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, 2016

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 AG

(Exact name of Registrant as specified in its charter)

Switzerland
(Jurisdiction of incorporation)

Bahnhofstrasse 21
6300 Zug
Switzerland
(Address of principal executive offices)

Thomas Meyer
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Bahnhofstrasse 21
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(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

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

Title of each class	Name of each exchange on which registered
Common Shares, nominal value CHF 0.40 per share	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: 34,329,704

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post 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 ☒

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

US 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 AG

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 AG" or "Auris," the "Company," "we," "our," "ours," "us" or similar terms refer to Auris Medical Holding AG (formerly Auris Medical AG), together with its subsidiaries. The trademarks, trade names and service marks appearing in this Annual Report are property of their respective owners.

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;
- our need for substantial additional funding before we can expect to become profitable from sales of our products;
- our dependence on the success of Keyzilen® (AM-101) and AM-111, which are still in clinical development and may eventually prove to be unsuccessful, including the likelihood that the TACTT3 clinical trial with Keyzilen® will not meet its endpoints;
- the chance that we may become exposed to costly and damaging liability claims resulting from the testing of our product candidates in the clinical 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 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 AM-111, 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 failure to enter into new strategic relationships;
- 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 comply with the requirement under our term loan facility with Hercules, including repayment of amounts outstanding when due; and
- other risk factors discussed under “Item 3. Key Information—D. Risk factors”.

Although we believe that the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Forward-looking statements speak only as of the date they are made, and we do not undertake any obligation to update them in light of new information or future developments or to release publicly any revisions to these statements in order to reflect later events or circumstances or to reflect the occurrence of unanticipated events.

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, 2016 and 2015 and for each of the years in the three-year period ended December 31, 2016 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 as of December 31, 2016, December 31, 2015 and December 31, 2014, and for the years ended December 31, 2013 and 2012 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,				
	2016	2015	2014	2013	2012
	(in thousands of CHF except for share and per share data)				
Profit or Loss and Other Comprehensive Loss:					
Research and development	(24,777)	(26,536)	(17,705)	(13,254)	(3,987)
General and administrative	(5,447)	(4,342)	(4,489)	(1,362)	(624)
Operating loss	**(30,223)**	**(30,878)**	**(22,194)**	**(14,616)**	**(4,611)**
Interest income	68	37	52	74	8
Interest expense	(829)	(8)	(56)	(53)	(2)
Foreign currency exchange gain/(loss), net	(100)	1,144	4,012	(104)	3
Revaluation gain from derivative financial instruments	291	–	–	–	–
Loss before tax	**(30,793)**	**(29,705)**	**(18,186)**	**(14,699)**	**(4,602)**
Income tax gain	131	–	–	–	–
Income tax expense	–	–	–	(306)	–
Net loss attributable to owners of the Company	**(30,662)**	**(29,705)**	**(18,186)**	**(15,005)**	**(4,602)**
Other comprehensive loss:					
Items that will never be reclassified to profit or loss:					
Remeasurements of defined benefits liability	(394)	(54)	(1,101)	(58)	(55)
Items that are or may be reclassified to profit or loss:					
Foreign currency translation differences	(20)	(13)	(105)	32	22
Other comprehensive loss	**(414)**	**(67)**	**(1,206)**	**(26)**	**(32)**
Total comprehensive loss attributable to owners of the Company	**(31,076)**	**(29,772)**	**(19,392)**	**(15,031)**	**(4,635)**
Net loss per share(1)					
Net loss per share, basic and diluted(2)	(0.89)	(0.92)	(0.66)	(1.01)	(0.40)
Weighted-average number of shares used to compute net loss per common share, basic and diluted	34,329,280	32,299,166	27,692,494	14,917,064	11,581,450

(1) For periods prior to the closing of our initial public offering, net loss per share includes preferred shares, which were converted on a one-for-one basis upon the closing of our initial public offering.

(2) 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,				
	2016	2015	2014	2013	2012
	(in thousands of CHF)				
Statement of Financial Position Data:					
Cash and cash equivalents	32,442	50,237	56,934	23,866	64
Total assets	35,658	52,812	59,493	26,252	866
Total liabilities	21,515	8,070	6,210	17,219	1,110
Share capital	13,732	13,722	11,604	6,487	4,633
Total shareholders' equity attributable to owners of the Company	14,143	44,741	53,283	9,034	(244)

Exchange Rate Information

The following table sets forth, for the periods indicated, the high, low, average and period-end exchange rates for the purchase of U.S. dollars expressed in CHF per U.S. Dollar. The rates were derived from the U.S. Federal Reserve Bank's reported exchange rates. On March 3, 2017, the exchange rate as reported by the U.S. Federal Reserve Bank was CHF 1.0118 to $1.00.

	Period-end	Average for period	Low	High
		(CHF per U.S. dollar)		
Year Ended December 31:				
2012	0.9155	0.9377	0.8949	0.9957
2013	0.8904	0.9269	0.8856	0.9814
2014	0.9934	0.9147	0.8712	0.9934
2015	1.0017	0.9628	0.8488	1.0305
2016	1.0160	0.9848	0.9536	1.0334
Month Ended:				
September 30, 2016	0.9694	0.9732	0.9655	0.9804
October 31, 2016	0.9890	0.9876	0.9740	0.9951
November 30, 2016	1.0187	0.9963	0.9682	1.0187
December 31, 2016	1.0160	1.0194	1.0065	1.0334
January 31, 2017	0.9888	1.0075	0.9888	1.0266
February 28, 2017	1.0022	1.0010	0.9894	1.0109
March, 2017 (through March 3, 2017)	1.0118	1.0103	1.0072	1.0120

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.

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 30.7 million, CHF 29.7 million and CHF 18.2 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of CHF 112.3 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 we have incurred while building our business infrastructure. 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 and pre-clinical development and seek to obtain regulatory approval and commercialization of our product candidates Keyzilen® and AM-111. In our financial year ended December 31, 2016, we incurred CHF 24.8 million in research and development costs, and we expect that our total operating expense in 2017 will be in the range of CHF 28 to CHF 32 million.

To date, we have financed our operations through the initial public offering and a follow-on offering of our common shares, private placements of equity securities and short- and long-term loans. Most recently, on July 19, 2016, we entered into a Loan and Security Agreement with Hercules Technology Growth Capital, Inc., or Hercules. The agreement provides us with a senior secured term loan facility for up to $20 million. As of December 31, 2016, we have drawn $12.5 million under the facility.

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. We are in the late stages of clinical development for our product candidates, but it may be several years, if ever, before we complete pivotal clinical trials, 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 for, and commercialize, Keyzilen® or AM-111. 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, including successfully completing Phase 3 clinical trials of Keyzilen® or AM-111;
- obtaining marketing approvals for our product candidates, including Keyzilen® or AM-111, for which we 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 U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or 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 Keyzilen®, AM-111 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 quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our 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 are currently advancing our product candidates Keyzilen® and AM-111 through clinical development. We expect our research and development expenses to remain significant in connection with our ongoing activities, particularly as we continue our ongoing, and initiate new, trials of Keyzilen® and AM-111 and initiate pre-clinical and clinical development of other product candidates. We expect that our total operating expense in 2017 will be in the range of CHF 28 to 32 million. As of December 31, 2016, our cash and cash equivalents were CHF 32.4 million. We believe that our existing cash and cash equivalents (including the net proceeds from the equity offering completed in February 2017) will enable us to fund our operating expenses and capital expenditure requirements at least until the first quarter of 2018. 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” and our audit report may have to be qualified accordingly. 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. Should the Company’s assets fall short of its liabilities as evidenced by the Company’s standalone Swiss GAAP accounts, the board of directors will have to immediately take steps to restructure the business or if it fails to do, file for bankruptcy. If the board of directors fails to take appropriate action, under Swiss law, in case of such over-indebtedness, the auditors may, according to Swiss law, file for bankruptcy on the Company’s behalf. 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 late-stage clinical programs, obtain regulatory approval for Keyzilen® and AM-111 and commercialize our product candidates Keyzilen® and AM-111. If we receive regulatory approval for Keyzilen® or AM-111, 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, such as our term loan agreement with Hercules, 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 have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We began our current operations in 2003. Our operations to date have been limited to financing and staffing our company, developing our technology and developing Keyzilen®, AM-111 and our other 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.

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

We depend entirely on the success of Keyzilen® and AM-111, which are still in clinical development. If our clinical trials are unsuccessful, we do not obtain regulatory approval or we are unable to commercialize Keyzilen® and AM-111, 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 Keyzilen® and AM-111, which are still in clinical development. Our ability to generate product revenues, which we do not expect will occur for at least the next few years, if ever, will depend heavily on successful clinical development, obtaining regulatory approval and eventual commercialization of these product candidates. We currently generate no revenues from sales of any drugs, and we may never be able to develop or commercialize a marketable drug. The success of Keyzilen®, AM-111 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 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 Keyzilen® or AM-111, which would materially adversely affect our business, financial condition and results of operations.

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 product candidates are prolonged or delayed, we may be unable to obtain required regulatory approvals, and therefore be unable to commercialize our product candidates on a timely basis or at all.

To obtain the requisite regulatory approvals to market and sell any of our 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 product candidates. Keyzilen® and AM-111 are in Phase 3 clinical development.

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 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 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. For example, although Keyzilen® achieved favorable results in our Phase 2 efficacy trial, in August 2016, we announced that the Phase 3 TACTT2 clinical trial of Keyzilen® did not meet its two co-primary efficacy endpoints of statistically significant changes in tinnitus loudness and tinnitus burden compared to placebo. There can be no assurances that TACTT3, our ongoing Phase 3 clinical trial with Keyzilen® will meet its primary efficacy endpoints. In addition, 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. In the case of our late-stage clinical product candidates, results may differ in general on the basis of the larger number of clinical trial sites and additional countries and languages involved in Phase 3 clinical trials.

In the case of Keyzilen®, our endpoints in Phase 3 clinical trials are based on patient reported outcomes, some of which are captured daily from trial participants with electronic diaries. Based on insights from our continuing analysis of the TACTT2 trial, we believe the high frequency of tinnitus loudness ratings over an extended period of time may have caused a number of patients to excessively focus on their tinnitus symptoms, thereby influencing the measured outcome. In addition, low compliance with daily reporting requirements may impact the trials' validity or statistical power.

Under the SPA with the FDA, we agreed to use the Tinnitus Functional Index, or TFI, as a co-primary efficacy endpoint in the TACTT2 trial and a secondary efficacy endpoint in the TACTT3 trial. Based on our ongoing analysis of the TACTT2 clinical trial results, we are amending our protocol for the TACTT3 Phase 3 clinical trial of Keyzilen® to elevate the change in the TFI score from a key secondary endpoint to an alternate primary efficacy endpoint. We used a different tinnitus questionnaire in the previous clinical trials with Keyzilen® (Tinnitus Handicap Inventory 12, THI-12, a 12-item short version of the 25-item Tinnitus Handicap Inventory, or THI). Unlike the THI-12, the TFI was developed and validated broadly in accordance with the FDA's guidance for patient-reported outcome measures and with the explicit aim of measuring treatment-related changes in tinnitus. In addition, the TFI covers all important domains of negative tinnitus impact including sleep difficulties, whereas the THI-12 does not include any sleep-related item. In spite of the methodological superiority of the TFI and a 2011 study by Meikle et al. showing a high correlation between THI and TFI scores with higher responsiveness to change of the latter, there is no assurance that outcomes with the TFI will be qualitatively and quantitatively similar or the same as those that would result with the THI-12. In the TACTT2 trial, treatment with Keyzilen® did not result in a clinically meaningful change in TFI in the overall trial population.

For calculating the statistical power of the extended TACTT3 trial, we made certain hypotheses regarding the size of the true treatment effect of Keyzilen® over placebo and the related standard deviations. For the TFI, those were based on actual outcomes for the subpopulations in the TACTT2 trial, whereas the standard deviation was taken at the 80% confidence level (meaning that the probability is 80% that the true standard deviation is not higher). The statistical power for detecting a true treatment effect of at least 5 TFI points in the overall trial population or in the subpopulation with severe or extreme tinnitus or of at least 7 TFI points in the subpopulation with otitis media related tinnitus was calculated at 87%; for true treatments effects of 0.5 in the TLQ the power is greater than 90%. We believe the underlying assumptions to be reasonable since they are based on actual patient data with Keyzilen® from TACTT2. However, we cannot know what the true effects of Keyzilen® will be in TACTT3; if the true effects turn out to be less than hypothesized, then the trial's power (i.e the chance of achieving a significant result in either the overall population or in one or both of the defined subpopulations) would be reduced and if the true effects turn out to be greater than hypothesized, then power would be increased. Further, the use of the Hochberg procedure to control for Type I error for testing endpoints not only for the entire trial population, but also for two subpopulations, means that not all tested groups will be tested at the same significance level; if the population with the least significant p-value does not reach the specified level of significance (0.04 for the TFI and 0.01 for TLQ), then the other two populations with lower p-values will be tested at a more stringent significance level. This means that the statistical hurdle could be highest for the best performing population. The Hochberg procedure, a method applied to statistical testing to control for multiplicity, avoids the need for pre-specification of a hierarchy among the three populations for analysis, providing more flexibility than with other methods and allowing the possibility of achieving success in a subpopulation.

In the case of AM-111, we are evaluating the safety and efficacy in an idiopathic condition which implies a considerable heterogeneity in the etiology and natural history of the condition. This may have an impact on the safety and efficacy outcomes of our Phase 3 clinical trials. In addition, in HEALOS and ASSENT, we extended the time window for enrollment into each clinical trial, from up to 48 hours to up to 72 hours, in response to results from the Phase 2 trial showing an increasing treatment effect the later the treatment was given. This was due to declining spontaneous recovery rates while the effects with active treatment held steady. Although spontaneous recovery is expected to decline further between 48 and 72 hours, we have no assurance that improvement achieved with the active treatment will remain stable. Based on discussions with the FDA and EMA, we moved the primary endpoint from Day 7 in the Phase 2 trial to later time points in the Phase 3 trials: to Day 28 in HEALOS and to Day 91 in ASSENT. In the Phase 2 trial, a therapeutic effect of AM-111 was observed in a clinically meaningful and statistically significant way in the relevant patient population on Day 3, and the majority of the effect was achieved by Day 7; however, superior results were also observed at later time points. Therefore, we expect to be able to demonstrate a therapeutic effect at the later time points in the Phase 3 trials. However, this expectation is based on the assumption that hearing recovery patterns will be similar to the Phase 2 trial, and there is no assurance that this will be the case.

Whereas in our Phase 2 trial we had full placebo control for the primary endpoint at Day 7 and an oral corticosteroid could only be administered as a reserve therapy in case of insufficient hearing recovery to that point, such trial design is not feasible in certain countries due to the use of oral corticosteroids as standard of care. Hence, in the planned ASSENT trial, oral corticosteroids will be offered as background therapy to all study participants. Although there is no clear evidence for the efficacy of oral corticosteroids in the treatment of idiopathic sudden sensorineural hearing loss, or ISSNHL, we have assumed a small impact of background therapy on hearing recovery when calculating the number of patients that are required to demonstrate AM-111’s efficacy in a statistically significant and clinically meaningful way. We cannot rule out the possibility that the background therapy will enhance hearing recovery more substantially, and that in consequence the trial may not demonstrate the therapeutic benefit of AM-111. We will conduct an interim analysis at the midpoint of enrollment, and the study protocol allows for adjusting the size of the trial if suggested by the interim analysis; however, the required adjustment may be too large to be considered feasible and we may have to change the trial design significantly or stop the trial altogether.

Orphan drug designation for AM-111 was granted by the FDA and EMA for the treatment of acute sensorineural hearing loss, or ASNHL, an umbrella term that comprises hearing loss from acute acoustic trauma, or AAT, surgery-induced trauma or ISSNHL. We estimate ISSNHL to be the largest of the three subgroups. The broader, more general designation of ASNHL is based on the common pathophysiologic pathway shared by the three subgroups. Although we expect to obtain regulatory approval for the entire indication of ASNHL based on confirmatory efficacy and safety data that covers only one or two rather than all three of the subgroups, there can be no assurance that regulatory agencies will concur with this assumption at the time of the marketing approval procedure. In that case, it may not be sufficient to conduct HEALOS and ASSENT in the subgroup of ISSNHL, as is currently planned.

Based on our ongoing analysis of the TACTT2 clinical trial results, we are amending our protocol for the ongoing TACTT3 Phase 3 clinical trial of Keyzilen® and intend to enroll an additional 120 patients, which will cause our product development costs to increase. If we are required to make further changes to the trial design of, or conduct additional clinical trials or other testing of Keyzilen®, AM-111 or any other product candidate that we develop beyond the trials and testing that we 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 Keyzilen®, AM-111 or our other 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 Keyzilen® and we may be required to obtain additional funds to complete 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 Keyzilen®, AM-111 or any other 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 trials of Keyzilen® and AM-111 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 2.4% of patients enrolled in the Keyzilen® Phase 2 program, in 2.5% in the TACTT2 clinical trial with Keyzilen® and in 4.5% of patients in the AM-111 Phase 2 clinical trial); all (Keyzilen®) or most (AM-111) 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. In our Phase 3 clinical trials of Keyzilen®, we enroll patients with acute inner ear tinnitus, meaning patients with symptom duration of three months or less, due to traumatic injury to their cochlea or otitis media. Thus, we must identify, recruit, enroll and dose patients with tinnitus caused by a pre-determined universe of factors in a limited time frame. Our product candidate AM-111, which is intended for patients with acute inner ear hearing loss, which is also known as acute sensorineural hearing loss or ASNHL, has orphan drug designation for the treatment of ASNHL, which means that the potential patient population is more limited. In our late-stage clinical program with AM-111, the enrollment window is 72 hours from onset, meaning that we must enroll patients in a short time frame. This short enrollment window may negatively impact our enrollment rate.

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 AM-111 for the treatment of ASNHL from the FDA and the EMA, and we may rely on obtaining and maintaining orphan drug exclusivity for AM-111, 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 AM-111, we may be subject to earlier competition and our potential revenue will be reduced.

AM-111 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 AM-111 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. 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.

The orphan drug designation for AM-111 relates to ASNHL, an umbrella term comprising acute acoustic trauma, ISSNHL and surgery-induced trauma based on a common pathophysiologic pathway. Our Phase 3 late-stage program is only enrolling patients suffering from ISSNHL, which represent the largest of the three ASNHL subgroups. Based on their outcomes, we may obtain marketing authorization only for the ISSNHL subgroup, and additional studies may be required to obtain marketing authorization for the entire ASNHL indication.

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 are currently primarily focused on the development of Keyzilen® and AM-111 for the treatment of acute inner ear tinnitus and acute inner ear hearing loss, respectively. 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 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 two product candidates in late-stage clinical development. Keyzilen® is in Phase 3 clinical development for the treatment of acute inner ear tinnitus under a SPA from the FDA (TACTT2) and based on scientific advice from the EMA (TACTT3). AM-111 is in Phase 3 clinical development for the treatment of acute sensorineural hearing loss for which we received feedback from the FDA and EMA on multiple occasions. We are not permitted to market or promote any of our 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 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 or acute inner ear hearing loss 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.

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 or acute inner ear hearing loss. 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 or acute inner ear hearing loss, 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. We have designed our Phase 3 trials for Keyzilen® and AM-111 to include endpoints that we believe are clinically justified and meaningful. Specifically, with regard to Keyzilen®, the EMA indicated that a statistically significant improvement in tinnitus loudness that is supported by several secondary variables would demonstrate a clinically meaningful result. The FDA indicated that an improvement in tinnitus loudness supported by a co-primary efficacy point, such as the TFI questionnaire, would be clinically meaningful. The TACTT2 clinical trial with Keyzilen® did not meet the two co-primary efficacy endpoints of statistically significant changes in tinnitus loudness and tinnitus burden compared to placebo. Additionally, no product has been approved for marketing based upon such guidance and we cannot be certain that Keyzilen® will be approved even if it were to demonstrate such results in TACTT3, its second Phase 3 trial, in particular because of the results of TACTT2.

With regard to AM-111, the FDA and EMA have indicated that a 10 dB improvement in hearing thresholds 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 AM-111 will be approved even if it were to demonstrate such results in its Phase 3 trial.

Some of our conclusions regarding the potential efficacy of Keyzilen® in our completed TACTT2 clinical trial of Keyzilen® for the treatment of acute inner ear tinnitus in certain subgroups are based on retrospective analyses of the results of these trials, which are generally considered less reliable indicators of efficacy than pre-specified analyses.

After determining that we did not achieve the co-primary efficacy endpoints in our completed TACTT2 clinical trial of Keyzilen® for the treatment of acute inner ear tinnitus, we performed retrospective analyses that we believe show treatment effects on TFI in favor of Keyzilen® in case of greater tinnitus severity 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 severe or extreme tinnitus poses greater risk of bias as such subgroup was not pre-specified in the trial design.

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. As a result, even if TACTT3 provides confirmatory results for the subgroup of severe to extreme tinnitus, the TACTT2 results and the retrospective analysis could negatively impact the evaluation by the EMA or the FDA of our anticipated applications for marketing approval for Keyzilen®.

If Keyzilen® is only shown to be efficacious in certain subgroups, such as patients with otitis media-related tinnitus or greater tinnitus severity, we may only be able to obtain approval for these limited patient populations, which would reduce the market potential for Keyzilen® and could materially adversely affect our business, financial condition and results of operations.

While our TACTT2 clinical trial with Keyzilen® did not meet the two co-primary efficacy endpoints of statistically significant changes in tinnitus loudness and tinnitus burden compared to placebo, we believe that the trial data show treatment effects on TFI in favor of Keyzilen® for the subgroups of patients with otitis media-related tinnitus or greater tinnitus severity. As a result, our amended trial protocol for TACTT3 includes these two subgroups in confirmatory statistical testing along with the overall trial population.

If the TACTT3 results were to show clinically meaningful treatment effects in these subgroups but fail to show efficacy in the overall trial population, we may not be able to receive regulatory approval for a patient population that is as broad as originally intended. If Keyzilen® were to receive marketing approval for these more limited patient populations, its market potential would be diminished. We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of Keyzilen®, our lead product candidate. As a result, approval for a more limited patient population could materially adversely affect our business, financial condition and results of operations.

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, the active pharmaceutical ingredient of Keyzilen®, is an isomer of Ketamine, and may be affected by the safety of the drugs related to them. Although Ketamine has 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, Ketamine, or reconsideration of known toxicities of Ketamine in the setting of new indications, could result in increased regulatory scrutiny of Keyzilen®. For example, Ketamine is regulated by the Drug Enforcement Administration, or DEA, under the Controlled Substances Act as a Schedule III drug. DEA scheduling is a separate process that can delay when a drug may become available to patients beyond a New Drug Application, or 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 Controlled Substances Act, such scheduling could negatively impact the ability or willingness of physicians to prescribe Keyzilen® and our ability to commercialize it.

Our special protocol assessment agreement with the FDA for our Phase 3 clinical trial of Keyzilen® does not guarantee any particular outcome from regulatory review, including ultimate approval and may not lead to a faster development or regulatory review or approval process.

We obtained agreement from the FDA on an SPA for the design of our U.S. Phase 3 trial of Keyzilen®. We also designed our Phase 3 clinical trials for Keyzilen® based on scientific advice that we received from the EMA. The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate the proposed design and size of Phase 3 clinical trials that are intended to form the primary basis for determining a drug product's efficacy. However, a SPA agreement does not guarantee approval of a product candidate and even if the FDA agrees to the design, execution, and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, an SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor company fails to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by the sponsor in a request for the SPA change or are found to be false or omit relevant facts. In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

On August 18, 2016, we announced that the TACTT2 clinical trial with Keyzilen® did not meet the two co-primary efficacy endpoints of statistically significant changes in tinnitus loudness and tinnitus burden compared to placebo. TACTT2 was designed as a randomized, double-blind, placebo-controlled trial in acute inner ear tinnitus following traumatic cochlear injury or otitis media. The trial was conducted primarily in North America and randomized 343 patients to receive either Keyzilen® 0.87 mg/mL or placebo in a 3:2 ratio. Based on insights

from our continuing analysis of the TACTT2 trial, we amended the clinical trial protocol for TACTT3, the ongoing second Phase 3 clinical trial with Keyzilen®. TACTT3 was originally designed as congruent with the design of TACTT2 regarding outcome measures and the patient population to be enrolled but it differed in that the improvement in the TFI score was not a co-primary efficacy endpoint, that it had a slightly smaller size (300 instead of 330 patients) and it also includes a separate stratum of patients suffering from post-acute inner ear tinnitus. In the amended trial protocol, the change in TFI score is elevated from a key secondary endpoint to an alternate primary efficacy endpoint and the trial size has been increased by 60 patients in each of Stratum A (acute tinnitus stage) and Stratum B (post-acute tinnitus stage) to enhance statistical sensitivity to the effects of treatment. Additionally, in order to corroborate the TACTT2 results showing clinically meaningful treatment effect under the TFI over placebo for patients with otitis media-related tinnitus and greater tinnitus severity, the severity subgroup will be included in confirmatory statistical testing in TACTT3 along with the overall study population and the already pre-specified subgroup of patients with otitis media-related tinnitus.

We cannot be sure of how the FDA, EMA or other regulatory authorities will view the TACTT2 results, including the results that we believe show treatment effects on TFI in favor of Keyzilen® for specific subgroups. Additionally, we cannot assure you that the protocol amendments to TACTT3 will be viewed favorably by the FDA, EMA or other regulatory authorities or that the TACTT3 clinical trial will succeed. These uncertainties could significantly delay or prevent any potential approval for Keyzilen®.

In early December 2016, we had two meetings with the FDA relating to the Keyzilen® program. Through a Type C Meeting, the FDA confirmed that, as per standard practice, two positive confirmatory trials would be required to submit a NDA. The FDA did not provide feedback on the TACTT3 protocol amendment because the trial is being conducted in Europe and is not under the IND Application. Data from trials that were not filed under the IND may be used for an NDA, provided they meet requisite legal and regulatory requirements such as adherence to cGCP regulations.

Even if we are able to include TACTT3 in a NDA with the FDA, due to the fact that TACTT3 was not assessed by the FDA as part of the SPA process, and in spite of the congruence between the trials, we cannot exclude that even if TACTT3 is successful, the differences in outcomes between the two pivotal trials may affect the FDA's assessment (for example, from cultural differences in patient attitudes or perceptions as TACTT3 is being conducted outside North America). If the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trials differently than we do, the FDA may not deem the data sufficient to support an application for regulatory approval. A revocation or alteration in our existing SPA could significantly delay or prevent approval of our application. Our SPA with the FDA and the scientific advice from the EMA does not ensure that Keyzilen® will receive marketing approval or that the approval process will be faster than conventional regulatory procedures.

As a result, if TACTT3 is not successful, we may not be able to obtain marketing approval, and even if TACTT3 is successful, we may not be able to obtain marketing approval without any further data, which could materially adversely affect our business, financial condition and results of operations.

The number of patients with safety data from chronic intermittent use of Keyzilen® may fail to reach the levels specified and requested by the FDA.

The FDA has requested safety data from chronic intermittent use of Keyzilen® by a minimum of 300 patients treated for six months and a minimum of 100 patients treated for one year, to support a new drug application filing for Keyzilen® in the treatment of acute peripheral tinnitus. In order to address this request, we offered all participants completing the TACTT2 and TACTT3 clinical trials that met certain criteria the option to roll over into an open label follow-on safety study (AMPACT1 and AMPACT2, respectively) and receive up to three treatment cycles with Keyzilen® over a period of up to nine months. Together with the three-month TACTT trial duration, this would cover up to 12 months of exposure. Enrollment in AMPACT1 and AMPACT2 has been completed. Since a higher than expected number of TACTT trial participants was willing and eligible for enrollment into the AMPACT studies, we reduced the number of available treatment cycles in AMPACT2 from three to one by way of a protocol amendment in the first quarter 2016. We are confident of meeting the requested number of patients with chronic intermittent use data. However, we have no control over the actual number of treatment cycles that the AMPACT participants will have received as we remain blinded as to treatment allocation in TACTT3, AMPACT1 and AMPACT2. Hence, the number of patients with safety data over six months and over 12 months may or may not reach the levels specified and requested by the FDA. In case of insufficient numbers, this will become a review issue at the time of the NDA submission. Although we plan to apply for an indication of acute inner ear tinnitus, rather than chronic inner ear tinnitus, we cannot ensure that the FDA will be satisfied with the data supporting our NDA if we are not able to enroll sufficient numbers of patients in AMPACT1 and AMPACT2.

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 him 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.

Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.

In the United States and the European Union, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system. These changes could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval.

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Health Care Reform Law, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of

healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The Health Care Reform Law, among other things, increased rebates a manufacturer must pay to the Medicaid program, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, established a Medicare Part D coverage gap discount program, in which manufacturers must provide 50% point-of-sale discounts on products covered under Part D and implemented payment system reforms including a national pilot program on payment bundling to encourage hospitals, physicians and other providers to improve the coordination, quality and efficiency of certain healthcare services through bundled payment models. Further, the law imposed a significant annual fee on companies that manufacture or import branded prescription drug products, expanded eligibility criteria for Medicaid programs, and created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. Substantial provisions affecting compliance were enacted, which may affect our business practices with health care practitioners. Continued pressure on pharmaceutical pricing is expected and may also increase our regulatory burdens and operating costs.

Other legislative changes have been proposed and adopted in the United States since the Health Care Reform Law was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our customers and accordingly, our financial operations. Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

Furthermore, it is possible that following the inauguration of President Trump on January 20, 2017, legislation will be introduced and passed by the Republican-controlled Congress repealing the Health Care Reform Law in whole or in part and signed into law by President Trump, consistent with statements made by him during his presidential campaign and subsequently indicating his intention to do so within a short time following his inauguration. Because of the continued uncertainty about the implementation of the Health Care Reform Law, including the potential for further legal challenges or repeal of that legislation, we cannot quantify or predict with any certainty the likely impact of the Health Care Reform Law or its repeal on our business model, prospects, financial condition or results of operations, in particular on the pricing, coverage or reimbursement of any of our product candidates that may receive marketing approval. We also anticipate that Congress, state legislatures, and third-party payors may continue to review and assess alternative healthcare delivery and payment systems and may in the future propose and adopt legislation or policy changes or implementations effecting additional fundamental changes in the healthcare delivery system. We cannot assure you as to the ultimate content, timing, or effect of changes, nor is it possible at this time to estimate the impact of any such potential legislation.

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.

On June 23, 2016, the UK public voted in a referendum to leave the European Union. The UK government subsequently announced its intention to serve notice of withdrawal from the European Union no later than March 2017. As a consequence of such withdrawal notice, EU law will cease to apply to the UK from the date of entry into force of a withdrawal agreement, or two years after UK's submission of the withdrawal notification. As a result, the UK is likely to remain within the European Union for at least the next two years, and, therefore there will likely be no major legal implications for the life sciences sector in the short term. In the long term, however, the effects may be more severe, in particular if the UK cannot agree the terms of a continued close association with the European Union and/or chooses not to incorporate existing EU rules into national law and/or to no longer align themselves with European law. The administrative burden for pharmaceutical companies could increase significantly because regulatory requirements, for example clinical trial authorizations and marketing authorization applications, may need to be fulfilled under a new and different legal framework for the UK. Existing marketing authorizations granted in the European Union under the centralized procedure prior to the exit may potentially not be recognized anymore by the UK.

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, 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 EU 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.

We believe that our key competitors are Otonomy, Inc., or Otonomy, and Sound Pharmaceuticals, Inc., or Sound Pharma, both U.S. companies developing pharmaceutical treatments for ear disorders. In October 2013, Otonomy announced the launch of a development program for the treatment of tinnitus, OTO-311, which is based on the NMDA receptor antagonist gacyclidine and may directly compete with our Keyzilen® product candidate. According to a recent public filing, Otonomy intends to develop a polymer-based formulation of gacyclidine that will provide a full course of treatment from a single intratympanic injection. OTO-311 is currently being evaluated in a Phase 1 trial. OTO-311's competitive strength will ultimately depend on the demonstration of clinical efficacy and safety and its comparison with Keyzilen®. Further, we intend to rely on our patent applications with broad disclosures to pursue claims relating to the use of polymers with NMDA antagonists in controlled-release topical compositions for the treatment of tinnitus. Otonomy is also developing OTO-104, which is a polymer-based formulation of dexamethasone for intratympanic treatment of Ménière's disease. OTO-104 is currently in Phase 3 of clinical development. If OTO-104 is approved prior to AM-125, we

will have to compete against it in the treatment of Ménière's disease. In addition, OTO-104 is being evaluated by Otonomy for the treatment of certain types of hearing loss and may compete against AM-111.

In June 2006, Sound Pharma began clinical testing of an oral treatment for hearing loss (SPI-1005, ebselen). Its active substance mimics and prompts production of the glutathione peroxidase enzyme. In February 2014, Sound Pharma announced positive outcomes from a placebo-controlled Phase 2 clinical trial with SPI-1005 in the prevention and treatment of temporary inner ear hearing loss from listening to loud music with a mobile digital media player. Although AM-111 targets permanent rather than transient hearing loss, SPI-1005 and Sound Pharma's SPI-5557 which it intends to develop for sever to profound hearing loss may become competing products if Sound Pharma seeks and manages to demonstrate clinical efficacy also in the prevention and treatment of permanent inner ear hearing loss.

Sensorion is developing SENS-401, a 5-HT3 antagonist with anti-inflammatory properties, for the oral treatment of sudden sensorineural hearing loss. The project is currently in Phase 1 of clinical development and obtained orphan drug designation from the EMA. Sensorion is also developing SENS-111, a histamine H4 receptor antagonist, for the oral treatment of acute vertigo crises and recently initiated a Phase 2 trial to enroll patients with acute unilateral vestibulopathy. If successful, SENS-401 may compete against AM-111, and SENS-111 may compete against AM-125.

There are several companies developing treatments for hearing loss. Strekin AG, a privately held Swiss company, announced in April 2016 that it plans to develop STR001, an agonist of the peroxisome proliferator, for surgery induced hearing loss and that it commenced a Phase 2 program in Germany and France. Nordmark, a German company, is developing Ancrod, the biologically active substance from the venom of the Malayan Pit Viper (*Calloselasma rhodostoma*), for the treatment of sudden sensorineural hearing loss and has initiated Phase 2 program. Both, STR001 and Ancrod have the potential to compete with AM-111.

There exist a variety of drug products that are licensed or used off-label for the treatment of vestibular disorders and Ménière's disease, including steroids, diuretics, anti-emetics or anti-nausea medications. In many countries outside the United States, oral betahistine is the standard of care and licensed for the treatment of Ménière's disease and vestibular vertigo. 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. In December 2016, Castle Creek Pharmaceuticals, LLC announced the in-licensing of Arlevert, a fixed-dose combination of cinnarizine, a calcium channel antagonist, and dimenhydrinate, an antihistamine, from Hennig Arzneimittel GmbH & Co. KG, a German company, and its intention to develop it as a treatment for vertigo in the United States market. Arlevert is approved and has been marketed for a long time in various countries outside the US.

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 Keyzilen®, AM-111 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 Keyzilen®, AM-111 or any other product candidate that we commercialize and, if available, that the reimbursement rates will be adequate.

In Germany, for example, the relatively recent "Act on Reorganization of the Pharmaceutical Market" ("AMNOG") requires manufacturers intending to bring a product with a new active ingredients into market to submit scientific evidence of the added benefit for patients. Only if the so-called "Federal Joint Committee" (*Gemeinsamer Bundesausschuss*) comes to the conclusion that our products indeed have a new benefit for patients, we will be allowed to negotiate the price directly with the public health insurers; otherwise, a maximum reimbursement rate will be fixed by the health administration authorities. If we are unable to obtain adequate levels of coverage and reimbursement for our product candidates, their marketability will be negatively and materially impacted.

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 Keyzilen®, AM-111 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 Keyzilen®, AM-111 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 AM-111 require multiple outpatient procedures to administer the drug;
- cost-effectiveness;
- patient diagnostics and screening infrastructure in each market, particularly as Keyzilen® and AM-111 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 Keyzilen® and AM-111 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 Keyzilen® and AM-111 could be smaller than our estimates of the potential market opportunity. If the actual market for Keyzilen® and AM-111 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 Keyzilen®, AM-111 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

We have several areas of disagreement with Xigen, and consequently our relationship with Xigen may be adversely affected, we could potentially lose our right to commercialize AM-111 and our business, commercialization prospects and financial condition may be adversely affected.

We have several areas of disagreement with Xigen S.A., or Xigen, with whom we have an agreement 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 differ from Xigen in our interpretation of the definition of the Area. We interpret “Area,” as it pertains to pharmaceutical products, as not limited to local administration to the inner ear, but inclusive of the use of pharmaceutical products generally for the treatment of ear disorders (and that the limitation of “local administration to the inner ear” applies only to “drug delivery devices and formulations”). Xigen has adopted the interpretation that the license is limited to local administration for both pharmaceutical products and drug delivery and formulations. This difference in interpretation has no impact on our current or planned use of AM-111 delivered locally via intratympanic treatment.

In addition, in October 2013, Xigen assigned certain of the patents relevant to the agreement to Xigen Inflammation Ltd., an unaffiliated entity organized in Cyprus. We consider this transfer to be in breach of the agreement since our prior written approval was not sought, although Xigen Inflammation Ltd. has confirmed to us that the assignment of patents is without prejudice to our license for local administration. In the past, Xigen has also requested from us quantities of AM-111 for certain analyses, although we believe the quantities requested exceed what laboratories would generally require for such tests.

The agreement contains a confidentiality provision restricting the disclosure of the terms of the agreement. We believe that Xigen may have waived the confidentiality provision of the agreement by disclosing the terms of the agreement to Xigen Inflammation Ltd., although Xigen has denied that any disclosure of the agreement has been made to the assignee despite the assignee’s assurance that the assignment was without prejudice to our license for local administration. Despite this, in connection with our initial public offering, we sought Xigen’s consent to disclose certain provisions of the agreement and file a redacted version of the agreement with the SEC. Xigen, however, was only willing to provide its consent if we agreed to limit the scope of the definition of “Area,” desist from claims that the transfer of patents to Xigen Inflammation Ltd. was in breach of the agreement and provide Xigen with certain quantities of the active substance of AM-111 for analysis.

We believe Xigen’s demands were unreasonable and unwarranted, and therefore we were not able to come to an agreement with Xigen prior to disclosing certain provisions of the agreement in the prospectus relating to our initial public offering and filing a redacted version of the agreement. Xigen may consider such disclosure to be a breach of the confidentiality provision of the agreement. The agreement is governed by Swiss law, and the venue is Solothurn, Switzerland. In the opinion of our Swiss counsel, while there can be no assurances, this disclosure by us does not rise to the level of material breach that would allow Xigen to repudiate the agreement.

We cannot predict the result of these disagreements with Xigen and any litigation that may result. While Xigen has taken no action as of the date of this Annual Report, Xigen may attempt to repudiate the contract and initiate a claim for damages against us. According to our Swiss counsel, Xigen would have to show that it had suffered a loss due to the disclosure of the redacted agreement and certain provisions of the agreement in the prospectus associated with our initial public offering, and the damages could be equal to the amount of the effective direct damage that Xigen proves it has suffered.

These disagreements, and in particular any resulting litigation, could result in substantial legal expenses, distraction to our management and employees and potentially the loss of our right to commercialize AM-111. No assurance can be given that these disagreements and any resulting litigation will not have a material adverse effect on our business, commercialization prospects for AM-111 and our other product candidates and our financial condition. For a description of our agreement with Xigen, please see “Item 4. Information on the Company—B. Business overview—Collaboration and License Agreements—Xigen.”

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 AM-111.

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.

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 AM-111 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 Keyzilen® and AM-111. 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 Keyzilen® and AM-111, and others for the manufacturing and supply of pre-filled syringes. 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 Keyzilen®, AM-111 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.

The drug substance and drug 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 drug substance or drug 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 Keyzilen® and AM-111. We currently have a relationship with one supplier each, for the supply of the active pharmaceutical ingredients and the hyaluronic acid component of Keyzilen® and AM-111. We are reliant upon single source third-party contract manufacturing organizations to manufacture and supply the drug substance and drug product and components thereof for each of Keyzilen® and AM-111. We do not currently have any other suppliers for the drug substance or drug 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 Keyzilen® and AM-111, we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. Specifically, Xigen is concurrently developing another indication for XG-102, the active substance of AM-111. Since for each product only a single patent can be selected for patent term extension, there may be a conflict of interest with respect to patent selection for extending patent terms covering two different indications of XG-102. It is possible that Xigen may select a patent that does not provide the longest patent term for the AM-111 indication developed by us. 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 5 and 10 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 Keyzilen®, AM-111, or any of our other product candidates. Our issued patents and pending patent applications are expected to expire for Keyzilen® between 2024 and 2028 and for AM-111 between 2020 and 2027, prior to any patent term extensions to which we may be entitled under applicable laws.

Janssen, a subsidiary of Johnson & Johnson, has been testing Esketamine in a spray formulation for intranasal treatment of treatment-resistant depression in several clinical trials to date, with a Phase 3 program expected to complete in early 2018. In November 2014, the FDA designated Esketamine a 'breakthrough therapy' for this indication. In the event that Janssen's confirmatory trials are successful and the company receives marketing authorization prior to us receiving marketing authorization for Keyzilen®, we would lose the potential benefit of a five-year marketing exclusivity period that we would otherwise expect to obtain.

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 make 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. The effects of these changes are currently unclear as the USPTO must still implement various regulations, the courts have yet to address any of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. 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 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® and AM-111 are approved, competitors could file ANDAs for generic versions of Keyzilen® and AM-111, or 505(b)(2) NDAs that reference Keyzilen® and AM-111, respectively. If there are patents listed for Keyzilen® and AM-111 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 AM-111. 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 AM-111 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 AM-111. 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.

On July 20, 2015, the USPTO declared Patent Interference No. 106,030 involving our issued U.S. patent No. 9,066,865 (the "'865 Patent") and Otonomy's U.S. patent application No. 13/848,636 (the "'636 Application"). The patent interference identified claims 1-9 in the '865 Patent as interfering with claims 38, 43 and 46-50 of the '636 Application. The '865 Patent discloses methods of treating inner or middle ear diseases with intratympanic injections of poloxamer-based compositions. The claims of the '865 Patent are directed to the use of fluoroquinolone antibiotics in poloxamer 407 compositions under certain specifications. On January 26, 2017, the USPTO issued a decision on the interference granting Auris benefit of priority. As a result of the decision,

judgment was entered against Otonomy and all claims in the ’636 Application were refused. In addition, claims 1-8 of the ’865 Patent were cancelled as the result of the USPTO’s determination that the written description of the specification lacked full scope support for treating middle or inner ear disease with fluoroquinolone. However, claim 9, which is directed to a method of treating viral and bacterial infections with intratympanic injection of a fluoroquinolone antibiotic in a poloxamer 407 composition under certain specifications, was affirmed. The USPTO’s decision is not final and may be appealed. Although we are still analyzing what effect, if any, the cancellation of claims 1-8 of the ’865 Patent will have on the remainder of the ’865 patent family, we do not expect the interference proceedings to impact our intellectual property portfolio relating to Keyzilen® and AM-111.

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, Thomas Jung, Chief Development Officer, Andrea Braun-Scherhag, Head Regulatory & Quality Affairs and Hernan Levett, 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 our home country, Switzerland, may restrict our ability to attract, motivate and retain the required level of qualified personnel. In Switzerland, new legislation affecting public companies has been passed that, among other things, (a) imposes an annual binding shareholders' "say on pay" vote with respect to the compensation of executive management, including executive officers and the board of directors, (b) prohibits severance, advances, transaction premiums and similar payments to executive officers and directors and (c) requires companies to specify various compensation-related matters in their articles of association, thus requiring them to be approved by a shareholders' vote. 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. The market price of our common shares may fluctuate significantly 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; 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.

Certain principal shareholders and members of our executive team and board of directors own a majority 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 65% 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 our company, certain decisions relating to our capital structure, the approval of certain significant corporate transactions and certain amendments to our articles of association. 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 56% of our common shares 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. We have also entered into a registration rights agreement pursuant to which we have agreed under certain circumstances to file a registration statement to register the resale of common shares held by certain of our shareholders, as well as to cooperate in certain public offerings of such common shares. We have also filed registration statements to register all 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. If a large number of our 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 have broad discretion in the use of our cash and cash equivalents and may not use them effectively.

Our management has broad discretion in the use of our cash and cash equivalents and could spend them in ways that do not improve our results of operations or enhance the value of our common shares. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common shares to decline and delay the development of our product candidates. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

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 and shareholders 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 limitation pursuant to Swiss law or by our articles of association. 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 Swiss corporation. The rights of our shareholders may be different from the rights of shareholders in companies governed by the laws of U.S. jurisdictions.

We are a Swiss corporation. Our corporate affairs are governed by our articles of association and by the laws governing companies incorporated in Switzerland. The rights of our shareholders and the responsibilities of members of our board of directors may be different from the rights and obligations of shareholders and directors of companies governed by the laws of U.S. jurisdictions. In the performance of its duties, our board of directors is required by Swiss law to consider the interests of our company, our shareholders, our employees and other stakeholders, in all cases with due observation of the principles of reasonableness and fairness. It is possible that some of these parties will have interests that are different from, or in addition to, your interests as a shareholder. Swiss corporate law limits the ability of our shareholders to challenge resolutions made or other actions taken by our board of directors in court. Our shareholders generally are not permitted to file a suit to reverse a decision or an action taken by our board of directors but are instead only permitted to seek damages for breaches of

fiduciary duty. As a matter of Swiss law, shareholder claims against a member of our board of directors for breach of fiduciary duty would have to be brought in Zug, Switzerland, or where the relevant member of our board of directors is domiciled. In addition, under Swiss law, any claims by our shareholders against us must be brought exclusively in Zug, Switzerland.

Our common shares are issued under the laws of Switzerland, which may not protect investors in a similar fashion afforded by incorporation in a U.S. state.

We are organized under the laws of Switzerland. There can be no assurance that Swiss law will not change in the future or that it will serve to protect investors in a similar fashion afforded under corporate law principles in the U.S., which could adversely affect the rights of investors.

U.S. shareholders may not be able to obtain judgments or enforce civil liabilities against us or our executive officers or members of our board of directors.

We are organized under the laws of Switzerland and our jurisdiction of incorporation is Zug, Switzerland. Moreover, a number of our directors and executive officers and a number of directors of each of our subsidiaries are not residents of the United States, and all or a substantial portion of the assets of such persons are located outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon us or upon such persons or to enforce against them judgments obtained in U.S. courts, including judgments in actions predicated upon the civil liability provisions of the federal securities laws of the United States. We have been advised by our Swiss counsel that there is doubt as to the enforceability in Switzerland of original actions, or in actions for enforcement of judgments of U.S. courts, of civil liabilities to the extent predicated upon the federal and state securities laws of the United States. Original actions against persons in Switzerland based solely upon the U.S. federal or state securities laws are governed, among other things, by the principles set forth in the Swiss Federal Act on International Private Law. This statute provides that the application of provisions of non-Swiss law by the courts in Switzerland shall be precluded if the result is incompatible with Swiss public policy. Also, mandatory provisions of Swiss law may be applicable regardless of any other law that would otherwise apply.

Switzerland and the United States do not have a treaty providing for reciprocal recognition and enforcement of judgments in civil and commercial matters. The recognition and enforcement of a judgment of the courts of the United States in Switzerland is governed by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides in principle that a judgment rendered by a non-Swiss court may be enforced in Switzerland only if:

- the non-Swiss court had jurisdiction pursuant to the Swiss Federal Act on Private International Law;
- the judgment of such non-Swiss court has become final and non-appealable;
- the judgment does not contravene Swiss public policy;
- the court procedures and the service of documents leading to the judgment were in accordance with the due process of law; and
- no proceeding involving the same position and the same subject matter was first brought in Switzerland, or adjudicated in Switzerland, or was earlier adjudicated in a third state and this decision is recognizable in Switzerland.

Our status as a Swiss corporation means that our shareholders enjoy certain rights that may limit our flexibility to raise capital, issue dividends and otherwise manage ongoing capital needs.

Swiss law reserves for approval by shareholders certain corporate actions over which a board of directors would have authority in some other jurisdictions. For example, the payment of dividends and cancellation of treasury shares must be approved by shareholders. Swiss law also requires that our shareholders themselves resolve to, or authorize our board of directors to, increase our share capital. While our shareholders may authorize share capital that can be issued by our board of directors without additional shareholder approval, Swiss law limits this authorization to 50% of the issued share capital at the time of the shareholders' authorization. The authorization, furthermore, has a limited duration of up to two years and must be renewed by the shareholders from time to time thereafter in order to be available for raising capital. Additionally, Swiss law grants pre-emptive rights to existing shareholders to subscribe for new issuances of shares. In certain circumstances, including those explicitly described in our articles of association, our board of directors may withdraw such pre-emptive rights. Shareholders who believe pre-emptive rights were improperly withdrawn

may sue us for damages or may attempt to block the registration of the issuance of new shares in the commercial register which may delay or exclude the share issuance. Swiss law also does not provide as much flexibility in the various rights and regulations that can attach to different categories of shares as do the laws of some other jurisdictions. These Swiss law requirements relating to our capital management may limit our flexibility, and situations may arise where greater flexibility would have provided benefits to our shareholders.

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 Securities Exchange Act of 1934, as amended, or 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 Swiss laws and regulations with regard to such matters and intend to furnish quarterly financial information to the SEC, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including (i) the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act; (ii) the sections of the Exchange Act requiring insiders to file public reports of their stock ownership and trading activities and liability for insiders who profit from trades made in a short period of time; and (iii) the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K, upon the occurrence of specified significant events. In addition, foreign private issuers are not required to file their annual report on Form 20-F until four months after the end of each 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.

Swiss 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.

Although Swiss law also requires that we adopt a compensation committee, we follow home country requirements with respect to such committee. 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. We follow Swiss law requirements with respect to disclosure of compensation for our directors and executive officers. Swiss 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).

Additionally, in accordance with Swiss 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).

Furthermore, in accordance with Swiss law and generally accepted business practices, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders. 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. Our articles of association provide for an independent proxy holder elected by our shareholders, who may represent our shareholders at a general meeting of shareholders, and we must provide shareholders with an agenda and other relevant documents for the general meeting of shareholders. However, Swiss law does not have a regulatory regime for the solicitation of proxies and company solicitation of proxies is prohibited for public companies in Switzerland, 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 are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to "emerging growth companies" will make our common shares less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act. For as long as we continue to be an "emerging growth company," we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We could be an "emerging growth company" until 2019, although circumstances could cause us to lose that status earlier, including if the market value of our common shares held by non-affiliates exceeds $700 million as of any June 30 (the end of our second fiscal quarter) before that time, in which case we would no longer be an "emerging growth company" as of the following December 31 (our fiscal year end). We cannot predict if investors will find our common shares less attractive because we may rely on these exemptions. If some investors find our common shares less attractive as a result, there may be a less active trading market for our common shares and the price of our common shares may be more volatile.

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 an "emerging growth company" under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an "emerging growth company" until 2019. 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 our 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.

We believe that we were a "passive foreign investment company," or PFIC, for U.S. federal income tax purposes for our 2015 and 2016 taxable years, 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 2016 taxable year, and we expect to be a PFIC for our current year and for the foreseeable future. In addition, we may, directly or indirectly, hold equity interests in other PFICs, or Lower-tier PFICs. Under the Internal Revenue Code of 1986, as amended, or the Code, 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 additional information, see "Item 10. Material U.S. Federal Income Tax Considerations for U.S. Holders."

ITEM 4. INFORMATION ON THE COMPANY

A. History and development of the Company

We are a clinical-stage biopharmaceutical company focused on the development of novel products for the treatment of inner ear disorders. Our most advanced product candidates are in Phase 3 clinical development. Keyzilen® (AM-101) is being developed for the treatment of acute inner ear tinnitus and has received fast track designation from the FDA. AM-111 is being developed for the treatment of acute inner ear hearing loss and has been granted orphan drug status by the FDA and the EMA and has been granted fast track designation by the FDA. AM-125 is being developed for the treatment of vestibular disorders. In addition, we are pursuing early stage projects for the treatment of tinnitus and rhinology.

We believe we are currently the clinically most advanced company working on inner ear therapeutics. We believe that Keyzilen® and AM-111 are the only drug candidates that have demonstrated positive efficacy in randomized placebo-controlled proof of concept clinical trials in acute inner ear tinnitus and acute inner ear hearing loss. Our products are protected through intellectual property rights and, in addition, orphan drug status has been granted to AM-111.

Our product candidates Keyzilen® and AM-111 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.

Our product candidate AM-125 is administered with a metered spray into the nose. 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.

Keyzilen® is targeting acute inner ear 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.

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 Tinnitus Functional Index, TFI, compared to placebo. However, the TACTT2 trial data showed treatment effects on TFI in favor of Keyzilen® for certain subgroups and support the positive safety profile established in the Phase 2 trials. Following analysis of TACTT2 data, we have amended the protocol of Efficacy and Safety of Keyzilen® (AM-101) in the Treatment of Acute Peripheral Tinnitus 3, or TACTT3, the second Phase 3 clinical trial with Keyzilen®. Under the amended protocol, the trial size will be increased, certain patient subgroups will be included in confirmatory testing and the TFI will be elevated from a key secondary endpoint to an alternate primary efficacy endpoint. We expect to have top-line results from the expanded TACTT3 trial in early 2018. In the two open label follow-on trials, AMPACT1 and AMPACT2, the last subjects completed the trial in September and December 2016, respectively. We expect that the topline data from AMPACT1 and AMPACT2 will become available in the second quarter of 2017. See “Item 4. Information on the Company – Business Overview – Keyzilen® Phase 3 Clinical Program.”

We are also developing AM-111 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. We are conducting two pivotal Phase 3 trials in the treatment of idiopathic sudden sensorineural hearing loss, or ISSNHL, titled HEALOS and ASSENT. HEALOS is enrolling 255 patients in Europe and Asia and ASSENT is enrolling 300 patients in the United States, Canada and South Korea. As of September 2016, HEALOS had recruited 50% of patients, and we expect to have top-line data from HEALOS in the third quarter of 2017. ASSENT started enrollment in June 2016, and we expect to have top-line data from the trial in the second half of 2018. We believe that, if approved, AM-111 could become the first approved pharmaceutical treatment for ASNHL. AM-111 received orphan drug designation for the treatment of ASNHL from both the FDA and the EMA.

We are a stock corporation organized under the laws of Switzerland. 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. Our principal office is located at Bahnhofstrasse 21, 6300 Zug, Switzerland, telephone number +41 41 729 71 94.

On August 11, 2014, we completed our initial public offering of common shares, selling an aggregate of 10,113,235 common shares, which included 713,235 common shares sold on August 19, 2014 pursuant to an over-allotment option granted to the underwriters. All of these common shares were sold at a price to the public of $6.00 per share, yielding gross proceeds of $60.7 million. On May 18, 2015, we completed an underwritten offering of 5,275,000 shares at an offering price of $4.75 per share, yielding gross proceeds of $25.1 million.

On June 1, 2016, we entered into a Controlled Equity Offering Sales Agreement with Cantor Fitzgerald & Co., or Cantor, pursuant to which we may offer and sell, from time to time, common shares with a nominal value of CHF 0.40 per share, having an aggregate offering price of up to $35 million through Cantor. Any common shares offered and sold will be issued pursuant to our shelf registration statement on Form F-3 as supplemented by a prospectus supplement, dated June 1, 2016. In the year ended December 31, 2016, we did not offer or sell any common shares under the Controlled Equity Offering Sales Agreement.

On July 19, 2016, we entered into a Loan and Security Agreement with Hercules for a secured term loan facility of up to $20.0 million. An initial tranche of $12.5 million was drawn on July 19, 2016, concurrently with the execution of the loan agreement. The loan matures on January 2, 2020 and bears interest at a minimum rate of 9.55% per annum, and is subject to the variability of the prime interest rate. In connection with the loan facility, we issued Hercules a warrant to purchase up to 241,117 of our common shares at an exercise price of $3.94 per share. As of December 31, 2016, the warrant was exercisable for 156,726 common shares. Upon Hercules making the second advance under the loan facility, the warrant shall become exercisable for the additional 84,391 common shares. The warrant expires on July 19, 2023. The loan is secured by a pledge of the shares of Auris Medical AG, our principal operating subsidiary, all intercompany receivables owed to us by our Swiss subsidiaries and a security assignment of our bank accounts.

On February 2, 2017, we entered into an asset purchase agreement with Otifex Therapeutics Pty. Ltd, or Otifex, an Australian company, pursuant to which we agreed to purchase and Otifex has agreed to sell us certain preclinical and clinical assets related to a formulation for the intranasal application of Betahistine, which we refer to as AM-125. See “Item 4. Information on the Company – Business Overview – AM-125 in Vestibular Disorders.”

On February 21, 2017, we completed a public offering of 10,000,000 common shares with a nominal value of CHF 0.40 each and 10,000,000 warrants, each warrant entitling its holder to purchase 0.70 of a common share. The net proceeds to the Company from the Offering were approximately $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 additional common shares and/or 1,500,000 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 warrants.

B. Business overview

Strengths

We believe we are a leader in the development of novel therapeutic products for inner ear disorders due to several factors.

- ***First mover advantage.*** With two product candidates in late stage clinical development, we believe we are currently the clinically most advanced company working on inner ear therapeutics. We believe that Keyzilen® and AM-111 are the only drug candidates that have demonstrated positive efficacy in randomized placebo-controlled proof of concept clinical trials in acute inner ear tinnitus and acute inner ear hearing loss. As a result, we believe that, if approved, we will be the first to market with FDA or EMA-approved products for these indications.

- ***Barriers to entry.*** Our product candidates are protected not only through intellectual property rights but also potentially by the orphan drug status granted to AM-111 as well as by the know-how across several disciplines that is required to formulate and reliably deliver drugs to the inner ear. Our proprietary gel formulation, its manufacturing and its application are part of our intellectual property, know-how and competitive advantage. In addition, we believe that our intellectual property broadly directed to polymer-based formulations for the treatment of middle or inner ear disorders will serve as barriers to entry beyond our current product candidates.

- ***Efficient commercialization.*** Given that the market for our therapeutic product candidates can be efficiently accessed through a limited number of specialist ENT physicians and specialist neurotologists, we intend to build our own sales force in order to commercialize our tinnitus and rhinology product candidates, if approved, in the United States and key European markets.

- ***Experienced management.*** Having been focused on developing therapeutic products for inner ear indications for over a decade, we believe that our senior management provides us with significant capabilities. Our Chief Executive Officer and founder, Thomas Meyer, has played several pivotal roles in our development and evolution. Prior to Auris Medical, he was the CEO of Disetronic, a fast growing Swiss diabetes care company sold to Roche in 2003. Other key members of our management team bring significant experience in clinical, product development and regulatory affairs in biopharmaceutical companies.

Strategy

Our goal is to become the leading biopharmaceutical company focused on developing and commercializing novel therapeutics to treat inner ear and related disorders. The key elements of our strategy to achieve this goal are:

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

- ***Use drug delivery techniques and proprietary drug formulations for effective, safe and rapid local administration.*** We are developing treatments for inner ear disorders based on intratympanic injections into the middle ear. This short outpatient procedure allows us to deliver therapeutic concentrations of drug in a highly targeted fashion with only minimal systemic exposure. We are using proprietary, fully biocompatible and biodegradable gel formulations for optimum middle ear tolerance and effective diffusion of active substances into the inner ear. We are also developing spray formulations for intranasal delivery of drugs that can reach the inner ear through the bloodstream more effectively than oral administration.

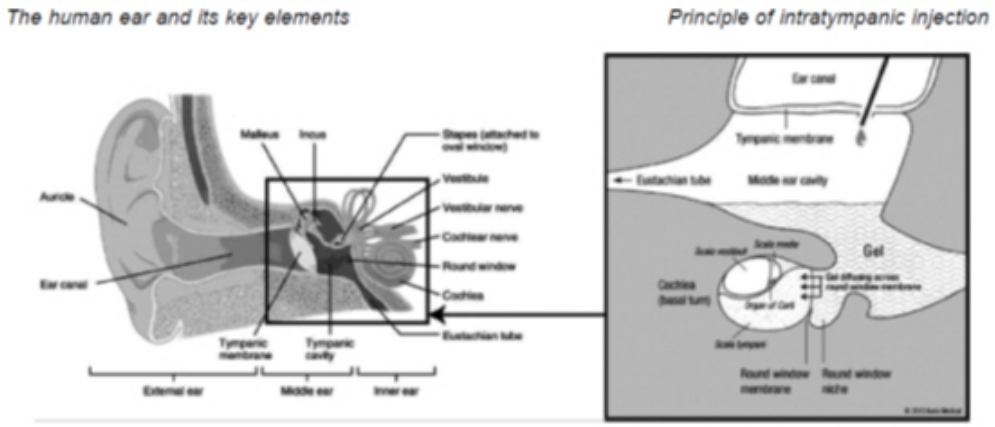
- ***Bring Keyzilen® (AM-101), AM-111 and AM-125 to market.*** We plan to focus most of our resources on the development and commercialization of our two lead product candidates: Keyzilen® and AM-111, which are in Phase 3 clinical development. In addition, we are developing AM-125 for the treatment of vestibular disorders and we are working on several early stage projects.

- ***Build an efficient commercial infrastructure to maximize the value of our product candidates.*** We intend to build commercial operations in select markets. In those markets, we expect our commercial operations to include specialty sales forces targeting ENTs and specialists in neurotology both in hospitals and in private practice. In other markets, we expect to seek partnerships that would maximize our products' commercial potential.

- ***Expand our pipeline through internal development, academic collaborations, in-licensing and acquisitions.*** Through our work with academic research partners on the pathophysiology of tinnitus and hearing loss and clinical development we have gained novel insights that will help us both to create new pipeline products that act by way of novel mechanisms as well as to expand the therapeutic focus for our existing product candidates beyond their current indications. We plan to further maximize our commercial potential through product life cycle management, and with licensing or acquisition of compounds that could augment our product offering in ENT disorders.

The Inner Ear

We have focused our drug discovery and development efforts on targeting the inner ear, which 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.



The human ear and its key elements (left). The external ear captures sound waves, amplifies and directs them through the ear canal to the ear drum, also known as the tympanic membrane, which transfers them further via the three small bones of the ossicular chain to the oval window of the inner ear. Here, the sound waves enter the fluid filled cochlea, travel up the turns and down again and are dissipated by the round window membrane. On their way through the cochlea, the sound waves are transduced by inner hair cells into neural activity by excitation of the cochlear nerve.

Principle of intratympanic injection (right). For the administration, the patient is positioned with the ear pointing up to ensure that the round window membrane is at the bottom of the middle ear. Following local anesthesia of the ear drum the drug is injected by the ENT into the middle ear, where it collects in the bottom part, allowing for the active substance to cross the round window membrane.

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 semicircular 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

Inner ear disorders, including hearing loss, tinnitus, Ménière's Disease and balance disorders, 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, 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%) US 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. Furthermore, according to the 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. Approximately 615,000 individuals in the United States are currently diagnosed with Ménière's disease and 45,500 cases are newly diagnosed each year.

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 despite the fact that according to a 2007 report by the consulting firm NeuroInsights, hearing loss ranks among the top ten neurologic disorders by worldwide prevalence, ranking above attention deficit disorders, Alzheimer's disease and multiple sclerosis. 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 and tinnitus 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. There has been a dearth of knowledge about the pathophysiology of tinnitus and hearing loss, 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, there is 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 patient reported outcomes, or 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.

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 intratympanic injection to deliver our product candidates to the inner ear reduces systemic exposure. We target specific types of tinnitus and hearing loss that are addressable with drug-based therapies. We have worked with regulatory agencies to develop an acceptable clinical trial paradigm assessing subjective endpoints culminating, for example, in our SPA for the TACTT2 trial.

Our Localized Delivery Solution for the Inner Ear for the Treatment of Tinnitus and Hearing Loss

The inner ear is a protected part of the body, analogous to the eye. It is hidden in the temporal bone, behind the middle ear and the ear drum. In addition, it is very tiny: the cochlea measures about the size of the fingernail on the little finger. Therefore, therapeutically targeting the inner ear is not easy. There is currently no FDA or EMA approved drug therapy for the treatment of tinnitus or hearing loss on the market.

The blood labyrinth barrier is a major physiological divider separating the inner ear from systemic circulation, critically preserving the inner ear's microenvironment. Systemic drug dose levels capable of having a therapeutic effect on the inner ear are often high enough to cause adverse side effects.

An alternative approach is to administer drugs locally by intratympanic injection to maximize efficacy and minimize systemic side effects. With intratympanic administration, the drug is injected via a needle through the anesthetized ear drum into the middle ear cavity. The drug then diffuses across the semi-permeable round window membrane (RWM) into the inner ear. Our lead product candidates are administered by intratympanic injection. We chose this approach after thorough evaluation of all available alternatives because it offers the optimal combination of access, convenience, physician familiarity and safety. We formulated our product candidates specifically with intratympanic delivery in mind.

One of the key shortcomings of current intratympanic approaches is the use of injectable solutions that may easily drain off via the Eustachian tube, thus preventing or reducing effective diffusion into the cochlea. With our proprietary gel formulations for intratympanic injections we overcome this "draining off," facilitate contact with the RWM and achieve effective diffusion into the cochlea.

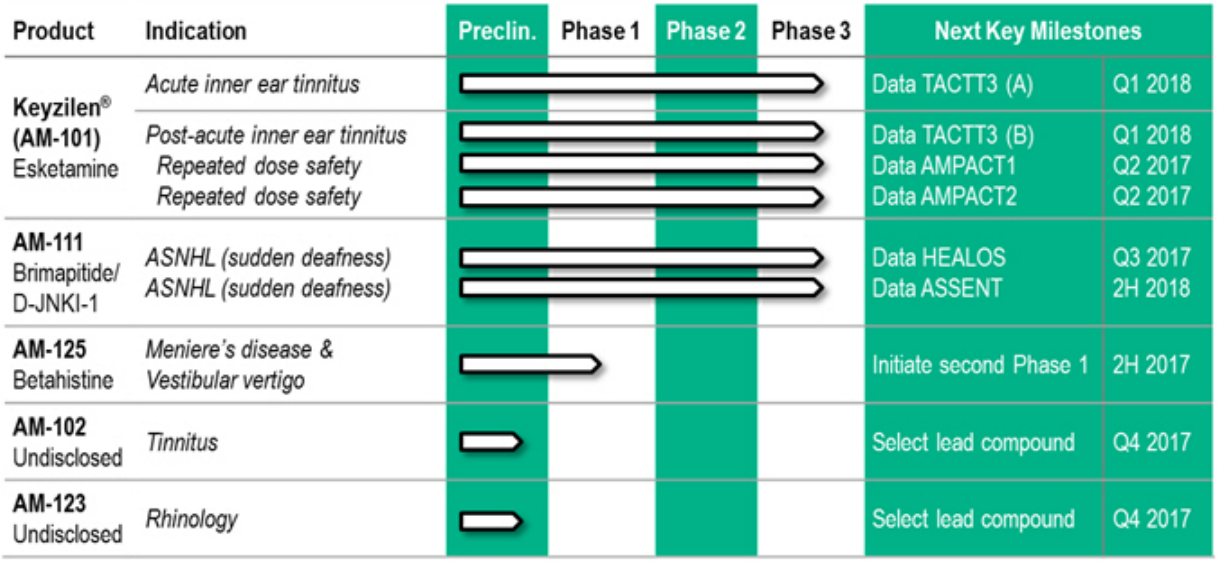
Both Keyzilen® and AM-111 are formulated in a viscous gel of sodium hyaluronate that is biocompatible, biodegradable, and isotonic (that is, having the same salt concentration and therefore not causing any pressure build up on either side of the RWM). The gel has a neutral pH which helps minimize potential irritation to the ear. We selected its viscosity in a way that the free movement of the ossicular chain, which transfers the vibrations of the eardrum to the inner ear, is not impacted. The presence of highly viscous gels in the middle ear may cause transient conductive hearing loss.

In addition, in the case of AM-111, we are employing D-TAT, a peptidic active transporter technology that allows the transport of a large molecule to the inner ear that would normally be blocked by the RWM. This novel use of D-TAT brings peptides not only behind the RWM but inside cells in the inner ear. To our knowledge, we are the first company to be delivering intracellular peptides to the inner ear using an active transporter such as D-TAT.

The intratympanic injection procedure by which our therapeutics are delivered to the RWM is a minimally invasive procedure that is relatively simple to perform by an experienced ENT specialist. Most ENT physicians and neurotologists have a high degree of comfort with intratympanic injection and it is well-accepted by patients. A billable procedure, intratympanic injection is routinely reimbursed under a broader reimbursement code. For the injection, patients lie on a stretcher or on a reclined exam chair, treated ear up; the injection is performed under local anesthesia of the eardrum by an ENT specialist using a microscope. Following the procedure, patients rest for 20 to 30 minutes to ensure maximum physical contact of the drug with the RWM. The tympanic membrane heals rapidly, usually within a few days, and the procedure may be performed several times. Often performed in children suffering from ear infections, the reversible opening of the eardrum is one of the most frequent ENT procedures.

Our Product Candidates

The following table summarizes our product development pipeline(1):



(1) Dates of key milestones are indicative and subject to change.

Keyzilen® in Tinnitus

Our most advanced clinical program is Keyzilen®, Esketamine gel for injection, which is in Phase 3 clinical trials in 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 patient reported outcomes associated with tinnitus in two Phase 2 clinical trials. Based on our SPA agreement with the FDA and scientific advice from the EMA, we have initiated two pivotal clinical trials with highly similar design, one in North America (TACTT2) and one in Europe, which we refer to as TACTT3. Keyzilen® has the potential to be the first drug to gain approval for treating acute inner ear tinnitus.

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 patients in the United States have tinnitus symptoms severe enough to seek medical attention and about two million patients 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, and annual service-connected disability payments for tinnitus to veterans from all periods of service are expected to exceed $2.75 billion by the end of 2016.

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. Royal National Institute for the Deaf 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 active pharmaceutical ingredient 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.

The NMDA receptor was first validated as a target for the treatment of tinnitus using an animal behavioral model of tinnitus triggered by salicylate, the active substance of aspirin. Salicylate is known to trigger temporary tinnitus when administered in high doses. The animal model demonstrated that local administration of different NMDA antagonists to the inner ear allowed for suppression of salicylate induced tinnitus. Together with INSERM, we developed a much more clinically relevant model of tinnitus induced by acute acoustic trauma, or AAT. Unlike salicylate-induced tinnitus, AAT triggers glutamate excitotoxicity and may lead to irreversible damage to sensory cells. It does not result in tinnitus in all cases, but where it sets in, it may be permanent. In our pre-clinical trials, we demonstrated that Keyzilen®was able to suppress this type of tinnitus. Further pre-clinical work demonstrated that tinnitus could be suppressed even when drug was administered after the onset of tinnitus.

Toxicology and tolerability studies confirmed that Keyzilen® had no impact on hearing, even at much higher doses than those needed for suppressing tinnitus. Animal biodistribution studies showed rapid diffusion of the active substance into the cochlea. Concentrations decreased over several days due to clearance.

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. The development of Keyzilen® has benefitted from the long-standing clinical use of Ketamine and Esketamine as well as the wealth of published pharmacology, pharmacokinetic and safety data. 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.

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. Patient reported outcomes, or 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 100 (“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 will serve as a co-primary efficacy endpoint in our TACTT2 trial.

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 and after unsuccessful steroid treatment. The primary objective of the trial was to evaluate the safety of intratympanically delivered Keyzilen®. This first clinical 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

TACTT0 was conducted at 28 European sites between March 2009 and May 2011. This trial was a double-blind, randomized, placebo controlled, multiple dose, parallel group, Phase 2 clinical trial. It enrolled patients with persistent inner ear tinnitus as a result of AAT, OM, or idiopathic inner ear hearing loss, or ISSNHL, occurring not more than three months prior, and with a MML of at least 5 dB. 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 (approximately eighty per treatment group). The improvement in the MML was the primary efficacy endpoint. The improvement in subjective tinnitus loudness and in tinnitus annoyance were co-primary efficacy endpoints.

In this trial, Keyzilen® further demonstrated a favorable safety profile. 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. In 93% of cases, the ear drum was fully closed five days after the last injection. Seven patients experienced a total of nine nonfatal serious adverse events, of which four occurred in the placebo group. All serious adverse events were considered either not related or unlikely related to treatment. In the placebo group, one patient died because of cardiomyopathy, which was considered unrelated.

Efficacy analysis revealed a differentiated picture. Overall, the trial failed to demonstrate a treatment benefit based on the change in the MML as there was no difference in outcomes between treatment groups. However, further analysis of certain pre-specified outcome variables and subgroups revealed consistent differences between changes in the MML and changes in PROs and substantial variability in MML measures. Unlike the MML, the PROs, including tinnitus loudness and tinnitus annoyance, indicated different outcomes in treatment groups. In addition, outcomes differed consistently between patients with tinnitus triggered by AAT or OM, and those with tinnitus caused by ISSNHL. In case of the latter, no treatment effects were evident. Lastly, outcomes in unilateral tinnitus patients (one ear affected) were superior to those in bilateral tinnitus patients.

The further efficacy analysis focused on the subgroup of patients with tinnitus caused by AAT or OM (n=118), that is, patients with well-established cochlear origin of tinnitus. It also focused primarily on unilateral tinnitus patients (n=84) since they allowed for a direct measure of a treatment effect, free from any interference arising from the other, untreated ear in bilateral tinnitus. For this AAT-and OM-subgroup, the trial demonstrated a dose-dependent and persistent improvement in PROs. Patients in this subgroup who received Keyzilen® at a dose level of 0.81 mg/mL showed a statistically significant improvement 90 days post-treatment in subjective tinnitus loudness and tinnitus annoyance as well as in tinnitus-related sleep difficulties and overall tinnitus impact compared with placebo. The improvement was dose dependent and statistically significant across all PROs in the analysis of covariance, or ANCOVA, statistical test. The ANCOVA model is commonly used in statistics for testing for differences between multiple treatment groups, and takes into account the baseline value of the respective test variable (covariate). Similar, but less pronounced outcomes were observed when also bilateral tinnitus cases were included; the improvement in tinnitus loudness, sleep difficulties and overall tinnitus impact in the enlarged subgroup was still statistically significant.

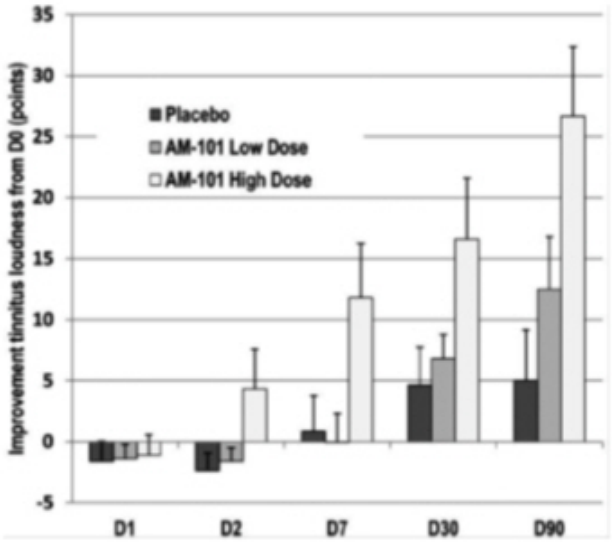
Improvement in tinnitus PROs

		Keyzilen®	
	Placebo	**Low Dose**	**High Dose**
Point improvement in tinnitus loudness (0-100 point scale)			
LS means (n)	1.4 (23)	16.0 (25)	24.1 (29)
LS mean difference (95% confidence interval)		14.6 (1.4, 27.7)	22.7 (10.3, 35.1)
P-value		0.0308*	0.0005***
Point improvement in tinnitus annoyance (0-100 point scale)			
LS means (n)	10.8 (23)	21.7 (25)	27.8 (29)
LS mean difference (95% confidence interval)		10.9 (1.4, 23.2)	17.0 (5.4, 28.6)
P-value		0.0805	0.0047**
Point improvement in difficulties falling asleep (0-100 point scale)			
LS means (n)	11.8 (21)	29.8 (15)	38.7 (22)
LS mean difference (95% confidence interval)		18.1 (2.5, 33.6)	26.9 (13.0, 40.9)
P-value		0.0234*	0.0003***
Point improvement in tinnitus impact (0-24 point scale)			
LS means (n)	2.5 (22)	5.5 (25)	5.9 (27)
LS mean difference (95% confidence interval)		3.0 (0.1, 5.8)	3.4 (0.8, 6.0)
P-value		0.0400*	0.0124*

*ANCOVA results for changes in PROs from baseline to Day 90 in patients with unilateral tinnitus following AAT or OM. Shown are least square (LS) means for treatment groups, differences for the active groups compared with placebo including 95% confidence interval and the p-value: * significant at 0.05 level; ** significant at 0.01 level; *** significant at 0.001 level. P-value is a conventional statistical method for measuring the statistical significance of clinical results. In clinical trials, the "p-value" is the probability that the result was obtained by chance. By convention, a "p-value" that is less than 0.05 is considered statistically significant. Tinnitus loudness, annoyance and difficulties falling asleep were rated by patients on a scale from 0 to 100 and tinnitus impact by the THI-12 questionnaire (maximum score 24 points).*

The improvement in PROs was gradual over the 90 day observation period. At Day 90 the mean improvement in tinnitus loudness was 48% in the Keyzilen® 0.81 mg/mL group compared to 9% in the placebo group.

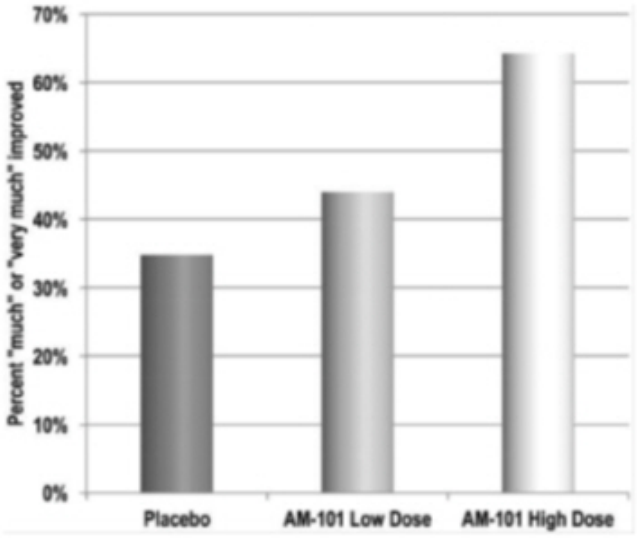
Improvement in tinnitus loudness over time



Mean improvement of tinnitus loudness from baseline in patients with unilateral tinnitus following AAT or OM (n=84). Shown are changes from baseline D0 (before first injection) to D1 (before second injection), D2 (before third injection) and the follow-up visits at D7, D30 and D90. Whiskers: standard error mean.

64% of patients in the high dose group rated their tinnitus severity at Day 90 compared to baseline as “much improved” or “very much improved”, compared with 34% of patients in the placebo group. The majority of placebo treated patients reported only “somewhat improved” tinnitus severity.

Global patient impression of change in tinnitus severity



Percentage of patients with unilateral tinnitus following AAT or OM (n=76) reporting at Day 90 “much improved” or “very much improved” tinnitus severity compared with baseline.

Further analysis of efficacy results in the ISSNHL subgroup showed an unexpectedly high rate of spontaneous remission and substantial heterogeneity in outcomes. When patients with certain pre-specified tinnitus characteristics were excluded, a treatment effect was even observed with a majority of ISSNHL-tinnitus patients. 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 with established cochlear origin (such as AAT and OM).

TACTT1

TACTT1, our second double-blind, randomized, placebo-controlled Phase 2 clinical trial, was conducted between 2011 and 2013 in the United States, Belgium, Germany and Poland to complement the TACTT0 trial. The trial was not powered to demonstrate statistical significance between treatment groups, but rather designed to evaluate whether repeated doses were better than a single dose in attenuating tinnitus. Therefore no statistical hypotheses were defined, but the trial was expected to indicate relevant efficacy trends.

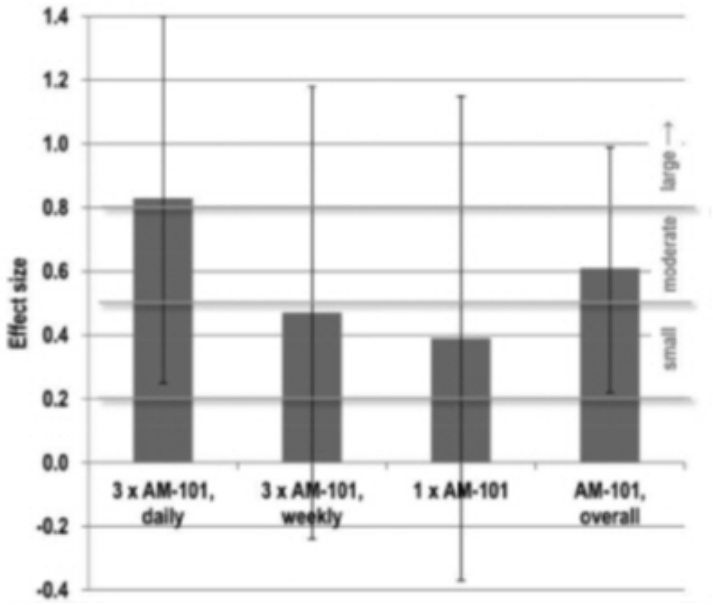
Enrollment consisted of 85 patients suffering from acute inner ear tinnitus following AAT or OM. Tinnitus after barotrauma and middle ear surgery were added as traumatic cases in addition to AAT.

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. Each cohort had its own placebo group, and the placebo groups were pooled for certain statistical analyses describes below. Unlike TACTT0, this trial allowed bilateral treatment where tinnitus was present in both ears. The outcome measures in TACTT1 reflected insights gained from TACTT0. Specifically, subjective tinnitus loudness was selected as the primary efficacy measure, while the highly variable MML was monitored as a secondary read out.

TACTT1 demonstrated the safety and tolerability outcomes observed in the preceding trials. Again, there were no systemic side effects. One non-fatal serious adverse event was observed in the active treatment group; it was considered unrelated to the treatment. It further demonstrated the gradual improvement in PROs in Keyzilen® treated groups that had already been observed in TACTT0. The ANCOVA model in the primary efficacy analysis showed no statistically significant trend for improvement in subjective tinnitus loudness related to the number of injections (single dose Keyzilen®, triple dose Keyzilen® and placebo pooled; p=0.084).

When comparing the improvement in tinnitus loudness in patients with unilateral tinnitus following traumatic injury to the cochlea or OM, treatment effects in TACTT1 were smaller than in TACTT0. The effect size was 0.83 where Keyzilen® had been administered three times over three consecutive days in TACTT0, 0.47 for three injections in weekly intervals (TACTT1) and 0.39 with single dose administration (TACTT1). The effect size is a commonly used standardized measure of the magnitude of observed effect to compare outcomes across different trials. Effect sizes between 0.5 and 0.8 are considered moderate, and above 0.8 as large. The observed differences in effect sizes suggest that repeated and concentrated application of Keyzilen® and hence concentrated inhibition of cochlear NMDA receptors provides superior treatment benefits. Over the two Phase 2 clinical trials, Keyzilen® 0.81 mg/mL showed a statistically significant improvement in the AAT and OM group of patients when compared against placebo (p=0.002).

Effect size of tinnitus loudness improvement in TACTT0 and TACTT1



Effect size of tinnitus loudness improvement from baseline to 90 days after last treatment administration for three different dose regimens – three doses over three consecutive days, three doses over two weeks, single dose – and pooled together in patients with unilateral tinnitus following AAT or OM (n=118) in the TACTT0 and TACTT1 trials. Effect size is calculated as mean difference in tinnitus loudness improvement between patients treated with Keyzilen®0.81 mg/mL and patients treated with placebo, standardized by the standard deviation. Whiskers: 95% confidence interval.

As in the TACTT0 trial, psychoacoustic measures such as MML were marked by high variability, confirming their limited suitability and reliability as efficacy outcome measure.

Keyzilen® Phase 3 Clinical Program

We have initiated two pivotal trials with Keyzilen® with highly similar designs, one in North America (TACTT2) and one in Europe (TACTT3). TACTT2 enrolled approximately 330 patients, while TACTT3 Stratum A (Europe) has enrolled approximately 300 patients, both during the acute stage. Trial participants receive three injections of Keyzilen® 0.87 mg/mL or placebo over three to five days and are followed for 84 days.

In addition, TACTT3 Stratum B is exploring 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, approximately 330 patients will be enrolled in TACTT3 Stratum B pre- and post-interim analysis.

Two further trials, AMPACT1 and AMPACT2 (Keyzilen® in the Post-Acute Treatment of Peripheral Tinnitus) are nine-month open label extension trials conducted at the same sites as for TACTT2 and TACTT3. These extension trials will be open to participants who complete the TACTT2 or the TACTT3 trial and will evaluate the safety and local tolerance of up to three treatment cycles, each with three repeated doses of Keyzilen® 0.87 mg/mL. In AMPACT1 and AMPACT2, the last subjects completed the trial in September and December 2016, respectively. We expect topline data from AMPACT1 and AMPACT2 in the second quarter of 2017.

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 new drug application, or 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. Therefore, we have designed these trials to provide further evidence of safety over a longer duration and also to study the effect of repeated administration over up to four treatment cycles in total.

On August 18, 2016, we announced that the Phase 3 TACTT2 clinical trial with our lead product candidate, Keyzilen® (AM-101), did not meet the two co-primary efficacy endpoints of statistically significant changes in tinnitus loudness and tinnitus burden compared to placebo. TACTT2 was designed as a randomized, double-blind, placebo-controlled trial in acute inner ear tinnitus following traumatic cochlear injury or otitis media. The trial was conducted primarily in North America and randomized 343 patients to receive either Keyzilen® 0.87 mg/mL or placebo in a 3:2 ratio. The co-primary endpoints were the change in subjective tinnitus loudness, measured by the TLQ and the change in tinnitus burden from baseline to Day 84, measured by the TFI.

Treatment with Keyzilen® did not demonstrate a statistically significant difference in tinnitus improvement as compared to placebo for either co-primary efficacy endpoint. In TACTT2, baseline values for TLQ and TFI were 6.44 and 52.4 points in the Keyzilen® group, and 6.47 and 50.2 points in the placebo group. Treatment with Keyzilen® resulted in a reduction in tinnitus loudness of 0.63 points, compared to a reduction of 0.80 points for placebo (p-value of 0.321). With respect to tinnitus burden, treatment with Keyzilen® resulted in a 9.67 point reduction, as measured by the TFI, compared to a reduction of 10.63 points for placebo (p-value of 0.565). A reduction of 13 points as measured by the TFI was defined as clinically meaningful by the developers of the TFI. By convention, a p-value that is less than 0.05 is considered statistically significant.

Keyzilen® was well tolerated with no drug-related serious adverse events. The trial's primary safety endpoint, incidence of clinically meaningful hearing deterioration, was low with no statistically significant difference from the placebo group (p-value of 0.82), supporting the safety profile of Keyzilen®.

While we are continuing to analyze the TACTT2 results, we believe we have identified two principal sources for the outcome: (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. We believe the daily capture of TLQ data may have caused a number of patients to excessively focus on their tinnitus symptoms. 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.

However, the TACTT2 trial data show treatment effects on TFI in favor of Keyzilen® for specific subgroups. In the pre-specified subgroup of patients suffering from tinnitus following otitis media, treatment with Keyzilen® resulted in a reduction of 14.76 points in the TFI from baseline, as compared to 6.19 points for placebo (p-value of 0.048). In active-treated patients who suffered at baseline from severe or extreme tinnitus (a subgroup independent of tinnitus etiology that was not pre-specified), as determined by the Patient Global Impression of Severity, a 15.53 point reduction was observed, as compared to 11.48 points for placebo (p-value of 0.238).

Based on insights from our continuing analysis of the TACTT2 trial, we submitted a protocol amendment to regulatory agencies in Europe for TACTT3, the ongoing second Phase 3 clinical trial with Keyzilen®. In the amended trial protocol, the change in TFI score has been elevated from a key secondary endpoint to an alternate primary efficacy endpoint such that both the TLQ and the TFI will be alternate primary efficacy endpoints. In order to corroborate the TACTT2 results showing clinically meaningful treatment effects based on the TFI for patients with otitis media-related tinnitus and those with severe to extreme tinnitus at baseline, these two subgroups will be included in confirmatory statistical testing in TACTT3 along with the overall study. Type I error (false positive) control will be provided across the three populations (overall study population, otitis media-related tinnitus and severe to extreme tinnitus) by application of the Hochberg procedure. The Hochberg procedure, a method applied to statistical testing to control for multiplicity, avoids the need for pre-specification of a hierarchy among the three populations for analysis, providing more flexibility than with other methods and allowing the possibility of achieving success in a subpopulation. Additionally, the trial size will be increased by 60 patients in each of Stratum A (acute tinnitus stage) and Stratum B (post-acute tinnitus stage) to enhance statistical sensitivity to the effects of treatment.

As of December 31, 2016, TACTT3 has enrolled more than 300 patients in Stratum A and approximately 330 patients in Stratum B. As in TACTT2, TLQ is determined based on averaged daily ratings around study visits; however, fewer additional data will be captured from the newly enrolled patients in between study visits in order to lighten their burden. Top-line results from the expanded TACTT3 trial are expected in early 2018.

In early December 2016, we had two meetings with the U.S. Food and Drug Administration, or FDA, relating to the Keyzilen® program. Through a Type C Meeting, the FDA confirmed that, as per standard practice, two positive confirmatory trials would be required to submit a New Drug Application, or NDA. The FDA did not provide feedback on the TACTT3 protocol amendment because the trial is being conducted in Europe and is not under the Investigational New Drug, or IND Application. Data from trials that were not filed under the IND may be used for an NDA, provided they meet requisite legal and regulatory requirements such as adherence to Good Clinical Practice, or GCP, regulations. In a separate meeting with the FDA, alignment was achieved on key items of the Keyzilen® Chemistry, Manufacturing, and Controls section for a future NDA.

Even if the protocol amendment for TACTT3 is approved by the applicable regulatory agencies, we cannot assure you that the TACTT3 clinical trial will be successful. Additionally, we cannot be certain that Keyzilen® will be approved, even if it the TACTT3 clinical trial is considered successful.

AM-111 in Hearing Loss

AM-111 is being developed for the treatment of ASNHL. 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.

AM-111 contains a synthetic D-form peptide (Brimapitide or D-JNKI-1) that protects sensorineural structures in the inner ear from stress-induced damage. AM-111 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 ASNHL.

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 for acute acoustic trauma. The latter is known as ISSNHL for idiopathic sudden sensorineural hearing loss. Together they can be defined as acute sensorineural hearing loss or 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 issued in 2012 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 colleagues 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 – AM-111

We are developing AM-111 as a treatment for acute inner ear hearing loss. AM-111 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 S.A. (Switzerland). Like Keyzilen®, AM-111 is delivered in a biocompatible gel formulation via intratympanic injection. We have established the safety and preliminary efficacy of AM-111 in a Phase 2 clinical trial. We are preparing for the late stage clinical development of AM-111 in acute inner ear hearing loss. The acute stage of hearing loss represents a window in time in which the inner ear can be protected from permanent hearing loss. AM-111 received orphan drug designation by both EMA and FDA in 2005 and 2006, respectively.

Therapeutic rationale for AM-111 in hearing loss

The proprietary active pharmaceutical ingredient of AM-111 is 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. D-JNKI-1 comprises an active transporter sequence, or D-TAT, that enables AM-111 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. AM-111 was shown to remain pharmacologically active for several days inside the cochlea. The D-form is necessary for AM-111 to cross the RWM.

By attenuating inflammation and protecting cells from apoptosis, we believe that AM-111 reinforces natural recovery processes and helps to prevent or minimize permanent damage respectively chronic hearing loss. AM-111'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 AM-111 in close collaboration with academic partners and various contract research organizations, or CROs. D-JNKI-1 was invented by Xigen S.A. 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.

The primary efficacy endpoint in our Phase 2 clinical trial was hearing loss recovery from baseline to Day 7 at the three worst affected frequencies. The percentage improvement of the patient's hearing across an average of three frequencies was measured relative to baseline hearing loss. This percentage improvement and the percentage of patients with complete remission (hearing recovery to within 10 dB of the pre-ASNHL level) at Day 7 were co-primary endpoints. We also monitored change in the speech discrimination score, or SDS, which measures the correct understanding of 20 monosyllabic words presented to patients, as well as subjective tinnitus loudness as secondary outcome variables.

AM-111 Clinical Development

We have successfully completed two clinical trials of AM-111 that demonstrated its favorable safety profile and efficacy in treating ASNHL. We have benefited several times from engaging in a protocol assistance procedure with the EMA, most recently for the design of the Phase 3 clinical development. We are conducting two pivotal Phase 3 trials in the treatment of idiopathic sudden sensorineural hearing loss, titled HEALOS and ASSENT. HEALOS is enrolling patients in Europe and Asia and ASSENT has commenced enrollment in the U.S., Canada and South Korea.

The design of our pivotal Phase 3 clinical trials is based on the outcomes from our Phase 2 clinical trial and our discussions with the EMA and FDA. We have decided to make some adjustments to the definition of the target patient population to ensure that the trial enrolls only those subjects who have a clear medical need and in whom a clinically meaningful therapeutic benefit can be shown.

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 AM-111 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. AM-111 was well tolerated by all trial participants, regardless of the dose. Adverse events occurred in only small numbers and were either unrelated or considered unlikely to be related to the treatment. The Phase 1/2 trial provided the first indications of therapeutic benefit of AM-111 in humans.

Phase 2 Clinical Trial

To further evaluate the efficacy and safety of AM-111 we conducted a Phase 2b clinical trial between March 2009 and 2012. Since pre-clinical tests had demonstrated AM-111'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.

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. AM-111 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 trial consisted of a baseline assessment and four follow-up visits on Days 3, 7, 30, and 90. The primary efficacy endpoint was hearing loss recovery from baseline to Day 7 at the three worst affected frequencies. The percentage improvement of PTA relative to baseline hearing loss and the percentage of patients with complete remission (PTA recovering to within 10 dB of the pre-ASNHL level) at Day 7 were co-primary endpoints. We also monitored change in the speech discrimination score, or SDS, measuring the correct understanding of 20 monosyllabic words presented to patients, and subjective tinnitus loudness as secondary outcome variables.

AM-111 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 were no apparent differences in the frequency of adverse events between placebo and AM-111 treated patients at any time points, 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. For nine patients, non-fatal serious adverse events were recorded (two, four and three patients in the placebo, AM-111 Low Dose and AM-111 High Dose, respectively). All serious adverse events were considered unlikely related or not related to the treatment with the exception of two ("deafness neurosensory", one in the placebo and one in the AM-111 High Dose group). All serious adverse events except two (diagnosis of internal auditory canal tumor, respectively neurofibromatosis type II, not related) had recovered or were recovering. The most common serious adverse event was "deafness neurosensory," as some severe or profound hearing loss patients with insufficient recovery, acute relapse or ongoing deterioration were hospitalized in Poland for infusion therapy in line with customary medical practice.

The trial demonstrated a statistically significant and clinically relevant improvement for the primary as well as the co-primary endpoints in patients with severe to profound ASNHL (those patients with hearing loss of at least 60 dB) treated with AM-111 0.4 mg/mL compared with placebo.

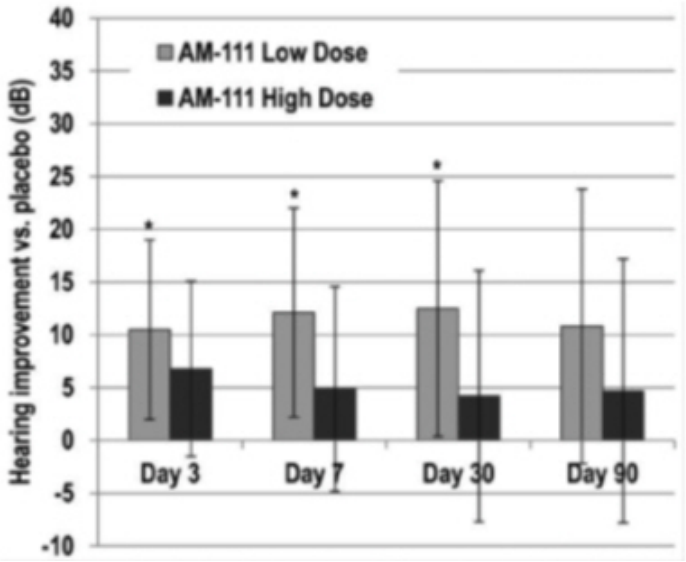
Improvement in hearing and speech discrimination

		AM-111	
	Placebo	Low Dose	High Dose
Absolute hearing improvement, dB	17.9 (30)	29.9 (29)	22.7 (33)
LS means (n)			
LS mean difference (95% confidence interval)		12.1 (2.2, 22.0)	4.9 (-4.8, 14.6)
P-value		0.017*	0.319
Relative hearing improvement, %			
LS means (n)	30.9 (30)	50.4 (29)	37.6 (33)
LS mean difference (95% confidence interval)		19.5 (3.0, 35.9)	6.6 (-9.6, 22.8)
P-value		0.021*	0.419
Frequency complete hearing recovery, %			
Mean (n)	13.3 (30)	31.0 (29)	24.2 (33)
Odds ratio (95% confidence interval)		5.5 (1.1, 29.0)	1.6 (0.4, 6.7)
P-value		0.044*	0.530
Speech discrimination score improvement, % points			
LS means (n)	9.1 (29)	27.4 (29)	23.2 (33)
LS mean difference (95% confidence interval)		18.3 (3.1, 33.4)	14.1 (0.7, 28.9)
P-value		0.019*	0.061*

*ANCOVA results for changes in hearing (absolute and relative to initial hearing loss) and speech discrimination score from baseline to Day 7 as well as frequency of complete hearing recovery in patients with severe to profound hearing loss. Shown are mean values for treatment groups (least square (LS) means for ANCOVA), differences for the active groups compared with placebo (odds ratio from logistic regression for frequency of complete hearing recovery) including 95% confidence interval and the p-value: * significant at 0.05 level.*

A clinically relevant and statistically significant therapeutic effect of AM-111 Low Dose was apparent at Day 3; it continued to Day 30 and leveled off somewhat by Day 90, but still remained clinically relevant.

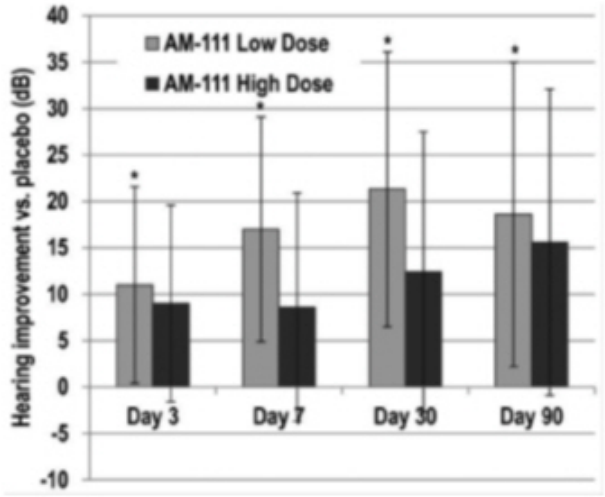
Improvement in hearing over time



*Treatment effect of AM-111 as difference in hearing recovery over placebo from baseline to follow-up visits in patients with severe to profound hearing loss (n=92). A difference of 10 dB is considered clinically relevant. Whiskers: 95% confidence interval. * Significant at 5% level when compared to placebo.*

At Day 90, 42% of patients had achieved complete recovery as compared to 26% in the placebo group. The High Dose group overall showed improvement between the Low Dose and the placebo groups, without reaching statistical significance. Sensitivity analysis showed that the therapeutic effect did not depend on early treatment: in patients who were treated more than 24 hours after ASNHL onset the treatment effect actually was larger as the rate of spontaneous recovery decreased.

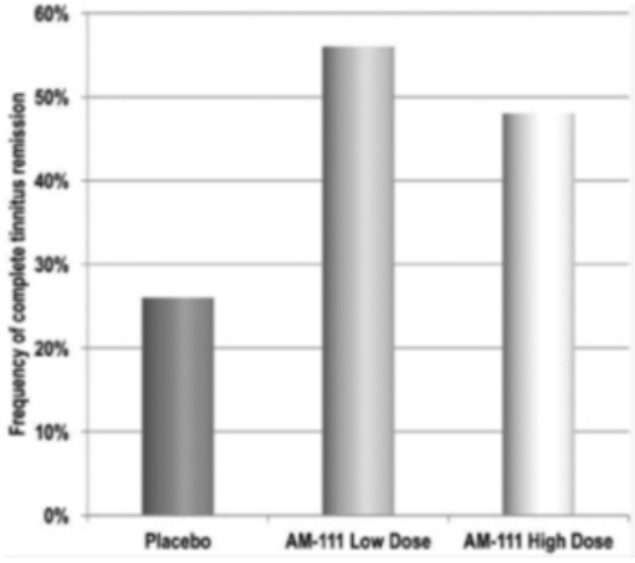
Improvement in hearing over time – ASNHL onset 24 to 48 hours before



*Treatment effect of AM-111 as difference in hearing recovery over placebo from baseline to follow-up visits in patients with severe to profound hearing loss treated 24 to 48 hours post ASNHL onset (n=66). A difference of 10 dB is considered clinically relevant. Whiskers: 95% confidence interval. * Significant at 5% level when compared to placebo.*

The superior hearing recovery in the AM-111 0.4 mg/mL group vs. placebo was supported by more frequent complete tinnitus remission. This finding, which was not yet apparent in the previous smaller Phase 1/2 clinical trial, suggests that preservation of sensory cochlear cells may help to prevent permanent tinnitus and hearing loss at the same time.

Complete tinnitus remission



Percentage of severe to profound hearing loss patients and tinnitus at baseline whose tinnitus was completely resolved by Day 90 (n=77).

In contrast to the patients with severe to profound hearing loss at baseline, there was no therapeutic benefit observed in patients with mild to moderate hearing loss (i.e. less than 60 dB) due to unexpectedly strong spontaneous recovery. Patients with mild hearing loss recovered essentially all of their initial hearing loss naturally, and those with moderate levels recovered most of it. In hindsight, the inclusion criteria for hearing loss severity had been set too low. Although there is consensus that spontaneous recovery can be substantial in ISSNHL, no reliable data had been available prior to our Phase 2b clinical trial, partly due to the dearth of placebo-controlled trials.

In the present trial, patients in the Low Dose group initially appeared to show greater improvement than those in the High Dose group. The difference, however, was not statistically significant for absolute PTA improvement and was much smaller or absent for the other efficacy outcomes.

Late Stage Clinical Program

Based on Phase 2 clinical trial outcomes, we prepared and initiated a late stage clinical program pursuant to which we are conducting confirmatory testing of AM-111 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, a concentration between 0.4 and 2.0 mg/mL may be even more effective than the low dose.

We have enrolled more than 50% of patients in a pivotal Phase 3 trial called HEALOS (Efficacy and Safety of AM-111 in the treatment of Acute Inner Ear Hearing Loss) in European and Asian countries which aims at enrolling approximately 255 patients. A single dose of either 0.4 mg/mL or 0.8 mg/mL of AM-111 is compared to placebo in patients suffering from acute severe to profound hearing loss with ISSNHL as the onset factor and an enrollment time window that has been set at 48 to 72 hours. The primary efficacy endpoint is the improvement of pure tone hearing thresholds from baseline to Day 28.

In parallel, we are enrolling up to 300 patients in ASSENT (Efficacy and Safety of AM-111 as Acute Sudden Sensorineural Hearing Loss Treatment) in the US, Canada and South Korea. A single dose of either 0.4 mg/mL or 0.8 mg/mL of AM-111 is compared to placebo in patients suffering from acute severe to profound hearing loss with ISSNHL as the onset factor and an enrollment time window of 72 hours. The primary efficacy endpoint is the improvement of pure tone hearing thresholds from baseline to Day 91. In contrast to HEALOS, where patients with insufficient hearing recovery have the option of receiving a course of oral corticosteroids as reserve therapy, all patients in ASSENT may receive oral corticosteroids as a background therapy. An interim analysis will be conducted after 150 patients have completed the trial.

AM-125 in Vestibular Disorders

Vestibular Disorders and Ménière's Disease

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. According to the 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. 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 are benign paroxysmal positional vertigo, or BPPV, or positional vertigo, labyrinthitis, vestibular neuronitis and Ménière's disease.

Ménière's disease is a chronic condition characterized by severe episodic vertigo, tinnitus, and fluctuating hearing loss. Additional symptoms include a sensation of fullness in the ear, gait problems, postural instability, drop attacks and nausea. According to the NIDCD, more than 600,000 individuals in the United States are currently diagnosed with Ménière's disease and 45,500 cases are newly diagnosed each year. The causes of Ménière's disease are not well understood. A characteristic pathological finding in affected patients is a distension of inner ear structures, the so called endolymphatic hydrops. There exist a variety of drug products that are licensed or used off-label for the treatment of vestibular disorders and Ménière's disease, including steroids, diuretics, anti-emetics or anti-nausea medications. In many countries outside the United States, oral betahistine is the standard of care and licensed for the treatment of Ménière's disease and vestibular vertigo.

Our Solution - AM-125

On February 2, 2017, we entered into an asset purchase agreement with Otifex, pursuant to which we have agreed to purchase and Otifex has agreed to sell various assets related to betahistine dihydrochloride in a spray formulation, which we intend to develop for intranasal treatment of Ménière's disease and vestibular vertigo under the name AM-125.

The assets include data from a randomized placebo controlled dose escalating Phase 1 clinical trial in 40 healthy volunteers. The trial demonstrated good tolerability of intranasal betahistine and a significantly higher betahistine concentrations in blood plasma than reported for oral betahistine administration. 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 more than 80 countries world-wide for the treatment of Ménière'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.

We intend to discuss the regulatory requirements for AM-125 with the FDA and other health authorities to further define the development program before conducting the next clinical trial. We believe that, if approved, AM-125 could become the first betahistine product for the treatment of Ménière's disease in the United States.

Competition

We believe that we are the clinically most advanced company in the emerging field of inner ear therapeutics and that our innovative technology, knowledge, experience and scientific resources provide us with competitive advantages. However, we may face competition from different sources with respect to our product candidates Keyzilen® (AM-101), AM-111 and AM-125 and our pipeline products or any product candidates that we may seek to develop or commercialize in the future. Because there are a variety of means to block the activity of NMDA receptors or the JNK pathway, our patents and other proprietary protections for Keyzilen® and AM-111 may not prevent development or commercialization of all viable product candidates that are different from our lead product candidates.

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.

There exist no FDA or EMA approved products for the treatment of acute inner ear tinnitus or acute inner ear hearing loss; however, some drug products such as pentoxifylline, gingko biloba, corticosteroids, betahistine, trimetazidine or piracetam are frequently prescribed off-label. Some of them are even licensed as tinnitus or hearing loss treatments in certain countries of the European Union. A variety of drug products that are licensed or used off-label for the treatment of vestibular disorders and Ménière's disease exist, including steroids, diuretics, anti-emetics or anti-nausea medications. In many countries outside the United States, oral betahistine is the standard of care and licensed for the treatment of Ménière's disease and vestibular vertigo.

Possible competitors may be biotechnology and pharmaceutical 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 or acute inner ear hearing loss. 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.

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 Tinnitus Retraining Therapy (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, among others, the following drug product candidates that are currently in clinical development:

- Autifony Therapeutics Ltd. has a Kv3 potassium channel agonist product candidate (AUT00063) that is designed for oral administration. In 2014 Autifony initiated a Phase 2 study with AUT00063 in patients with post-acute tinnitus. Following an interim analysis, Autifony announced in October 2015 that it would halt enrollment in its Phase 2 trial due to a lack of efficacy.

- Otonomy Inc. acquired an early stage NMDA receptor antagonist product candidate (NST-001, gacyclidine) from Neurosystec Inc. in October 2013 and, according to public information, is planning to develop it as OTO-311 for intratympanic injection. According to public information, Otonomy intends to develop a polymer-based formulation of gacyclidine for the treatment of tinnitus that will provide a full course of treatment from a single intratympanic injection. OTO-311 is currently being evaluated in a Phase 1 trial; initiation of a Phase 2 trial is planned but no launch date has been announced.

Based on publicly available information, OTO-311 will target a similar group of tinnitus patients. Its competitive strength will ultimately depend on the demonstration of clinical efficacy and safety and its comparison with Keyzilen®. Further, we intend to rely on our patent applications with broad disclosures to pursue claims relating to the use of polymers with NMDA antagonists in controlled-release topical compositions for the treatment of tinnitus. Further 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, among others, the following product candidates:

- AudioCure Pharma GmbH has a ß-carboline product candidate (AC-002) and other chemical entities derived from it in pre-clinical development that is designed for intratympanic treatment of noise induced hearing loss in a gel-based formulation.

- Autifony Therapeutics Ltd. has a Kv3 potassium channel agonist product candidate (AUT00063) that is designed for oral administration. Autifony is expected to initiate a Phase 2 trial with AUT00063 in the treatment of speech-in-noise deficits in elderly patients.

- GenVec, Inc. is developing CGF166, E1-, E3-, E4-deleted human adenovector serotype 5 (Ad5) backbone in collaboration with Novartis and has initiated a Phase 1/2 study for the treatment of hearing loss and vestibular dysfunction. The first patient was treated in October 2014.

- Nordmark, a German company, is developing Ancrod, the biologically active substance from the venom of the Malayan Pit Viper (Calloselasma rhodostoma), for the treatment of sudden sensorineural hearing loss and has initiated a Phase 2 program.

- Sound Pharmaceuticals, Inc. has a product candidate (SPI-1005, ebselen), that mimics and prompts production of the enzyme glutathione peroxidase and is designed for oral administration, and that has been tested for the prevention and treatment of temporary inner ear hearing loss in a Phase 2 clinical trial.

- Otologic Pharmaceutics, Inc. has a product candidate (HPN-07) designed for treatment of acute hearing loss by way of oral administration. A Phase 1 trial was to be initiated in 2014, but no further information is publicly available on its status.

- Sensorion, a French company, is developing R-azasetron besylate for the treatment of sudden sensorineural hearing loss. 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.

- Strekin AG, a privately held Swiss company, has an agonist of the peroxisome proliferator (STR001) that it plans to develop for surgery induced haring loss. A Phase 2 trial was initiated in 2016.

In addition, Otonomy, Inc. announced the development of a product for age related treatment of hearing loss and Decibel Therapeutics, Inc. and Frequency, both U.S. companies, announced development programs for hearing loss that could potentially compete with AM-111.

We believe that AM-111 is the only product candidate administered after an incidence of hearing loss that so far has demonstrated in a randomized, placebo controlled clinical trial a clinically relevant and statistically significant improvement in patients with severe to profound ASNHL and to have a therapeutic effect on tinnitus as well. To our knowledge, we are also the only company to have obtained orphan drug designation for a product candidate in the treatment of ASNHL in the United States. 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.

Vestibular Disorders

- Otonomy is developing a polymer-based formulation for the steroid dexamethasone (OTO-104) for patients with Ménière’s disease and is conducting two Phase 3 trials in this indication.

- Sensorion is developing SENS-111, a histamine H4 receptor antagonist, for the oral treatment of acute vertigo crises and recently initiated a Phase 2 trial to enroll patients with acute unilateral vestibulopathy.

- Castle Creek Pharmaceuticals, LLC, a U.S. company, announced in December 2016 the in-licensing of Arlevert, a fixed-dose combination of cinnarizine, a calcium channel antagonist, and dimenhydrinate, an antihistamine, from Hennig Arzneimittel GmbH & Co. KG, a German company, and its intention to develop it as a treatment for vertigo for the U.S. market. Arlevert is approved and has been marketed for a long time in various countries outside the U.S.

The developments of Otonomy, Sensirion and Castle Creek 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 Ménière's disease, including steroids, diuretics, anti-emetics or anti-nausea medications as well as oral betahistine, the standard of care for treatment of Ménière's disease and vestibular vertigo 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.

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. For more information, please see "Item 3. Key Information—D. Risk factors—Risks Related to Intellectual Property."

As of December 31, 2016, we own five issued U.S. patents and nine pending U.S. patent applications along with foreign counterparts of such patents and applications in various jurisdictions. We co-own four 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, we co-own two of our pending applications with Xigen pursuant to the terms of our collaboration and license agreement.

In addition, as of December 31, 2016, we have exclusively licensed from Xigen twelve issued U.S. patents and three 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 acute sensorineural hearing loss.

With respect to our issued patents in the United States and Europe, 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.

The patent portfolios for our two leading product candidates as well as other related filings as of December 31, 2016 are summarized below.

Keyzilen®

We are the owner or co-owner of patents and patent applications relating to Ketamine or its use in inner ear tinnitus. In particular, we have an agreement entitled "Co-Ownership/Exploitation Agreement" with INSERM with respect to its Ketamine patent portfolio. We have rights to four issued U.S. patents and one pending U.S. applications 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.

AM-111

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 twelve issued U.S. patents and three pending U.S. applications 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 AM-111 are expected to expire between 2020 and 2027, prior to any patent term extensions to which we may be entitled under applicable laws. In addition, we co-own two patent families with Xigen related to use of JNK ligand peptides for the treatment of Ménière's disease or tinnitus.

We have several areas of disagreement with Xigen, including (i) our interpretation of the scope of the exclusive worldwide license granted to us by Xigen, (ii) the assignment by Xigen of certain of the patents covered by the license and (iii) Xigen's refusal to grant its consent for the disclosure of certain provisions of our agreement in the prospectus associated with our initial public offering and the filing of a redacted version of the agreement with the SEC. Although the difference in interpretation over the scope of the license has no impact on our current or planned use of AM-111 and we have been assured by Xigen and its assignee that the assignment of patents is without prejudice to our license, these areas of disagreement could adversely affect our relationship with Xigen and our business, commercialization prospects and financial conditions. Although Xigen has not taken any action as of the date of this Annual Report, any resulting litigation could result in substantial legal expenses and potentially the loss of our right to commercialize AM-111. For a discussion of these issues, please refer to "Item 3. Key Information—D. Risk factors —Risks Related to our Reliance on Third Parties—We have several areas of disagreement with Xigen, and consequently our relationship with Xigen may be adversely affected, we could potentially lose our right to commercialize AM-111 and our business, commercialization prospects and financial condition may be adversely affected."

Additional Patents and Applications

In addition to the Keyzilen® and AM-111 patent portfolios, we own one issued and four U.S. patent applications directed to poloxamer-based compositions with actives including fluoroquinolone antibiotics, steroids, or gacyclidine. Although these applications are not directed to our Keyzilen® or AM-111 products, they can provide a competitive advantage in the relevant market.

On July 20, 2015, the USPTO declared Patent Interference No. 106,030 involving our issued U.S. patent No. 9,066,865 (the "'865 Patent") and Otonomy's U.S. patent application No. 13/848,636 (the "'636 Application"). The patent interference identified claims 1-9 in the '865 Patent as interfering with claims 38, 43 and 46-50 of the '636 Application. The '865 Patent discloses methods of treating inner or middle ear diseases with intratympanic injections of poloxamer-based compositions. The claims of the '865 Patent are directed to the use of fluoroquinolone antibiotics in poloxamer 407 compositions under certain specifications. On January 26, 2017, the USPTO issued a decision on the interference granting Auris benefit of priority. As a result of the decision, judgment was entered against Otonomy and all claims in the '636 Application were refused. In addition, claims 1-8 of the '865 Patent were cancelled as the result of the USPTO's determination that the written description of the specification lacked full scope support for treating middle or inner ear disease with fluoroquinolone. However, claim 9, which is directed to a method of treating viral and bacterial infections with intratympanic injection of a fluoroquinolone antibiotic in a poloxamer 407 composition under certain specifications, was affirmed. The USPTO's decision is not final and may be appealed. Although we are still analyzing what effect, if any, the cancellation of claims 1-8 of the '865 Patent will have on the remainder of the '865 patent family, we do not expect the interference proceedings to impact our intellectual property portfolio relating to Keyzilen® and AM-111. See "Item 3. Key Information—D. Risk factors—Risks Related to Intellectual Property.

We have acquired one United States patent from Otifex directed to intranasal application of betahistine for eustachian tube dysfunction and we have filed a patent application directed at the application of the formulation for vestibular disorders.

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.

Janssen, a subsidiary of Johnson & Johnson, has been testing Esketamine in a spray formulation for intranasal treatment of treatment-resistant depression in several clinical trials to date, with a Phase 3 program starting in 2015. In November 2014, the FDA designated Esketamine a 'breakthrough therapy' for this indication. In the event that Janssen's confirmatory trials are successful and the company receives marketing authorization prior to us receiving marketing authorization for Keyzilen®, we would lose the potential benefit of a five year market exclusivity period that we would otherwise expect to obtain.

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 AM-111 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.

We have obtained U.S. trademark registrations for Auris, Auris Medical, Auris Medical Cochlear Therapies (and Design) and Keyzilen®.

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 Institut National de la Santé et de la Recherche Médicale, or 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.

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 S.A., or 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 active pharmaceutical ingredient for AM-111 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 AM-111. In October 2013, Xigen assigned certain of the patents relevant to the agreement to Xigen Inflammation Ltd, Cyprus, an unaffiliated party.

There have been several areas of disagreement with Xigen, primarily related to interpreting the definition of the Area, the transfer of patents to Xigen Inflammation Ltd. and to the disclosure of certain provisions of the agreement in the context of our initial public offering. For a discussion of these issues, please refer to "Item 3. Key Information—D. Risk factors —Risks Related to our Reliance on Third Parties—We have several areas of disagreement with Xigen, and consequently our relationship with Xigen may be adversely affected, we could potentially lose our right to commercialize AM-111 and our business, commercialization prospects and financial condition may be adversely affected."

Manufacturing

We currently rely on and expect to continue to rely on third parties for the supply of raw materials and to manufacture drug supplies for clinical trials of our product candidates, including Keyzilen® and AM-111. 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 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, 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 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, both in hospitals and in private practice. In other markets, we expect to seek partnerships that would maximize our products' commercial potential.

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

Clinical trials typically 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, or PDUFA, 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 Active Pharmaceutical Ingredient, or 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.

Special Protocol Assessment

The FDA and an IND sponsor may agree in writing on the design and size of clinical studies intended to form the primary basis of a claim of effectiveness in an NDA. This process is known as a special protocol assessment, or SPA. Upon a specific request for an SPA by an IND sponsor, the FDA will evaluate the protocol. If an SPA agreement is reached, however, it is not a guarantee of product approval by the FDA or approval of any permissible claims about the product. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement. In particular, the SPA agreement is not binding on the FDA if previously unrecognized public health concerns later come to light, other new scientific concerns regarding product safety or efficacy arise, the IND sponsor fails to comply with the protocol agreed upon, or the relevant data, assumptions, or information provided by the IND sponsor when requesting an SPA agreement change, are found to be false statements or misstatements, or are found to omit relevant facts. An SPA agreement may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA, or if the FDA determines that a substantial scientific issue essential to determining the safety or effectiveness of the drug was identified after the testing began.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the US, or if it affects more than 200,000 individuals in the US there is no reasonable expectation that the cost of developing and making a drug product available in the US for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA or if our drug candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the European Union has similar but not identical benefits in that jurisdiction.

DEA Regulation

The Drug Enforcement Administration, or DEA, regulates drugs that are controlled substances. Controlled substances are those drugs that appear on one of the five schedules promulgated and administered by the DEA under the Controlled Substances Act, or CSA, such as Ketamine, which is a Schedule III controlled substance. The CSA governs, among other things, the inventory, distribution, recordkeeping, handling, security and disposal of controlled substances. Any drug that acts on the central nervous system has the potential to become a controlled substance, and scheduling by the DEA is a separate process that may delay the commercial launch of a drug even after FDA approval of the NDA. Companies with a scheduled drug are subject to periodic and ongoing inspections by the DEA and similar state drug enforcement authorities to assess ongoing compliance with the DEA's regulations. Any failure to comply with these regulations could lead to a variety of sanctions, including the revocation or a denial of renewal of any DEA registration, injunctions, or civil or criminal penalties.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;

- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Other Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state healthcare laws govern certain business practices in the biopharmaceutical industry. These laws include, but are not limited to, anti-kickback, false claims, data privacy and security, and transparency statutes and regulations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any good, facility, item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term “remuneration” has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and our practices may not in all cases meet all of the criteria for a statutory exception or safe harbor protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Several courts have interpreted the statute’s intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. A person or entity does not need to have actual knowledge of the statute or the specific intent to violate it in order to have committed a violation. In addition, 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 civil False Claims Act (discussed below). Further, the civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal false claims laws, including the civil False Claims Act, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-covered, uses. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, prohibits knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of, or payment for, healthcare benefits, items or services.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, imposes certain requirements on certain types of individuals and entities relating to the privacy, security and transmission of individually identifiable health information. In addition, certain state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act requires that certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

Also, many states have similar healthcare statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Certain states require the posting of information relating to clinical studies, pharmaceutical companies to implement a comprehensive compliance program that includes a limit on expenditures for, or payments to, individual medical or health professionals and track and report gifts and other payments made to physicians and other healthcare providers. If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion of products from reimbursement under government programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products will be sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Pharmaceutical Coverage, Pricing and Reimbursement

In both domestic and foreign markets, our sales of any approved 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 other 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.

C. Organizational structure

The registrant corporation, Auris Medical Holding AG, has four wholly owned subsidiaries 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 headquarters are in Zug, Switzerland. We also lease approximately 5,900 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 focused on the development of novel products for the treatment of inner ear disorders. Our most advanced product candidates are in Phase 3 clinical development. Keyzilen® (AM-101) is being developed for the treatment of acute inner ear tinnitus and has received fast track designation from the FDA. In two Phase 2 clinical trials, Keyzilen® demonstrated a favorable safety profile and statistically significant improvement in tinnitus loudness and other patient reported outcomes. In August 2016, we announced that the trial Efficacy and Safety of Keyzilen® (AM-101) in the Treatment of Acute Peripheral Tinnitus 2 (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 support the positive safety profile established in the Phase 2 trials. See "Item 4. Information on the Company – Business Overview – Keyzilen® Phase 3 Clinical Program."

Following analysis of the TACTT2 data, we amended the protocol for the TACTT3 trial, the second Phase 3 clinical trial with Keyzilen®. TACTT3 is being conducted in several European countries. Under the amended protocol, the trial size will be increased, certain patient subgroups will be included in confirmatory testing and the TFI will be elevated from a key secondary endpoint to an alternate primary efficacy endpoint. We have commenced enrollment under the amended protocol and expect to have top-line results from the expanded TACTT3 trial in early 2018.

We are also developing AM-111 for acute inner ear hearing loss. We are conducting two pivotal Phase 3 trials in the treatment of idiopathic sudden sensorineural hearing loss, titled HEALOS and ASSENT. HEALOS is enrolling 255 patients in Europe and Asia, and ASSENT is enrolling 300 patients in the United States, Canada and South Korea. As of September 2016, HEALOS had enrolled 50% of patients, and we expect to have top-line data from HEALOS in the third quarter of 2017. ASSENT started enrollment in June 2016, and we expect to have top-line data from the trial in the second half of 2018.

On February 2, 2017, we entered into an asset purchase agreement with Otifex, pursuant to which we agreed to purchase and Otifex has agreed to sell us certain preclinical and clinical assets related to a formulation for the intranasal application of Betahistine, which we refer to as AM-125. See "Item 4. Information on the Company – Business Overview – AM-125 in Vestibular Disorders."

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, 2016, we had cash and cash equivalents of CHF 32.4 million. Based on our current plans, we do not expect to generate royalty or product revenues unless and until we obtain marketing approval for, and commercialize, Keyzilen®, AM-111 or any of our other product candidates.

As of December 31, 2016, we had an accumulated deficit of CHF 112.3 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 Institut National de la Santé et de la Recherche Médicale, or 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 S.A., or Xigen, pursuant to which Xigen granted us an exclusive worldwide license to use specified compounds to develop, manufacture and commercialize "pharmaceutical products as well as drug delivery devices and formulations for local administration of therapeutic substances to the inner ear for the treatment of ear disorders" (the Area). We also have a right of first refusal to license certain additional compounds developed by Xigen which may be used for the Area, specifically any cell permeable inhibitors to effectively block certain signal pathways in apoptotic processes.

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

Otifex

On February 2, 2017, we entered into an asset purchase agreement with Otifex, pursuant to which we agreed to purchase and Otifex has agreed to sell us certain preclinical and clinical assets related to a formulation for the intranasal application of Betahistine, which we refer to as AM-125. We plan to develop the formulation for vestibular disorders. The asset purchase agreement provides for an upfront payment and a development milestone payment which, in the aggregate equal an amount less than $500,000.

Financial Operations Overview

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 and drug substances 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.

We expect that our operating expenses in 2017 will be in the range of CHF 28 to 32 million, the majority of which we expect to be research and development expense. Our research and development expense mainly relates to the following key programs:

- *Keyzilen® (AM-101).* We are conducting a Phase 3 clinical development program with Keyzilen® comprising two Phase 3 trials and two open label follow-on trials. In August 2016, we announced that the 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. We expect top-line results of the amended TACTT3 trial in early 2018. In the two open label follow-on trials, AMPACT1 and AMPACT2, the last subjects completed the trial in September and December 2016, respectively. We expect that the topline data from AMPACT1 and AMPACT2 will become available in the second quarter of 2017. We anticipate that our research and development expenses in connection with these clinical trials will be lower in 2017 than in 2016, reflecting the lower number of active trials.
- *AM-111*. We are conducting two pivotal Phase 3 trials in the treatment of ISSNHL, titled HEALOS and ASSENT. HEALOS is enrolling 255 patients in Europe and Asia, and ASSENT is enrolling 300 patients in the United States, Canada and South Korea. HEALOS had enrolled 50% of the target patient number in September 2016, and we expect to have top-line data from HEALOS in the third quarter of 2017. ASSENT started enrollment in June 2016, and we expect to have top-line data from the trial in the second half of 2018. We anticipate that our research and development expenses in connection with the two AM-111 trials in 2017 will be comparable to those in the previous year.
- *AM*-125. We plan to initiate a Phase 1 trial in healthy volunteers in 2017 to test the safety and tolerability of AM-125. We expect to obtain the results of the study in the first half 2018.

Other research and development expenses mainly relate to our pre-clinical studies of AM-102 and AM-123. The expenses mainly consist of costs for production of the pre-clinical compounds and costs paid to academic research institutions in conjunction with pre-clinical testing.

For the years ended December 31, 2016, 2015 and 2014, we spent CHF 15.3, CHF 19.7 and CHF 12.5 million, respectively, on research and development expenses related to Keyzilen®. For the same time periods, we spend CHF 9.4 million, CHF 6.4 million and CHF 4.8 million, respectively, on research and development expenses related to AM-111. In addition, we incurred research and development expenses related to our earlier stage products. These expenses exclude the milestone payment to Xigen for AM-111 as it was capitalized. Research and development expenses are expected to remain at significant levels as we advance the clinical development of Keyzilen®, AM-111 and AM-125. 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 Keyzilen®, AM-111 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 preclinical 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.

We expect that our general and administrative expense will increase in the future as our business expands and we incur additional costs associated with operating as a public company. These public company-related increases will likely include costs of additional personnel, additional legal fees, accounting and audit fees, managing directors' and supervisory directors' liability insurance premiums and costs related to investor relations.

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. We expect to continue this investment philosophy.

Interest expense

Our interest expense consists principally of bank charges and interest expenses due to the Loan and Security Agreement with Hercules.

Revaluation gain/(loss) from derivative financial instruments

In connection with the Hercules Loan and Security Agreement, the Company issued Hercules a warrant to purchase up to 241,117 of its common shares at an exercise price of $3.94 per share. Revaluation gain/(loss) show the changes in fair value of the warrant issued to Hercules.

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.

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.

We determine the net interest expense or income on the net defined benefit liability or 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 or asset, taking into account any changes in the net defined benefit liability or 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.

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, 2016 and 2015

	Year Ended December 31,		
	2016	2015	Change
	(in thousands of CHF)		%
Research and development	(24,777)	(26,536)	(7%)
General and administrative	(5,447)	(4,342)	25%
Operating loss	**(30,223)**	**(30,878)**	**(2%)**
Interest income	68	37	84%
Interest expense	(829)	(8)	10,263%
Foreign currency exchange gain/(loss), net	(100)	1,144	(109%)
Revaluation gain/(loss) from derivative financial instruments	291	–	–
Loss before tax	**(30,793)**	**(29,705)**	**4%**
Income tax gain	131	–	–
Net loss attributable to owners of the Company	**(30,662)**	**(29,705)**	**3%**
Other comprehensive loss:			
Items that will never be reclassified to profit or loss			
Remeasurements of defined benefits liability	(394)	(54)	630%
Items that are or may be reclassified to profit or loss			

	Year Ended December 31,		
	2016	2015	Change
	(in thousands of CHF)		%
Foreign currency translation differences	(20)	(13)	54%
Other comprehensive loss	**(414)**	**(67)**	**518%**
Total comprehensive loss attributable to owners of the Company	**(31,076)**	**(29,772)**	**4%**

Research and development expense

	Year Ended December 31,		
	2016	2015	Change
	(in thousands of CHF)		%
Research and development expense			
Clinical projects	(16,639)	(20,808)	(20%)
Preclinical projects	(546)	(468)	17%
Drug manufacture and substance	(2,609)	(1,866)	40%
Employee benefits	(2,855)	(2,140)	33%
Other research and development expenses	(2,128)	(1,253)	70%
Total	**(24,777)**	**(26,536)**	**(7%)**

Research and development expense decreased by 7% from CHF 26.5 million in 2015 to CHF 24.8 million in 2016. 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 2015 and 2016 are mainly due to the following factors:

- *Clinical projects*. In 2016 we incurred lower clinical expenses related to our Phase 3 clinical program with Keyzilen® than in 2015. Expenses decreased in 2016 primarily due to lower service and milestone costs charged by contracted service providers, reflecting the completion of the TACTT2 trial and progress in our open label follow-on studies AMPACT1 and AMPACT2. The decrease of Keyzilen® related expenses was partially offset by an increase of cost related to our Phase 3 clinical program with AM-111 reflecting the progress in recruitment in HEALOS and the initiation of patient recruitment in the ASSENT trial.

- *Preclinical projects*. In 2016 preclinical expenses increased due to an increase in activities in our early stage program AM-102.

- *Drug manufacture and substance*. In 2016, drug manufacturing expenses increased due to the validation of the Keyzilen® drug product manufacturing process, work performed for the AM-111 drug product validation as well as the production of clinical supplies for the AM-111 trials.

- *Employee benefits*. Employee benefits increased in 2016 due to an increase in headcount and higher compensation expenses.

General and administrative expense

	Year Ended December 31,		
	2016	2015	Change
	(in thousands of CHF)		%
General and administrative expense			
Employee benefits	(2,175)	(1,503)	45%
Administration expenses	(2,970)	(2,387)	24%
Other	(302)	(452)	(33%)
Total	**(5,447)**	**(4,342)**	**25%**

General and administrative expenses increased by 25% from CHF 4.3 million in 2015 to CHF 5.4 million in 2016.

- *Employee benefits*. Headcount continued to increase in 2016 in line with the expansion of administrative staff and the management team. Employee benefits also reflect an increase in share-based payments and pension charges.

- *Administration expenses.* The increase reflects higher legal, consulting and auditing expenses associated with operating as a public company.

- *Other*. In 2016, these expenses, which comprise facility, business development and travel costs, decreased from previous year's level.

We expect that general and administrative expense will increase in the future as our business expands and we continue to increase headcount as well as continue to incur additional costs associated with operating as a public company.

Interest income

Interest income increased due to higher interest rates on short-term deposits.

Interest expense

Interest expense increased substantially in 2016, as a result of the Hercules Loan and Security Agreement. On June 19, 2016, we drew $12.5 million under the facility. The loan was initially recognized at transaction value less the fair value of the warrant as of the transaction date and less directly attributable transactions costs. Following the initial recognition, the loan is measured at amortized cost using the effective interest method. Changes in amortized cost as well as interest paid to Hercules are recognized as interest expense. In addition, we recognized bank charges as interest expense.

Foreign currency exchange gain/(loss), net

Foreign currency exchange gains/(loss), net decrease in 2016 due to lower foreign exchange losses on the Company's U.S. dollar denominated cash and cash equivalents.

Revaluation gain/(loss) from derivative financial instruments

In connection with the Hercules Loan and Security Agreement, the Company issued Hercules a warrant to purchase up to 241,117 of its common shares at an exercise price of $3.94 per share. As of December 31, 2016, the warrant was exercisable for 156,726 common shares and the fair value of the warrant amounted to CHF 117,132. Since its initial recognition, the fair value decreased by CHF 291,048 resulting in a gain in the corresponding amount (fair value as of July 19, 2016: CHF 408,180).

Income tax gain

Income tax gain reflects the reassessment of deferred tax assets and liabilities booked in the 2014 and 2015 fiscal years.

Remeasurements of defined benefits liability

Remeasurements of the net defined benefits liability, which comprise actuarial gains and losses, the return on plan assets (excluding interest) and the effect of the asset ceiling (if any, excluding interest), increased by 630% from 2015 to 2016. The increase was due a change in the discount rate and a change in demographic assumptions.

Foreign currency translation differences

Foreign currency translation differences increased by 54% from 2015 to 2016. 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, 2015 and 2014

	Year Ended December 31,		
	2015	2014	Change
	(in thousands of CHF)		%
Research and development	(26,536)	(17,705)	50%
General and administrative	(4,342)	(4,489)	(3%)
Operating loss	**(30,878)**	**(22,194)**	**39%**
Interest income	37	52	(30%)
Interest expense	(8)	(56)	(86%)
Foreign currency exchange gain/(loss), net	1,144	4,012	(71%)
Loss before tax	**(29,705)**	**(18,185)**	**(63%)**
Income tax expense	–	–	–
Net loss attributable to owners of the Company	**(29,705)**	**(18,185)**	**63%**
Other comprehensive loss:			
Items that will never be reclassified to profit or loss			

	Year Ended December 31,		
	2015	2014	Change
	(in thousands of CHF)		%
Remeasurements of defined benefits liability, net of taxes of CHF 0	(54)	(1,102)	(95%)
Items that are or may be reclassified to profit or loss			
Foreign currency translation differences, net of taxes of CHF 0	(13)	(105)	(88%)
Other comprehensive loss	**(67)**	**(1,207)**	**(94%)**
Total comprehensive loss attributable to owners of the Company	**(29,772)**	**(19,392)**	**54%**

Research and development expense

	Year Ended December 31,		
	2015	2014	Change
	(in thousands of CHF)		%
Research and development expense			
Clinical projects	(20,808)	(12,142)	71%
Preclinical projects	(468)	(1,160)	(60%)
Drug manufacture and substance	(1,866)	(1,384)	35%
Employee benefits	(2,140)	(1,718)	25%
Other research and development expenses	(1,253)	(1,301)	(4%)
Total	**(26,535)**	**(17,705)**	**50%**

Research and development expense increased 50% from CHF 17.7 million in 2014 to CHF 26.5 million in 2015. Our research and development expense is dependent on the development phases of our research projects and therefore fluctuates significantly from year to year. The variances in expense between 2014 and 2015 are mainly due to the following factors:

- *Clinical projects*. In 2015, we incurred significantly higher clinical expenses than in 2014, primarily due to higher service and milestone costs charged by contracted service providers in connection with the late stage Keyzilen® clinical trials, reflecting higher patient enrollment rates when compared with the previous reporting period and trial progress. For AM-111, we also incurred higher expenses related to the start of patient recruitment in the Phase 3 HEALOS trial.

- *Preclinical projects*. In 2015, we incurred significantly lower expenses as several toxicology studies were completed in 2014.

- *Drug manufacture and substance*. In 2015, we incurred higher expenses primarily related to the production of validation batches for Keyzilen®, which were partly offset by lower expenses for AM-111 due to fluctuations in the timing of raw material purchases and the manufacture of clinical trial supplies.

- *Employee benefits*. Headcount continued to increase in 2015 to support expanded project management activities.

General and administrative expense

	Year Ended December 31,		
	2015	2014	Change
	(in thousands of CHF)		%
General and administrative expense			
Employee benefits	(1,503)	(1,137)	32%
Administration expenses	(2,387)	(2,014)	18%
Initial public offering expenses, expensed	–	(822)	(100%)
Other	(452)	(516)	(12%)
Total	**(4,342)**	**(4,489)**	**(3%)**

General and administrative expenses decreased by 3% from CHF 4.5 million in 2014 to CHF 4.3 million in 2015.

- *Employee benefits*. Headcount continued to increase in 2015 in line with the expansion of administrative staff established after becoming a publicly listed company. Employee benefits also reflect an increase in share-based payments and pension charges.

- *Administration expenses*. The increase reflects higher consulting and auditing expenses associated with operating as a public company.

- *Initial public offering expenses, expensed*. These initial public offering expenses were expensed in the three months ended March, 31, 2014, as management determined that successful completion was not deemed more likely than not. No such expenses were incurred in 2015.

- *Other*. In 2015, these expenses were on aggregate broadly in line with 2014 and comprise facility, business development and travel costs.

We expect that general and administrative expense will increase in the future as our business expands and we continue to increase headcount as well as continue to incur additional costs associated with operating as a public company.

Interest income

Interest income decreased from CHF 0.05 million in 2014 to CHF 0.04 million in 2015 due to the lower interest rates on short-term deposits.

Interest expense

Interest expense decreased substantially in 2015, as convertible loans had been converted in 2014. In 2014 we recognized interest expenses in the amount of CHF 0.05 million on the convertible loans.

Foreign currency exchange gains/(losses), net

Foreign currency exchange gains/(losses), net decreased in 2015 due to lower foreign exchange gains on the Company's U.S. dollar denominated cash and cash equivalents.

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 95% from 2014 to 2015. The decline was due to higher return on plan assets offset by lower actuarial losses on changes in experience adjustments and actuarial gains from changes in economic assumptions.

Foreign currency translation differences

Foreign currency translation differences decreased by 88% from 2014 to 2015. 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, 2016 and 2015

The table below summarizes our consolidated statement of cash flows for the years ended December 31, 2016 and 2015:

	Year Ended December 31,	
	2016	2015
	(in thousands of CHF)	
Net cash used in operating activities	(29,454)	(28,727)
Net cash used in investing activities	(177)	(43)
Net cash from financing activities	11,439	20,919

	Year Ended December 31,	
	2016	2015
	(in thousands of CHF)	
Net effect of currency translation on cash	397	1,155
Cash and cash equivalents at the beginning of the period	50,237	56,934
Cash and cash equivalents at the end of the period	**32,442**	**50,237**

The increase in cash used in operating activities from CHF 28.8 million in 2015 to CHF 29.5 million in 2016 reflects the change in working capital.

Cash used in investing activities reflects, in both 2016 and 2015, cash used in the purchase of property, plant and equipment (manufacturing equipment, leasehold improvements and office furniture) offset by interest received.

Cash from financing activities in 2016 reflects the net proceeds (CHF 12.0 million) from the drawdown of a $12.5 million tranche under the Loan and Security Agreement with Hercules and accounts for interest payments to Hercules as well as share issuance cost incurred in connection with restricted shares issued as a management bonus. Cash from financing activities in 2015 reflects the net proceeds (CHF 21.1 million) from our public offering of 5,275,000 common shares at a price of $4.75 per share. The proceeds were partially offset by issuance costs associated with the offering.

Comparison of the years ended December 31, 2015 and 2014

The table below summarizes our consolidated statement of cash flows for the years ended December 31, 2015 and 2014:

	Year Ended December 31,	
	2015	2014
	(in thousands of CHF)	
Cash used in operating activities	(28,727)	(19,316)
Net cash used in investing activities	(43)	(1,186)
Net cash from financing activities	20,919	49,609
Net effect of currency translation on cash	1,155	3,962
Cash and cash equivalents at the beginning of the period	56,934	23,866
Cash and cash equivalents at the end of the period	**50,237**	**56,934**

The increase in cash used in operating activities from CHF 19.3 million in 2014 to CHF 28.8 million in 2015 was mainly due to an increase in research and development expenses as well as general and administrative expenses other than share-based payments (non-cash item).

Cash used in investing activities reflects, in both 2015 and 2014, cash used in the purchase of property, plant and equipment (manufacturing equipment and office furniture) offset by interest received. In 2014, it includes a CHF 1.125 million cash milestone payment to Xigen.

Cash from financing activities in 2015 reflects the net proceeds (CHF 21.1 million) from our public offering of 5,275,000 common shares at a price of $4.75 per share. The proceeds were partially offset by issuance costs associated with the offering. In 2014, net cash from financing activities was CHF 49.6 million, reflecting the net effect of proceeds from our initial public offering in August 2014.

Cash and funding sources

The table below summarizes our sources of financing for the years ended December 31, 2016, 2015 and 2014.

	Equity Capital and Preferred Shares	Loans	Total
		(in thousands of CHF)	
2016	–	11,987	11,987
2015	21,071	–	21,071
2014	50,038	–	50,038
Total	**71,109**	**11,987**	**83,096**

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 matures on January 2, 2020 and bears interest at a minimum rate of 9.55% per annum, and is subject to the variability of the prime interest rate. The loan is 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 241,117 of our common shares at an exercise price of $3.94 per share. As of December 31, 2016, the warrant is exercisable for 156,726 common shares.

On June 1, 2016, we entered into a Controlled Equity Offering Sales Agreement with Cantor, pursuant to which we may offer and sell, from time to time common shares, with a nominal value of CHF 0.40 per share, having an aggregate offering price of up to $35 million through Cantor. Any common shares offered and sold will be issued pursuant to our shelf registration statement on Form F-3 as supplemented by a prospectus supplement, dated June 1, 2016. In the year ended December 31, 2016, we did not offer or sell any common shares under the Controlled Equity Offering Sales Agreement.

On May 20, 2015, we completed a public offering of 5,275,000 common shares at a price to the public of $4.75 per share. The net proceeds of the public offering were CHF 21.1 million.

Our sources of financing in 2014 included the initial public offering of 10,113,235 common shares providing net proceeds (after underwriting fees, initial public offering and share issuance costs) of CHF 49.60 million.

We have no 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 believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements at least until the first quarter of 2018. 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 late-stage Keyzilen® and AM-111 clinical program, obtain regulatory approval for Keyzilen® and AM-111 and to commercialize our product candidates Keyzilen® and AM-111. If we receive regulatory approval for Keyzilen® or AM-111, 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. Likewise, if we are unable to refinance amounts outstanding under our existing term loan facility before such amounts are due we may be unable to repay such amounts, which could result in foreclosure of the collateral pledged to secure such loan.

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

Expenditures on the research programs of the Company are not capitalized, they are expensed when incurred.

Expenditures on the Company’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 Company intends to and has sufficient resources to complete development and to use or sell the asset. For the development projects of the Company, these criteria are generally only met when regulatory approval for commercialization is obtained. Given the current stage of the development projects, no development expenditures have yet been capitalized. 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 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 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

Share Options

The Company maintains various share-based payment plans in the form of stock option plans 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. The vesting of share options is conditional on the employee completing a period of service of three and four years respectively, from the grant date, in accordance with Plans A and C. Under the Company's Equity Incentive Plan ("the 2014 Plan"), 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 in 2015 and 2016 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 (nominal value) and share premium.

Valuation of share options

The fair value of our shares 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 common shares as of each grant date.

In our historical financing rounds, we have mainly relied on the prior sale of stock method where the Company and new investors negotiate the Company's valuation at arm's length. Typical considerations in this method may include the type and amount of equity sold, the estimated volatility, the estimated time to liquidity, the relationship of the parties involved, the timing compared to the common shares valuation date and the financial condition and structure of the Company at the time of the sale.

Following the completion of our initial public offering, 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.

JOBS Act exemptions

On April 5, 2012, the JOBS Act was signed into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an "emerging growth company." As an emerging growth company, we are electing to take advantage of the following exemptions:

- not providing an auditor attestation report on our system of internal controls over financial reporting;
- not providing all of the compensation disclosure that may be required of non-emerging growth public companies under the U.S. Dodd-Frank Wall Street Reform and Consumer Protection Act;
- not disclosing certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the Chief Executive Officer's compensation to median employee compensation; and
- not complying with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements (auditor discussion and analysis).

These exemptions will apply until 2019 or until we no longer meet the requirements of being an "emerging growth company," whichever is earlier. We would cease to be an emerging growth company if we have more than $1.0 billion in annual revenue, have more than $700 million in market value of our common shares held by non-affiliates or issue more than $1.0 billion of non-convertible debt over a three-year period.

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 operating lease mentioned below.

F. Tabular disclosure of contractual obligations

The following table presents information relating to our contractual obligations as of December 31, 2016:

	Payments Due by Period				
	Less Than 1 Year	1-3 Years	3-5 Years	More than 5 Years	Total
	(in thousands of CHF)				
Operating lease obligations (1)	161	261	364	0	786
Loan and Borrowings (2)	2,213	10,040	1,226	0	13,479
Derivative Financial Instruments (2)			117	0	117
Total	**2,374**	**10,301**	**1,707**	**0**	**14,382**

(1) Operating lease obligations consist of payments pursuant to an operating lease agreements relating to our lease of office space and are not accounted for on the balance sheet. The lease term of our lease in Basel, Switzerland, is 5 years and expires on September 30, 2021, with an option to extend for another five years. The lease may be terminated effective September 30, 2019 and is otherwise non-cancellable.

(2) Loan and borrowings consist of amortization payments and end of term charges due under the Hercules Loan and Security Agreement. The loan matures on January 2, 2020 and bears interest at a minimum rate of 9.55% per annum, and is subject to the variability of the prime interest rate. Interest payments are not included in the table presented above. The derivative financial instrument reflects the fair value of the warrants granted to Hercules.

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. Additionally, under the terms of our asset purchase agreement with Otifex, we are obligated to make a development milestone payment of $200,000 upon successful achievement of a target related to the betahistine spray formulation. 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.

G. Safe harbor

See "Forward-Looking Statements."

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and senior management

The following table presents information about our executive officers and directors. The term of each of our directors is one year and, accordingly, will expire at the time of our 2017 annual shareholder meeting. With the exception of Mr. Arnold and Mr. Healy, all directors have indicated that they will stand for re-election.

Name	Position	Age	Initial Year of Appointment
Executive Officers[1]			
Thomas Meyer	Chairman and Chief Executive Officer	49	2003
Andrea Braun-Scherhag	Head Regulatory & Quality Affairs	50	2016
Thomas Jung	Chief Development Officer	57	2016
Hernan Levett	Chief Financial Officer	41	2017
Anne Sabine Zoller[2]	General Counsel	37	2015
Non-Executive Directors			
Armando Anido	Director	59	2016
Wolfgang Arnold	Director	75	2007
James I. Healy	Vice-Chairman and Director	52	2013
Oliver Kubli	Director	44	2010
Berndt A.E. Modig	Director	58	2015
Antoine Papiernik	Director	50	2013
Calvin W. Roberts	Director	64	2015

(1) Effective August 31, 2016, Sven Zimmermann resigned his position as Chief Financial Officer of the Company and effective September 30, 2016, Bettina Mirella Stubinski resigned her position as Chief Medical Officer of the Company.

(2) Anne Sabine Zoller will resign from her position as General Counsel effective April 30, 2017.

Unless otherwise indicated, the current business addresses for our executive officers and directors is Auris Medical Holding AG, Bahnhofstrasse 21, 6300 Zug, Switzerland.

Executive Officers

Thomas Meyer, Founder, Chairman 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 holds a Ph.D. (Dr.rer.pol.) in business administration from the University of Fribourg, Switzerland.

Andrea Braun-Scherhag, Head Regulatory & Quality Affairs: Ms. Braun leads the Company's regulatory affairs, quality and pharmacovigilance departments. Prior to joining the Company, Ms. Braun was Head of Global Regulatory Affairs and Vice President at Alvotech. Prior to Alvotech, she spent 15 years in various regulatory affairs functions at Roche, most recently as Head of EU Regulatory Affairs, and five years in regulatory affairs at DSM Nutritional Products. Ms. Braun received her state examination in pharmacy from the University of Heidelberg, Germany, and holds a Ph.D. in immunology from the University of Basel, Switzerland.

Thomas Jung, Chief Development Officer: Mr. Jung leads the Company's clinical, preclinical and pharmaceutical development activities and the Company's chemistry, manufacturing and controls team. Prior to joining Auris Medical, Mr. Jung served as the Chief Medical Officer at Delenex Therapeutics AG and spent 13 years at Novartis, most recently as Head, Translational Medicine for the European Union. Since 2012, Mr. Jung serves as a member of the Board of Directors of AIMM Therapeutics and since 2016 as a member of the Scientific Advisory Committee of Topas Therapeutics GmbH. He is a board-certified dermatologist and is an Associate Professor for Dermatology at the University of Göttingen, Germany. He holds a Ph.D. and M.D. degree from the Philipps-University Marburg, Germany.

Hernan Levett, Chief Financial Officer: Mr. Levett joined the Company on January 1, 2017 as Chief Financial Officer. Prior to joining Auris Medical, Mr. Levett served as Head of Group Controlling at Acino Pharma AG. Prior to Acino, he served as Vice President of Finance and Administration Europe at InterMune International AG and spent 10 years at Novartis, most recently as Chief Financial Officer of Novartis Chile SA.

Mr. Levett is a certified public accountant and holds an accounting degree from the University of Buenos Aires, Argentina.

Anne Sabine Zoller, General Counsel: Ms. Zoller joined the Company as Senior Legal Counsel in April 2015 and was appointed General Counsel in August 2015. Prior to joining Auris Medical, Ms. Zoller was a Corporate/M&A Counsel with Straumann Group, a dental implant company headquartered in Basel, and an attorney in the Corporate/M&A team of Homburger AG, a Zurich based law firm. She obtained a Ph.D. in law from the University of Zurich and holds an M.B.A. degree.

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 serves 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 and Chairman of the Compensation Committee of Aviragen Therapeutics (formely: Biota Pharmaceuticals, Inc.). He was a member of the Board of Directors of Adolor Corporation until it was sold to Cubist Pharmaceuticals. Mr. Anido holds a BS in Pharmacy and an MBA from West Virginia University.

Wolfgang Arnold, Director: Dr. Arnold has been a member of our board of directors since 2007. He is a professor emeritus in otolaryngology and head and neck surgery, and an internationally renowned expert in the field of inner ear disorders. Dr. Arnold has authored or co-authored more than 365 peer-reviewed scientific and medical articles and more than 10 textbooks. From 1981 to 1992 he served as Head of the Department of Otorhinolaryngology, Head & Neck Surgery, Cantonal Hospital of Lucerne (Switzerland) and from 1992 to 2007 he served as Director of the Department of Otolaryngology, Head and Neck Surgery of the Technical University of Munich, Germany. He is still practicing today. Dr. Arnold holds an M.D. from the University of Munich.

James I. Healy, Vice-Chairman: Dr. Healy has been a member of our board of directors since April 2013. Dr. Healy has been a General Partner of Sofinnova Ventures, a venture capital firm, since June 2000. Prior to June 2000, Dr. Healy held various positions at Sanderling Ventures, Bayer Healthcare Pharmaceuticals (as successor to Miles Laboratories) and ISTA Pharmaceuticals, Inc. Dr. Healy is currently on the board of directors of Ascendis Pharma A/S, Coherus Bioscience, Inc., Edge Therapeutics, Inc., Natera, Inc., Observa SA and several private companies. Previously, he served as a board member of Amarin Corporation plc., Hyperion Therapeutics, Inc., CoTherix, Inc., Durata Therapeutics, Inc., InterMune, Inc., Movetis NV and several private companies. Dr. Healy was nominated to our board of directors by Sofinnova Ventures. Dr. Healy holds an M.D. and a Ph.D. in Immunology from the Stanford School of Medicine and holds a B.A. in molecular biology and a B.A. in Scandinavian Studies from the University of California at Berkeley.

Oliver Kubli, Director: Mr. Kubli has been a member of our board of directors since June 2010. He is a Managing Director and Head Portfolio Management Healthcare Funds & Mandates at Bellevue Asset Management AG. Mr. Kubli is the Senior Portfolio Manager for several public health care funds. Prior to joining Bellevue Asset Management, Mr. Kubli was Head Portfolio Management Healthcare Funds & Mandates of Adamant Biomedical Investments AG. Before joining Adamant in 2008, he held various management positions at ZKB and was responsible for the global health care sector within the bank's Asset Management Division. Mr. Kubli started his career as a financial analyst and portfolio manager with UBS and Swiss Re. He is a chartered financial analyst (CFA) and holds a B.A. in Business Administration from the University of Applied Sciences, Zürich/Winterthur, Switzerland.

Berndt A.E. Modig, Director, Chairman of the Audit Committee: Mr. Modig was elected to our board of directors in 2015. Mr. Modig is the Managing Director of Schoodic Management BV and has been the Chief Executive Officer of Pharvaris BV since April 2016. He was the Chief Financial Officer of Prosensa Holding N.V., a company dedicated to the development of treatments of neuromuscular and neurodegenerative disorders such as Duchenne Muscular Dystrophy, from 2010 up to its sale to Biomarin. Prior to that, he was the Chief Financial Officer of Jerini AG, another publicly listed biotechnology company, and held various management positions in industry, finance and private equity groups. He started his professional career in the auditing practice of Price Waterhouse. Berndt Modig is a member of the Board of Directors and the Audit Committee of Affimed N.V., a member of the Board of Directors and Chairman of the Audit Committee of Axovant Sciences, Ltd., a Vice-Chairman of the Board of Directors of Kiadis Pharma N.V. and a Chairman of its Audit Committee, and a member of the Board of Directors of Onco BioTek. Mr. Modig is a Certified Public Accountant and has an M.B.A. from INSEAD.

Antoine Papiernik, Director, Member of the Compensation Committee: Mr. Papiernik has been a member of our board of directors since April 2013. He is a Managing Partner at Sofinnova Partners, a French venture capital firm, which he joined in 1997. He serves on the boards of directors of Reflexion Medical Inc., MD Start, Shockwave Medical, Inc., Pixium Vision, ReCor Medical, ProQR Therapeutics BV, Mainstay Medical Ltd., Gecko Biomedical and Rgenix Inc. Mr. Papiernik was nominated to our board of directors by Sofinnova Partners. He has an M.B.A. from the Wharton School of Business.

Calvin W. Roberts, Director: Dr. Roberts was elected to our board of directors in 2015. Mr. Roberts, M.D., is Chief Medical Officer at Bausch + Lomb and Senior Vice President and Chief Medical Officer, Eye Care of Valeant Pharmaceuticals. He joined Bausch + Lomb in 2011. 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. He is the author of over 50 peer-reviewed articles. Dr. Roberts has been a member of the Board of Directors and the Audit Committee of Alimera Sciences, Inc., since it was founded in 2003.

B. Compensation

For the year ended December 31, 2016, 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 2,235,682 (2015: CHF 2,071,071).

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 88,838 in the year ended December 31, 2016 (2015: CHF 78,721).

We incorporate by reference into this Annual Report the information in “Item 2.3 — Compensation awarded to the Board of Directors in 2016” and “Item 3.4 —Compensation awarded to the Executive Management Committee” of Exhibit 99.4 to our report on Form 6-K filed with the SEC on March 14, 2017.

Employment Agreements

We have entered into employment agreements with our executive officers Thomas Meyer, Andrea Braun-Scherhag, Thomas Jung, Hernan Levett and Anne Sabine Zoller. The employment agreements provide for the compensation that our executive officers are entitled to receive, including certain equity grants, and contain termination notice periods of seven days for the first three months and then afterwards six-months’ notice. The Company will have title to the intellectual property rights developed in connection with the executive officer’s employment, if any. There is an 18 month non-compete period following the end of employment in our agreement with Mr. Meyer and a 12 month non-compete period following the end of employment in our agreement with Mr. Jung.

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, we established the 2014 Plan 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. As of December 31, 2016, the maximum number of shares available for issuance under the 2014 Plan was 3,936,047 common shares. The option exercise price for options under the 2014 Plan is determined by the compensation committee at the time of grant, but shall not be less than the nominal value of a share of common stock on the grant date.

Plan administration. The 2014 Plan is administered by our compensation committee. Approval of the committee is required for all grants of awards under the 2014 Plan. 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 2014 Plan.

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 2014 Plan provides that upon a change of control of the Company (as defined in the 2014 Plan) 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 2014 Plan). 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 2014 Plan subject, in certain circumstances, to required shareholder approval or the consent of an affected participant.

Prior Plans

In 2013 we established Stock Option Plan C, or Plan C, and in 2008 we established Stock Option Plan A, or Plan A and Stock Option Plan B, or Plan B. We refer to Plan A, Plan B and Plan C together as the Prior Plans. Each of the Prior Plans permits the grant of options, or Options, which are subject to transfer restrictions. As of December 31, 2016, there were 92,500 common shares underlying outstanding Options granted pursuant to Plan A and 121,250 common shares underlying outstanding Options granted pursuant to Plan C. There are no outstanding Options under Plan B, which was abolished in 2015. Following our initial public offering, we ceased issuing any new grants under Stock Option Plan C and adopted a new omnibus equity incentive plan under which we have the discretion to grant a broad range of equity-based awards to eligible participants.

Plan Administration. Under each of the Prior Plans, an Option, which can only be granted with the approval of our board of directors, is evidenced by an option agreement signed by the participant to indicate his or her acceptance of the Option subject to the terms and conditions of the applicable Prior Plan.

Eligibility. Under Plan A and Plan C, Options may be granted to directors, employees, advisors and agents of the Company.

Option Exercise Price. The exercise price of each Option is set forth in the applicable option agreement. The exercise prices for currently granted and unexercised Options range from USD 1.39 to USD 5.98.

Vesting Period. Under Plan A and Plan C, the option period commences on the date of grant and lasts for five years and six years, respectively. Options granted under Plan A vested and became immediately exercisable upon the closing of our initial public offering. Under Plan C, Options vest four years after grant.

Amendment. Our board of directors has the authority to amend each of the Prior Plans.

Indemnification

Subject to Swiss law, Article 17 of our articles of association provides for indemnification of the existing and former members of our board of directors, executive management, and their heirs, executors and administrators, against liabilities arising in connection with the performance of their duties in such capacity, and permits us to advance the expenses of defending any act, suit or proceeding to members of our board of directors and executive management. We also have entered into indemnification agreements with each of the members of our board of directors and executive officers in the form filed as Exhibit 4.3 to this Annual Report.

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 composed of eight members, see "Item 6. Directors, Senior Management and Employees—A. Directors and senior management." Each director is elected for a one year term. Our articles of association require our directors to retire once they have reached 75 years of age, subject to a special exception being granted by the general meeting of shareholders for up to two additional terms of office. The current members of our board of directors were appointed at a shareholders meeting held on April 8, 2016 for a one-year term ending at the next annual shareholders meeting.

We are a foreign private issuer. As a result, in accordance with the Nasdaq stock exchange listing requirements, we comply with 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 Berndt A.E. Modig, Oliver Kubli 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. Modig serves as chairman of the committee. The audit committee consists exclusively of members of our board of directors who are financially literate, and Mr. Modig and Mr. Kubli are considered "audit committee financial experts" as defined by the SEC. Our board of directors has determined that Mr. Modig, Mr. Kubli 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, Jim Healy and Antoine Papiernik, 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. Swiss law requires that we adopt a compensation committee, so in accordance with Nasdaq Listing Rule 5615(a)(3), we follow home country requirements with respect to the compensation committee. 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, 2016, we had 24 employees (21.5 full time equivalents), 13 of whom hold M.D. or Ph.D. degrees. 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 10, 2017, 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 10, 2017 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 10, 2017 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. As of March 10, 2017, 34,006,385 common shares, or approximately 77%, are held by two holders in the United States. Unless otherwise indicated below, the address for each beneficial owner is Auris Medical Holding AG, Bahnhofstrasse 21, 6300 Zug, Switzerland.

The percentage of common shares beneficially owned is based on 44,329,704 common shares issued and outstanding as of March 10, 2017. Each common share confers the right on the holder to cast one vote at a general meeting of shareholders and no shareholder has different voting rights.

Shareholder	Shares Beneficially Owned	
	Number	Percent
5% Shareholders		
Sofinnova Venture Partners VIII, L.P. (1)	9,218,175	20.79%
Sofinnova Capital VII FCPR (2)	5,384,450	12.15%
Empery Asset Management, LP (3)	4,250,000	9.59%
Executive Officers and Directors		
Thomas Meyer, Ph.D. (5)	7,672,500	17.31%
Armando Anido, M.B.A (6)	3,750	*
Wolfgang Arnold, M.D. (7)	57,657	*
James I. Healy, M.D., Ph.D. (8)	9,237,082	20.84%
Oliver Kubli, C.F.A.(9)	2,213,532	4.99%
Antoine Papiernik, M.B.A. (10)	5,384,450	12.15%
Berndt A.E. Modig, M.B.A (6).	12,500	*
Calvin W. Roberts, M.D.(11)	67,742	*
Andrea Braun-Scherhag	4,300	*
Thomas Jung, M.D.	–	–
Hernan Levett, CPA	–	–
Anne Sabine Zoller, Dr.iur.	–	–

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

(1) Consists of 7,818,175 common shares and warrants to purchase an additional 1,400,000 common shares. James I. Healy and the other managing members of Sofinnova Management VIII, L.L.C., which is the general partner of Sofinnova Venture Partners VIII, L.P., share the power to vote or dispose of these shares and therefore may be deemed to have voting and investment power with respect to such shares. Each of the managing members disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein, if any. The address for Sofinnova Venture Partners VIII, L.P. and Sofinnova Management VIII, L.L.C. is 2800 Sand Hill Road, Suite 150, Menlo Park, California 94025, USA.

(2) Consists of 5,384,450 common shares held by Sofinnova Capital VII FCPR. Sofinnova Partners SAS, a French corporation and the management company of Sofinnova Capital VII FCPR, may be deemed to have sole voting and investment power, and Denis Lucquin, Antoine Papiernik, Rafaèle Tordjman and Monique Saulnier, the managing partners of Sofinnova Partners SAS, may be deemed to have shared voting and investment power with respect to such shares. All of the managing partners of Sofinnova Partners SAS disclaim beneficial ownership of such shares except to the extent of their pecuniary interest therein. The address for Sofinnova Capital VII FCPR is 16-18 Rue du Quatre Septembre, 75002 Paris, France.

(4) Based on a Schedule 13G filed with the SEC on February 14, 2017 by Empery Asset Management, LP. Consists of 2,500,000 common shares and warrants to purchase an additional 1,750,000 common shares. The address of Empery Asset Management, L.P. is 1 Rockefeller Plaza, Suite 1205, New York, New York 10020, USA.

(5) Consists of 7,242,500 common shares, warrants to purchase 350,000 common shares and options to purchase 50,000 shares under the Company's Stock Option Plan A and options to purchase 30,000 common shares under the Company's Equity Incentive Plan.

(6) Consists of options to purchase common shares under the Company's Equity Incentive Plan.

(7) Consists of 32,500 common shares options to purchase an additional 6,250 common shares under the Company's Stock Option Plan A and options to purchase an additional 18,907 common shares under the Company's Equity Incentive Plan.

(8) Consists of 7,818,175 common shares and warrants to purchase an additional 1,400,000 common shares held by Sofinnova Venture Partners VIII, L.P. Dr. Healy is a managing member of Sofinnova Management VIII, L.L.C., the general partner of Sofinnova Venture Partners VIII, L.P., and may be considered to have beneficial ownership of Sofinnova Venture Partners VIII, L.P.'s interest in us. Dr. Healy disclaims beneficial ownership of all shares held by Sofinnova Venture Partners VIII, L.P., except to the extent of his pecuniary interest therein. Also, consists of options to purchase 18,907 common shares under the Company's Equity Incentive Plan held by Dr. Healy.

(9) Based on a Schedule 13G/A filed with the SEC on February 14, 2017 by Swisscanto Fondsleitung AG, Swisscanto Holding AG and Zurcher Kantonalbank. Swisscanto Fondsleitung AG, Swisscanto Holding AG and Zurcher Kantonalbank sponsor BB Adamant Global Biotech, BB Adamant Global Generika, BB Adamant Global Medtech and Services and Swisscanto (CH) Equity Fund Global Health Care (the "ZKB Funds"). Investment power over the 2,169,625 common shares held by the ZKB Funds is exercised by Bellevue Asset Management AG, an independent manager. The address of Swisscanto Fondsleitung AG, Swisscanto Holding AG and Zurcher Kantonalbank is Bahnhofstrasse 9, 8001 Zurich, Switzerland.

Mr. Kubli is a Senior Portfolio manager for the ZKB Funds. He disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein. Also, consists of 18,750 common shares acquired by Mr. Kubli pursuant to the exercise of Plan A options to purchase an additional 6,250 shares under the Company's Stock Option Plan A and options to purchase an additional 18,907 common shares under the Company's Equity Incentive Plan held by Mr. Kubli.

(10) Consists of 5,384,450 common shares held by Sofinnova Capital VII FCPR. Mr. Papiernik disclaims any beneficial ownership of the shares held by Sofinnova Capital VII FCPR except to the extent of his pecuniary interest therein.

(11) Consists of 15,242 shares jointly owned by Calvin W. Roberts and Andrea Colvin Roberts. Also, consists of 20,000 shares held by Calvin W. Roberts, MD PC Pension Plan, 10,000 shares held by The David Roberts Trust and 10,000 shares held by The Joanna Roberts Trust. Calvin Roberts is a trustee for each of Calvin W. Roberts, MD PC Pension Plan, The David Roberts Trust and The Joanna Roberts Trust. Also, consists of options to purchase an additional 12,500 common shares under the Company's Equity Incentive Plan.

Holders

As of March 10, 2017, we had nine shareholders of record of our common stock.

Significant Changes in Ownership by Major Shareholders

We have experienced significant changes in the percentage ownership held by major shareholders as a result of our public offerings. Prior to our initial public offering in August 2014, our principal shareholders were Thomas Meyer (34.9%), Sofinnova Venture Partners VIII, L.P. (19.3%), Sofinnova Capital VII FCPR (18.6%), the ZKB Funds (11.4%) and entities affiliated with Idinvest Partners (9.1%).

In August 2014, we completed our initial public offering and listed our common shares on the Nasdaq Global Market. In the initial public offering, we issued and sold 10,113,325 common shares, including 713,235 common shares sold to the underwriters pursuant to the underwriters' over-allotment option. In May 2015, we completed a public offering of 5,275,000 common shares. In February 2017, we completed a public offering of 10,000,000 common shares and warrants to purchase 7,000,000 common shares. While none of our existing shareholders sold common shares in the public offerings, certain shareholders purchased common shares in the public offering. Additionally, the percentage ownership held by certain shareholders decreased as a result of the issuance of the common shares sold by us in the public offerings.

B. Related party transactions

The following is a description of related party transactions we have entered into since January 1, 2016 with any of our members of our board of directors or management and the holders of more than 5% of our common shares.

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.

Indemnification Agreements

We have entered into indemnification agreements with our directors and executive officers. The indemnification agreements and our articles of association 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."

Registration Rights Agreement

We have entered into a registration rights agreement with certain of our existing shareholders pursuant to which granted them customary registration rights for the resale of the common shares held by certain of our existing shareholders.

Demand registration rights. Certain of our shareholders that are party to the Registration Rights Agreement (the "RRA Shareholders") are entitled to request that we effect up to an aggregate of two demand registrations under the Registration Rights Agreement, covering the RRA Shareholders' ordinary shares that are subject to transfer restrictions under Rule 144 ("registrable securities"). The demand registration rights are subject to certain customary conditions and limitations, including customary underwriter cutback rights and deferral rights. No demand registration rights exist while a shelf registration is in effect.

Piggyback registration rights. If we propose to register any ordinary shares (other than in a shelf registration or on a registration statement on Form F-4, S-4 or S-8), the RRA Shareholders are entitled to notice of such registration and to include their registrable securities in that registration. The registration of RRA Shareholders' registrable securities pursuant to a piggyback registration does not relieve us of the obligation to effect a demand registration. The managing underwriter has the right to limit the number of registrable securities included in a piggyback registration if the managing underwriter believes it would interfere with the successful marketing of the ordinary shares.

Form F-3 registration rights. When we are eligible to use Form F-3, one or more RRA Shareholders have the right to request that we file a registration statement on Form F-3. RRA Shareholders will have the right to cause us to undertake underwritten offerings from the shelf registration, but no more than one underwritten offering in a six-month period. Each underwritten takedown constitutes a demand registration for purposes of the maximum number of demand registrations we are obligated to effectuate.

Subject to limited exceptions, the Registration Rights Agreement provides that we must pay all registration expenses in connection with a demand, piggyback or shelf registration. The Registration Rights Agreement contains customary indemnification and contribution provisions.

Controlled Equity Offering[SM]

Thomas Meyer, our Chief Executive Officer, or the Share Lender, has entered into a share lending agreement with Cantor to facilitate the timely settlement of common shares sold under the Controlled Equity Offering Sales Agreement with Cantor. Pursuant to the terms of the share lending agreement, the Share Lender will lend common shares to Cantor so that those common shares may be delivered by Cantor to purchasers of common shares sold in any offering under the Controlled Equity Offering Sales Agreement. Cantor will return common shares to the Share Lender upon the issuance of new common shares by the Company to Cantor. Neither the Company nor the Share Lender will receive any compensation for this arrangement. In the year ended December 31, 2016, we did not offer or sell any common shares under the Controlled Equity Offering Sales Agreement.

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. The standalone financial statements of the Company have been prepared in accordance in Swiss law and have been filed as Exhibit 99.5 to our report on Form 6-K filed with the SEC on March 14, 2017.

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.

On July 20, 2015, the USPTO declared Patent Interference No. 106,030 involving our issued U.S. patent No. 9,066,865 (the "'865 Patent") and Otonomy's U.S. patent application No. 13/848,636 (the "'636 Application"). The patent interference identified claims 1-9 in the '865 Patent as interfering with claims 38, 43 and 46-50 of the '636 Application. The '865 Patent discloses methods of treating inner or middle ear diseases with intratympanic injections of poloxamer-based compositions. The claims of the '865 Patent are directed to the use of fluoroquinolone antibiotics in poloxamer 407 compositions under certain specifications. On January 26, 2017, the USPTO issued a decision on the interference granting Auris benefit of priority. As a result of the decision, judgment was entered against Otonomy and all claims in the '636 Application were refused. In addition, claims 1-8 of the '865 Patent were cancelled as the result of the USPTO's determination that the written description of the specification lacked full scope support for treating middle or inner ear disease with fluoroquinolone. However, claim 9, which is directed to a method of treating viral and bacterial infections with intratympanic injection of a fluoroquinolone antibiotic in a poloxamer 407 composition under certain specifications, was affirmed. The USPTO's decision is not final and may be appealed.

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, require the approval of the annual general meeting of shareholders.

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

The following table sets forth the high and low closing prices as reported in USD by Nasdaq for the periods presented:

	High	Low
Year Ended December 31:		
2014 (since August 6)	7.23	3.51
2015	6.38	3.02
2016	7.79	0.90
Year Ended December 31, 2015:		
First Quarter	6.38	3.51
Second Quarter	6.05	4.33
Third Quarter	5.56	3.50
Fourth Quarter	5.00	3.02
Year Ended December 31, 2016:		
First Quarter	7.79	3.36
Second Quarter	4.33	3.13
Third Quarter	5.35	1.58
Fourth Quarter	1.75	0.90
Month Ended:		
September 30, 2016	1.82	1.58
October 31, 2016	1.75	1.06
November 30, 2016	1.24	0.90
December 31, 2016	1.45	1.07
January 31, 2017	1.24	1.06
February 28, 2017	1.27	0.79
March, 2017 (through March 10, 2017)	0.78	0.67

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”.

D. Selling shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the issue

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. Share capital

Not applicable.

B. Memorandum and articles of association

When we refer to our articles of association in this annual report on Form 20-F, we refer to our amended and restated articles of association dated as of February 24, 2017.

We are registered with the commercial register of the canton of Zug, Switzerland, under the company number CHE-108.297.413. Our purpose as stated in article 2 of our articles of association is to hold investments of all kinds in Switzerland and abroad, particularly in relation to pharmaceutical products and services. Moreover, our corporation may transact any business conducive to developing the corporation or furthering the corporation’s purpose. We may also arrange financing for our own or third-party account, in particular we may grant loans to Group companies, as well as provide guarantees or surety bonds of any sort of such financing.

Ordinary Capital Increase, Authorized and Conditional Share Capital

Under Swiss law, we may increase our share capital (*Aktienkapital*) with a resolution of the general meeting of shareholders (ordinary capital increase) that must be carried out by the board of directors within three months in order to become effective. In the case of subscription and increase against payment of contributions in cash, a resolution passed by an absolute majority of the shares represented at the general meeting of shareholders is required. In the case of subscription and increase against contributions in kind or to fund acquisitions in kind, when shareholders’ statutory pre-emptive rights are withdrawn or where transformation of reserves into share capital is involved, a resolution passed by two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal amount of the shares represented is required.

Our shareholders, by a resolution passed by two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal amount of the shares represented, may empower our board of directors to issue shares of a specific aggregate nominal amount up to a maximum of 50% of the share capital in the form of:

- conditional capital (*bedingtes Kapital*) for the purpose of issuing shares in connection with, among other things, (i) option and conversion rights granted in connection with loans, warrants, convertible bonds or other financial market instruments issued by the Company or one of our subsidiaries or (ii) grants of rights to employees, members of our board of directors or consultants of the Group to subscribe for new shares (conversion or option rights); and/or

- authorized capital (*genehmigtes Kapital*) to be utilized by the board of directors within a period determined by the shareholders but not exceeding two years from the date of the shareholder approval.

Pre-emptive Rights

Pursuant to the Swiss Code of Obligations, or CO, shareholders have pre-emptive rights (*Bezugsrechte*) to subscribe for new issuances of shares. With respect to conditional capital in connection with the issuance of conversion rights, convertible bonds or similar debt instruments, shareholders have advance subscription rights (*Vorwegzeichnungsrechte*) for the subscription of conversion rights, convertible bonds or similar debt instruments.

A resolution passed at a general meeting of shareholders by two-thirds of the shares represented and the absolute majority of the nominal value of the shares represented may authorize our board of directors to withdraw or limit pre-emptive rights and/or advance subscription rights in certain circumstances.

If pre-emptive rights are granted, but not exercised, the board of directors may allocate the pre-emptive rights as it elects.

With respect to our authorized share capital, the board of directors is authorized by our articles of association to withdraw or to limit the pre-emptive rights of shareholders, and to allocate them to third parties or to the Company, in the event that the newly issued shares are used for a purpose set forth in our articles of association.

Our Authorized Share Capital

At our ordinary general meeting of shareholders on April 8, 2016, the shareholders approved an amendment to our authorized share capital. The new provision, as amended on February 24, 2017, (article 3a of the articles of association) reads as follows (translation of the binding original German version):

"*The Board of Directors is authorized at any time until 8 April 2018 to increase the share capital by a maximum aggregate amount of CHF 2,860,000.00 through the issuance of not more than 7,150,000 registered shares, which will have to be fully paid-in, with a nominal value of CHF 0.40 each.*

Increases in partial amounts are permitted. The Board of Directors may issue new shares also by means of underwriting or in any other manner by one or more banks and subsequent offer to shareholders or third parties. The Board of Directors determines the type of contributions, the issue price, the time of the issue, the conditions for the exercise of the pre-emptive rights, the allocation of pre-emptive rights which have not been exercised, and the date on which the dividend entitlement starts. The Board of Directors is authorized to permit, to restrict or to deny the trade with pre-emptive rights.

If pre-emptive rights are granted, but not exercised, the Board of Directors may use the respective shares in the interest of the Corporation.

The Board of Directors is authorized to restrict or to exclude the pre-emptive rights of the shareholders, and to allocate them to third parties or to the Corporation, in the event of use of the shares for the purpose of: a) expanding the shareholder base in certain capital markets or in the context of the listing, admission to official trading or registration of the shares at domestic or international stock exchanges; b) granting an over-allotment option ("greenshoe") to one or several underwriters in connection with a placement of shares; c) share placements, provided the issue price is determined by reference to the market price; d) the participation of employees, Members of the Board of Directors or consultants of the Corporation or of one of its Group companies according to one or several equity incentive plans issued by the Board of Directors; e) the acquisition of companies, company assets, participations, the acquisition of products, intellectual property rights, licenses or new investment projects or for public or private share placements for the financing and/or refinancing of such transactions; f) for raising equity capital in a fast and flexible manner as such transaction would be difficult to carry out, or could be carried out only at less favorable terms, without the exclusion of the pre-emptive rights of the existing shareholders; or g) the acquisition of a participation in the Corporation by a strategic partner (including in the case of a public takeover offer)."

Within the limits of Swiss law, the general meeting of shareholders may increase or alter the authorization granted to the board of directors. See "Ordinary Capital Increase, Authorized and Conditional Share Capital."

Our Conditional Share Capital

Conditional Share Capital for Warrants and Convertible Bonds

At our ordinary general meeting of shareholders on April 8, 2016, the shareholders approved an amendment to our conditional share capital for financing purposes. The new provision, as amended on February 24, 2017, (article 3b of the articles of association) reads as follows (translation of the binding original German version):

"*The Corporation's share capital shall be increased by a maximum aggregate amount of CHF 4,860,000.00 through the issuance of not more than 12,150,000 registered shares, which will have to be fully paid-in, with a nominal value of CHF 0.40 each, by the exercise of option and conversion rights which are granted in connection with bonds, similar obligations, loans or other financial market instruments or contractual obligations of the Corporation or one of its Group companies, and/or by the exercise of option rights issued by the Corporation or one of its Group companies ("Financial Instruments"). The pre-emptive rights of shareholders are excluded. The holders of Financial Instruments are entitled to the new shares. The conditions of the Financial Instruments shall be determined by the Board of Directors.*

When issuing Financial Instruments the Board of Directors is authorized to limit or exclude the advance subscription rights of shareholders:

a) for the purpose of financing or refinancing the acquisition of enterprises, divisions thereof, or of participations, products, intellectual property rights, licenses, cooperations or of newly planned investments of the Corporation;

b) if the issue occurs on domestic or international capital markets including private placements; or

c) for purposes of an underwriting of the Financial Instruments by a banking institution or a consortium of banks with subsequent offering to the public.

To the extent that the advance subscription rights are excluded, i) the Financial Instruments are to be placed at market conditions; ii) the exercise period, the conversion period or the exchange period of the Financial Instruments may not exceed 10 years as of the date of the issue; and iii) the conversion price, the exchange price or other exercise price of the Financial Instruments must be determined by reference to the market price."

Conditional Share Capital for Equity Incentive Plans

At our ordinary general meeting of shareholders on April 8, 2016, the shareholders approved an amendment to our conditional share capital for equity incentive plans. The new provision (last paragraph of article 3b of the articles of association) reads as follows (translation of the binding original German version):

"*The Corporation's share capital shall, to the exclusion of the pre-emptive rights and advance subscription rights of shareholders, be increased by a maximum aggregate amount of CHF 1,989,674.80 through the issuance of not more than 4,974,187 registered shares, which shall be fully paid-in, with a nominal value of CHF 0.40 each, by issuance of shares upon the exercise of options or pre-emptive rights thereof, which have been issued or granted to employees, Members of the Board of Directors or consultants of the Corporation or of one of its Group companies according to one or several equity incentive plans or regulations issued by the Board of Directors. The details shall be determined by the Board of Directors*."

Uncertificated Securities

Our shares are uncertificated securities (*Wertrechte*, within the meaning of art. 973c of the CO) and, when administered by a financial intermediary (*Verwahrungsstelle*, within the meaning of the Federal Act on Intermediated Securities, "FISA"), qualify as intermediated securities (*Bucheffekten*, within the meaning of the FISA). In accordance with art. 973c of the CO, we maintain a non-public register of uncertificated securities (*Wertrechtebuch*). We may at any time convert uncertificated securities into share certificates (including global certificates), one kind of certificate into another, or share certificates (including global certificates) into uncertificated securities. If registered in our share register, a shareholder may at any time request from us a written confirmation in respect of the shares. Shareholders are not entitled, however, to request the printing and delivery of certificates.

Participation certificates and profit sharing certificates

The Company has not issued any non-voting equity securities, such as participation certificates (*Partizipationsscheine*) or profit sharing certificates (*Genussscheine*), nor has it issued any preference shares (*Vorzugsaktien*).

No Additional Capital Contributions

Under Swiss law, shareholders are not obliged to make any capital contribution in excess of the subscription amount.

General Meeting of Shareholders

Ordinary/extraordinary meetings and powers

The general meeting of shareholders is our supreme corporate body. Under Swiss law, ordinary and extraordinary general meetings of shareholders may be held. Under Swiss law, an ordinary general meeting of shareholders must be held annually within six months after the end of a corporation's financial year. In our case, this means on or before June 30.

The following powers are vested exclusively in the general meeting of shareholders:

- adopting and amending our articles of association;
- electing the members of the board of directors, the chairman of the board of directors, the members of the compensation committee, the auditors and the independent proxy;
- approving the annual report, the annual statutory financial statements and the consolidated financial statements, and deciding on the allocation of profits as shown on the balance sheet, in particular with regard to dividends and bonus payments to members of the board of directors;
- approving the compensation of members of the board of directors and executive management, which under Swiss law is not necessarily limited to the executive officers;
- discharging the members of the board of directors and executive management from liability with respect to their tenure in the previous financial year;
- dissolving the Company with or without liquidation;
- deciding matters reserved to the general meeting of shareholders by law or our articles of association or that are presented to it by the board of directors.

An extraordinary general meeting of shareholders may be called by a resolution of the board of directors or, under certain circumstances, by the Company's auditor, liquidator or the representatives of convertible bond holders, if any. In addition, the board of directors is required to convene an extraordinary general meeting of shareholders if shareholders representing at least ten percent of the share capital request such general meeting of shareholders in writing. Such request must set forth the items to be discussed and the proposals to be acted upon. The board of directors must convene an extraordinary general meeting of shareholders and propose financial restructuring measures if, based on the Company's stand-alone annual statutory balance sheet, half of our share capital and reserves are not covered by our assets.

Voting and Quorum Requirements

Shareholder resolutions and elections (including elections of members of the board of directors) require the affirmative vote of the absolute majority of shares represented at the general meeting of shareholders, unless otherwise stipulated by law.

A resolution of the general meeting of the shareholders passed by two-thirds of the shares represented at the meeting, and the absolute majority of the nominal value of the shares represented is required for:

- amending the Company's corporate purpose;
- creating or cancelling shares with preference rights or amending rights attached to such shares;

- cancelling or amending the transfer restrictions of registered shares;
- creating authorized or conditional share capital;
- increasing the share capital out of equity, against contributions in kind or for the purpose of acquiring specific assets and granting specific benefits;
- limiting or suppressing shareholder's pre-emptive rights;
- changing our domicile;
- dissolving or liquidating the Company.

The same voting requirements apply to resolutions regarding transactions among corporations based on Switzerland's Federal Act on Mergers, Demergers, Transformations and the Transfer of Assets, or the Merger Act (including a merger, demerger or conversion of a corporation) see "Compulsory Acquisitions; Appraisal Rights."

In accordance with Swiss law and generally accepted business practices, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders. To this extent, our practice varies from the requirement of Nasdaq Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting stock.

Notice

General meetings of shareholders must be convened by the board of directors at least twenty days before the date of the meeting. The general meeting of shareholders is convened by way of a notice appearing in our official publication medium, currently the Swiss Official Gazette of Commerce. Registered shareholders may also be informed by ordinary mail. The notice of a general meeting of shareholders must state the items on the agenda, the proposals to be acted upon and, in case of elections, the names of the nominated candidates. Except in the limited circumstances listed below, a resolution may not be passed at a general meeting without proper notice. This limitation does not apply to proposals to convene an extraordinary general meeting of shareholders or to initiate a special investigation. No previous notification is required for proposals concerning items included in the agenda or for debates that do not result in a vote. The notice period for a general meeting of shareholders may be waived if all shareholders are present or represented at such meeting.Agenda Requests

Pursuant to Swiss law, one or more shareholders whose combined shareholdings represent the lower of (i) one tenth of the share capital or (ii) an aggregate nominal value of at least CHF 1,000,000, may request that an item be included in the agenda for an ordinary general meeting of shareholders. To be timely, the shareholder's request must be received by us at least 45 calendar days in advance of the meeting. The request must be made in writing and contain, for each of the agenda items, the following information:

- a brief description of the business desired to be brought before the ordinary general meeting of shareholders and the reasons for conducting such business at the ordinary general meeting of shareholders;
- the name and address, as they appear in the share register, of the shareholder proposing such business; and
- all other information required under the applicable laws and stock exchange rules.

Our business report, the compensation report and the auditor's report must be made available for inspection by the shareholders at our registered office no later than 20 days prior to the general meeting of shareholders. Shareholders of record are notified of this in writing.

Voting Rights

Each of our shares entitles a holder to one vote, regardless of its nominal value. The shares are not divisible. The right to vote and the other rights of share ownership may only be exercised by shareholders (including any nominees) or usufructuaries who are entered in our share register at cut-off date determined by the board of directors. Those entitled to vote in the general meeting of shareholders may be represented by the independent proxy holder (annually elected by the general meeting of shareholders), another registered shareholder or third person with written authorization to act as proxy or the shareholder's legal representative. The chairman has the power to decide whether to recognize a power of attorney. The Board of Directors issues the regulations on the determination of shareholder status, on proxies and voting instructions, and on the issue of voting cards.

Dividends and Other Distributions

Our board of directors may propose to shareholders that a dividend or other distribution be paid but cannot itself authorize the distribution. Dividend payments require a resolution passed by an absolute majority of the shares represented at a general meeting of shareholders. In addition, our auditors must confirm that the dividend proposal of our board of directors conforms to Swiss statutory law and our articles of association.

Under Swiss law, we may pay dividends only if we have sufficient distributable profits brought forward from the previous business years (*Gewinnvortrag*), or if we have distributable reserves (*frei verfügbare Reserven*), each as evidenced by our audited stand-alone statutory balance sheet prepared pursuant to Swiss law, and after allocations to reserves required by Swiss law and the articles of association have been deducted. We are not permitted to pay interim dividends out of profit of the current business year.

Distributable reserves are generally booked either as "free reserves" (*freie Reserven*) or as "reserve from capital contributions" (*Reserven aus Kapitaleinlagen*). Under the CO, if our general reserves (*allgemeine Reserve*) amount to less than 20% of our share capital recorded in the commercial register (i.e., 20% of the aggregate nominal value of our issued capital), then at least 5% of our annual profit must be retained as general reserves. The CO permits us to accrue additional general reserves. Further, a purchase of our own shares (whether by us or a subsidiary) reduces the distributable reserves in an amount corresponding to the purchase price of such own shares. Finally, the CO under certain circumstances requires the creation of revaluation reserves which are not distributable.

Distributions out of issued share capital (i.e., the aggregate nominal value of our issued shares) are not allowed and may be made only by way of a share capital reduction. Such a capital reduction requires a resolution passed by an absolute majority of the shares represented at a general meeting of shareholders. The resolution of the shareholders must be recorded in a public deed and a special audit report must confirm that claims of our creditors remain fully covered despite the reduction in the share capital recorded in the commercial register. The share capital may be reduced below CHF 100,000 only if and to the extent that at the same time the statutory minimum share capital of CHF 100,000 is reestablished by sufficient new fully paid-up capital. Upon approval by the general meeting of shareholders of the capital reduction, the board of directors must give public notice of the capital reduction resolution in the Swiss Official Gazette of Commerce three times and notify creditors that they may request, within two months of the third publication, satisfaction of or security for their claims. The reduction of the share capital may be implemented only after expiration of this time limit.

Our board of directors determines the date on which the dividend entitlement starts. Dividends are usually due and payable shortly after the shareholders have passed the resolution approving the payment, but shareholders may also resolve at the ordinary general meeting of shareholders to pay dividends in quarterly or other installments.

Transfer of Shares

Shares in uncertificated form (*Wertrechte*) may only be transferred by way of assignment. Shares that constitute intermediated securities (*Bucheffekten*) may only be transferred when a credit of the relevant intermediated securities to the acquirer's securities account is made in accordance with the relevant provisions of the FISA. Article 4 of our articles of association provides that in the case of securities held with an intermediary such as a registrar, transfer agent, trust corporation, bank or similar entity, any transfer, grant of a security interest or usufructuary right in such intermediated securities and the appurtenant rights associated therewith requires the cooperation of the intermediary in order for such transfer, grant of a security interest or usufructuary right to be valid against us.

Voting rights may be exercised only after a shareholder has been entered in our share register (*Aktienbuch*) with his or her name and address (in the case of legal entities, the registered office) as a shareholder with voting rights. Any acquirer of our shares who is not registered in our share register as a shareholder with voting rights will still be entitled to dividends and other rights with financial value with respect to such shares.

Inspection of Books and Records

Under the CO, a shareholder has a right to inspect our share register with respect to his own shares and otherwise to the extent necessary to exercise his shareholder rights. No other person has a right to inspect our share register. Our books and correspondence may be inspected with the express authorization of the general meeting of shareholders or by resolution of the board of directors and subject to the safeguarding of our business secrets.

Special Investigation

If the shareholders' inspection rights as outlined above prove to be insufficient in the judgment of the shareholder, any shareholder may propose to the general meeting of shareholders that specific facts be examined by a special commissioner in a special investigation. If the general meeting of shareholders approves the proposal, we or any shareholder may, within 30 calendar days after the general meeting of shareholders, request a court in Zug, Switzerland, our registered office, to appoint a special commissioner. If the general meeting of shareholders rejects the request, one or more shareholders representing at least 10 percent of the share capital or holders of shares in an aggregate nominal value of at least CHF 2,000,000 may request that the court appoint a special commissioner. The court will issue such an order if the petitioners can demonstrate that the board of directors, any member of the board of directors or our executive management infringed the law or our articles of association and thereby caused damages to the Company or the shareholders. The costs of the investigation would generally be allocated to us and only in exceptional cases to the petitioners.

Compulsory Acquisitions; Appraisal Rights

Business combinations and other transactions that are governed by the Swiss Merger Act (i.e., mergers, demergers, transformations and certain asset transfers) are binding on all shareholders. A statutory merger or demerger requires approval of two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal value of the shares represented.

Swiss corporations may be acquired by an acquirer through the direct acquisition of the share capital of the Swiss corporation. The Swiss Merger Act provides for the possibility of a so-called "cash-out" or "squeeze-out" merger if the acquirer controls 90% of the outstanding shares. In these limited circumstances, minority shareholders of the corporation being acquired may be compensated in a form other than through shares of the acquiring corporation (for instance, through cash or securities of a parent corporation of the acquiring corporation or of another corporation). Following a statutory merger or demerger, pursuant to the Merger Act, shareholders can file an appraisal action against the surviving company. If the consideration is deemed inadequate, the court will determine an adequate compensation payment.

In addition, under Swiss law, the sale of "all or substantially all of our assets" by us may require the approval of two-thirds of the number of shares represented at a general meeting shareholders and the absolute majority of the nominal value of the shares represented. Whether a shareholder resolution is required depends on the particular transaction, including whether the following test is satisfied:

- a core part of the Company's business is sold without which it is economically impracticable or unreasonable to continue to operate the remaining business;
- the Company's assets, after the divestment, are not invested in accordance with the Company's statutory business purpose; and
- the proceeds of the divestment are not earmarked for reinvestment in accordance with the Company's business purpose but, instead, are intended for distribution to the Company's shareholders or for financial investments unrelated to the Company's business.

Board of Directors

Our articles of association provide that the board of directors shall consist of at least three and not more than nine members.

The members of the board of directors and the chairman are elected annually by the general meeting of shareholders for a period until the completion of the subsequent ordinary general meeting of shareholders and are eligible for re-election. Each member of the board of directors must be elected individually. Unless an exception is granted by the general meeting of shareholders, only persons who have not completed their seventy-fifth year of age on the election date are eligible for election. Under Swiss law, a member of the Board of Directors is not required to be a shareholder.

Powers

The board of directors has the following non-delegable and inalienable powers and duties:

- the ultimate direction of the business of the Company and issuing of the relevant directives;
- laying down the organization of the Company;
- formulating accounting procedures, financial controls and financial planning, to the extent required for the governance of the Company;
- nominating and removing persons entrusted with the management and representation of the Company and regulating the power to sign for the Company;
- the ultimate supervision of those persons entrusted with management of the Company, with particular regard to adherence to law, our articles of association, and regulations
- and directives of the Company;
- issuing the annual report and the compensation report, and preparing for the general meeting of shareholders and carrying out its resolutions; and
- informing the court in case of over-indebtedness.

The board of directors may, while retaining such non-delegable and inalienable powers and duties, delegate some of its powers, in particular direct management, to a single or to several of its members, managing directors, committees or to third parties who need be neither members of the board of directors nor shareholders. Pursuant to Swiss law and Article 13 of our articles of association, details of the delegation and other procedural rules such as quorum requirements must be set in the organizational rules issued by the board of directors.

Indemnification of Executive Management and Directors

Subject to Swiss law, Article 17 of our articles of association provides for indemnification of the existing and former members of the board of directors, executive management and their heirs, executors and administrators, against liabilities arising in connection with the performance of their duties in such capacity, and permits us to advance the expenses of defending any act, suit or proceeding to our directors and executive management.

In addition, under general principles of Swiss employment law, an employer may be required to indemnify an employee against losses and expenses incurred by such employee in the proper execution of their duties under the employment agreement with the employer.

We have entered into indemnification agreements with each of the members of our board of directors and executive management. The indemnification agreements and our articles of association require us to indemnify our directors and executive officers to the fullest extent permitted by law.

Conflict of Interest, Management Transactions

Swiss law does not provide for a general provision regarding conflicts of interest. However, the CO contains a provision that requires our directors and executive management to safeguard the Company’s interests and imposes a duty of loyalty and duty of care on our directors and executive management. This rule is generally understood to disqualify directors and executive management from participation in decisions that directly affect them. Our directors and executive officers are personally liable to us for breach of these provisions. In addition, Swiss law contains provisions under which directors and all persons engaged in the Company’s management are liable to the Company, each shareholder and the Company’s creditors for damages caused by an intentional or negligent violation of their duties. Furthermore, Swiss law contains a provision under which payments made to any of the Company’s shareholders or directors or any person associated with any such shareholder or director, other than payments made at arm’s length, must be repaid to the Company if such shareholder or director acted in bad faith.

Our board of directors has adopted a Code of Business Conduct and Ethics that covers a broad range of matters, including the handling of conflicts of interest.

Principles of the Compensation of the Board of Directors and the Executive Management

Pursuant to Swiss law, our shareholders must annually resolve on the approval of the compensation of the board of directors and the persons whom the board of directors has, fully or partially, entrusted with the management of the Company. The board of directors must issue, on an annual basis, a written compensation report that must be reviewed together with a report on our business by our auditor. The compensation report must disclose all compensation, loans and other forms of indebtedness granted by the Company, directly or indirectly, to current or former members of the board of directors and executive management to the extent related to their former role within the Company or not on customary market terms.

The disclosure concerning compensation, loans and other forms of indebtedness must include the aggregate amount for the board of directors and the executive management as well as the particular amount for each member of the board of directors and executive officer, specifying the name and function of each respective person.

Certain forms of compensation are prohibited for members of our board of directors and executive management, such as:

- severance payments provided for either contractually or in the articles of association (compensation due until the termination of a contractual relationship does not qualify as severance payment);
- advance compensation;
- incentive fees for the acquisition or transfer of corporations or parts thereof by the Company or by companies being, directly or indirectly, controlled by us;
- loans, other forms of indebtedness, pension benefits not based on occupational pension schemes and performance-based compensation not provided for in the articles of association; and
- equity securities and conversion and option rights awards not provided for in the articles of association.

Compensation to members of the board of directors and executive management for activities in entities that are, directly or indirectly, controlled by the Company is prohibited if the compensation (i) would have been prohibited if it was paid directly by the Company, (ii) is not provided for in the articles of association or (iii) has not been approved by the general meeting of shareholders.

The general meeting of shareholders annually votes on the proposals of the board of directors with respect to:

- the maximum aggregate amount of compensation of the board of directors for the subsequent term of office; and
- the maximum aggregate amount of compensation of the executive management for the subsequent financial year.

The board of directors may submit for approval at the general meeting of shareholders deviating or additional proposals relating to the same or different periods.

In the event that at the general meeting of shareholders the shareholders do not approve a proposal of the board of directors, the board of directors must form a new proposal for the maximum aggregate compensation and the particular compensation for each individual, taking into account all relevant factors, and submit the new proposal for approval by the same general meeting of shareholders, at a subsequent extraordinary general meeting or the next ordinary general meeting of shareholders.

In addition to fixed compensation, members of the board of directors and executive management may be paid variable compensation, depending on the achievement of certain performance criteria. The performance criteria may include individual targets, targets of the Company or parts thereof and targets in relation to the market, other companies or comparable benchmarks, taking into account the position and level of responsibility of the recipient of the variable compensation. The board of directors or, where delegated to it, the compensation committee shall determine the relative weight of the performance criteria and the respective target values.

Compensation may be paid or granted in the form of cash, shares, financial instruments, in kind, or in the form of other types of benefits. The board of directors or, where delegated to it, the compensation committee shall determine grant, vesting, exercise and forfeiture conditions.

Borrowing Powers

Neither Swiss law nor our articles of association restrict in any way our power to borrow and raise funds. The decision to borrow funds is made by or under the direction of our board of directors, and no approval by the shareholders is required in relation to any such borrowing.

Repurchases of Shares and Purchases of Own Shares and Other Limitations on the Rights to Own Securities

The CO limits our right to purchase and hold our own shares. We and our subsidiaries may purchase shares only if and to the extent that (i) we have freely distributable reserves in the amount of the purchase price; and (ii) the aggregate nominal value of all shares held by us does not exceed 10 percent of our share capital. Pursuant to Swiss law, where shares are acquired in connection with a transfer restriction set out in the articles of association, the foregoing upper limit is 20 percent. We currently do not have any transfer restriction in our articles of association. If we own shares that exceed the threshold of 10 percent of our share capital, the excess must be sold or cancelled by means of a capital reduction within two years.

Shares held by us or our subsidiaries are not entitled to vote at the general meeting of shareholders but are entitled to the economic benefits applicable to the shares generally, including dividends and pre-emptive rights in the case of share capital increases.

Swiss law and/or our articles of association do not impose any restrictions on the exercise of voting or any other shareholder right by shareholders resident outside Switzerland.

Notification and Disclosure of Substantial Share Interests

The disclosure obligations generally applicable to shareholders of Swiss corporations under the Swiss Financial Market Infrastructure Act do not apply to us since our shares are not listed on a Swiss exchange.

Pursuant to art. 663c of the CO, Swiss corporations whose shares are listed on a stock exchange must disclose their significant shareholders and their shareholdings in the notes to their balance sheet, where this information is known or ought to be known. Significant shareholders are defined as shareholders and groups of shareholders linked through voting rights who hold more than five percent of all voting rights.

C. Material contracts

Except as otherwise disclosed in this annual report on Form 20-F (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

There are no Swiss governmental laws, decrees or regulations that restrict, in a manner material to us, the export or import of capital, including any foreign exchange controls, or that generally affect the remittance of dividends or other payments to non-residents or non-citizens of Switzerland who hold our common shares.

E. Taxation

The following summary contains a description of the material 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 Switzerland and regulations thereunder and on the tax laws of the United States and regulations thereunder as of the date hereof, which are subject to change.

Swiss Tax Considerations

This summary of material Swiss tax consequences is based on Swiss law and regulations and the practice of the Swiss tax administration as in effect on the date hereof, all of which are subject to change (or subject to changes in interpretation), possibly with retroactive effect. The summary does not purport to take into account the specific circumstances of any particular shareholder or potential investor and does not relate to persons in the business of buying and selling common shares or other securities. The summary is not intended to be, and should not be interpreted as, legal or tax advice to any particular potential shareholder/s, and no representation with respect to the tax consequences to any particular shareholder/s is made.

Current and prospective shareholders are advised to consult their own tax advisers in light of their particular circumstances as to the Swiss tax laws, regulations and regulatory practices that could be relevant for them in connection with the acquiring, owning and selling or otherwise disposing of common shares and receiving dividends and similar cash or in-kind distributions on common shares (including dividends on liquidation proceeds and stock dividends) or distributions on common shares based upon a capital reduction (*Nennwertrückzahlungen*) or reserves paid out of capital contributions (*Reserven aus Kapitaleinlagen*) and the consequences thereof under the tax laws, regulations and regulatory practices of Switzerland.

Taxation of Auris Medical Holding AG

Auris Medical Holding AG is a Swiss based company, taxed as a holding company in the Canton of Zug. The company is taxed at a current effective income tax rate of 7.83% (including direct federal as well as cantonal/communal taxes), whereby a participation relief applies to dividend income from qualifying subsidiaries, and a current annual capital tax rate of 0.003% which is levied on the net equity of the company.

Switzerland is currently in the process of reforming certain elements of its corporate tax law which may impact the taxation of Auris Medical Holding AG (including the abolition of the holding taxation at cantonal/communal level). Whether and when such new rules will enter into force is not known.

Taxation of Common Shares: Swiss Federal Withholding Tax on Dividends and Distributions

Dividend payments and similar cash or in-kind distributions on the common shares (including dividends on liquidation proceeds and stock dividends) that the Company makes to shareholders are subject to Swiss federal withholding tax (*Verrechnungssteuer*) at a rate of 35% on the gross amount of the dividend. The Company is required to withhold the Swiss federal withholding tax from the dividend and remit it to the Swiss Federal Tax Administration. Distributions based upon a capital reduction (*Nennwertrückzahlungen*) and reserves paid out of capital contributions (*Reserven aus Kapitaleinlagen*) are not subject to Swiss federal withholding tax.

The Swiss federal withholding tax may also apply to gains realized upon a repurchase of shares by the Company, on the difference between the repurchase price and the nominal value of the shares (*Nennwertprinzip*); a different basis of taxation may apply under the capital contribution principle (*Kapitaleinlageprinzip*).

The Swiss federal withholding tax is refundable or creditable in full to a Swiss tax resident corporate and individual shareholder as well as to a non-Swiss tax resident corporate or individual shareholder who holds the common shares as part of a trade or business carried on in Switzerland through a permanent establishment or fixed place of business situated for tax purposes in Switzerland, if such person is the beneficial owner of the distribution and, in the case of a Swiss tax resident individual who holds the common shares as part of his private assets, duly reports the gross distribution received in his individual income tax return or, in the case of a person who holds the common shares as part of a trade or business carried on in Switzerland through a permanent establishment or fixed place of business situated for tax purposes in Switzerland, recognizes the gross dividend distribution for tax purposes as earnings in the income statements and reports the annual profit in the Swiss income tax return.

If a shareholder who is not a Swiss resident for tax purposes and does not hold the common shares in connection with the conduct of a trade or business in Switzerland through a permanent establishment or fixed place of business situated, for tax purposes in Switzerland, receives a distribution from the Company, the shareholder may be entitled to a full or partial refund or credit of Swiss federal withholding tax incurred on a taxable distribution if the country in which such shareholder is resident for tax purposes has entered into a treaty for the avoidance of double taxation with Switzerland and the further prerequisites of the treaty for a refund have been met. Shareholders not resident in Switzerland should be aware that the procedures for claiming treaty benefits (and the time required for obtaining a refund or credit) may differ from country to country.

Besides the bilateral treaties, Switzerland has entered into an agreement with the European Community providing for measures equivalent to those laid down in Council Directive 2003/48/EC on taxation of savings income in the form of interest payments and the Council Directive 90/435/EWG on the taxation of parent companies and subsidiaries of different Member States. This agreement contains in its Article 15 provisions on taxation of dividends which apply with respect to EU member states and provides for an exemption of Withholding Tax for companies under certain circumstances.

Individual and Corporate Income Tax on Dividends

Swiss resident individuals holding the common shares as part of their private assets who receive dividends and similar distributions (including stock dividends and liquidation proceeds), which are not repayments of the nominal value (*Nennwertrückzahlungen*) of the common shares or reserves paid out of capital contributions (*Reserven aus Kapitaleinlagen*) are required to report such payments in their individual income tax returns and are liable to Swiss federal, cantonal and communal income taxes on any net taxable income for the relevant tax period. Furthermore, for the purpose of the Direct Federal Tax, dividends, shares in profits, liquidation proceeds and pecuniary benefits from shares (including bonus shares) are included in the tax base for only 60% of their value (*Teilbesteuerung*), if the investment amounts to at least 10% of nominal capital of the Company. Most Swiss cantons have introduced similar partial taxation measures at cantonal and communal levels.

Swiss resident individuals as well as non-Swiss resident individual taxpayers holding the common shares in connection with the conduct of a trade or business in Switzerland through a permanent establishment or fixed place of business situated, for tax purposes, in Switzerland, are required to recognize dividends, distributions based upon a capital reduction (*Nennwertrückzahlungen*) and reserves paid out of capital contributions (*Reserven aus Kapitaleinlagen*) in their income statements for the relevant tax period and are liable to Swiss federal, cantonal and communal individual or corporate income taxes, as the case may be, on any net taxable earnings accumulated (including the payment of dividends) for such period. Furthermore, for the purpose of the Direct Federal Tax, dividends, shares in profits, liquidation proceeds and pecuniary benefits from shares (including bonus shares) are included in the tax base for only 50% (*Teilbesteuerung*), if the investment is held in connection with the conduct of a trade or business or qualifies as an opted business asset (*gewillkürtes Geschäftsvermögen*) according to Swiss tax law and amounts to at least 10% of nominal capital of the Company. All cantons have introduced similar partial taxation measures at cantonal and communal levels.

Swiss resident corporate taxpayers as well as non-Swiss resident corporate taxpayers holding the common shares in connection with the conduct of a trade or business through a permanent establishment or fixed place of business situated, for tax purposes, in Switzerland, are required to recognize dividends, distributions based upon a capital reduction (*Nennwertrückzahlungen*) and reserves paid out of capital contributions (*Reserven aus Kapitaleinlagen*) in their income statements for the relevant tax period and are liable to Swiss federal, cantonal and communal corporate income taxes on any net taxable earnings accumulated for such period. Swiss resident corporate taxpayers as well as non-Swiss resident corporate taxpayers holding the common shares in connection with the conduct of a trade or business through a permanent establishment or fixed place of business situated, for tax purposes, in Switzerland may be eligible for participation relief (*Beteiligungsabzug*) in respect of dividends and distributions based upon a capital reduction (*Nennwertrückzahlungen*) and reserves paid out of capital contributions (*Reserven aus Kapitaleinlagen*) if the common shares held by them as part of a Swiss business have an aggregate market value of at least CHF 1 million or represent at least 10% of the share capital of the Company or give entitlement to at least 10% of the profits and reserves of the Company, respectively.

Recipients of dividends and similar distributions on the common shares (including stock dividends and liquidation proceeds) who neither are residents of Switzerland nor during the current taxation year have engaged in a trade or business in Switzerland and who are not subject to taxation in Switzerland for any other reason are not subject to Swiss federal, cantonal or communal individual or corporate income taxes in respect of dividend payments and similar distributions because of the mere holding of the common shares.

Wealth and Annual Capital Tax on Holding of Common Shares

Swiss resident individuals and non-Swiss resident individuals holding the common shares in connection with the conduct of a trade or business in Switzerland through a permanent establishment or fixed place of business situated, for tax purposes, in Switzerland, are required to report their common shares as part of their wealth and will be subject to cantonal and communal wealth tax to the extent the aggregate taxable net wealth is allocable to Switzerland.

Swiss resident corporate taxpayers and non-Swiss resident corporate taxpayers holding the common shares in connection with the conduct of a trade or business in Switzerland through a permanent establishment or fixed place of business situated, for tax purposes, in Switzerland, will be subject to cantonal and communal annual capital tax on the taxable capital to the extent the aggregate taxable capital is allocable to Switzerland.

Individuals and corporate taxpayers not resident in Switzerland for tax purposes and not holding the common shares in connection with the conduct of a trade or business in Switzerland through a permanent establishment or fixed place of business situated, for tax purposes, in Switzerland, are not subject to wealth or annual capital tax in Switzerland because of the mere holding of the common shares.

Capital Gains on Disposal of Common Shares

Swiss resident individuals who sell or otherwise dispose of the common shares realize a tax-free capital gain, or a non-deductible capital loss, as the case may be, provided that they hold the common shares as part of their private assets. Under certain circumstances, the sales proceeds may be recharacterised into taxable investment income (e.g., professional securities dealer, etc.).

Capital gains realized on the sale of the common shares held by Swiss resident individuals, Swiss resident corporate taxpayers as well as non-Swiss resident individuals and corporate taxpayers holding the common shares in connection with the conduct of a trade or business in Switzerland through a permanent establishment or fixed place of business situated, for tax purposes, in Switzerland, will be subject to Swiss federal, cantonal and communal individual or corporate income tax, as the case may be. This also applies to Swiss resident individuals who, for individual income tax purposes, are deemed to be professional securities dealers for reasons of, inter alia, frequent dealing and debt-financed purchases. Capital gains realized by resident individuals who hold the common shares as business assets might be entitled to reductions or partial taxations similar to those mentioned above for dividends (*Teilbesteuerung*) if certain conditions are met (e.g., holding period of at least one year and participation of at least 10% of nominal capital).

Swiss resident corporate taxpayers as well as non-Swiss resident corporate taxpayers holding the common shares in connection with the conduct of a trade or business, through a permanent establishment or fixed place of business situated, for tax purposes, in Switzerland, are required to recognize such capital gain in their income statements for the relevant tax period. Corporate taxpayers may qualify for participation relief on capital gains (*Beteiligungsabzug*), if the common shares sold during the tax period represent at least 10% of the Company's share capital or if the common shares sold give entitlement to at least 10% of the Company's profit and reserve and were held for at least one year. The tax relief applies to the difference between the sale proceeds of common shares by the Company and the initial costs of the participation (*Gestehungskosten*).

Individuals and corporations not resident in Switzerland for tax purposes and not holding the common shares in connection with the conduct of a trade or business in Switzerland through a permanent establishment or fixed place of business situated, for tax purposes, in Switzerland, are not subject to Swiss federal, cantonal and communal individual income or corporate income tax, as the case may be, on capital gains realized on the sale of the common shares.

Gift and Inheritance Tax

Transfers of common shares may be subject to cantonal and/or communal inheritance or gift taxes if the deceased or the donor or the recipient were resident in a Canton levying such taxes and, in international circumstances where residency requirements are satisfied, if the applicable tax treaty were to allocate the right to tax to Switzerland.

Swiss Issuance Stamp Duty

The Company is subject to paying to the Swiss Federal Tax Administration a 1% Swiss federal issuance stamp tax (*Emissionsabgabe*) on any increase of the nominal capital of the Company (with or without issuance of shares) or any other equity contributions received by the Company (regardless of whether or not any compensation is paid to the shareholder in connection with the contribution). Certain costs incurred in connection with the issuance of shares (if any) may be deductible. There are several exemptions from issuance stamp tax that may apply under certain circumstances (e.g., certain intercompany reorganizations).

Swiss Securities Transfer Tax

The purchase or sale (or other financial transfer) of the common shares, whether by Swiss residents or non-Swiss residents, may be subject to Swiss securities transfer tax of up to 0.15%, calculated on the purchase price or the proceeds if the purchase or sale occurs through or with a Swiss bank or other Swiss securities dealer as defined in the Swiss Federal Stamp Duty Act as an intermediary or party to the transaction unless an exemption applies.

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 Internal Revenue Code of 1986, as amended, or 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 voting stock;
- 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, and the income tax treaty between Switzerland and the United States, or the Treaty, 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 who is eligible for the benefits of the Treaty 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 or trust the income of which is subject to U.S. federal income taxation regardless of its source.

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 "passive foreign investment company," or PFIC, for U.S. federal income tax purposes for our 2015 and 2016 taxable years, and we expect to be a PFIC for our current taxable year and for the foreseeable future. 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 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. 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*."

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 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 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 information will be available for any Lower-tier PFIC.

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 discussed below 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. 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). The amount of a dividend will include any amounts withheld by us in respect of Swiss taxes. 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. The amount of any dividend income paid in Swiss Francs will be the U.S. dollar amount calculated by reference to the exchange rate in effect on the date of receipt, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted into U.S. dollars on the date of receipt, a U.S. Holder should not be required to recognize foreign currency gain or loss in respect of the dividend income. A U.S. Holder may have foreign currency gain or loss if the dividend is converted into U.S. dollars after the date of receipt.

Subject to applicable limitations, some of which vary depending upon the U.S. Holder's circumstances, Swiss income taxes withheld from dividends on common shares at a rate not exceeding the rate provided by the Treaty may be creditable against the U.S. Holder's U.S. federal income tax liability. Swiss taxes withheld in excess of the rate applicable under the Treaty will not be eligible for credit against a U.S. Holder's federal income tax liability. The rules governing foreign tax credits are complex, and U.S. Holders should consult their tax advisers regarding the creditability of foreign taxes in their particular circumstances. In lieu of claiming a foreign tax credit, U.S. Holders may, at their election, deduct foreign taxes, including the Swiss withholding tax, in computing their taxable income, subject to generally applicable limitations under U.S. law. An election to deduct foreign taxes instead of claiming foreign tax credits applies to all foreign taxes paid or accrued in the taxable year.

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.

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.

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 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 the effect, if any, of this legislation on 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. You may inspect and copy reports and other information filed with the SEC at the Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. In addition, 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.

Additionally, pursuant to Swiss law, any shareholder of record has the right to receive a free copy of this Annual Report and to inspect this Annual Report at any time at our registered offices in Zug.

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.

Interest rate risk

Interest expense pursuant to borrowings under the loan and security agreement with Hercules Capital, Inc. is subject to the variability of the prime rate as reported by the Wall Street Journal. An increase or decrease of the prime rate reported effective July 19, 2016 by 50 basis points, with all other factors held constant, would have resulted in a CHF 28,276 increase or decrease of the net annual result. In 2015, the Company had no borrowings at variable interest rates.

Other than the interest rate risk related to the loan and security agreement, we are not currently exposed to significant interest rate risk because we have no fixed rate financial liabilities at fair value through profit or loss and no derivatives. Our only variable interest-bearing financial asset is cash at banks. The effect of an increase or decrease in interest rates would only have an immaterial effect in profit or loss.

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, 2016, a 5% increase or decrease in the USD/CHF exchange rate with all other variables held constant would have resulted in a CHF 872,443 (2015: CHF 2,135,522) 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 180,595 (2015: CHF 127,692) increase or decrease in the net annual result.

We have subsidiaries in the United States and Ireland, 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

On August 11, 2014, we completed our initial public offering of common shares pursuant to a Registration Statement on Form F-1, as amended (Registration No. 333-197105) that was declared effective on August 5, 2014. Under the registration statement, we sold an aggregate of 10,113,235 common shares, which included 713,235 common shares sold on August 19, 2014 pursuant to an over-allotment option granted to the underwriters. All of these common shares were sold at a price to the public of $6.00 per share, yielding gross proceeds of $60.7 million or net proceeds of $56.4 million (CHF 51.3 million) after underwriting discounts and commissions. Jefferies LLC and Leerink Partners LLC were joint book-running managers for the initial public offering. We paid the offering expenses in connection with the initial public offering, which were approximately CHF 2.1 million ($2.3 million), and which included SEC registration fees, FINRA filing fees, Nasdaq listing fees and expenses, legal fees and expenses, printing expenses, transfer agent fees and expenses, accounting fees and expenses as well as other miscellaneous fees and expenses, but excluded the underwriting discounts and commissions.

Between the effective date of the Registration Statement and December 31, 2016, we used the entire net proceeds of our initial public offering, to fund research and development expenses for Keyzilen® and AM-111 and general administrative expenses. None of the net proceeds were used to make payments (other than compensation paid to our executive officers, directors and an affiliate of one of our directors, each as described in this Annual Report), directly or indirectly, to (i) any of our directors, officers or their associates, (ii) any persons owning 10% or more of our common shares or (iii) any of our affiliates.

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, 2016.

C. Attestation Report of the Registered Public Accounting Firm

This Annual Report does not include an attestation report of our registered public accounting firm due to an exemption provided to emerging growth companies under the JOBS Act.

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 Berndt A.E. Modig and Oliver Kubli are audit committee financial experts, as that term is defined by the SEC, and are 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

	2016	2015
Audit Fees	348	743
Total fees	**348**	**743**

For the year ended December 31, 2013, KPMG AG was the Company's auditor for the IFRS and statutory accounts. At the ordinary annual general meeting on April 22, 2014, the shareholders appointed Deloitte AG as the Company's auditor for the year ended December 31, 2014. Deloitte AG's was reelected at the ordinary annual general meeting on April 22, 2015 and April 8, 2016.

In 2015, we were billed CHF 582,000 by Deloitte AG in connection with our annual filing, as well as interim reviews, group audit, statutory audits, offerings on Form F-1 and the shelf registration on Form F-3 and CHF 161,000 by KPMG AG in connection with our annual filing, as well as offerings on Form F-1 and the shelf registration on Form F-3. In 2016, we were billed CHF 306,000, by Deloitte AG in connection with our annual filing as well as interim reviews, group audit, statutory audits and work in connection with our controlled equity offering program and CHF 42,000 by KPMG AG in connection with our annual filing.

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.

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 2016, no purchases of our equity securities were made by or on behalf of Auris Medical Holding AG 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 Global 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

Swiss 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 will 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

Although Swiss law also requires that we have a compensation committee, we will follow home country requirements with respect to such committee. As a result, our practice will vary 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

In accordance with Swiss law and generally accepted business practices, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders. 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 articles of association provide for an independent proxy holder elected by our shareholders, who may represent our shareholders at a general meeting of shareholders, and we must provide shareholders with an agenda and other relevant documents for the general meeting of shareholders. However, Swiss law does not have a regulatory regime for the solicitation of proxies and company solicitation of proxies is prohibited for public companies in Switzerland, thus our practice will vary 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

We follow Swiss law requirements with respect to disclosure of compensation for our directors and executive officers. Swiss 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	Articles of Association of Auris Medical Holding AG, (incorporated by reference to exhibit 1.1 of the Auris Medical Holding AG Report on Form 6-K filed with the Commission on April 11, 2016)
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 July 19, 2016, between Auris Medical Holding AG and Hercules Capital, Inc. (incorporated by reference to exhibit 10.2 of the Auris Medical Holding AG report on Form 6-K filed with the Commission on July 19, 2016)
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	English language translation of Lease Agreement between Auris Medical AG and Privera AG (incorporated by reference to exhibit 10.10 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 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)
4.6	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)
4.7*	English language translation of Termination of Lease Agreement between Auris Medical AG and Privera AG
4.8*	English language translation of Lease Agreement between Auris Medical AG and PSP Management AG
4.9	Controlled Equity Offering[SM] 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 27, 2016)
4.10	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)
4.11	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)
4.12	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)
4.13	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)
4.14	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)
8.1	List of subsidiaries (incorporated by reference to exhibit 21.1 of the Auris Medical Holding AG registration statement on Form F-1 (Registration no. 333-197105) filed with the Commission on June 27, 2014)
12.1*	Certification of Thomas Meyer pursuant to 17 CFR 240.13a-14(a)
12.2*	Certification of Hernan Levett 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 Hernan Levett pursuant to 17 CFR 240.13a-14(b) and 18 U.S.C. 1350
15.1*	Consent of Deloitte AG
15.3	“Item 2.3 — Compensation awarded to the Board of Directors in 2016” and “Item 3.4 — Compensation awarded to the Executive Management Committee in 2016” of Exhibit 99.4 to our report on Form 6-K filed with the Commission on March 14, 2017

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* 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 AG

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

Date: March 14, 2017

Index to Consolidated Financial Statements

Audited Consolidated Financial Statements—Auris Medical Holding AG (formerly Auris Medical AG)

As of December 31, 2016 and 2015 and for the years ended December 31, 2016, 2015, and 2014

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Auris Medical Holding AG

We have audited the accompanying consolidated statements of financial position of Auris Medical Holding AG and its subsidiaries (the "Company") as of December 31, 2016 and 2015, and the related consolidated statements of profit or loss and other comprehensive loss, changes in equity, and cash flows for each of the three years in the period ended December 31, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, 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. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of Auris Medical Holding AG and its subsidiaries as of December 31, 2016 and 2015, and the results of their operations, and their cash flows for each of the three years in the period ended December 31, 2016, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Deloitte AG

/s/ Matthias Gschwend
Auditor in Charge

/s/ Adrian Kaeppeli

Zurich, Switzerland
March 10, 2017

AURIS MEDICAL HOLDING AG

Consolidated Statement of Profit or Loss and Other Comprehensive Loss
For the Years Ended December 31, 2016, 2015 and 2014
(in CHF)

	Note	2016	2015	2014
Research and development	16	(24,776,763)	(26,536,176)	(17,704,461)
General and administrative	17	(5,446,512)	(4,341,570)	(4,489,051)
Operating loss		**(30,223,275)**	**(30,877,746)**	**(22,193,512)**
Interest income	19	67,565	36,562	52,133
Interest expense	19	(828,547)	(7,985)	(55,810)
Foreign currency exchange gain/(loss), net	19	(100,097)	1,144,106	4,012,174
Revaluation gain from derivative financial instruments	19, 24	291,048	–	–
Loss before tax		**(30,793,306)**	**(29,705,063)**	**(18,185,015)**
Income tax gain	20	131,055	–	–
Net loss attributable to owners of the Company		**(30,662,251)**	**(29,705,063)**	**(18,185,015)**
Other comprehensive loss:				
Items that will never be reclassified to profit or loss				
Remeasurements of defined benefit liability,				
net of taxes of CHF 0	18	(394,102)	(53,916)	(1,101,468)
Items that are or may be reclassified to profit or loss				
Foreign currency translation differences,				
net of taxes of CHF 0		(19,723)	(12,712)	(105,104)
Other comprehensive loss, net of taxes of CHF 0		**(413,825)**	**(66,628)**	**(1,206,572)**
Total comprehensive loss attributable to owners of the Company		**(31,076,076)**	**(29,771,691)**	**(19,391,587)**
Basic and diluted loss per share	21	(0.89)	(0.92)	(0.66)

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

AURIS MEDICAL HOLDING AG

Consolidated Statement of Financial Position
As of December 31, 2016 and 2015
(in CHF)

	Note	December 31, 2016	December 31, 2015
ASSETS			
Non-current assets			
Property and equipment	7	369,294	222,570
Intangible assets	8	1,482,520	1,482,520
Other non-current receivables		114,778	38,066
Total non-current assets		**1,966,592**	**1,743,156**
Current assets			
Other receivables	9	296,531	650,716
Prepayments	10	952,595	181,044
Cash and cash equivalents	11	32,442,222	50,237,300
Total current assets		**33,691,348**	**51,069,060**
Total assets		**35,657,940**	**52,812,216**
EQUITY AND LIABILITIES			
Equity			
Share capital	12	13,731,881	13,721,556
Share premium		112,838,815	112,662,910
Foreign currency translation reserve		(83,544)	(63,821)
Accumulated deficit		(112,344,303)	(81,578,733)
Total shareholders' equity attributable to owners of the Company		**14,142,849**	**44,741,912**
Non-current liabilities			
Loan	24	10,151,498	–
Derivative financial instruments	24	117,132	–
Employee benefits	18	2,092,434	1,575,833
Deferred tax liabilities	20	196,582	327,637
Total non-current liabilities		**12,557,646**	**1,903,470**
Current liabilities			
Loan	24	2,212,706	–
Trade and other payables	14	1,837,997	1,205,522
Accrued expenses	15	4,906,742	4,961,312
Total current liabilities		**8,957,445**	**6,166,834**
Total liabilities		**21,515,091**	**8,070,304**
Total equity and liabilities		**35,657,940**	**52,812,216**

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

AURIS MEDICAL HOLDING AG

Consolidated Statement of Changes in Equity
As of December 31, 2016, 2015 and 2014
(in CHF)

	Note	Share Capital	Share Premium	Foreign Currency Translation Reserve	Accumulated Deficit	Total Equity
As of January 1, 2014		**6,487,130**	**35,608,210**	**53,995**	**(33,115,689)**	**9,033,646**
Total comprehensive loss						
Net loss		–	–	–	(18,185,015)	(18,185,015)
Other comprehensive loss		–	–	(105,104)	(1,101,468)	(1,206,572)
Total comprehensive loss		**–**	**–**	**(105,104)**	**(19,286,483)**	**(19,391,587)**
Transactions with owners of the Company						
Issue of ordinary shares associated with Initial Public Offering ("IPO")		4,045,294	47,261,446	–	–	51,306,740
Issuance costs associated with IPO		–	(1,815,056)	–	–	(1,815,056)
Conversion of convertible loan		1,043,180	12,717,655	–	–	13,760,835
Share issuance costs		–	(136,697)	–	–	(136,697)
Share based payments		–	–	–	270,747	270,747
Share options exercised		28,552	225,613	–	–	254,165
Balance at December 31, 2014		**11,604,156**	**93,861,171**	**(51,109)**	**(52,131,426)**	**53,282,793**
As of January 1, 2015		**11,604,156**	**93,861,171**	**(51,109)**	**(52,131,426)**	**53,282,793**
Total comprehensive loss						
Net loss		–	–	–	(29,705,063)	(29,705,063)
Other comprehensive loss		–	–	(12,712)	(53,916)	(66,628)
Total comprehensive loss		**–**	**–**	**(12,712)**	**(29,758,979)**	**(29,771,691)**
Transactions with owners of the Company						
Capital increase from follow-on offering		2,110,000	19,604,877	–	–	21,714,877
Transaction costs	12	–	(643,796)	–	–	(643,796)
Share issuance costs		–	(211,142)	–	–	(211,142)
Share based payments	13	–	–	–	311,671	311,671
Share options exercised	13	7,400	51,800	–	–	59,200
Balance at December 31, 2015		**13,721,556**	**112,662,910**	**(63,821)**	**(81,578,733)**	**44,741,912**
As of January 1, 2016		**13,721,556**	**112,662,910**	**(63,821)**	**(81,578,733)**	**44,741,912**
Total comprehensive loss						
Net loss		–	–	–	(30,662,251)	(30,662,251)
Other comprehensive loss		–	–	(19,723)	(394,102)	(413,825)
Total comprehensive loss		–	–	**(19,723)**	**(31,056,353)**	**(31,076,076)**
Transactions with owners of the Company						
Issue of bonus shares	13	10,325	177,767	–	–	188,092
Share issuance costs	13	–	(1,862)	–	–	(1,862)
Share based payments	13	–	–	–	290,783	290,783
Balance at December 31, 2016		**13,731,881**	**112,838,815**	**(83,544)**	**(112,344,303)**	**14,142,849**

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

AURIS MEDICAL HOLDING AG

Consolidated Statement of Cash Flows
For the Years Ended December 31, 2016, 2015, and 2014
(in CHF)

	Note	2016	2015	2014
Cash flows from operating activities				
Net loss		**(30,662,251)**	**(29,705,063)**	**(18,185,015)**
Adjustments for:				
Depreciation	16, 17	97,600	92,777	73,984
Unrealized foreign currency exchange (gain)/loss, net		99,091	(1,167,227)	(4,066,452)
Net interest expense/(income)	19	748,840	(36,390)	(2,498)
Share based payments	13	290,783	311,671	270,747
Employee benefits		122,501	111,321	(19,211)
Fair value derivative financial instruments	24	(291,048)	–	–
Income tax gain	20	(131,055)	–	–
		(29,725,539)	**(30,392,911)**	**(21,928,445)**
Changes in:				
Other receivables		277,483	(146,244)	(17,634)
Prepayments		(771,551)	84,126	(82,033)
Trade and other payables		632,474	(2,028,862)	2,279,626
Accrued expenses		133,522	3,756,744	432,449
Net cash used in operating activities		**(29,453,611)**	**(28,727,147)**	**(19,316,037)**
Cash flows from investing activities				
Purchase of property and equipment	7	(244,324)	(79,920)	(113,496)
Purchase of intangibles	8	–	–	(1,125,000)
Interest received	19	67,553	36,562	52,133
Net cash from/(used in) investing activities		**(176,771)**	**(43,358)**	**(1,186,363)**
Cash flows from financing activities				
Proceeds from exercise of options	12	–	59,200	254,165
Share issuance costs	12	(1,862)	(211,142)	(136,697)
Proceeds from issue of loan with warrant	24	11,986,671	–	–
Proceeds from follow-on offering, net of underwriting fees and follow-on offering costs	12	–	21,071,081	–
Proceeds from IPO, net of underwriting fees and IPO costs		–	–	50,037,847
Share issuance costs IPO		–	–	(546,163)
Interest paid	19, 24	(546,170)	(172)	–
Net cash from financing activities		**11,438,639**	**20,918,967**	**49,609,152**
Net (decrease)/increase in cash and cash equivalents		**(18,191,743)**	**(7,851,538)**	**29,106,752**
Cash and cash equivalents at beginning of the period		50,237,300	56,934,325	23,865,842
Net effect of currency translation on cash		396,665	1,154,513	3,961,731
Cash and cash equivalents at end of the period		**32,442,222**	**50,237,300**	**56,934,325**

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

AURIS MEDICAL HOLDING AG

1. Reporting entity

Auris Medical Holding AG (the "Company") is a corporation (*Aktiengesellschaft*) organized in accordance with Swiss law and domiciled in Switzerland. The Company's registered address is Bahnhofstrasse 21, 6300 Zug. 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
- 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

On April 22, 2014, we changed our 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.

The Group is primarily involved in the development of pharmaceutical products for the treatment of inner ear and vestibular disorders, in particular tinnitus and hearing loss. Its most advanced projects are in the late stage of clinical development.

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 10, 2017.

Basis of measurement

The consolidated financial statements are prepared on the historical cost basis, except for the revaluation to fair value of certain financial assets. 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.

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.

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 207,445, the Group has not recorded any deferred tax assets in relation to these tax losses. 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 2014 and 2015 fiscal years.

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. Generally 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. Given the current stage of the Group's development projects, no development expenditures have yet been capitalized. The Group has capitalized certain milestone payments with regard 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.

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 pharmaceutical products for the treatment of inner ear and vestibular 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:

Currency		Geographical area	Reporting entities	December 31, 2016	December 31, 2015	December 31, 2014
CHF	Swiss Franc	Switzerland	3	1.0000	1.0000	1.0000
USD	Dollar	United States	1	1.0196	1.0014	0.9895
EUR	Euro	Europe	1	1.0723	1.0875	1.2027

Average exchange rates for the year for the most significant foreign currencies:

Currency		Geographical area	Reporting entities	2016	2015	2014
CHF	Swiss Franc	Switzerland	3	1.0000	1.0000	1.0000
USD	Dollar	United States	1	0.9855	0.9613	0.9150
EUR	Euro	Europe	1	1.0901	1.0659	1.2144

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. Given the current stage of the development projects, no development expenditures (other than certain milestone payments) have been capitalized in 2014 and 2015. Intellectual property-related costs for patents are part of the expenditure for 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 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 and available-for-sale financial assets. The classification depends on the nature and purpose of the financial assets and is determined at the time of initial recognition.

Recognition and derecognition of non-derivative financial assets and liabilities

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

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

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

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

Non-derivative financial assets and liabilities—measurement

Loans and receivables

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 any impairment 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.

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 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.

Convertible loans

The component parts of convertible loans issued by the Company are classified separately as financial liabilities and equity in accordance with the substance of the contractual arrangement. At the date of issue, the fair value of the liability component is estimated using the prevailing market interest rate for a similar non-convertible instrument. This amount is recorded as a liability on an amortized cost basis using the effective interest method until extinguished upon conversion or at the instrument’s maturity date. The equity component is determined by deducting the amount of the liability component from the fair value of the compound instrument as a whole. This is recognized and included in equity, net of income tax effects, and is not subsequently remeasured.

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.

Available-for-sale financial assets

Impairment losses on available-for-sale financial assets are recognized by reclassifying the losses accumulated in the fair value reserve to profit or loss. The amount reclassified is the difference between the acquisition cost (net of any principal repayment and amortization) and the current fair value, less any impairment loss previously recognized in profit or loss.

Derivative Financial Instruments

Derivative financial instruments 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.

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 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 various share-based payment plans in the form of stock option plans 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. The vesting of share options is conditional on the employee completing a period of service of three and four years respectively, from the grant date, in accordance with Stock Option Plans A and C. Under the Auris Medical Holding AG 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 in 2016 and in 2015 vest after a period of one year after the grant date. Stock Option Plan B was created to provide shares for share based compensation plans; it was used in the years 2008, 2009 and 2014 and has been abolished in 2015.

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 (nominal value) and share premium.

Valuation of share options

Following the completion of our initial public offering, 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.

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.

Leases

Leases in which a significant portion of the risks and rewards of ownership are retained by the lessor are classified as operating leases. Payments made under operating leases (net of any incentives received from the lessor) are charged to profit or loss on a straight-line basis over the period of the lease.

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 the current year, the following revised standards have been adopted in these financial statements. Adoption has not had a significant impact on the amounts reported in these financial statements but may impact the accounting for future transactions and arrangements.

IAS 1 amendments	Presentation of Financial Statements
Various	Annual Improvements to IFRSs:2012-2014 Cycle
IAS 16 & 38 amendments	Property Plant and Equipment, Intangible Assets
IFRS 10,12, & IAS 28 amendments	Consolidated Financial Statements, Disclosure of Interests in Other Entities
IFRS 14	Regulatory Deferral Accounts
IFRS 11 amendment	Joint Arrangement
IAS 16 & 41 amendments	Property Plant and Equipment, Agriculture
IAS 27 amendments	Consolidated and Separate Financial Statements

A number of new standards, amendments to standards and interpretations are effective for annual periods beginning after January 1, 2017, 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 2	Amendment to IFRS 2, Classification and Measurement of Share-based Payment Transaction	1)	January 1, 2018	To be determined
IFRS 9	Financial Instruments	1)	January 1, 2018	To be determined
IFRS 15	Revenue from Contracts with Customers	1)	January 1, 2018	To be determined
IFRS 15	Amendments to IFRS 15 Contracts with Customers	1)	January 1, 2018	To be determined
IFRS 16	Leases	1)	January 1, 2019	To be determined
IAS 7	Amendments to IAS 7, Statement of Cash Flows	1)	January 1, 2017	FY 2017
IAS 12	Amendments to IAS 12, Income Taxes	1)	January 1, 2017	FY 2017
IFRS 4 / IFRS 9	Amendments to IFRS 4, Insurance Contracts	1)	January 1, 2018	To be determined

1) The impact on the consolidated financial statements of the Group cannot yet be determined with sufficient reliability.

5. Financial instruments and risk management

The following table shows the carrying amounts of financial assets and financial liabilities:

Financial assets	December 31, 2016	December 31, 2015
Available for sale		
Current financial assets	–	–
Loans and receivables		
Cash and cash equivalents	32,442,222	50,237,300
Other receivables	134,900	592,792
Total financial assets	**32,577,122**	**50,830,092**
Financial liabilities		
At amortized cost		
Trade and other payables	1,837,997	1,205,522
Accrued expenses	4,652,033	4,917,074
Loan	12,364,204	–
At fair value through profit and loss		
Derivative financial instruments	117,132	–
Total financial liabilities	**18,971,366**	**6,122,596**

Fair values

The carrying amount of cash and cash equivalents, other receivables, trade and other payables and accrued expenses 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 2016 and 2015 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 analyses the remaining contractual maturities of financial liabilities, including estimated interest payments as of December 31, 2016 and 2015. 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, 2016					
Trade and other payables	1,837,997	1,837,997	–	–	1,837,997
Accrued expenses	4,652,033	3,632,752	1,019,281	–	4,652,033
Loan and borrowings	12,364,204	311,013	8,725,772	6,834,249	15,871,034
Derivative financial instruments	117,132	–	–	117,132	117,132
Total	**18,971,366**	**5,781,762**	**9,745,053**	**6,951,381**	**22,478,196**

	Carrying amount	Less than 3 months	Between 3 months and 2 years	2 years and later	Total
December 31, 2015					
Trade and other payables	1,205,522	1,205,522	–	–	1,205,522
Accrued expenses	4,917,074	4,780,737	136,337	–	4,917,074
Total	**6,122,596**	**5,986,259**	**136,337**	**–**	**6,122,596**

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, 2016 and December 31, 2015, 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 and EUR) 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, 2016	December 31,2015
Financial assets		
Cash and cash equivalents	32,442,222	50,237,300
Other receivables	134,900	592,792
Total	**32,577,122**	**50,830,092**

As of December 31, 2016 and December 31, 2015 other receivables consisted of other non-current receivables from third party and deposits for rent. As of December 2015, other receivables also included advance payments to suppliers.

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:

	2016		2015	
in CHF	**USD**	**EUR**	**USD**	**EUR**
Other receivables	–	–	158,625	286,313
Cash and cash equivalents	31,124,874	444,075	44,643,328	193,366
Trade and other payables	(501,249)	(847,892)	(284,620)	(189,393)
Accrued expenses	(1,031,096)	(2,964,552)	(2,046,276)	(2,638,638)
Loan and borrowings	(12,364,204)	–	–	–
Derivative financial instruments	(117,132)	–	–	–
Net statement of financial position exposure - asset/(liability)	**17,111,193**	**(3,368,369)**	**42,471,057**	**(2,348,352)**

As of December 31, 2016, a 5% increase or decrease in the USD/CHF exchange rate with all other variables held constant would have resulted in a CHF 872,443 (2015: CHF 2,135,522) 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 180,595 (2015: CHF 127,692) increase or decrease in the net result.

The Company has subsidiaries in the United States 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.

Interest rate risk

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 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 loan agreement. The loan matures on January 2, 2020 and bears interest at a minimum rate of 9.55% per annum, and is subject to the variability of the prime interest rate. The Company's exposure to interest rates on financial assets and financial liabilities is resulting from loan and cash at banks. As of December 31, 2016 an increase or decrease in interest rates on financial obligations by 50 basis points effective July 19, 2016 with all other variables held constant would have resulted in a CHF 28,276 (2015: immaterial effect) increase or decrease in the net result.

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, 2016	December 31, 2015
Switzerland	1,966,592	1,743,156
Total	**1,966,592**	**1,743,156**

Non-current assets exclude financial instruments.

7. Property and Equipment

	Production equipment	Office furniture and EDP	Leasehold improvements	Total
At cost				
As of January 1, 2015	**230,249**	**182,042**	**17,132**	**429,423**
Additions	53,250	26,670	–	79,920
As of December 31, 2015	**283,499**	**208,712**	**17,132**	**509,343**
Additions	**–**	24,994	219,330	244,324
As of December 31, 2016	**283,499**	**233,706**	**236,462**	**753,667**
Accumulated depreciation				
As of January 1, 2015	**(73,592)**	**(114,539)**	**(5,865)**	**(193,996)**
Charge for the year	(54,037)	(35,334)	(3,406)	(92,777)
As of December 31, 2015	**(127,629)**	**(149,873)**	**(9,271)**	**(286,773)**
Charge for the year	(56,700)	(33,837)	(7,063)	(97,600)
As of December 31, 2016	**(184,329)**	**(183,710)**	**(16,334)**	**(384,373)**
Net book value				
As of December 31, 2015	**155,870**	**58,839**	**7,861**	**222,570**
As of December 31, 2016	**99,170**	**49,996**	**220,128**	**369,294**

As of December 31, 2016, and 2015 no items of property and equipment were pledged. Refer to note 24 for security provided to Hercules Capital, Inc under the Loan and Security Agreement.

8. Intangible assets

	Licences
At cost	
As of January 1, 2015	1,482,520
As of December 31, 2015	1,482,520
As of December 31, 2016	1,482,520
Accumulated amortization and impairment losses	
As of December 31, 2015	–
As of December 31, 2016	–
Net book value	
As of December 31, 2015	1,482,520
As of December 31, 2016	1,482,520

Intangible assets comprise upfront and milestone payments related to licenses. In 2013 a milestone 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.

No amortization or impairment was recorded in 2016 and 2015.

9. Other receivables

	December 31, 2016	December 31, 2015
Advance payments to suppliers	–	465,624
Value added tax receivable	132,570	82,468
Withholding tax receivable	23,644	13,522
Deposit credit cards	79,900	–
Other	60,417	89,102
Total other receivables	**296,531**	**650,716**

Other receivables were not considered impaired in the years under review.

10. Prepayments

	December 31, 2016	December 31, 2015
Advance payments to supplier	759,716	–
Clinical projects and related activities	41,681	–
Insurance	151,198	179,674
Other	–	1,370
Total prepayments	**952,595**	**181,044**

11. Cash and cash equivalents

	December 31, 2016	December 31, 2015
Cash in bank accounts	32,441,968	50,235,869
Cash on hand	254	1,431
Total cash and cash equivalents	**32,442,222**	**50,237,300**

12. Capital and reserves

Share capital

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

	December 31, 2016		December 31, 2015	
	Number	CHF	Number	CHF
Common shares with a nominal value of CHF 0.40 each	34,329,704	13,731,881	34,303,891	13,721,556
Total	**34,329,704**	**13,731,881**	**34,303,891**	**13,721,556**

	Common Shares (Number)	
	2016	2015
As of January 1	34,303,891	29,010,391
Common shares issued or for stock options exercises with a nominal value of CHF 0.40 each		18,500
Common shares issued for the follow-on offering with a nominal value of CHF 0.40 each		5,275,000
Restricted shares issue for bonus purposes nominal value of CHF 0.40 each	25,813	
Total, as of December 31	**34,329,704**	**34,303,891**

Follow-On Offering on Nasdaq Global Market

On May 20, 2015, the Company completed a public offering of 5,275,000 shares, yielding net proceeds after underwriting discounts of USD 23.6 million (CHF 21.7 million). Offering costs associated with the follow-on amounted to CHF 643,796. Following the offering (and settlement of the employee options mentioned below) there were 34,303,891 common shares of the Company outstanding as of December 31, 2015.

Issuance of common shares upon exercise of options

In 2015, beneficiaries of Stock Option Plan A exercised their right to acquire common shares of the Company at CHF 3.20 per share. This resulted in an increase in the number of outstanding common shares of 18,500 and an increase in the share capital of CHF 7,400. Total proceeds from the exercise to the Company were CHF 59,200.

Issuance of common shares with restrictions

For the business year 2015, 25,813 restricted common shares with a nominal value of CHF 0.40 were awarded and issued on January 7, 2016 under the Equity Incentive Plan for the purpose of share based bonus payments. The shares are fully vested on the grant date but remain subject to transfer restrictions for a period until January 7, 2019. The Company recorded a payroll charge of CHF 188,092 in 2015.

Controlled Equity Offering

On June 1, 2016, we entered into a Controlled Equity Offering^{SM} Sales Agreement (the “Sales Agreement”) with Cantor Fitzgerald & Co. (“Cantor”), pursuant to which we may offer and sell, from time to time common shares, with a nominal value of CHF 0.40 per share, having an aggregate offering price of up to $35 million through Cantor. Any common shares offered and sold will be issued pursuant to our shelf registration statement on F-3 (Registration No. 333-206710) as supplemented by a prospectus supplement, dated June 1, 2016. In 2016, we did not offer or sell any common shares under the Sales Agreement.

Authorized share capital

After the follow-on offering in May 2015 and as of December 31, 2015, the authorized capital amounted to CHF 1,204,706 or 3,011,765 registered shares with a nominal value of CHF 0.40 each.

On April 8, 2016, the annual general meeting of shareholders revised the provisions related to authorized and contingent capital of the Company and approved an increase and extension of the authorized share capital. As of December 31, 2016, the Company's authorized capital amounted to CHF 6,860,000 and allowed to Board of Directors, subject to the terms and conditions set forth in the Articles of Association, to issue up to 17,150,000 fully paid registered shares with a nominal value of CHF 0.40 each.

Conditional share capital

The share capital may be increased by the issuance of up to 5,000,000 fully paid registered Common Shares with a nominal value of CHF 0.40 per share and to the maximum amount of CHF 2,000,000 in execution of subscription rights, which may be granted to employees, members of the Board of Directors as well as key service providers (see Note 13 for further reference).

The Company's share capital may be further increased by the issuance of up to 12,150,000 fully paid registered Common Shares with a nominal value of CHF 0.40 per share and to the maximum amount of CHF 4,860,000 in execution of conversion rights in connection with warrants and convertible bonds of the Company. For the terms of the warrant issued to Hercules, refer to Note 24.

13. Share based compensation

Description

On November 21, 2008, the Company established share option programs ("Stock Option Plans A and B") for employees, members of the Board of Directors as well as key service providers to purchase shares in the Company. Stock Option Plan A was amended and superseded by an updated version effective November 24, 2009, and replaced with amendments by Stock Option Plan C for any future option grants effective April 5, 2013. Grants under Stock Option Plan A and subsequently under Stock Option Plan C were offered in each year with vesting periods of three and four years; grants under Stock Option Plan B were made in 2008, 2009 and 2014 only. Stock Option Plan B was abolished in 2015 and no grants under Stock Option Plan B were made in 2015. In 2014, the Group introduced a further equity incentive plan, the EIP. The Company granted 555,660 options in 2016 (2015: 234,750) under the EIP.

For the business year 2015, the Company granted 25,813 restricted shares to employees under the Equity Incentive Plan on January 7, 2016. The grant price for these awards was the closing price of our shares on January 7, 2016 (USD 7.08) and resulted in a total payroll charge of CHF 188,092. These shares vest upon grant and have a sale restriction for a period of 3 years.

Holders of vested options are entitled to purchase common shares of the Company. For the stock option plans that were in place before the IPO, the exercise price corresponded to the value per share at the most recent financing round. 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 are as follows:

Plan	Number of options outstanding	Vesting conditions	Contractual life of options
Stock option Plan A	92,500	3 years' service from grant date	5 years
Stock option Plan C	121,250	4 years' service from grant date	6 years
Equity Incentive Plan Board	102,500	1 year service from grant date	8 years
Equity Incentive Plan Employees / Board*	360,945	2 years' service from grant date (50%)	8 years
Equity Incentive Plan Employees / Board*	360,945	3 years' service from grant date (50%)	8 years

* 25,000 options issued to Bettina Stubinski, the former Chief Medical Officer of the Company, have vested early, on December 29, 2016 and will expire on March 29, 2017.

Measurement of fair values

The fair value of the options was measured based on the Black-Scholes formula.

	Stock Option Plan			
	Equity Incentive Plan 2016	Equity Incentive Plan 2016	Equity Incentive Plan 2015	Equity Incentive Plan 2015
Fair value at grant date	USD 0.308 (1 year vesting) USD 0.472 (2 year vesting) USD 0.583 (3 year vesting)	USD 1.094 (1 year vesting) USD 1.560 (2 year vesting) USD 1.888 (3 year vesting)	USD 1.161 (1 year vesting) USD 1.679 (2 year vesting) USD 2.052 (3 year vesting)	USD 2.289 (2 year vesting) USD 2.773 (3 year vesting)
Share price at grant date	USD 1.03	USD 3.66	USD 4.33	USD 5.75
Exercise price	USD 1.39	USD 3.92	USD 4.68	USD 5.98
Expected volatility	100.93%	82.00%	74.20%	74.20%
Expected life	1,2 and 3 years	1,2 and 3 years	1, 2 and 3 years	2 and 3 years
Expected dividends	–	–	–	–
Risk-free interest rate	1.84%	1.83%	2.28%	2.06%

The Company has historically been a private company and started trading publicly in August 2014. Therefore, for the March 2015 grants under the EIP the Company lacks significant Company-specific historical and implied volatility information. For the aforementioned grants, the Company estimates expected volatility based on comparable public company data for these grants. For September 2015 award under the EIP and any grant thereafter, the Company used its own historic 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 290,783 in 2016 (2015: CHF 311,671, 2014: 270,747).

The number and weighted average exercise prices (in CHF) of options under the share option programs for Stock Option Plan A, Stock Option Plan C and the EIP are as follows:

	2016			2015		
	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	629,010	4.92	5.42	419,010	4.61	4.86
Expired during the year	(17,500)	0	0	0	0	0
Forfeited during the year	(129,030)	0	0	(6,250)	0	0
Exercised during the year	0	0	0	(18,500)	3.20	0
Granted during the year	555,660	1.99	7.81	234,750	5.31	7.61
Outstanding at December 31	**1,038,140**	**3.36**	**6.14**	**629,010**	**4.92**	**5.42**
Exercisable at December 31	199,005	4.56	3.11	71,250	4.15	1.31

The range of exercise prices for outstanding options was CHF 1.35 to CHF 6.01 as of December 31, 2016 and CHF 3.20 to CHF 6.01 as of December 31, 2015.

14. Trade and other payables

	December 31, 2016	December 31, 2015
Trade accounts payable - third parties	1,733,319	965,472
Other	104,678	240,050
Total trade and other payables	**1,837,997**	**1,205,522**

15. Accrued expenses

	December 31, 2016	December 31, 2015
Accrued research and development costs including milestone payments	4,307,089	4,403,622
Professional fees	316,470	291,629
Accrued vacation & overtime	115,749	44,238
Employee benefits incl. share based payments	138,960	188,092
Board of Directors fees	1,529	-
Other	26,945	33,731
Total accrued expenses	**4,906,742**	**4,961,312**

16. Research and development expense

	December 31, 2016	December 31, 2015	December 31, 2014
Pre-clinical projects	546,429	468,326	1,160,058
Clinical projects	16,639,304	20,808,025	12,141,571
Drug manufacturing and substance	2,608,814	1,866,148	1,383,581
Employee benefits and expenses	2,854,624	2,140,664	1,718,212
Lease expenses	84,344	42,953	68,082
Patents and trademarks	941,836	824,201	665,023
Regulatory projects	1,043,287	331,822	519,104
Depreciation tangible assets	58,125	54,037	48,830
Total research and development expense	**24,776,763**	**26,536,176**	**17,704,461**

17. General and administrative expense

	December 31, 2016	December 31, 2015	December 31, 2014
Employee benefits and expenses	2,174,543	1,502,900	1,136,677
Business development	45,649	72,562	237,720
Travel expenses	158,774	257,454	169,602
Administration expenses	2,969,796	2,386,791	2,014,178
IPO expenses, expensed	–	–	822,367
Lease expenses	63,695	59,665	35,072
Depreciation tangible assets	39,475	38,740	25,153
Capital tax expenses	(5,420)	23,458	48,281
Total general and administrative expenses	**5,446,512**	**4,341,570**	**4,489,051**

As of March 31, 2014, management determined that a successful completion of an IPO was not deemed to be more likely than not thus CHF 822,367 were expensed in the first quarter of 2014.

18. Employee benefits

	December 31, 2016	December 31, 2015	December 31, 2014
Salaries	3,662,180	2,833,741	2,259,112
Pension costs	342,805	282,517	118,755
Other social benefits	301,537	191,079	131,939
Share based payments costs	290,783	311,671	270,748
Recruitment costs	391,035	–	–
Other personnel expenditures	40,827	24,557	74,334
Total employee benefits	**5,029,167**	**3,643,565**	**2,854,888**

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. In 2014 and 2015 the rate was 1.75% and 1.25% in 2016.

The assets are invested by the collective foundation in a diversified portfolio that respects the requirements of the Swiss BVG. 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.

The following tables present information about the net defined benefit liability and its components:

Change in defined benefit obligation

	2016	2015
Defined benefit obligation at January 1	5,427,776	4,895,667
Service costs	319,173	261,778
Plan participants' contribution	218,275	171,196
Interest cost	62,916	58,943
Actuarial losses	417,937	7,750
Transfer-out amounts	(1,276,315)	(353,925)
Transfer-in amounts of new employees	1,953,079	386,367
Defined benefit obligation at December 31	**7,122,841**	**5,427,776**

The defined benefit obligation includes only liabilities for active employees. The weighted average modified duration of the defined benefit obligation at December 31, 2016 is 21.7 years (2015: 22.4 years).

Change in fair value of plan assets

	2016	2015
Fair value of plan assets at January 1	3,851,943	3,485,069
Interest income	47,994	44,070
Return on plan assets excluding interest income	23,835	(46,164)
Employer contributions	220,306	171,196
Plan participants' contributions	218,275	171,196
Transfer-out amounts	(1,276,315)	(353,925)
Transfer-in amounts of new employees	1,953,079	386,367
Administration expense	(8,710)	(5,866)
Fair value of plan assets at December 31	**5,030,407**	**3,851,943**

Net defined benefit liability recognized in the statement of financial position

	December 31, 2016	December 31, 2015
Present value of funded defined benefit obligation	7,122,841	5,427,776
Fair value of plan assets	(5,030,407)	(3,851,943)
Net defined benefit liability	**2,092,434**	**1,575,833**

Defined Benefit Cost

	2016	2015	2014
Service cost	319,173	261,778	111,513
Net interest expense	14,922	14,873	4,188
Administration expense	8,710	5,866	3,054
Total defined costs for the year recognized in profit or loss	**342,805**	**282,517**	**118,755**

Remeasurement of the Defined Benefit Liability

	2016	2015	2014
Actuarial loss (gain) arising from changes in financial assumptions	412,396	(167,623)	699,456
Actuarial loss arising from experience adjustments	264,417	175,375	784,766
Actuarial gain arising from demographic assumptions	(258,876)	–	–
Return on plan assets excluding interest income	(23,835)	46,164	(382,755)
Total defined benefit cost for the year recognized in the other comprehensive loss	**394,102**	**53,916**	**1,101,467**

Assumptions

At December 31	**2016**	**2015**	**2014**
Discount rate	0.70%	1.10%	1.20%
Future salary increase	1.10%	1.10%	1.50%
Pension indexation	0.00%	0.00%	0.00%
Mortality and disability rates	BVG2015G	BVG 2010G	BVG 2010G

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,	2016	2015
Chance in assumption	0.25 % increase	0.25 % increase
Discount rate	(324,057)	(248,110)
Salary increase	42,181	39,749
Pension indexation	201,221	148,095
Change in assumption	+ 1 year	+ 1 year
Life expectancy	167,161	106,136

19. Finance income and finance expense

	2016	2015	2014
Interest income	67,565	36,562	52,133
Net foreign currency exchange gain	843,950	1,806,206	4,164,189
Revaluation gain from derivative financial instruments	291,048	–	–
Total finance income	**1,202,563**	**1,842,768**	**4,216,322**
Interest expense related parties	–	–	49,635
Interest expense (incl. Bank charges)	828,547	7,985	6,175
Net foreign currency exchange loss	944,047	662,100	152,015
Total finance expense	**1,772,594**	**670,085**	**207,825**
Finance income/(expense), net	**(570,031)**	**1,172,683**	**4,008,497**

In 2014, interest expense on convertible loans of CHF 49,635 did not result in a net cash outflow. In 2016, net foreign currency exchange gains contain translation gains of CHF 396,665 (2015: CHF 1,154,513; 2014: CHF 3,961,731) which arose on the Company's USD and EUR denominated cash and cash equivalents. In 2016, interest expenses include interest paid to Hercules Capital, Inc. under the Loan and Security Agreement in an amount of CHF 546,170.

20. Taxation

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

	2016	2015	2014
Deferred income tax expense	–	(32,761)	(32,761)
Deferred income tax gain	131,055	32,761	32,761
	131,055	**–**	**–**

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 21.5% in 2016 (2015: 21.9%, 2014: 23%) as summarized in the following table:

Reconciliation	2016	2015	2014
Loss before income tax	(30,793,306)	(29,705,063)	(18,185,015)
Income tax at statutory tax rates applicable to results in the respective countries	6,629,237	6,493,569	4,177,780
Effect of unrecognized temporary differences	(27,072)	(105,395)	(273,073)
Effect of unrecognized taxable losses	(6,360,837)	(6,438,609)	(4,160,118)
Effect of previously unrecognised deferred tax asset	131,055		
Effect of expenses deductible for tax purposes	2,505		
Effect of expenses not considerable for tax purposes	23,716		
Effect of impact from application of different tax rates	(267,695)		
Effect of unrecognized deferred tax due to change in income tax rate	–		156,005
Effect of unrecognized taxable losses in equity	146	50,435	99,406
Income tax (expense)/income	**131,055**	**–**	**–**

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, 2016	December 31, 2015
Intangible assets	(327,637)	(327,637)
Hercules Loan Facility and Warrant	(76,390)	–
Total	**(404,027)**	**(327,637)**

Deferred Tax Asset	December 31, 2016	December 31, 2015
Net operating loss (NOL)	207,445	–
Total	**207,445**	**–**
Deferred Tax, net	**(196,582)**	**(327,637)**

Deferred Tax 2016	Opening Balance	Recognized in Profit or Loss	Recognized in Equity	Closing Balance
Intangible assets	(327,637)	–	–	(327,637)
Hercules Loan Facility and Warrant	–	(76,390)	–	(76,390)
Net operating loss (NOL)	–	207,445	–	207,445
Total	**(327,637)**	**131,055**	**–**	**(196,582)**

Deferred Tax 2015	Opening Balance	Recognized in Profit or Loss	Recognized in Equity	Closing Balance
Intangible assets	(327,637)	–	–	(327,637)
Provisions	(32,761)	32,761	–	–
Net operating loss (NOL)	32,761	(32,761)	–	–
Total	**(327,637)**	**–**	**–**	**(327,637)**

As of December 31, 2016, the Group had total gross tax loss carry forwards amounting to CHF 115.4 million (2015: CHF 86 million), of which CHF 114.3 million related to Auris Medical AG, Auris Medical Holding AG and Otolanum AG in Switzerland and CHF 1.1 million to Auris Medical Inc. in the United States (2015: CHF 84.9 million for Auris Medical AG and Otolanum AG and CHF 1.1 million for Auris Medical Inc.).

The Group’s tax loss carry-forwards with their expiry dates are as follows:

	December 31, 2016	December 31, 2015
Within 1 year	1,859,601	1,686,986
Between 1 and 2 years	9,928,391	3,613,999
Between 3 and 7 years	102,542,641	79,651,641
More than 7 years	1,087,543	1,073,609
Total	**115,418,176**	**86,026,235**

The tax effect of the major unrecognized temporary differences and loss carry-forwards is presented in the table below:

	December 31, 2016	December 31, 2015
Deductible temporary differences		
Employee benefit plan	450,227	348,259
Stock option plans	–	183,023
Total potential tax assets	**450,227**	**531,282**
Taxable unrecognized temporary differences		
Property and equipment	–	–
Total unrecognized potential tax liabilities	–	–
Offsetting potential tax liabilities with potential tax assets	–	–
Net potential tax assets from temporary differences not recognized	450,227	531,282
Potential tax assets from loss carry-forwards not recognized	25,082,968	19,049,472
Total potential tax assets from loss carry-forwards and temporary differences not recognized	**25,533,195**	**19,580,754**

21. Loss per share

	December 31, 2016	December 31, 2015	December 31, 2014
Loss attributable to owners of the Company	(30,662,251)	(29,705,063)	(18,185,015)
Weighted average number of shares outstanding	34,329,280	32,299,166	27,692,494
Basic and diluted loss per share	**(0.89)**	**(0.92)**	**(0.66)**

For the years ended December 31, 2016 and 2015 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) and the warrant issued to Hercules (Note 24) as they would be anti-dilutive. As of December 31, 2016, the Company has 1,038,140 options outstanding under its stock option plans. The average number of options outstanding between January 1, 2016 and December 31, 2016 was 769,529 (524,010 for the period between January 1, 2015 and December 31, 2015). As of December 31, 2016, the Company issued warrants to purchase up to 241,117 of its common shares outstanding.

22. Commitments and contingencies

Operating lease commitments

On October 1, 2016, the Group entered into a lease for a new office space under an operating lease agreement. The lease has a five year fixed term, subject to a one-time cancellation option effective as per September 30, 2019. Effective December 31, 2016, the Group entered into a termination agreement related to a lease entered into on April 1, 2013.

The future minimum lease payments under non-cancellable operating leases that are not accounted for in the statement of financial position were as follows:

	December 31, 2016	December 31, 2015
Within one year	161,110	100,572
Between one and five years	607,161	114,465
Total	**768,271**	**215,037**

Office lease expenses of CHF 148,039, CHF 107,450 and CHF 99,072 were booked in 2016, 2015 and 2014, 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.

Compensation of the members of the Board of Directors and Management

In 2016, the total compensation paid to management amounted to CHF 1,871,406 (2015: CHF 1,619,208; 2014: CHF 1,220,677). The fees paid to members of the Board of Directors in 2016 for their activities as board members totaled CHF 364,276 (2015: CHF 329,827; 2014: CHF 143,647).

Up to the Company's IPO, non-executive directors received part or all of their remuneration in stock options; travel and out of pocket expenses were reimbursed in cash by the Group. Executive directors and directors delegated and remunerated by a shareholder for its representation on the Board were not entitled to any specific remuneration for their Board membership and work. Following the IPO, the Board's remuneration policy was modified in that all non-executive directors received remuneration for their work as members of the Board as well as of the newly constituted Compensation Committee and Audit Committee.

	Executive Management			Board of Directors			Total		
	2016	2015	2014	2016	2015	2014	2016	2015	2014
Short term benefits	1,554,850	1,363,796	1,008,817	325,493	268,810	81,567	1,880,343	1,632,606	1,090,384
Post-employee benefits years	88,838	78,721	63,386	–	–	–	88,838	78,721	63,386
Share-based payment charge	217,981	176,691	148,474	103,380	61,017	62,080	321,361	237,708	210,554
Total	**1,861,669**	**1,619,208**	**1,220,677**	**428,873**	**329,827**	**143,647**	**2,290,542**	**1,949,035**	**1,364,324**

In 2016, CHF 321,361 (2015: CHF 237,708; 2014: CHF 210,554) was expensed for grants of stock options to members of the Board of Directors and management. The 2016 share based payment charge shown above excludes adjustments for instruments forfeited in 2016 due to termination of service. Contributions to pension schemes amounted to CHF 88,838, CHF 78,721 and CHF 63,386 during the years 2016, 2015 and 2014, respectively. No termination benefits or other long term benefits were paid.

Members of the Board of Directors and management held 656,355, 457,510 and 287,510 stock options as of December 31, 2016, 2015, and 2014, respectively.

For the business year 2015, the Company granted 25,813 (2014: 20,881) restricted shares to employees under the Equity Incentive Plan (2014: Stock Option Plan B). The grant price for the 2015 awards was the closing price of our shares on January 7, 2016 (USD 7.08) and resulted in a total payroll charge of CHF 188,092 (2014: CHF 92,565). These shares vest upon grant and have a sale restriction for a period of 3 years. For the 2016 business year, no restricted shares were issued.

Controlled Equity Offering℠

Thomas Meyer, our Chief Executive Officer, or the Share Lender, has entered into a share lending agreement with Cantor to facilitate the timely settlement of common shares sold under the Sales Agreement with Cantor. Pursuant to the terms of the share lending agreement, the Share Lender will lend common shares to Cantor so that those common shares may be delivered by Cantor to purchasers of common shares sold in the offering. Cantor will return common shares to the Share Lender upon the issuance of new common shares by the Company to Cantor. Neither the Company nor the Share Lender will receive any compensation for this arrangement.

24. Loan and Warrant

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 matures on January 2, 2020 and bears interest at a minimum rate of 9.55% per annum, and is subject to the variability of the prime interest rate. The loan is secured by a pledge of the shares in 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.

The loan was initially recognized at transaction value less the fair value of the warrant as of the transaction date and less directly attributable transactions costs. Following the initial recognition, the loan is measured at amortized cost using the effective interest method. As of December 31, 2016, the loan is valued at CHF 12,364,204. Of the CHF 12,364,204 an amount of CHF 2,212,706, reflecting amortization payments due within the next 12 months, is classified as current liability and the remainder as non-current liability. In connection with the loan facility, the Company issued Hercules a warrant to purchase up to 241,117 of its common shares at an exercise price of $3.94 per share. As of July 19, 2016, the warrant is exercisable for 156,726 common shares. Upon Hercules making the second advance under the loan facility, the warrant shall become exercisable for the additional 84,391 common shares. The warrant expires on July 19, 2023. The fair value calculation of the warrant is based on the Black-Scholes option pricing model. Assumptions are made regarding inputs such as volatility and the risk free rate in order to determine the fair value of the warrant. As the warrant is part of the loan transaction, its initial fair value was deducted from the loan proceeds and accounted for as non-current

financial liability. Following the initial recognition, the warrant is measured at fair value and changes in fair value are shown as profit or loss.

As of December 31, 2016 the fair value of the warrant amounts to CHF 117,132. Since its initial recognition, the fair value decreased by CHF 291,048 resulting in a gain in the corresponding amount (fair value as of July 19, 2016: CHF 408,180).

25. Events after the balance sheet date

Interference Proceedings

On July 20, 2015, the USPTO declared Patent Interference No. 106,030 involving the Company's issued U.S. patent No. 9,066,865 (the "'865 Patent") and Otonomy's U.S. patent application No. 13/848,636 (the "'636 Application"). The patent interference identified claims 1-9 in the '865 Patent as interfering with claims 38, 43 and 46-50 of the '636 Application. The '865 Patent discloses methods of treating inner or middle ear diseases with intratympanic injections of poloxamer-based compositions. The claims of the '865 Patent are directed to the use of fluoroquinolone antibiotics in poloxamer 407 compositions under certain specifications. On January 26, 2017, the USPTO issued a decision on the interference granting Auris benefit of priority. As a result of the decision, judgment was entered against Otonomy and all claims in the '636 Application were refused. In addition, claims 1-8 of the '865 Patent were cancelled as the result of the USPTO's determination that the written description of the specification lacked full scope support for treating middle or inner ear disease with fluoroquinolone. However, claim 9, which is directed to a method of treating viral and bacterial infections with intratympanic injection of a fluoroquinolone antibiotic in a poloxamer 407 composition under certain specifications, was affirmed. The USPTO's decision is not final and may be appealed. Although the Company is still analyzing what effect, if any, the cancellation of claims 1-8 of the '865 Patent will have on the remainder of the '865 patent family, the Company does not expect the interference proceedings to impact its intellectual property portfolio relating to Keyzilen® and AM-111. However, given that the USPTO's decision is subject to appeal, there can be no assurance that the final outcome of the interference proceedings will not have a material adverse effect on the Company's intellectual property portfolio.

Otifex

On February 2, 2017, the Company entered into an asset purchase agreement with Otifex, pursuant to which the Company agreed to purchase and Otifex has agreed to sell certain preclinical and clinical assets related to a formulation for the intranasal application of Betahistine, which the Company refers to as AM-125. The Company plans to develop the formulation for vestibular disorders. The asset purchase agreement provides for an upfront and a development milestone payment which, in the aggregate, equal an amount less than $500,000.

Equity Offering

On February 21, 2017, the Company completed a public offering of (the "Offering") 10,000,000 common shares with a nominal value of CHF 0.40 each and 10,000,000 warrants, each warrant entitling its holder to purchase 0.70 of a common share. The net proceeds to the Company from the Offering were approximately CHF 9.2 million ($9.1 million), after deducting underwriting discounts and other estimated offering expenses payable by the Company.

Roth Capital Partners, LLC (the "Underwriter") was granted a 30-day option to purchase up to 1,500,000 additional common shares and/or 1,500,000 additional warrants. All of the common shares and warrants in the Offering were sold by the Company. 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 warrants.

The warrants are exercisable beginning on the date of issuance, and at any time up to five years from the date of issuance. Each warrant represents the right to purchase 0.70 of a common share at an exercise price equal to $1.20 per share. The exercise price is subject to adjustment upon the occurrence of certain events; provided that in no event will the exercise price per share be lower than the nominal value of a common share at the time of exercise.

PRIVERA

Addendum No. 1

to the lease agreement dated	15 January 2013	
Property	Falknerstrasse 2/4, 4001 Basel	
	Office space on the 3rd floor / Ref. No. 21003.01.430010	
between	Assetimmo Immobilien Anlagestiftung, Zurich	"Lessor"
represented by	PRIVERA AG,	"Agent"
	Mühlematt Shopping	
	Mühlemattstrasse 22	
	4104 Oberwil	
and	Auris Medical AG	"Lessee"
	Falknerstrasse 2/4	
	4001 Basel	
Regarding	**Termination of lease**	
	as of 31 December 2016	

By way of amendment to the Lease Agreement, the following is agreed:

1. **Termination of lease**
   The existing/current lease based on the lease agreement dated 15 January 2013 between the abovementioned Parties is terminated by mutual agreement as of 31 December 2016.

2. **Special provisions**
   This Addendum No. 1 does not become legally valid unless and until Scope Solutions AG signs a lease agreement for a lease commencing as of 1 January 2017 for the abovementioned office space as the subsequent tenant.

3. **Further contractual provisions**
   In all other respects, the provisions of the lease agreement of 15 January 2013 apply.

4. **Official copies of Agreement**
   The present Addendum No. 1 is issued and signed in two counterparts with the same wording, with the Lessee and the Lessor each receiving one counterpart thereof.

Oberwil, 1 December 2016 / PKUM

For the Lessor: The Agent
PRIVERA AG

[signature] [signature]

The Lessee
Auris Medical AG

[signature]
Anne Sabine Zoller
General Counsel

Commercial Lease Agreement

Principal lease: office space
Reference number: 6007.01.0401.07
Commencement of lease: 01 October 2016
Subject to VAT

1 Lessor

PSP Real Estate AG
Seestrasse 353
8038 Zurich

VAT No. CHE-116.310.369 VAT

2 Represented by

PSP Management AG
Baslerstrasse 44
4600 Olten

3 Lessee

Lessee 1
Auris Medical AG
Falknerstrasse 4
4001 Basel

VAT No. CHE-455.709.593 VAT

VAT No.

4 Property

Dornacherstr. 210, 4053 Basel

Initials [initials]

5 Table of contents

6 Leased properties; rent; ancillary space; purpose of use; ancillary costs

6.1 Leased properties and rents

Property type	Floor	Prop. No.	Reference No.	Area, approx. m^2	Price, m^2/year	Francs per year	Francs per month
Office space	4th		6007.01.0401.07	568.00	230.00	130,639.80	10,886.65
Total net rent						130,639.80	10,886.65
Advance payment for heating/operating costs						11,400.00	950.00
VAT, 8%						11,363.40	946.95
Total gross rent, incl. VAT						153,403.20	12,783.60

The agreed base net rent refers to the leased property in bare construction condition.

6.2 Supplementary space

The total leased space stated includes the following supplementary space:

Reference No. 6007.01.0401.07 approx. 36 m^2 share of approx. 72 m^2 general corridor and restroom facilities

6.3 Ancillary space for shared use

The following space and facilities are available for shared use without separate rent being charged therefor:

Stairway and three passenger elevators

Any operating costs with regard to the shared-use space and facilities will be borne proportionally by the users or the Lessee, as the case may be.

6.4 Intended use

The leased premises must only be used as office space. The only specification stipulated on a binding basis with the intended use is the Lessee’s right of use, regardless of the contractually defined finish condition of the leased property.

6.5 Payment of rent; default

The rent is due on the first day of each month (due date). The Lessee is considered to have paid the rent on time if the Lessor can dispose of the money on the due date. The Lessor is entitled to charge the Lessee default interest of 5% (from the due date onward) if payment is received after the due date.

All rent payments will always be applied to the item that has been open the longest, irrespective of the designated purpose of the payment.

6.6 Basis of rent

Swiss Consumer Price Index: Base year 2015 Status 31 May 2016 Point 100.6

6.7 Rent adjustments

The net rent is indexed at a rate of 100.00%.

The net rent can be adjusted in accordance with the changes in the Swiss Consumer Price Index once annually, upon one month's notice, with the first effective date being 01 January 2018. Rent adjustments are calculated according to the following formula:

Current index - index from last adjustment
---------- x 100.00 = rent adjustment as a percentage
Index from last adjustment

It is not possible for the rent to be adjusted to below the base net rent stipulated upon the commencement of the Agreement as part of the indexing of the rent.

Rent increases based on additional services provided by the Lessor or due to the introduction of new duties or contributions under public law can also be asserted during the fixed term of the Agreement.

"Additional services" means all facilities, installations, or construction-related adjustments that are applied or created as additions to the previous condition, irrespective of whether the Lessor occasions this on its own initiative or in fulfillment of any changes in statutory provisions that may apply. Such rent increases will take place upon one month's prior notice, effective as of the first day of the next month, and will be announced to the Lessee in the form stipulated therefor.

If necessary, advance contributions to heating and operating costs and flat fees for ancillary costs can also be adjusted during the fixed term of the Agreement upon one month's prior notice, in the form stipulated therefor, effective as of the first day of the next month, with this being based on the actual costs in the case of advance payments for heating and operating costs and according to the average value for the previous three years in the case of flat fees for ancillary costs.

6.8 Value-added tax

The Lessee owes the Lessor value-added tax at the then-applicable rate (currently 8%) on the compensation that is relevant for VAT purposes pursuant to Art. 24 of the Swiss Value-Added Tax Act [*Mehrwertsteuergesetz* (MWSTG)], i.e. the agreed net rent and the ancillary costs. In the event of changes in the VAT rate, the Lessor shall implement the new rate as of the time of the change in the law and shall notify the Lessee thereof at least one month in advance.

The Lessee confirms that it will use the leased property, by way of application of Art. 22 (2) (b) MWSTG, for business purposes and not exclusively for private purposes during the entire term of the Lease Agreement. If the option in favor of application of VAT ceases to apply for a reason caused by the Lessee, the Lessee shall be liable to the Lessor for the full amount of damage arising therefrom.

6.9 Ancillary costs

The term "ancillary costs" means heating, hot water, and operating costs.

To the extent that advance contributions are agreed above for the heating, hot water, and operating costs, the Lessor shall settle accounts for these costs once annually. The reference date for the settlement of accounts for heating, hot water, and operating costs is 31 December.

The costs of heating and hot water include all cost types pursuant to Art. 5 of the Swiss Ordinance on Rental and Lease of Residential and Business Space [*Verordnung über die Miete und Pacht von Wohn- und Geschäftsräumen* (VMWG)] plus decalcification of any individual boilers present in the leased property (every three years) and a billing fee for heating and hot water costs for the management in the amount of 3% plus VAT.

The operating costs include the following cost types:

- Building caretaker services, including VAT, rent for the caretaker's space, incidentals;
- Cleaning the generally accessible rooms and spaces, including cleaning supplies and replacement lamps;
- Periodic container cleaning;
- Cleaning of glass and metal façades or façade parts;
- General electricity/water consumption/wastewater/sewage/refuse, including corresponding base fees;
- Garden maintenance, removal of garden waste, and garden cleaning;
- Removal of snow and ice, including salt;
- Service subscription fees for elevator facilities, including operation of the elevator phone, ventilation facilities, including periodic cleaning of distribution pipes and consumable supplies, sliding doors, fire extinguishers, pumps, emergency lighting systems and equipment;
- Filters and service for water treatment units;
- Preventive flushing of the sewage system and feed/discharge lines;
- Cleaning and consumable supplies for general restroom facilities;
- Costs of security service;
- Billing fee for management, 3.5% + VAT.

The statement of accounts for heating, hot water, and operating costs is considered to be approved with regard to all services and costs covered therein to the extent that the Lessee does not object thereto in writing to the Lessor or the Lessor's representative within 30 days after receipt thereof. The Lessee has the right to inspect, or to have an authorized representative inspect, the detailed statement of accounts and the corresponding documentation in the original on the premises of the Lessor or its representative.

Additional charges must be paid within 30 days after receipt of the statement. Refunds will be made within 45 days, subject to setoff.

During the heating period, the heating must not be turned off entirely in any room. No reductions in heating costs can be made for heaters turned down by the Lessee.

6.10 Duties and fees

Duties and fees caused exclusively by the operation of the Lessee's business must be paid by the Lessee, even if they are charged to the Lessor.

If the operation of the Lessee's business entails disproportionate use of water, the Lessor is permitted to order that a separate water meter be installed at the Lessee's expense, even during the term of the lease. Accounts will be settled with regard to water use together with the operating costs.

Costs that are billed directly to the Lessee by a provider or government agency (including cable networks) and are not listed in the Agreement must be paid directly by the Lessee.

7 Commencement of lease; term of lease

Commencement of lease: 01 October 2016
The rent is owed from this point onward. Should the delivery take place before then, especially for the performance of the Lessee's finishing work, the risk shall pass to the Lessee upon delivery.

End of lease: 30 September 2021
The lease is subject to a fixed term to terminate without prior notice on 30 September 2021.

8 One-time right of termination on the Lessee's part

The Lessee is granted the right to terminate the present Lease Agreement one time as follows:

Notice period for termination:	12 months
One time, effective as of:	30 September 2019

If the Lessee intends to make use of this right, the Lessee's notice of termination must be rendered by certified/registered mail. It is considered valid if it is received by the Lessor or is ready for pick-up at the post office no later than on the last day before the notice period for termination begins. If the Lease Agreement has been entered into with multiple Lessees, the notice of termination must be signed by all Lessees.

If the Lessee makes use of this right of termination, the Lessor has the right to demand a penalty payment of CHF 50,000.00 (share of Lessee's finishing work without the amount of CHF 5,000.00 for the installation of the partition walls for the new entrance corridor).

9 Premature return of the leased property

If the Lessee wishes to dissolve the lease without complying with the agreed time limits and deadlines and to return the leased property prematurely, the Lessee is liable for the rent, ancillary costs, and the other obligations of the Lessee up until such time as the property is leased to a different tenant, but not beyond the expiration of the Agreement or – if agreed – the next date of termination possible under the Agreement, unless the Lessee proposes a substitute tenant that is acceptable to the Lessor, solvent and willing to take on the Lease Agreement on the same terms and conditions (Art. 264 of the Swiss Code of Obligations [*Obligationenrecht* (OR)]. The costs of placing advertisements, advertising and additional activities that are associated with the unscheduled leasing of the property to a new tenant shall be borne by the Lessee that is moving out.

The Lessor has 30 days to review the substitute tenant and engage in the associated clarifications.

10 Renewal option

The Lessee is granted the option to renew by an additional five years, meaning from 01 October 2021 until 30 September 2026. The Lessee can exercise this option no later than 30 September 2020, and not before six (6) months before this date, by way of registered/certified mail; otherwise, the renewal option shall cease to apply. If the option is not exercised or ceases to apply, the lease shall terminate without prior notice on 30 September 2021.

If the Lessee validly exercises the renewal option, the Lessor is entitled to adjust the rent to the market conditions then in effect as of the commencement of the new term of the Agreement. It is not possible for the rent to fall below the rent applicable at the relevant point in time.

The new rent will be sent to the Lessee no later than 30 days after the renewal option is validly exercised, along with a new Lease Agreement for the Lessee to countersign. If the Lessee does not return the countersigned new Lease Agreement within 30 days from delivery thereof, the renewal option shall cease to apply and the lease shall terminate on the contractually agreed terms without prior notice of termination being required.

If the renewal option is exercised and a new Lease Agreement comes into existence, the lease shall terminate upon the expiration of the new term thereof without prior notice of termination being required.

The option right is only available to the Lessee personally. If the Lessee transfers the lease to a third party within the meaning of Art. 263 OR, or if more than 50% of the leased space is sub-leased, the renewal option shall cease to apply.

11 Provision of security

To safeguard all of the Lessor's claims arising from the lease pursuant to the present Lease Agreement and the relevant annexes hereto, the Lessee shall provide an irrevocable, abstract bank guarantee payable upon first demand within the meaning of Art. 111 OR from a bank accepted in writing by the Lessor beforehand and recognized in Switzerland in the amount of CHF 76,700.00 or, in the same scope, security within the meaning of an interest-bearing savings account pursuant to Art. 257 e OR for the duration of the lease plus 12 months.

In the event that the lease is transferred (Art. 263 OR), the Lessor is permitted to demand that the security be increased to cover the Lessor's claims.

The security is due before the keys are delivered. If security is not provided, the Lessor is entitled to refuse to deliver the leased property and to proceed according to Art. 107 et seqq. OR.

12 Plans; calculation of space

The attached plan dated 14 June 2016 constitutes an integral element of the present Lease Agreement and shall be signed by both Parties.

Deviations in space, if any, do not justify an adjustment of the rent.

The leased space is calculated as follows:
SIA Documentation d 0165

13 Lessor's finishing work (bare construction); Lessee's finishing work; contractors' liens

13.1 Lessor's finishing work (bare construction 2)

The leased property is leased out as bare construction 2, consisting of the following components:

- Floor: Raw concrete floor
- Walls: Enclosing walls, base plaster, raw
- Ceiling: Raw concrete ceiling
- Electrical: Lessee's responsibility from floor-level distributor / empty wall duct
- Heating: Radiators
- Windows: Aluminum/wood windows

All finishing work on the leased property in excess of the bare construction defined above is part of the Lessee's finishing work and lies within the Lessee's exclusive sphere of responsibilities.

According to the will of both Parties, the bare construction condition defined above corresponds to the condition of the lease property that is suitable for the presupposed use.

The Lessee is obligated to tolerate the placement of ducts, pipes, cables, etc., in the ceiling cavity and floor without compensation.

13.2 Lessee's finishing work (finishing work assumed by the Lessee; structural changes; contractors' liens)

13.2.1 Installation and finishing work assumed by the Lessee

All installation and finishing work beyond the above-described Lessor's finishing work (bare construction) that already exists at the time of commencement of the lease and installations that have been performed by the Lessor or a previous tenant shall be delivered to the Lessee free of charge in their current condition in accordance with the delivery record that is to be drawn up. These items are part of the "Lessee's finishing work," and have not been taken into account in setting the base net rent. The Lessor assumes no liability for the Lessee's finishing work.

13.2.2 Structural changes made by the Lessee

The Lessee is entitled to finish and/or convert the leased property according to its needs at its own expense, with the Lessor's prior written approval being required for the respective conversion and finishing projects. Corresponding plans at a scale of 1:50, cost estimates, and detailed construction specifications must be presented to the Lessor for this.

To the extent that changes to the leased property by the Lessee require construction-related or other official permits or authorizations, all costs associated therewith shall be borne by the Lessee. If approval or authorization for finishing work to be performed by the Lessee is rendered dependent on the fulfillment of conditions imposed by government agencies or by law and these conditions necessitate additional construction-related or other measures, e.g. for reasons associated with fire regulations, or for safety, ecological, historical preservation or other reasons (additional emergency exit doors, disabled-accessible construction, sprinkler systems, fire alarm systems, use of equipment and materials specified for ecological reasons, removal of equipment and materials that are hazardous to health, such as asbestos, etc.), all costs associated therewith shall be borne exclusively by the Lessee. No compensation is owed by the Lessor upon the end of the Agreement, even if the corresponding measures are not reversed.

The Lessee is obligated, at its own expense, to comply with all statutory provisions concerning the finishing and/or conversion work, such as the municipal and cantonal building codes, SIA standards and guidelines of relevant specialized associations, SUVA rules and regulations, fire codes and regulations, etc., and to obtain all necessary official permits and authorizations. Particular attention must be paid to the structural engineering of the building (floor load, load-bearing elements, etc.). Where approved interventions in the general parts of the building take place, especially in the areas of structural engineering, installations and the building envelope, the Lessor has the right to specify the planners, entrepreneurs, products, and systems used.

Other tenants must be given the utmost consideration when performing the finishing or conversion work. The Lessee is obligated to notify the other tenants in the building with sufficient lead time and in detail with regard to the upcoming construction emissions. Noise-intensive work and any interruptions in pipes or other lines (electricity, water, fiber optic, etc.) must be coordinated with the other tenants in the building. In commercial buildings with a residential portion, performance of the Lessee's work is permitted only Monday through Friday and only during normal working hours.

The Lessee shall bear all costs arising directly or indirectly from its construction activities; this also includes connection fees for water, electrical, sewage, etc. The Lessee is moreover liable, including in the case of careful and considerate performance of the relevant work, for any claims that may be asserted by other tenants or third parties (e.g. neighbors) (reduction of rent and/or damages, neighbors' rights) to the extent that such claims are rightly asserted with citation of the relevant legal provisions. The Lessee moreover undertakes to participate in any legal dispute that may be initiated vis-à-vis the Lessor in this regard upon provision of third-party notice and to assume the legal dispute at its own risk and expense if the Lessor so requests.

The Lessee is liable for all property damage, personal injury, and financial losses that may arise in connection with construction measures on the Lessee's part. The Lessee is therefore obligated to take out construction principal's liability insurance and insurance for the term of the construction at its own expense for every construction project.

For the purpose of reporting the Lessee's finishing work to the cantonal building insurance authority, the Lessee is obligated to provide to the Lessor, no later than three months after the completion of the construction, a statement of accounts for construction organized according to the construction cost plan published by the Swiss Zentralstelle für Baurationalisierung and an adjusted set of finishing specifications.

In the event of any electrical installations by the Lessee, the Lessee is responsible for ensuring that all statutory provisions in this regard are complied with. To this end, the Lessee is obligated to have a safety certification prepared, and to send it to the Lessor, at the Lessee's own expense no later than three months after the completion of these installations.

If a change in the leased property by the Lessee leads to reassessment of the building (additional premiums for building insurance) or to an increase in public fees or contributions as a result of an increase in value due to the Lessee's finishing work, these additional costs shall be borne by the Lessee.

13.2.3 Contractors' liens

The Lessee shall ensure that the contractors, entrepreneurs and suppliers involved do not register any contractors' liens. If this occurs nonetheless, the Lessee is required to ensure that these liens are deleted immediately and at the Lessee's own expense already at the time of provisional entry in the Land Register. If it fails to do so, the Lessee is liable to the Lessor for the damage and/or losses arising therefrom.

In the case of larger investments, the Lessor is entitled to demand that the Lessee provide, before construction begins, a confirmation from a bank accepted by the Lessor in writing in advance and recognized in Switzerland that documents that the estimated construction amount has been secured and according to which this bank is obligated to pay the invoices of contractors and suppliers directly.

14 Lessor's maintenance obligations

The Lessor's maintenance obligations are limited to the Lessor's finishing work as defined above, meaning the bare construction. In this regard, the Lessor is obligated to maintain the leased property (not including finishing work by the Lessee) in usable condition. The Lessee must report any defects to the Lessor.

In the event of suddenly emerging defects that represent an emergency that cannot be postponed, the Lessee is obligated to immediately notify the caretaker and the management or, in their absence, to take itself or cause to be taken the precautions that are absolutely necessary to avert consequential damage and/or losses, to the extent possible and reasonable. If it fails to do so, the Lessee is liable for consequential damage and/or losses.

The Lessor is entitled to perform necessary repairs, adjustments and renovations in the leased property and with regard to the associated facilities and installations and in and on the general parts of the building unimpeded, provided it has given advance notice that is appropriate to the scope thereof.

The Lessee is required to tolerate at all times any work that is necessary to maintain the physical condition of the property and cannot be postponed. If the Lessee refuses to allow contractors to access the leased property, the Lessee may be held liable for any additional costs and consequential damage and/or losses.

15 Lessee's maintenance obligations

The costs of maintenance and replacements with regard to the Lessee's finishing work, meaning any and all installations and finishing work performed by the Lessee as well as its installations, facilities and equipment, shall be borne expressly and exclusively by the Lessee. The Lessee is obligated to maintain the Lessee's finishing work during the entire term of the lease in such a way that the appearance of the leased property is always in qualitatively and aesthetically perfect condition. The Lessor is permitted to demand that the Lessee perform the necessary work if the condition of such facilities and equipment threatens to damage the leased premises or other parts of the property. If it fails to do so, the Lessor is permitted to order the work on its own and charge the costs to the Lessee.

Furthermore, the Lessee is responsible for minor cleaning, repairs and improvements (termed “minor maintenance”) on the bare construction as necessary for the customary use of the leased premises. Such maintenance work must be performed in a workmanlike manner, including if others are commissioned to perform it. Minor maintenance includes the following in particular:

a) Periodic cleaning of the windows and display windows (inside and outside), shutters, blinds, balconies and decks as well as drains, restroom facilities, doors and mailboxes as well as signage and advertising equipment, clearing blockages in wastewater lines to the main line, decalcification of individual boilers.

b) All further minor repairs that do not exceed 1% of the annual net rent (on an indexed basis) in the individual case.

16 Risk of damage and/or losses; insurance

The Lessor shall insure the leased property without furniture, fixtures and equipment with the cantonal building insurance authority – or, in cantons where there is no such established authority, with a private insurance company – against fire and elemental damage.

Additional building insurance premiums due to the Lessee’s finishing work will be passed through to the Lessee annually. The building insurance premium is calculated based on the construction account statement to be prepared by the Lessee and/or the building insurance estimate for the Lessee’s finishing work and in accordance with the then-applicable rates applied for the relevant insurance. If the Lessee fails to send the construction account statement to the Lessor as agreed, the Lessee shall bear the risk of all damage and/or losses suffered by the Lessee’s finishing work, and the Lessor rejects all liability in this regard.

The Lessee shall bear the risk for all damage and/or losses due to fire, water, explosion, moisture, break-in, theft, etc. suffered by the Lessee’s finishing work, the Lessee’s fixtures, equipment and installations, and/or the goods belonging to the Lessee that the Lessee has brought onto the premises. The Lessee shall take out corresponding insurance policies at its own expense.

The Lessee shall moreover bear, as a basic principle, the risk for all panes of glass in its leased premises. Shattered or broken panes of glass must be replaced with glass of the same characteristic features and quality. The Lessee is not released from the obligation to replace such panes accordingly unless it proves that the damage was caused by improper installation or by tension in the frame.

The Lessor will take out and maintain insurance coverage for liability claims vis-à-vis third parties only to the extent to which the Lessor can be held liable. The rest is the Lessee’s responsibility.

17 Cleaning

The periodic complete cleaning of the leased property and the windows and rolling shutters pertaining to the leased property (inside and outside) as well as signs, lighted signs and mailboxes is the Lessee’s responsibility and must be performed by the Lessee at its own expense.

If general parts of the building are dirty or infested with pests because the Lessee does not fulfill this cleaning obligation or does not do so adequately, the Lessee is liable for all direct and consequential damage and/or losses.

If common areas are available to multiple tenants, they must arrange for cleaning and replacement of consumable supplies among themselves; the Lessor reserves the right to arrange this work and is entitled to charge the tenants proportionally for the costs arising in this respect as part of the ancillary costs.

18 Delivery

The Lessor shall deliver the leased premises to the Lessee in the contractually owed condition and clean. The Lessee shall have no claim to receive the leased premises in like-new condition.

The blinds and windows will be cleaned by the Lessor before the property is delivered.

A record of delivery will be prepared. The Lessee must report any defects in the leased premises that are not listed in the record to the Lessor via registered/certified mail within ten days after the start of the lease. This does not apply to hidden defects, which must be reported in writing without delay after they are discovered. If no such reports are made, the leased property is considered to have been delivered in the condition stated in the record.

19 List of keys

The record of delivery will list the keys/badges delivered. The Lessee must replace any keys/badges that are lost during the term of the lease at its own expense no later than as of the end of the term thereof. In such a case, the Lessor is entitled to change or replace the locking system and the keys/badges at the Lessee's expense. Any additional keys/badges made must be turned over to the

Lessor when the Lessee moves out, without any compensation being paid therefor.

20 Approvals from the authorities responsible for trades; statutory provisions for industrial operations and of the fire and health code and inspection authorities

The Lessee is obligated to obtain, directly and at its own expense, all permits and approvals required for the use of the leased premises and for its operations and to comply therewith.

21 Use of the leased premises

21.1 Duty of care and consideration

The Lessee must use the leased premises with the utmost care and must keep them in good and clean condition. The Lessee is only permitted to use the leased premises for the contractually agreed purpose. The Lessee is liable for any damage and/or losses arising through improper use thereof or use thereof in breach of contract.

The Lessee must demonstrate consideration for fellow tenants and neighbors in its use of the leased premises. The Lessee is prohibited from using machines, apparatus and equipment or engaging in any trade or commercial business that causes noise, vibrations or shocks, bothersome fumes or foul odors. The Lessee agrees to comply with any house rules that may be established by the Lessor.

Before heavy goods and items such as safes, machines, etc. are brought into the leased property, the Lessee must clarify the load limits for the floors with the Lessor; the Lessee shall bear the costs of any expert report from the construction engineer that may be needed. Appropriate underlays or insulation must be placed under heavy furnishings to protect the floors and, where applicable, to prevent noise, vibrations and shocks.

22 Use of the courtyard, forecourt, premises and facilities outside the leased premises

22.1 Fundamental provisions

Unless otherwise agreed in writing, the Lessee is not permitted to place or store objects outside the leased premises. In particular, access to the building and courtyard, vehicle passage, building and basement or other open areas and spaces must not be blocked with objects of any kind. If the Lessor grants its permission therefor as an exception, the Lessee shall be liable for any and all damage and/or losses arising from the storage.

Vehicles of any kind belonging to the Lessee, its employees and its customers must only be parked in the parking spaces designated by the Lessor.

22.2 Incoming and outgoing deliveries

Incoming and outgoing deliveries of goods must be performed carefully and must only be performed in the locations designated by the Lessor. The Lessee must eliminate any soiling due to incoming and outgoing deliveries of goods immediately and without any particular request to that effect being issued. Any damage and/or losses that are sustained must be reported without delay to the Lessor, which will cause them to be remedied at the Lessee's expense.

The use of the passenger and freight elevators is subject to the rules posted there. In particular, users must comply with the load rules.

22.3 Waste

Waste of all kinds must only be placed in the locations designated by the Lessor and must be placed there in an appropriate manner. If necessary, the Lessee is obligated to procure appropriate containers and to provide them regularly for emptying.

23 Fire escape

Any fire escape that may be present must only be used in the event of a fire or other emergency in which the main stairs are not accessible. The door to the fire escape must be kept clear at all times. Storage of any kind along emergency escape routes is prohibited.

24 Signage; advertising

The Lessee shall assume the costs of producing standardized name signs for the doorbell, mailbox, elevator, etc.

The façade, roof, roof overhangs, wall projections, technical space, and stairway walls are not included in the lease, and the Lessee is not permitted to use them.

Company and advertising signs, posters, display windows, placards and the like must not be installed except with the Lessor's prior written approval and in the locations designated by the Lessor. The costs of installation, operation, maintenance and replacement associated therewith shall be borne by the Lessee. The Lessor's approval encompasses the nature, size, color, form and material, and moreover the orientation and sequence of signs. In the case of façade repairs or modifications, the Lessee must remove and reinstall the signs and lettering at its own expense. It is the Lessee's responsibility to obtain any official permits or authorizations that may be required and to bear the costs arising therefrom. Upon the end of the lease, the Lessee must remove the signs and lettering in a workmanlike manner at its own expense and restore the original condition; in particular, it must cleanly patch all holes and clean the surface below the signs.

In the case of façade advertising, the Lessor is entitled to demand that the Lessee pay rent accordingly.

The Lessee shall bear the electricity costs associated with any lighted signs. The Lessee shall ensure that electricity is supplied via a separate meter and charged directly to the Lessee by the supplier. In the event of fire involving lighted signs, the Lessee shall bear any and all consequential damage and/or losses arising therefrom.

25 Deposit process; setoff

The Lessee is not permitted to unilaterally reduce the rent.

If the Lessor fails to comply with its maintenance obligations pursuant to the section titled “Lessor’s maintenance obligations,” the Lessee must set an appropriate time limit for the Lessor to do so in writing, accompanied by a threat that if the time limit expires without producing the desired result, the Lessee will deposit future rent payments or portions thereof with the body designated by the canton.

The Lessor must also be notified in writing when the deposit has been made.

Rent payments that have been deposited shall devolve on the Lessor if the Lessee does not assert its claims vis-à-vis the Lessor with the conciliation authority within 30 days from the time at which the first rent payment deposited fell due.

The Lessor is permitted to demand that the conciliation authority release rent payments that have been wrongly deposited as soon as the Lessee notifies the Lessor of the deposit.

26 Subleasing

Subleasing the leased premises in whole or in part (Art. 262 OR) is permitted only within the scope of the contractually agreed intended use thereof and only with the Lessor’s prior written consent. The Lessee shall provide the Lessor, with adequate lead time before entering into any planned agreement, with a corresponding written request stating the personal details of the sub-lessee and the terms of the agreement. After the sublease agreement comes into existence, the Lessee shall provide the Lessor with a copy of the agreement without being requested to do so.

The Lessee is liable to the Lessor for ensuring that the sub-lessee does not use the leased premises in any manner other than the manner in which the Lessee itself is permitted to use them. The Lessor is permitted to urge the sub-lessee to do this directly.

27 Transferring the lease

Transferring the lease is permitted only within the scope of the contractually agreed intended use and requires the Lessor’s written consent (Art. 263 OR). Before entering into an agreement to transfer the lease to a third party, the Lessee shall notify the Lessor of the third party’s personal details and sphere of activity. Furthermore, the Lessee shall provide the Lessor with a detailed listing of the Lessee’s finishing work, installations and apparatus that are to be assumed by the third party, along with the compensation to be paid therefor. The written request must be supplemented by an extract from the commercial register or debt collection register and must be submitted approximately 30 days in advance so that the Lessor has sufficient time to review any objections.

The Lessor is permitted to deny its consent to the transfer if the Lessee accepts a promise of remuneration from the proposed subsequent tenant that does not have equivalent consideration as its subject (especially “key money”).

If the Lessor consents, the third party shall assume the lease in the Lessee’s stead. After that, the Lessee will be released from its obligations vis-à-vis the Lessor. However, the Lessee will be jointly and severally liable with the third party up until the time at which the lease expires or can be terminated, whether according to the contract or by law, up to a maximum of two years.

28 Right of inspection

In the case of negotiations regarding sale and leasing the property to a new tenant and to safeguard ownership rights, the Lessor or its representative is entitled to enter the premises during customary business hours upon 48 hours' prior notice. If the Lessee is absent, the keys must be kept available.

29 Restoration and return of the leased premises

29.1 Restoration

There is no obligation to reverse the finishing work that already exists upon commencement of the lease (and is assumed from the previous tenant). The Lessee agrees only to reverse the finishing work that it has undertaken during the term of the lease, which it will do in a workmanlike and timely manner prior to the time of return. The Lessee must cause floor coverings that pertain to the leased premises to be cleaned in a workmanlike manner.

The Lessor may waive its right to demand that the bare construction be restored in whole or in part in writing (but not orally). In this case, the Lessee is obligated to leave the Lessee's finishing work whose reversal is being waived in the leased property in full. The Lessee's finishing work shall become the Lessor's property without any compensation being paid therefor upon the end of the contract in this case.

If the Lessee violates its obligation to put the leased property in the contractually agreed condition in due time, the Lessor is not obligated to set a cure period for the Lessee to meet the return obligation. Instead, the Lessor is permitted to cause the work and measures necessary to establish the aforementioned condition in due time to be performed itself at the Lessee's expense. In this case, claims for damages are reserved, especially an obligation of payment corresponding to the rent until such time as the contractually agreed condition is established or until the premises are leased to another tenant, if the late return of the leased property has made it impossible to deliver the leased property to the subsequent tenant on time and the latter thereafter rescinds the contract; furthermore, the Lessee must compensate the Lessor for the damage and/or losses suffered by any subsequent tenant in connection therewith.

19.2 Return

The leased property must be returned, entirely cleared, vacated, and cleaned and in the contractually owed condition, together with all keys/badges by 12:00 p.m. on the last day of the lease at the latest. If the date of return falls on a Saturday, Sunday or governmentally acknowledged day off or holiday, the return must take place by 12:00 p.m. on the next local working day at the latest.

After the expiration of the lease, the Lessee shall have neither a right to be present on the premises nor a right to dispose thereof.

Upon the return of the premises, the Lessor shall draft a record of assumption of possession. Defects for which the Lessee is to be held responsible will be listed in this record. The Lessor is permitted to assert claims on the Lessee for hidden defects that the Lessor does not discover, despite a careful acceptance procedure, until after taking possession of the premises, even after the fact, provided that these defects are reported to the Lessee immediately after discovery thereof.

The Lessor is permitted to demand that the Lessee participate in preparing a joint record of return upon assuming possession of the leased premises. If the Lessee refuses to participate therein, the Lessor is permitted to have the findings of a government agency recorded at the Lessee's expense.

30 Share of costs of finishing work

The Lessor shall bear a share of the costs of the Lessee's planned finishing work in the lump sum of CHF 55,000.00, including VAT. This amount also includes the installation of the new partition walls for the new entrance corridor (at CHF 5,000.00) so that the length of the emergency escape route is complied with. Disbursement shall take place after construction is complete and after the Lessee issues an invoice that is compliant with the provisions on VAT and on the condition that the Lessee has paid the contractors and entrepreneurs (including architects, planners and the like) involved in the finishing work. Upon request, the Lessee must provide corresponding proof of payment. The Lessor is entitled to withhold payment until such proof is provided.

In addition, the costs of a new entrance door to the leased property and the installation of a meter for the leased property will be at the Lessor's expense.

31 Applicable law; place of jurisdiction

Unless otherwise agreed herein, the provisions of the Swiss Code of Obligations (Art. 253 et seqq. OR) apply. The place of jurisdiction for all disputes arising out of this Agreement is the location of the leased property.

32 Supplementary provisions

The Lessee is permitted to install a handrail in one of the ladies' restrooms. Construction modifications must be removed at the Lessor's request, and the Lessee must restore the original condition, by the end of the term of the lease.

33 Amendments; addenda; prior agreements and understandings

Amendments and addenda to this Lease Agreement (including any cancellation of this written form reservation) are not valid unless made in written form.

The present Lease Agreement supersedes any and all prior agreements, understandings and confirmations by the Parties, whether oral or in writing.

34 Annexes

The following annex, which was issued to the Lessee and is expressly acknowledged by the Parties, constitutes an integral element of this Lease Agreement:

1. Contractual annex plan of the 4th floor dated 14 June 2016

35 Signatures

By signing below, the Lessee confirms that it has read and understood the entire contractual document, including annexes.

Olten, 14 June 2016/CHQ0744

The Lessor, represented by PSP Management AG	[signature] Lessee 1 Auris Medical AG [stamp:] **Thomas Meyer**	[signature] [stamp:] **Anne Sabine Zoller** General Counsel
[signature]	Chairman and CEO	

This Agreement is not legally valid unless and until it is signed by all Parties.

Exhibit 12.1

CERTIFICATION

I, Thomas Meyer, certify that:

1. I have reviewed this annual report on Form 20-F of Auris Medical Holding AG;

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 14, 2017

/s/ Thomas Meyer
Thomas Meyer
Chief Executive Officer

Exhibit 12.2

CERTIFICATION

I, Hernan Levett, certify that:

1. I have reviewed this annual report on Form 20-F of Auris Medical Holding AG;

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 14, 2017

/s/ Hernan Levett
Hernan Levett
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, 2016 (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 AG, 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 AG.

Date: March 14, 2017

/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, 2016 (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.

Hernan Levett, the Chief Financial Officer of Auris Medical Holding AG, 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 AG.

Date: March 14, 2017

/s/ Hernan Levett
Name: Hernan Levett
Chief Financial Officer

Exhibit 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-198037, and 333-200805 on Form S-8 and No. 333-206710 on Form F-3 of our report dated March 10, 2017, relating to the consolidated financial statements of Auris Medical Holding AG appearing in this Annual Report on Form 20-F of Auris Medical Holding AG for the year ended December 31, 2016.

Deloitte AG

/s/ Matthias Gschwend
Auditor in Charge

/s/ Adrian Kaeppeli

Zurich, Switzerland

March 14, 2017