EDISON

Auris Medical Holding

Initiation of coverage

Treating vertigo

Pharma & biotech

Auris Medical is a clinical-stage biopharmaceutical company developing pharmacotherapies for neurologic disorders of the inner ear. The company's primary focus is on the development of intranasal betahistine for the treatment of acute vertigo. Oral betahistine dihydrochloride has been prescribed in Europe for decades for all types of vertigo, with an average 26% market share. We initiate at $117.6m or $4.89 per basic share based on a risk-adjusted NPV analysis of these two programs.

Year end	Revenue (CHFm)	PBT* (CHFm)	EPS* (CHF)	DPS (CHF)	P/E (x)	Yield (%)
12/16	0.0	(31.0)	(0.90)	0.0	N/A	N/A
12/17	0.0	(25.9)	(0.54)	0.0	N/A	N/A
12/18e	0.0	(11.7)	(0.48)	0.0	N/A	N/A
12/19e	0.0	(11.8)	(0.39)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

AM-125: Intranasal betahistine for acute vertigo

Each year, an estimated 2.6m visits to the emergency department (ED) are associated with acute dizziness and vertigo in the US. Oral betahistine is the most commonly prescribed medication for all types of vertigo in Europe, but was withdrawn from the US market in 1972 due to unsubstantiated efficacy results upon which approval was based. Auris is developing an intranasal formulation of betahistine, bypassing the digestive tract where the compound is readily metabolised to increase effectiveness.

AM-201: Co-administration with antipsychotics

Auris is also developing AM-201, an intranasal betahistine formulation, for co-administration with olanzapine to counteract adverse effects. Not only is olanzapine an antipsychotic prescribed for the treatment of schizophrenia and bipolar disorders, it is also a histamine-H1 receptor antagonist, which regulates food intake and wakefulness. Consequently, olanzapine is associated with significant weight gain (ie on average ~2.96±3.08kg), drowsiness and somnolence.

Acute hearing loss and tinnitus take a back seat

Auris recently deprioritized its AM-111 and Keyzilen Phase III programs for the treatment of acute inner ear hearing loss and tinnitus, respectively, subsequent to missing critical endpoints. The company strongly believes in both programs and intends to identify a strategic partner for the AM-111 program and external grant funding for the Keyzilen program before continuing with development in the future.

Valuation: $117.6m or $4.89 per basic share

We arrive at an initial valuation of $117.6m or $4.89 per basic share ($3.20 per diluted share) based on a risk-adjusted NPV analysis of Auris's two Phase I clinical programs in the US and European markets. Accordingly, we forecast significant financing needs (CHF65m) to bring both programs from Phase I through to commercialization.

1 November 2018

Price	**US$0.63**
Market cap	**US$15m**
	US$1.01/CHF
Net cash ($m) at 30 June 2018 (plus July 2018 offering)	7.0
Shares in issue	24.1m
Free float	75%
Code	EARS
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	71.7	139.7	(91.9)
Rel (local)	86.5	150.4	(92.2)

52-week high/low	US$9.3 US$0.2

Business description

Auris Medical is a Swiss biopharmaceutical company developing neurotology therapeutics. The company is developing intranasal betahistine in a Phase I trial for mental disorder supportive care and is entering Phase II for vertigo; both are designed to demonstrate proof-of-concept.

Next events

Initiate AM-201 PK/PD study	Q119
Initiate AM-125 Phase II study	Q119
AM-125 Phase II top-line data readout	Q319

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Investment summary

Company description: Focus on neurotology and mental health

Auris Medical is a development-stage biopharmaceutical company with a historical focus on the development of pharmacotherapies for neurological disorders of the inner ear. The company was founded in 2003 in Zug, Switzerland, and publically listed on the NASDAQ in 2014. Presently, Auris Medical is engaged in four pipeline programs with a primary focus on the development of intranasal betahistine for the treatment of vertigo (AM-125) and for the treatment of antipsychotic drug-induced weight gain and somnolence (AM-201). Both indications are entering Phase II and Phase I trials respectively, and are designed to demonstrate proof-of-concept (POC). The company has two additional Phase III programs including AM-111 for acute inner ear hearing loss, which has previously been granted orphan drug status by the FDA and EMA, and Keyzilen (AM-101) for acute inner ear tinnitus. Both of these programs have recently been deprioritized.

Valuation: $117.6m or $4.89 per basic share

We arrive at an initial valuation of $117.6m or $4.89 per basic share ($3.20 per diluted share) based on a risk-adjusted NPV analysis of its two intranasal betahistine clinical programs. Based on our estimations, we value the AM-125 development program at the highest in Europe where we assign a 45% probability of success because the oral formulation of betahistine is the most commonly prescribed medication for treatment of Meniere's disease (MD) and vertigo. We expect to include the two Phase III programs in our valuation when the company identifies a path forward.

Financials: CHF65m needed over next several years

The company's expenses are largely driven by its R&D activities, which totalled CHF19.2m in FY17. As per guidance from Auris, total operational expenses for FY18 are estimated to be approximately half of the year prior (FY17: CHF24.4m). This decrease is driven by the swift change in strategy to focus on Phase I development programs. The company ended Q218 (30 June) with CHF4.4m in cash and equivalents and CHF3.6m in debt. After the end of H118, Auris received an additional CHF6.14m in net proceeds from the July 2018 public offering. We project Auris Medical will need CHF65m in additional capital to bring both Phase I programs through to commercialization.

Sensitivities: A range of development phases

There are inherent risks associated with Auris's business, although they are typical for a development-stage drug company. The company is developing an intranasal formulation of betahistine, which is a drug with an established mechanism of action. Oral betahistine is currently the most widely used medication in Europe for treatment of MD, benign paroxysmal positional vertigo (BPPV), and peripheral vestibular vertigo of known and unknown origin. However, betahistine was withdrawn from the US market by the FDA in 1972 due to unsubstantiated efficacy results in vertigo upon which approval was based. Both the Keyzilen (AM-101) and AM-111 Phase III development programs have previously missed clinical trial end points, which according to the company was due to issues with study design and unexpectedly high placebo response in the severe hearing loss population, respectively. Nonetheless, the company remains excited about these two programs, is encouraged by existing data and intends to move the programs forward within the next few years via a strategic partnership for the AM-111 program and external grant funding for Keyzilen. There is also substantial financial risk due to the CHF65m in additional cash needed before profitability, which may result in substantial dilution.

Treating otolaryngology disorders

Auris Medical's pipeline consists of four main programs across a range of development stages and indications (Exhibit 1). The majority of its pipeline is concentrated on the development of pharmacotherapies for disorders of the inner ear. The company's primary focus is on the development of intranasal betahistine for two distinct indications: the treatment of acute vertigo and in mental disorder supportive care in co-administration with olanzapine to prevent and/or treat antipsychotic drug-induced weight gain, drowsiness and somnolence. In 2017, Auris acquired intranasal betahistine from Otifex Therapeutics, which did not have the capacity to develop the program. The company has demonstrated that intranasal betahistine has greater bioavailability than oral betahistine and therefore expects to demonstrate a superior therapeutic benefit. Furthermore, it has temporarily deprioritized its Keyzilen and AM-111 Phase III programs as it plans to rebuild each case due to missed primary endpoints and drive both of these programs forward through strategic partnerships within the next few years.

Exhibit 1: Auris Medical pipeline

Product	Indication	Agent	Stage	Notes
AM-125*	Acute vertigo	Intranasal betahistine dihydrochloride	Phase I	Acquired AM-125 assets from Otifex Therapeutics in July 2017. In a previous randomized, double-blind, placebo-controlled Phase I trial, intranasal betahistine was well tolerated with dose escalation. Announced Phase I trial results in October 2018 and expects initiate Phase II TRAVERS trial in Q119.
AM-201*	Olanzapine-induced weight gain, drowsiness/somnolence	Intranasal betahistine dihydrochloride	Phase I	Expects to initiate randomized, placebo-controlled Phase I trial in healthy volunteers to evaluate the safety and PK/PD effects of AM-201 in co-administration with olanzapine in early 2019.
AM-111	Acute inner ear hearing loss	Brimapitide otic gel for intratympanic use	Phase III	HEALOS trial completed in 2017 and did not meet its primary endpoint, which according to the company was due to the unexpectedly high placebo response in the severe hearing loss population. However, post-hoc data show clinically meaningful and nominally significant improvement in the profound hearing loss population. AM-111 has previously been granted orphan drug designation by the FDA and EMA, and was granted fast track designation by the FDA. In May 2018, the EMA CHMP endorsed plans for a single pivotal Phase III trial, while the FDA endorsed the end points, statistics and size of the trial in late August 2018. Intends to move program forward via strategic partnering.
Keyzilen (AM-101)	Acute inner ear tinnitus	Esketamine hydrochloride otic gel for intratympanic use	Phase III	TACTT2 and TACTT3 trials completed in 2016 and 2018, respectively, and did not meet primary end points. According to the company, this was due to issues with subjective outcomes and patient selection. Intends to run POC study and validate objective measurement tools as basis for pivotal trial via external grant funding.
AM-102	Tinnitus	Undisclosed	Preclinical	Expects to select lead compound in Q418.

Source: Auris Medical. Notes: * Highest priority programs; CHMP= Committee for Medicinal Products for Human Use; POC= proof-of-concept.

Intranasal betahistine for acute vertigo attacks

Acute vertigo/dizziness is one of the most common causes of visits to the ED. Vertigo is a condition described as a false sensation of spinning and unsteadiness often accompanied by nausea and vomiting that is thought to originate from vestibular (inner ear) disorders. Each year in the US, roughly 2.6m visits to the ED are associated with dizziness/vertigo. In adults aged 18–79, the annual incidence is approximately 1.4%; this substantially increases with age and is roughly 2 to 3 times more common in women than in men.[1] Approximately 25% of those presenting with vertigo/dizziness symptoms are attributable to vestibular diagnoses.[2] In the ED, acute vertigo due

[1] Neuhauser, H. (2016). The epidemiology of dizziness and vertigo. *Handbook of Clinical Neurology Neuro-Otology,* 67-82.

[2] Tehrani, A. S., et al. (2013). Rising Annual Costs of Dizziness Presentations to U.S. Emergency Departments. *Academic Emergency Medicine,20*(7), 689-696.

to BPPV (dislodged calcium carbonate ear crystals migrate to fluid-filled canals) is treated with vestibular rehabilitation (patterned head-trunk positioning manoeuvres or canalith repositioning therapy), which moves displaced canaliths to stop the symptoms and is effective about 80% of the time. In Europe, oral betahistine is the most commonly prescribed medication for treatment of MD (34.8%), BPPV (24.6%), peripheral vestibular vertigo of unknown origin (23.6%) and for other vertigo of peripheral vestibular origin (22.8%).[3] Because oral betahistine is not approved in the US, alternative treatment regimens to alleviate acute vertigo symptoms include antihistamines such as Antivert (meclizine), Dramamine (dimenhydrinate), Phenergan (promethazine), and Benadryl (diphenhydramine), prescription anti-nausea medications including Reglan (metoclopramide) and Zofran (ondansetron), as well as prescription sedative medications such as Valium (diazepam), Ativan (lorazepam), or Klonopin (clonazepam). Unlike betahistine, these alternative regimens have drawbacks such as severe daytime drowsiness and targeting nausea relief as opposed to the underlying concern.

Betahistine dihydrochloride (betahistine), which is a structural analogue of histamine, is a neuromodulatory transmitter of the histaminergic system that regulates cerebral functions such as circadian rhythm, cardiovascular regulation, and food intake. Outside of the US, betahistine is approved and marketed (Serc, Betaserc, Hiserk) in the oral form for the management of vertigo. Vertigo may affect patients differently depending on the underlying cause of the condition including BPPV, MD, and vestibular neuritis. Although betahistine is not approved by the FDA, it can be obtained through compounding pharmacies with a prescription in the US.

Histamine receptors (H1, H2, and H3) are found diffusely throughout the central vestibular system (ie the brain and brain stem) and pharmacological evidence suggests these histamine receptors also exist in the peripheral vestibular system (the inner ear and pathways to the brainstem).[4] Betahistine dually acts as a partial postsynaptic H1 receptor agonist and potent presynaptic H3 receptor antagonist,[5] and as previously demonstrated in preclinical animal models and clinical trials, leads to increased cerebrovascular blood flow via dilatation of precapillary arterioles and improves microcirculation of the cochlear and vestibular systems.[6] Nonetheless, several studies examining the efficacy of oral betahistine for the management of vertigo attacks have reported inconsistent outcomes.

In a recent post-marketing observational study investigating the effectiveness of oral betahistine in 305 patients with vestibular vertigo prescribed the recommended dose (ie 48 mg/day) in Russia and Ukraine, the frequency of monthly vertigo attacks decreased significantly from baseline to day 60 of treatment ($p<0.001$).[7] Similarly, a review of 17 studies comprising a total of 1,025 patients with vertigo of multiple aetiologies suggests there may be a positive effect of betahistine in reducing vertigo symptoms; however, the authors also highlight that quality of evidence available is weak.[8] Although studies have demonstrated mixed results, we assume efficacy must be seen at least in acute indications as results are seen rather quickly and European physicians continue to prescribe the drug with an average 26% market share across all types of vertigo.

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[3] Agus, S., Benecke, H., Thum, C., & Strupp, M. (2013). Clinical and Demographic Features of Vertigo: Findings from the REVERT Registry. *Frontiers in Neurology,4*.

[4] Samy, H. (2015). Pharmacotherapy of vestibular disorders. *Advanced Arab Academy of Audio-Vestibulogy Journal,2*(2), 39.

[5] Lacour, M. (2013). Betahistine treatment in managing vertigo and improving vestibular compensation: Clarification. *Journal of Vestibular Research,23*, 139-151.

[6] Arrang, J., et al. (1985). Actions of betahistine at histamine receptors in the brain. *European Journal of Pharmacology,111*(1), 73-84.

[7] Parfenov, V. A., et al. (2017). Effectiveness of betahistine (48 mg/day) in patients with vestibular vertigo during routine practice: The VIRTUOSO study. *Plos One,12*(3).

[8] Murdin, L., Hussain, K., Schilder AGM. Betahistine for symptoms of vertigo. *Cochrane Database of Systemic Reviews 2016*.

Because orally administered betahistine is readily and almost completely absorbed by the gastrointestinal tract on its first pass and its metabolites (ie 2-pyridylacetic acid, or 2-PAA) are pharmacologically inactive, higher doses of the drug have been investigated to increase effectiveness.[9] A trial demonstrated that the recommended dose of 48mg/day of betahistine was not effective and higher doses between 192mg/day (eight tablets per day at 24mg each) to 960 mg/day (40 tablets per day at 24mg each) of betahistine were needed to minimize the frequency of vertigo attacks in patients with severe MD over six months.[10] However, the efficacy of high-dose treatment plans for MD and symptoms of vertigo have not been validated. Because the efficacy of oral betahistine is highly dose and time dependent, it is postulated that bypassing the catabolism of the compound at the digestive barrier could significantly improve its effectiveness and convenience.

IP, previous studies and the AM-125 clinical program

As per the agreement with Otifex Therapeutics, Auris Medical purchased several assets related to intranasal betahistine including preclinical and clinical data and intellectual property rights for an upfront payment and future development milestone payments totalling approximately $500,000. The development work for AM-125 details the composition matter for the intranasal delivery of betahistine over a range of doses for the treatment of otological and neurological disorders. The patent application (US patent application no. 15/887,388) is pending in the US with a priority filing date of February 2017, which would provide coverage in the US through 2037. Similarly, the international patent (international publication no. WO 2018/141922) should provide coverage in Europe through 2037. Aside from patent coverage, there may be data exclusivity of up to five and 10 years in the US and in Europe, respectively.

In Auris Medical's non-clinical pharmacokinetic study in Beagle dogs, concentrations of betahistine were measured in blood plasma following intranasal administration of the compound at doses up to 120mg and oral administration up to 48mg/kg, which is the maximum approved daily dose. The study demonstrated that the absolute bioavailability of oral betahistine reached 2% to 6% (Exhibit 2), while it reached 27% to 82% with intranasal betahistine. This suggests a relative increase of bioavailability of five to 35 times over oral administration (Exhibit 3).

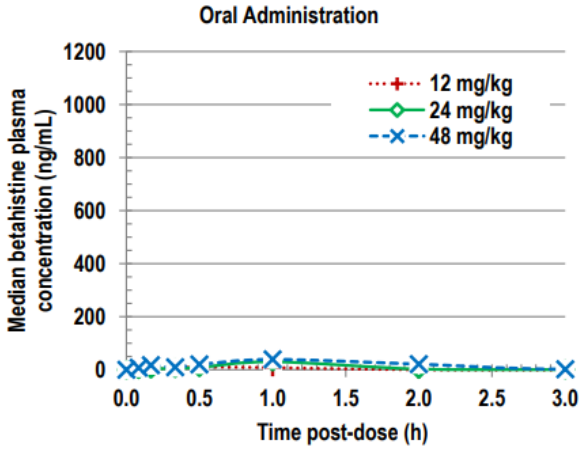
Moreover, Auris Medical compared human pharmacokinetic outcomes of intranasal betahistine from a previous Phase I trial in eight healthy volunteers per dose group (single dose, volume of 100 µl per dose) conducted by Otifex Therapeutics to data from an independent Phase I clinical trial in 20 healthy female volunteers dosed with 48mg oral betahistine three times daily.[11] Although the juxtaposition of these data suggests the relative bioavailability of intranasal betahistine is 20 to 40 times higher (NB: this is dose adjusted) than with oral administration (Exhibit 4), a controlled clinical trial is the only way to establish superior clinical efficacy of intranasal administration over oral administration of the drug.

[9] Serc Product Monograph. Date of Revision January 8, 2016 and Control No. 180426

[10] Adrion, C., et al. (2016). Efficacy and safety of betahistine treatment in patients with Meniere's disease: primary results of a long term, multicentre, double blind, randomised, placebo controlled, dose defining trial (BEMED trial). *The BMJ*, *352*, h6816.

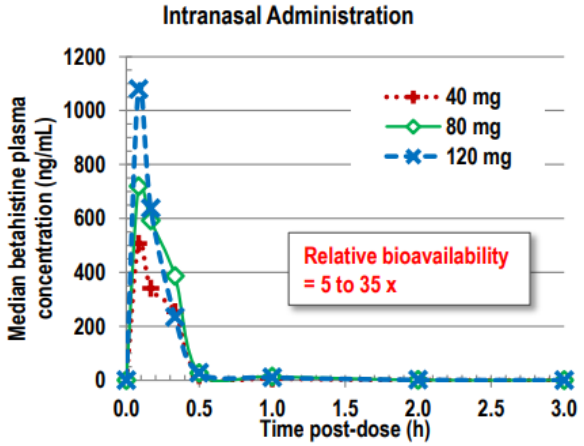
[11] Barak, N., Beck, Y., & Albeck, J. H. (2016). Betahistine decreases olanzapine-induced weight gain and somnolence in humans. *Journal of Psychopharmacology,30*(3), 237-241.

Exhibit 2: Oral administration of betahistine in Beagle dogs



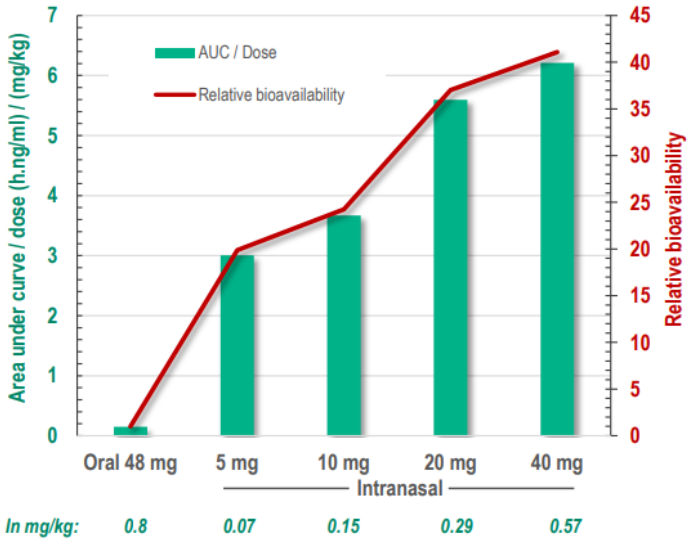
Source: Auris Medical

Exhibit 3: Intranasal administration of betahistine in Beagle dogs



Source: Auris Medical

Exhibit 4: Comparison of previous Phase I trials in healthy human volunteers



Source: Auris Medical

Auris Medical recently completed its randomized, placebo-controlled Phase I clinical trial in 72 healthy volunteers (Exhibit 5) and reported top-line data including pharmacokinetics and maximum tolerated does with single and repeated dosing on 17 October 2018. The trial was divided into three parts: the first included the administration of escalating doses of oral betahistine to 384 mg, the second included intranasal betahistine administration to determine the maximum tolerated dose with single and repeated dosing, and the third included dose escalation of repeated doses of AM-125 three times daily for three days.

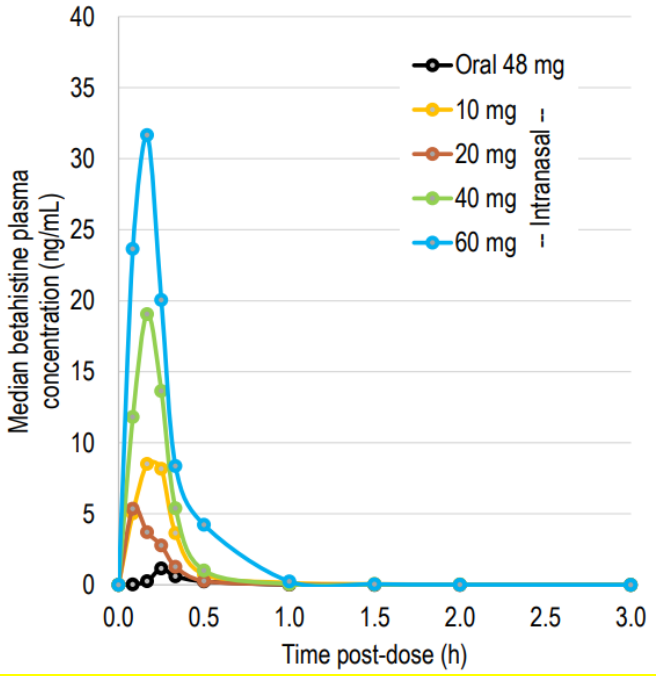
Exhibit 5: AM-125 Phase I in 72 healthy volunteers

	Dose
Group 1	Single dose intranasal betahistine (10, 20, 40, 60 mg, 100 µl) or placebo
	3x daily intranasal betahistine (5, 10, 20, 40 mg, 100 µl) or placebo for three days
Group 2	Oral betahistine (48mg) or placebo

Source: Auris Medical

Single doses (10, 20, 40, 60 mg) of intranasal betahistine demonstrated 6 to 29 times superior relative bioavailability (0.056<p<0.0001) over a single 48mg oral dose of oral betahistine as illustrated by the median betahistine plasma concentration (Exhibit 6). The company did not present data on repeated doses, but explained the profile was similar. Adverse events (AE) were mild to moderate, described as transient and included sneezing and nasal congestion, which corresponded to dose. One patient withdrew from the trial due to an AE, however no serious AEs were reported. According to Auris, the maximum tolerated repeated dose based on local tolerability in the nose was identified and set at 40 mg; the maximum tolerated single dose was not reached at 60mg.

Exhibit 6: Single-dose AM-125 demonstrates superior bioavailability to oral betahistine



Source: Auris Medical

Following these encouraging Phase I data, Auris expects to initiate its Phase II clinical trial in 138 patients with surgically-induced acute vertigo following the removal of vestibular schwannoma (ie a noncancerous tumour located on the main nerve leading from the inner ear to the brain, also known as acoustic neuroma). Vestibular schwannoma surgery triggers acute vertigo which can leave patients with the loss of peripheral vestibular input on one side. Surgical complications may include vision or hearing problems as well as nausea. Patients spend approximately three days in the hospital following the surgery and recovery time may take anywhere from six to 12 weeks, though this varies from patient to patient. Previous studies have demonstrated the ability of oral betahistine to shorten the time required to achieve vestibular compensation in patients who underwent unilateral vestibular neurectomy.[12]

Auris Medical's randomized, controlled double-blind Phase II trial, called TRAVERS, will be divided into two parts (Exhibit 7). Part A of the trial, which the company plans to initiate in Q119, will include 50 patients who will be administered 5 steps with AM-125 three times daily and 16 patients who will receive 48mg three times daily. The company anticipates top-line data readout in Q319, expects to determine a dose response curve and select a low dose and a high dose of AM-125 for the second part of the trial, which will be measured against placebo. The company plans to enrol 72 patients in

[12] Redon, C., et al. (2011). Betahistine Treatment Improves the Recovery of Static Symptoms in Patients With Unilateral Vestibular Loss. *The Journal of Clinical Pharmacology,51*(4), 538-548.

part B of the trial. Furthermore, Auris expects to receive EMA feedback on the TRAVERS trial in Q418 and plans to initiate Part A of trial thereafter.

Exhibit 7: TRAVERS Phase II trial outline

	No. patients	Dose (3x daily)	Time frame	Primary endpoints	Secondary endpoints
Part A	50 (experimental)	5 doses up to 40 mg with AM-125	4 weeks	Standing on foam, tandem Romberg test	Tandem gait, subjective visual deviation and subjective questionnaires
	16 (placebo)	48mg oral betahistine			
Part B	72	High dose and low dose (determined by interim analysis) vs placebo (48mg oral betahistine)	4 weeks	Standing on foam, tandem Romberg test	Tandem gait, subjective visual deviation and subjective questionnaires

Source: Auris Medical

Intranasal betahistine for mental health supportive care

Olanzapine is approved for the treatment of schizophrenia and bipolar disorder for adolescents and adults in the US and EU. Schizophrenia is a mental disorder characterised by a breakdown in the relation between thought, emotion, and behaviour that leads to a false sense of perception, inappropriate actions and feelings, and withdrawal from reality into delusion. It has a worldwide incidence of about 1.5 per 10,000 people. However, an estimated 40% of these individuals go untreated each year. Likewise, the worldwide incidence of bipolar disorder, which is characterized by sporadic periods of elation and depression, is an estimated 22 per 100,000 persons.[13]

In 2017, an estimated 7m prescriptions of olanzapine were supplied in the US, which is roughly equivalent to 657,000 people having a prescription that year (note: this estimate includes generics, branded and reformulations of olanzapine).[14] In a study comparing second-generation antipsychotics (SGAs) for first episode psychosis, schizophrenia patients treated with olanzapine, risperidone and quetiapine demonstrated significant weight gain (≥7% body weight) following 12 weeks and 52 weeks of treatment (Exhibit 8).[15] Negative side effects may compel patients to discontinue treatment regimens and may in turn encourage relapse.

Exhibit 8: Schizophrenic patients demonstrating more than 7% body weight gain on SGAs

Drug	Percent of patients experiencing weight gain at 12 weeks (%)	Percent of patients experiencing weight gain at 52 weeks (%)
Olanzapine	59.8	80.0
Risperidone	32.5	57.6
Quetiapine	29.2	50.0

Source: Adapted from Patel, J. K., et al. (2009)

The efficacy of olanzapine, which is just one of nine SGA drugs approved by the FDA for the first-line treatment of schizophrenia and bipolar disorders, is mediated via a combination of dopamine and serotonin type 2 (5HT2) antagonism. Interestingly, olanzapine (and other atypical antipsychotics) is also a histamine-H1 receptor antagonist, which regulates central functions including food intake, body temperature control and circadian rhythm,[16] and consequently common side effects of the drug include significant weight gain, drowsiness and somnolence.

Because betahistine acts as a partial postsynaptic H1 receptor agonist, it is postulated that the co-administration of oral betahistine with olanzapine may offset undesirable side effects. In a female Sprague Dawley rat model, rats were orally administered olanzapine (1 mg/kg) and/or betahistine

[13] World Health Organization (WHO).

[14] Symphony Health.

[15] Patel, J. K., et al. (2009). Metabolic profiles of second-generation antipsychotics in early psychosis: Findings from the CAFE study. *Schizophrenia Research,111*(1-3), 9-16.

[16] Barak, N., Beck, Y., & Albeck, J. H. (2016). Betahistine decreases olanzapine-induced weight gain and somnolence in humans. *Journal of Psychopharmacology,30*(3), 237-241.

(2.67 mg/kg) or vehicle for 14 days. Rats treated with olanzapine only demonstrated a significant increase in total weight gain over the control group ($p<0.01$), while the olanzapine and betahistine co-administration groups demonstrated a significantly lower weight gain than the olanzapine-only treatment group ($p<0.05$) by about 45%.[17] These findings suggest the co-administration of olanzapine and betahistine may partially reduce antipsychotic-induced weight gain.

Oral betahistine for antipsychotic-induced weight gain has been clinically evaluated in several trials, including two conducted by Obecure, a now-defunct Israeli company. In a Phase II double blind placebo-controlled trial enrolled 36 patients (men and women aged 16 to 45 years and BMI range of 18.5–35kg/m^2) diagnosed as having schizophrenia and prescribed to treatment with olanzapine. Eligible patients were randomized into one of two treatment groups and administrated either betahistine (24mg two times daily) or placebo in addition to once-daily, individually prescribed olanzapine treatment plans. In total, 36 patients completed the safety portion of the trial, while 35 patients were included in the intention to treat (ITT) population.[18] Betahistine was safe and well tolerated. Antipsychotic effects, as measured by PANSS and CGI, demonstrate that there was no statistical difference between the betahistine and placebo groups, thus elucidating betahistine does not interfere with the effectiveness of olanzapine. Nevertheless, mean change in body weight between baseline and week 16 of the betahistine and placebo groups of the ITT population were not statistically significant. The authors of this study highlight that the missed clinical significance was due in part to the small patient population size and low dose of betahistine.

Thereafter, a Phase I trial was conducted to evaluate higher doses of betahistine. In the Phase I double blind, placebo-controlled trial, 43 healthy female subjects (aged 18 to 45 years) with a BMI range of 18.6–27kg/m^2 were randomized into one of two treatment groups either receiving a once-daily co-administration of oral olanzapine (10mg/day) and betahistine (144mg/day) or oral olanzapine and placebo. The mean change in body weight from baseline to day 28 was 37% lower in the betahistine plus olanzapine group (1.24±0.33 kg weight gain) than in the placebo plus olanzapine group (1.93±0.85 kg weight gain) ($p=0.0489$).[16] The mean increase in somnolence observed was 60% less for the oral betahistine plus olanzapine group than the placebo plus olanzapine group ($p=0.042$) as measured by the Epworth Sleepiness Scale. Interestingly, oral betahistine has also been investigated as an obesity drug. However, in a study in obese women, betahistine did not effectively reduce food intake or appetite.[19]

IP and the AM-201 clinical program

In April 2018, Auris Medical purchased two US patents relevant to compositions for weight management (US patent no. 7,728,015) and methods of reducing olanzapine-induced weight gain (US patent no. 7,737,165), which should provide coverage through 2024. However, further details of this agreement have not been disclosed. We expect this drug formulation to be granted New Chemical Exclusivity (NCE) in the US, which will provide five years of market exclusivity, and we expect 10 years of market exclusivity in the European market. Nonetheless, the 2017 patent application covering the formulation of intranasal betahistine is also relevant for AM-201 and should therefore provide coverage through 2037 in both the US and in Europe. If intranasal administration of betahistine demonstrates superior pharmacokinetics as it bypasses the catabolism of the compound at the digestive barrier, compared to oral delivery it may also more readily offset weight gain and somnolence associated with olanzapine.

[17] Deng, C., Lian, J., Pai, N., & Huang, X. (2012). Reducing olanzapine-induced weight gain side effect by using betahistine: A study in the rat model. *Journal of Psychopharmacology,26*(9), 1271-1279.

[18] Barak, N., et al. (2016). A Randomized, Double-Blind, Placebo-Controlled Pilot Study of Betahistine to Counteract Olanzapine-Associated Weight Gain. *Journal of Clinical Psychopharmacology,36*(3), 253-256.

[19] Ali, A. H., et al. (2010). Acute effects of betahistine hydrochloride on food intake and appetite in obese women: a randomized, placebo-controlled trial. *The American Journal of Clinical Nutrition*, *92*(6), 1290–1297.

The AM-201 development program will utilize the same product as AM-125; however, the dose for the two distinct indications may differ. Auris is developing AM-201 primarily for the prevention of antipsychotic-induced weight gain, while its secondary targets include drowsiness and additional metabolic side effects. The company expects to receive pre-IND feedback from the FDA in Q418 and subsequently plans to begin enrolling healthy volunteers in its pharmacokinetics and pharmacodynamics Phase I trial in Q119 (Exhibit 9). The company expects to enrol 50 healthy volunteers at one site in Europe. The primary efficacy endpoint is weight gain while PK analysis will demonstrate potential drug-drug interaction. It expects to complete this Phase I trial in Q219 with data readout expected in Q319. The company plans to submit an IND thereafter. Concurrently, it is laying the groundwork for its Phase II randomized controlled trial in which the primary endpoint will be weight gain in either adolescents or adults. It is important to note that if the trial is efficacious for olanzapine-induced weight gain, it may also work for other atypical antipsychotics that produce similar adverse effects.

Exhibit 9: AM-201 Phase I PK/PD trial design

Screening	Olanzapine titration	Maintenance
▪ Male and female healthy volunteers ▪ 18-50 years of age ▪ BMI 18-25 kg/m2	▪ Titrate up to 10 mg (7.5mg) once daily within first week ▪ Replace subjects who do not tolerate olanzapine or gain a clinically relevant amount of weight/ high glucose level	▪ Maintain olanzapine dose for three weeks

Source: Auris Medical

Seeking strategic partnerships for Phase III programs

Auris Medical is also developing AM-111 and Keyzilen (AM-101) for the treatment of acute inner ear hearing loss and tinnitus, respectively. Inner ear hearing loss and tinnitus are often a result of acute injury (eg from noise exposure, vascular compromise or inflammation); they are therefore focuses of neurotology. AM-111 has received orphan drug designation from both the FDA and EMA for the treatment of acute sensorineural hearing loss (ASNHL), hearing loss from acoustic trauma, sudden deafness (idiopathic sudden sensorial hearing loss, ISSNHL) and surgery-induced acoustic trauma. This designation would provide seven and 10 years of market exclusivity in the US and in Europe, respectively. Additionally, the FDA has granted both AM-111 and Keyzilen fast-track designation, which enables early and frequent meetings with the FDA to discuss development and ensure the collection of appropriate data, which may lead to accelerated approval.

AM-111 and HEALOS

AM-111 is a biocompatible and biodegradable composition of brimapitide, also known as D-JNKI-1, an inhibitor of the jun-N-terminal protein kinase (JNK) pathway involved in sensory cell death, or apoptosis, following chemical or mechanical stress. Animal studies suggest that blocking the JNK/stress-activated protein kinase-mediated cell death pathway with brimapitide prevents hair cell death and permanent hearing loss caused by sound trauma, cochlear ischemia, bacterial infection, cochlear inflammation (labyrinthitis) and cochlear implantation trauma.[20,21,22]

[20] Wang, J., et al (2006). Inhibition of the c-Jun N-Terminal Kinase-Mediated Mitochondrial Cell Death Pathway Restores Auditory Function in Sound-Exposed Animals. *Molecular Pharmacology,71*(3), 654-666.

[21] Omotehara, Y., et al (2011). Protection Against Ischemic Cochlear Damage by Intratympanic Administration of AM-111. *Otology & Neurotology,32*(9), 1422-1427.

[22] Barkdull, G. C., et al. (2007). AM-111 Reduces Hearing Loss in a Guinea Pig Model of Acute Labyrinthitis. *The Laryngoscope,117*(12), 2174-2182.

In 2013, Auris Medical completed its randomized, double-blind, placebo-controlled Phase II clinical trial in 210 patients aged 18 to 60 years with ASNHL of at least 30dB due to acoustic trauma within 48 hours of onset.[23] Patients were randomized to receive either a single intratympanic injection of AM-111 at 0.4mg/mL or 0.2mg/mL, or placebo. Intratympanic injection of AM-111 was considered safe and well tolerated. Although AM-111 treatment did not demonstrate otoprotection in patients with mild-to-moderate ASHL (pure tone average <60dB), the study found that AM-111 at 0.4mg/mL showed a statistically significant and clinically relevant improvement in hearing thresholds and speech discrimination between baseline and day seven among those with severe-to-profound ASHL (pure tone average ≥60dB). The authors highlighted that the lack of significance was likely due to spontaneous hearing recovery in mild-to-moderate ASNHL. These results provided a foundation for the Phase III trial.

In 2017, Auris Medical completed its European Phase III HEALOS trial, which investigated the safety and effectiveness of the intratympanic administration of AM-111 in 256 patients (aged 18 to 65 years) suffering from severe-to-profound ISSNHL within 72 hours of onset. Patients were randomized to receive either a single intratympanic injection of AM-111 at 0.4 mg/mL or 0.8 mg/mL, or placebo gel. However, AM-111 did not meet the primary efficacy endpoint of a significant improvement in hearing from baseline to day 28 compared to placebo in either treatment groups (Exhibit 10).

Exhibit 10: HEALOS trial outcomes

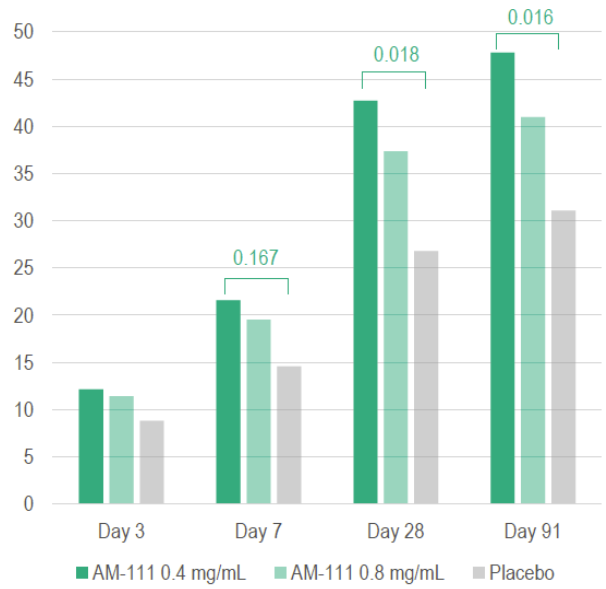
Treatment group	Day 28 hearing frequencies (dB)	Statistical analysis versus placebo
Placebo	33.4	N/A
0.4 mg/mL	38.4	p=0.226
0.8 mg/mL	36.6	p=0.448

Source: Auris Medical

Post-hoc analysis demonstrated that a subpopulation of patients with profound hearing loss (pure tone average ≥90dB at baseline) experienced clinical and statistically significant improvement in the AM-111 0.4mg/mL treatment group (Exhibit 11). Following the results of the HEALOS trial, the company terminated the ASSENT trial in the US and met with the FDA and EMA to discuss the development and regulatory path forward. Auris Medical proposed running a Phase III placebo-controlled pivotal trial with AM-111 0.4mg/mL in patients with profound acute hearing loss and received positive feedback from both organizations. The trial is expected to take around 2-2.5 years. The company has stated that it plans to identify a strategic partner before moving forward.

[23] Suckfuell, M., et al. (2014). Efficacy and Safety of AM-111 in the Treatment of Acute Sensorineural Hearing Loss. *Otology & Neurotology,35*(8), 1317-1326.

Exhibit 11: Post-hoc analysis of subpopulation with profound hearing loss



Source: Auris Medical

Keyzilen and the TACTT trials

Auris Medical is also developing Keyzilen (AM-101), an otic gel formulation of esketamine hydrochloride, for the treatment of acute inner ear tinnitus. Esketamine (an enantiomer of ketamine) is a small-molecule N-Methyl-D-aspartate (NMDA) receptor antagonist. Cochlear NMDA receptors are activated by the excessive release of neurotransmitters from inner hair cell post-synapses, which become excitotoxic to the primary auditory neuron.[24] These exitotoxic events may emanate from acoustic trauma, salicylate toxicity (salicylate is the active component of NSAIDS such as aspirin) or other events associated with sudden deafness. Activity imbalance between NMDA and non-NMDA receptors can lead to hyperactivity of the auditory nerve and thus the initiation of tinnitus activity. Auris Medical has previously conducted two Phase II and two Phase III trials in both the US and in Europe investigating the safety and efficacy of Keyzilen for acute inner ear tinnitus.

In a Phase II trial, 248 patients (aged 16 to 65 years) with persistent tinnitus following acute acoustic trauma, sudden deafness or acute otitis media with onset less than three months prior were randomized to receive either three intratympanic injections of Keyzilen at 0.27mg/mL (78 patients) or 0.81mg/mL (84 patients), or placebo (86 patients) over three consecutive days.[25] Intratympanic injections of Keyzilen were well tolerated. The study failed to meet the primary endpoint, which was a change in the minimum masking level (ie the volume at which an external noise masks the perception of tinnitus, MML) from baseline to day 90 follow up. Notably, however, 42% of the patients in the high-dose group experienced an improvement (ie a reduction) in tinnitus loudness, a co-primary endpoint, of 50% or more between baseline and follow up at day 90. A second exploratory Phase II trial was designed to evaluate the dosing regimen for Keyzilen by testing single- and triple-dose injections over two weeks instead of three days.[26] Eighty-five patients were randomised into four groups (single-dose placebo, triple-dose placebo, single-dose Keyzilen,

[24] Bing, D., et al (2015). Cochlear NMDA Receptors as a Therapeutic Target of Noise-Induced Tinnitus. *Cellular Physiology and Biochemistry,35*(5), 1905-1923.

[25] Heyning, P. V., et al. (2014). Efficacy and Safety of AM-101 in the Treatment of Acute Inner Ear Tinnitus—A Double-Blind, Randomized, Placebo-Controlled Phase II Study. *Otology & Neurotology,35*(4), 589-597.

[26] Staecker, H., et al. (2015). Selecting Appropriate Dose Regimens for AM-101 in the Intratympanic Treatment of Acute Inner Ear Tinnitus. *Audiology and Neurotology,20*(3), 172-182.

triple-dose Keyzilen). The study found that patient-reported outcomes such as tinnitus loudness and annoyance in the Keyzilen groups showed a consistent improvement over placebo, however, the trial was not powered to demonstrate statistical significance.

On the back of established results, the company increased the concentration of esketamine from 0.81mg/mL to 0.87mg/mL, which was simply a technical adjustment, for the TACTT2 and TACTT3 Phase III trials. Auris Medical, the EMA and FDA, agreed to abandon the MML endpoint and focus instead on tinnitus loudness and a questionnaire measuring tinnitus impact. For the TACTT2 trial 343 patients (aged 18 years and older) with persistent tinnitus following traumatic cochlear injury onset less than three months prior were randomized to receive either three intratympanic injections of Keyzilen at 0.87mg/mL (204 patients), or placebo (139 patients) over three to five days.[27] The injections over this period were well tolerated; however, the study missed the primary efficacy endpoint, which was a change in patient-reported tinnitus loudness improvement from baseline to follow up at day 84 (p=0.32). In parallel, Auris ran a sister trial, TACTT3, that enrolled patients with persistent tinnitus following traumatic cochlear injury onset less than three to six months prior. Following results from TACTT2, enrolment for TACTT3 was re-opened to make some changes to the protocol and add about 20% more patients. The trial read out in March 2018 and produced similar results.

In response to FDA request for safety data from chronic intermittent use of Keyzilen for up to 12 months, Auris Medical conducted two open label extension studies, AMPACT1 and AMPACT2, which enrolled patients who completed the TACTT2 and TACTT3 trials respectively. The primary safety endpoint of both trials was incidence of clinically relevant hearing deterioration five weeks after the start of a treatment cycle, which was 6% in AMPACT1 and 4-8% in AMPACT2. The majority of the adverse events related to Keyzilen and/or the treatment procedure were either mild or moderate. The trials suggested a therapeutic benefit and demonstrated that the more treatment cycles the patients received the greater the decrease in tinnitus functional index (TFI). The trials also provided evidence of the existence of a treatment time window such that earlier initiation of treatment resulted in more tinnitus reduction (Exhibit 12).

Exhibit 12: Average TFI decrease from baseline

Original enrolment period	AMPACT1	AMPACT2
Up to 3 months from onset	8.2	7.6
Between 3 and 6 months from onset	N/A	3.5
Between 6 and 12 months from onset	N/A	2.5

Source: Auris Medical. Notes: TFI= Tinnitus functional index.

The company adamantly believes in the program and has stated the primary endpoints of the TACTT trials were most likely missed due to issues in study design including the switch from visit-based to daily ratings of tinnitus loudness in the context of a special protocol assessment with the FDA. The company also believes the lack of objective tools to measure patient eligibility for these trials may have also biased the outcomes. Auris Medical has temporarily deprioritized the Keyzilen development program and plans to run a POC study without including daily ratings of tinnitus loudness and to validate objective measurement tools as a basis for a pivotal trial potentially via external funding from a research grant.

Sensitivities

Auris Medical has shifted away from late-stage clinical development as it recently deprioritized both the Keyzilen (AM-101) and AM-111 Phase III development programs as a result of missing key clinical trial endpoints. Nonetheless, the company is encouraged by the existing Phase II data from

[27] Staecker, H., et al. (2017). Safety of Repeated-Dose Intratympanic Injections with AM-101 in Acute Inner Ear Tinnitus. *Otolaryngology-Head and Neck Surgery,157*(3), 478-487.

the Keyzilen program and the HEALOS data from the AM-111 program and remains excited about these two programs. Auris is determined to drive the AM-111 program forward via a strategic partner and progress the Keyzilen program via a POC study with financial support from an external grant.

In the near term, the primary risks associated with Auris Medical are clinical given the early stage of its two primary development programs. However, some risks are relatively alleviated considering that betahistine hydrochloride has an established mechanism of action and its oral formulation the most widely prescribed medication in the European market for the treatment of MD, BPPV and peripheral vestibular vertigo of known and unknown origin. Auris is addressing the fact that oral betahistine (48mg) was withdrawn from the US market by the FDA in 1972 due to unsubstantiated evidence in vertigo with its intranasal formulation that has demonstrated higher bioavailability and thus may show superior therapeutic benefit. This leaves an opportunity to tap into the US market where there are currently no betahistine products on the market. There is also a substantial financial risk due to the CHF65m in additional cash needed to bring the two intranasal betahistine programs from Phase I development through to commercialization, which may result in substantial dilution.

Valuation

We arrive at an initial valuation of $117.6m or $4.89 per basic share ($3.20 per diluted share). Our valuation is derived from a risk-adjusted NPV analysis on the future earnings of its two lead clinical programs, and as standard practice, this includes costs associated with each asset (Exhibit 13). We model commercialization for AM-125 and AM-210 in both the US and Europe. The probability of success for each clinical asset is predicted based on Edison's research principles and an analysis of the underlying asset in each specific market. In all cases, our valuations of individual assets include associated costs (R&D, SG&A). We assume a total of CHF22m and CHF25m in clinical trial costs for the acute vertigo and mental health disorder support in co-administration with olanzapine indications, respectively.

Our valuation is based on launch pricing of the intranasal betahistine in the range of $500-$1,000 per year. We estimate peak sales of CHF200m for AM-125 with a 25% penetration into the US and European markets of patients, with acute vertigo requiring additional treatment following failed ED head-positioning manoeuvres. Further to this, we estimate 30% and 45% probability of successes in the US and the EU, respectively, considering oral betahistine is widely used throughout Europe and the intranasal administration of the drug may increase efficacy. We also consider the convenience of a nasal administration over taking up to ~20 pills each day to alleviate symptoms. We estimate peak sales of CHF270m for AM-201 with a 20% penetration into the US and European markets of patients prescribed olanzapine (based on number of patients prescribed olanzapine in the US in 2017) and those who experience significant weight gain (≥7% body weight). We apply a 12.5% discount rate, our standard for development-stage companies. We expect to make adjustments to our valuation with efficacy data and expect to add the AM-111 and Keyzilen Phase III programs in our valuation when the company identifies a path forward.

Exhibit 13: Valuation of Auris Medical

Program	Market	Indication	Clinical stage	Probability of success	Launch year	Peak sales ($m)	rNPV ($m)
AM-125	US	Acute vertigo	Phase I	30%	2023	88.73	$21.6
AM-125	Europe	Acute vertigo	Phase I	45%	2022	113.12	$54.7
AM-201	US	Mental health supportive care	Phase I	20%	2024	128.72	$14.5
AM-201	Europe	Mental health supportive care	Phase I	20%	2025	143.85	$19.7
Total							**110.62**
Net cash and equivalents (as of 30 June 2018 plus July 2018 public offering) ($m)							7.01
Total firm value ($m)							117.6
Total basic shares (as of June 2018 plus July 2018 public offering, m)							24.1
Value per basic share ($)							4.89
Options and warrants (as of June 2018 plus July 2018 public offering, m)							12.7
Total diluted shares (m)							36.8
Value per diluted share ($)							3.20

Source: Edison Investment Research

Financials

The company's expenses are largely driven by its R&D activities, which totalled CHF19.2m in FY17. However, Auris has guided that total operational expenses are forecast to total approximately CHF10m to CHF12m for FY18, which is down roughly half versus the same period last year (FY17: CHF24.4m). This decrease is driven by the shift away from Phase III development to focus on early-stage clinical programs. Auris reported CHF5m in R&D expenditure for the first half of the year. Auris Medical ended Q218 (30 June) with CHF4.4m in cash and equivalents and CHF3.6m in debt. Following the end of the quarter, the company received an additional CHF6.15m in net proceeds from the July 2018 public offering. Our forecasts model a total CHF65m in financing needs through 2023, which we record as illustrative debt, to bring the two intranasal betahistine programs from Phase I to commercialization (Exhibit 14). However, these financing needs may be offset by potential strategic partnering. Auris may also draw down from its $10m equity line established with Lincoln Park Capital Fund. We forecast slight increases R&D expenditure to about CHF6m in 2019 and CHF11m in 2020 primarily associated with the advancement of AM-125 into Phase II and the initiation of the AM-201 Phase I program, which is expected in Q119.

Exhibit 14: Financial summary

CHF'000s	2016	2017	2018e	2019e
Year end 31 December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	0	0	0	0
Cost of Sales	0	0	0	0
Gross Profit	0	0	0	0
Research and development	(24,777)	(19,211)	(7,128)	(6,732)
Selling, general & administrative	(5,447)	(5,150)	(4,512)	(4,557)
EBITDA	(30,321)	(24,484)	(11,732)	(11,473)
Operating Profit (before amort. and except.)	(30,223)	(24,361)	(11,640)	(11,381)
Intangible Amortisation	0	0	0	0
Exceptionals/Other	0	0	0	0
Operating Profit	(30,223)	(24,361)	(11,640)	(11,381)
Net Interest	(761)	(1,586)	(60)	(400)
Other (change in fair value of warrants)	191	1,520	3,431	0
Profit Before Tax (norm)	(30,984)	(25,947)	(11,700)	(11,781)
Profit Before Tax (IFRS)	(30,793)	(24,427)	(8,269)	(11,781)
Tax	131	18	17	0
Deferred tax	(414)	322	1,066	0
Profit After Tax (norm)	(30,853)	(25,929)	(11,682)	(11,781)
Profit After Tax (IFRS)	(31,076)	(24,087)	(7,186)	(11,781)
Average Number of Shares Outstanding (m)	34.3	48.4	24.4	30.6
EPS - normalised (CHF)	(0.90)	(0.54)	(0.48)	(0.39)
EPS - IFRS (CHF)	(0.91)	(0.50)	(0.29)	(0.39)
Dividend per share (CHF)	0.0	0.0	0.0	0.0
Gross Margin (%)	N/A	N/A	N/A	N/A
EBITDA Margin (%)	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A
BALANCE SHEET				
Fixed Assets	1,967	1,959	2,154	2,062
Intangible Assets	1,483	1,629	1,664	1,664
Tangible Assets	369	253	161	69
Other	115	77	329	329
Current Assets	33,691	15,868	5,865	2,618
Stocks	0	0	0	0
Debtors	297	241	82	116
Cash	32,442	14,973	5,302	2,021
Other	953	653	481	481
Current Liabilities	(8,957)	(10,426)	(6,972)	(5,414)
Creditors	(6,745)	(5,884)	(5,472)	(5,414)
Short term borrowings	(2,213)	(4,542)	(1,500)	0
Long Term Liabilities	(12,558)	(9,563)	(1,565)	(11,565)
Long term borrowings	(10,151)	(5,584)	0	(10,000)
Other long term liabilities	(2,406)	(3,979)	(1,565)	(1,565)
Net Assets	14,143	(2,162)	(518)	(12,299)
CASH FLOW				
Operating Cash Flow	(30,071)	(25,827)	(11,252)	(11,781)
Net Interest	749	1,569	845	0
Tax	(131)	(18)	(17)	0
Capex	(244)	(153)	(20)	0
Acquisitions/disposals	0	0	0	0
Financing	11,439	10,308	10,076	0
Dividends	0	0	0	0
Other	68	(2,034)	0	0
Net Cash Flow	(18,192)	(16,154)	(367)	(11,781)
Opening net debt/(cash)	(38,251)	(20,078)	(4,847)	(3,802)
HP finance leases initiated	0	0	0	0
Exchange rate movements	(397)	1,316	152	0
Other	416	(393)	(829)	0
Closing net debt/(cash)	(20,078)	(4,847)	(3,802)	7,979

Source: Company reports, Edison Investment Research

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Management team

CEO, Founder, and Chairman: Thomas Meyer	CFO: Hernan Levett
Dr Thomas Meyer founded the company in 2007 and currently serves as the chief executive and Chairman of the Board of Directors. Prior to founding Auris Medical he served as CEO Disetonic Group, which is a Swiss supplier of precision infusion and injection systems. Dr Meyer holds a PhD in business administration from the University of Fribourg, Switzerland.	Mr Hernan Levett has served as the company's chief financial officer since January 2017. Prior to joining Auris Medical, he spent 10 years at Novartis, and most recently served as CFA of Novartis Chile SA. Mr Levett is a CPA and earned his MNA at Universidad de San Andres.
Director of Translational Research: Ilja Hohenfeld	**Medical Director: Andrea Vondraskova**
Mr Ilja Hohenfeld joined Auris Medical in 2012 as senior clinical project manager and in 2017 became the company's director of translational research. Prior to joining Auris Medical, he spent eight years in various roles with ICON Clinical Research, and served as clinical project manager and global trial leader at Actelion. He holds a PhD in natural sciences from the Max Planck Institute of Molecular Physiology, Dortmund, Germany.	Dr Andrea Vondraskova has served as the company's medical director since the beginning of 2017. Prior to joining Auris Medical, she spent 18 years in the pharmaceutical industry in various roles with pharmaceutical companies, CROs, and a regulatory agency. She did her training as a general practitioner at the Faculty of Medicine, Charles University, in Prague, Czech Republic, and obtained a Master of Science in clinical pharmacology/pharmaceutical medicine at the University of Surrey, UK.

Principal shareholders	(%)
Sofinnova Venture Partners VIII, LP	14.73
Thomas Meyer, PhD	12.56
Empery Asset Management, LP	7.69
Sabby Volatility Warrant Master Fund, Ltd	6.38

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