Media Release

PRIME designation granted by European Medicines Agency for RG6042 for treatment of Huntington's disease

- **European Medicines Agency PRIME (PRIority MEdicines) status is granted to medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options**
- **RG6042 has the potential to be the first therapy targeting the underlying cause of Huntington's disease, a fatal neurodegenerative rare disease**
- **Third PRIME designation for a Roche medicine**

Basel, 3 August 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Medicines Agency (EMA) has granted PRIME (PRIority MEdicines) designation for the company's investigational medicine RG6042 (formerly known as IONIS-HTTRx) for the treatment of people with Huntington's disease (HD). RG6042 has demonstrated its ability to reduce the toxic mutant huntingtin protein (mHTT), which is believed to be the underlying cause of HD, in a Phase I/IIa study.[1] PRIME is a designation implemented by the EMA to support data generation and development plans for promising medicines, providing a pathway for accelerated evaluation by the agency, and thus potentially enable them to reach patients earlier.[2]

"We are very pleased that the European Medicines Agency has granted PRIME designation for RG6042, as there is an urgent medical need to find treatment options for families affected by Huntington's disease," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "Preliminary data on RG6042 were the first to show that levels of toxic mutant huntingtin protein can be lowered in adults with Huntington's disease, and we are working closely with the EMA and other health authorities to initiate a global phase III study as soon as possible."

PRIME designation for RG6042 is primarily based on the data from an exploratory Phase I/IIa trial of RG6042 that demonstrated a significant reduction in mHTT, which breaks down the nerve cells in the brain.[1] The study demonstrated a mean 40% (up to 60%) reduction of the specific HD protein in the cerebrospinal fluid (CSF) of adult patients treated with RG6042 for three months at the two highest doses. Furthermore, levels of mHTT measured in the CSF were still declining in the majority of treated patients (~70%) as of the last measurement in the study.[3] RG6042 was well tolerated in this short initial study.[1] These data were shared at the CHDI 13th Annual HD Therapeutics Conference in March 2018,[3] and updated results were presented at the American Academy of Neurology (AAN) Annual Meeting in April 2018.[4]

Roche will initiate a pivotal phase III study to evaluate RG6042 in a larger patient population to further characterise the safety profile and determine if it can slow the progression of HD in adults.

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About RG6042
RG6042 is a second-generation modified antisense oligonucleotide (ASO) designed to reduce the production and levels of mHTT protein by targeting human HTT mRNA.[5] RG6042 is the result of a comprehensive drug discovery programme between Roche and Ionis Pharmaceuticals focused on optimising the potency, specificity and tolerability of an ASO targeting human HTT mRNA. RG6042 is the most advanced compound in clinical development to target toxic mutant huntingtin protein (mHTT), which is believed to be the underlying cause of HD. Treatment with RG6042 has the potential to slow or stop disease progression in all people with HD.[1]

About Huntington's disease
Huntington's disease is a rare genetic, progressive condition that causes the nerve cells in the brain to break down, which severely affects a person's everyday functions such as mobility and thinking.[6] It has a devastating impact on people living with the disease, and the hereditary nature of HD means it profoundly affects entire families.[6] As the disease progresses, people with HD may develop personality changes, difficulty walking and swallowing, as well as having a significant cognitive impact.[6] Survival ranges from approximately 10-20 years following motor onset of the disease.[6]

There is no known cure for HD and no approved therapies that treat the underlying cause. The estimates for the number of people affected by Huntington's vary between geographic regions. Huntington's disease is the most common monogenic neurological disorder in the developed world, with an estimated prevalence of ~3.5–7/100,000 in North America, Western Europe, and Australia.[7]

About Roche in neuroscience
Neuroscience is a major focus of research and development at Roche. The company's goal is to develop treatment options based on the biology of the nervous system to help improve the lives of people with chronic and potentially devastating diseases. Roche has more than a dozen investigational medicines in clinical development for diseases that include multiple sclerosis, Alzheimer's disease, spinal muscular atrophy, Parkinson's disease, Huntington's disease and autism spectrum disorder.

About Roche
Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. Thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines.

Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine years in a row by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 billion. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

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References

[1] Ionis Pharmaceuticals. 2018. Press release: IONIS-HTT Rx (RG6042) top-line data demonstrate significant reductions of disease-causing mutant Huntingtin protein in people with Huntington's disease. [Internet; cited 2018 July]. Available from: http://ir.ionispharma.com/node/23401/pdf
[2] European Medicines Agency. PRIME Designation. [Internet; cited 2018 July]. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000660.jsp&mid=WC0b01ac05809f8439.
[3] CHDI 13th Annual HD Therapeutics Conference 2018. Press Release: Ionis Pharmaceuticals Licenses IONIS-HTT Rx to Partner Following Successful Phase 1/2a Study in Patients with Huntington's Disease. [Internet; cited 2018 July]. Available from: https://chdifoundation.org/ionis-pharmaceuticals-licenses-ionis-htt-rx-to-partner-following-successful-phase-12a-study-in-patients-with-huntingtons-disease/. (Data on file)
[4] Ionis Pharmaceuticals. 2018. Press release: New Data from IONIS-HTT Rx Phase 1/2 Study Demonstrates Correlation Between Reduction of Disease-causing Protein and Improvement in Clinical Measures of Huntington's Disease. [Internet; cited 2018 July]. Available from: http://ir.ionispharma.com/node/23661/pdf.
[5] Leavitt B, Tabrizi S, Kordasiewicz H et al. Discovery and early clinical development of ISIS-HTTRx, the first HTT-lowering drug to be tested in patients with Huntington's disease (PL01.002). Neurology 2016;86(Suppl. 16):PL01.002. [Internet; cited 2018 July]. Available from: http://n.neurology.org/content/86/16_Supplement/PL01.002.
[6] NHS Choices. Huntington's disease: Overview. [Internet; cited 2018 July]. Available from: https://www.nhs.uk/conditions/huntingtons-disease/.
[7] Rawlins M, et al. The Prevalence of Huntington's Disease. Neuroepidemiology 2016;46:144-153.

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