

MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG**Novartis announces landmark EU approval for one-time gene therapy Luxturna® to restore vision in people with rare inherited retinal disease**

- *Luxturna* (voretigene neparvovec) is the first gene therapy to treat an inherited retinal disease, indicated for children and adults with vision loss caused by mutations in both copies of the RPE65 gene and sufficient viable retinal cells¹*
- *Nearly 60% of patients have severe forms of the disease, with severe visual impairment occurring shortly after birth²*
- *As a one-time treatment, Luxturna restores vision and improves sight in children and adults with a sustained effect and favorable safety profile^{3,4}*

Basel, November 23, 2018 – Novartis announced today that the European Commission (EC) approved Luxturna, a one-time gene therapy for the treatment of patients with vision loss due to a genetic mutation in both copies of the *RPE65* gene and who have enough viable retinal cells. The authorization is valid in all 28 member states of the EU, as well as Iceland, Liechtenstein and Norway. Luxturna was developed and is commercialized in the US by Spark Therapeutics.

People born with mutations in both copies of the *RPE65* gene can experience profound sight loss from an early age, with the majority of patients progressing to total blindness³. Research shows that vision impairment and blindness in children frequently cause social isolation, emotional distress, loss of independence, or hazards such as falls and injuries⁵. The working copy of the *RPE65* gene provided by Luxturna can restore vision and improve sight in children and adults with sufficient viable retinal cells³.

“Today’s approval is momentous for patients given that there have been no pharmacological treatment options to date to treat this form of LCA,” said Christina Fasser, president of Retina International, an umbrella organization of more than 43 patient organizations worldwide promoting research to find treatments for inherited retinal degenerative diseases. “Access to this treatment has the potential to reduce the substantial physical, emotional and financial burden this disease has on patients and their families.”

“As a clinician who has worked for over 20 years with patients with inherited retinal disease and their families, I’ve seen firsthand the profound impact blindness can have on quality of life. It’s exciting to practice medicine at a time when we can offer options to children and adults facing blindness,” said Dr Bart Leroy, ophthalmologist and clinical geneticist, Professor and Head, Department of Ophthalmology at Ghent University Hospital, Ghent, Belgium and Director of Retinal Degenerations Clinic at Children’s Hospital of Philadelphia, Philadelphia, PA. “After more than 20 years of gene therapy research, there is finally a promising future ahead for the treatment of rare genetic eye disorders.”

“EU approval of the one-time gene therapy Luxturna marks a milestone in reimagining medicine and can bring real value to patients, their families and society as a whole,” said Paul Hudson, CEO, Novartis Pharmaceuticals. “Novartis is committed to working with patients, caregivers, health systems and physicians to establish access to this gene therapy for RPE65 patients, as we believe it can help restore sight and improve vision in children and adults who currently have no treatment options.”

The EC decision is based on a positive CHMP opinion that looked at data from a Phase 1 clinical trial, its follow-up trial, and the first randomized, controlled Phase 3 gene therapy trial for an inherited disease³. In the Phase 3 clinical trial vision improvement was recorded as early as 30 days following treatment³. At 1 year, compared to the control group, patients treated with voretigene neparvovec improved by 1.6 light levels on the binocular multi-luminance mobility test (MLMT), the trial’s novel, patient-centric, primary endpoint³. Vision improved by one or more light levels for 90% of patients treated with voretigene neparvovec, and 65% were able to successfully navigate the MLMT at the lowest light level of 1 lux at 1 year³.

Decisions from national reimbursement bodies on Luxturna for patients with vision loss due to a genetic mutation in both copies of the *RPE65* gene are expected in 2019 and 2020. Novartis is working closely with all stakeholders to help ensure that eligible patients can start benefitting from this treatment as quickly as possible once reimbursement decisions are available in 2019 and 2020. A range of resources and innovative reimbursement and access approaches are also being explored in order to provide as much support as possible to both patients and healthcare professionals.

About *RPE65* mutation-associated inherited retinal disease

Inherited retinal diseases are a group of rare blinding conditions caused by more than 250 different genes⁶, often disproportionately affecting children and young adults³. Mutations in both copies of the *RPE65* gene affect approximately 1 in 200,000 people⁷.

Mutations in both copies of the *RPE65* gene can lead to blindness. Early in the disease patients can suffer from night blindness (nyctalopia), loss of light sensitivity, loss of peripheral vision, loss of sharpness or clarity of vision, impaired dark adaptation and repetitive uncontrolled movements of the eye (nystagmus)⁸. Patients with mutations in both copies of the *RPE65* gene may be diagnosed, for instance, with subtypes of either Leber congenital amaurosis or retinitis pigmentosa⁹. A genetic test is needed to confirm that vision loss is caused by mutations in the *RPE65* gene³.

About the multi-luminance mobility test (MLMT)

The MLMT measures changes in patient relevant functional vision by asking patients to navigate a course accurately and at a reasonable pace at seven different levels of illumination, ranging from 400 lux (corresponding to a brightly lit office) to one lux (corresponding to a moonless summer night)³.

About Luxturna’s mechanism of action

Luxturna is the first EU-approved treatment for this disease and is designed to provide a working copy of the *RPE65* gene to act in place of the mutated *RPE65* gene³.

About the Novartis and Spark Therapeutics licensing and supply agreement

In January 2018, Spark Therapeutics entered into a licensing and supply agreement with Novartis covering development, registration and commercialization rights to Luxturna in markets outside the US. Upon the transfer of the marketing authorization from Spark Therapeutics to Novartis, Novartis can commercialize Luxturna in the EU/EEA. Novartis already has exclusive rights to pursue development, registration and commercialization in all other countries outside the US, and Spark Therapeutics will supply the gene therapy to Novartis.

About Novartis in ophthalmology

For more than 70 years, patients, caregivers and healthcare providers worldwide have looked to Novartis for state-of-the-art treatments in eye diseases. We continue to invest in science as well as in strategic alliances to help ensure patients have access to screening, diagnosis, and our eye medicines. Our commitment to vision extends globally across ages, from premature infants to seniors, from rare diseases to those affecting millions, from eye drops to gene therapies. Our aspiration: reimagining eye care to help *everyone* see possibilities.

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About Novartis

Novartis is reimagining medicine to improve and extend people’s lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world’s top companies investing in research and development. Novartis products reach nearly 1 billion people globally and we are finding innovative ways to expand access to our latest treatments. About 125 000 people of more than 140 nationalities work at Novartis around the world. Find out more at www.novartis.com.

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*Luxturna is a trademark of Spark Therapeutics, Inc. and is registered in the United States and in the EU

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