

### **Hybrigenics' specific inhibitors of Ubiquitin-Specific Protease 7 (USP7) are cytotoxic for human cancer cell lines *in vitro***

**The mechanism of USP7 inhibition and the resulting decrease in viability of human cancer cells *in vitro* are published in Chemistry & Biology**

**Paris, 24 April 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 publication of a peer-reviewed research article in *Chemistry & Biology*, a highly respected scientific journal of the Cell Press group, on Hybrigenics' new generation of USP7 inhibitors (Reverdy *et al.*, *Chemistry & Biology*, 2012, 19 (4), 467-477; doi:10.1016/j.chembiol.2012.02.007)

This new chemical series discovered by Hybrigenics exerts its inhibition by direct irreversible covalent linkage to the active site of USP7 in a selective manner: no other tested USPs or deubiquitinating enzymes were inhibited. The *in vitro* treatment of SJSa and U2OS human osteosarcoma cell lines by these compounds reproduced the anti-proliferative effects obtained by inhibition of USP7 gene expression. Furthermore, the viability of DU 145 human prostate cancer and HCT116 human colon cancer cell lines was altered by USP7 inhibition and apoptosis (programmed cell death) was also triggered in HCT116 cells.

The cytotoxicity of one of Hybrigenics' USP7 inhibitors has already been reported on human chronic lymphocytic leukemia (CLL) cells by Professor Tatjana Stankovic, from the University of Birmingham (UK) School of Cancer Sciences, at the 14<sup>th</sup> International Workshop on CLL last year (cf. Hybrigenics' press release of Oct. 28, 2011). The full chemical series is protected by European, American and worldwide patent applications filed simultaneously on January 15, 2010. Examination procedures are on track and should secure Hybrigenics' intellectual property of this series up to 2030.

In the same issue of *Chemistry & Biology*, Drs. Robert Menard and Traian Sulea, from the Biotechnology Research Institute in Montreal, Canada, published a detailed preview analysis (Menard and Sulea., *Chemistry & Biology*, 2012, 19 (4), 437-438; doi:10.1016/j.chembiol.2012.04.001) with these comments: "*all these results strongly suggest that the discovered compound displays an appreciable level of potency and selectivity towards USP7...*" and "*...identification of inhibitors that bind selectively to USP7 [...] can be viewed as a step in the right direction and opens an exciting avenue toward potential therapeutic interventions.*"

# HYBRIGENICS

## Press Release

### About Hybrigenics

Hybrigenics ([www.hybrigenics.com](http://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<sup>®</sup>, 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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**Ticker: ALHYG**



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