Phase 1 and 2 Clinical Trials for AC102 Treating SSNHL

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Introduction

- The pathology of Sudden Sensorineural Hearing Loss (SSNHL) includes:
  - Permanent loss of outer hair cells (OHCs, Fig. 1A)
  - Synaptic disconnection of inner hair cells (IHCs) from the auditory nerve (Fig. 1B)
- Currently, SSNHL is mostly treated with corticosteroids which lack reliable efficacy data and therefore remain unapproved by regulatory authorities
- Preclinically, AC102 almost completely reversed noise-induced hearing loss by counteracting apoptotic death of OHCs and reversing synaptic disconnection of IHCs

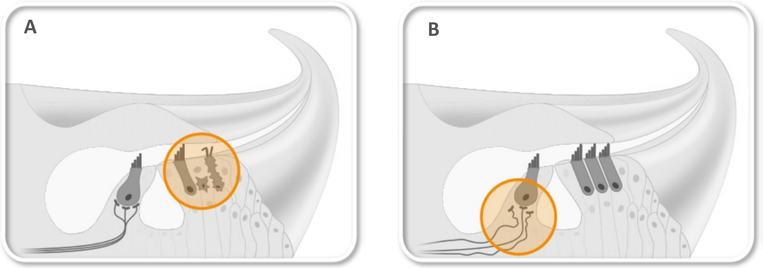

Fig 1: Pathology of SSNHL

Phase 1: Study Design

- In this open-label study, AC102 was compared to placebo in 42 male and female healthy volunteers (aged 18-40 years)
- Subjects received either AC102 in a thermosensitive gel or gel alone via a single intratympanic (IT) injection into one ear in increasing concentrations and volumes
- Endpoints were:
  - Safety and tolerability of AC102, including extensive assessment of audiological and vestibular function
  - Plasma pharmacokinetics of a single-dose of AC102 (IT). Blood samples were collected up to 24 hours after AC102 administration and analyzed using LC-MS

Phase 1: Results

- No Serious Adverse Events (SAEs) were observed
- AC102 and placebo gels were well tolerated
- Treatment Emergent Adverse Events (TEAEs) occurred almost equally in both groups, were mild and often in line with the IT procedure and/or the gel in the middle ear

Main TEAEs Included:

- Otoscopically, small bleedings after IT injection
- The injection hole healed without consequences by day 4
- No trends were noted for clinical laboratory evaluations, vital signs, and ECGs
- No clinically significant otoscopy or tympanometry findings at EOS
- AC102 plasma levels were dose-dependent and decreased over 24h

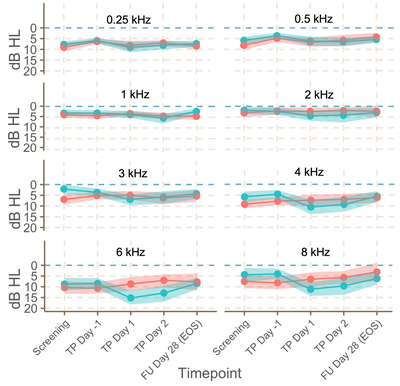

Fig 2: Average air-conduction thresholds

- A temporary (usually < 4 days) and mild, volume dependent rise in hearing threshold mainly at higher frequencies occurred in both groups, indicating the presence of gel in the middle ear
- Functional measurements confirmed no significant changes in OHC or auditory neural pathway function

Phase 2 Clinical Study in ISSNHL

- AC102 is currently being evaluated in a Phase 2 trial
- In this randomized and blinded two-arm study, the efficacy, safety, and tolerability of AC102 will be compared to the standard oral corticosteroid medication. This ensures that all patients are treated
- Approx. 200 patients with moderately-severe to profound idiopathic SSNHL will be enrolled
- Key audiological endpoints include hearing thresholds (PTA) and word recognition which are both crucial for understanding of speech
- Data Safety Monitoring Board (DSMB) reported no safety concerns after evaluation of the first 20 patients
- Up to 50 European sites in Austria, Bulgaria, Czech Republic, Germany, Netherlands, Poland and Serbia

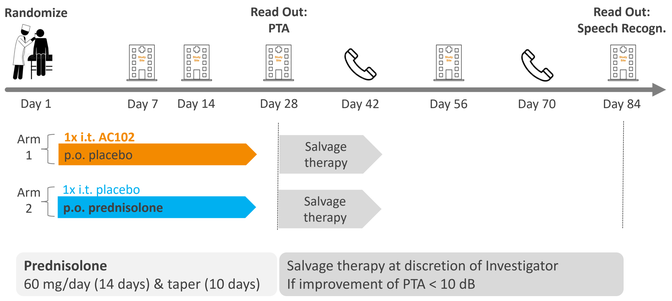

Fig 4: European Study Sites and Potential US Expansion

Conclusions

- Preclinical models indicate AC102 is a promising candidate for SSNHL treatment
- Phase 1 trial demonstrated IT administered AC102 was well tolerated in healthy volunteers. DSMB confirmed results in SSNHL patients
- A Phase 2 trial is underway to examine the efficacy of AC102 in patients with ISSNHL
- AudioCure plans to expand AC102 Phase 2 study sites to the USA

Please find more information on the AC102-201 study here

www.audiocure.com www.clinicaltrials.gov/study/NCT05776459 trials@audiocure.com