

Hybrigenics presents new *in vitro* results on inecalcitol in chronic myeloid leukemia at the AACR meeting in Philadelphia, USA

- **Inecalcitol synergizes *in vitro* with dasatinib and nilotinib to inhibit the growth of stem cells isolated from chronic myeloid leukemia patients**
- **Results are presented today at the Annual Meeting of the American Association for Cancer Research by Prof. A. Turhan, from Inserm U935 and Paris-Sud University**

Paris, 20 April 2015 – Hybrigenics (ALHYG), a bio-pharmaceutical company listed on the Alternext market of Euronext Paris, with a focus on research and development of new treatments against proliferative diseases, today announces the presentation by the Inserm U935 research group of Prof. Ali Turhan, Head of the Division of Hematology, Paris-Sud Kremlin-Bicetre University Hospital, of the *in vitro* effects of inecalcitol on the growth of human chronic myeloid leukemia (CML) progenitors and stem cells in culture, at the Annual Meeting of the American Association for Cancer Research in Philadelphia, Pennsylvania, USA.

Inecalcitol had already been shown to preferentially inhibit the proliferation of CML progenitors and stem cells isolated from CML patients at diagnosis and cultured *in vitro*, as compared to normal myeloid progenitors and stem cells isolated from healthy volunteers. Furthermore, this activity was synergistic with the inhibition exerted *in vitro* by imatinib (Gleevec®, Novartis), the first generation inhibitor of the Bcr-Abl tyrosine-kinase, the reference treatment of CML (see Hybrigenics' press release of December 09, 2013). On the basis of these initial results, a clinical Phase II study of inecalcitol in combination with imatinib has recently been launched in CML patients (see Hybrigenics' press release of January 20, 2015).

In the present study by the same group of researchers, a synergy to inhibit the growth of progenitors and stem cell isolated from CML patients has been demonstrated *in vitro* between inecalcitol and dasatinib (Sprycel®, BMS) or nilotinib (Tasigna®, Novartis), two other inhibitors of the Bcr-Abl tyrosine-kinase of a more recent generation than imatinib. By contrast, the combination of inecalcitol and dasatinib or nilotinib had no effect on normal myeloid progenitors.

"These preliminary observations extend the synergistic potential of inecalcitol and tyrosine-kinase inhibitors to dasatinib and nilotinib, in addition to imatinib," said Prof. Ali Turhan.

"If positive, the ongoing clinical Phase II study of inecalcitol with imatinib could lead the way to testing the combination of inecalcitol with any tyrosine-kinase inhibitor indicated for the treatment of CML," said Jean-François Dufour-Lamartinie, Hybrigenics' Head of Clinical R&D.

About chronic myeloid leukemia

Chronic myeloid leukemia (CML), also known as chronic myelogenous leukemia, is a type of cancer that starts in the bone marrow, invades the blood and then other parts of the body such as the spleen. CML evolves slowly at the beginning and, without treatment, ends by deteriorating into acute ("blast") phases, causing deadly anemia, coagulation impairment or lack of defense against infections.

CML is an orphan adult leukemia. In the United States, 6,000 new cases are diagnosed every year and a total of 34,000 patients are presently living with the disease; the 5-year survival rate is 60% and about 800 patients die from CML every year (LLS Facts and Figures, 2015). In Europe, the incidence is 1.02 patient per year per 100,000 inhabitants (EuTOS, 2014). CML has orphan disease regulatory status in Europe, Japan and the United States.

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CML is characterized by the over-production of all types of white blood cells (except lymphocytes) originating from a single stem cell, which starts escaping proper regulations. In all CML patients, the loss of cell control results from the same accidental "exchange" of "bits" of chromosomes (translocation between chromosomes number 9 and 22), which gives rise to the abnormal fusion gene called BCR-ABL. The product of this gene, the Bcr-Abl protein is a hyper-functional tyrosine-kinase which continuously stimulates cell proliferation. The inhibitors of the Bcr-Abl tyrosine-kinase, such as imatinib (Gleevec®), are used to treat CML patients and the BCR-ABL gene transcripts are well-established biomarkers of the blood concentration of residual CML cells.

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 metastatic 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.

HYBRIGENICS is listed on the Alternext market of Euronext Paris

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