# Hybrigenics presented at the ASH Annual Meeting the potency of inecalcitol to induce CD38 on Multiple Myeloma cell lines

- **37 out of 38 human multiple myeloma (MM) cell lines responded to inecalcitol, a vitamin D receptor agonist, by an average of 5-fold increase in CD38 surface density**
- **The single MM cell line unresponsive to inecalcitol lacks vitamin D receptors**
- **Patent applications have been filed worldwide on the CD38-inducing properties of inecalcitol**

**Paris, France, on December 11th, 2017 – Hybrigenics (ALHYG),** a bio-pharmaceutical company listed on the Euronext Growth market of Euronext Paris, with a focus on research and development of new anticancer treatments, presented on December 9th at the 59th Annual Meeting of the American Society of Hematology (ASH) in Atlanta, United States, *in vitro* results showing the reproducibility and the potency of inecalcitol to stimulates the expression of the CD38 antigen at the surface of human multiple myeloma (MM) cell lines in culture.

Initial results have already been published on line (cf. Hybrigenics news, November 2nd, 2017; https://ash.confex.com/ash/2017/webprogram/Paper101424.html). Additional data have been included in the poster presentation on December 9.

Myelomax (Nantes, France) has tested inecalcitol, Hybrigenics' vitamin D receptor (VDR) agonist, on its full panel of human MM cell lines *in vitro:* 37 out of 38 cell lines have significantly responded to inecalcitol by an average of 5-fold increase in CD38 antigen density at the surface of the cells. The only MM cell line which did not respond to inecalcitol was shown to lack VDR, thereby demonstrating that inecalcitol is acting exclusively through the VDR pathway to stimulate CD38.

Furthermore, inecalcitol was compared to all-*trans* retinoic acid (ATRA) *in vitro* on MM cell lines: inecalcitol was on average 2 to 3 times more efficacious than ATRA to stimulate CD38 in the same range of concentrations, and 10- to 100-times higher concentrations of ATRA were necessary to achieve the same maximal stimulation of CD38 than with inecalcitol. ATRA is the only drug currently being tested to stimulate CD38 in a clinical trial in MM with the objective to enhance the therapeutic efficacy of daratumumab (Darzalex®, J&J), the reference anti-CD38 monoclonal antibody in this indication.

Two simultaneous patent applications have been filed, in the United States and according to the Euro-PCT worldwide procedure, to claim the therapeutic use of inecalcitol in combination with anti-CD38 drugs in MM, but also in Acute Myeloid Leukemia (AML; cf. Hybrigenics' press release of December 05, 2016) and some forms of classical Hodgkin Lymphoma and B-Acute Lymphoblastic Leukemia, based on the stimulation of CD38 by inecalcitol in representative human cell lines.

*"Since our discovery last year of the stimulation of CD38 by inecalcitol on human AML cell lines, we have extended this finding in collaboration with Myelomax to nearly all Multiple Myeloma cell lines tested. The potency of inecalcitol was much higher than that of all-*trans *retinoic acid, the only drug in clinical trial in combination with daratumumab to look for a synergistic therapeutic efficacy based on the induction of CD38. In front of this potent and unexpected effect, we filed a patent on the therapeutic use of inecalcitol in combination with anti-CD38 antibodies such as daratumumab,"* said Remi Delansorne, Hybrigenics' CEO.

## About Hybrigenics

Hybrigenics (www.hybrigenics.com) is a bio-pharmaceutical company listed (ALHYG) on the Euronext Growth market of Euronext Paris, focusing its internal R&D programs on innovative targets and therapies for the treatment of proliferative diseases.

Hybrigenics' development program is based on inecalcitol, a vitamin D receptor agonist active by oral administration. Inecalcitol has been tested in chronic lymphocytic leukemia patients, an indication for which inecalcitol has received orphan drug status in Europe and the United States. Two clinical Phase II studies of inecalcitol are currently ongoing in chronic myeloid leukemia and acute myeloid leukemia. Oral inecalcitol has shown excellent tolerance and strong presumption of efficacy for the first-line treatment of metastastic castrate-resistant prostate cancer in combination with Taxotere®, which is the current gold-standard chemotherapeutic treatment for this indication.

Hybrigenics' research program is exploring the role of enzymes called Ubiquitin-Specific Proteases (USP) in the balance between degradation and recycling of proteins called onco-proteins due to their involvement in various cancers. Hybrigenics is evaluating the interest of inhibitors of USP as anti-cancer drug candidates. Hybrigenics has collaborated with Servier on one particular USP in oncology. In this R&D program, two milestones have been reached and additional milestones may be achieved until registration of a potential drug.

Hybrigenics Pharma Inc., based in Cambridge, Mass., is the U.S. subsidiary of Hybrigenics.

**Hybrigenics** is listed on the Euronext Growth market of Euronext Paris

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