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Phase I/II study to evaluate the safety and biological activity of HORA-PDE6B in patients with *PDE6B* retinitis pigmentosa (MIM#613801)

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Abstract

Purpose : Inherited retinal dystrophies are the major causes of incurable blindness in the Western world, a heterogeneous group of pathologies ultimately leading to photoreceptor degeneration and death. Among the autosomal recessive retinitis pigmentosa (RP), the *PDE6B* gene, encoding the β subunit of rod phosphodiesterase accounts for about 4-5% of these conditons[c] and currently have no effective treatment. HORA.PDE6B (AAV2/5.hPDE6B) is investigational gene replacement therapy product which aims to deliver the non-mutated gene to the target retinal cells leading to synthetise the functional protein. By restoring normal cell function, the treatment goal is preserve or improve visual function and delay or halt disease progression in patients. The purpose of this study is to evaluate safety and the biological activity of HORA.PDE6B in patients with RP harbouring mutations in the *PDE6B* gene. We report the first results of this ongoing study.

Methods : This first-in-human study (NCT03328130) is a 3-year, prospective, interventional, single centre, open-label, dose-ranging study evaluating safety and biological activity of a unilateral subretinal administration of HORA-PDE6B in *PDE6B* RP patients. After a screening visit, the patients undergo 9 visits in the first year and then an annual assessment. The visual function evaluations include distance visual acuity, reading speed, colour vision test, pupillometry, static, kinetic and bicolour visual field, electroretinogram, microperimetry, dark adaptation and a mobility tests and the retinal structural evaluations include slit lamp examination, fundoscopy, colour fundus photography, indocyanin green and fluorescein angiographies, autofluorescence and spectral domain optical coherence tomography. Additionally, the NEI-VFQ-25 will be administered and functional magnetic resonance imaging will be performed.

Results : Since the first patient enrolled on November 06, 2017, three additional patients out of twelve patients have been enrolled and treated in Ophthalmology Clinic, University Hospital of Nantes – France. We will share the demographic and safety data of the three first patients enrolled in this Phase I/II study.

Conclusions : The design and flowchart of this first Phase I/II gene therapy study for *PDE6B* mutation related retinitis pigmentosa and the very preliminary data of the first patients enrolled will be presented.

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