AM-125.

The assets include preclinical and clinical data as well as certain intellectual property rights. In a Phase 1 clinical trial conducted by Otifex in 40 healthy volunteers intranasal betahistine showed good tolerability and significantly higher betahistine concentrations in blood plasma than reported for oral betahistine administration.

Therapeutic rationale for AM-125 in vertigo

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

Vertigo endpoints

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

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

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

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

Clinical development of AM-125

In 2018, we conducted a second Phase 1 clinical trial with AM-125 in 72 healthy volunteers. The randomized double blind placebo controlled trial demonstrated superior bioavailability over a range of four intranasal betahistine doses compared to oral betahistine, with plasma exposure being 5 to 29 times higher (unadjusted for dose; p-value between 0.056 and $p < 0.0001$). Further, it confirmed the favorable safety profile of intranasal betahistine and showed that the treatment was well tolerated when administered three times daily for three days. One group of study participants received a single dose of intranasal betahistine or placebo and, following a wash-out period, three doses 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. The other group of study participants received oral betahistine or placebo for reference. Pharmacokinetic parameters in blood plasma were determined for betahistine and its metabolites, and relative bioavailability for intranasal betahistine was calculated compared to oral betahistine 48 mg, which is the maximum approved daily dose as marketed worldwide (ex U.S.).

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

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

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

Enrollment into TRAVERS has been impacted by the COVID-19 pandemic, as the type of neurosurgery required for participation in the trial is classified as an elective procedure and hence was postponed and as many participating sites temporarily reduced or suspended clinical research activities. The effect was particularly felt in the spring of 2020 and then again in early 2021.

We have discussed the regulatory requirements for AM-125 during a pre-Investigational New Drug (“IND”) meeting with the FDA and in the context of scientific advice meetings with the EMA and two European national health authorities to further define the development program. We expect to have further exchanges with regulatory agencies following conclusion of the TRAVERS trial, upon which we aim to obtain an IND. We believe that, if approved, AM-125 could become the first betahistine product for the treatment of acute peripheral vertigo in the United States.

AM-201 in Antipsychotic-Induced Weight Gain

Antipsychotic-induced weight gain

The use of second generation antipsychotic drugs such as olanzapine or clozapine can be associated with severe side effects such as weight gain, metabolic dysregulation and somnolence. These side effects not only have a negative effect on patients’ compliance with medication, but expose them to additional hazards: weight gain is strongly correlated with metabolic dysregulation leading to diabetes and cardiovascular disease; and somnolence may severely impact quality of life, affecting learning, social interactions or tasks such as driving or operating machinery. These adverse events are mainly attributed to the histamine H1 receptor antagonistic properties of these agents. Treatment with these antipsychotic drugs reduces the activity of the H1 receptor, which in turn causes increased eating and weight gain.

According to the U.S. prescription information for olanzapine, accumulated evidence shows that patients gain on average 2.6 kg over a treatment duration of 6 weeks. During long-term treatment (≥ 48 weeks) patients gain on average 5.6 kg as shown in a review published by Citrome and colleagues published in the journal Clinical Drug Investigations in 2011. Over that time period, 64%, 32%, and 12% of patients treated with olanzapine gain at least 7%, 15%, or 25% of their baseline body weight, respectively.

The concerns about antipsychotic-induced weight gain and consequent metabolic changes have led the FDA to highlight these risks as warnings in the prescribing information of certain antipsychotics and call for regular monitoring of glycemic control, lipid profile and weight. These concerns are also reflected in treatment guidelines, which do not recommend olanzapine or clozapine as first-line treatments, despite the fact that meta-analyses such as one by Leucht and colleagues published in 2013 in the journal Lancet show that they are among the most effective treatments for schizophrenia.

Our Solution—AM-201

In May 2018, we announced the expansion of our intranasal betahistine development program beyond the treatment of vertigo into mental health supportive care indications. Under project code AM-201 we intend to develop intranasal betahistine 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. We have discussed our development plan for AM-201 with the FDA during a Pre-IND meeting. In its written response, the FDA supported the planned conduct of a multiple dose Phase 1 trial with AM-201 administered to healthy subjects in combination with olanzapine to evaluate the pharmacokinetics, pharmacodynamics, and safety, and to establish proof-of-concept. Further, the FDA endorsed weight gain normalized to baseline body weight versus placebo as reasonable primary efficacy endpoint for a subsequent Phase 2 trial.

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 October 2019, we announced interim results from the first 50 participants in the trial. The study demonstrated good safety and tolerability of AM-201 and revealed relevant reductions in olanzapine-induced weight gain and daytime sleepiness. The trial then proceeded to the next higher and final dose level of 30 mg tested in an additional 30 healthy volunteers. 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. We expect to file for an IND in alignment with the IND filing for AM-125.

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 – AM-301

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

The key component of AM-301 is a naturally occurring substance. Through a specialized testing laboratory, we performed an experiment with SARS-CoV-2, where the key component was added in various concentrations to a suspension of the virus for various time periods. Unbound virus particles were then collected from the suspension and transferred onto cell cultures for incubation, allowing for viral replication. The experiment showed that after only 5 minutes of contact between AM-301's key component and the virus suspension the viral infectious load was reduced by up to 99%.

Following formulation development, we tested AM-301 for its capability to prevent or mitigate SARS-CoV-2 infection of nasal epithelial cells, which are part of the nasal mucosa and the first barrier against continuously inhaled substances such as pathogens and allergens. The experiment was performed over four days on reconstituted human nasal epithelia, which are frequently used to study the effects of human respiratory viruses. In saline-treated control cultures, Sars-CoV-2 replicated efficiently, resulting in a rapid increase in viral titer (as measured by the Median Tissue Culture Infectious Dose, TCID50). In contrast, daily treatment with AM-301, beginning right before inoculation, showed effective protection against viral infection. 48 hours post-infection, average virus titers were 90.0% lower than those observed in controls ($p<0.01$). 72 hours and 96 hours post-infection, average virus titers were 99.2 and 99.4% lower, respectively ($p<0.001$). Even when unbound virus was not removed daily through apical washing, allowing the virus to accumulate in the culture for 4 days, the reduction in viral titer was 92.4% compared to saline-treated controls ($p<0.001$).

Based on these *in vitro* results, we believe that AM-301 could help to reduce the risks of exposure from airborne transmission of SARS-CoV-2. It is estimated that about 90% of air is inhaled via the nose, and it has been established that infection with SARS-CoV-2 via the nose is a major transmission pathway for Covid-19. We are currently conducting and planning additional studies to evaluate further AM-301's effects against SARS-CoV-2 as well as other types of viruses.

In January 2021 we announced the initiation of a clinical investigation of AM-301 in allergic rhinitis. The clinical investigation is an open-label randomized cross-over study that will enroll 36 patients with allergic rhinitis to grass pollen. Study participants will be administered a single dose of AM-301 nasal spray or a comparator product (one puff into each nostril) prior to controlled pollen exposure for four hours in an allergen challenge chamber. The challenge will be repeated with the alternate treatment following a wash-out period. The difference in the Total Nasal Symptom Score (TNSS) between the two treatments over the 4-hour exposure will serve as the primary efficacy endpoint; the investigation shall aim to demonstrate clinical non-inferiority of AM-301 to the comparator product.

We believe that AM-301 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. We are currently conducting and planning additional studies to evaluate further AM-301's preventative effects for allergy management.

Since AM-301 does not contain any active substance, we believe that it will be regulated and marketed as an "over-the-counter" medical device. Following the conduct of further studies in safety and efficacy, the Company is targeting submission of regulatory applications to the U.S. Food and Drug Administration ("FDA") and regulatory authorities in other jurisdictions in 2021.

Keyzilen® in Tinnitus

Our clinical program with Keyzilen®, Esketamine gel for injection, is in Phase 3 development in acute inner ear tinnitus, subject to our ability to obtain non-dilutive funding or partnering. Esketamine is a potent, small molecule non-competitive NMDA receptor antagonist. Keyzilen® is formulated in a biocompatible gel and delivered via intratympanic injection. It has demonstrated a favorable safety profile and positive effect on PROs associated with tinnitus in two Phase 2 clinical trials. The Phase 3 clinical development program comprised two pivotal clinical trials with highly similar design, one in North America (TACTT2) and one in Europe, which we refer to as TACTT3.

Tinnitus

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

Tinnitus is categorized as acute during the first three months and chronic when it persists for more than three months. The distinction between acute and chronic is based on the clinical observation that spontaneous recovery or complete remission of tinnitus is much more likely to occur in the first days, weeks and months following its onset. The chances of spontaneous recovery decline exponentially as the acute phase progresses. In the chronic stage, improvement is much more unlikely, and the therapeutic focus shifts from curing to managing the disorder. In some cases, tinnitus originates inside the cochlea, or the periphery of the auditory system, but then becomes "centralized," that is, the phantom sound persists even long after the initial source of the sensation has been removed.

Tinnitus is a symptom that can be triggered by a variety of diseases or incidents such as noise trauma, infection, inflammation, vascular problems, temporomandibular joint dysfunction, head trauma or whiplash injury. In the majority of cases the tinnitus originates in the cochlea, but the precise mechanisms of tinnitus generation are still the subject of considerable debate and remain to be fully elucidated. In our development we are focusing on one particular, well-defined type of tinnitus generation based on glutamate excitotoxicity.

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.

Current Therapies and Unmet Need

Tinnitus treatments may be categorized according to whether they treat the underlying cause or provide symptomatic relief. It is rarely possible to treat the underlying cause. When it is possible, treatment often involves a surgical procedure to resect tumors or vascular abnormalities. In contrast, treatments to provide symptomatic relief are highly diverse, reflecting the general lack of understanding of the underlying pathophysiology.

Currently, the most widely employed treatment options include counseling, cognitive behavioral therapy, various forms of sound therapies, tinnitus retraining therapy, or TRT, herbal and vitamin supplements, ginkgo biloba, vasodilators, steroids, benzodiazepines and tricyclic antidepressants.

Sound-based therapies and TRT are some of the most commonly employed treatments for tinnitus. TRT is a non-pharmacological intervention that employs low-level sound emitted by a so-called "masking device" worn behind or in the ear. TRT also incorporates patient counseling to help habituate patients to their tinnitus. In those cases in which it is effective, TRT takes one to two years before patients "learn" to ignore tinnitus without the aid of a masking device. TRT can cost $2,500 to $3,000, including the masking devices. After an initial period of enthusiasm in the 1980s, masking devices declined in popularity among clinicians because it became clear that many patients who agreed to try them were nonusers six months later. While classic sound based therapies are based on broadband sound, newer therapies use sound individually tailored to the hearing loss and tinnitus characteristics.

Although there are no approved drugs in the United States for the treatment of tinnitus, there is widespread off-label use of drugs approved for other indications. The U.K. Charity Action on Hearing Loss reports that more than three million prescriptions are written each year in the United States and Europe for drugs that purport to offer tinnitus relief, drugs for which there is no proven efficacy.

The local anesthetic and antiarrhythmic drug lidocaine is the only substance to date that is known to attenuate tinnitus, albeit only temporarily. This illustrates that tinnitus can be addressed using pharmacological intervention. However, lidocaine causes severe vertigo and other side effects, preventing its widespread clinical use.

Our Solution—Keyzilen® (AM-101)

Therapeutic rationale for Keyzilen® in tinnitus

The API of Keyzilen® is Esketamine hydrochloride, a well-known small molecule non-competitive NMDA receptor antagonist. As described above, acoustic trauma and other insults to the inner ear have been shown in animal studies to activate cochlear NMDA receptors. The antagonist effect of Esketamine towards the NMDA receptor aims to suppress the aberrant activity of the auditory nerve and thus diminish tinnitus.

Ketamine has been used clinically for decades as an anesthetic and analgesic. Esketamine is the S-enantiomer of Ketamine and was introduced in a small number of markets outside the United States as a more potent NMDA receptor antagonist with more favorable side effects than racemic Ketamine. We are using Esketamine in doses that result in systemic exposure several orders of magnitude lower than those seen when Esketamine is used as an anesthetic at clinically safe doses. In March 2019, the first esketamine drug product was approved by the FDA – esketamine intranasal spray for treatment of treatment-resistant depression (SPRAVATO).

Tinnitus endpoints

Given the lack of existing tinnitus treatments, there have been no fully validated or universally accepted outcome measures for clinical trials. There are two fundamental types of efficacy outcome variables. PROs such as the visual or numerical rating of tinnitus loudness or tinnitus questionnaires provide direct subjective measures of tinnitus and its impact on sleep, relaxation, communication, emotions, social interactions and other factors. For example, patients are asked a single question to rate the loudness of their tinnitus “right now” on a scale from 0 (“no tinnitus heard”) to 10 (“tinnitus extremely loud”). Among several tinnitus questionnaires, the 25 item TFI is one of the most recent. It was developed and validated broadly in line with the PRO guidelines of the FDA and was introduced in 2011 by Meikle et al. following extensive validation work, as described in the journal Ear & Hearing. Alternatively, measures commonly referred to as psychoacoustic may be performed by an audiologist, which is why they are considered “semi-objective.” They seek to determine how loud a masking sound has to be to cover the tinnitus (minimum masking level, or MML) or how loud the tinnitus is compared to reference sound (equal loudness match).

In our Phase 2 clinical trials, PROs showed good responsiveness and consistent results, whereas psychoacoustic measures proved highly variable and unreliable. Therefore, following discussions with the FDA and EMA, it was agreed that our Phase 3 clinical program for Keyzilen® would be based on PROs with the improvement of subjective tinnitus loudness being defined as the primary efficacy endpoint. As part of the SPA with the FDA, it was agreed that improvement as measured by the TFI questionnaire would serve as a co-primary efficacy endpoint in our TACTT2 trial in order to confirm the clinical meaningfulness of a reduction in tinnitus loudness.

Keyzilen® Clinical Development

Phase 1/2

We conducted the first clinical evaluation of Keyzilen® in a Phase 1/2 double blind, randomized, placebo-controlled trial that included dose escalation from 0.03 to 0.81 mg/mL. The trial enrolled 24 patients suffering for up to three months from severe or disabling permanent inner ear tinnitus caused by AAT or sudden deafness (also called idiopathic sudden sensorineural hearing loss, or ISSNHL) and after unsuccessful steroid treatment.. The trial showed that single doses of intratympanically administered Keyzilen® were well tolerated up to the highest tested dose of 0.81 mg/mL. Only small traces of Esketamine and its primary metabolite were detected in blood samples within the first hours following treatment administration.

Phase 2

Following successful completion of our Phase 1/2 trial, we conducted two multi-center Phase 2 trials, one in Europe (Treatment of Acute Inner Ear Tinnitus 0 or TACTT0) and the other in Europe and the United States (which we refer to as TACTT1).

TACTT0 was conducted as a double-blind, randomized, placebo controlled, multiple dose, parallel group, Phase 2 clinical trial at 28 European sites between March 2009 and May 2011. It enrolled patients with persistent inner ear tinnitus as a result of AAT, otitis media (OM), or ISSNHL, occurring not more than three months prior. Trial participants received three intratympanic administrations of Keyzilen® at dose levels of either 0.27 mg/mL or 0.81 mg/mL or placebo over three consecutive days. A total of 248 patients were randomized. As described by van de Heyning and colleagues in a 2014 article in Otology & Neurotology, Keyzilen® was well tolerated and had no negative impact on hearing. Adverse events were mostly local and related primarily to anticipated temporary changes in tinnitus loudness and muffled hearing following the intratympanic injection procedure. These effects usually resolved with closure of the ear drum.

The trial further showed a dose-dependent reduction in PROs such as subjective tinnitus loudness and the THI-12 questionnaire measuring tinnitus impact in the subpopulation of patients with tinnitus induced by AAT or OM, but not in the subpopulation of tinnitus induced by ISSNHL. In the latter, an unexpectedly high rate of spontaneous remission and substantial heterogeneity in outcomes were observed. Contrary to the PROs the minimum masking levels failed to indicate any treatment effect.

Given the high variability and the uncertainty over the precise trigger of the tinnitus in ISSNHL, we decided to continue clinical development exclusively in tinnitus following AAT and OM. In addition, we decided to focus on PROs for efficacy endpoints as we had determined – in a separate study – that the MML was not reliable enough.

TACTT1, our second double-blind, randomized, placebo-controlled Phase 2 clinical trial, enrolled 85 patients suffering from acute inner ear tinnitus following cochlear trauma or OM to complement the TACTT0 trial, notably by evaluating efficacy trends with different treatment schemes.

Patients received single (Cohort 1) or multiple (Cohort 2: three injections over two weeks) doses of Keyzilen® at a dose level of 0.81 mg/mL or placebo.

As described by Staecker and colleagues in an article in Audiology & Neurotology in 2015, TACTT1 further confirmed the safety and tolerability of the treatment and demonstrated the gradual improvement in PROs in Keyzilen®treated groups that had already been observed in TACTT0. Spreading the three treatment administrations over two weeks rather than three days as applied in TACTT0 appeared to provide less therapeutic benefit.

Keyzilen® Phase 3 Clinical Program

We have conducted two pivotal trials with Keyzilen® with highly similar designs, one in North America (TACTT2) and one in Europe (TACTT3). TACTT2 enrolled 343 patients, while TACTT3 Stratum A (Europe) randomized 372 patients, both during the acute stage. Both trials were designed as a randomized, double-blind, placebo-controlled trial in acute inner ear tinnitus following traumatic cochlear injury or otitis media. Trial participants received three injections of Keyzilen® 0.87 mg/mL or placebo in a 3:2 ratio over three to five days and were followed for 84 days. The TACTT2 trial was conducted primarily in North America, the TACTT3 trial was conducted exclusively in Europe.

In addition, TACTT3 Stratum B explored the potential efficacy of Keyzilen® during the post-acute stage (tinnitus onset between three and 12 months) since data from our Phase 2 clinical program suggested that Keyzilen® might be effective beyond the three month acute stage. An Independent Data Review Committee conducted an interim analysis after enrollment of 150 patients. The interim analysis showed positive efficacy signals, with higher activity levels observed in the early post-acute stage (three to six months) compared to the late post-acute stage (six to 12 months). Based on recommendations from the Independent Data Review Committee, TACTT3 Stratum B continued solely with enrollment of patients with tinnitus onset three to six months prior. In total, 369 patients were randomized in TACTT3 Stratum B pre- and post-interim analysis.

Two further trials, AMPACT1 and AMPACT2 (Keyzilen® in the Post-Acute Treatment of Peripheral Tinnitus) were nine-month open label extension trials conducted at the same sites as for TACTT2 and TACTT3. These extension trials were open to participants who completed the TACTT2 or the TACTT3 trial (the latter until summer 2016) and evaluated the safety and local tolerance of up to three treatment cycles, each with three repeated doses of Keyzilen® 0.87 mg/mL.

The extension trials were designed in response to the FDA's request for safety data from chronic intermittent use by tinnitus patients in support of a NDA filing. Although we do not have any plans to seek a label for such use, the FDA considered such unintended use likely to occur.

In August 2016 we announced outcomes from the Phase 3 TACTT2 clinical trial. Keyzilen® was well tolerated with no drug-related serious adverse events. The trial's primary safety endpoint, incidence of clinically meaningful hearing deterioration, was met. However, the trial did not meet the two co-primary efficacy endpoints of statistically significant changes in tinnitus loudness and the TFI questionnaire compared to placebo.

Following the outcomes from the TACTT2 trial, we amended our protocol for the TACTT3 Phase 3 clinical trial of Keyzilen®. The change in TFI score was elevated from a key secondary endpoint to a primary efficacy endpoint, the trial size was increased to enhance statistical sensitivity to the effects of treatment, and the subgroup of patients with otitis media-related tinnitus was included in confirmatory statistical testing along with the overall study population. The change in tinnitus loudness was downgraded from a primary to a secondary efficacy endpoint. As in TACTT2, tinnitus loudness was initially rated on a daily basis; however, the rating frequency was subsequently reduced in between study visits in order to lighten the burden of patients and reduce the potential impact of the frequent measures. Enrollment into the TACTT3 trial was resumed in early 2017 and completed in September 2017.

In March 2018 we announced that the TACTT3 trial did not meet its primary efficacy endpoint of a statistically significant improvement in the Tinnitus Functional Score from baseline to Day 84 in the active treated group compared to placebo either in the overall population or in the otitis media subpopulation. 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.

We consider that additional studies with Keyzilen® will be necessary to move the program forward, and that the way how outcomes are measured Keyzilen® will need to be improved in order to provide more robust efficacy data. 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 following traumatic cochlear injury 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®. We intend to fund further development of Keyzilen® either through partnerships or research grants.

Sonsuvi® (AM-111) in Hearing Loss

Sonsuvi® is being developed for the treatment of ASNHL, subject to our ability to obtain non-dilutive funding or partnering. In sensorineural hearing loss, there is damage to the sensory cells of the inner ear or the auditory nerve. Sensorineural hearing loss is also called "inner ear hearing loss". Hearing loss is a heterogeneous disorder of many forms with a variety of causes. 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.

Hearing Loss

Hearing loss, like tinnitus, is a heterogeneous disorder of many forms with diverse etiology. There are two general categories: conductive hearing loss in which sound waves are not conducted efficiently to the inner ear due to build-up of earwax, fluid, or a punctured eardrum; and sensorineural hearing loss, in which there is damage to the inner ear or the auditory nerve. Acute hearing loss can occur in either category. Hearing loss is amenable to pharmaceutical intervention (and thus relevant to our drug development) only when it is sensorineural in origin. ASNHL is often accompanied by tinnitus.

There are two main types of acute hearing loss: hearing loss induced by trauma, such as from a loud rock concert or an explosion; and hearing loss that arises from unknown origins, that is, idiopathically, based on causes suspected to include changes in blood flow to the inner ear, bacterial and viral infections, autoimmune disease and others. The former is known as AAT. The latter is known as ISSNHL. Together they can be defined as ASNHL. In both cases, the onset is sudden. And in both cases, part of the initial hearing loss tends to recover naturally in the days and weeks following the loss; however, some of the loss may remain and, over time, become chronic in nature and less amenable to therapeutic intervention.

ASNHL differs from age-related hearing loss or hearing loss driven by chronic exposure to noise. Those types of hearing loss arise more slowly or on the basis of repeated insults, in slow motion. By contrast, in the case of ASNHL, the effects are felt immediately. This difference in the speed of progression is significant since sudden hearing losses are noticed much more readily.

ASNHL involves a variety of pathologic processes such as massive release of free reactive oxygen species, excessive and pathological stimulation of receptors on neurons by neurotransmitters like glutamate, and inflammation. These reactions, in turn, can damage sensorineural structures of the inner ear such as the sensitive inner and outer hair cells and nerve cells that line the interior of the cochlea. If the stress incident is severe enough, it may lead to permanent cochlear injury with irreversible loss of hair cells and nerve cells. Cell death occurs primarily through so-called programmed cell death, which is driven by damaged cells (apoptosis), and to a lesser extent also through necrosis, which is a passive consequence of gross injury to the cell.

JNK is a signal transmitting enzyme that is stress-activated and regulates a number of important cellular activities. Stresses to the cochlea such as those described above, if severe enough, can activate the JNK signal transduction pathway, leading to the activation of transcription factors such as c-jun and c-fos that are found in the cell nucleus. This activation, in turn, activates genes encoding inflammatory molecules or promoting cell death.

Current Therapies and Unmet Need

Sensorineural hearing loss may have a serious impact on people's personal and professional lives. Severe to profound hearing loss can result in high societal costs, mostly due to reduced work productivity, as reported in 2000 in the International Journal of Technology Assessment in Healthcare. Yet no treatment currently exists that has unequivocal evidence of efficacy for AAT or ISSNHL. There is no FDA- or EMA-approved drug on the market for sensorineural hearing loss. The only remaining therapeutic option is a hearing aid or, in cases of deafness or near-deafness, a cochlear implant.

A patient with the acute form of hearing loss may recover on his or her own, especially if the loss is of low or moderate intensity and severity. This is due to intrinsic repair mechanisms inside the cochlea. However, in other cases the patient may recover only partially or not at all. In those cases, in the absence of effective treatment, acute hearing loss will become chronic and irreversible. There is currently no possibility to regrow or replace sensory structures inside the inner ear that are not recovered in the weeks immediately following the loss.

For ASNHL, non-specific treatments are frequently prescribed, mostly on an off-label empirical basis. These may include glucocorticoids and steroids such as prednisolone or dexamethasone; vasodilators such as pentoxyfilline; rheologics; ionotropics and local anesthetics; antioxidants and thrombolytics.

In the United States, most frequently oral prednisolone is administered for the treatment of ASNHL. Corticosteroids are intended to reduce inflammation and swelling in the ear that may be related to hearing loss. The U.S. treatment guideline by the American Academy of Otolaryngology/Head & Neck Surgery for ISSNHL lists oral steroids and hyperbaric oxygen as treatment options, but refrains from recommending them in light of the low evidence level for their efficacy. Indeed, Nosrati-Zarenoe and Hultcrantz presented in 2012 in the journal Otology and Neurotology the results of a Swedish placebo controlled trial with oral prednisolone in the treatment of ISSNHL that showed no therapeutic effect on hearing loss from active treatment.

Our Solution—Sonsuvi® (AM-111)

We are developing Sonsuvi® as a treatment for acute inner ear hearing loss. Sonsuvi® contains a synthetic D-form peptide (D-JNKI-1) that acts as a c-Jun N-terminal Kinase (JNK) ligand, thereby protecting sensorineural structures in the inner ear from stress-induced damage. We are developing D-JNKI-1 under a worldwide exclusive license for the treatment of ear disorders from Xigen (Switzerland). Like Keyzilen®, Sonsuvi® is delivered in a biocompatible gel formulation via intratympanic injection. We have established the safety and preliminary efficacy of Sonsuvi® in a Phase 2 and in a Phase 3 clinical trial. The acute stage of hearing loss represents a window in time in which the inner ear can be protected from permanent hearing loss. Sonsuvi® received orphan drug designation by both EMA and FDA in 2005 and 2006, respectively, and was granted fast track designation by the FDA in 2017.

Therapeutic rationale for Sonsuvi® in hearing loss

The proprietary API of Sonsuvi® is brimapitide (D-JNKI-1), a 31 amino acid synthetic D-form peptide that binds to JNK and inhibits activation of transcription factors such as c-jun and c-fos, thereby protecting sensorineural structures from stress-induced inflammation and apoptosis. Brimapitide comprises an active transporter sequence, or D-TAT, that enables Sonsuvi® to cross the round window membrane quickly, diffuse widely throughout the cochlea, transfect sensorineural cells effectively and reach its target inside the cell nucleus. The D-form of the peptide provides for protease resistance and hence enhanced stability. Sonsuvi® was shown to remain pharmacologically active for several days inside the cochlea. The D-form is necessary for Sonsuvi® to cross the RWM.

By attenuating inflammation and protecting cells from apoptosis, we believe that Sonsuvi® reinforces natural recovery processes and helps to prevent or minimize permanent damage respectively chronic hearing loss. Sonsuvi®'s otoprotective effect has been demonstrated in various animal models of cochlear stress, including AAT, acute labyrinthitis (inflammation), drug ototoxicity (aminoglycosides), bacterial infection, cochlear ischemia and cochlear implantation trauma.

We conducted our pre-clinical development program for Sonsuvi® in close collaboration with academic partners and various CROs. Brimapitide was invented by Xigen in Lausanne, Switzerland. In 2003, we signed a Collaboration and License Agreement with Xigen, under which we in-licensed worldwide exclusive rights for use of D-JNKI-1 in the treatment of ear disorders. Under the agreement with Xigen, we have exchanged various pre-clinical and clinical data.

Hearing loss endpoints

Unlike tinnitus, where measures of therapeutic outcomes have to rely on PROs, the evaluation of hearing is based on psychoacoustic measures performed by audiologists. Audiometric procedures and equipment are highly standardized around the world; hearing thresholds are typically determined by presenting pure tones in the 250 Hz to 8 kHz range through headphones or ear inserts (air conduction) or through a vibrator placed behind the ear or on the forehead (bone conduction). An increase in volume of 10 dB is perceived as twice as loud. In other words, a person whose hearing thresholds improved by 10 dB can hear sounds at half the intensity level that was necessary before. A change of this magnitude is generally considered to be clinically relevant. In addition to pure tone audiometry usually speech audiometry is conducted, in which the audiologist measures a patient's ability to hear and correctly understand a series of monosyllabic words.

Sonsuvi® Clinical Development

We have completed three clinical trials of Sonsuvi® that demonstrated its favorable safety profile and efficacy in treating more severe types of ASNHL. We have benefited several times from engaging in a protocol assistance procedure with the EMA and exchanges with the FDA. The design of our pivotal Phase 3 clinical trials was based on the outcomes from our Phase 2 clinical trial and our discussions with the EMA and FDA.

Phase 1/2 Clinical Trial

A Phase 1/2 clinical trial was conducted at two centers in Germany in January 2006, with 11 patients suffering from AAT due to New Year's firecracker accidents. Patients had at least 30 dB hearing loss by pure tone audiometry (average of 4 and 6 kHz) and were treated within 24 hours of onset.

Trial participants received a single dose of Sonsuvi® at either 0.4 mg/mL or 2 mg/mL in a biocompatible gel formulation by intratympanic injection into the most affected ear. The primary endpoint of the trial was the recovery of hearing thresholds from baseline to Day 30. Sonsuvi® was well tolerated by all trial participants, regardless of the dose. The Phase 1/2 trial provided the first indications of therapeutic benefit of Sonsuvi® in humans.

Phase 2 Clinical Trial

To further evaluate the efficacy and safety of Sonsuvi® we conducted a Phase 2b clinical trial between 2009 and 2012. Since pre-clinical tests had demonstrated Sonsuvi®'s otoprotective effects in many different types of cochlear stress, the patient population was expanded from AAT cases to also include patients affected by ISSNHL. In addition, based on observations from our Phase 1 clinical trial, we expanded the allowed time window from 24 to 48 hours from onset. The design for this Phase 2b trial was discussed with the EMA under a protocol assistance procedure.

As described by Suckfuell and colleagues in an article in Otology & Neurotology in 2014, the trial enrolled 210 participants who suffered from ASNHL (unilateral ISSNHL, uni-or bilateral AAT) with hearing loss of at least 30 dB at the average of the three worst affected frequencies (pure tone average; PTA) and onset not more than 48 hours previously. Sonsuvi® was dosed at 0 mg/mL (placebo), 0.4 mg/mL (Low Dose) and 2.0 mg/mL (High Dose). All patients without a clinically relevant hearing recovery on Day 7 were given the option to take a course of oral prednisolone as a reserve therapy. The primary efficacy endpoint was hearing loss recovery from baseline to Day 7 at the three worst affected frequencies. The trial consisted of a baseline assessment and four follow-up visits on Days 3, 7, 30, and 90.

Sonsuvi® demonstrated a favorable safety profile in this trial. There were no statistically significant differences in the occurrence of clinically relevant hearing deterioration in the treated ear. Also, there was no apparent difference in the frequency of adverse events between placebo and Sonsuvi® treated patients at any time point, no systemic side effects and no negative impact on balance or tinnitus. There were transient procedure related effects such as ear discomfort or pain, incision site complications or middle ear infection in less than 5% of cases.

Overall, the trial did not meet its primary efficacy endpoint. Analysis of PTA improvement by hearing loss severity in accordance with a commonly used hearing loss classification revealed unexpectedly strong spontaneous recovery for lesser severities: by Day 7, placebo-treated patients enrolling with mild-to-moderate hearing loss (PTA <60 dB) had recovered more than three quarters of their initial loss, whereas for patients with severe to profound hearing loss (PTA ≥60 dB), it was only about one quarter. Post-hoc analyses in the severe-to-profound hearing loss subgroup demonstrated superiority of Sonsuvi® 0.4 mg/mL over placebo for the primary endpoint, improvement in absolute PTA, as well as for co-primary efficacy endpoints, hearing improvement relative to the initial hearing loss and frequency of complete hearing recovery. Further, the improvement in word recognition scores was nominally significant as well as the frequency of complete tinnitus remission.

The Sonsuvi® 2.0 mg/mL group overall showed improvement between the Sonsuvi® 0.4 mg/mL and the placebo groups, without reaching statistical significance. However, differences between the two active treatment groups were nominally not significant.

Phase 3 Clinical Program

Based on Phase 2 clinical trial outcomes, we initiated a Phase 3 clinical program including confirmatory testing of Sonsuvi® 0.4 mg/mL as well as exploring potential incremental therapeutic benefits from a higher concentration (0.8 mg/mL) in ISSNHL patients. Since a “bell shaped” dose response curve was observed in animal studies, testing a concentration between 0.4 and 2.0 mg/mL was expected to shed further light on the dose effect relationship in humans. In view of the high spontaneous recovery in the mild to moderate hearing loss subgroup observed in Phase 2, recruitment was limited to patients experiencing severe or profound ISSNHL, i.e. patients with more pronounced medical need. Further, the time window for inclusion was extended from up to 48 hours to up to 72 hours from ISSNHL onset as the magnitude of the therapeutic effect in Phase 2 did not appear to decrease when the later treatment was started. This enlargement also aligned the duration of the time window with the period over which ISSNHL can develop, which is defined, e.g. by the U.S. practice guideline for sudden sensorineural hearing loss, as 72 hours.

The first Phase 3 trial, called HEALOS, enrolled a total of 256 patients in several European and Asian countries. In November 2017, we announced that the HEALOS Phase 3 clinical trial did not meet the primary efficacy endpoint of a statistically significant improvement in hearing from baseline to Day 28 compared to placebo for either active treatment groups in the overall study population. 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. Further, patients treated with Sonsuvi® 0.4 mg/mL showed a nominally significantly lower incidence of no hearing improvement compared to placebo by Day 91 as well as a superior improvement in word recognition score. Outcomes with Sonsuvi® 0.8 mg/mL tended to be somewhat less pronounced than those observed for Sonsuvi® 0.4 mg/mL. Sonsuvi® was well tolerated and the primary safety endpoint was met.

Together with the outcomes of the HEALOS trial, we announced that ASSENT, the second Phase 3 clinical trial investigating Sonsuvi®, was terminated early in order to avoid the need for substantial protocol changes and interruptions of enrollment pending feedback from health authorities on the regulatory pathway. ASSENT was planned to enroll a total of 300 patients in the US, Canada and South Korea. In contrast to HEALOS and the Phase 2 trial, where patients with insufficient hearing recovery had the option of receiving a course of oral corticosteroids as reserve therapy, all patients in ASSENT would receive oral corticosteroids as a background therapy. At the time of early termination, the ASSENT trial had recruited 56 patients.

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. We currently aim to implement the further development of Sonsuvi® through strategic partnering, special purpose vehicle financing, grant funding or a combination thereof. There is no guarantee that we will be successful in any pursuit of such transactions or that we will be able to continue our efforts to develop and commercialize Sonsuvi® in the future on a non-dilutive basis, or that any alternative course of action will lead to the success of the program.

Competition

We may face competition from different sources with respect to our product candidates Keyzilen® (AM-101), Sonsuvi® (AM-111), AM-125, AM-201, AM-301 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 acute inner ear tinnitus, hearing loss, vertigo, allergic rhinitis or viral infections. Any 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.

Vestibular Disorders

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

- Otonomy is developing a polymer-based formulation for the steroid dexamethasone (Otividex; OTO-104) for patients with Meniere's disease. In August 2017 Otonomy announced that a Phase 3 clinical trial conducted in the United States had failed to show a treatment effect of OTO-104 against placebo and that a European Phase 3 clinical trial was terminated early. In November 2017 the company announced that the European study showed a statistically significant reduction in the count of definitive vertigo days. In February 2020 the company announced that a new Phase 3 trial with OTO-104 had failed to reach its primary efficacy endpoint.

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

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.

Antipsychotic-induced weight gain

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

- ALKS-3831 is a fixed-dose combination of olanzapine and samidorphan, a novel opioid system modulator, which is being developed by Alkermes Inc. with the specific aim of providing the therapeutic benefits of olanzapine with less weight gain than olanzapine monotherapy. In November 2018 Alkermes announced that the ENLIGHTEN-2 phase 3 trial with ALKS-3831 had met its coprimary endpoints of mean % body weight change from baseline and % of patients with ≥10% weight gain. The reported reduction in weight gain over 6 months was 37% versus olanzapine monotherapy. In November 2019, Alkermes filed an NDA with the FDA for US approval; in January 2021, the FDA accepted the resubmission of an amended NDA. If approved, AM-201 will compete against ALKS 3831.

If approved, ALKS-3831 will reach the market well before AM-201. We believe that our product may provide various benefits over ALKS-3831, notably that it does not come in a fixed dose combination, allowing for dosing flexibility, has a different mode of action, providing potentially also effects on daytime sleepiness, another side effect of olanzapine and that it may be used with other antipsychotic drugs than olanzapine.

As weight gain is associated with immediate metabolic side effects it is advisable to prevent antipsychotic-induced weight gain rather than seek to treat the overweight once it has developed. Weight monitoring, dietary and lifestyle changes as well as behavioral and cognitive counseling present the most effective non-pharmacologic ways to prevent and also treat antipsychotic weight gain. Pharmacologic approaches include the switch to an alternative antipsychotic treatment strategy, which however can be associated with a loss of efficacy or the appearance of other side effects. Limited evidence for efficacy with metformin as an exploratory adjuvant to prevent antipsychotic-induced weight gain has been demonstrated.

Allergic rhinitis and upper respiratory airway infections

We believe that our main competitors for AM-301 are Marinomed Biotech AG or Marinomed, Trutek Corp. or Trutek, Nasaleze Ltd. or Nasaleze, Nasus Pharma Ltd. or Nasus Pharma, and larger companies such as GSK, Bayer, Sanofi, Procter & Gamble, Reckitt Benckiser, and Johnson & Johnson. These companies already market a variety of OTC drug or drug-free products for the management of allergic rhinitis and/or protection against certain viruses. E.g. Nasaleze and Nasus Pharma market nasal sprays based on hydroxypropylmethylcellulose (HPMC) powder which serves to establish a barrier on the nasal mucosa. Marinomed is marketing through various licensees a nasal spray based on carrageenan, a sulfated polymer from red seaweed, for protection against certain respiratory viral infections. Trutek is marketing a gel that is applied around the nostrils and above the upper lip to prevent airborne particles from entering the nose. 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.

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. Based on publicly available information, we have further identified the following drug product candidate that is currently in clinical development:

- Otonomy Inc. acquired an early stage NMDA receptor antagonist product candidate (NST-001, gacyclidine) from Neurosystec Inc. in October 2013. Following OTO-311's evaluation in a Phase 1 trial and a subsequent change in formulation, Otonomy initiated a Phase 1/2 trial with the modified drug product OTO-313 in 2019. In July 2020 Otonomy announced the results from a Phase 1/2 trial and in November 2020 the initiation of a Phase 2 trial for the first quarter of 2021. Based on publicly available information, OTO-313 will target a similar group of tinnitus patients.

Progress in the development of Keyzilen® and in particular market approval may attract increased interest in developing treatments for acute inner ear tinnitus and may lead to the arrival of new competitors.

Acute inner ear hearing loss

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

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

- Sensorion, a French company, is developing SENS-401 (R-azasetron besylate) for the treatment of sudden sensorineural hearing loss by way of oral administration. In 2019, the company initiated a Phase 2 trial, the conclusion of which is expected by the company for the fourth quarter of 2021. Sensorion has received orphan drug designation by the EMA for sudden sensorineural hearing loss.

- Southern Illinois University has an antioxidant product candidate (D-methionine) that is designed for oral administration in the prevention and treatment of noise induced hearing loss and currently being tested in a late stage study with the Department of Defense. Enrolment was completed and the study terminated in April 2019; no results have been published so far.

- Strekin AG, a privately held Swiss company, has an agonist of the peroxisome proliferator (STR001) that it plans to develop for sudden sensorineural haring loss. The company announced the completion of enrollment in a Phase 3 trial; however, no results have been published so far. Strekin has received orphan drug designation by the EMA for sudden sensorineural hearing loss.

- Frequency Therapeutics is developing FX-322, a small molecule for the regeneration cochlear hair cells through activation of progenitor cells already present in the cochlea. After a Phase 1/2 trial had showed improvement in some measures of hearing loss, the company initiated a Phase 2 clinical trial in patients with mild to moderately severe acquired SNHL, and two Phase 1b trials in patients with severe SNHL or mild to moderately severe age-related hearing loss. Results from the trials are expected through 2021. If successful, STR001 and FX-322 may compete against Sonsuvi®.

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, 2020, we own eleven issued U.S. patents and seven pending U.S. patent applications along with foreign counterparts of particular patents and applications in various jurisdictions. We co-own three of our issued U.S. patents, and one of our pending patent applications with INSERM, along with their foreign counterparts, pursuant to the terms of our co-ownership and exploitation agreement.

In addition, as of December 31, 2020, we have exclusively licensed from Xigen eleven issued U.S. patents and one pending U.S. patent applications, along with their foreign counterparts in various jurisdictions that cover the composition of matter or method of use of JNK ligand peptides in a limited field including the intratympanic treatment of ASNHL.

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

Intranasal Betahistine

We have acquired one patent from Otifex directed to intranasal application of betahistine for Eustachian tube dysfunction that is issued in the United States. In addition, we purchased 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-301

In 2020, we filed two provisional US patent applications relating to the formulation and use of AM-301; we expect to file additional one or more provisional applications in 2021 and to convert the most recent provisional application into a non-provisional application.

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 three issued U.S. patents and one pending U.S. application and corresponding patents and applications in other jurisdictions including Europe, Eurasia, Australia, Canada, Japan, Brazil, China, South Korea, Israel, India, Mexico, Philippines, Russia, South Africa and New Zealand, covering formulation and use of Ketamine. Our issued patents and pending patent applications relating to Keyzilen® are expected to expire between 2024 and 2028, prior to any patent term extensions to which we may be entitled under applicable laws.

Sonsuvi®

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

Proprietary Rights

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

In March 2019, the FDA approved esketamine in a spray formulation for treatment-resistant depression (SPRAVATO). The product was developed by Janssen, a subsidiary of Johnson & Johnson. Therefore we can no longer expect to obtain the potential benefit of a five year market exclusivity period.

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 Auris Medical, 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

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. We alone are entitled to grant manufacturing or sales licenses for any patents to our subsidiaries and/or third parties. 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. See “Item 4. Information on the Company—B. Business Overview—Collaboration and License Agreements—INSERM.”

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. Further, pursuant to our agreement, we and Xigen agreed to enter into a supply agreement within a specified period after the date of the agreement, which period has since passed, pursuant to which Xigen would supply us with licensed compounds. We did not enter into such a supply agreement with Xigen. Xigen supplied us with the API for Sonsuvi® for a period of time, but we presently are receiving our supply from an alternative supplier.

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. Either we or Xigen may terminate the agreement for the other party's material breach or bankruptcy, in the event of force majeure, or after a specified period following the date of the agreement, if we are not progressing any activities with respect to the licensed compound. This period has passed for Sonsuvi®. In August 2019 Xigen was acquired by Kuste Biopharma SAS, or Kuste, a French company. In February 2021, we were notified by Kuste of its decision to terminate the agreement effective May 10, 2021 due to the alleged lack of any development work since August 2018. We consider that the purported termination is without effect and that the agreement continues to be in full force and effect in accordance with its terms. We have retained legal counsel and intend to defend our interests, as appropriate and necessary.

Manufacturing

We currently rely on and expect to continue to rely on third parties for the supply of raw materials and to manufacture supplies for clinical trials of our product candidates, including AM-125, AM-201, AM-301, Keyzilen® and Sonsuvi®. For the foreseeable future, we expect to continue to rely on such third parties for the manufacture of any of our product candidates on a clinical or commercial scale, if any of our product candidates receives regulatory approval or clearance. 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 manufacture of our 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 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 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 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 do not have a commercialization infrastructure. If any of our drug product candidates is granted marketing approval, we intend to focus our initial commercial efforts in the United States and select European markets, which we believe represent the largest market opportunities for us. In those markets, we expect our commercial operations to include our own specialty sales force that we will specifically develop to target ENTs and specialists in neurotology and neurology, both in hospitals and in private practice. In other markets, we expect to seek partnerships that would maximize our products' commercial potential.

For the commercialization of our AM-301 nasal spray device, which we intend to initiate in 2021 subject to regulatory clearance and approvals, respectively, we plan to rely on commercial partners with presence in "over-the-counter" markets and / or providers of "go to market" services. We may be unable to secure appropriate or timely support and as a result experience a delay of the product launch or product sales below our expectations. Further, as an "OTC" product, the purchase of AM-301 by consumers is unlikely to be eligible for reimbursement by health insurance plans and will therefore have to be purchased out of their own pockets. We expect the lack of reimbursement coverage to reduce the pool of potential buyers.

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 a 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 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 IRB, either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries. The FDA, the IRB or the clinical trial sponsor may suspend or terminate clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the study. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

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

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

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

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

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

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

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

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

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

Device Approval Process

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

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

AM-301 is also intended for use in the reduction of the intranasal infectious viral load following inspiration of airborne viruses such as SARS-CoV-2. Since there may be no valid predicate device available for this intended use, we may have to submit a de novo request to the FDA. Under the de novo pathway, we would have to prove that AM-301 does not present substantial risk to the patient rather than just demonstrating substantial equivalence with the safety of the relevant predicate device(s), which may require additional testing. The review by the FDA would take a minimum of 150 days in the de novo process compared to a minimum of 90 days in 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.

Many foreign countries in which we intend to market AM-301 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 will repeal and replace the MDD with effect from May 26, 2021. The MDR clearly envisages, among other things, stricter controls of medical devices, including strengthening of the conformity assessment procedures, increased expectations with respect to clinical data for devices and pre-market regulatory review of high-risk devices. The MDR also envisages greater control over notified bodies and their standards, increased transparency, more robust device vigilance requirements and clarification of the rules for clinical investigations. Under transitional provisions, medical devices with notified body certificates issued under the MDD prior to May 26, 2021 may continue to be placed on the market for the remaining validity of the certificate, until May 27, 2024 at the latest. After the expiry of any applicable transitional period, only devices that have been CE marked under the MDR may be placed on the market in the EU.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000, there is no reasonable expectation that sales of the drug in the United States will be sufficient to offset the costs of developing and making the drug available in the United States. Orphan drug designation must be requested before submitting an NDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If the FDA approves a sponsor’s marketing application for a designated orphan drug for use in the rare disease or condition for which it was designated, the sponsor is eligible for a seven-year period of marketing exclusivity, during which the FDA may not approve another sponsor’s marketing application for a drug with the same active moiety and intended for the same use or indication as the approved orphan drug, except in limited circumstances, such as if a subsequent sponsor demonstrates its product is clinically superior. During a sponsor’s orphan drug exclusivity period, competitors, however, may receive approval for drugs with different active moieties for the same indication as the approved orphan drug, or for drugs with the same active moiety as the approved orphan drug, but for different indications. Orphan drug exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for a drug with the same active moiety intended for the same indication before we do, unless we are able to demonstrate that grounds for withdrawal of the orphan drug exclusivity exist, such as that our product is clinically superior. Further, if a designated orphan drug receives marketing approval for an indication broader than the rare disease or condition for which it received orphan drug designation, it may not be entitled to exclusivity.

Pharmaceutical Coverage, Pricing and Reimbursement

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

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

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

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

Healthcare Reform

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

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

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

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

Other Regulatory Requirements

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

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

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

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

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

Other Healthcare Laws

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

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

C. Organizational structure

The registrant corporation, Auris Medical Holding Ltd., had seven wholly-owned subsidiaries as of December 31, 2020, 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 500 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 the information under "Item 3. Key Information—A. Selected Financial Data" and 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-stage biopharmaceutical company dedicated to developing therapeutics that address important unmet medical needs in neurotology, rhinology and allergy and CNS disorders. We are focusing on the development of intranasal betahistine for the treatment of vertigo (AM-125, in Phase 2) and for the prevention of antipsychotic-induced weight gain and somnolence (AM-201, post Phase 1b). Through our affiliate Altamira Medica, we are developing a nasal spray for protection against airborne viruses and allergens (AM-301).

To date, we have financed our operations through public offerings of our common shares, private placements of equity securities, and short- and long-term loans. We have no products approved for commercialization and have never generated any revenues from royalties or product sales. As of December 31, 2020, we had cash and cash equivalents of CHF 11.3 million. Based on our current plans, we do not expect to generate royalty or product revenues unless and until we obtain marketing approval or clearance for, and commercialize, AM-125, AM-201, AM-301, Keyzilen®, or Sonsuvi®, or any of our other product candidates.

As of December 31, 2020, we had an accumulated deficit of CHF 160.6 million. We expect to continue incurring losses as we continue our clinical and pre-clinical development programs, apply for marketing approval for our product candidates and, subject to obtaining regulatory approval of our product candidates, build a sales and marketing force in preparation for the potential commercialization of our product candidates.

Collaboration and License Agreements

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. See “Item 4. Information on the Company—B. Business Overview—Collaboration and License Agreements—Xigen.”

Otifex

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

Anti-psychotic induced weight-gain

On April 24, 2018, we entered into an asset purchase agreement pursuant to which we agreed to purchase two patents related to the treatment of anti-psychotic induced weight-gain which we refer to as AM-201. The transaction closed in April 2018.

Financial Operations Overview

We expect our regular total cash need in 2021 to be in the range of CHF 11.5 to 13.0 million for our expected total operating expenses of CHF 7 to 8 million and our expected capitalized research and development costs of CHF 4.5 to 5 million. Further cash needs may arise in 2021 related to the manufacture of AM-301 as well as marketing and sale activities as we intend to commercialize the product in selected markets; these cash needs may initially not be covered by cash flows from product revenues.

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 and amortization of tangible and intangible fixed assets used to develop our product candidates.

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

- AM-125 for Vertigo. The "TRAVERS" Phase 2 trial will enroll 118 patients suffering from acute vertigo following surgical removal of a vestibular schwannoma, a tumor growing behind the inner ear, resection of the vestibular nerve (vestibular neurectomy) or surgical removal of parts of the inner ear (labyrinthectomy). It is conducted in several European countries and Canada. The TRAVERS trial started recruitment during the third quarter of 2019. In September 2020 we announced the results of an interim analysis from Part A of the trial, which comprised a dose escalation – 1, 10 or 20 mg or placebo – in 33 patients. The interim analysis showed a dose-dependent improvement in balance as well as good safety and tolerability of ascending doses of AM-125. Based on the results from the interim analysis, we selected the two highest doses, 10 and 20 mg, for testing against placebo in 72 patients in Part B of the trial. Prior to starting Part B of the trial in October 2020, we tested oral betahistine (48 mg) open label for reference purposes. Enrollment into TRAVERS has been impacted by the COVID-19 pandemic, as the type of neurosurgery required for participation in the trial is classified as an elective procedure and hence was postponed and as many participating sites temporarily reduced or suspended clinical research activities. The effect was particularly felt in spring 2020 and then again in early 2021. We expect to complete enrollment in the third quarter of 2021.

- AM-201 for Antipsychotic-Induced Weight Gain. We conducted a Phase 1b trial in Europe with AM-201 in antipsychotic-induced weight gain. Participants received either AM-201 (1, 2.5, 5, 10, 20 or 30 mg) or placebo in parallel with oral olanzapine (10 mg) once a day for four weeks. In October 2019, we announced interim results from the first 50 participants in the trial. The study demonstrated good safety and tolerability of AM-201 and revealed relevant reductions in olanzapine-induced weight gain and daytime sleepiness. The trial then proceeded to the next higher and final dose level of 30 mg tested in an additional 30 healthy volunteers. 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).

- AM-301 for Protection Against Airborne Allergens and Viruses: In September 2020 we announced the launch of the development of AM-301, a drug-free nasal spray for protection against airborne viruses and allergens. Following formulation development, we tested AM-301 in vitro in reconstituted human nasal epithelia infected with SARS-CoV-2. Daily treatment with AM-301, beginning right before inoculation, showed effective protection against viral infection: 48 hours post-infection, average virus titers were 90.0% lower than those observed in controls ($p<0.01$). 72 hours and 96 hours post-infection, average virus titers were 99.2 and 99.4% lower, respectively ($p<0.001$). In January 2021 we initiated an open-label randomized cross-over study with AM-301 that will enroll 36 patients with allergic rhinitis to grass pollen. Study participants will be administered a single dose of AM-301 nasal spray or a comparator product prior to controlled pollen exposure for four hours in an allergen challenge chamber. The challenge will be repeated with the alternate treatment following a wash-out period. We expect results from the study in the second quarter of 2021. In addition, various pre-clinical and clinical assessments are either planned or ongoing in 2021.

- *Sonsuvi® (AM-111)* for Acute Inner Ear Hearing Loss. Following 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. We currently aim to implement the further development of Sonsuvi® through strategic partnering thereof. Pending such funding, we expect our research and development expenses in connection with the Sonsuvi® program to remain minimal.

- *Keyzilen® (AM-101).* We conducted a Phase 3 clinical development program with Keyzilen® comprising two Phase 3 trials and two open label follow-on trials. We completed enrollment of the last of these trials (TACTT3) in September 2017. In March 2018 we announced that preliminary top-line data from the TACTT3 trial indicated that the study did not meet its primary efficacy endpoint of a statistically significant improvement in the Tinnitus Functional Score from baseline to Day 84 in the active treated group compared to placebo either in the overall population or in the otitis media subpopulation. 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 following traumatic cochlear injury and provide confirmatory efficacy data to support a filing for marketing authorization. In September 2019 we announced that we had 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®. We intend to fund further development of Keyzilen® either through partnerships or research grants. Pending such funding, we expect our research and development expenses in connection with the Keyzilen® program to remain minimal.

Other research and development expenses mainly relate to our pre-clinical studies of AM-102 (second generation tinnitus treatment). The expenses mainly consist of costs for production of the pre-clinical compounds and costs paid to academic and other research institutions in conjunction with pre-clinical testing.

For the years ended December 31, 2020, 2019 and 2018, we also spent CHF 2.7 million, CHF 4.3 million and CHF 3.5 million, respectively, on research and development expenses related to our intranasal betahistine program (before capitalization of expenses related to AM-125). For the year ended December 31, 2020, we spent CHF 0.8 million on research and development expenses related to AM-301. For the same time periods, we spent CHF 0.1 million, CHF 0.5 million, and CHF 1.7 million, respectively, on research and development expenses related to Keyzilen®. For the same time periods, we spent CHF 0.1 million, CHF 0.1 million, and CHF 1.5 million, respectively, on research and development expenses related to Sonsuvi®. In addition, we incurred research and development expenses related to our earlier stage products.

Following a marked reduction in research and development expenses related to the conclusion of the Phase 3 trials with Keyzilen® and Sonsuvi®, their level is expected to start increasing again from 2021 onward as we advance the clinical development with AM-125, AM-201, and AM-301. At this time, we cannot reasonably estimate the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, or the period, if any, in which material net cash inflows may commence from, any of our product candidates. This is due to numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

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

A change in the outcome of any of these variables with respect to the development of AM-125, AM-201, AM-301, Keyzilen®, and Sonsuvi®, or any other product candidate that we may develop could mean a significant change in the costs and timing associated with the development of such product candidate. For example, if the FDA or other regulatory authority were to require us to conduct pre-clinical and clinical studies beyond those which we currently anticipate will be required for the completion of clinical development or if we experience significant delays in enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of the clinical development.

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 2020, our interest expense consisted principally of interest on the convertible loan provided by FiveT. In 2019, our interest expense consisted principally of bank charges and interest expenses due to the Loan and Security Agreement with Hercules. On January 31, 2019, we made the final payment to Hercules under the facility, comprising the last amortization payment as well as an end of term charge. In March 2021, we issued common shares in full satisfaction of the convertible loan provided by FiveT.

Revaluation loss/gain from derivative financial instruments

Expenses related to fair value measurement of derivatives embedded in the FiveT convertible loan of CHF 2,248,257 were recorded as financial expenses in profit or loss.

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

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

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

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

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

Foreign currency exchange gain/(loss), net

Our foreign currency exchange gain/(loss), net, consists primarily of unrealized gains or losses on our USD and EUR denominated cash and cash equivalents.

Transaction costs

Transaction costs are shown as costs if they are not directly attributable to the equity transaction. Transaction costs increased by CHF 219,615 in the year ended December 31, 2020 compared to the previous year, due to the write off of the remaining capitalized derivate financial instrument related to a commitment purchase agreement with LPC dated May 2, 2018 (the “2018 Commitment Purchase Agreement”). The agreement was formally still effective as of December 31, 2020, but no more in use.

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, 2020 and 2019

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

Research and development expense

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

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

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

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

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

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

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

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

General and administrative expense

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

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

Interest income

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

Interest expense

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

Foreign currency exchange gain/(loss), net

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

Revaluation gain/(loss) from derivative financial instruments

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

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

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

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

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

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

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

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

Income tax 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), decreased 64% from 2019 to 2020. The loss in 2020 is primarily due to an actuarial loss arising from experience adjustment.

Foreign currency translation differences

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

Comparison of the years ended December 31, 2019 and 2018

	Year Ended December 31,		
	2019	2018	Change
	(in thousands of CHF)		%
Research and development	(3,325)	(6,690)	(50)%
General and administrative	(3,934)	(4,264)	(8)%
Operating loss	**(7,259)**	**(10,954)**	**(34)%**
Interest income	18	—	(100)%
Interest expense	(29)	(1,070)	(97)%
Foreign currency exchange loss, net	(219)	(140)	57%
Revaluation loss from derivative financial instruments	664	1,350	(51)%
Transaction Costs	—	(520)	(100)%
Loss before tax	**(6,825)**	**(11,334)**	**(40)%**
Income tax gain/(expense)	194	(162)	(220)%
Net loss attributable to owners of the Company	**(6,631)**	**(11,496)**	**(42)%**
Other comprehensive loss:			
Items that will never be reclassified to profit or loss			
Remeasurements of defined benefits liability	(72)	1,277	(106)%
Items that are or may be reclassified to profit or loss			
Foreign currency translation differences	16	(11)	(245)%
Other comprehensive income/(loss)	(56)	1,266	(104)%
Total comprehensive loss attributable to owners of the Company	**(6,687)**	**(10,230)**	**(35)%**

Research and development expense

	Year Ended December 31,		
	2019	2018	Change
	(in thousands of CHF)		%
Research and development expense			
Clinical projects	(993)	(846)	17%
Pre-clinical projects	(182)	(873)	(79)%
Drug manufacture and substance	(481)	(2,185)	(78)%
Employee benefits	(1,374)	(1,653)	(17)%
Other research and development expenses	(295)	(1,132)	(74)%
Total	**(3,325)**	**(6,689)**	**(50)%**

Research and development expense decreased by 50% from CHF 6.7 million in 2018 to CHF 3.3 million in 2018. 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 2018 and 2019 are mainly due to the following factors:

- Capitalization of internal costs for AM-125. In the year ended December 31, 2019, we capitalized direct costs related to our AM-125 program for a total amount of CHF 3.2 million, compared to CHF 1.9 million in the year ended December 31, 2018.

- Clinical projects. In the year ended December 31, 2019, we incurred lower service and milestone costs for our Keyzilen® and Sonsuvi® studies, mainly reflecting the completion of our late-stage clinical trials as well as the capitalization of direct cost related to the AM-125 program.

- Pre-clinical projects. In the year ended December 31, 2019, pre-clinical expenses increased by 79% due to an increase in activities in our intranasal betahistine program.

- Drug manufacture and substance. In the year ended December 31, 2019, costs related to raw material purchases and expenses decreased by 78% mainly due to higher costs for process validation related to lower AM-111 project activities and the capitalization of directs costs in our AM-125 program.

- Employee benefits. Employee benefit costs decreased in 2019 due to lower headcount and lower recruiting fees.

- Other research and development expenses. Other research and development expenses decreased by CHF 0.8 million in the year ended December 31, 2019 compared to the year ended December 31, 2018 primarily due to a reduction in regulatory related activities. Further we capitalized legal costs related for patent registration related to the AM-125 program.

General and administrative expense

	Year Ended December 31,		
	2019	2018	Change
	(in thousands of CHF)		%
General and administrative expense			
Employee benefits	(1,011)	(1,084)	(7)%
Business development	(114)	(44)	159%
Travel expenses	(103)	(71)	45%
Administration expenses	(2,653)	(2,798)	(5)%
Lease expenses	(27)	(52)	(48)%
Depreciation tangible assets	(11)	(187)	(94)%
Capital tax expenses	(15)	(29)	(48)%
Total	**(3,934)**	**(4,265)**	**(8)%**

General and administrative expenses decreased by 8% from CHF 4.3 million in 2018 to CHF 3.9 million in the year ended December 31, 2019. The decrease is related to lower employee benefits due to lower headcount and employee benefit-related expenses, partly offset by consultancy costs related to the Redomestication.

Interest income

Interest income increased in the year ended December 31, 2019 compared to year the ended December 31, 2018 due to interest earned in the year ended December 31, 2019 on short-term deposits.

Interest expense

Interest expense related to the Hercules Loan and Security Agreement decreased substantially in the year ended December 31, 2019 to CHF 0.03 million compared to CHF 1.1 million in the year ended December 31, 2018, driven by the early repayment of the loan as well as the payment of the end of term charge on January 31, 2019.

Foreign currency exchange gain/(loss), net

Foreign currency exchange loss decreased in 2019 mainly due to the depreciation of the USD and EUR against the Swiss Franc.

Revaluation gain/(loss) from derivative financial instruments

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

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

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

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

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

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

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

Income tax expense

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

Remeasurements of defined benefits liability

Remeasurements of the net defined benefits liability, which comprise actuarial gains and losses, the return on plan assets (excluding interest) and the effect of the asset ceiling (if any, excluding interest), decreased 106% from 2018 to 2019. The loss was primarily due to a reduction in headcount.

Foreign currency translation differences

Foreign currency translation differences decreased by 245% from 2018 to 2019. 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. To date, we have not generated any 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, 2020 and 2019

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

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

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

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

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

Comparison of the years ended December 31, 2019 and 2018

The table below summarizes our consolidated statement of cash flows for the years ended December 31, 2019 and 2018:

	Year Ended December 31,	
	2019	**2018**
	(in thousands of CHF)	
Cash used in operating activities	(8,393)	(13,232)
Net cash used in investing activities	(3,001)	(1,823)
Net cash from financing activities	7,378	5,733
Net effect of currency translation on cash	8	(258)
Cash and cash equivalents at the beginning of the period	5,393	14,973
Cash and cash equivalents at the end of the period	**1,385**	**5,393**

The decrease in cash used in operating activities from CHF 13.2 million in 2018 to CHF 8.4 million in 2019 reflects the impact of lower operating expenses primarily driven by lower research and development related expenses.

Cash used in investing activities increased from CHF 1.8 million in 2018 to CHF 3.0 million in 2018. The increase is primarily due to higher investments in intangible assets in 2019.

Cash from financing activities in 2019 increased as the repayment of the loan towards Hercules decreased from CHF 9.3 million to CHF 1.5 million. The cash inflow from our funding sources decreased from CHF 15.4 million to CHF 8.8 million as a result of lower equity raises.

Cash and funding sources

The table below summarizes our sources of financing for the years ended December 31, 2020, 2019 and 2018.

	Equity Capital and Preference Shares	Loans	Total
	(in thousands of CHF)		
2020	15,438	1,550	16,988
2019	8,845	—	8,845
2018	15,441	—	15,441
Total	39,724	1,550	41,274

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

On September 8, 2020, FiveT provided a convertible loan to our subsidiary Altamira. The loan had a principal amount of CHF 1.5 million, a duration of 18 months, and carried an interest rate of 8% p.a. Under the terms of the agreement, FiveT had the right to convert the loan or parts thereof including accrued interest into common shares of either Altamira or Auris Medical Holding Ltd., subject to additional provisions and certain restrictions. On December 2, 2020, FiveT converted principal of CHF 895,455 into 737,000 shares of Auris Medical Holding Ltd. at a 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.

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

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

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

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

On November 30, 2018, we entered into the A.G.P. Sales Agreement with A.G.P. Pursuant to the terms of the A.G.P. Sales Agreement, as amended on April 5, 2019, we may offer and sell our common shares, from time to time through A.G.P. by any method deemed to be an "at-the-market" offering as defined in Rule 415(a)(4) promulgated under the Securities Act. Pursuant to the A.G.P. Sales Agreement, we may sell common shares up to a maximum aggregate offering price of $25.0 million. In 2020, we sold 1,628,827 shares under the ATM for aggregate proceeds of $1.9 million. As of the date of this Annual Report, we have sold 1,758,618 of our common shares for an aggregate offering price of $3.2 million pursuant to the A.G.P. Sales Agreement.

On November 27, 2018 and December 11, 2018, we entered into purchase agreements with FiveT Capital AG, providing for the issuance and sale by us of an aggregate of 165,750 of our common shares for an aggregate purchase price of $1.6 million in two separate registered direct offerings.

On July 17, 2018, we completed a public offering of 897,435 common shares, Series A warrants each entitling its holder to purchase 0.35 of a common share for an aggregate of 314,102 common shares, and Series B warrants entitling its holder to purchase 0.25 of a common share for an aggregate of 224,358 common shares. The net proceeds to us from the July 2018 Registered Offering were approximately $6.2 million, after deducting underwriting discounts and other offering expenses payable by us. Since the July 2018 Registered Offering, certain Series A warrant holders exercised their warrant shares to purchase 145,226 common shares of the Company and certain Series B warrant holders exercised warrant shares to purchase 143,221 common shares. On June 30, 2020, the outstanding Series B warrants from the July 17, 2018 offering expired without further warrants being exercised.

On May 2, 2018, we entered into the LPC Purchase agreement and the registration rights agreement with LPC (the "Registration Rights Agreement"). Pursuant to the Purchase Agreement, LPC agreed to purchase common shares for up to $10,000,000 over the 30-month term of the Purchase Agreement. As of the date of this Annual Report, we have issued an aggregate of 463,000 common shares for aggregate proceed of $1.7 million to LPC under the LPC Purchase Agreement. The Purchase Agreement replaced the Purchase Agreement that we entered into with LPC on October 10, 2017 (the "2017 Commitment Purchase Agreement"), which was terminated as a result of the Merger. Under the 2017 Commitment Purchase Agreement, LPC agreed to subscribe for up to $13,500,000 of our common shares, and prior to its termination, we had issued an aggregate of 2,600,000 (pre-merger) common shares for aggregate proceeds of $1.8 million to LPC under the 2017 Commitment Purchase Agreement.

On January 30, 2018, we completed a public offering of 62,499 common shares and a concurrent offering of warrants, each warrant entitling its holder to purchase 0.6 common shares. The net proceeds to the Company from the January 2018 Registered Offering were approximately $4.9 million, after deducting placement agent fees and other estimated offering expenses payable by the Company. As of December 31, 2020, the outstanding warrants issued in the January 2018 offering were exercisable for up to 37,501 common shares (assuming we decide to round up fractional common shares to the next whole common share) at an exercise price of $100.00 per common share.

On October 16, 2017, in a separate private placement, we issued 1,744,186 (pre-merger) common shares to LPC for aggregate proceeds of $1,500,000.

On February 21, 2017, we completed a public offering of 10,000,000 (pre-merger) common shares and 10,000,000 (pre-merger) warrants, each warrant entitling its holder to purchase 0.70 of a common share. The net proceeds to us from the offering were approximately CHF 9.1 million, after deducting underwriting discounts and other estimated offering expenses payable by us. The underwriter was granted a 30-day option to purchase up to 1,500,000 (pre-merger) additional common shares and/or 1,500,000 (pre-merger) additional warrants. On February 15, 2017, the underwriter partially exercised its option in the amount of 1,350,000 (pre-merger) warrants. As of December 31, 2020, the outstanding warrants issued in the February 2017 offering were exercisable for up to 39,725 common shares at an exercise price of $240.00 per common share.

On July 19, 2016, the Company entered into a Loan and Security Agreement for a secured term loan facility of up to $20.0 million with Hercules as administrative agent and the lenders party thereto. An initial tranche of $12.5 million was drawn on July 19, 2016, concurrently with the execution of the loan agreement. The loan was to mature on January 2, 2020 and bore interest at a minimum rate of 9.55% per annum and was subject to the variability of the prime interest rate. The loan was secured by a pledge of the shares of Auris Medical AG owned by the Company, all intercompany receivables owed to the Company by its Swiss subsidiaries and a security assignment of the Company's bank accounts. In connection with the loan facility, we issued Hercules a warrant to purchase up to 783 of our common shares at an exercise price of $788.00 per share. On January 31, 2019, we made the final payment to Hercules under the facility, comprising the last amortization payment as well as an end of term charge. With the final payment, all covenants and collaterals in favor of Hercules have been lifted. In addition, Hercules agreed to return the warrant held by Hercules exercisable for 783 common shares at an exercise price of $788.00 per common share for no consideration to us in exchange for our payment to Hercules.

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

Funding requirements

We expect that we will need additional funding. We expect our total cash need in 2021 to be in the range of CHF 11.5 to 13.0 million for our expected total operating expenses of CHF 4.5 to 5.5 million and our expected capitalized research and development costs of CHF 7 to 7.5 million. Further cash needs may arise in 2021 related to the manufacture of AM-301 as well as marketing and sales activities as we intend to commercialize the product in selected markets; these cash needs may initially not be covered by cash flows from product revenues.

As of the date of this Annual Report we have warrants outstanding, which are exercisable for an aggregate of 246,102 common shares at a weighted average exercise price of $60.03 per share, an equity commitment to sell up to $8.9 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 $21.8 million of additional common shares.

The COVID-19 outbreak and its impact on the global financial markets may limit our ability to raise additional funds to continuously fund our operations and complete the research and development of all of our product candidates. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future 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 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 complete our development programs with AM-125, AM-201, AM-301, Keyzilen®, and Sonsuvi®, obtain regulatory approval for them and to commercialize our product candidates AM-125, AM-201, AM-301, Keyzilen ®, Sonsuvi® or any other product candidate. If we receive regulatory approval for AM-125, AM-201, AM-301, Keyzilen ®, or Sonsuvi®, and if we choose not to grant any licenses to partners, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize. Additional funds may not be available on a timely basis, on favorable terms, or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long-term business strategy. If we are not able to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

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

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

Significant accounting policies and use of estimates and judgment

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

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

Intangible assets

Research and development

The project stage forms the basis for the decision as to whether costs incurred for the Company's development projects can be capitalized. For AM-201, AM-301, Keyzilen®, and Sonsuvi® clinical development expenditures are not capitalized until the Company obtains regulatory approval or clearance (i.e. approval to commercially use the product), as this is considered to be essentially the first point in time where it becomes probable that future revenues can be generated. For the AM-125 program, however, given the current stage of the development project, the nature of the development approach and the fact that there is an existing market, direct development expenditures have been capitalized, including certain expenses related to the patenting of intellectual property.

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

Licenses, Intellectual Property and Data rights

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

Measurement

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

Subsequent expenditure

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

Amortization

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

Income tax

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

Current tax

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

Deferred tax

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

- temporary differences on the initial recognition of assets or liabilities in a transaction that is not a business combination and that affects neither accounting nor taxable profit or loss;

- temporary differences related to investments in subsidiaries to the extent that the Company is able to control the timing of the reversal of the temporary differences and it is probable that they will not reverse in the foreseeable future; and

- taxable temporary differences arising on the initial recognition of goodwill.

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

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

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

Employee benefits

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

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

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

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

Share-based compensation

Stock Options

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

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

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

Valuation of stock options

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

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

Recent accounting pronouncements

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

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

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

D. Trend information

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

E. Off-balance sheet arrangements

As of the date of this Annual Report, we do not have any, and during the periods presented we did not have any, off-balance sheet arrangements except for the lease agreements for which the short-term lease exemption is applied.

F. Tabular disclosure of contractual obligations

The following table presents information relating to our contractual obligations as of December 31, 2020:

	Payments Due by Period				
	Less Than 1 Year	1-3 Years	3-5 Years	More than 5 Years	Total
	(in thousands of CHF)				
Lease obligations (1)	26	—	—	—	26
Loan (2)	50	—	—	—	50
Total	**76**	**—**	**—**	**—**	**76**

(1) Lease obligations consist of payments pursuant to short-term lease agreement until the date of termination of the contract as of June 30, 2021.
(2) In March 2020 the Company obtained an interest-free "COVID-19" loan from UBS Switzerland, guaranteed by the Swiss government. The loan may be repaid at any time with a maximum term of 5 years. The company decided to repay the loan as of June 30, 2021.

Under the terms of our collaboration and license agreement with Xigen, we are obliged to make development milestone payments on an indication-by-indication basis of up to CHF 1.5 million upon the successful completion of a Phase 2 clinical trial 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, upon receiving marketing approval for a product. The milestones are not included in the table above as they have not met the recognition criteria for provisions and the timing of these is not yet determinable as it is dependent upon the achievement of earlier mentioned milestones.

Under the terms of the asset purchase agreement with Otifex Therapeutics Pty Ltd, we are obliged to make a development milestone payment of $200,000 if use of the purchased formulation is supported by the results from toxicology studies over three to six months.

G. 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 2020 annual general meeting. All directors have indicated that they 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	53	2003
Elmar Schaerli	Chief Financial Officer	49	2019
Non-Executive Directors			
Armando Anido	Director	63	2016
Mats Blom	Director	56	2017
Alain Munoz	Director	70	2018
Calvin W. Roberts	Director	68	2015

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

Executive Officers

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

Elmar Schaerli, Chief Financial Officer: Mr. Schaerli has served as Auris Medical's Chief Financial Officer since November 2019. Mr. Schaerli has acquired almost 30 years of both private and public finance and accounting experience in the biotech and medtech industry. In 2003 he founded ante treuhand ag, a Swiss fiduciary company supporting companies primarily in health care and technology and has since served as its CEO.

Non-Executive Directors

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

Mats Blom, Director: Mats 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) 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) Amryt Pharma Plc (AMYT.L) and OxThera AB. He is a member of the scientific advisory board of Valneva (VLA.PA).

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

B. Compensation

For the year ended December 31, 2020, 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 947,701 (2019: CHF 1,214,846).

For the year ended December 31, 2020, 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 26,870 (2019: CHF 42,560).

Compensation awarded to the Board of Directors in 2020

The total compensation of the members of the board of directors in 2020 is outlined below:

In CHF	Cash Compensation	Social Contributions	Stock Options(2)	Total
Thomas Meyer, PhD, Chairman(1)	—	—	—	—
Armando Anido, MBA	40,869	—	14,287	55,156
Mats Blom, MBA	40,869	—	14.287	55,156
Alain Munoz, MD	40,869	—	14,287	55,156
Calvin W. Roberts, MD	40,869	—	14,287	55,156
Total	**163,476**	—	**57,148**	**220,624**

(1) Disclosed under "Compensation Awarded to Our Executive Officers" below. The Chief Executive Officer does not receive any additional compensation for the exercise of the office of the Chairman.
(2) In 2020, 43,605 options were granted to each eligible member of the Board of Directors. 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 2020

The total compensation and the highest individual compensation to our executive officers in 2020 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)	363,600	46,230	69,470	177,048	656,347
Executive Officers Total(4)	**401,681**	**46,230**	**74,326**	**204,840**	**727,077**

(1) The variable compensation is paid in shares of the company.
(2) 2020 option grants. 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, 2020, we had two executive officers.

Employment Agreements

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

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

Equity Incentive Plans

Equity Incentive Plan

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

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

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

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

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

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

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

Indemnification

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

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

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

C. Board practices

Board Composition and Election of Directors

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

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

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

Committees of the Board of Directors

Audit Committee

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

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

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

- reviewing, in conjunction with the Chief Executive Officer and Chief Financial Officer of the Company, the Company's disclosure controls and procedures and internal control over financial reporting;

- establishing procedures for the receipt, retention and treatment of complaints received by the Company regarding accounting, internal accounting controls or auditing matters, and the confidential, anonymous submission by employees of the Company of concerns regarding questionable accounting or auditing matters;

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

The audit committee meets at least four times per year.

Compensation Committee

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

D. Employees

As of December 31, 2020, we had 9 employees (8.1 full time equivalents). None of our employees is subject to a collective bargaining agreement or represented by a trade or labor union. We consider our relations with our employees to be good.

E. Share ownership

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

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major shareholders

The following table presents information relating to the beneficial ownership of our common shares as of March 15, 2021 by:

- each person, or group of affiliated persons, known by us to own beneficially 5% or more of our outstanding common shares;

- each of our executive officers and directors; and

- all executive officers and directors as a group.

The number of common shares beneficially owned by each entity, person, executive officer or director is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any common shares over which the individual has sole or shared voting power or investment power as well as any common shares that the individual has the right to acquire within 60 days of March 15, 2021 through the exercise of any option, warrant or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all common shares held by that person.

Common shares that a person has the right to acquire within 60 days of March 15, 2021 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 Auris Medical Holding Ltd., Clarendon House, 2 Church Street, Hamilton HM 11, Bermuda.

The percentage of common shares beneficially owned is based on 12,869,587 common shares issued and outstanding as of March 15, 2021. 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)	755,442	5.87%
Armando Anido, M.B.A (2)	15,713	*
Mats Blom, M.B.A. (3)	15,697	*
Alain Munoz, M.D. (4)	15,530	*
Calvin W. Roberts, M.D. (5)	15,725	*
Elmar Schaerli, CPA	—	*
All current directors and executive officers as a group (7 persons)	818,107	6.36%

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

(1) Consists of 638,179 common shares, warrants to purchase 91,494 common shares and options to purchase 25,769 common shares under the EIP.
(2) Consists of options to purchase common shares under the Company's EIP.
(3) Consists of options to purchase common shares under the Company's EIP.
(4) Consists of 62 common shares owned by Alain Munoz and options to purchase common shares under the Company's EIP.
(5) Consists of 76 common shares jointly owned by Calvin W. Roberts and Andrea Colvin Roberts. Also, consists of 100 common shares held by Calvin W. Roberts, MD PC Pension Plan. Calvin Roberts is a trustee for Calvin W. Roberts, MD PC Pension Plan. Also consists of options to purchase common shares under the Company's EIP.

Holders

As of March 15, 2021, we had four shareholders of record of our common shares.

Significant Changes in Ownership by Major Shareholders

None

B. Related party transactions

Related Person Transaction Policy

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

Indemnification Agreements

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

Employment Agreements

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

Mandate Agreement

Ante Treuhand AG ("Ante Treuhand") provides the Chief Financial Officer to the Company. The Chief Financial Officer is an employee of Ante Treuhand and is not paid directly by the Company. Fees paid to Ante Treuhand for CFO services were CHF 173,030 in 2020 compared to CHF 11,770 in 2019 (for two months). Fees paid to Ante Treuhand for other services provided during the year ended December 31, 2020 were CHF 3,025 compared to CHF 28,611 in 2019.

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.

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."

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." Our registered office is located at Clarendon House, 2 Church Street, Hamilton HM 11, Bermuda.

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

Since the Redomestication, other than the 2019 Reverse Share Split and as otherwise described herein, 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, 2020, our authorized share capital consisted of 25,000,000 common shares, par value CHF 0.01 per share, and 20,000,000 preference shares, par value CHF 0.02 per share, and there were 11,417,159 common shares issued and outstanding, excluding 1,038,537 common shares issuable upon exercise of options and 1,143,537 common shares issuable upon exercise of warrants, and no preference shares issued and outstanding. All the Company's issued and outstanding shares are fully paid in.

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

Common Shares

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

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

Preference Shares

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

Dividend Rights

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

Variation of Rights

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

Transfer of Shares

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

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

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

Meeting of Shareholders

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

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

Access to Books and Records and Dissemination of Information

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

Election and Removal of Directors

Our Bye-laws provide that our board shall consist of three directors or such greater number as the board may determine. Our board of directors currently consists of 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 will serve as branch registrar and transfer agent.

Untraced Shareholders

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

Certain Provisions of Bermuda Law

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

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

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

Comparison of Corporate Law

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

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

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

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

Directors' fiduciary duties

A director of a Delaware corporation has a fiduciary duty to the corporation and its shareholders. This duty has two components:

the duty of care; and
the duty of loyalty.

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.

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

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

The Companies Act provides that shareholders may take action by written consent, except in respect of the removal of an auditor from office before the expiry of his term or in respect of a resolution passed for the purpose of removing a director before the expiration of his term of office. A resolution in writing is passed when it is signed by the members of the company who at the date of the notice of the resolution represent such majority of votes as would be required if the resolution had been voted on at a meeting or when it is signed by all the members of the company or such other majority of members as may be provided by the bye-laws of the company.

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 Auris Medical's board must give notice of the intention to propose the person for election in accordance with the Bye-laws.
Cumulative voting	
Under the Delaware General Corporation Law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation provides for it.	Under Bermuda law, the voting rights of shareholders are regulated by the company's Bye-laws and, in certain circumstances, by the Companies Act. The Bye-laws provide for a plurality of voting for elections of directors, and cumulative voting for elections of directors is not permitted.
Removal of directors	
A Delaware corporation with a classified board may be removed only for cause with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise.	Under the Bye-laws, a director may be removed, with cause, by the shareholders, provided notice of the shareholders meeting convened to remove the director is given to the director. The notice must contain a statement of the intention to remove the director and must be served on the director not less than fourteen days before the meeting. The director is entitled to attend the meeting and be heard on the motion for his removal.
Transactions with interested shareholders	
The Delaware General Corporation Law generally prohibits a Delaware corporation from engaging in certain business combinations with an "interested shareholder" for three years following the date that such person becomes an interested shareholder. An interested shareholder generally is a person or group who or which owns or owned 15.0% or more of the corporation's outstanding voting stock within the past three years.	There is no similar law in Bermuda. The Bye-laws contain provisions regarding "business combinations" with "interested shareholders" which are described above under "mergers and similar arrangements."
Dissolution; Winding up	
Unless the board of directors of a Delaware corporation approves the proposal to dissolve, dissolution must be approved by shareholders holding 100.0% of the total voting power of the corporation. Only if the dissolution is initiated by the board of directors may it be approved by a simple majority of the corporation's outstanding shares. Delaware law allows a Delaware corporation to include in its certificate of incorporation a supermajority voting requirement in connection with dissolutions initiated by the board.	A Bermuda company may be wound up by the Bermuda court on application presented by the company itself, its creditors (including contingent or prospective creditors) or its contributories. The Bermuda court has authority to order winding up in a number of specified circumstances including where it is, in the opinion of the Bermuda court, just and equitable to do so. A Bermuda company limited by shares may be wound up voluntarily when the shareholders so resolve in general meeting. In the case of a voluntary winding up, the company shall, from the commencement of the winding up, cease to carry on its business, except so far as may be required for the beneficial winding up thereof.

Variation of rights of shares

A Delaware corporation may vary the rights of a class of shares with the approval of a majority of the outstanding shares of such class, unless the certificate of incorporation provides otherwise.

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

Amendment of governing documents

A Delaware corporation's governing documents may be amended with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise.

A Bermuda company's memorandum of association and Bye-laws may be amended by resolutions of the board of directors and the shareholders, subject to the company's bye-laws.

Inspection of Books and Records

Shareholders of a Delaware corporation, upon written demand under oath stating the purpose thereof, have the right during the usual hours for business to inspect for any proper purpose, and to obtain copies of list(s) of shareholders and other books and records of the corporation and its subsidiaries, if any, to the extent the books and records of such subsidiaries are available to the corporation.

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

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

C. Material contracts

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

D. Exchange controls

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

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

E. Taxation

The following summary contains a description of the material Bermuda, Swiss and U.S. federal income tax consequences of the acquisition, ownership and disposition of common shares, but it does not purport to be a comprehensive description of all the tax considerations that may be relevant to a decision to purchase common shares. The summary is based upon the tax laws of Bermuda and regulations thereunder, of Switzerland and regulations thereunder and on the tax laws of the United States and regulations thereunder as of the date hereof, which may be subject to change.

Bermuda Tax Considerations

At the present time, there is no Bermuda income or profits tax, withholding tax, capital gains tax, capital transfer tax, estate duty or inheritance tax payable by us or by our shareholders in respect of our shares. We have received an assurance from the Minister of Finance of Bermuda under the Exempted Undertakings Tax Protection Act 1966 that, in the event that any legislation is enacted in Bermuda imposing any tax computed on profits or income, or computed on any capital asset, gain or appreciation or any tax in the nature of estate duty or inheritance tax, such tax shall not, until March 31, 2035, be applicable to us or to any of our operations or to our shares, debentures or other obligations except insofar as such tax applies to persons ordinarily resident in Bermuda or is payable by us in respect of real property owned or leased by us in Bermuda.

Swiss Tax Considerations

With the deletion of Auris Medical Holding AG from the Swiss Commercial Register as of December 9, 2020, our taxability in Switzerland has ceased.

Material U.S. Federal Income Tax Considerations for U.S. Holders

The following is a description of the material U.S. federal income tax consequences to the U.S. Holders described below of owning and disposing of common shares, but it does not purport to be a comprehensive description of all tax considerations that may be relevant to a particular person's decision to hold the common shares. This discussion applies only to a U.S. Holder that holds common shares as capital assets for U.S. federal income tax purposes. In addition, it does not describe all of the tax consequences that may be relevant in light of the U.S. Holder's particular circumstances, including alternative minimum tax consequences, the potential application of the provisions of the Code, known as the Medicare contribution tax and tax consequences applicable to U.S. Holders subject to special rules, such as:

- certain financial institutions;
- dealers or traders in securities who use a mark-to-market method of tax accounting;
- persons holding common shares as part of a straddle, wash sale, conversion transaction or persons entering into a constructive sale with respect to the common shares;
- persons whose functional currency for U.S. federal income tax purposes is not the U.S. dollar;
- entities classified as partnerships for U.S. federal income tax purposes;
- tax-exempt entities, including an "individual retirement account" or "Roth IRA";
- persons that own or are deemed to own ten percent or more of our stock by vote or value;
- persons who acquired our common shares pursuant to the exercise of an employee stock option or otherwise as compensation; or
- persons holding shares in connection with a trade or business conducted outside of the United States.

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

This discussion is based on the Code, administrative pronouncements, judicial decisions, final, temporary and proposed Treasury regulations, all as of the date hereof, any of which is subject to change, possibly with retroactive effect.

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

- an individual who is a citizen or resident of the United States;

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

- an estate the income of which is subject to U.S. federal income taxation regardless of its source.

- a trust with respect to which a U.S. court is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of its substantial decisions, or that has a valid election in effect to be treated as a U.S. person under applicable U.S. Treasury Regulations.

U.S. Holders should consult their tax advisers concerning the U.S. federal, state, local and non-U.S. tax consequences of owning and disposing of common shares in their particular circumstances.

Passive Foreign Investment Company Rules

We believe that we were a PFIC for U.S. federal income tax purposes for our 2020 taxable year, and we expect to be a PFIC for our current taxable year and for the foreseeable future. However, our actual PFIC status for the current or any future taxable year is uncertain and cannot be determined until after the end of such taxable year. In addition, we may, directly or indirectly, hold equity interests in other PFICs, or Lower-tier PFICs. In general, a non-U.S. corporation will be considered a PFIC for any taxable year in which (i) 75% or more of its gross income consists of passive income or (ii) 50% or more of the average quarterly value of its assets consists of assets that produce, or are held for the production of, passive income. For purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as if it held its proportionate share of the assets of the other corporation and received directly its proportionate share of the income of the other corporation. Passive income generally includes dividends, interest, rents, royalties and capital gains.

Under attribution rules, assuming we are a PFIC, 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.

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 our common shares are "regularly traded" on a "qualified exchange," a U.S. Holder may make a mark-to-market election that would result in tax treatment different from the general tax treatment for PFICs described above. Our common shares will be treated as "regularly traded" in any calendar year in which more than a de minimis quantity of the common shares is traded on a qualified exchange on at least 15 days during each calendar quarter. Nasdaq, on which the common shares are currently listed, is a qualified exchange for this purpose. U.S. Holders should consult their tax advisers regarding the availability and advisability of making a mark-to-market election in their particular circumstances and the consequences to them if the common shares are delisted from Nasdaq (see "Item 3. Key Information—D. Risk Factors—Risks Related to Our Business and Industry—Our common shares may be involuntarily delisted from trading on The Nasdaq Capital Market if we fail to comply with the continued listing requirements. A delisting of our common shares is likely to reduce the liquidity of our common shares and may inhibit or preclude our ability to raise additional financing" above). In particular, U.S. Holders should consider carefully the impact of a mark-to-market election with respect to their common shares given that we may have Lower-tier PFICs for which a mark-to-market election may not be available.

If a U.S. Holder makes the mark-to-market election, the U.S. Holder generally will recognize as ordinary income any excess of the fair market value of the common shares at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the common shares over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. Holder makes the election, the U.S. Holder's tax basis in the common shares will be adjusted to reflect the income or loss amounts recognized. Any gain recognized on a sale or other disposition of common shares in a year in which we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark to-market election). Distributions paid on common shares will be treated as discussed below under "*Taxation of Distributions*." Once made, the election cannot be revoked without the consent of the Internal Revenue Service 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 will provide the information necessary for a U.S. Holder to make a QEF Election with respect to us and will use commercially reasonable efforts to cause each Lower-tier PFIC which we control to provide such information with respect to such Lower-tier PFIC. However, no assurance can be given that such QEF Election information will be available for any Lower-tier PFIC and we cannot guarantee that we will continue to provide such determination or information in future years.

If a U.S. Holder makes a QEF Election with respect to a PFIC, the U.S. Holder will be currently taxable on its *pro rata* share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is classified as a PFIC. If a U.S. Holder makes a QEF Election with respect to us, any distributions paid by us out of our earnings and profits that were previously included in the U.S. Holder's income under the QEF Election will not be taxable to the U.S. Holder. A U.S. Holder will increase its tax basis in its common shares by an amount equal to any income included under the QEF Election and will decrease its tax basis by any amount distributed on the common shares that is not included in its income. In addition, a U.S. Holder will recognize capital gain or loss on the disposition of common shares in an amount equal to the difference between the amount realized and its adjusted tax basis in the common shares. U.S. Holders should note that if they make QEF Elections with respect to us and Lower-tier PFICs, they may be required to pay U.S. federal income tax with respect to their common shares for any taxable year significantly in excess of any cash distributions received on the shares for such taxable year. U.S. Holders should consult their tax advisers regarding making QEF Elections in their particular circumstances.

Furthermore, if we were a PFIC or, with respect to a particular U.S. Holder, were treated as a PFIC for the taxable year in which we paid a dividend or the prior taxable year, the preferential dividend rate with respect to dividends paid to certain non-corporate U.S. Holders will not apply.

If we were a PFIC for any taxable year during which a U.S. Holder held common shares, such U.S. Holder would be required to file an annual information report with such U.S. Holder's U.S. Federal income tax return on IRS Form 8621.

U.S. Holders should consult their tax advisers concerning our PFIC status and the tax considerations relevant to an investment in a PFIC.

Taxation of Distributions

As discussed above under "Item 8. Financial Information—Dividends and Dividend Policy," we do not currently expect to make distributions on our common shares. In the event that we do make distributions of cash or other property, subject to the PFIC rules described above, distributions paid on common shares, other than certain *pro rata* distributions of common shares, will be treated as dividends to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Because we may not calculate our earnings and profits under U.S. federal income tax principles, we expect that distributions generally will be reported to U.S. Holders as dividends. The U.S. dollar amount of any dividend will be treated as foreign-source dividend income to U.S. Holders and will not be eligible for the dividends-received deduction generally available to U.S. corporations under the Code. Dividends will be included in a U.S. Holder's income on the date of the U.S. Holder's receipt of the dividend.

Sale or Other Disposition of Common Shares

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

Information Reporting and Backup Withholding

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

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

Information Reporting with Respect to Foreign Financial Assets

Certain U.S. Holders who are individuals and certain entities may be required to report information relating to an interest in our common shares, subject to certain exceptions (including an exception for common shares held in accounts maintained by certain U.S. financial institutions). U.S. Holders should consult their tax advisers regarding whether or not they are obligated to report information relating to their ownership and disposition of the common shares.

F. Dividends and paying agents

Not applicable.

G. Statement by experts

Not applicable.

H. Documents on display

We are subject to the informational requirements of the Exchange Act. Accordingly, we are required to file reports and other information with the SEC, including annual reports on Form 20-F and reports on Form 6-K. The SEC maintains an Internet website that contains reports and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

Under Bermuda law shareholders have the right to inspect the bye-laws of the company, minutes of general meetings and the company's audited financial statements, which must be presented to the annual general meeting. The register of members of a company is also open to inspection by shareholders and by members of the general public without charge. The register of members is required to be open for inspection for not less than two hours in any business day (subject to the ability of a company to close the register of members for not more than thirty days in a year).

As a foreign private issuer, we are exempt under the Exchange Act from, among other things, the rules prescribing the furnishing and content of proxy statements, and our executive officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we will not be required under the Exchange Act to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act.

I. Subsidiary information

Not applicable.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Credit Risk

We manage credit risk on a group basis. Credit risk arises from cash and cash equivalents and deposits with banks, as well as from other receivables. Our policy is to invest funds in low risk investments including interest bearing deposits. Only independent banks and financial institutions are used and banks with which we currently hold term deposits have a minimum S&P rating of "A". Receivables are not past due and not impaired and include only well-known counterparties.

We hold cash and cash equivalents in our principal operating currencies (CHF, USD and EUR).

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, 2020, a 5% increase or decrease in the USD/CHF exchange rate with all other variables held constant would have resulted in a CHF 455,241 (2019: CHF 19,664) 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 13,648 (2019: CHF 28,841) increase or decrease in the net annual result.

We have subsidiaries in the United States, Ireland and Australia, whose net assets are exposed to foreign currency translation risk. Due to the small size of these subsidiaries the translation risk is not significant.

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt securities

Not applicable.

B. Warrants and rights

Not applicable.

C. Other securities

Not applicable.

D. American Depositary Shares

Not applicable.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

A. Defaults

No matters to report.

B. Arrears and delinquencies

No matters to report.

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

E. Use of Proceeds

Not applicable.

ITEM 15. CONTROLS AND PROCEDURES

A. Disclosure Controls and Procedures

As of the end of the period covered by this Annual Report, an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act) was performed under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, our principal executive officer and principal financial officer, respectively. There are inherent limitations to the effectiveness of any system of disclosure controls and procedures, including the possibility of human error and the circumvention or overriding of the controls and procedures. Accordingly, even effective disclosure controls and procedures can only provide reasonable assurance of achieving their control objectives.

Based on the evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective, as of the end of the period covered by this Annual Report, in providing a reasonable level of assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods in SEC rules and forms, including providing a reasonable level of assurance that information required to be disclosed by us in such reports is accumulated and communicated to our management, including our principal executive officer and our principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

B. Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) of the Exchange Act. Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based upon criteria established in *Internal Control – Integrated Framework* (2013) by the Committee of Sponsoring Organizations of the Treadway Commission. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our internal control over financial reporting was effective as of December 31, 2020.

C. Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting.

D. Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) that occurred during the period covered by this Annual Report that has materially affected, or is reasonably likely to materially affect, internal control over financial reporting.

ITEM 16. [RESERVED]

ITEM 16A. Audit committee financial expert

Our board of directors has determined that Mats Blom is the audit committee financial expert, as that term is defined by the SEC, and is independent for the purposes of SEC and Nasdaq rules.

ITEM 16B. Code of ethics

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics which covers a broad range of matters including the handling of conflicts of interest, compliance issues and other corporate policies such as insider trading and equal opportunity and non-discrimination standards. Our Code of Business Conduct applies to all of our directors, executive officers and employees. We have published our Code of Business Conduct and Ethics on our website, *www.aurismedical.com*. The information contained on our website is not a part of this Annual Report.

ITEM 16C. Principal Accountant Fees and Services

	2020	2019
Audit fees	252	152
Audit-related fees	99	245
Total fees	**351**	**397**

In 2020 we were billed CHF 252,100 by Deloitte AG in connection with audit services for our annual filing as well as interim reviews, group audit, and statutory audits plus CHF 98,800 in connection with audit-related services for work in connection with our equity offerings and registration statements. In 2019, we were billed CHF 152,495, by Deloitte AG in connection with our annual filing as well as interim reviews, group audit, and statutory audits plus CHF 244,900 in connection with audit related services in the context of registration statement fillings and issuance of shares and other statutory required audit reports.

Pre-Approval Policies and Procedures

To ensure the independence and objectivity of the Company's external auditors, the provision of all non-audit services by the external auditors are pre-approved by the Audit Committee.

ITEM 16D. Exemptions from the listing standards for audit committees

Not applicable.

ITEM 16E. Purchases of equity securities by the issuer and affiliated purchasers

In 2020, no purchases of our equity securities were made by or on behalf of Auris Medical Holding 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).

ITEM 16H. Mine safety disclosure

Not applicable.

PART III

ITEM 17. Financial statements

We have responded to Item 18 in lieu of this item.

ITEM 18. Financial statements

Financial Statements are filed as part of this Annual Report, see page F-1.

ITEM 19. Exhibits

(a) The following documents are filed as part of this registration statement:

1.1	Memorandum of Continuance of the registrant (incorporated herein by reference to exhibit 1.2 of the Auris Medical Holding Ltd. Annual Report on Form 20-F filed with the Commission on March 14, 2019)
1.2	Bye-laws of the Registrant (incorporated herein by reference to exhibit 1.3 of the Auris Medical Holding Ltd. Annual Report on Form 20-F filed with the Commission on March 14, 2019)
2.1	Form of Registration Rights Agreement between Auris Medical Holding AG and the shareholders listed therein (incorporated by reference to exhibit 4.1 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-197105) filed with the Commission on July 21, 2014)
2.2	Warrant Agreement, dated as of March 13, 2018, between Auris Medical Holding AG and Hercules Capital, Inc. (incorporated by reference to exhibit 2.2 of the Auris Medical Holding AG Annual Report on Form 20-F filed with the Commission on March 22, 2018)
2.3	Registration Rights Agreement, dated as of October 10, 2017 between Auris Medical Holding AG and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.3 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on October 11, 2017)
2.4	Purchase Agreement, dated as of May 2, 2018 between Auris Medical Holding AG and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on May 2, 2018)
2.5	Registration Rights Agreement, dated as of May 2, 2018 between Auris Medical Holding AG and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.2 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on May 2, 2018)
2.6	Form of Pre-Funded Warrant (incorporated by reference to exhibit 4.6 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-225676) filed with the Commission on July 12, 2018)
2.7	Form of Series A Warrant (incorporated by reference to exhibit 4.7 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-225676) filed with the Commission on July 12, 2018)
2.8	Form of Series B Warrant (incorporated by reference to exhibit 4.8 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-225676) filed with the Commission on July 12, 2018)
2.9	Form of Common Warrant (incorporated by reference to exhibit 4.1 of the Auris Medical Holding Ltd. report on Form 6-K filed with the commission on May 16, 2019)
2.10	Form of Pre-Funded Warrant (incorporated by reference to exhibit 4.2 of the Auris Medical Holding Ltd. report on Form 6-K filed with the commission on May 16, 2019)
2.11	Form of Common Warrant Agent Agreement (incorporated by reference to exhibit 4.3 of the Auris Medical Holding Ltd. report on Form 6-K filed with the commission on May 16, 2019)
2.12	Form of Pre-Funded Warrant Agent Agreement (incorporated by reference to exhibit 4.4 of the Auris Medical Holding Ltd. report on Form 6-K filed with the commission on May 16, 2019)
2.13*	Description of Securities Registered under Section 12 of the Exchange Act
2.14	Purchase Agreement, dated as of April 23, 2020 between Auris Medical Holding Ltd. and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.1 of the Auris Medical Holding Ltd. report on Form 6-K furnished with the Commission on April 23, 2020)
2.15	Registration Rights Agreement, dated as of April 23, 2020 between Auris Medical Holding Ltd. and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.2 of the Auris Medical Holding Ltd. report on Form 6-K furnished with the Commission on April 23, 2020)

4.1†	Collaboration and License Agreement, dated October 21, 2003, between Auris Medical AG and Xigen SA (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-197105) filed with the Commission on June 27, 2014)
4.2†	Co-Ownership and Exploitation Agreement, dated September 29, 2003, between Auris Medical AG and INSERM (incorporated by reference to exhibit 10.2 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-197105) filed with the Commission on June 27, 2014)
4.3	Form of Indemnification Agreement (incorporated by reference to exhibit 99.4 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on May 11, 2016)
4.4	Stock Option Plan A (incorporated by reference to exhibit 10.11 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-197105) filed with the Commission on June 27, 2014)
4.5	Stock Option Plan C (incorporated by reference to exhibit 10.12 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-197105) filed with the Commission on June 27, 2014)
4.6	Equity Incentive Plan, as amended (incorporated by reference to exhibit 99.1 to the Auris Medical Holding AG registration statement on Form S-8 (Registration no. 333-217306) filed with the Commission on April 14, 2017)
4.7	English language translation of Lease Agreement between Auris Medical AG and PSP Management AG (incorporated by reference to exhibit 4.8 of the Auris Medical Holding AG Annual Report on Form 20-F filed with the Commission on March 14, 2017)
4.8	Controlled Equity OfferingSM Sales Agreement, dated as of June 1, 2016, between Auris Medical Holding AG and Cantor Fitzgerald & Co. (incorporated by reference to exhibit 1.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on June 1, 2016)
4.9	Share Lending Agreement, dated as of June 1, 2016, between Thomas Meyer and Cantor Fitzgerald & Co. (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on June 1, 2016)
4.10	Loan and Security Agreement, dated as of July 19, 2016, between Auris Medical Holding AG, the several banks and other financial institutions or entities from time to time parties to the agreement and Hercules Capital, Inc. (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on July 19, 2016)
4.11	Consent and Waiver, dated as of March 8, 2018, between Auris Medical Holding AG, the several banks and other financial institutions or entities from time to time parties to the agreement and Hercules Capital, Inc. (incorporated by reference to exhibit 4.12 of the Auris Medical Holding AG Annual Report on Form 20-F filed with the Commission on March 22, 2018)
4.12	Joinder Agreement dated as of March 13, 2018 to the Loan and Security Agreement, dated as of July 19, 2016, between Auris Medical Holding AG, the several banks and other financial institutions or entities from time to time parties to the agreement and Hercules Capital, Inc. (incorporated by reference to exhibit 4.13 of the Auris Medical Holding AG Annual Report on Form 20-F filed with the Commission on March 22, 2018)
4.13	Share Pledge Agreement, dated July 19, 2016, between Auris Medical Holding AG and Hercules Capital, Inc. (incorporated by reference to exhibit 10.3 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on July 19, 2016)
4.14	Claims Security Assignment Agreement, dated July 19, 2016, between Auris Medical Holding AG and Hercules Capital, Inc. (incorporated by reference to exhibit 10.4 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on July 19, 2016)
4.15	Bank Account Claims Security Assignment Agreement, dated July 19, 2016, between Auris Medical Holding AG and Hercules Capital, Inc. (incorporated by reference to exhibit 10.5 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on July 19, 2016)
4.16	Purchase Agreement, dated as of October 10, 2017 between Auris Medical Holding AG and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on October 11, 2017)
4.17	Purchase Agreement, dated as of October 10, 2017 between Auris Medical Holding AG and Lincoln Park Capital Fund, LLC (incorporated by reference to exhibit 10.2 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on October 11, 2017)
4.18	Placement Agency Agreement, dated as of January 28, 2018, between Auris Medical Holding AG and Ladenburg Thalmann & Co. Inc. (incorporated by reference to exhibit 1.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on January 30, 2018)
4.19	Securities Purchase Agreement, dated as of January 26, 2018 by and among Auris Medical Holding AG and the investors named therein (incorporated by reference to exhibit 10.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on January 30, 2018)

4.20	Agreement and Plan of Merger, dated as of February 9, 2018 by and among Auris Medical Holding AG and Auris Medical NewCo Holding AG (incorporated by reference to exhibit 99.3 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on February 9, 2018)
4.21	Share Transfer Agreement, dated as of February 9, 2018 by and between Thomas Meyer and Auris Medical Holding AG (incorporated by reference to exhibit 4.22 of the Auris Medical Holding AG Annual Report on Form 20-F filed with the Commission on March 22, 2018)
4.22	Sales Agreement, dated as of November 30, 2018, between Auris Medical Holding AG and A.G.P./Alliance Global Partners (incorporated by reference to exhibit 1.1 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on November 30, 2018)
4.23	Form of Indemnification Agreement (incorporated by reference to exhibit 10.23 of the Auris Medical Holding Ltd. registration statement on Form F-1 (Registration no. 333-229465) filed with the Commission on March 20, 2019)
4.24	Amendment No. 1 to Sales Agreement, dated as of April 5, 2019, between Auris Medical Holding Ltd. and A.G.P./Alliance Global Partners (incorporated by reference to exhibit 1.1 of the Auris Medical Holding Ltd. report on Form 6-K filed with the Commission on April 5, 2019)
4.25	Convertible Loan Agreement, dated as of September 7, 2020, by and among Auris Medical Holding Ltd., Altamira Medica AG and FiveT Capital Holding AG (incorporated by reference to exhibit 99.1 of the Auris Medical Holding Ltd. report on Form 6-K furnished with the Commission on September 8, 2020)
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*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document

* Filed herewith

† Confidential treatment requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

(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.

AURIS MEDICAL HOLDING LTD.

By: /s/ Thomas Meyer
Name: Thomas Meyer
Title: Chief Executive Officer

Date: March 31, 2021

Index to Consolidated Financial Statements

Audited Consolidated Financial Statements — Auris Medical Holding Ltd.

As of December 31, 2020 and 2019 and for the years ended December 31, 2020, 2019, and 2018

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Auris Medical Holding Ltd.

Opinion on the Financial Statements

We have audited the accompanying consolidated statements of financial position of Auris Medical Holding Ltd. and subsidiaries (the "Company") as of December 31, 2020 and 2019, 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, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Retrospective adjustment of loss per share information

As discussed in Note 21 to the financial statements, the basic and diluted loss per share in the accompanying 2018 financial statements have been retrospectively adjusted to reflect the reverse-split ratio of 10 to 1 following the Merger on March 13, 2018, and the reverse-split ratio of 20 to 1 following the reverse share split on May 1, 2019.

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 Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

INTANGIBLE ASSETS - CAPITALIZED DEVELOPMENT EXPENDITURE – refer to note 2 (section development expenditures), note 3 (section intangible assets), and note 8 (intangible assets) to the financial statements

Description of the Matter

The Company capitalized development expenditure for AM-125, a product candidate for the treatment of vertigo, in the amount of CHF 2,166,054 for the year ended December 31, 2020. The total carrying value of internally developed intangible assets was CHF 7,021,685 as of December 31, 2020.

We identified the Company's accounting treatment of capitalized development expenditure as a critical audit matter. This required a high degree of auditor judgment and an increased extent of effort when performing audit procedures to evaluate the reasonableness of management's judgements of technical feasibility, intention and ability to complete the development of AM-125 and to generate future economic profits from the intangible asset.

How We Addressed the Matter in Our Audit

We performed the following audit procedures amongst others, to address this critical audit matter:

- We assessed, with the assistance of our IFRS specialist, whether the Company's accounting policy and treatment is in line with IFRS and the underlying nature of the development of AM-125;
- We evaluated whether technical feasibility criteria is met through assessment of the nature of the development approach of AM-125 and the results from ongoing studies;
- We evaluated new or contradictory evidence that would affect the intention and ability to complete the development of AM-125 or to generate profits in the future, including review of minutes of meetings of the board of directors and inquiries with management and project managers throughout the year, and;
- We tested a sample of capitalized research and development costs to evaluate if they fulfil the criteria of being directly attributable to the development of AM-125 and evaluate whether amounts agree to supporting documentation and the confirmations received from clinical research organisations (CRO) to determine whether only costs related to the development of AM-125 are capitalized.

LOAN AND DERIVATIVE FINANCIAL INSTRUMENTS - DETERMINATION OF ACCOUNTING TREATMENT OF CONVERTIBLE LOAN AGREEMENT AND VALUATION OF CONVERSION RIGHT - refer to note 3 (convertible loans), and note 25 (loan) to the financial statements

Description of the Matter

On September 7, 2020, the Company and its affiliate Altamira Medica AG ("Altamira") entered into a convertible loan agreement with FiveT Capital AG ("FiveT") to raise CHF 1,500,000 to fund the initial development of AM-301. Under the convertible loan agreement, FiveT has the right to convert the outstanding principal amount, including interest, into the Company's common shares or alternatively into Altamira shares. The pricing of conversion into common shares is at the lower of 150% of the share price at close of the disbursement date (USD 1.35 fixed on September 8, 2020) and 95% of the average price of 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 common shares. The pricing of a conversion into Altamira shares is at the lower of CHF 3.00 and the issue price of a qualified financing round, meaning that a third-party investor will hold at least 10% of Altamira shares after completion of such financing round.

The Company elected to not designate the entire hybrid contract as at fair value through profit and loss. Consequently, the hybrid contract is separated between the host contract (loan agreement) and the embedded derivative (conversion right). The loan is measured at amortized cost and the embedded derivative is measured at fair value through profit and loss. The Company estimated the fair value of the conversion right using a Monte-Carlo simulation. The simulation is based on several assumptions including estimates of the Company's normalized equity volatility, expected exercise date, the expected execution date, the calculation of the repayment amount, as well as assumptions regarding the early repayment trigger and to the conversion option in Altamira shares.

We identified the Company's accounting treatment and the valuation assumptions used in the valuation of the conversion right as a critical audit matter due to the unobservable inputs management uses to estimate the fair value. This required a high degree of auditor judgment and an increased extent of effort to audit and evaluate the appropriateness of the inputs.

How We Addressed the Matter in Our Audit

We performed the following audit procedures amongst others, to address this critical audit matter:

- We assessed the appropriateness of management's methodology and model with the assistance of our fair value specialists;
- We assessed, with the assistance of our fair value specialists the reasonableness of the significant assumptions related to management's valuation of the derivative, including, among others:
  - whether the normalized equity volatility used by management was reasonable by comparing the assumption used by management with objective evidence based on publicly available data of share prices;
  - whether the expected exercise date was modelled in line with the valuation methodology;
  - whether the early repayment trigger was appropriately considered in the valuation model, and;
  - whether management's judgment used to estimate the probability that the lender would use the conversion right in exchange for subsidiary shares of Altamira Medica AG instead of Auris Medical Holding Ltd. shares was reasonable.

Deloitte AG

/s/ Matthias Gschwend
Auditor in Charge

/s/ Adrian Kaeppeli

Zurich, Switzerland
March 31, 2021

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, 2020, 2019 and 2018
(in CHF)

	Note	2020	2019	2018
Other operating income		174,475	—	—
Research and development	16	(2,862,979)	(3,325,281)	(6,689,589)
General and administrative	17	(2,594,662)	(3,933,863)	(4,264,534)
Operating loss		**(5,283,166)**	**(7,259,144)**	**(10,954,123)**
Interest income	19	258	17,882	—
Interest expense	19	(135,151)	(28,628)	(1,070,177)
Foreign currency exchange loss, net		(333,553)	(219,573)	(139,870)
Revaluation gain/(loss) from derivative financial instruments	19, 24, 25, 26	(2,250,222)	663,725	1,350,071
Transaction costs	19	(219,615)	—	(520,125)
Loss before tax		**(8,221,449)**	**(6,825,738)**	**(11,334,224)**
Income tax gain/(loss)	20	21,284	193,837	(162,177)
Net loss attributable to owners of the Company		**(8,200,165)**	**(6,631,901)**	**(11,496,401)**
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	18	(26,118)	(72,010)	1,277,192
Items that are or may be reclassified to profit or loss				
Foreign currency translation differences, net of taxes of CHF 0		88,862	16,446	(10,964)
Other comprehensive income/(loss), net of taxes of CHF 0		**62,744**	**(55,564)**	**1,266,228**
Total comprehensive loss attributable to owners of the Company		**(8,137,421)**	**(6,687,465)**	**(10,230,173)**
Basic and diluted loss per share	21	(1.36)	(2.28)	(14.46)

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

Consolidated Statement of Financial Position
As of December 31, 2020 and 2019
(in CHF)

	Note	December 31, 2020	December 31, 2019
ASSETS			
Non-current assets			
Property and equipment	7	46,636	66,672
Intangible assets	8	9,115,410	6,765,613
Other non-current receivables		20,001	20,001
Total non-current assets		**9,182,047**	**6,852,286**
Current assets			
Other receivables	9	80,861	335,299
Prepayments	10	277,589	434,231
Derivative financial instruments		—	219,615
Cash and cash equivalents	11	11,258,870	1,384,720
Total current assets		**11,617,320**	**2,373,865**
Total assets		**20,799,367**	**9,226,151**
EQUITY AND LIABILITIES			
Equity			
Share capital	12	114,172	1,650,380
Share premium		177,230,300	157,191,707
Foreign currency translation reserve		61,297	(27,565)
Accumulated deficit		(160,635,879)	(152,778,389)
Total shareholders' (deficit)/equity attributable to owners of the Company		**16,769,890**	**6,036,133**
Non-current liabilities			
Derivative financial instruments	26	6,318	4,353
Employee benefit liability	18	867,376	760,447
Deferred tax liabilities	20	125,865	147,149
Total non-current liabilities		**999,559**	**911,949**
Current liabilities			
Loan	25	523,920	—
Derivative financial instruments	25	310,439	—
Trade and other payables	14	762,453	938,247
Accrued expenses	15	1,433,106	1,339,822
Total current liabilities		**3,029,918**	**2,278,069**
Total liabilities		**4,029,477**	**3,190,018**
Total equity and liabilities		**20,799,367**	**9,226,151**

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

Consolidated Statement of Changes in Equity
As of December 31, 2020, 2019 and 2018
(in CHF)

	Note	Share Capital	Share Premium	Foreign Currency Translation Reserve	Accumulated Deficit	Total Equity / (Deficit)
As of January 1, 2018		**19,349,556**	**114,648,228**	**(33,047)**	**(136,126,946)**	**(2,162,209)**
Total comprehensive loss						
Net loss		—	—	—	(11,496,401)	(11,496,401)
Other comprehensive income / (loss)		—	—	(10,964)	1,277,192	1,266,228
Total comprehensive loss		**—**	**—**	**(10,964)**	**(10,219,209)**	**(10,230,173)**
Transactions with owners of the Company						
Reorganization of group structure		(24,347,208)	24,347,208	—	—	—
Capital increase / Exercise of warrants		5,707,988	11,550,874	—	—	17,258,862
Transaction costs		—	(1,259,587)	—	—	(1,259,587)
Share based payments	13	—	—	—	42,757	42,757
Balance at December 31, 2018		**710,336**	**149,286,723**	**(44,011)**	**(146,303,398)**	**3,649,650**
As of January 1, 2019		**710,336**	**149,286,723**	**(44,011)**	**(146,303,398)**	**3,649,650**
Total comprehensive loss						
Net loss		—	—	—	(6,631,901)	(6,631,901)
Other comprehensive income / (loss)		—	—	16,446	(72,010)	(55,564)
Total comprehensive loss		**—**	**—**	**16,446**	**(6,703,911)**	**(6,687,465)**
Transactions with owners of the Company						
Capital increase / Exercise of warrants		940,044	8,853,599	—	—	9,793,643
Transaction costs		—	(948,615)	—	—	(948,615)
Share based payments	13	—	—	—	228,920	228,920
Balance at December 31, 2019		**1,650,380**	**157,191,707**	**(27,565)**	**(152,778,389)**	**6,036,133**
As of January 1, 2020		**1,650,380**	**157,191,707**	**(27,565)**	**(152,778,389)**	**6,036,133**
Total comprehensive loss						
Net loss		—	—	—	(8,200,165)	(8,200,165)
Other comprehensive income / (loss)		—	—	88,862	(26,118)	62,744
Total comprehensive loss		**—**	**—**	**88,862**	**(8,226,283)**	**(8,137,421)**
Transactions with owners of the Company						
Reduction par value		(1,973,044)	1,973,044	—	—	—
Capital increase / Exercise of warrants		429,466	15,645,530	—	—	16,074,996
Transaction costs		—	(636,858)	—	—	(636,858)
Conversion of loan		7,370	3,056,877	—	—	3,064,247
Share based payments	13	—	—	—	368,793	368,793
Balance at December 31, 2020		**114,172**	**177,230,300**	**61,297**	**(160,635,879)**	**16,769,890**

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

Consolidated Statement of Cash Flows
For the Years Ended December 31, 2020, 2019, and 2018
(in CHF)

	Note	2020	2019	2018
Cash flows from operating activities				
Net loss		**(8,200,165)**	**(6,631,901)**	**(11,496,401)**
Adjustments for:				
Depreciation	16, 17	20,036	30,823	72,713
Unrealized foreign currency exchange loss, net		10,818	21,290	211,214
Net interest expense	19	127,160	1,205	1,052,787
Loss on disposal of property and equipment		—	—	78,133
Share based payments	13	368,793	226,601	27,730
Transaction costs	19	219,615	—	520,125
Employee benefits		80,811	40,150	(37,491)
Revaluation loss/(gain) derivative financial instruments	19, 25, 26	2,250,222	(663,725)	(1,350,071)
Income tax loss/(gain)	20	(21,284)	(193,837)	162,177
		(5,143,994)	**(7,169,394)**	**(10,759,084)**
Changes in:				
Other receivables		254,438	(18,925)	(18,390)
Prepayments		156,661	(82,948)	301,628
Trade and other payables		(175,878)	(898,088)	635,516
Accrued expenses		65,303	(224,077)	(3,391,834)
Net cash used in operating activities		**(4,843,470)**	**(8,393,432)**	**(13,232,164)**
Cash flows from investing activities				
Purchase of property and equipment	7	—	(63,600)	—
Purchase of intangibles	8	(2,315,232)	(2,955,036)	(1,891,115)
Proceeds from disposals of property and equipment		—	—	68,160
Interest received	19	258	17,882	—
Net cash from / (used) in investing activities		**(2,314,974)**	**(3,000,754)**	**(1,822,955)**
Cash flows from financing activities				
Proceeds from offerings and warrant exercises	12, 26	16,074,996	9,793,643	17,447,499
Transaction costs	12	(636,858)	(948,615)	(2,006,577)
Proceeds from loans	25	1,522,931	—	—
Repayment of loan			(1,463,328)	(9,272,328)
Interest paid	19, 24	—	(3,745)	(435,993)
Net cash from financing activities		**16,961,069**	**7,377,955**	**5,732,601**
Net increase / (decrease) in cash and cash equivalents		**9,802,625**	**(4,016,231)**	**(9,322,518)**
Cash and cash equivalents at beginning of the period		1,384,720	5,393,207	14,973,369
Net effect of currency translation on cash		71,525	7,744	(257,644)
Cash and cash equivalents at end of the period		**11,258,870**	**1,384,720**	**5,393,207**

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

1. Reporting entity

Auris Medical Holding Ltd. (the "Company") is an exempted company incorporated in Bermuda and is subject to Bermuda law. The Company's registered address is Clarendon House, 2 Church Street, Hamilton HM11, Bermuda. These consolidated financial statements comprise the Company and its subsidiaries (together referred to as the "Group" and individually as "Group entities"). The Company is the ultimate parent of the following Group entities:

- Auris Medical AG, Basel, Switzerland (100%) with a nominal share capital of CHF 2,500,000
- Otolanum AG, Zug, Switzerland (100%) with a nominal share capital of CHF 100,000
- Zilentin AG, Zug, Switzerland (100%), with a nominal share capital of CHF 100,000
- Altamira Medica AG, Zug, Switzerland (100%), with a nominal share capital of CHF 1,000,000
- Auris Medical Inc., Chicago, United States (100%) with a nominal share capital of USD 15,000
- Auris Medical Ltd., Dublin, Ireland (100%) with a nominal share capital of EUR 100
- Auris Medical Pty Ltd, Collingwood, Australia (100%), with a nominal share capital of AUD 100

On April 22, 2014, the Company changed its name from Auris Medical AG to Auris Medical Holding AG. On May 21, 2014 the domicile of Auris Medical Holding AG was transferred from Basel to Zug. On March 13, 2018, the Company ("Auris OldCo") merged (the "Merger") into Auris Medical NewCo Holding AG ("Auris NewCo"), a newly incorporated, wholly-owned Swiss subsidiary following shareholder approval at an extraordinary general meeting of shareholders held on March 12, 2018. Following the Merger, Auris NewCo, the surviving company, had a share capital of CHF 122,347.76, divided into 6,117,388 (pre-2019 Reverse Share Split) common shares with a nominal value of CHF 0.02 (pre-2019 Reverse Share Split) each. Pursuant to the Merger, the Company's shareholders received one common share with a nominal value of CHF 0.02 (pre-2019 Reverse Share Split) of Auris NewCo for every 10 of the Company's common shares held prior to the Merger, effectively resulting in a "reverse stock split" at a ratio of 10-for-1. Auris NewCo changed its name to "Auris Medical Holding AG" following consummation of the Merger. Following shareholder approval at an extraordinary general meeting of shareholders held on March 8, 2019 and upon the issuance of a certificate of continuance by the Registrar of Companies in Bermuda on March 18, 2019, the Company discontinued as a Swiss company and, pursuant to Article 163 of the Swiss Federal Act on Private International Law and pursuant to Section 132C of the Companies Act 1981 of Bermuda (the "Companies Act"), continued existence under the Companies Act as a Bermuda company with the name "Auris Medical Holding Ltd." (the "Redomestication"). The common shares of Auris Medical Holding Ltd. trade on the Nasdaq Capital Market under the trading symbol "EARS."

The Company is primarily involved in the development of therapeutics that address important unmet medical needs in neurotology, rhinology and allergy and CNS disorders. The Company is focusing on the development of intranasal betahistine for the treatment of vertigo (AM-125, in Phase 2) and for the prevention of antipsychotic-induced weight gain and somnolence (AM-201, post Phase 1b). Through its affiliate Altamira Medica, the Company is developing a nasal spray for protection against airborne viruses and allergens (AM-301). In addition, it has two Phase 3 programs under development, subject to its ability to obtain non-dilutive funding or partnering: (i) Keyzilen® (AM-101), which is being developed for the treatment of acute inner ear tinnitus and (ii) Sonsuvi® (AM-111), which is being developed for the treatment of acute inner ear hearing loss.

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 as well as unissued 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.

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 of the Company on March 30, 2021.

Basis of measurement

The consolidated financial statements are prepared on the historical cost basis, except for the revaluation to fair value of certain financial liabilities. Historical cost is generally based on the fair value of the consideration given in exchange for goods and services. The principal accounting policies adopted are set out below.

In addition, for financial reporting purposes, fair value measurements are categorized into Level 1, 2 or 3 based on the degree to which the inputs to the fair value measurements are observable and the significance of the inputs to the fair value measurement in its entirety, which are described as follows:

- Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities that the entity can access at the measurement date
- Level 2 inputs are inputs, other than quoted prices included within Level 1, that are observable for the asset or liability, either directly or indirectly; and
- Level 3 inputs are unobservable inputs for the asset or liability.

Functional and reporting currency

These consolidated financial statements are presented in Swiss Francs ("CHF"), which is the Company's functional ("functional currency") and the Group's reporting currency.

Redomestication

The Redomestication of the Company from Switzerland to Bermuda is a continuance of its business. Therefore, the consolidated financial statements present the operation of Auris Medical Holding AG for the time before the Redomestication and of Auris Medical Holding Ltd for the time following the Redomestication.

2019 Reverse Share Split

The Company effected the 2019 Reverse Share Split of its common shares at a ratio of 1-for-20. No fractional common shares were issued as fractional common shares were settled in cash. Impacted amounts and share information included in the consolidated financial statements and notes thereto have been adjusted for the reverse share split as if such reverse share split occurred on the first day of the periods presented. Certain amounts in the notes to the consolidated financial statements may be slightly different than previously reported due to rounding of fractional shares as a result of the reverse share split.

Use of estimates and judgments

The preparation of financial statements in conformity with IFRS requires management to make judgments, estimates and assumptions that affect the application of accounting policies and the reported amounts of assets, liabilities, income and expenses. Actual results may differ from these estimates.

Estimates and underlying assumptions are reviewed on an ongoing basis. Revisions of accounting estimates are recognized in the period in which the estimates are revised and in any future periods affected.

Information about judgments made in applying accounting policies that have the most significant effects on the amounts recognized in the consolidated financial statements are described below.

Income taxes

As disclosed in Note 20 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 476,363 (31.12.2019: CHF 91,851), 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 2020 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. For AM-201, AM-301, AM-101 and AM-111 clinical development expenditures are not capitalized until the Group obtains regulatory approval (i.e. approval to commercially use the product), as this is considered to be essentially the first point in time where it becomes probable that future revenues can be generated. For the Group's intranasal betahistine program for the treatment of vertigo (AM-125), however, the development is primarily focused on the delivery route and formulation and not the drug itself (already an approved generic) and aims to demonstrate higher bioavailability through intranasal delivery. Given the nature of the development approach and the fact that there is an existing market in which oral betahistine for the treatment of vertigo has been approved, direct development expenditures have been capitalized. In addition, the Group has capitalized certain milestone payments with regarding to license payments.

As of each reporting date, the Group estimates the level of service performed by the vendors and the associated costs incurred for the services performed. As part of the process of preparing the Group's financial statements, the Group is required to estimate its accrued expenses. This process involves reviewing contracts, identifying services that have been performed on the Group's behalf and estimating the level of service performed and the associated cost incurred for the service when it has not yet been invoiced or otherwise notified of the actual cost.

Employee benefits

The Group maintains a pension plan for all employees in Switzerland through payments to a legally independent collective foundation. This pension plan qualifies under IFRS as defined benefit pension plan.

The Group's net obligation in respect of defined benefit plans is calculated by estimating the amount of future benefit that employees have earned in return for their service in the current and prior periods, discounting that amount and deducting the fair value of any plan assets. The Company makes relevant actuarial assumptions with regard to the discount rate, future salary increases and life expectancy.

Research and Development and Accrued Expenses

The Company records the costs associated with research, nonclinical and clinical trials, and manufacturing process development as incurred. These costs are a significant component of the Company's research and development expenses, with a substantial portion of the Company's on-going research and development activities being conducted by third party service providers, including contract research and manufacturing organizations.

The Company accrues for expenses resulting from obligations under agreements with contract research organizations ("CROs"), contract manufacturing organizations ("CMOs"), and other outside service providers for which payment flows do not match the periods over which materials or services are provided to the Company. Accrued expenses are recorded based on estimates of services received and efforts expended pursuant to agreements established with CROs, CMOs, and other outside service providers. These estimates are typically based on contracted amounts applied to the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the services. The Company makes significant judgments and estimates in determining the accrued expense balance in each reporting period. In the event advance payments are made to a CRO, CMO, or outside service provider, the payments will be recorded as prepayments which will be expensed as the contracted services are performed. Inputs, such as the services performed, the number of patients enrolled, or the trial duration, may vary from the Company's estimates. As actual costs become known, the Company adjusts its prepayments and accrued expenses.

3. Significant accounting policies

The accounting policies set out below have been applied consistently to all periods presented in these consolidated financial statements, unless otherwise indicated.

Basis of consolidation

Subsidiaries

Subsidiaries are entities controlled by the Group. The Group controls an entity when it is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity. The financial statements of subsidiaries are included in the consolidated financial statements from the date on which control commences until the date on which control ceases.

Transactions eliminated on consolidation

All inter-company balances, transactions and unrealized gains on transactions have been eliminated in consolidation. Unrealized losses are also eliminated unless the transaction provides evidence of an impairment of the asset transferred.

Segment reporting

A segment is a distinguishable component of the Group that engages in business activities from which it may earn revenues and incur expenses, including revenues and expenses that relate to transactions with any of the Group's other components.

The Chief Executive Officer is determined to be the Group's Chief Operating Decision Maker ("CODM"). The CODM assesses the performance and allocates the resources of the Group as a whole, as all of the Group's activities are focusing on the development of therapeutics for the treatment and prevention of ear, nose, throat and related disorders. Financial information is only available for the Group as a whole. Therefore, management considers there is only one operating segment under the requirements of IFRS 8, Operating Segments.

Foreign currency

Foreign currency transactions

Items included in the financial statements of Group entities are measured using the currency of the primary economic environment in which the entity operates. Foreign currency transactions are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of such transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognized in profit or loss. Non-monetary items that are measured based on historical cost in a foreign currency are not re-translated.

Foreign operations

Assets and liabilities of Group entities whose functional currency is other than CHF are included in the consolidation by translating the assets and liabilities into the reporting currency at the exchange rates applicable at the end of the reporting period. Income and expenses are translated at average exchange rates (unless this average is not a reasonable approximation of the cumulative effect of the rates prevailing on the transaction dates, in which case income and expenses are translated at the dates of the transaction).

These foreign currency translation differences are recognized in Other Comprehensive 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, 2020	December 31, 2019	December 31, 2018
CHF	Swiss Franc	Switzerland	5	1.0000	1.0000	1.0000
USD	Dollar	United States	1	0.8840	0.9674	0.9827
EUR	Euro	Europe	1	1.0817	1.0855	1.1283
AUD	Dollar	Australia	1	0.6822	—	—

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

Currency		Geographical area	Reporting entities	2020	2019	2018
CHF	Swiss Franc	Switzerland	5	1.0000	1.0000	1.0000
USD	Dollar	United States	1	0.9581	0.9938	0.9768
EUR	Euro	Europe	1	1.0825	1.1128	1.1573
AUD	Dollar	Australia	1	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 or the shorter remaining lease term for leasehold improvements. The applicable estimated useful lives are as follows:

Production equipment	5 years
Office furniture and electronic data processing equipment (“EDP”)	3 years
Leasehold improvements	5 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. This has been the general assessment for AM-201, AM-301, AM-101, and AM-111. For the AM-125 program for the treatment of vertigo it is the Group's assessment that the criteria mentioned above are met and therefore direct development expenditures have been capitalized for AM-125 in 2018, 2019 and 2020. Intellectual property-related costs for patents are part of the expenditure for research and development projects. Therefore, the costs for the prosecution and registration of patents are expensed when incurred as long as the research and development project concerned does not meet the criteria for capitalization. In case of AM-125, where in 2019 a US patent was issued and a related EU application was allowed, prosecution and registration costs have been capitalized as the criteria have been met.

Licenses, intellectual property and data rights

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

Measurement

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

Subsequent expenditure

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

Amortization

All licenses of the Group have finite lives. Amortization will commence once the Group's intangible assets are available for use which will be the case after regulatory approvals are obtained and the related products are available for use. Amortization of licenses is calculated on a straight-line basis over the period of the expected benefit or until the license expires, whichever is shorter. The estimated useful life is 10 years or the remaining term of patent protection. The Group assesses at each statement of financial position date whether intangible assets which are not yet ready for use are impaired.

Impairment of non-financial assets

Property and equipment and intangible assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. For the purpose of assessing impairment, assets are grouped at the lowest levels for which there are separately identifiable cash flows (cash-generating units). An impairment loss is recognized as the amount by which the asset's carrying amount exceeds its recoverable amount. The recoverable amount is the higher of an asset's fair value less costs to sell or value in use. Impairment losses are recognized in profit or loss. Assets that were previously impaired are reviewed for possible reversal of the impairment at each reporting date. Any increase in the carrying amount of an asset will be based on the depreciated historical costs had the initial impairment not been recognized.

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. The date of initial application (i.e. the date on which the Company has assessed its existing financial assets and financial liabilities in terms of IFRS 9 requirements) is January 1, 2018. Accordingly, the Company has applied the requirements of IFRS 9 to instruments that continue to be recognized at January 1, 2018 whereas for the year ended December 31, 2017 IAS 39 was applied.

Recognition and derecognition of non-derivative financial assets and liabilities

The Group initially recognizes loans and receivables and debt securities issued on the date when they are originated. All other financial assets and financial liabilities are initially recognized on the trade date.

The Group derecognizes a financial asset when the contractual rights to the cash flows from the asset expire, or it transfers the rights to receive the contractual cash flows in a transaction in which substantially all of the risks and rewards of ownership of the financial asset are transferred, or it neither transfers nor retains substantially all of the risks and rewards of ownership and does not retain control over the transferred asset. Any interest in such derecognized financial assets that is created or retained by the Group is recognized as a separate asset or liability.

The Group derecognizes a financial liability when its contractual obligations are discharged, cancelled, or expired.

Financial assets and financial liabilities are offset and the net amount presented in the statement of financial position when, and only when, the Group has a legal right to offset the amounts and intends either to settle them on a net basis or to realize the asset and settle the liability simultaneously.

Non-derivative financial assets and liabilities—measurement

Loans and receivable

These are non-derivative financial assets with fixed or determinable payments that are not quoted in an active market. Loans and receivables are initially recognized at fair value plus any directly attributable transaction costs. Subsequent to initial recognition, they are measured at amortized cost using the effective interest method, less expected losses.

Cash and cash equivalents

The Group considers all short-term, highly liquid investments that are readily convertible into known amounts of cash and which are subject to an insignificant risk of changes in value with original maturities of three months or less at the date of the purchase to be cash equivalents.

Non-derivative financial liabilities—measurement

Non-derivative financial liabilities are initially recognized at fair value less any directly attributable transaction costs. Subsequent to initial recognition, these liabilities are measured at amortized cost using the effective interest method.

Convertible loans

In a convertible loan classified as a hybrid contract containing a host and a separated embedded derivative, both classified as liability, the carrying amount of the host contract at initial recognition is the difference between the carrying amount of the hybrid contract and the fair value of the embedded derivative. Transaction costs that relate to the issue of the convertible loan are allocated to the host and embedded derivative in proportion to the allocation of the gross proceeds. Transaction costs relating to the embedded derivative are immediately recognized in profit and loss. Transaction costs relating to the host contract are included in the carrying amount of the liability. The host contract is then subsequently measured at amortized cost, using the effective interest method.

Share capital

All shares of the Company are registered shares and classified as part of shareholders' equity. Incremental costs directly attributable to the issue of the Company's shares, net of any tax effects, are recognized as a deduction from equity. The warrants are classified as a financial liability at fair value through profit or loss and the cost allocated to the liability component will be immediately expensed to the income statement.

The Company has not paid any dividends since its inception and does not anticipate paying dividends in the foreseeable future.

Repurchase and reissue of ordinary shares (treasury shares)

When shares recognized as equity are repurchased, the amount of the consideration paid, which includes directly attributable costs, net of any tax effects, is recognized as a deduction from equity. Repurchased shares are classified as treasury shares and are presented in the treasury share reserve. When treasury shares are sold or reissued subsequently, the amount received is recognized as an increase in equity and the resulting surplus or deficit (calculated as the difference between initial cost and fair value) on the transaction is presented within share premium.

Impairment of non-derivative financial assets

Financial assets are assessed at each reporting date to determine whether there is objective evidence of impairment.

Objective evidence that financial assets are impaired includes:

- default or delinquency by a debtor;
- indications that a debtor or issuer will enter bankruptcy;
- adverse changes in the payment status of borrowers or issuers;
- the disappearance of an active market for a security; or
- observable data indicating that there is measurable decrease in expected cash flows from a group of financial assets.

Financial assets measured at amortized cost

The Group considers evidence of impairment for these assets at an individual asset level. An impairment loss is calculated as the difference between an asset's carrying amount and the present value of the estimated future cash flows discounted at the asset's original effective interest rate. Losses are recognized in profit or loss and reflected in an allowance account. When the Group considers that there are no realistic prospects of recovery of the asset, the relevant amounts are written off. If the amount of impairment loss subsequently decreases and the decrease can be related objectively to an event occurring after the impairment was recognized, then the previously recognized impairment loss is reversed through profit or loss.

Derivative Financial Instruments

Derivative financial instruments (assets) are accounted as the cost to obtain the rights from a third party to issue shares under the purchase agreement and changes in fair value are shown as profit or loss. The fair value calculation of the derivative financial instrument (asset) is adjusted on the utilization of the asset based on total dollar amount of the purchase agreement.

Derivative financial instruments (liabilities) are accounted at fair value and changes in fair value are shown as profit or loss. The fair value calculation of the derivative financial instruments is based on the Black-Scholes option pricing model. Assumptions are made for volatility and the risk free rate in order to estimate the fair value of the instrument. Transaction cost related to derivative financial instruments are recorded through profit and loss.

Embedded Derivatives

Derivatives may be embedded in another contractual arrangement. The Group accounts for an embedded derivative separately from the host contract when:

- The host contract is not an asset in the scope of IFRS 9
- The host contract is not itself carried at fair value through profit and loss (FVPL)
- The terms of the Embedded Derivative would meet the definition of a derivative if they were contained in a separate contract
- The economic characteristics and risks of the embedded derivative are not closely related to the economic characteristics and risks of the host

The separated embedded derivatives were measured at fair value by an independent consultant applying a simulation –based valuation approach. Assumptions are made for volatility, risk free rate and other features of the instrument. All changes in the fair value of embedded derivatives were recognized in profit and loss.

Income tax

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

Current tax

Current tax comprises the expected tax payable or receivable on the taxable income or loss for the year and any adjustment to tax payable or receivable in respect of previous years. It is measured using tax rates enacted or substantively enacted at the reporting date.

Deferred tax

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

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

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

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

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

Employee benefits

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

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

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

Remeasurements of the net defined benefit liability, which comprise actuarial gains and losses, the return on plan assets (excluding interest) and the effect of the asset ceiling (if any, excluding interest), are recognized immediately in Other Comprehensive Income. Past service costs, including curtailment gains or losses, are recognized immediately in general and administrative expenses within the operating results. Settlement gains or losses are recognized in general and administrative expenses within the operating results. The Group determines the net interest expense (income) on the net defined benefit liability (asset) for the period by applying the discount rate used to measure the defined benefit obligation at the beginning of the annual period or in case of any significant events between measurement dates to the then-net defined benefit liability (asset), taking into account any changes in the net defined benefit liability (asset) during the period as a result of contributions and benefit payments. Net interest expense and other expenses related to defined benefit plans are recognized in profit or loss.

Share-based compensation

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

The share-based compensation plans qualify as equity settled plans. The grant-date fair value of share-based payment awards granted to employees is recognized as an expense, with a corresponding increase in equity, over the period that the employees become unconditionally entitled to the awards. Under the Auris Medical Holding Ltd. Long Term Equity Incentive Plan (the "Equity Incentive Plan" or "EIP"), 50% of granted share options granted to employees vest after a period of service of two years from the grant date and the remaining 50% vest after a period of service of three years from the grant date. Share options granted to members of the Board of Directors granted from 2016 onwards vest after a period of one year after the grant date.

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

Valuation of share options

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

Provisions

Provisions are recognized when the Group has a present obligation (legal or constructive) as a result of a past event, where it is more likely than not that an outflow of resources will be required to settle the obligation, and where a reliable estimate can be made of the amount of the obligation. Provisions are not recognized for future operating losses. Provisions are measured at the present value of the expenditures expected to be required to settle the obligation using a pre-tax rate that reflects current market assessments of the time value of money and the risks specific to the liability.

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 2020, the following revised standards have been adopted:

IFRS 3	Amendments to IFRS 3, Definition of a business
IAS 1/IAS 8	Amendments to IAS 1 and IAS 8, Definition of material
IFRS 9/IAS 39/IFRS 7	Amendments to IFRS 9, IAS 39 and IFRS7, Interest Rate Benchmark Reform – Phase 1
IFRS 16	COVID-19 Rent-related Concessions (Amendments to IFRS 16)
Conceptual Framework	Amendments to References to the Conceptual Framework (Various Standards)

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, 2021, 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 9/IAS 39/IFRS 7/IFRS 4/IFRS 16	Amendments to IFRS 9/IAS 39/IFRS 7/IFRS 4/IFRS 16, Interest Rate Benchmark Reform – Phase 2	1)	January 1, 2021	FY 2021
IAS 16	Amendments to IAS 16, Proceeds before Intended Use	1)	January 1,2022	FY 2022
IAS 37	Amendments to IAS 37, Onerous contracts – Costs of Fulfilling a Contract	1)	January 1, 2022	FY 2022
IFRS 3	Amendments to IFRS 3, References to the Conceptual Framework	1)	January 1, 2022	FY 2022
IFRS 1, IFRS 9, IFRS 16, IAS 41	Annual improvements to IFRS Standards 2018-2020 Cycle	1)	January 1, 2022	FY 2022
IFRS 17	Insurance contracts	1)	January 1, 2023	FY 2023
IAS 1	Amendments to IAS 1, Classification of Liabilities as Current or Non-current	1)	January 1, 2023	FY 2023

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, 2020	December 31, 2019
Financial assets		
Cash and cash equivalents	11,258,870	1,384,720
Loans and receivables		
Other receivables	10,040	80,040
Total financial assets	**11,268,910**	**1,464,760**
Financial liabilities		
At amortized cost		
Trade and other payables	762,453	938,247
Accrued expenses	1,433,106	1,339,822
Loan	523,920	—
At fair value through profit and loss		
Derivative financial instruments	316,757	4,353
Total financial liabilities	**3,036,236**	**2,282,422**

Fair values

The carrying amount of cash and cash equivalents, other receivables, trade and other payables, accrued expenses and loan is a reasonable approximation of their fair value due to the short-term nature of these instruments.

Financial risk factors

The Group's activities expose it to a variety of financial risks: market risk, credit risk, interest rate and liquidity risk. The Group's overall risk management program focuses on the unpredictability of financial markets and seeks to minimize potential adverse effects on the Group's financial performance. Management identifies, evaluates and controls financial risks. No financial derivatives have been used in 2020 and 2019 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, 2020 and 2019. 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, 2020					
Trade and other payables	762,453	762,453	—	—	762,453
Accrued expenses	1,433,106	1,433,106	—	—	1,433,106
Loan and borrowings	523,920	473,920	50,000		523,920
Derivative financial instruments	316,757	310,439	—	6,318	316,757
Total	**3,036,236**	**2,979,918**	**50,000**	**6,318**	**3,036,236**

	Carrying amount	Less than 3 months	Between 3 months and 2 years	2 years and later	Total
December 31, 2019					
Trade and other payables	938,247	938,247	—	—	938,247
Accrued expenses	1,339,822	1,339,822	—	—	1,339,822
Loan and borrowings	—	—	—	—	—
Derivative financial instruments	4,353	—	—	4,353	4,353
Total	**2,282,422**	**2,278,069**	**—**	**4,353**	**2,282,422**

Fair value measurement

	Fair values as at		Fair	
Financial assets / liabilities	**December 31, 2020**	**December 31, 2019**	**value hierarchy**	**Valuation technique(s) and key input(s)**
Derivative financial liabilities – Warrants from public offerings	Liability 6,318	Liability 4,353	Level 2	Black-Scholes option pricing model The share price is determined by Company's NASDAQ quoted-price. The strike price and maturity are defined by the contract. The volatility assumption is driven by Company's historic quoted share price and the risk free rate is estimated based on observable yield curves at the end of each reporting period.
Derivative financial liabilities – Embedded derivatives	310,439	—	Level 3	Monte Carlo simulation model The valuation is based on input parameters classified as level 3. Input parameters include the historical volatility of AMHL shares, risk-free rate, expected remaining life, expected exercise date and share prices of AMHL at valuation dates.
Derivative financial asset	Asset —	Asset 219,615	Level 3	The fair value is equal to the price paid to the counter party for obtaining the right 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 volatility of 5%.

	Dec 31, 2020		Dec 31, 2019	
	Increase/Decrease in volatility assumption	Effect on result before taxes on CHF	Increase/Decrease in volatility assumption	Effect on result before taxes on CHF
Change in volatility	+5%	2,770	-	
	-5%	-5,475	-	

Changes in liabilities arising from financing activities

			Non-cash changes		
	01.01.2020	Financing Cash Flows [1)]	Fair value revaluation	Other changes [2)]	31.12.2020
Derivative financial instrument	4,353	—	219,315	93,089	316,757
Loans	—	1,522,931	—	(999,011)	523,920
Total	**4,353**	**1,522,931**	**219,315**	**(905,922)**	**840,677**

			Non-cash changes		
	01.01.2019	Financing Cash Flows [1)]	Fair value revaluation	Other changes [2)]	31.12.2019
Derivative financial instrument	675,328	—	(663,725)	(7,250)	4,353
Loans	1,435,400	(1,463,328)	—	27,928	—
Total	**2,110,728**	**(1,463,328)**	**(663,725)**	**20,678**	**4,353**

1) The financing cash flows are from loan borrowings or loan repayments.
2) Other non-cash changes include recognition of derivative, partial conversion and amortization of convertible loan, accrued interest and Foreign Exchange-Difference.

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 other receivables. The Company's policy is to invest funds in low risk investments including interest bearing deposits. Other receivables were current as of December 31, 2020 and December 31, 2019, 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, 2020	December 31, 2019
Financial assets		
Cash and cash equivalents	11,258,870	1,384,720
Other receivables	10,040	80,040
Total	**11,268,910**	**1,464,760**

As of December 31, 2020 and December 31, 2019 other receivables consisted in a bank deposit for guaranteeing credit card liabilities.

Market risk

Currency risk

The Group operates internationally and is exposed to foreign exchange risk arising from various exposures, primarily with respect to US Dollar and Euro. 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:

	2020		2019	
in CHF	**USD**	**EUR**	**USD**	**EUR**
Cash and cash equivalents	9,214,709	694,287	1,041,695	125,631
Other receivables	479	—	154,063	—
Trade and other payables	(75,712)	(397,853)	(51,527)	(526,637)
Accrued expenses	(34,648)	(569,400)	(750,949)	(175,826)
Net statement of financial position exposure -asset/(liability)	**9,104,828**	**(272,966)**	**393,282**	**(576,832)**

As of December 31, 2020, a 5% increase or decrease in the USD/CHF exchange rate with all other variables held constant would have resulted in a CHF 455,241 (2019: CHF 19,664) 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 13,648 (2019: CHF 28,841) 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, 2020	**December 31, 2019**
Switzerland	9,030,778	6,852,286
Australia	151,269	—
Total	**9,182,047**	**6,852,286**

Non-current assets exclude financial instruments.

7. Property and Equipment

	Production equipment	Office furniture and EDP	Total
At cost			
As of January 1, 2019	**289,888**	**233,706**	**523,594**
Additions	63,600	—	63,600
Disposals	—	—	**—**
As of December 31, 2019	**353,488**	**233,706**	**587,194**
Additions	—	—	**—**
Disposals	—	—	**—**
As of December 31, 2020	**353,488**	**233,706**	**587,194**
Accumulated depreciation			
As of January 1, 2019	**(270,408)**	**(219,291)**	**(489,699)**
Charge for the year	(20,083)	(10,740)	(30,823)
Disposals	—	**—**	—
As of December 31, 2019	**(290,491)**	**(230,031)**	**(520,522)**
Charge for the year	(16,481)	(3,555)	(20,036)
Disposals	—	—	—
As of December 31, 2020	(306,972)	(233,586)	(540,558)
Net book value			
As of December 31, 2019	**62,997**	**3,675**	**66,672**
As of December 31, 2020	**46,516**	**120**	**46,636**

As of December 31, 2020, and 2019 no items of property and equipment were pledged.

8. Intangible assets

	Licenses	IP & Data rights	Patents	Internally generated	Total
At cost					
As of January 1, 2019	**1,482,520**	**193,989**	**—**	**1,858,731**	**3,535,240**
Additions	—	—	239,593	2,990,780	3,230,373
As of December 31, 2019	**1,482,520**	**193,989**	**239,593**	**4,849,511**	**6,765,613**
Exchange differences				6,120	6,120
Additions	—	—	177,623	2,166,054	2,343,677
As of December 31, 2020	**1,482,520**	**193,989**	**417,216**	**7,021,685**	**9,115,410**
Accumulated amortization and impairment losses					
As of December 31, 2019	**—**	**—**	**—**	**—**	**—**
As of December 31, 2020	**—**	**—**	**—**	**—**	**—**
Net book value					
As of December 31, 2019	**1,482,520**	**193,989**	**239,593**	**4,849,511**	**6,765,613**
As of December 31, 2020	**1,482,520**	**193,989**	**417,216**	**7,021,685**	**9,115,410**

Intangible assets comprise upfront and milestone payments related to licenses. In 2013 a milestone payment of CHF 1,125,000 related to the AM-111 program was recorded. 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.

On February 2, 2017, the Company entered into an asset purchase agreement with Otifex Therapeutics Pty Ltd ("Otifex"), pursuant to which the Company agreed to purchase and Otifex has agreed to sell to the Company certain pre-clinical and clinical assets related to a formulation for the intranasal application of betahistine, which the Company refers to as AM-125, as well as intellectual property rights. The Otifex transaction closed in July 2017 and the Company recorded CHF 146,580 as intangibles related to this transaction.

On December 6, 2018, in two related transactions, the Company acquired an Orphan Drug Designation for betahistine in the treatment of obesity associated with Prader-Willi syndrome (PWS). In a related transaction, on May 15, 2019, the Company acquired two U.S. Patents relating to the use of betahistine for the treatment of depression and attention-deficit / hyperactivity disorder (ADHD), respectively. The Company recorded CHF 47,409 as intangibles related to these transactions.

In 2019, a US patent on AM-125 was issued and a related EU application was allowed. As a consequence, we started to capitalize prosecution and registration costs. In 2020, we capitalized CHF 177,623 (2019: CHF 239,593).

Commencing with the business year 2018, the Company recorded intangibles related to direct development expenditure of its AM-125 program. The capitalized amount for the year ended December 31, 2020 was CHF 2,343,677 (2019: CHF 3,230,373).

No amortization or impairment was recorded in 2020 and 2019.

9. Other receivables

	December 31, 2020	December 31, 2019
Advance payments to suppliers	479	—
Value added tax receivable	38,337	26,438
Withholding tax receivable	6,087	24,113
Deposit credit cards	10,040	80,040
Other	25,918	204,708
Total other receivables	**80,861**	**335,299**

Other receivables were not considered impaired in the years under review.

10. Prepayments

	December 31, 2020	December 31, 2019
Advance payments to suppliers	5,020	40,461
Clinical projects and related activities	164,916	265,842
Insurance	104,590	114,016
Other	3,063	13,912
Total prepayments	**277,589**	**434,231**

11. Cash and cash equivalents

	December 31, 2020	December 31, 2019
Cash in bank accounts	11,258,870	1,383,182
Cash on hand	—	1,538
Total cash and cash equivalents	**11,258,870**	**1,384,720**

12. Capital and reserves

Share capital

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

	December 31, 2020		December 31, 2019	
	Number	**CHF**	**Number**	**CHF**
Common shares with a par value of CHF 0.01 each	11,417,159	114,172	—	—
Common shares with a nominal value of CHF 0.40	—	—	4,125,949	1,650,380
Total	**11,417,159**	**114,172**	**4,125,949**	**1,650,380**

	Common Shares (Number)	
	2020	**2019**
As of January 1	4,125,949	1,775,839
Public offering	—	2,161,280
Exercise of warrants	1,263,845	—
LPC equity line	1,610,120	89,880
ATM program	1,628,827	98,950
Share-based payments (bonus)	51,418	—
Conversion convertible loan	737,000	—
Registered direct offering	2,000,000	—
Total, as of December 31	**11,417,159**	**4,125,949**

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

On December 1, 2020, a tranche of the convertible loan provided by FiveT (please refer to note 25) in the amount of CHF 895,455 was converted into 737,000 common shares at a conversion price of $1.35.

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

On May 15, 2019, the Company completed a public offering of (i) 440,000 common shares with a par value of CHF 0.40 each, together with warrants to purchase 440,000 common shares, and (ii) 1,721,280 pre-funded warrants, with each pre-funded warrant exercisable for one common share, together with warrants to purchase 1,721,280 common shares, including 110,000 common shares and warrants to purchase 110,000 common shares sold pursuant to a partial exercise by the underwriters of the underwriters' over-allotment option (the "May 2019 Registered Offering"). The exercise price for the pre-funded warrants was CHF 0.01 per common share and for the warrants CHF 4.34. The net proceeds to us from the May 2019 Registered Offering were approximately $7.7 million, after deducting underwriting discounts and other offering expenses payable by us. All pre-funded warrants were exercised in 2019. In December 2020, 1,263,845 warrants were exercised, leaving 897,435 warrants outstanding as of December 31, 2020. These remaining 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 2020, we sold 1,628,827 shares under the ATM. As of the date of this Annual Report, we have sold 1,758,618 of our common shares for an aggregate offering price of $3.2 million pursuant to the A.G.P. Sales Agreement. In 2019, we sold 98,954 shares for an aggregate offering price of $978,415. The related transaction costs of CHF 71,161 were charged to equity.

On November 27, 2018 and December 11, 2018, the Company entered into purchase agreements with FiveT Capital AG, providing for the issuance and sale by us of an aggregate of 165,750 of its common shares for an aggregate purchase price of CHF 1.6 million in two separate registered direct offerings.

On July 17, 2018 the Company completed a public offering of 897,435 common shares with a nominal value of CHF 0.40, Series A warrants each entitling its holder to purchase 0.35 of a common share for an aggregate of 314,102 common shares, and Series B warrants entitling its holder to purchase 0.25 of a common share for an aggregate of 224,358 common shares (the "July 2018 Registered Offering"). As of December 31, 2019, the exercise price for the Series A Warrants was CHF 7.80 per common share and the exercise price for the Series B Warrants was CHF 3.95 per common share (which exercise price was automatically adjusted due to the May 2019 Registered Offering). Since the July 2018 Registered Offering, certain Series A warrant holders exercised their warrant shares to purchase 145,226 common shares of the Company and certain Series B warrant holders exercised warrant shares to purchase 143,221 common shares. On June 18, 2020, the Series B warrants expired without further warrants being exercised. The net proceeds to the Company from the July 2018 Registered Offering were approximately CHF 6.2 million, after deducting underwriting discounts and other offering expenses payable by us. The Company had transaction costs amounting to CHF 851,692. The transaction costs were recorded as CHF 742,833 in equity for the issuance of common shares and CHF 108,809 to finance expense in the statement of profit or loss and comprehensive loss for the issuance of the warrants.

On May 2, 2018 the company entered into a purchase agreement (the "2018 Commitment Purchase Agreement") and a registration rights agreement (the "2018 Registration Rights Agreement") with Lincoln Park Capital LLC ("LPC"). Pursuant to the 2018 Commitment Purchase Agreement, LPC agreed to purchase common shares for up to $10,000,000 over the 30-month term of the 2018 Commitment Purchase Agreement. As of the date of these consolidated financial statements, the Company has issued an aggregate of 89,880 common shares for aggregate proceeds of CHF 286,450 to LPC under the 2018 Commitment Purchase Agreement. The 2018 Commitment Purchase Agreement replaces the 2017 Commitment Purchase Agreement (as defined below), 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 common shares and prior to its termination, the Company had issued an aggregate of 2,600,000 (pre-merger) common shares for aggregate proceeds of CHF 1.7 million to LPC under the 2017 Commitment Purchase Agreement. The Company had transaction costs amounting to CHF 349,907. The payment of CHF 252,351 was recorded as a derivative financial instrument and classified as a non-current asset and CHF 97,556 to finance expense in the statement of profit or loss and comprehensive loss. During the financial year 2019, the Company had sold 89,880 of its common shares for an aggregate offering price of $ 286,450. The related transaction costs of CHF 2,859 were charged to equity.

On January 30, 2018, the Company completed a public offering of 62,499 common shares and concurrent offering of warrants, each warrant entitling its holder to purchase 0.6 common shares (the "January 2018 Registered Offering"). The net proceeds to the Company from the January 2018 Registered Offering were approximately CHF 4.5 million, after deducting placement agent fees and other estimated offering expenses payable by the Company. As of December 31, 2020, the outstanding warrants issued in the January 2018 Registered Offering were exercisable for up to 37,501 common shares (assuming the Company rounds up fractional common shares to the next whole common share) at an exercise price of $100.00 per common share. As of December 31, 2019 the outstanding warrants were exercisable for up to 37,501 common shares at an exercise price of $100.00 per common share. The Company had transaction costs amounting to CHF 654,985. The transaction costs were recorded as CHF 341,226 in equity for the issuance of the common shares and CHF 313,760 to finance expense in the statement of profit or loss and comprehensive loss for the issuance of the warrants.

Authorized share capital

On January 24, 2019, our board of directors determined that it would be in our best interest to change our legal seat and jurisdiction of incorporation, respectively, from Switzerland to Bermuda (the "Redomestication"). The Company's Memorandum of Continuance and the Bye-laws that were adopted at an extraordinary meeting of shareholders held on March 8, 2019 provided for an authorized share capital of 200,000,000 common shares and 20,000,000 preference shares. Following a reverse share split at a ratio of 20-for-1 on May 1, 2019, a decision by the annual general meeting of shareholders on June 4, 2020 to increase the authorized share capital and the reduction of the par value of June 30, 2020, our authorized share capital consists of 25,000,000 common shares, par value CHF 0.01 per share, and 20,000,000 preference shares, par value CHF 0.02 per share.

13. Share-based compensation

Description

In 2014, the Group introduced an equity incentive plan (the ("EIP") as amended in 2017 and 2019. In September 2019, all employees and directors of the Company opted-in to forfeit all option grants received prior to 2019 in exchange for new options (the "September 2019 Conversion Grant"). The number of new options was calculated on a value neutral basis using the Black-Scholes model. Including the September 2019 Conversion Grant, the Company granted 390,620 options in 2019 under the EIP. Plan C was terminated in 2019. The last outstanding options under Plan C were replaced by the September 2019 Conversion Grant. In 2020, the Company granted 726,637 options under the EIP.

Holders of vested options are entitled to purchase common shares of the Company. Under the Equity Incentive Plan, the Board of Directors defined the exercise price as the average daily closing price of the Company's shares during the 30 days preceding the date of grant. All options are to be settled by the physical delivery of shares. The key terms and conditions related to the grants under these programs at December 31, 2020 are as follows:

Plan	Number of options outstanding	Vesting conditions	Contractual life of options
Equity Incentive Plan Board	237,083	1 year service from grant date	6 years
Equity Incentive Plan Management & Staff	399,738	2 years' service from grant date (50%)	8 years
Equity Incentive Plan Management & Staff	399,738	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 2020	Equity Incentive Plan 2020	Equity Incentive Plan 2019	Equity Incentive Plan 2019
Fair value at grant date	USD 0.325 (2 year vesting) [1)] USD 0.391 (3 year vesting) [1)]	USD 0.258 (1 year vesting) [2)] USD 0.514 (2 year vesting) [2)] USD 0.578 (3 year vesting) [2)]	USD 0.715 (1 year vesting) [1)] USD 1.006 (2 year vesting) [1)] USD 1.193 (3 year vesting) [1)]	USD 1.495 (1 year vesting) [2)] USD 2.196 (2 year vesting) [2)] USD 2.596 (3 year vesting) [2)]
Share price at grant date	USD 0.79	USD 0.92	USD 1.76	USD 3.35
Exercise price	USD 0.878	USD 0.825	USD 2.07	USD 5.75
Expected volatility	84.96%	72.72%	119.41%	156.26%
Expected life	2 and 3 years	1, 2 and 3 years	1, 2 and 3 years	1, 2 and 3 years
Expected dividends	—	—	—	—
Risk-free interest rate	0.82%	0.61%	1.62%	2.29%

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 368,793 in 2020 (2019: CHF 228,920, 2018: CHF 42,757).

Share based compensation loss related to employee stock options amounted to CHF 351,401 in 2020 (2019: CHF 226,601, 2018: CHF 27,730).

Share based compensation expense of CHF 0 related to the purchase of intangibles was capitalized for the year ended December 31, 2020 (2019: CHF 2,319, 2018: 15,027).

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

	2020			2019		
	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	324,053	3.01	7.60	992,777	1.10	7.45
Replacement of historical grants	—	—	—	(992,777)	—	—
New grant with new exercise price	—	—	—	39,191	—	—
Expired during the year	—	—	—	—	—	—
Forfeited during the year	—	—	—	(66,567)	—	—
Exercised during the year	—	—	—	—	—	—
Granted during the year	714,484	0.87	—	351,429	3.30	—
Outstanding at December 31	**1,038,537**	**1.58**	**7.01**	**324,053**	**3.01**	**7.60**
Exercisable at December 31	37,576	—	—	—	—	—

The range of exercise prices for outstanding options was CHF 0.73 to CHF 27.93 as of December 31, 2020 and CHF 2.00 to CHF 5.56 as of December 31, 2019.

14. Trade and other payables

	December 31, 2020	**December 31, 2019**
Trade accounts payable - third parties	722,272	906,501
Other	40,181	31,746
Total trade and other payables	**762,453**	**938,247**

15. Accrued expenses

	December 31, 2020	**December 31, 2019**
Accrued research and development costs including milestone payments	1,105,089	1,019,563
Professional fees	172,273	108,519
Accrued vacation & overtime	44,466	23,377
Employee benefits incl. share based payments	101,821	47,916
Other	9,457	140,447
Total accrued expenses	**1,433,106**	**1,339,822**

16. Research and development expense

	December 31, 2020	December 31, 2019	December 31, 2018
Pre-clinical projects	242,617	182,346	873,453
Clinical projects	476,972	993,085	846,235
Drug manufacturing and substance	614,744	481,453	2,185,292
Employee benefits and expenses	1,120,814	1,373,543	1,652,791
Lease expenses from short-term lease	34,147	26,057	65,921
Patents and trademarks	246,592	168,367	634,986
Regulatory projects	110,612	80,347	398,426
Depreciation tangible assets	16,481	20,083	32,485
Total research and development expense	**2,862,979**	**3,325,281**	**6,689,589**

Research and development expense were capitalized in the amount of CHF 2,343,677 during 2020 compared to CHF 3,230,373 in 2019.

17. General and administrative expense

	December 31, 2020	December 31, 2019	December 31, 2018
Employee benefits and expenses	811,373	1,010,708	1,084,112
Business development	95,663	113,959	43,816
Travel expenses	28,898	102,679	70,944
Administration expenses	1,645,530	2,653,914	2,797,526
Lease expenses from short-term lease	13,871	27,362	52,416
Depreciation tangible assets	3,555	10,740	186,520
Capital tax expenses	(4,228)	14,501	29,200
Total general and administrative expenses	**2,594,662**	**3,933,863**	**4,264,534**

18. Employee benefits

	December 31, 2020	December 31, 2019	December 31, 2018
Salaries	1,260,359	1,832,382	2,542,952
Pension costs	156,843	130,792	108,978
Other social benefits	116,290	217,448	188,138
Share based payments costs	351,401	226,601	27,730
Other personnel expenditures	47,295	(22,973)	(130,895)
Total employee benefits	**1,932,188**	**2,384,250**	**2,736,903**

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 2018, 1.00% in 2019 and 1.00% in 2020.

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

	2020	2019
Defined benefit obligation at January 1	3,087,947	3,085,625
Service costs	151,624	138,580
Plan participants' contribution	76,032	107,618
Interest cost	9,482	27,335
Actuarial losses	58,912	145,385
Transfer-out amounts	(201,310)	(445,457)
Transfer-in amounts of new employees	346,915	28,861
Defined benefit obligation at December 31	**3,529,602**	**3,087,947**

The defined benefit obligation includes only liabilities for active employees. The weighted average modified duration of the defined benefit obligation at December 31, 2020 is 21.9 years (2019: 22.6 years).

Change in fair value of plan assets

	2020	2019
Fair value of plan assets at January 1	2,327,500	2,437,338
Interest income	7,429	22,198
Return on plan assets excluding interest income	32,794	73,375
Employer contributions	76,032	107,618
Plan participants' contributions	76,032	107,618
Transfer-out amounts	(201,310)	(445,457)
Transfer-in amounts of new employees	346,915	28,861
Administration expense	(3,166)	(4,051)
Fair value of plan assets at December 31	**2,662,226**	**2,327,500**

Net defined benefit liability recognized in the statement of financial position

	December 31, 2020	December 31, 2019
Present value of funded defined benefit obligation	3,529,602	3,087,947
Fair value of plan assets	(2,662,226)	(2,327,500)
Net defined benefit liability	**867,376**	**760,447**

Defined Benefit Cost

	2020	2019	2018
Service cost	151,624	138,580	90,162
Net interest expense	2,053	5,137	14,541
Administration expense	3,166	4,051	6,009
Total defined costs for the year recognized in profit or loss	**156,843**	**147,768**	**110,712**

Remeasurement of the Defined Benefit Liability

	2020	2019	2018
Actuarial loss (gain) arising from changes in financial assumptions	13,031	360,541	(119,117)
Actuarial loss arising from experience adjustments	45,881	(215,156)	(1,792,265)
Actuarial gain arising from demographic assumptions	—	—	—
Return on plan assets excluding interest income	(32,794)	(73,375)	634,190
Total defined benefit cost for the year recognized in the other comprehensive loss	**26,118**	**72,010**	**(1,277,192)**

Assumptions

At December 31	**2020**	**2019**	**2018**
Discount rate	0.20%	0.30%	0.95%
Future salary increase	0.60%	1.10%	1.10%
Pension indexation	0.00%	0.00%	0.00%
Mortality and disability rates	BVG2015G	BVG2015G	BVG2015G

Sensitivity analysis

Reasonably possible changes at the reporting date to one of the relevant actuarial assumptions, holding other assumptions constant, would have affected the defined benefit obligation by the amounts shown below.

December 31,	**2020**	**2019**
Change in assumption	0.25% increase	0.25% increase
Discount rate	(166,228)	(148,884)
Salary increase	13,602	14,395
Pension indexation	88,460	74,976
Change in assumption	+ 1 year	+ 1 year
Life expectancy	88,215	73,484

19. Finance income and finance expense

	2020	2019	2018
Interest income	258	17,882	—
Net foreign currency exchange gain	3,207,649	1,343,153	1,103,067
Revaluation gain from derivative financial instruments	—	663,725	1,350,071
Total finance income	**3,207,907**	**2,024,760**	**2,453,138**
Interest expense (incl. Bank charges)	135,151	28,628	1,070,177
Net foreign currency exchange loss	3,541,202	1,562,725	1,242,938
Revaluation loss from derivative financial instruments	2,250,222	—	—
Transaction costs	219,615	—	—
Total finance expense	**6,146,190**	**1,591,353**	**2,313,115**
Finance (expense)/income, net	**(2,938,283)**	**433,407**	**140,023**

In 2020, CHF 2,248,257 of the revaluation loss from derivative financial instruments is related to the revaluation of the financial derivatives embedded in the FiveT convertible loan (note 25), both at partial conversion and at year-end. CHF 1,965 of the revaluation loss is related to the revaluation of outstanding warrants from public offerings (note 26). In 2019 and 2018 there was a revaluation gain from derivative financial instruments of CHF 663,725 and CHF 1,350,071 respectively. In 2020, net foreign currency exchange gains contain translation gains of CHF 71,525 (2019: CHF 7,744; 2018: CHF 264,029) which arose on the Company's USD and EUR denominated cash and cash equivalents. In 2020, finance expenses did not include any interest paid (2019: CHF 3,745; 2018: CHF 435,993).

20. Taxation

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

	2020	2019	2018
Deferred income tax expense	(389,384)	(213,355)	(294,056)
Deferred income tax gain	410,668	407,192	131,879
	21,284	**193,837**	**(162,177)**

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 12.1% in 2020 (2019: 12.5%, 2018: 21.1%) as summarized in the following table:

Reconciliation	2020	2019	2018
Loss before income tax	(8,221,449)	(6,825,738)	(11,334,224)
Income tax at statutory tax rates applicable to results in the respective countries	991,120	854,636	2,397,177
Effect of unrecognized temporary differences	(302,557)	89,974	140,371
Effect of unrecognized taxable losses	(184,881)	(913,309)	(2,553,594)
Effect of utilization of previously unrecognized taxable losses	—	193,155	—
Effect of impairment of deferred tax assets	—	(131,055)	—
Effect of previously unrecognized deferred tax asset	97,458	20,977	114,116
Effect of expenses deductible for tax purposes	—	—	—
Effect of expenses not considerable for tax purposes	(47,894)	(29,549)	—
Effect of changes in local tax legislation and/or local tax rates	—	110,758	—
Effect of impact from application of different tax rates	(531,962)	(1,750)	(260,247)
Effect of unrecognized taxable losses in equity	—	—	—
Income tax gain/(loss)	**21,284**	**193,837**	**(162,177)**

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, 2020	December 31, 2019
Intangible assets	(252,174)	(212,844)
Deferred unrealized foreign exchange gains	(350,054)	—
Derivative financial asset	—	(26,156)
Total	**(602,228)**	**(239,000)**

Deferred Tax Asset	December 31, 2020	December 31, 2019
Net operating loss (NOL)	476,363	91,851
Total	**476,363**	**91,851**
Deferred Tax, net	**(125,865)**	**(147,149)**

Deferred Tax 2020	Opening Balance	Recognized in Profit or Loss	Recognized in Equity	Closing Balance
Intangible assets	(212,844)	(39,330)	—	(252,174)
Hercules Loan Facility	—	—	—	—
Deferred unrealized foreign exchange gains	—	(350,054)	—	(350,054)
Derivative financial asset	(26,156)	26,156	—	—
Net operating loss (NOL)	91,851	384,512	—	476,363
Total	**(147,149)**	**21,284**	**—**	**(125,865)**

Deferred Tax 2019	Opening Balance	Recognized in Profit or Loss	Recognized in Equity	Closing Balance
Intangible assets	(627,540)	414,696	—	(212,844)
Hercules Loan Facility	(889)	889	—	—
Derivative financial asset	(17,763)	(8,393)	—	(26,156)
Net operating loss (NOL)	305,206	(213,355)	—	91,851
Total	**(340,986)**	**193,837**	**—**	**(147,149)**

As of December 31, 2020, the Group had unrecognized tax loss carryforwards amounting to CHF 114.0 million (2019: CHF 151.5 million), of which CHF 113.0 million related to Auris Medical AG, Otolanum AG, Zilentin AG and Altamira Medica AG in Switzerland, CHF 1.0 million to Auris Medical Inc. in the United States and CHF 0.0 million to Auris Medical PTY in Australia (2019: CHF 150.4 million for Auris Medical AG, Auris Medical Holding Ltd. and Otolanum AG and CHF 1.1 million for Auris Medical Inc.).

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

	December 31, 2020	December 31, 2019
Within 1 year	19,575,171	22,405,533
Between 1 and 3 years	56,866,795	49,120,938
Between 3 and 7 years	36,701,692	78,872,116
More than 7 years	870,200	1,054,465
Total	**114,013,858**	**151,453,052**

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, 2020	December 31, 2019
Deductible temporary differences		
Employee benefit plan	113,106	99,162
Derivative financial instruments	36,973	—
Other accounts payable	258,303	—
Stock option plans	—	568
Total potential tax assets	**408,382**	**99,730**
Taxable unrecognized temporary differences		
Convertible loan	19,359	—
Total unrecognized potential tax liabilities	**19,359**	**—**
Offsetting potential tax liabilities with potential tax assets	(19,359)	—
Net potential tax assets from temporary differences not recognized	389,023	99,730
Potential tax assets from loss carry-forwards not recognized	14,896,367	19,611,272
Total potential tax assets from loss carry-forwards and temporary differences not recognized	**15,285,390**	**19,711,002**

21. Loss per share

	December 31, 2020	December 31, 2019	December 31, 2018
Loss attributable to owners of the Company	(8,200,165)	(6,631,901)	(11,496,401)
Weighted average number of shares outstanding *	6,014,146	2,909,056	795,043
Basic and diluted loss per share	**(1.36)**	**(2.28)**	**(14.46)**

* The basic and diluted loss per share for the year ended December 31, 2018 is revised to reflect the reverse-split ratio of 10 to 1 following the Merger on March 13, 2018 and the reverse-split ratio of 20 to 1 following the "reverse share split" on May 1, 2019.

For the years ended December 31, 2020 and 2019 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 13) as they would be anti-dilutive. As of December 31, 2020, the Company has 1,038,537 options outstanding under its stock option plans. The average number of options outstanding between January 1, 2020 and December 31, 2020 was 633,314 (812,167 for the period between January 1, 2019 and December 31, 2019). As of December 31, 2020, the Company had warrants to purchase up to 1,143,537 of its common shares issued and outstanding (as of December 31, 2019, the Company had warrants to purchase up to 2,488,520 common shares).

22. 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, 2020	December 31, 2019
Within one year	25,580	24,980
Between one and five years	—	—
Total	**25,580**	**24,980**

Office lease expenses of CHF 50,260, CHF 49,314 and CHF 118,337 were recorded in 2020, 2019 and 2018, respectively, in the consolidated statement of profit or loss and other comprehensive loss.

23. 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") provides the Chief Financial Officer to the Company. 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 2020 were CHF 173,030 (CHF 2019: 11,770). Fees paid to Ante Treuhand for other services provided during the year ended December 31, 2020 were CHF 3,025 (2019: CHF 28,611).

Compensation of the members of the Board of Directors and Management

In 2020, the total compensation paid to management amounted to CHF 522,237 (2019: CHF 934,179; 2018: CHF 1,403,250). The fees paid to members of the Board of Directors in 2020 for their activities as board members totaled CHF 163,476 (2019: CHF 170,755; 2018: CHF 287,384).

	Executive Management			Board of Directors			Total		
	2020	2019	2018	2020	2019	2018	2020	2019	2018
Short term benefits	407,147	717,905	1,002,707	163,476	170,755	200,421	570,623	888,660	1,203,128
Post-employee benefits years	26,870	42,560	55,278	—	—	—	26,870	42,560	55,278
Share-based payment charge	204,840	109,912	204,224	57,148	49,323	60,657	261,988	159,235	264,881
Total	**638,857**	**870,377**	**1,262,209**	**220,624**	**220,078**	**261,078**	**859,481**	**1,090,455**	**1,523,287**

In 2020, CHF 261,988 (2019: CHF 159,235; 2018: CHF 264,881) was expensed for grants of stock options to members of the Board of Directors and management. The 2020 share based payment charge shown above excludes adjustments for instruments forfeited in 2020 due to termination of service. Contributions to pension schemes amounted to CHF 26,870, CHF 42,560 and CHF 55,278 during the years 2020, 2019 and 2018, respectively. No termination benefits or other long-term benefits were paid.

Members of the Board of Directors and management held 769,101, 271,999 and 703,235 stock options as of December 31, 2020, 2019, and 2018, respectively.

24. Loan and Warrant

On July 19, 2016, the Company entered into a Loan and Security Agreement (the "Hercules Loan and Security Agreement") for a secured term loan facility of up to $20.0 million with Hercules Capital, Inc. as administrative agent ("Hercules") and the lenders party thereto. An initial tranche of $12.5 million was drawn on July 19, 2016, concurrently with the execution of the Hercules Loan and Security Agreement. Prior to its payoff in January 2019, the loan matured on January 2, 2020 and bore interest at a minimum rate of 9.55% per annum and was subject to the variability of the prime interest rate. The loan was secured by a pledge of the shares of Auris Medical AG owned by the Company, all intercompany receivables owed to the Company by its Swiss subsidiaries and a security assignment of the Company's bank accounts. On April 5, 2018 the Company entered into an agreement with Hercules whereby the terms of the Hercules Loan and Security Agreement were amended to eliminate the $5 million liquidity covenant in exchange for a repayment of $5 million principal amount outstanding under the Hercules Loan and Security Agreement. The loan was initially recognized at transaction value with deductions of the fair value of the warrant at transaction date and directly attributable transactions costs. Subsequent to initial recognition, the loan was measured at amortized cost using the effective interest method. On January 31, 2019, the Company made the final payment to Hercules under the facility, comprising the last amortization payment as well as an end of term charge. With the final payment, all covenants and collaterals in favor of Hercules have been lifted. In addition, Hercules agreed to return the warrant held by Hercules exercisable for 783 common shares at an exercise price of $788.00 per common share for no consideration to the Company in exchange for the Company's payment to Hercules. Due to the final payment and return of the warrant held by Hercules in January 2019, no warrants were outstanding and subject to revaluation on December 31, 2020. As of December 31, 2019, the fair value of the warrant amounted to CHF 0.00. There was no revaluation gain or loss for the twelve months ended December, 2020 (2019: revaluation gain of CHF 3,804). Since its initial recognition as of July 19, 2016, the fair value decreased by CHF 408,180 resulting in a revaluation gain in the corresponding amount (fair value as of July 19, 2016: CHF 408,180).

25. Loan

	December 31, 2020	December 31, 2019
Loan guaranteed by Swiss government (COVID-19)	50,000	—
Convertible Loan Agreement	473,920	—
Total	**523,920**	**—**

Convertible Loan Agreement

	December 31, 2020	December 31, 2019
Gross proceeds at disbursement date	1,500,000	—
Embedded derivative, separated	(230,974)	—
Transaction costs allocated to host	(22,495)	—
Carrying amount at initial recognition	**1,246,531**	**—**
Converted principal amount	(895,455)	—
Accrued interest at 8%	31,920	—
Amortization	90,924	—
Total	**473,920**	**—**

On September 7, 2020, our affiliate Altamira Medica AG ("Altamira") and Auris Medical Holding Ltd. ("the Company") entered into a convertible loan agreement with Five T Capital Holding AG ("FiveT") to raise CHF 1,500,000 to fund the initial development of AM-301. The loan has a term of 18 months and carries interest at 8% p.a., which shall not be paid in cash but added to the loan outstanding amount. At maturity, the unconverted outstanding amount of the loan including accrued interest shall become payable in cash. Altamira may choose to repay the total outstanding amount including the accrued interest at 130%, first time after 6 months with a prior written notice of 1 month. Prior to the expiry of the repayment notice period, the lender may convert the repayment amount.

Under the convertible loan agreement FiveT has the right to convert the outstanding principal amount including interest into the Company's common shares or alternatively into Altamira shares. The pricing of a conversion into our common shares is at the lower of 150% of the share price at close of the disbursement date ($1.35 fixed on September 8, 2020) and 95% of the average price of our common share at close of the 5 trading dates preceding the date of the conversion notice. However, the conversion price shall not be less than the higher of the par value and the backward-looking 3-month floor price of 75% of the average closing price of our common shares. The pricing of a conversion into Altamira shares is at the lower of CHF 3.00 and the issue price of a qualified financing round, meaning that a third-party investor will hold at least 10% of Altamira shares after completion of such financing round. The convertible loan agreement further contains a limitation on the conversion rights in the sense that they may not result in an ownership interest of more than 9.99% in the Company or 49.99% in Altamira. By December 31, 2020, an amount of CHF 895,455 has been converted into 737,000 common shares of the Company (at a conversion price of $1.35).

The convertible loan is classified as a hybrid contract containing a host that is a financial liability and embedded derivatives separated from the host and measured at fair value with all changes in fair value recognized in profit or loss. The embedded financial derivatives are valued by an independent consultant initially and at period end at fair value, applying a simulation-based valuation approach. The valuation of the embedded financial derivatives is based on input parameters, classified as Level 3. One of the significant inputs is the historical volatility of the Company's common shares. The underlying share price development has been simulated based on a Geometric Brownian Motion (GBM). In accordance with the GBM definition, a normalized, sustainable level of volatility was applied. The normalized volatility used as per December 31, 2020 was 90.9%, over a lookback period of 12 months. Other significant assumptions relate to the expected exercise date, the expected execution date, the calculation of the repayment amount, as well as assumptions with regards to the early repayment trigger and to the conversion option in Altamira shares. The embedded derivatives of the convertible loan are closely related to each other and are therefore accounted for as a single instrument (i.e., a compound derivative). Due to the conversion based on market share price, the conversion right may result in a variable number of conversion shares and the embedded derivatives are therefore classified as a financial liability.

The carrying amount of the host contract at initial recognition is the difference between the carrying amount of the hybrid contract and the fair value of the embedded derivatives. The host is then subsequently measured at amortized cost, using the effective interest rate method. As of December 31, 2020, the carrying amount (including accrued interest) of the host for the unconverted outstanding loan amounted to CHF 473,920 and is included in the balance sheet under current liabilities. The fair value of the embedded derivatives of the outstanding loan units amounted to CHF 310,439 and is included in current derivative financial instruments. Expenses related to fair value measurement of embedded derivatives of CHF 2,248,257 as well as effective interest and transaction costs of CHF 127,418 were recorded as financial expenses in profit or loss.

26. Warrants from Public Offering

On February 21, 2017, the Company completed a public offering (the "February 2017 Offering") of 10,000,000 (pre-merger) common shares with a nominal value of CHF 0.40 each and 10,000,000 (pre-merger) warrants, each warrant entitling its holder to purchase 0.70 of a common share. The net proceeds to the Company from the February 2017 Offering were approximately CHF 9.1 million ($ 9.1 million), after deducting underwriting discounts and other estimated offering expenses payable by us. The Company had transaction costs amounting to CHF 903,919. The transactions costs were recorded as CHF 397,685 in equity for the issuance of the common shares and CHF 506,234 to finance expense in the statement of profit or loss and comprehensive loss for the issuance of the warrants.

The underwriter was granted a 30-day option to purchase up to 1,500,000 (pre-merger) additional common shares and/or 1,500,000 (pre-merger) additional warrants. On February 15, 2017, the underwriter partially exercised its 30-day option to purchase additional common shares and/or warrants in the amount of 1,350,000 (pre-merger) warrants.

Consequently, the Company issued warrants to purchase up to 7,945,000 (pre-merger) of its common shares at an exercise price of $ 1.20 per share. The warrants are exercisable during a five-year period beginning on date of issuance. The fair value calculation of the warrants is based on the Black-Scholes option price model. Assumptions are made regarding inputs such as volatility and the risk-free rate in order to determine the fair value of the warrant. If a warrant is exercised, the Company will receive variable proceeds because the Company's functional currency is CHF and the exercise price is in USD, which results in the warrants being considered liability instruments. Therefore, the warrants were assigned fair values using the Black-Scholes model. The residual value was assigned to the common share sold along with each warrant in accordance with IAS 32 Financial instruments. The gross proceeds from the February 2017 offering were CHF 9,998,305 of which CHF 5,091,817 (fair value as of February 21, 2017) was assigned to the warrants and CHF 4,906,488 was assigned to equity.

As of December 31, 2020, the outstanding warrants issued in the 2017 February Offering are exercisable for up to 39,725 common shares at an exercise price of $240.00. As of December 31, 2020, the fair value of the warrants amounted to CHF 0.00 (2019: CHF 0.00). As the fair value remained unchanged, no revaluation gain or loss resulted for the year ended December 31, 2020.

On January 30, 2018, the Company issued warrants in connection with a direct offering of 62,499 common shares, each warrant entitling its holder to purchase 0.6 common shares at an exercise price of $100.00 per common share. As of December 31, 2020, the outstanding warrants issued in such offering were exercisable for up to 37,501 common shares at an exercise price of $100.00 per common share. As of December 31, 2020 the fair value of the warrants amounted to CHF 6,318 (2019: CHF 4,353). The revaluation loss of the derivative for the twelve months ended December 31, 2020 amounted to CHF 1,965 (2019: revaluation gain of CHF 285,298). Since its initial recognition on January 30, 2018, the fair value of the warrants has decreased by CHF 2,477,429 resulting in a gain in the corresponding amount (fair value as of January 30, 2018: CHF 2,483,747).

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

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

As of December 31, 2019, 143,221 Series B exercised warrants were subject to revaluation at the time that they were exercised and the fair value amounted to CHF 3,005,348. Since its initial recognition on July 17, 2018 the fair value of the warrants has increased by CHF 2,433,099, resulting in a loss in the corresponding amounts (fair value as of July 17, 2018: CHF 572,249). On June 18, 2020, the Series B warrants expired without further warrants being exercised.

Due to the expiry on June 18, 2020, no Series B warrants were outstanding and subject to revaluation on December 31, 2020. As of December 31, 2019, the number of Series B warrants outstanding subject to revaluation were 34,535 and the fair value amounted to CHF 0.00. Accordingly, there was no revaluation gain or loss on these warrants for the year ended December 31, 2020 (2019: revaluation gain of CHF 215,572).

27. Events after the balance sheet date

The COVID-19 pandemic continues to delay enrollment of patients into our “TRAVERS” phase 2 trial with AM-125. Candidates for trial participation undergo certain types of neurosurgery, which are elective procedures. In early 2021, several sites participating in the “TRAVERS” trial have postponed elective procedures and temporarily reduced or suspended clinical research activities. Although sites are expected to catch up on enrollment once COVID-19 related restrictions are relaxed, the Company expects that final results from the trial will become only available in the third quarter of 2021, at the earliest.

On January 15, 2021, we filed a prospectus supplement with the SEC to issue up to $8.0 million in common shares under the at-the-market offering program in place with A.G.P. for a total of $25.0 million. Under the previous registration, we had issued an aggregate of 1,758,618 of our common shares for gross proceeds of approximately $3.25 million.

On February 8, 2021, we notified FiveT about our early repayment of the convertible loan as of March 8, 2021. FiveT made use of their right to convert the loan during the notice period and converted the remaining principal plus accrued interest into 516,814 common shares as of March 4, 2021.

In August 2019 Xigen, the licensor of the active substance for our Sonsuvi® product candidate, 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 license agreement under which we are developing Sonsuvi® 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 license 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.

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 Auris Medical Holdings Ltd. ("Auris," "Auris Medical," 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 (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."

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." Our registered office is located at Clarendon House, 2 Church Street, Hamilton HM 11, Bermuda.

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

Since the Redomestication, other than the 2019 Reverse Share Split and as otherwise described herein, 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, 2020, our authorized share capital consisted of 25,000,000 common shares, par value CHF 0.01 per share, and 20,000,000 preference shares, par value CHF 0.01 per share, and there were 11,455,578 common shares issued and outstanding, excluding 324,053 common shares issuable upon exercise of options and 1,143,537 common shares issuable upon exercise of warrants, and no preference shares issued and outstanding. All of the Company's issued and outstanding shares are fully paid-in.

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

Common Shares

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

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

Preference Shares

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

Dividend Rights

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

Variation of Rights

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

Transfer of Shares

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

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

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

Meeting of Shareholders

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

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

Access to Books and Records and Dissemination of Information

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

Election and Removal of Directors

Our Bye-laws provide that our board shall consist of three directors or such greater number as the board may determine. Our board of directors currently consists of 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 will serve as branch registrar and transfer agent.

Untraced Shareholders

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

Certain Provisions of Bermuda Law

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

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

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

Comparison of Corporate Law

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

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Mergers and similar arrangements	
Under the Delaware General Corporation Law, with certain exceptions, a merger, consolidation, sale, lease or transfer of all or substantially all of the assets of a corporation must be approved by the board of directors and a majority of the outstanding shares entitled to vote thereon. A shareholder of a Delaware corporation participating in certain major corporate transactions may, under certain circumstances, be entitled to appraisal rights pursuant to which such shareholder may receive cash in the amount of the fair value of the shares held by such shareholder (as determined by a court) in lieu of the consideration such shareholder would otherwise receive in the transaction. The Delaware General Corporation Law also provides that a parent corporation, by resolution of its board of directors, may merge with any subsidiary, of which it owns at least 90.0% of each class of capital stock without a vote by the shareholders of such subsidiary. Upon any such merger, dissenting shareholders of the subsidiary would have appraisal rights.	The amalgamation or merger of a Bermuda company with another company or corporation (other than certain affiliated companies) requires the amalgamation or merger agreement to be approved by the company's board of directors and by its shareholders. Unless the company's bye-laws provide otherwise, the approval of 75% of the shareholders voting at a general meeting is required to approve the amalgamation or merger agreement, and the quorum for such meeting must be two persons holding or representing more than one-third of the issued shares of the company. The Bye-laws provide that a merger or an amalgamation (other than with a wholly owned subsidiary or as described below) that has been approved by the board must only be approved by a majority of the votes cast at a general meeting of the shareholders at which the quorum shall be two or more persons present in person and representing in person or by proxy issued and outstanding voting shares. The Bye-laws contain provisions regarding "business combinations" with "interested shareholders". Pursuant to our Bye-laws, in addition to any other approval that may be required by applicable law, any business combination with an interested shareholder within a period of three years after the date of the transaction in which the person became an interested shareholder must be approved by Auris Medical's board and authorized at an annual or special general meeting by the affirmative vote of at least 66 and 2/3rds% of Auris Medical's issued and outstanding voting shares that are not owned by the interested shareholder, unless: (i) prior to the time that the shareholder becoming an interested shareholder, our board of directors approved either the business combination or the transaction that resulted in the shareholder becoming an interested shareholder; or

	(ii) upon consummation of the transaction that resulted in the shareholder becoming an interested shareholder, the interested shareholder owned at least 85% of our issued and outstanding voting shares at the time the transaction commenced. For purposes of these provisions, "business combinations" include mergers, amalgamations, consolidations and certain sales, leases, exchanges, mortgages, pledges, transfers and other dispositions of assets, issuances and transfers of shares and other transactions resulting in a financial benefit to an interested shareholder. An "interested shareholder" is a person that beneficially owns 15% or more of our issued and outstanding voting shares and any person affiliated or associated with us that owned 15% or more of our issued and outstanding voting shares at any time three years prior to the relevant time. Under Bermuda law, in the event of an amalgamation or merger of a Bermuda company with another company or corporation, a shareholder of the Bermuda company who did not vote in favor of the amalgamation or merger and who is not satisfied that fair value has been offered for such shareholder's shares may, within one month of notice of the shareholders meeting, apply to the Supreme Court of Bermuda to appraise the fair value of those shares. Note that each share of an amalgamating or merging companies carries the right to vote in respect of an amalgamation or merger whether or not is otherwise carries the right to vote.
Shareholders' suits	
Class actions and derivative actions generally are available to shareholders of a Delaware corporation for, among other things, breach of fiduciary duty, corporate waste and actions not taken in accordance with applicable law. In such actions, the court has discretion to permit the winning party to recover attorneys' fees incurred in connection with such action.	Class actions and derivative actions are generally not available to shareholders under Bermuda law. The Bermuda courts, however, would ordinarily be expected to permit a shareholder to commence an action in the name of a company to remedy a wrong to the company where the act complained of is alleged to be beyond the corporate power of the company or illegal, or would result in the violation of the company's memorandum of association or bye-laws. Furthermore, consideration would be given by a Bermuda court to acts that are alleged to constitute a fraud against the minority shareholders or, for instance, where an act requires the approval of a greater percentage of the company's shareholders than that which actually approved it. When the affairs of a company are being conducted in a manner which is oppressive or prejudicial to the interests of some part of the shareholders, one or more shareholders may apply to the Supreme Court of Bermuda, which may make such order as it sees fit, including an order regulating the conduct of the company's affairs in the future or ordering the purchase of the shares of any shareholders by other shareholders or by the company. The Bye-laws contain a provision by virtue of which Auris Medical's shareholders waive any claim or right of action that they have, both individually and on Auris Medical's behalf, against any director or officer in relation to any action or failure to take action by such director or officer, except in respect of any fraud or dishonesty of such director or officer.

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

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
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	
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.	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.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
Shareholder action by written consent	
A Delaware corporation may, in its certificate of incorporation, eliminate the right of shareholders to act by written consent.	The Companies Act provides that shareholders may take action by written consent, expect in respect of the removal of an auditor from office before the expiry of his term or in respect of a resolution passed for the purpose of removing a director before the expiration of his term of office. A resolution in writing is passed when it is signed by the members of the company who at the date of the notice of the resolution represent such majority of votes as would be required if the resolution had been voted on at a meeting or when it is signed by all the members of the company or such other majority of members as may be provided by the bye-laws of the company.
Shareholder proposals	
A shareholder of a Delaware corporation has the right to put any proposal before the annual meeting of shareholders, provided it complies with the notice provisions in the governing documents. A special meeting may be called by the board of directors or any other person authorized to do so in the governing documents, but shareholders may be precluded from calling special meetings.	Shareholder(s) may, as set forth below and at their own expense (unless the company otherwise resolves), require the company to: (i) give notice to all shareholders entitled to receive notice of the annual general meeting of any resolution that the shareholder(s) may properly move at the next annual general meeting; and/or (ii) circulate to all shareholders entitled to receive notice of any general meeting a statement in respect of any matter referred to in the proposed resolution or any business to be conducted at such general meeting. The number of shareholders necessary for such a requisition is either: (i) any number of shareholders representing not less than 5% of the total voting rights of all shareholders entitled to vote at the meeting to which the requisition relates; or (ii) not less than 100 shareholders. Pursuant to the Bye-laws, any shareholder or shareholders holding or representing not less than 5% of the total voting rights wishing to propose for election as a director someone who is not an existing director or is not proposed by Auris Medical's board must give notice of the intention to propose the person for election in accordance with the Bye-laws.
Cumulative voting	
Under the Delaware General Corporation Law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation provides for it.	Under Bermuda law, the voting rights of shareholders are regulated by the company's bye-laws and, in certain circumstances, by the Companies Act. The Bye-laws provide for a plurality of voting for elections of directors, and cumulative voting for elections of directors is not permitted.
Removal of directors	
A Delaware corporation with a classified board may be removed only for cause with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise.	Under the Bye-laws, a director may be removed, with cause, by the shareholders, provided notice of the shareholders meeting convened to remove the director is given to the director. The notice must contain a statement of the intention to remove the director and must be served on the director not less than fourteen days before the meeting. The director is entitled to attend the meeting and be heard on the motion for his removal.

DELAWARE CORPORATE LAW	BERMUDA CORPORATE LAW
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	
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.

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 require the board of directors to adopt a resolution or resolutions, pursuant to authority expressly vested in the board of directors by the provisions of the company's certificate of incorporation.

The authorized share capital of a Bermuda company is determined by the company's shareholders.

Exhibit 8.1

SUBSIDIARIES OF THE REGISTRANT

Name of Subsidiary	Jurisdiction of Incorporation or Organization
Auris Medical AG	Switzerland
Otolanum AG	Switzerland
Zilentin AG	Switzerland
Altamira Medica AG	Switzerland
Auris Medical Inc.	Illinois
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 Auris Medical Holding 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: March 31, 2021

/s/ Thomas Meyer
Thomas Meyer
Chief Executive Officer

Exhibit 12.2

CERTIFICATION

I, Elmar Schaerli, certify that:

1. I have reviewed this annual report on Form 20-F of Auris Medical Holding 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: March 31, 2021

/s/ Elmar Schaerli
Elmar Schaerli
Chief Financial Officer

Exhibit 13.1

CERTIFICATION

The certification set forth below is being submitted in connection with Auris Medical Holding AG's annual report on Form 20-F for the year ended December 31, 2020 (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 Auris Medical Holding 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 Auris Medical Holding Ltd.

Date: March 31, 2021

/s/ Thomas Meyer

Name: Thomas Meyer
Chief Executive Officer

Exhibit 13.2

CERTIFICATION

The certification set forth below is being submitted in connection with Auris Medical Holding AG's annual report on Form 20-F for the year ended December 31, 2020 (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.

Elmar Schaerli, the Chief Financial Officer of Auris Medical Holding 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 Auris Medical Holding Ltd.

Date: March 31, 2021

/s/ Elmar Schaerli
Name: Elmar Schaerli
Chief Financial Officer

Exhibit 15.1

Deloitte AG
General-Guisan-Quai 38
8022 Zurich
Switzerland

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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 and 333-249347 on Form F-3 of our report dated March 31, 2021, relating to the financial statements of Auris Medical Holding Ltd. appearing in this Annual Report on Form 20-F for the year ended December 31, 2020.

Deloitte AG

/s/ Matthias Gschwend
Auditor in Charge

/s/ Adrian Kaeppeli

Zurich, Switzerland
March 31, 2021