

Basel, Switzerland, and Barcelona, Spain – 07 April 2014

Roche and Oryzon announce collaboration to develop epigenetics-based medicines

- **Collaboration spans research, development and commercialization of LSD1 inhibitors for oncology, haematology and non-malignant conditions**
- **Lead agent ORY-1001 currently in phase I/IIa study in AML**

Roche (SIX: RO, ROG; OTCQX: RHHBY) and Oryzon Genomics SA today announced they have entered into a worldwide collaboration to research, develop and commercialize inhibitors of Lysine Specific Demethylase-1 (LSD1; KDM1A), an epigenetic modulator that regulates gene expression.

The lead molecule, ORY-1001, was granted orphan drug status by EMA in August 2013 and is currently in phase I/IIA for acute myeloid leukaemia (AML). Roche will have sole responsibility for developing and commercializing ORY-1001 and/or its backup compounds. The agreement includes the licensing of two patent families that Oryzon has created in its pioneering research in LSD1, and includes options for other Oryzon programs to be incorporated in future. The agreement also includes an initial two-year collaborative research program between Oryzon and Roche's New York-based Translational Clinical Research Center (TCRC), Roche's hub for research and early development activities in North America, to better understand the potential of LSD1 inhibitors in oncology and haematology.

John Reed, Roche's Head of Pharma Research and Early Development, commented, "Oryzon is working at the leading edge of LSD1 inhibition, a technology with great potential to bring genuine patient benefit. Our TCRC in New York has been launched with a mandate to identify partnerships that drive innovation, providing an industry-leading conduit between sources of breakthrough science and the broader Roche organization. This collaboration on LSD1 inhibition with Oryzon fulfils that mandate perfectly."

Carlos Buesa, CEO of Oryzon, added, "We are excited to work with Roche in developing ORY-1001 to make a significant difference for patients with AML and, hopefully, for patients in other disease areas as well. Roche is the global leader in oncology and haematology, with a tremendous expertise in clinical development; this was the primary reason to prioritize this alliance. The collaboration is recognition of our cutting-edge science and our experience in epigenetics, an approach that we believe holds great promise for many patient groups."

Under the terms of the agreement, Oryzon will receive an upfront payment and near-term milestones totalling \$21 million, plus potential development, commercial and sales milestone payments across haematology, cancer and non-malignant indications that could exceed \$500 million, together with tiered royalties on sales which range up to mid-double digits.

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About epigenetics

Epigenetics is a term used to describe functionally relevant changes to the genome that do not involve a change in the nucleotide sequence. Examples of epigenetic mechanisms include DNA methylation or histone modification, each of which alters how genes are expressed and consequently read or not read without altering the underlying DNA sequence. These epigenetic changes may last through cell divisions for the duration of the cell's life, and may also last for multiple generations even though they do not involve changes in the underlying DNA sequence. Epigenetics is an active field of cancer research. The lysine-specific demethylase 1 (LSD1), which demethylates a histone, is an indispensable epigenetic governor involved in regulation of key cellular processes including proliferation and differentiation.

About LSD1 inhibition

LSD1 is also called an "eraser", for it removes signals in the histone, provoking changes in the reading context of the chromosome and turning off genes. Aberrant "erasing" activity may lead to disease. In mixed lineage leukaemia (e.g., AML, ALL) LSD1 has been identified as playing a pivotal role. Drugs inhibiting LSD1 produced changes in gene expression leading to differentiation of leukemic blasts cells into normal differentiated cells, reducing proliferation and reducing viability of leukemic stem cells.

About ORY-1001

ORY-1001 is a highly selective and potent LSD1 inhibitor which can be orally administered to patients. ORY-1001 affects AML stem cells, a sub-population of cancer cells that has been proposed to be responsible for frequent relapses of the disease. ORY-1001 also significantly reduces tumour cell load and increases survival time in mouse models of Acute Lymphoblastic Leukaemia. LSD1 has been also related with other malignancies such as solid tumours and other haematological diseases.

About the Translational and Clinical Research Center (TCRC)

The TCRC is Roche's hub for research and early development activities in North America, underscoring the center's importance to Roche. The TCRC staff comprises some 250 highly experienced drug developers who are focused on early clinical development of Roche drug candidates. In addition to advancing Roche's existing portfolio, the TCRC experts aim to access external innovation by identifying collaborations ranging from very early discovery platforms through advanced stage molecules.

About Oryzon

Founded in 2000 in Barcelona, Spain, Oryzon (www.oryzon.com) is a privately held, clinical stage biotechnology company considered as the European champion in Epigenetics with a strong portfolio in the field. Its LSD program is currently covered by 18 patent families. The company has a second program in LSD1 inhibition devoted to Alzheimer's and Huntington's disease that is expected to enter in Clinical trials in 2015. The company has also a strong technological platform for biomarker identification. With a core in genomics, the company performs biomarker and target validation for a variety of malignant and neurodegenerative diseases. Under our current business model, Oryzon develops new drugs against these targets till Phase II.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in *in vitro* diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. Twenty-four medicines developed by Roche are included in the World Health Organisation Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and chemotherapy.

In 2013 the Roche Group employed over 85,000 people worldwide, invested 8.7 billion Swiss francs in R&D and posted sales of 46.8 billion Swiss francs. 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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For further information:

Oryzon

Emili Torrell, Business Development Officer, etorrell@oryzon.com

Roche Partnering

Diana Gibson, Head of Roche Partnering Communications, diana.gibson@roche.com