HYBRIGENICS

Press Release

Hybrigenics reports initial results from clinical Phase 2 trial of oral inecalcitol in moderate to severe psoriasis

Paris, 04 June 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 the first results of the placebo-controlled double-blind clinical Phase II efficacy study of oral inecalcitol at the single dose of 4 mg per day in moderate to severe psoriasis.

The primary endpoint was the Psoriasis Area and Severity Index (PASI) which is a composite scoring system taking into account the area of the psoriatic lesions and their thickness, redness and scaling. A patient is considered as a "responder" if his PASI has been decreased by at least 50% during treatment (PASI 50). A PASI decline of more than 75% (PASI 75) is considered clinically relevant.

Of the total 60 enrolled patients, 57 (20 placebo and 37 inecalcitol) have completed their treatment for at least 10 weeks and up to 16 weeks. One early study withdrawal was due to grade 3 hypercalcemia caused by inecalcitol within the first week of treatment. Of the 37 patients treated with oral inecalcitol, 24 patients (65%) showed a PASI 50 response and, among them, 10 patients (27%) had a PASI 75 clinical improvement. However, these results were not statistically different from the placebo group, in which women had an unexpectedly strong improvement of their disease with a PASI 75 rate of 63% vs. 17% observed in placebo-treated men, which is more in line with usual values from the literature on psoriasis studies of similar duration.

Blood levels of inflammatory biomarkers such as IL-4, IL-10, IL-12, IL-17, interferon-gamma (IFN-γ) and tumor necrosis factor alpha (TNF-α) are currently being assayed in samples from all patients, as well as the levels of vitamin D receptor in white blood cells. Biopsies of skin lesions have been taken in subsets of patients and their histo-pathological examination is also ongoing. This additional data will be available in the coming weeks and may shed some light on the reasons for the strong placebo effect observed in women, and why there weren't more PASI 50 responders progressing to PASI 75 clinical improvement.

In addition, levels of parathyroid hormone (parathormone, PTH) were measured, since PTH levels had decreased below the lower limit of the normal range, and sometimes even below the limit of quantification (LoQ), in all prostate cancer patients treated by 4 mg per day of oral inecalcitol in a clinical tolerance Phase IIa study (see Hybrigenics' press release of September 20, 2010).

During the entire treatment period (16 weeks) and still one month later, after the follow-up period, the PTH levels of each of the 20 patients on placebo changed by less than 50% from their initial value and remained within the normal range. By contrast, the PTH levels of each of the 37 patients receiving inecalcitol decreased by more than 50% during the treatment. PTH levels were decreased below the normal range in 34 inecalcitol-treated patients (92%) and below LoQ in 24 of them (65%). This PTH lowering effect was highly statistically significant as compared with placebo at all times during treatment ($p < 0.001$), even as soon as week 4, the earliest time point measured. This pharmacological effect of inecalcitol was totally and rapidly reversible because all PTH levels were back within the normal range after the one-month follow-up period.

"*Two-thirds of inecalcitol-treated psoriasis patients showed some degree of response (PASI 50) but only one fourth had a clinically-relevant improvement (PASI 75) at week 12 or at week 16. A hypothesis could be that a longer duration of treatment might be necessary for inecalcitol to fully improve all the responders*", commented Dr Jean-François Dufour-Lamartinie, Hybrigenics' Head of clinical R&D. He added: "*the confirmation of inhibition of normal PTH secretion by inecalcitol, a fast, strong and straightforward effect observed in all treated patients, without any placebo effect, deserves further clinical investigation in chronic kidney disease patients who suffer from pathologically elevated PTH levels*".

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 active by oral administration. Oral inecalcitol is currently being studied in a clinical trial for the treatment of moderate-to-severe psoriasis. Oral inecalcitol is also planned to be tested in chronic lymphocytic leukemia patients. Oral inecalcitol has already 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.

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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HYBRIGENICS is listed on the Alternext by NYSE Euronext Paris

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