

Hybrigenics launches Phase II clinical study of inecalcitol in chronic myeloid leukemia

Paris, 19 January 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 launch of clinical Phase II study of inecalcitol in chronic myeloid leukemia (CML), an orphan blood cancer mostly affecting adults.

The rationale for this clinical Phase II study in CML results from the antiproliferative effects of inecalcitol and its synergy with imatinib demonstrated by Prof. A. Thuran's INSERM U935 research group on *in vitro* cultures of CML stem cells directly taken from CML patients (cf. Hybrigenics' press release of December 09, 2013). The results recently obtained in the clinical Phase II study of inecalcitol in chronic lymphocytic leukemia (CLL) at the dose of 2 milligram per day, *i.e.* 52% of patients experiencing stabilization or decrease of blood leukemic lymphocytes counts (cf. Hybrigenics' press release of July 16, 2014), have also supported the idea to test inecalcitol in CML, the main other adult chronic leukemia.

In the clinical Phase II study in CML, oral inecalcitol will be given at the dose of 4 milligram per day to patients already under treatment by oral imatinib (Gleevec®) for more than two years, but who still present a residual disease as measured in the blood by the specific CML biomarker called BCR-ABL. The objective of the treatment with inecalcitol is to improve the patients' condition by further reducing the BCR-ABL biomarker to 10 times lower or even undetectable levels, which could be the sign of a possible cure. The CML patients will be treated for one year.

The clinical Phase II study in CML will be implemented in at least 5 centres in France, including Paris-Sud 11 Kremlin-Bicetre University Hospital (Division of Hematology, Prof. A. Thuran), and coordinated by Prof. H.-A. Johnson-Ansah from Caen University Hospital. The goal of the study is to enrol 54 patients within one year.

"It took Hybrigenics just over one year to translate the synergy of inecalcitol with imatinib on chronic myeloid leukemic (CML) stem cells discovered at the lab bench into the launch of this Phase II study of its potential benefits for the patients. We also took into account the recent results of the clinical Phase II study of inecalcitol in chronic lymphocytic leukemia (CLL) to design this trial in CML, a new potential orphan indication," said Remi Delansorne, Hybrigenics' CEO.

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.

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 hyper-functional and continuously stimulates cell proliferation. The inhibitors of the Bcr-Abl protein, 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.

HYBRIGENICS

Press Release

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. Oral 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.

Hybrigenics has a research collaboration with Servier on deubiquitinating enzymes and their inhibitors in oncology, neurology, psychiatry, rheumatology, ophthalmology, diabetes and cardiovascular diseases. Hybrigenics continues to build on its pioneer research position in the field of ubiquitin-specific proteases by exploring their role in other areas of particular relevance, such as inflammation and virology.

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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