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## Press Release

### **A NEW APPROACH TO CANCER THERAPY – Results of a placebo-controlled clinical trial published in Nature Communications**

The serendipitous discovery of HAMLET has provided novel insights into how to kill tumor cells without harming healthy tissues. The protein-lipid complex Alpha1-oleate, derived from HAMLET, is now identified as a molecule with significant therapeutic potential. The successful clinical translation and results of a placebo-controlled clinical bladder cancer trial has now been published in Nature Communications ([link](https://www.nature.com/articles/s41467-021-23748-y)).

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The HAMLET complex, discovered in human milk, is formed by the protein alpha-lactalbumin and the fatty acid oleic acid. Early investigations in tumor cells and animal models detected potent therapeutic effects of HAMLET and clinical studies provided further evidence of efficacy.

The synthetic, peptide-based drug candidate Alpha1H is the N-terminal part of HAMLET and reproduces its tumor-killing properties. Detailed molecular characterization of the Alpha1-oleate complex in collaboration with Trinity College Dublin and NTU, Singapore has now allowed for full translation into the clinic in a placebo-controlled clinical trial. The clinical trial program is conducted by Professor M. Babjuk, Charles University and Motol Hospital, Prague in collaboration with The HAMLET group at Lund University and Hamlet Pharma.

Potent effects of the complex were demonstrated in patients with non-muscle invasive bladder cancer (NMIBC). Highly significant differences between the Alpha1-oleate treated patients and the placebo group were detected for several crucial efficacy variables. The complex induced rapid shedding (within 2 hours) of tumor cells and tumor fragments into the urine, resulting in a significant reduction in tumor size.

Treatment was shown to be safe, as no drug-related side effects were observed. The Alpha1-oleate complex is attractive to cancer cells, which internalize it, but end up being killed. Healthy cells are less responsive and extensive toxicity studies have failed to detect adverse effects in the bladder. This low toxicity was confirmed here, as no drug-related side effects were observed in the treatment group. Alpha1-oleate triggered apoptotic cell death in the tumor and by gene expression analysis, massive inhibition of multiple cancer biofunctions was observed.

Bladder cancer is the 4th most common malignancy in the United States and the 5th in Europe. Bladder cancer is associated with the highest life time treatment costs per

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patient of all cancers, followed by colorectal-, breast- and prostate cancer. More than 80% of the patients recur after complete surgical removal of the first tumor and 15% progress to muscle invasive disease. Only three drugs have been approved for non-muscle-invasive disease in about 30 years and access to these drugs is limited by insufficient supply, including BCG immuno-therapy and common chemotherapeutics such as Mitomycin and Epirubicin.

The Food and Drug Administration has declared bladder cancer a great, unmet medical need. This study identifies alpha1-oleate treatment as a novel therapeutic concept and therapeutic option specifically in non-muscle invasive bladder cancer. In view of the low toxicity observed so far, liberal intra-vesical administration in early stage NMIBC might be an interesting approach to postponing the introduction of more toxic and invasive therapeutic options.

*“We hope that the readers will be as fascinated by this new therapeutic concept as we are. Publishing this translational study in such a high profile journal inspires our efforts to make Alpha1H available to cancer patients in the future,”* says Professor Catharina Svanborg, Lund University.

*“This is an important milestone for HAMLET Pharma and we are grateful to all, who have made this possible. We need more evidence but hopefully this could be the gentle chemotherapy of the future,”* says Mats Persson, CEO of Hamlet Pharma Ltd.

### **For more information, please contact**

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### **About HAMLET Pharma**

HAMLET Pharma, listed on Spotlight, develops drugs based on the unique tumoricidal protein-lipid complex, HAMLET, formed by two natural and harmless molecules found in breast milk. Development focuses primarily on drugs, for the treatment and prevention of cancer. HAMLET kills tumour cells and has proven safe in proof-of-concept studies in animal models. Alpha1H is the synthetic variant of HAMLET, which has enabled development of the agent for clinical trials. Alpha1H kills different types of tumour cells and has demonstrated therapeutic effects on bladder cancer in animal models. Hamlet Pharma has one ongoing Phase I/II clinical trial with Alpha1H in patients with bladder cancer, a costly form of cancer that is difficult to treat and intends to expand its activities into other types of cancer. The first results from the ongoing

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clinical Phase I/II study shows no side effects of Alpha1H, indicating that the treatment is safe and well tolerated. Alpha1H also demonstrated clinical efficacy compared with patients who received placebo. In addition, Hamlet Pharma develops BAMLET, which is a molecular complex formed by bovine  $\alpha$ -lactalbumin and oleic acid. Data from animal models suggest that local BAMLET treatment may be effective against colon cancer.



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