HYBRIGENICS

Press Release

Hybrigenics targets chronic lymphocytic leukemia (CLL) as the third therapeutic indication for its oral inecalcitol

Hybrigenics filed a clinical trial application to test inecalcitol, a vitamin D receptor agonist, in CLL patients

Hybrigenics started a collaboration with Necker Institute, Paris, on vitamin D receptor and CLL

Paris, 19 January 2012 – Hybrigenics (ALHYG), a bio-pharmaceutical company listed on Alternext (NYSE-Euronext) in Paris, with a focus on research and development of new treatments against proliferative diseases, today announces that it has filed a clinical trial application at the new French National Drug Safety Agency to test inecalcitol, a vitamin D receptor agonist, in chronic lymphocytic leukemia (CLL) patients. A first response from the agency is expected before end of March 2012. World-wide, more than 70,000 new patients are diagnosed each year with CLL, for which a real cure does not exist. CLL is designated as an orphan disease in the United States.

The open-label clinical study would enrol 50 patients across 6 centres in France and be coordinated by Prof. Hermine, Head of Clinical Haematology at Necker Hospital in Paris, with the endorsement and active participation of the French Cooperative Group on CLL. Patients would receive 4 mg/day of inecalcitol for at least 6 months and/or until progression of the disease. In parallel, Hybrigenics started a research collaboration with the Necker Institute to assess the vitamin D receptor (VDR) status of CLL cells and to correlate their responsiveness to inecalcitol treatment with the level of VDR expression.

The rationale for investigating inecalcitol in CLL stems from a recent clinical observation that a patient, whose CLL cells over-expressed VDR, responded positively to a treatment with high oral doses of natural vitamin D every two weeks (Arlet *et al*., 2012, British Journal of Haematology, 156: 148-9; e-pub: 25 Aug 2011). A control patient whose CLL cells expressed low levels of VDR remained unresponsive to the same high doses of vitamin D. The frequency of natural vitamin D administrations is usually limited by the high risk of developing hypercalcemia. By contrast, Hybrigenics has shown that inecalcitol can be administered every day at high doses without such risk. Therefore, it can be envisaged that daily oral inecalcitol might prove effective in patients with CLL cells over-expressing VDR.

"We seized this opportunity to test oral inecalcitol in a third therapeutic indication: chronic lymphocytic leukemia, after castrate-resistant prostate cancer and moderate-to-severe psoriasis. All three diseases have in common long-term cell hyper-proliferation, which inecalcitol may slow down. It is very easy to collect repeated samples of CLL cells in blood and therefore to monitor at regular intervals their VDR status and their responsiveness to inecalcitol treatment as biomarkers of efficacy," said Dr. Jean-François Dufour-Lamartinie, Head of Clinical R&D.

About Chronic Lymphocytic Leukemia (CLL)

CLL is the most frequent form of leukemia (cancerous proliferative disease of circulating blood cells) and accounts for about 35% of all leukemic patients. Annual estimates of newly diagnosed CLL cases amount to close to 15,000 in the United States (American Leukemia Lymphoma Society, Facts 2012), 14,000 in Europe and 70,000 world-wide (Globocan 2008).

People with CLL make too many lymphocytes (mononuclear white blood cells) of one single abnormal "family" (monoclonal) which are not fully developed (immature). Over time, these circulating CLL cells (monoclonal immature lymphocytes) in excess build up in the lymphatic system and cause large, swollen lymph nodes. They may also fill the bone marrow, reducing the number of normal white cells, red cells and platelets that can be made, thereby lowering their blood counts. CLL cannot usually be cured.

About inecalcitol

Inecalcitol is an anti-proliferative vitamin D receptor agonist with a non-calcemic activity by oral administration at doses up to 4 milligrams per day, as observed in a completed Phase IIa clinical study in first-line metastatic castrate-resistant prostate cancer patients, in combination with Taxotere®.

The anti-proliferative effectiveness of oral inecalcitol is further being explored in a phase II study in patients with moderate-to-severe psoriasis. All patients have been enrolled in the study and first results are expected in Q3, 2012

About Hybrigenics

Hybrigenics (www.hybrigenics.com) is a bio-pharmaceutical company listed (ALHYG) on Alternext (NYSE-Euronext) in Paris, focusing its internal R&D programs on innovative targets and therapies for the treatment of proliferative cancerous or non-cancerous diseases.
Hybrigenics' current development program is based on inecalcitol, a vitamin D receptor agonist, 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 is also being developed to treat moderate-to-severe psoriasis by oral administration.
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 SAS, a fully-owned subsidiary, 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, its sophisticated bioinformatics tools and extensive database, along with its chemical library and chemical screening platform

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ISIN: FR0004153930
Ticker: ALHYG

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