HYBRIGENICS

Press Release

Hybrigenics receives FDA green light for Phase II clinical study of inecalcitol in Acute Myeloid Leukemia in the United States

- **This double-blind placebo-controlled Phase II clinical study focused on older or frail Acute Myeloid Leukemia patients will be conducted in France and in the United States with the same clinical protocol**
- **Hybrigenics was granted authorization by the FDA in the minimum regulatory time of just one month after filing its Investigational New Drug application**

Paris, 11 January 2016 – Hybrigenics (FR0004153930 - ALHYG), a bio-pharmaceutical company listed on the Alternext market of Euronext Paris, with a focus on research and development of new treatments of proliferative diseases, today announces having received the authorization from the American Food and Drug Administration to perform a double-blind placebo-controlled clinical Phase II study of inecalcitol in elderly or frail acute myeloid leukemia (AML) patients in the United States. The study has recently already been approved by the French Drug Agency.

The objective of the study is to focus on the elderly or frail AML patients who are unfit to standard chemotherapy and who can only receive monthly cycles of intravenous perfusions of decitabine (Dacogen®, Johnson & Johnson). In addition to this treatment, they will receive oral inecalcitol or placebo. The primary endpoint will be overall survival. The total number of 110 patients to be included in the study is designed to be sufficiently powered to evidence potential efficacy on mortality. Prof. J. Cortes, Chair of the AML and CML sections, Department of Leukemia, University of Texas MD Anderson Cancer Center, Houston, will be the principal investigator in the United States. Hybrigenics was granted authorization by the American Food and Drug Administration for the Investigational New Drug (IND) application for this AML clinical study of inecalcitol in the minimum regulatory time of just one month after filing.

Last month, Hybrigenics had already received authorization by the French Drug Agency for the Investigational Medicinal Product Dossier (IMPD) of inecalcitol for the AML trial (see Hybrigenics' press release of December 14, 2015). Prof. O. Hermine, Chair of the Department of Hematology, Necker Hospital, Paris, will be the principal investigator of the study in France.

Inecalcitol has received Orphan Drug status for AML both in Europe and the Unites States on the basis of encouraging *in vitro* and *in vivo* preclinical results (cf. Hybrigenics' press releases of June 22 and August 08, 2015). The molecular basis of the synergy between decitabine, a hypomethylating agent, and inecalcitol has been established: decitabine "unmasks" the gene coding for vitamin D receptors (by reducing the methylation of its promoter region). As a consequence, more vitamin D receptors are expressed and available to be activated by inecalcitol (cf. Hybrigenics' press releases of June 20, 2014).

"*The authorization process for the clinical Phase II study of inecalcitol in elderly or frail acute myeloid leukemia patients has been as swift and fast with the American Food and Drug Administration as with the French Drug Agency. The unmet medical need for this category of patients is especially high, with intravenous decitabine as their only specific treatment option. We aim at increasing its efficacy by combining it with oral inecalcitol and thereby to improve patient care with this new additional treatment option,"* said Jean-François Dufour-Lamartinie, Hybrigenics' Head of Clinical R&D.

About Acute Myeloid Leukemia

Acute myeloid leukemia (AML) has recently become the most frequent form of leukemia and accounts for about 38% of all leukemic patients. Annual estimates of newly diagnosed AML cases amount to 20,830 in the United States (Cancer Facts and Figures 2015), 18,500 in Europe (RARECARE Working Group, 2012) and 110,000 world-wide (Globocan, 2012). AML is designated as an orphan disease in the United States, Europe and Japan.

AML is a type of cancer that affects the blood and bone marrow. AML is characterized by a fast-increasing overproduction of immature white blood cells, called myeloblasts. These cells rapidly crowd the bone marrow, soon preventing it from making normal blood cells. They can also spill out into the blood stream and circulate around the body. Due to their immaturity, they are unable to function properly to prevent or fight infection. Inadequate numbers of red cells and platelets being made by the marrow cause anemia, and easy bleeding and/or bruising. AML is sometimes called acute myelocytic, myelogenous or granulocytic leukemia.

AML can occur at any age but is more common in adults over the age of 60 years. Treatment needs to begin soon after AML is diagnosed, as it progresses very quickly. Chemotherapy is the main form of treatment for AML; occasionally, a stem cell transplant may be used. Despite available treatments, AML shows the lowest 5-year survival rate of all leukemias: 25% in the US and 19% in Europe.

About Hybrigenics

Hybrigenics (www.hybrigenics.com) is a bio-pharmaceutical group listed (ALHYG) on the Alternext market of Euronext Paris, focusing its internal R&D programs on innovative targets and therapies for the treatment of proliferative diseases and providing cutting-edge proteomic and genomic scientific services.

Hybrigenics' current development program is based on inecalcitol, a vitamin D receptor agonist active by oral administration. Oral inecalcitol has shown excellent tolerance and strong presumption of efficacy for the first-line treatment of metastastic castrate-resistant prostate cancer in combination with Taxotere®, which is the current gold-standard chemotherapeutic treatment for this indication. Inecalcitol has also been tested in chronic lymphocytic leukemia patients, an indication for which inecalcitol has received orphan drug status in Europe and the United States. A clinical Phase II study of inecalcitol is currently ongoing in chronic myeloid leukemia patients.

Hybrigenics has a research collaboration with Servier on deubiquitinating enzymes (DUBs) and their inhibitors in oncology, neurology, psychiatry, rheumatology, ophthalmology, diabetes and cardiovascular diseases. A first milestone has been achieved in a drug discovery program targeting one DUB in oncology.

Hybrigenics Services (www.hybrigenics-services.com) is the market leader in Yeast Two-Hybrid (Y2H) and related services to identify, validate and inhibit protein interactions for researchers in all areas of life sciences, using its ISO 9001-certified high-throughput Y2H screening platform.

Helixio (www.helixio.com), Hybrigenics' genomic branch, provides state-of-the-art services specialized in DNA chips, DNA or RNA target enrichment and next generation sequencing with an Illumina NextSeq500.

Hybrigenics Corp., based in Cambridge, Mass., is the American subsidiary of Hybrigenics.

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HYBRIGENICS is listed on the Alternext market of Euronext Paris

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