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Novartis to file for new Lucentis® (ranibizumab) indication in retinopathy of prematurity (ROP), a rare disease in premature infants that often leads to blindness

- *In the Phase III RAINBOW study, despite marginally missing statistical significance for the primary endpoint of demonstrating superiority of Lucentis® to laser surgery, Lucentis was shown to be an efficacious, safe and well-tolerated treatment for infants with ROP¹*
- *Laser surgery, the current standard of care for ROP in infants, destroys diseased retinal tissue responsible for elevated vascular endothelial growth factor (VEGF) whereas Lucentis is an anti-VEGF that directly targets and reduces VEGF²*
- *With 80% of patients achieving treatment success with 0.2mg Lucentis versus 66% with laser, these data are clinically relevant¹*
- *Novartis plans to file ex-US for a new indication in ROP to bring transformative treatment to premature infants facing severe vision loss - the first anti-VEGF product to seek an ROP indication*

Basel, September 22, 2018 – Novartis today announced results from a Phase III study of Lucentis® (ranibizumab) versus laser surgery (the current standard of care) at the 18th Congress of the European Society of Retina Specialists (EURETINA) in premature infants with retinopathy of prematurity (ROP), a rare disease but a leading cause of childhood blindness^{2,3}. Unlike laser surgery, which damages eye tissue and can be associated with significant complications such as high myopia, Lucentis pharmacologically targets and reduces the elevated intraocular level of vascular endothelial growth factor (VEGF), which is the underlying cause of the condition^{4,5,6}.

Although the RAINBOW Phase III study marginally missed statistical significance for the primary endpoint ($p=0.0254$, as opposed to the significance level of $p=0.025$), the difference in treatment success between the Lucentis 0.2mg and 0.1mg groups compared to laser surgery (80%, 75% and 66.2% respectively) is nevertheless considered clinically relevant by Novartis¹. Based on the favorable benefit-risk profile, Novartis plans to file for a new indication for Lucentis for the treatment of ROP to support this rare but important patient population.

“Laser surgery, the current standard of care, works by destroying the tissue in the eye that contributes to the elevation of VEGF. While it is an effective treatment, there is a clear unmet need for innovative ways to treat ROP without destroying retinal tissue. Lucentis demonstrated in the RAINBOW study that it is an efficacious and well tolerated option for the treatment of ROP that may offer new hope to parents of this vulnerable patient population,” said Professor Andreas Stahl, Senior Physician in Retinal Surgery and Head of the Angiogenesis Research Group at the Eye Center, University of Freiburg, Germany.

Retinopathy of prematurity affects premature infants in both developed and developing countries, with an estimated 23,800 to 45,600 infants newly diagnosed with irreversible vision impairment from ROP each year³. Caused by the abnormal development of retinal blood vessels in premature infants, disease progression is due to high levels of a growth factor called VEGF⁶. After premature birth, high VEGF levels can cause an infant's blood vessels in the retina to develop abnormally, which may lead to structural abnormalities such as retinal detachment, resulting in vision loss or blindness^{4,6}.

"The RAINBOW study is part of our ongoing commitment to addressing the most urgent needs in eye care. We look forward to filing outside the US for an indication in ROP, which may bring us one step closer to reimagining care for these premature infants," said Dirk Sauer, Development Unit Head, Novartis Ophthalmology.

About Lucentis

Lucentis (ranibizumab injection), the first anti-vascular endothelial cell growth factor (anti-VEGF) therapy licensed for ophthalmic use, revolutionized the treatment of nAMD and has helped reduce blindness due to nAMD by 50% in several parts of the world. More than a decade of innovation and six indications (nAMD, DME, BRVO, CRVO, mCNV and other CNV) later, Lucentis continues to preserve and resolve vision for patients around the globe. We continue to investigate the possibility of Lucentis to transform the treatment of even the youngest, most vulnerable patients.

Lucentis is available in more than 110 countries and is supported by a portfolio of 251 sponsored clinical studies and extensive real-world experience. The Lucentis clinical development program has enrolled more than 205,000 patients across indications with 5.4 million patient-treatment years of exposure since the therapy's launch in the United States in 2006. Lucentis was developed by Genentech and Novartis. Genentech has the rights to Lucentis in the United States. Novartis has rights in the rest of the world. Lucentis is a registered trademark of Genentech Inc.

About ROP

Retinopathy of prematurity (ROP) is a rare and potentially blinding disease caused by abnormal development of retinal blood vessels in premature babies (preterm infants)^{3,4,6}. The retina is the inner layer of the eye that receives light and turns it into visual messages that are sent to the brain⁷.

The retina develops late in the womb and very premature babies may have incomplete development of blood vessels needed to provide oxygen^{4,6}. VEGF is an important regulator of the development of new blood vessels (known as angiogenesis) and plays a key role in the progression of ROP. If the blood vessels do not develop normally during ROP, they can exert traction on the retina and lead to macular dragging, retinal detachment or other structural abnormalities resulting in vision loss or potentially blindness⁶.

About RAINBOW

The RAINBOW study, which was conducted in 26 countries, is a randomized, open-label, controlled, multicenter study designed to compare the efficacy and safety of intravitreal Lucentis (ranibizumab) with laser surgery in 225 patients with ROP. The trial compared two different concentrations of Lucentis, 0.1 mg and 0.2 mg, to the current standard of care, laser surgery. The outcomes of the study were measured at 24 weeks after starting the trial. A long-term extension trial is currently underway and expected to conclude by Q4 of 2022. The exact conclusion date is to be confirmed.¹

About Novartis 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

The foregoing release contains forward-looking statements that can be identified by words such as "dedicated to," "positive opinion," "so far," or similar terms, or by express or implied discussions regarding potential new indications or labeling for Lucentis, or regarding potential future revenues from Lucentis. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management 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 Lucentis will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that Lucentis will be commercially successful in the future. In particular, management's expectations regarding Lucentis could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected safety, quality or manufacturing issues, 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.

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