

# Innovative Treatments for Inner Ear Disorders



## **AM-125 : Intranasal Betahistine**

February 3, 2017

NASDAQ: EARS

# Forward-looking Statements

This presentation and the accompanying oral commentary contain “forward-looking” statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation and the accompanying oral commentary, including statements regarding our future financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “believe,” “will,” “may,” “estimate,” “continue,” “anticipate,” “intend,” “should,” “plan,” “might,” “approximately,” “expect,” “predict,” “could,” “potentially” or the negative of these terms or other similar expressions. Forward-looking statements appear in a number of places throughout this presentation and the accompanying oral commentary and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates AM-101 and AM-111, our intellectual property position, our ability to develop commercial functions, expectations regarding clinical trial data, our results of operations, cash needs, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us.

Forward-looking statements involve known and unknown risks, uncertainties, assumptions and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These include, but are not limited to, the timing and conduct of clinical trials of our product candidates, the clinical utility of our product candidates, including the likelihood that the TACTT3 trial may not meet its endpoints, the timing or likelihood of regulatory filings and approvals, the timing or likelihood of regulatory filings and approvals, our intellectual property position and our financial position, including the impact of any future acquisitions, dispositions, partnerships, license transactions or changes to our capital structure, including future securities offerings. These risks and uncertainties also include, but are not limited to, those described under the caption “Risk Factors” in our Annual Report on Form 20-F, in our Report on Form 6-K filed on November 10, 2016, and in future filings with the Securities and Exchange Commission. Forward-looking statements represent our management’s beliefs and assumptions only as of the date of this presentation. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

A stack of newspapers is shown, with the top page prominently displaying the word "NEWS" in a large, serif font, centered between two horizontal lines. Below this, the main headline is written in a bold, italicized sans-serif font.

# NEWS

***Auris Medical Expands Pipeline  
with Intranasal Betahistine for  
Meniere's Disease and  
Vestibular Vertigo***

# Strategic Fit within Clinical-Stage Pipeline

Product	Indication	Preclin.	Phase 1	Phase 2	Phase 3	Next Key Milestones	
<b>Keyzilen®</b> (AM-101) Esketamine	<i>Acute inner ear tinnitus</i>					Data TACTT3 (A)	Q1 2018
	<i>Post-acute inner ear tinnitus</i>					Data TACTT3 (B)	Q1 2018
	<i>Repeated dose safety</i>					Data AMPACT1	Q2 2017
	<i>Repeated dose safety</i>					Data AMPACT2	Q2 2017
<b>AM-111</b> Brimapitide/ D-JNKI-1	<i>ASNHL (sudden deafness)</i>					Data HEALOS	Q3 2017
	<i>ASNHL (sudden deafness)</i>					Data ASSENT	2H 2018
<b>AM-125</b> Betahistine	<i>Meniere's disease &amp; Vestibular vertigo</i>					Initiate second Phase 1	2H 2017
<b>AM-102</b> Undisclosed	<i>Tinnitus</i>					Select lead compound	Q4 2017
<b>AM-123</b> Undisclosed	<i>Rhinology</i>					Select lead compound	Q4 2017

# AM-125 for Vestibular Disorders

- Develop first intranasal betahistine spray for the treatment of Meniere's disease and vestibular vertigo
  - Delivery route has potential to offer significant efficacy and tolerability benefits
- Bring innovative formula to key markets and broaden availability of betahistine, including in US where compound is not approved<sup>1</sup>
- Oral betahistine is a widely-used medication for treating Meniere's disease and vestibular vertigo around the world
  - >130 million patients treated since launch



<sup>1</sup> NDA withdrawn in 1970 after the discovery that efficacy studies contained unsubstantiated information about some patients

# Meniere's Disease & Vestibular Vertigo



- **Meniere's disease:** chronic disorder of the inner ear characterized by episodes of vertigo, tinnitus, hearing loss, and fullness in the ear
  - ~615,000 Americans are currently diagnosed with Meniere's disease<sup>1</sup>
- **Vestibular vertigo:** symptoms resulting from dysfunction within the body's system of balance, including the misperception of movement or dizziness
  - ~35% of US adults over 40 years old (69 million Americans) have experienced some form of vestibular dysfunction<sup>2</sup>
  - In the US, there are almost 4 million visits per year to the ER for problems of dizziness or vertigo<sup>3</sup>

Source: <sup>1</sup> [www.nidcd.nih.gov/health/Menieres-disease](http://www.nidcd.nih.gov/health/Menieres-disease)

<sup>2</sup> Agrawal Y, et al. *Arch Intern Med.* 2009;169(10):938-944.

<sup>3</sup> Saber Tehrani AS, et al. *Acad Emerg Med.* 2013;20(7):689-96.



## AM-125 Development Opportunity

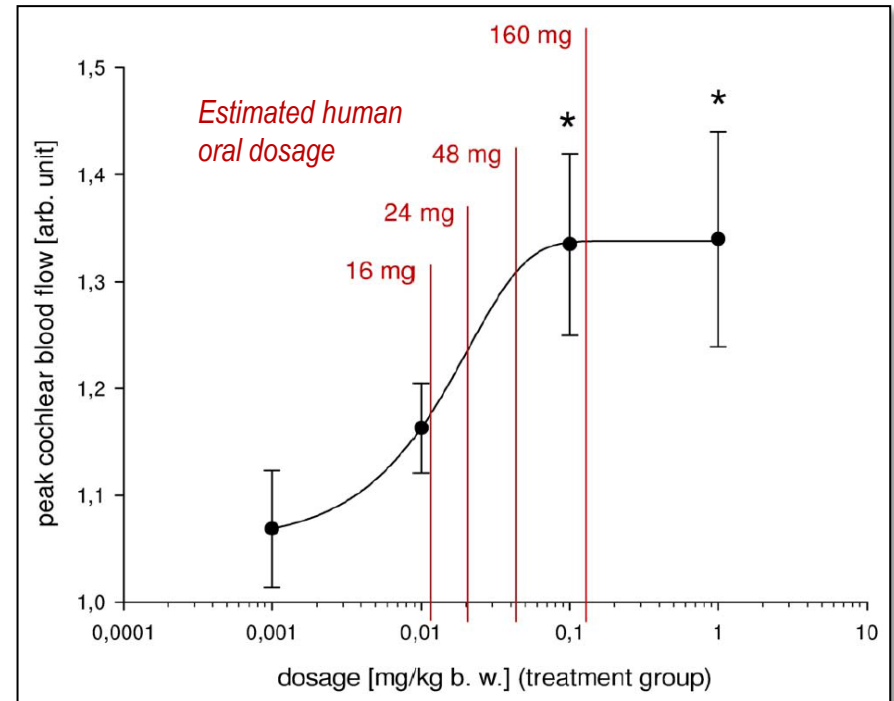
# Betahistine: Widely-Used Medication ex-US

- Betahistine is a structural analog of histamine that has been shown to:
  - Increase cochlear, vestibular and cerebral blood flow
  - Facilitate vestibular compensation
  - Inhibit neuronal firing in the vestibular nuclei
- Outside of the US, approved and prescribed for:
  - Meniere's disease
  - Vestibular vertigo



# Dose- and Time-Dependent Effects

- Pre-clinical and clinical studies show dose- and time-dependent efficacy
- Dose-dependent increase in vestibular and cochlear blood flow<sup>1,2</sup>
- Patients with severe Meniere's disease benefited from titration up to 288-480 mg/day<sup>3</sup>
- Clinical utility not fully exploited at current dose levels



Ihler et al., 2012

<sup>1</sup> Dziadziola JK et al. *Otolaryngol Head Neck Surg* 1999;120:400–405.

<sup>2</sup> Ihler F, et al. *PLoS One*. 2012;7(6):e39086.

<sup>3</sup> Lezius F, et al. *Eur Arch Otorhinolaryngol*. 2011;268(8):1237-40.

# First-Pass Effect Is Key Challenge

- Rapidly metabolized into 2-pyridylacetic acid (2-PAA; no known activity)
- Absolute bioavailability of oral betahistine estimated to be ~1% due to very high first-pass metabolism
  - Plasma levels are very low
  - $C_{\max}$  of betahistine after oral intake of 24 mg was  $< 0.5 \text{ ng/mL}$ <sup>1</sup>
- Limited ability to overcome first-pass effect with higher doses

<sup>1</sup> Chen XY, et al. *Xenobiotica*. 2003;33(12):1261-71.

# Improve Utility with Innovative Delivery

- Build on work performed by Otifex Therapeutics
  - Intranasal betahistine for Eustachian tube dysfunction
  - Efficacy trial did not show satisfactory results in this indication
- Dose-escalating, double-blind, placebo-controlled Phase 1 trial
  - Good tolerance
  - Plasma concentration significantly higher than with oral administration, increasing with dose
- Auris Medical acquiring preclinical and clinical assets and intellectual property
- Development program to be discussed with FDA and EMA
  - To initiate Phase 1 trial with repeated dosing over extended period of time

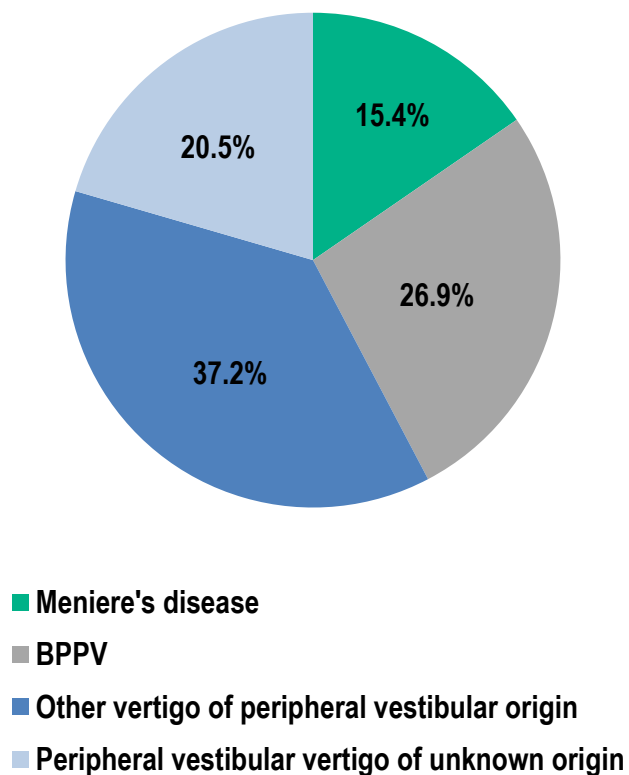


## AM-125 Market Opportunity

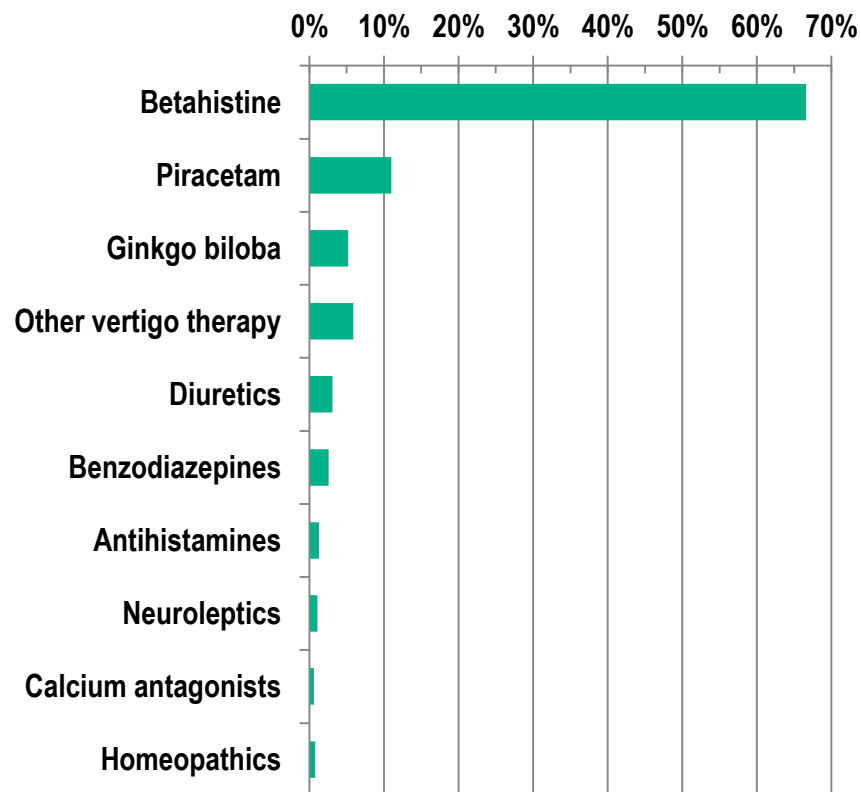
# Role of Betahistine in Vertigo Treatment

4,294 patients with vertigo were enrolled in the REVERT registry from 618 international centers across 13 countries over 28 months.<sup>1</sup>

## Vertigo Diagnosis



## Treatment Started



<sup>1</sup> Agus S, et al. *Front Neurol.* 2013;4:48.

# Estimated Global Market Opportunity >\$1B

- Current worldwide annual betahistine sales ~\$450 million (at manufacturer prices)
- Plan to launch AM-125 in United States and Europe
  - Estimate 2022 product launch, subject to regulatory feedback
- Market in rest of world through partnership agreements
- Global market opportunity for AM-125 estimated at >\$1 billion
- Builds on highly synergistic product portfolio of Keyzilen® and AM-111
  - Specialist salesforce reach to focus on ENT physicians / neurotologists

- Acquisition of intangible assets
  - Upfront payment and future development milestone payment (<\$500,000 in total)
- Moderate spending levels expected for AM-125 in 2017 and 2018
- 2017 operating expenses including AM-125 expected between CHF 28-32 million
- Cash at YE 2016 totaled more than CHF 30 million
- Maintain cash runway until Fall 2017

- **AM-125 intranasal delivery avoids first-pass effect with oral betahistine**
  - Expect rapid onset and improved efficacy
  - Expect better tolerability
- **Global development program, including United States**
  - Estimate 2022 product launch
  - Global market opportunity estimated at over \$1 billion
- **Third clinical-stage project**
  - Expanding beyond cochlear into vestibular therapies
  - Adds to AM-111 (sudden hearing loss) and Keyzilen® (acute inner ear tinnitus)
    - Phase 3, first-in-class therapies for major unmet needs



# Upcoming Milestones

**Second Quarter 2017**

- Complete enrollment of HEALOS

**Second Quarter 2017**

- Announce AMPACT open label study results

**Third Quarter 2017**

- Announce HEALOS top-line results

**Second Half 2017**

- Initiate Phase 1 trial with AM-125

**Early 2018**

- Announce TACTT3 top-line results



## Q&A



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Cochlear therapies