CLAIMS

1. Use of CHIR99021 or a pharmaceutically acceptable salt thereof and valproic acid (VPA) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating sensorineural hearing loss in a human patient, wherein:

    (a) the patient has a standard word recognition score of 90% or less prior to the treatment;
    (b) the sensorineural hearing loss is mild, moderate, moderately severe, or severe sensorineural hearing loss;
    (c) the average of the patient's hearing thresholds across 0.5kHz, 1kHz, 2kHz, and 4kHz is
        (i) at least 25 dB HL and no more than 40 dB HL when measured by pure tone audiometry prior to the treatment, for example greater than 25 dB HL and no more than 40 dB HL when measured by pure tone audiometry prior to the treatment,
        (ii) at least 40 dB HL and no more than 70 dB HL when measured by pure tone audiometry prior to the treatment, for example greater than 40 dB HL and no more than 70 dB HL when measured by pure tone audiometry prior to the treatment, or
        (iii) at least 70 dB HL and no more than 90 dB HL when measured by pure tone audiometry prior to the treatment, for example greater than 70 dB HL and no more than 90 dB HL when measured by pure tone audiometry prior to the treatment;
    (d) the patient has a words-in-noise score of 50% or less prior to the treatment; and/or
    (e) the patient has an audiogram with hearing thresholds in the following ranges when measured by pure tone audiometry:
        16kHz – 40 dB HL to 70 dB HL; and/or
        14kHz – 40 dB HL to 85 dB HL; and/or
        12kHz – 40 dB HL to 95 dB HL; and/or
        10kHz – 40 dB HL to 95 dB HL.

2. The use of claim 1, wherein the average of the patient's hearing thresholds across 0.5kHz, 1kHz, 2kHz, and 4kHz is at least 40 dB HL and no more than 55 dB HL when measured by pure tone audiometry prior to the treatment, for example greater than 40 dB HL and no more than 55 dB HL when measured by pure tone audiometry prior to the treatment.

3. The use of claim 1, wherein the average of the patient's hearing thresholds across 0.5kHz, 1kHz, 2kHz, and 4kHz is at least 55 dB HL and no more than 70 dB HL when measured by pure tone audiometry prior to the treatment, for example greater than 55 dB HL and no more than 70 dB HL when measured by pure tone audiometry prior to the treatment.

4. The use of any of claims 1-3, wherein the patient has a standard word recognition score of between 10% and 85%, 10% and 70%, 20% and 60%, 85% or less, or 60% or less, prior to the treatment.

5. The use of any of claims 1-4, wherein said treatment provides an improved standard word recognition score for the patient, wherein said improvement, if tested, would be at least 10%, wherein said percentage improvement is calculated using the following formula:

$$100 \times \left(\frac{patient's\ word\ recognition\ score\ after\ treatment}{patient's\ word\ recognition\ score\ prior\ to\ treatment} - 1\right).$$

6. The use of any of claims 1-5, wherein said treatment provides an improved words-in-noise score for the patient, wherein said improvement, if tested, would be at least 10%, wherein said percentage improvement is calculated using the following formula:

$$100 \times \left(\frac{patient's\ words\ in\ noise\ score\ after\ treatment}{patient's\ words\ in\ noise\ score\ prior\ to\ treatment} - 1\right).$$

7. The use of any of claims 1-6, wherein said treatment provides an improved hearing threshold at 8kHz, wherein said improvement, if tested, would be at least 5 dB relative to the patient's hearing threshold at 8kHz prior to the treatment, wherein said hearing threshold is measured by pure tone audiometry.

8. Use of CHIR99021 or a pharmaceutically acceptable salt thereof and valproic acid (VPA) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating sensorineural hearing loss in a human patient, wherein said treatment provides:

   (a) an improved standard word recognition score for the patient, wherein said improvement, if tested, would be at least 10%, wherein said percentage improvement is calculated using the following formula:

$$100 \times \left(\frac{patient's\ word\ recognition\ score\ after\ treatment}{patie\quad's\ word\ recognition\ score\ prior\ to\ treatment} - 1\right);$$

   (b) an improved words-in-noise score for the patient, wherein said improvement, if tested, would be at least 10%, wherein said percentage improvement is calculated using the following formula:

$$100 \times \left(\frac{patient's\ words\ in\ noise\ score\ after\ treatment}{pat\quad's\ words\ in\ noise\ score\ prior\ to\ treatment} - 1\right);\ \text{and/or}$$

   (c) an improved hearing threshold at 8kHz, wherein said improvement, if tested, would be at least 5 dB relative to the patient's hearing threshold at 8kHz prior to the treatment, wherein said hearing threshold is measured by pure tone audiometry.

9. The use of any of claims 1-8, wherein an improvement in hearing is provided within 90 days.

10. The use of any of claims 1-9, wherein an improvement in hearing is provided by a single administration.

11. The use of any of claims 1-10, wherein said compounds are to be administered to the middle ear, wherein optionally administration to the middle ear is by intratympanic injection.

12. The use of any of claims 1-11, wherein the pharmaceutically acceptable salt of valproic

acid is sodium valproate.

13. The use of any of claims 1-12, wherein the CHIR99021 and the VPA are formulated as a single composition, wherein optionally the composition comprises a poloxamer, for example Poloxamer 407.

14. The use of any of claims 1-13, wherein the sensorineural hearing loss is sudden sensorineural hearing loss, noise-induced hearing loss, age-related hearing loss, or drug-induced hearing loss.

15. The use of any of claims 1-14, wherein the CHIR99021 is at a concentration of 3.14 mg/ml and VPA is sodium valproate at a concentration of 88.6 mg/ml.

16. The use of any of claims 1-15, wherein the CHIR99021 or a pharmaceutically acceptable salt thereof and valproic acid (VPA) or a pharmaceutically acceptable salt thereof is administered at a volume of about 200 μL.

17. The use of any of claims 1-16, wherein an improvement in audibility and/or intelligibility function is maintained until at least 365 days.

18. The use of any of claims 1-17, wherein the treatment provides for treatment of tinnitus.