Novartis announces positive CHMP opinion for one-time gene therapy Luxturna® to treat children and adults with rare inherited retinal disease

- If approved in expected timeframe, Luxturna® (voretigene neparvovec) will be first and only gene therapy available in EU to treat a rare inherited retinal disease
- Children and adults living with inherited retinal disease caused by RPE65 gene mutations nearly all progress to complete blindness
- 93% of patients treated with Luxturna in the Phase 3 clinical trial had improved vision at 1 year

Basel, September 21, 2018 – Novartis today announced that the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion for the approval of voretigene neparvovec, 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. Luxturna was developed and is marketed in the US by Spark Therapeutics. If approved, voretigene neparvovec will be commercialized by Novartis in markets outside the U.S.

Inherited retinal diseases are a group of rare conditions that can lead to total blindness, often disproportionally affecting children and young adults. 50% of people with mutations in both copies of the RPE65 gene will be legally blind by the time they’re 16 years old. Voretigene neparvovec provides a working copy of the RPE65 gene to act in place of the mutated RPE65 gene. This working gene has the potential to restore vision and improve sight. Outside of the US, there are currently no approved pharmacologic treatment options for vision loss caused by RPE65 mutations.

“Inherited retinal diseases are a heterogenous group of degenerative conditions that represent the major cause of blindness in childhood and active working life. This opinion represents a hopeful milestone for current and future patients who may ultimately benefit from gene therapy,” 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.

“Today’s positive CHMP opinion represents a significant step in our journey toward advancing potentially life-changing cell and gene therapies in ophthalmology,” said Paul Hudson, CEO, Novartis Pharmaceuticals. “We look forward to working with Spark Therapeutics and the EMA to establish access and reimagine care for people in the EU who face the threat of total blindness from this inherited retinal disease.”

The positive CHMP opinion is based on data from a Phase 1 clinical trial, its follow-up trial, and a Phase 3 trial that together enrolled 43 patients with inherited retinal disease caused by...
mutations in both copies of the RPE65 gene\(^1\). The Phase 3 trial was the first randomized, controlled Phase 3 gene therapy trial for an inherited disease\(^1\).

A marketing authorization decision from the European Commission is anticipated within approximately two months of the positive CHMP opinion. If approved, the authorization will be valid in all 28 member states of the EU, as well as Iceland, Liechtenstein and Norway.

**About RPE65 mutation-associated inherited retinal disease**

Inherited retinal diseases are a group of rare blinding conditions caused by more than 220 different genes, often disproportionally affecting children and young adults\(^1\). Mutations in both copies of the RPE65 gene affect approximately 1 in 200,000 people\(^3\).

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)\(^4\). Patients with mutations in both copies of the RPE65 gene may be diagnosed, for instance, with subtypes of either Leber congenital amaurosis or retinitis pigmentosa\(^5\).

**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. Commercialization rights in the EU/EEA will be transferred to Novartis upon successful completion of EU registration and issuance of marketing authorization. Novartis already has exclusive rights to pursue development, registration and commercialization in all other countries outside the US, and Spark Therapeutics would 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.

**Disclaimer**

This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “potential,” “can,” “will,” “plan,” “expect,” “anticipate,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; our ability to
obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political and economic conditions; safety, quality or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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.

Novartis is on Twitter. Sign up to follow @Novartis at http://twitter.com/novartis
For Novartis multimedia content, please visit www.novartis.com/news/media-library
For questions about the site or required registration, please contact media.relations@novartis.com

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

References

Novartis Media Relations
Central media line: +41 61 324 2200
E-mail: media.relations@novartis.com

Eric Althoff
Novartis Global Media Relations
+41 61 324 7999 (direct)
+41 79 593 4202 (mobile)
eric.althoff@novartis.com

Amy Wolf
Global Head, Ophthalmology Communications
+41 61 696 5894 (direct)
+41 79 576 0723 (mobile)
amy.wolf@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central
Samir Shah +41 61 324 7944
Pierre-Michel Bringer +41 61 324 1065
Thomas Hungerbuehler +41 61 324 8425
Isabella Zinck +41 61 324 7188

North America
Richard Pulik +1 212 830 2448
Cory Twining +1 212 830 2417