



Our Technology

A disease modifying novel molecule

AudioCure Pharma develops novel pharmaceutical therapies for the prevention and treatment of a range of hearing impairments with high, unmet medical need. Our lead candidate is a novel molecule named AC102.

The primary focus of AudioCure's development program for AC102 is acute hearing loss and acute tinnitus. Currently there are no approved drug treatments available for these disorders. Our front-runner molecule has undergone comprehensive preclinical research which demonstrates that it acts upon the sensory cells and neurons that are central to the hearing process. As no other drug has shown any such action, AC102 has the potential to become the first breakthrough causative therapy (i.e. treatment aimed at eliminating the cause) for acute hearing loss and acute tinnitus. By treating these conditions as soon as possible after onset, it is our vision to prevent the development of long-term, chronic hearing impairments.

How AC102 works

Noise-induced hearing loss is caused when the sound waves of a loud noise damages the sensitive structures within the inner ear; namely the inner and outer hair cells, which are critical for the hearing process. Preclinical studies have demonstrated the unique potential of AC102 to tackle the damage to these key players.

Mechanisms of Action

- **AC102 protects and restores cells of the inner ear**

Outer hair cells within the cochlea sharpen and amplify sound pressure waves from the outer ear. This signal is then received by the inner hair cells which send it on to the brain via the auditory nerve. Therefore, the inner and outer hair cells and the neurons of the auditory nerve are critical to the hearing process. Following noise-induced hearing loss, AC102 acts upon all three of these cell types to either protect them from further damage or restore already damaged cells.

- **AC102 prevents outer hair cell apoptotic cell death**

Outer hair cells act as amplifiers in the hearing process. Damage by an acoustic trauma can lead to their programmed cell death, a process known as apoptosis. Once dead, these cells cannot be replaced and their amplification role is lost. Our studies demonstrate that AC102 significantly reduces apoptosis of outer hair cells following noise-induced hearing loss.



- **AC102 enhances protection and repair processes**

Following trauma, it is very important to both repair damaged cells and protect them from further damage. AC102 enhances factors that are central to these protection and repair processes, giving the cells of the auditory system a greater chance of survival after injury. AC102 reduces inflammation

- **AC102 reduces inflammation**

Acoustic trauma leads to an increase in pro-inflammatory factors in the inner ear which, in turn, results in inflammation. AC102 increases the release of anti-inflammatory factors that can help to counteract these damaging effects.

In summary, AC102 acts as an antagonist of the multitude of pathological processes leading to hearing loss.

Application

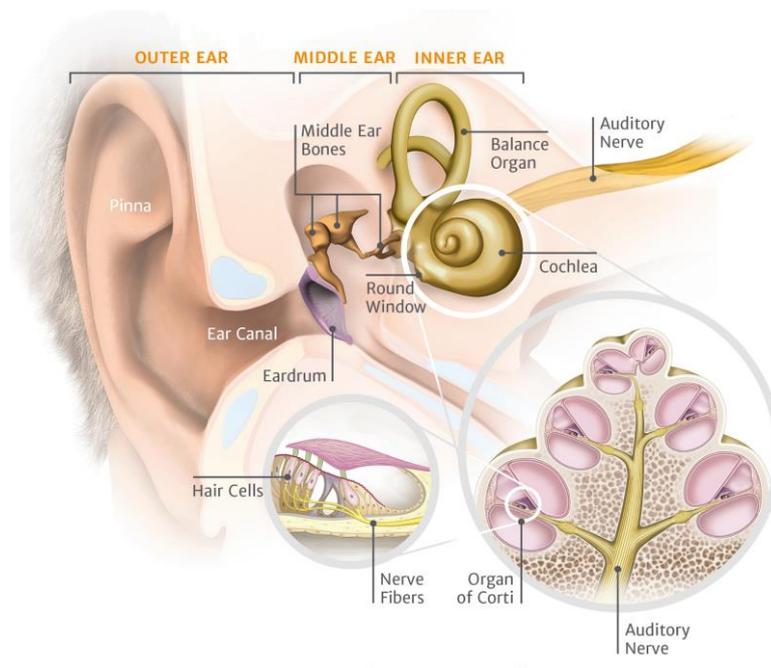
A specialized formulation and application provide targeted drug delivery

The inner ear is very well protected. Not only is it hidden away in the temporal bone but it is also separated from the systemic (blood) system by the blood labyrinth barrier. This barrier prevents systemically taken drugs (e.g. orally) from reaching the inner ear in dose levels sufficient to have a therapeutic effect. Therefore, to reach therapeutic levels in the inner ear, a systemic drug would have to be given at a very high dose, possibly leading to adverse side effects.

To avoid this, drugs can be delivered topically to the middle ear via intratympanic administration. This is a routine outpatient procedure for ENT specialists during which the drug is given into the middle onto the inner ear. From there, the drug can then diffuse across the so-called round window membrane into the inner ear.

Benefits of AudioCure's gel formulation:

- No requirement for repeated applications
- Drug is delivered directly to the round window membrane, quickly arriving at the targeted cells
- Minimal systemic exposure



Schematic of the ear highlighting the principal structures involved in hearing including magnifications of the cochlea and the hair cells within the Organ of Corti. (adapted from an image courtesy of MED-EL)

For further information, please visit www.audiocure.de

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