Auris Medical News Release

January 27, 2011 – Phase I/II clinical trial with AM-101 showing good safety in treatment of acute inner ear tinnitus

AM-101, Auris Medical’s investigational drug for the treatment for acute inner ear tinnitus, was well tolerated and safe in a phase I/II clinical trial and showed some first indications of therapeutic efficacy, as a recent article in the journal Audiology & Neurotology reports. The publication by the study’s principal investigators presents the design and principal results of the double-blind, randomized, placebo-controlled trial, which was conducted in 2007/08 in Germany.

Study design
The phase I/II study with AM-101 enrolled 24 patients suffering from persisting moderate to severe tinnitus following acute noise trauma or sudden deafness at 4 study centres (3 clinics of the German Bundeswehr and 1 private ENT practice). Their tinnitus had been refractory to a first-line corticoid treatment prior to study inclusion, and was not older than 3 months (i.e. still at an acute stage). Study participants were randomized to receive either AM-101 or placebo (ratio 2:1) in a single dose intratympanic injection. A total of 4 dose concentrations were tested under a dose escalation scheme from 30 to 810 μg/mL. Follow-up visits were performed 7, 30 and 60 days after treatment administration.

The primary objective of the study was to evaluate the safety of AM-101 delivered by intratympanic injection. Secondary objectives were a preliminary evaluation of the potential therapeutic benefit of AM-101 in the treatment of acute inner ear tinnitus as well as the determination of the systemic exposure from local drug administration.

Safety outcomes
Overall, AM-101 was well tolerated by study participants, irrespective of the administered dose. The incidence of adverse events (AEs) was low and similar in the verum and placebo arms. They were considered either unrelated or unlikely related to the treatment. No serious adverse events (SAEs) or AEs leading to withdrawal occurred during the study. AM-101 and its primary metabolite could be found in plasma samples obtained in the first hours following treatment in small amounts only (< 0.3 ng/mL), which confirmed the favourable safety profile of intra-tympanic injection. This minimally invasive procedure allows for a highly site specific treatment with low doses and only minimal systemic exposure.

Efficacy outcomes
The phase I/II study, while too small to allow for formal hypothesis testing, also provided some first indications of AM-101’s efficacy. Both the subjective tinnitus loudness as measured by a 10 point visual analog scale and the minimum masking level (MML) decreased, with the verum group showing larger improvements than the placebo group. The MML decreased continuously in the active treatment arm, with a total reduction of 3.7 dB to a final MML of 5.2 dB at the last visit. In the placebo arm, the mean MML decreased as well, but this was less pronounced, with a total reduction of 1.9 dB to a final MML of 6.6 dB. The median MML dropped from 9.5 dB to 3.0 dB in verum patients, while it fluctuated in the placebo arm around the baseline level to finish 1 dB higher at 7.5 dB. There was also a trend towards improvement in a tinnitus handicap questionnaire (THI-12), however, the magnitude was clearly lower. This discrepancy is likely due to...
the more long-term orientation of the questionnaire and / or the fact, that patients with bilateral tinnitus got only one of their ears treated, and hence one untreated ear influenced the outcome.

**About acute inner ear tinnitus**

Tinnitus, the perception of sound without external acoustic stimulation, is a symptom common to various ear or other diseases. Inner ear tinnitus may be provoked by various injuries to the cochlea, the organ of hearing, such as overexposure to noise or disruptions in its blood supply. 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 tinnitus that is older than one year is considered chronic.

Inner ear 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 contains a small molecule that selectively blocks N-methyl-D-aspartate (NMDA) receptors. 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, exposure to excessive noise, disturbances in inner ear blood supply (anoxia/ischemia), barotrauma, migration of pathogens from the inflamed middle ear into the inner ear, noise/vibration trauma resulting from middle ear surgery, or the administration of certain ototoxic drugs. It has been hypothesized that the upregulation of NMDA receptors induced by cochlear excitotoxicity is responsible for abnormal spontaneous “firing” of auditory nerve fibres, which is perceived as tinnitus.

A large double-blind, randomised, placebo-controlled phase IIb clinical trial with AM-101 is currently under way in Germany, Belgium, Poland and the Netherlands to further evaluate the treatment’s efficacy and safety. Patient enrolment in the study is expected to be completed during the first quarter of 2011.

**About Auris Medical**

Auris Medical is a Swiss biotechnology company developing specific pharmaceutical compounds for the prevention or treatment of inner ear disorders, an area of great unmet medical need. Around the world, many million people are suffering permanently from severe hearing loss and / or tinnitus, still lacking truly effective and safe treatments for their disorders. Auris Medical is currently focusing on the development of treatments for acute inner ear tinnitus (AM-101) and for acute sensorineural hearing loss (AM-111).


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