HYBRIGENICS

Press Release

Hybrigenics gives an update on the clinical development of inecalcitol

- **End of Phase II study in chronic lymphocytic leukemia (CLL)**
- **Authorization to start Phase II study in chronic myeloid leukemia (CML)**

Paris, 16 July 2014 – Hybrigenics SA (ALHYG), a bio-pharmaceutical company listed on the Alternext market of Euronext in Paris, with a focus on research and development of new treatments against proliferative diseases, today announces the end of the clinical Phase II study of inecalcitol in chronic lymphocytic leukemia (CLL) and the authorization by the French drug agency to start a clinical Phase II study in chronic myeloid leukemia (CML).

End of Phase II clinical study in chronic lymphocytic leukemia (CLL)

Out of the 24 enrolled patients in the CLL study, twenty-one evaluable patients have been treated for at least 4 months and up to 23 months with 2 mg/day of oral inecalcitol alone. Eleven patients (52%) showed a decrease or a stabilization of their blood lymphocyte counts (BLC); one out of these eleven patients achieved a -95% decrease in BLC after 10 months of treatment and another one had around -45% BLC reduction after 4 and 5 months of treatment. The BLC of 10 other patients (48%) have increased at a regular exponential pace without any influence of the treatment.

Seven patients dropped out of the study to receive immuno-chemotherapy: six in the group of patients with no obvious effect of the treatment and one at one year in the study after an initial phase of stabilization. Two patients experienced hypercalcemic adverse events (one grade 3 and one grade 4) attributable to inecalcitol after 15 and 17 months of treatment.

Authorization to start Phase II clinical study in chronic myeloid leukemia (CML)

The French drug agency has granted authorization to a Clinical Trial Application submitted by Hybrigenics to study oral inecalcitol in CML patients treated by oral imatinib (Gleevec®) with a stable but sub-maximal level of efficacy, as measured in blood by the Bcr-Abl biomarker. The objective is to add inecalcitol to imatinib to investigate if the Bcr-Abl biomarker can be furthered reduced down to levels where cure of the disease could be achieved.

Inecalcitol and imatinib have already demonstrated a synergistic inhibitory effect on CML stem cells isolated from patient blood and grown *in vitro* (cf. Hybrigenics' press release of December 09, 2013). The aim of the study is to translate this initial laboratory finding into clinical research in CML patients. Hybrigenics' objective is to enrol and treat the first CML patient before the end of 2014.

"*Treatment with inecalcitol seems to delineate two sets of patients of nearly equal proportion with regards to the evolution of the blood count of their leukemic lymphocytes. This result will be taken into account to design the next step of the clinical development of inecalcitol as an orphan drug in* chronic lymphocytic leukemia*. Meanwhile, Hybrigenics will start to evaluate the potential of inecalcitol in combination with imatinib (Gleevec®) in* chronic myeloid leukemia *patients, another orphan adult leukemia,"* said Remi Delansorne, Hybrigenics' CEO.

About Hybrigenics

Hybrigenics (www.hybrigenics.com) is a bio-pharmaceutical group listed (ALHYG) on the Alternext market of Euronext in 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.eu), Hybrigenics' genomic branch, provides state-of-the-art services specialized in DNA chips, DNA or RNA target enrichment and next generation sequencing.

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

***

HYBRIGENICS is listed on the Alternext market of Euronext Paris

ISIN: FR0004153930
Ticker: ALHYG

ALHYG
LISTED
NYSE
ALTERNEXT

Hybrigenics
Rémi Delansorne
CEO
Tel.: +33 (0)1 58 10 38 00
investors@hybrigenics.com

NewCap.
Financial communication
Julien Perez / Pierre Laurent
Tel.: +33 (0)1 44 71 94 94
hybrigenics@newcap.fr