

Hybrigenics' inecalcitol shows promising preclinical results against hormone-dependent prostate cancer

Preclinical results from Prof Koeffler's laboratory at the Cedars-Sinai Medical Center, University of California at Los Angeles, are presented today at the 14th Vitamin D Workshop in Brugge, Belgium

Paris, 08 October 2009 – Hybrigenics (ALHYG), a bio-pharmaceutical company listed on Alternext (NYSE-Euronext) in Paris, with a focus on research and development of new cancer treatments and specialized in protein interactions, announces today preclinical results demonstrating the potential of inecalcitol alone and in a synergistic combination with a cytotoxic platinum derivative, to inhibit the growth of a human hormone-dependent prostate cancer cell line. These results are presented today at the 14th Vitamin D Workshop in Brugge by Dr Ryoko Okamoto.

Dr Okamoto showed that inecalcitol was 11 times more potent than calcitriol, the naturally active metabolite of vitamin D, to inhibit the growth *in vitro* of the human hormone-dependent prostate cancer cell line named LNCaP. She also showed that 30 µg/mouse of inecalcitol three times per week for 11 weeks was well tolerated and that, by contrast, the maximum tolerated dose of calcitriol in mice was limited to 0.0625 µg/mouse. This means that inecalcitol was at least 480 times less toxic than calcitriol in the same experimental conditions. Dr Okamoto works in Prof Koeffler's Division of Hematology and Oncology at the Cedars-Sinai Medical Center of the UCLA School of Medicine.

In another set of experiments, inecalcitol was shown to be 25 times more potent *in vitro* on the same LNCaP human cell line than a platinum-based cytotoxic compound. When combined together, inecalcitol and the platinum derivative exerted synergistic inhibitory effects *in vitro* at low concentrations. Inecalcitol and the platinum derivative were subsequently administered in small non-toxic doses to mice inoculated with human LNCaP cells: each compound alone reduced tumor growth by half over 6 weeks. In combination, they produced a statistically significant decrease of 65 percent.

"Although still preliminary, these results from a leading international laboratory in the field of cancer applications of vitamin D analogues are very promising for two reasons: 1) inecalcitol may be active against hormone-dependent prostate cancer (and not only against hormone-refractory prostate cancer against which it is currently being developed in combination with Taxotere[®] chemotherapy), and 2) inecalcitol might also be successfully combined with platinum-based chemotherapeutics (and not only with taxanes like Taxotere[®])," said Remi Delansorne, Hybrigenics' CEO.

HYBRIGENICS

Press Release

About prostate cancer

Prostate cancer is the most common type of cancer in men. The latest documented figures are forecasts of 192,300 new cases and 27,400 deaths from prostate cancer for 2009 in the United States of America, and estimates of 345,900 new cases and 87,400 deaths in 2006 for all of Europe.

At the time of diagnosis, if the cancer is localized to the prostate, it can be definitively cured by surgery and/or radiotherapy. If the cancer has already spread beyond the prostate gland, treatments with anti-hormonal drugs initially manage to keep it under control, in a so-called "hormone-dependent" stage. However, after several months or years, tumor growth resumes despite anti-hormonal treatment: the prostate cancer has then escaped into a "hormone-refractory" stage, for which Taxotere[®]-based chemotherapy is the standard of care. The worldwide drug market for prostate cancer is more than \$ 3 billion per year, with an estimated 75/25 per cent split between hormone dependent/refractory stages, respectively.

About inecalcitol

Inecalcitol is an orally active agonist targeting the vitamin D receptor. The therapeutic rationale behind its development is to add its cytostatic potential to the established efficacy of the reference treatments of the two stages of prostate cancer: anti-hormonals (LH-RH agonists and anti-androgens) for the hormone-dependent stage and Taxotere[®]-based chemotherapy for the hormone-refractory stage.

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 cancer. Hybrigenics' development program is based on inecalcitol, a vitamin D analogue, for the treatment of hormone-refractory prostate cancer in combination with Sanofi-Aventis' Taxotere[®], which is the current gold-standard chemotherapeutic treatment for this indication. Hybrigenics' research program explores the role of enzymes known as ubiquitin-specific proteases (USP) in the degradation of onco-proteins, and the effectiveness of proprietary USP inhibitors in treating various types of cancer.

Hybrigenics is also 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.

HYBRIGENICS is listed on the Alternext by NYSE Euronext

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