Auris Medical News Release

Published analysis confirms positive results from Auris Medical's phase IIb study with AM-101 in treatment of acute inner ear tinnitus

Basel, Switzerland, March 31, 2014 – Auris Medical announced today that results from its phase IIb clinical trial with AM-101 in the treatment of acute inner ear tinnitus have been published in the specialist journal Otology & Neurotology[1]. The trial demonstrated that AM-101 was well tolerated and safe and established proof of concept in the treatment of tinnitus arising from traumatic acoustic injury to the cochlea and otitis media. In particular the trial showed persistent, clinically relevant and statistically significant improvement in several patient-reported tinnitus measures.

"We are very pleased to see the design and the detailed outcomes of our phase IIb trial with AM-101 published in a leading peer reviewed publication", commented Thomas Meyer, Auris Medical's founder and CEO. He added: "The trial provided us with a wealth of data and insights into the sensitivity and robustness of various clinical endpoints and the natural history of tinnitus in the acute stage. We incorporated these findings in the design of our recently started phase III trials, which will be another great step forward towards the development of the first specific therapeutic for tinnitus."

The double-blind, randomized, placebo-controlled, parallel-dose phase IIb trial with AM-101 was conducted at 28 study sites in Germany, Belgium, Poland and the Netherlands. A total of 248 patients suffering from persistent acute inner ear tinnitus were randomized to receive three i.t. injections of either AM-101 at 0.27 or 0.81 mg/mL or placebo over three consecutive days. Their tinnitus was triggered by acute acoustic trauma, sudden deafness (idiopathic sudden sensorineural hearing loss, ISSNHL) or otitis media and no older than three months. Trial participants were monitored over 90 days.

The trial demonstrated a dose-dependent and persistent improvement in several patient reported outcomes (PROs). Patients suffering from unilateral tinnitus following acute acoustic trauma or otitis media who received AM-101 0.81 mg/mL showed a gradual and statistically significant improvement 90 days post-treatment in tinnitus loudness, annoyance, tinnitus-related sleep difficulties and in overall tinnitus impact (THI-12 questionnaire) compared with placebo. In the analysis of covariance (ANCOVA), p-values were <0.02 for these outcomes. At Day 90, the mean improvement in tinnitus loudness was 48% in the high-dose group, compared to 28% in the low-dose group and 9% in the placebo group. Overall, 64% of patients in the high-dose group rated their tinnitus severity at Day 90 compared with baseline as "much improved" or "very much improved," compared with 44% and 35% of patients in the low-dose and placebo groups, respectively.

Treatment effects of AM-101 were somewhat less pronounced in patients with bilateral rather than unilateral tinnitus since only one ear was treated as a precautionary safety measure. Efficacy outcomes with pa-

[1] Van de Heyning P, Muehlmeier G, Cox T, Lisowska G, Maier H, Morawski K, Meyer T (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.
The article is directly accessible at http://journals.lww.com/otology-neurotology

tients suffering from tinnitus related to ISSNHL were not conclusive for that subgroup overall, owing to an unexpectedly large rate of spontaneous recovery and the heterogeneity in tinnitus origin. Psychoacoustic measures such as the minimum masking level turned out to be insufficiently reliable and did not show results that were consistent with PROs.

Furthermore, AM-101 showed good safety in the phase IIb trial, and the repeated intratympanic injections were well tolerated. Mean hearing thresholds improved slightly in all treatment groups; the frequency of clinically relevant hearing deterioration overall was low and not significantly different between groups. Adverse events were reported by similar proportions of patients across the treatment groups with no apparent clinically relevant differences in frequency, intensity, or relationship to the treatment. Local events accounted for greater than 50% of reported adverse events and related mostly to anticipated transient changes in tinnitus perception and hearing following the injection procedure. In 93% of cases, the eardrum was already fully closed again five days after the last injection.

About acute peripheral tinnitus

Tinnitus, the perception of sound without external acoustic stimulation, is a symptom common to various ear or other diseases. Peripheral (inner ear) tinnitus may be provoked by various injuries to the cochlea, the organ of hearing, such as overexposure to noise or inflammation. It may be short and just transitory; however, it may also become permanent. Tinnitus of less than three months of duration is considered acute, while older tinnitus is considered chronic.

Peripheral tinnitus may be only a slight nuisance, but often it has a serious impact on the ability to sleep, relax, or concentrate, or it may lead to tiredness, irritation, nervousness, despair, frustration, or even depression. As of today, there exists neither a universal standard of care for acute inner ear tinnitus, nor a truly proven, effective treatment method.

About AM-101

AM-101 is a small molecule N-methyl-D-aspartate (NMDA) receptor antagonist formulated in a biocompatible gel for intratympanic injection. Emerging evidence suggests that NMDA receptors in the cochlea play a major role in the occurrence of tinnitus following inner ear excitotoxicity, which is characterized by excessive synaptic release of glutamate, the principal neurotransmitter in the auditory system. Cochlear excitotoxicity may be triggered by, for example, trauma (e.g. exposure to excessive noise), neuroinflammation, disturbances in inner ear blood supply (anoxia/ischemia), or the administration of certain ototoxic drugs. It has been proposed that the upregulation of NMDA receptors induced by cochlear excitotoxicity is responsible for aberrant excitation of auditory nerve fibers, which is perceived as tinnitus.

The development of AM-101 is based on research conducted at the INSERM Institute for Neurosciences of Montpellier, France. The clinical development of AM-101 was initiated by Auris Medical in 2007 and comprises three clinical trials to date. In 2013, Auris Medical reached agreement with the US Food and Drug Administration (FDA) under a Special Protocol Assessment (SPA) for its pivotal TACTT2 study. Patents have been granted in more than 30 countries worldwide so far.

About Auris Medical

Auris Medical is a Swiss biopharmaceutical company dedicated to developing therapeutics that address important unmet medical needs in otolaryngology. The Company is currently focusing on the development

of treatments for acute peripheral tinnitus (AM-101) and for acute inner ear hearing loss (AM-111) by way of intratympanic injection with biocompatible gel formulations. In addition, Auris Medical is pursuing early-stage research and development projects. The Company was founded in 2003 and is headquartered in Basel, Switzerland.

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