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SUPPLEMENTARY SECTION

Title: OTO-201 for the Treatment of Acute Otitis Externa: Results from a Phase 3 Randomized Clinical Study

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INCLUSION CRITERIA

Subjects meeting all of the following criteria may be eligible for the study:

1. Subject is a male or female age 6 months or older
2. Subject has a clinical diagnosis of unilateral or bilateral AOE as defined by the 2014 AAO-HNS Clinical Practice Guideline: Acute Otitis Externa (Rosenfeld et al. 2014)
3. Subjects has a combined numerical score of ≥ 4 in at least 1 affected ear at the screening visit for tenderness, erythema and edema
    a. For subjects with bilateral AOE, only one ear must have met this criterion (e.g., subject may be enrolled with a numerical score of 4 in one ear and a numerical score of 1 in the contralateral ear; both ears will be assessed, cultured and treated with OTO-201 or Sham-Control)
4. Subject or subject's caregiver is willing to comply with the protocol and attend all study visits
5. Subject or subject's caregiver is able to provide written informed consent, including agreement to country specific privacy language compliant with the Health Insurance Portability and Accountability Act (HIPAA) or Personal Information Protection and Electronic Documents Act (PIPEDA), before the initiation of any study-related procedures
6. Female subjects of childbearing potential (i.e., not surgically sterile and/or not post-menopausal (≥12 months since last menstrual period and 45 years of age or older)) must have a negative pregnancy test before randomization. Women of childbearing potential who are not abstinent from sex with male partners may be entered into the study if they are using and willing to continue to use adequate contraceptive precautions for the duration of the study (e.g., oral contraceptives, contraceptive implant or injection, intrauterine device, condom and spermicide, or diaphragm and spermicide).
7. Subject of appropriate age is able to provide assent for participation in the study

EXCLUSION CRITERIA

Subjects meeting any of the following criteria are not eligible for participation:

1. Subject has known tympanic membrane perforation in either ear
2. Subject has severe otitis externa (OE) that either includes auricular cellulitis or chondritis or prevents administration of OTO-201
3. Subject has chronic OE, defined as either having 1 or more previous episodes of OE within the last 3 months or more than 3 previous episodes of OE within the last year
4. Subject has eczematoid OE
5. Subject has fungal OE, based on clinical signs

6. Subject has a history of known immunodeficiency disease
7. Subject has diabetes mellitus
8. Presence of any infection requiring systemic antimicrobial or antifungal agents
9. Use of antimicrobial ear drops to the affected ear within 1 week of the screening visit; use of disinfectants (e.g. alcohol, peroxide) is allowed but must be discontinued at screening and while on study
10. Use of systemic antimicrobial or antifungal agents within 1 week of the screening visit and within 2 weeks of the screening visits for Zithromax®
11. Subject has a history of allergy to ciprofloxacin or any of the components of OTO-201
12. Subject has any other clinically significant illness or medical condition that, in the opinion of either the investigator or medical monitor, would prohibit the subject from participating in the study
13. Subject has used an investigational drug or device in the month prior to screening
14. Subject is pregnant or lactating
15. Subject resides in the same household as another participating subject

In addition to these exclusion criteria, patients with baseline cultures growing group A streptococci will be excluded from the efficacy analysis and should be treated with standard of care (SOC), including systemic therapy as needed. Subjects will remain in the study and followed for safety.