EDISON

Auris Medical Holding

Financial update

Full-year results and near-term trial initiations

Pharma & biotech

Auris recently announced its full-year 2018 financial results and provided an update on its active intranasal betahistine programs. R&D expenditure for the year was down roughly 65% compared to FY17, which reflects the shift to focus on earlier-stage program development. Auris plans to initiate the AM-125 Phase II trial of intranasal betahistine for treating acute vertigo in Q119 following the finalisation of clinical site selection, which it states is nearly complete. Additionally, Auris plans to initiate its AM-201 Phase I trial for olanzapine-induced weight gain in Q119.

Year end	Revenue (CHFm)	PBT* (CHFm)	EPS* (CHF)	DPS (CHF)	P/E (x)	Yield (%)
12/17	0.0	(25.9)	(0.54)	0.0	N/A	N/A
12/18	0.0	(12.0)	(0.72)	0.0	N/A	N/A
12/19e	0.0	(11.6)	(0.58)	0.0	N/A	N/A
12/20e	0.0	(17.5)	(0.84)	0.0	N/A	N/A

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

TRAVERS trial initiation in Q119

Auris is developing AM-125, an intranasal formulation of betahistine for the treatment of acute vertigo. As AM-125 bypasses the digestive tract where the oral compound is readily metabolised, the intranasal formulation has demonstrated superior bioavailability over oral betahistine. The Phase II trial, TRAVERS, will include 138 patients with surgically induced acute vertigo following vestibular schwannoma excision. The trial is expected to initiate in Q119 following the completion of clinical site selection, with interim data expected in Q419.

Upcoming AM-201 PK/PD trial

Auris also is developing AM-201, an intranasal betahistine formulation, for co-administration with olanzapine to counteract adverse effects such as weight gain and sleepiness. The company plans to initiate the Phase I trial in Q119 in 50 healthy volunteers in Europe with top-line data expected in Q319.

Potential betahistine pipeline expansion

Auris recently acquired orphan drug designation for betahistine for the treatment of obesity associated with Prader-Willi syndrome (PWS) as well as two US patents covering the use of betahistine for the treatment of atypical depression and attention deficit hyperactivity disorder (ADHD). However, the company has noted these transactions will not affect its business strategy in the near term.

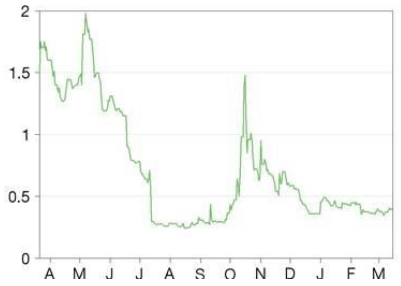
Valuation: $123.4m or $3.29 per basic share

We have revised our valuation to $123.4m or $3.29 per basic share ($2.74 per diluted share), from $119.8m or $3.92 per basic share ($3.19 per diluted share). The increase in overall valuation was primarily driven by rolling forward our NPVs. The increase in share count is attributed to the financial agreements with FiveT Capital and Alliance Global Partners (AGP), which consequently decreased the price per share.

21 March 2019

Price	**US$0.40**
Market cap	**US$15m**
	US$1/CHF
Net cash ($m) at 31 December 2018	3.96
Shares in issue	37.5m
Free float	82.8%
Code	EARS
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	9.3	(7.0)	(75.5)
Rel (local)	6.9	(13.9)	(76.0)
52-week high/low	US$2.0		US$0.2

Business description

Auris Medical is a Swiss biopharmaceutical company developing neurotology therapeutics. It 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-201 PK/PD top-line readout	Q319
AM-125 Phase IIa interim readout	Q419

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Edison profile page

AM-125 TRAVERS trial expected to initiate soon

Auris recently provided an update on its AM-125 clinical program for the treatment of acute vertigo. The TRAVERS trial is a randomised, controlled, double-blind Phase II trial divided into two parts (Exhibit 1) and will include 138 patients in total with surgically induced acute vertigo following the removal of vestibular schwannoma (which is a noncancerous tumour on the main nerve leading from the inner ear to the brain, also known as acoustic neuroma). Vestibular schwannoma surgery leads to loss of peripheral vestibular input, which triggers acute vertigo.

In Part A of the trial, which the company plans to initiate in Q119, 50 patients will be administered AM-125 in five dose cohorts or placebo three times daily and 16 patients will receive 48mg oral betahistine three times daily (open-label). Dosing will begin roughly three to four days after surgery. The company plans to report interim data in Q419 and 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. Then in Part B of the trial, the company plans to enrol 72 patients. Furthermore, Auris received EMA feedback on the TRAVERS trial and expects to initiate the study in Q119. The trial will be conducted in 15–18 sites in Europe and Canada. According to the company, selection of these clinical sites is nearly complete. If the study is successful, it could be an important catalyst for the program.

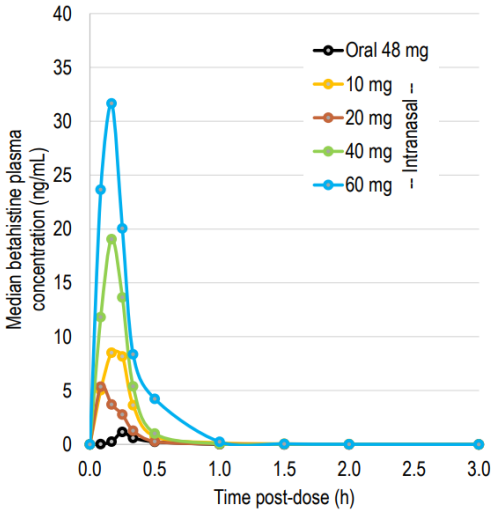
Exhibit 1: TRAVERS Phase II trial outline

	No. of patients	Dose (three times daily)	Timeframe	Primary endpoints	Secondary endpoints
Part A	50 (experimental)	Five doses up to 20mg with AM-125	Four 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	Four weeks	Standing on foam, tandem Romberg test	Tandem gait, subjective visual deviation and subjective questionnaires

Source: Auris Medical

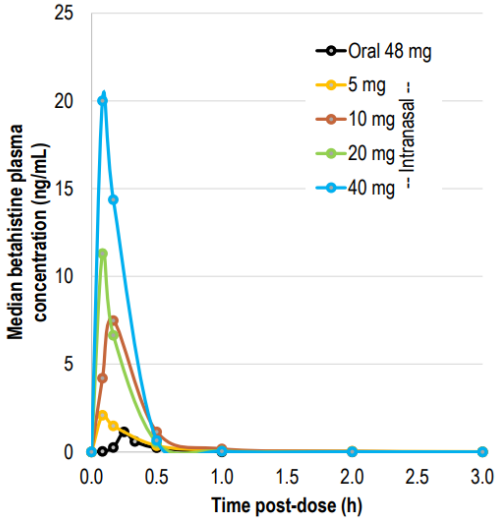
Auris previously demonstrated the superior bioavailability of AM-125, intranasal betahistine, compared to oral betahistine (48mg) in both single and multiple doses (Exhibits 2 and 3) in its Phase I trial. Adverse events (AEs) were mild to moderate, described as transient and included sneezing and nasal congestion, which corresponded to dose. One patient withdrew from the trial due to an AE, but 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 40mg; the maximum tolerated single dose was not reached at 60mg.

Exhibit 2: Single-dose AM-125 bioavailability vs oral betahistine



Source: Auris Medical

Exhibit 3: Multi-dose AM-125 bioavailability vs oral betahistine



Source: Auris Medical

AM-201 for olanzapine-induced weight gain

Concurrent to the AM-125 trial, Auris plans to initiate the Phase Ib pharmacokinetics/ pharmacodynamics (PK/PD) trial in AM-201, intranasal betahistine for the prevention of olanzapine-induced weight gain. The company intends to begin enrolling 50 healthy volunteers at one site in Europe in Q119 (Exhibit 4).

Exhibit 4: AM-201 Phase I PK/PD trial design

Screening	Olanzapine titration	Maintenance
■ Male and female healthy volunteers ■ 18–50 years of age ■ BMI 18–25kg/m^2	■ Titrate up to 10mg (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

The primary and secondary endpoints are weight gain and daytime sleepiness, respectively, whereas PK analysis will assess potential drug to drug interaction. The company expects to read out top-line data in summer 2019.

Potential betahistine program expansion

On 6 December 2018, Auris acquired orphan drug designation for betahistine for the treatment of obesity associated with PWS. PWS is rare genetic disorder characterised by hyperphagia, an abnormally increased appetite, which leads to early-onset obesity, developmental delay, hypogonadism and characteristic facial features. Prevalence estimates of PWS in the US and in Europe are one in 25,000[1] people and one in 45,000[2] people, respectively. Additionally, the company announced the signing of a binding letter of intent to acquire two US patents covering the use of betahistine for the treatment of atypical depression and ADHD. Atypical depression is a subtype of major depression that presents with at least two of the following symptoms: increased appetite/significant weight gain, hypersomnia, laden paralysis, or sensitivity to interpersonal rejection. Atypical depression occurs in roughly 40% of those diagnosed with major depressive

1 Butler, MG (1990) Prader-Willi syndrome: Current understanding of cause and diagnosis. *American Journal of Medical Genetics, 35*(3), 319–332.

2 Whittington, JE (2001) Population prevalence and estimated birth incidence and mortality rate for people with Prader-Willi syndrome in one UK health region. *Journal of Medical Genetics, 38*(11), 792–798.

disorder, which has an estimated prevalence of 6.7%[3] and 4.0%[4,5] of adults in the US and in Europe, respectively. ADHD is a mental disorder characterised by inattention, hyperactivity and impulsivity. According to the Centres for Disease Control, roughly 9.4% (or 6.1 million) of children (aged 2–17) have had ADHD in the US, whereas estimates for prevalence of ADHD in adults is 4.4%[3] in the US. Prevalence estimates are similar in Europe. We have no further information on these transactions and the company has indicated these dealings will not affect its business strategy in the near term. We expect the results of the current clinical programs to guide and potentially tailor intranasal betahistine pipeline expansion. We therefore do not include these in our valuation for now.

Valuation

We have adjusted our valuation to $123.4m or $3.29 per basic share ($2.74 per diluted share) from $119.8m or $3.92 per basic share ($3.19 per diluted share). The increase in overall valuation was primarily driven by rolling forward our NPVs. The increase in share count is attributed to the two purchase agreements with FiveT Capital AG announced in November and December 2018 and the market sales agreement with Alliance Global Partners (AGP) announced in November 2018, which consequently decreased the price per share.

Exhibit 5: 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	23.7
AM-125	Europe	Acute vertigo	Phase I	45%	2022	113.12	59.2
AM-201	US	Mental health supportive care	Phase I	20%	2024	128.72	15.4
AM-201	Europe	Mental health supportive care	Phase I	20%	2025	143.85	21.1
Total							119.48
Net cash and equivalents (As of 31 December 2018) ($m)							3.96
Total firm value ($m)							**123.44**
Total basic shares (as of 31 December 2018, m)							37.5
Value per basic share ($)							**3.29**
Options and warrants (as of 31 December 2018, m)							7.5
Total diluted shares (m)							45.0
Value per diluted share ($)							2.74

Source: Company reports, Edison Investment Research

Financials

Auris recently reported its fourth quarter and full FY18 results. The company reported R&D spend of CHF34,923 for Q418 and CHF6.7m for the full year, which is down significantly from the year before (Q417: CHF4.3m; FY17: CHF19.2m). This decrease reflects the capitalization of CHF1.9m in direct costs associated with the AM-125 program and the completion of the late-stage programs. G&A expenditure for the year was CHF4.3m, which is down roughly 17% from the year prior (CHF5.2m). As of 31 December 2018, Auris had CHF5.4m in cash and equivalents and CHF1.4m in debt. After the end of the quarter, Auris announced the full repayment of its loan facility with Hercules Capital.

[3] National Institute of Mental Health

[4] Kessler, RC and Bromet, EJ (2013) The epidemiology of depression across cultures. *Annual Review of Public Health, 34*(1), 119–138.

[5] Prevalence estimate of major depressive disorder in Europe is based on the average prevalence in France, Germany and Italy.

The company has guided towards operating expenditure in the range of CHF10m to CHF13m for FY19. In our forecasts, we model a total of CHF65m in financing needs through 2023, which we record as illustrative debt, to bring the two intranasal betahistine programs from Phase I to commercialisation (Exhibit 6). However, these financing needs may be offset by potential strategic partnering. Auris may also draw down from its Lincoln Park Capital Fund equity line (~$9.0m remaining). As per the market sales agreement between Auris and AGP announced in November 2018, the company may sell common shares through AGP for up to $25m. We forecast slight increases in R&D expenditure to about CHF7m in 2019 and CHF12m 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 6: Financial summary

CHF000s	2017	2018	2019e	2020e
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	(19,211)	(6,690)	(6,800)	(12,000)
Selling, general & administrative	(5,150)	(4,265)	(4,307)	(4,393)
EBITDA	(24,484)	(11,027)	(11,253)	(16,539)
Operating Profit (before amort. and except.)	(24,361)	(10,954)	(11,180)	(16,466)
Intangible Amortisation	0	0	0	0
Exceptionals/Other	0	0	0	0
Operating Profit	(24,361)	(10,954)	(11,180)	(16,466)
Net Interest	(1,586)	(1,070)	(400)	(1,000)
Other (change in fair value of warrants)	1,520	690	0	0
Profit Before Tax (norm)	(25,947)	(12,024)	(11,580)	(17,466)
Profit Before Tax (IFRS)	(24,427)	(11,334)	(11,580)	(17,466)
Tax	18	(162)	0	0
Deferred tax	322	1,266	0	0
Profit After Tax (norm)	(25,929)	(12,186)	(11,580)	(17,466)
Profit After Tax (IFRS)	(24,087)	(10,230)	(11,580)	(17,466)
Average Number of Shares Outstanding (m)	48.4	15.9	19.9	20.7
EPS - normalised (CHFc)	(53.60)	(72.04)	(58.26)	(84.49)
EPS - IFRS (CHF)	(0.50)	(0.72)	(0.58)	(0.84)
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	1,959	3,812	3,739	3,667
Intangible Assets	1,629	3,535	3,535	3,535
Tangible Assets	253	34	(39)	(112)
Other	77	243	243	243
Current Assets	15,868	6,065	3,111	1,587
Stocks	0	0	0	0
Debtors	241	320	114	173
Cash	14,973	5,393	2,646	1,063
Other	653	351	351	351
Current Liabilities	(10,426)	(4,563)	(3,117)	(3,986)
Creditors	(5,884)	(3,127)	(3,117)	(3,986)
Short term borrowings	(4,542)	(1,435)	0	0
Long Term Liabilities	(9,563)	(1,665)	(11,665)	(26,665)
Long term borrowings	(5,584)	0	(10,000)	(25,000)
Other long term liabilities	(3,979)	(1,665)	(1,665)	(1,665)
Net Assets	(2,162)	3,649	(7,931)	(25,397)
CASH FLOW				
Operating Cash Flow	(25,827)	(14,447)	(11,312)	(16,583)
Net Interest	1,569	1,053	0	0
Tax	(18)	162	0	0
Capex	(153)	(1,891)	0	0
Acquisitions/disposals	0	68	0	0
Financing	10,308	15,005	0	0
Dividends	0	0	0	0
Other	(2,034)	0	0	0
Net Cash Flow	(16,154)	(50)	(11,312)	(16,583)
Opening net debt/(cash)	(20,078)	(4,847)	(3,958)	7,354
HP finance leases initiated	0	0	0	0
Exchange rate movements	1,316	258	0	0
Other	(393)	(1,097)	0	0
Closing net debt/(cash)	(4,847)	(3,958)	7,354	23,937

Source: Auris Medical Holding reports, Edison Investment Research

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