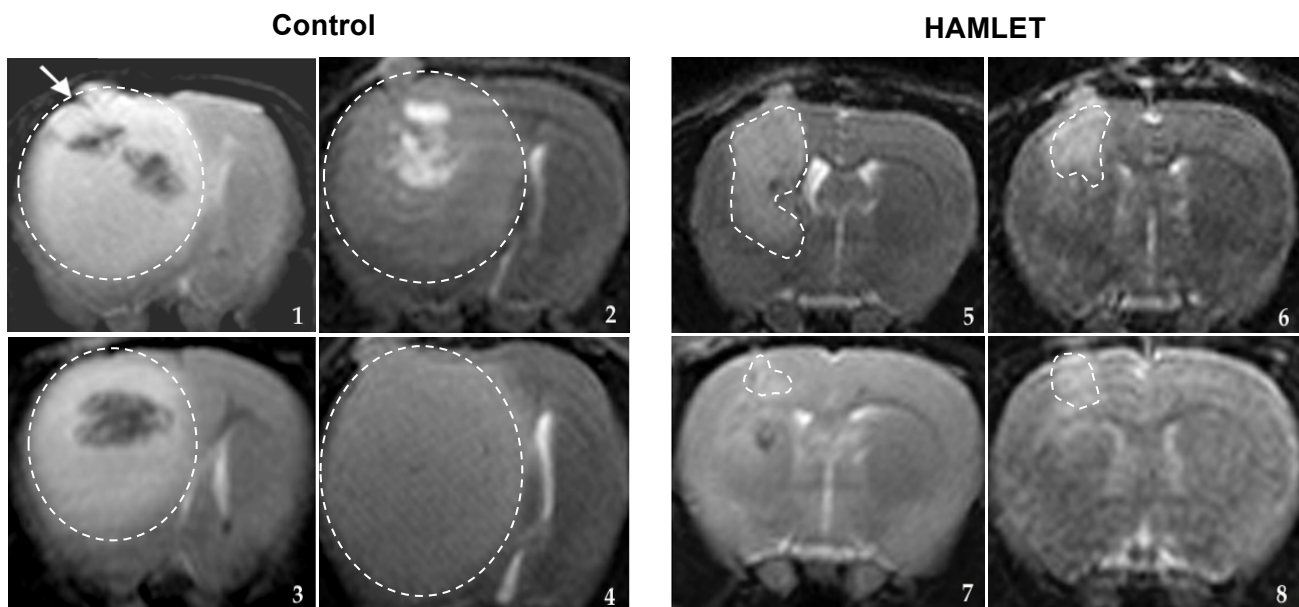


## Newsletter

### Brain tumor therapy – a new cancer indication for HAMLET Pharma

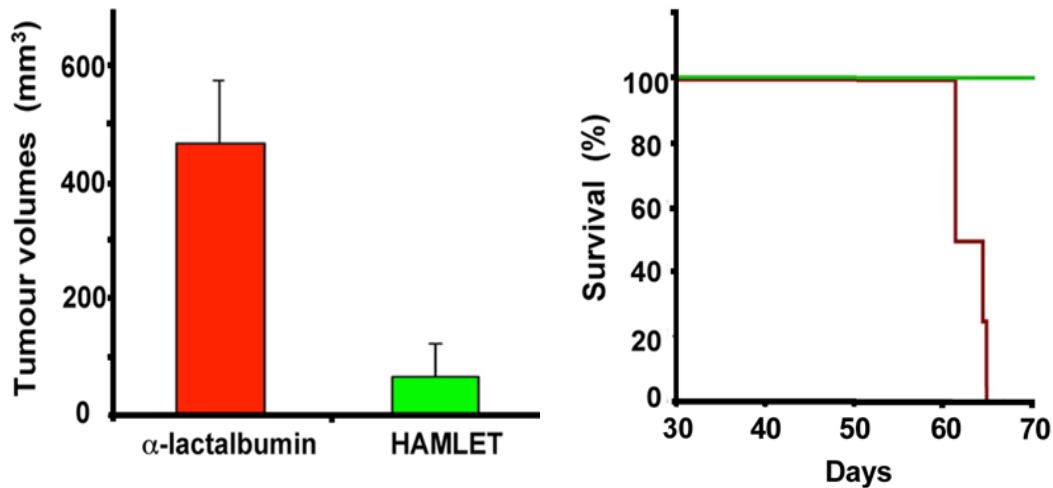
The prognosis of malignant brain tumors remains dismal, even though the development of effective therapies is a prioritized area both in academia and industry. Despite an aggressive treatment protocol consisting of surgery, radiation and chemotherapy, the median survival is only about 15 months. The failure of current therapies is thought to reflect the intrinsic drug and radiation resistance of the tumor cells, the toxicity of the drugs for normal brain tissue, and poor drug penetration from the blood stream through the blood-brain barrier. Further, the tumor cells are extremely invasive, and at the time of diagnosis, the tumor has spread throughout the brain and cannot be completely removed by surgery.

The properties of HAMLET suggest that it may be possible to overcome some of the problems of brain tumor therapy and should allow for a progress towards clinical studies in defined patient groups. *HAMLET shows high tumor specificity, appears to overcome the intrinsic resistance of brain tumor cells, has not shown toxicity for normal brain tissue and can be administered directly to the tumor tissue without having to pass the blood-brain barrier.*



MRI scans, 8 weeks after inoculation

**Figure 1. Effects of HAMLET therapy.** The MRI scans illustrate the differences in tumor size (dotted lines) between HAMLET treated animals (right panels) and controls.



**Figure 2. Effects on tumor volume and survival.** Comparison of HAMLET treatment (green) to controls (red).

Hamlet Pharma's interest in brain tumor therapy is based on successful preclinical research. Early studies showed that Hamlet effectively kills brain tumor cells in the laboratory, including cells that are the most difficult to treat with conventional methods. Hamlet also works therapeutically against human tumors in an animal model, where tumor cells grow invasively in the rat brain. We observed a marked reduction in tumor volume and an increased survival time in HAMLET treated animals compared to the control group, which received an inactive substance.

A second advantage of HAMLET is the diffusion of the substance throughout the brain. As brain tumor cells are known for their invasive properties and spread to remote areas of the brain, an ideal therapeutic agent should be administered along the migratory routes of the tumor cells. In preparation for future clinical studies, we have therefore examined the tissue distribution of infused HAMLET. HAMLET was shown to enter the brain tissue and to spread throughout the injected hemisphere. During infusion, no neurological symptoms or side effects were observed.

In conclusion, the results showed excellent drug penetration, no toxicity in surrounding brain tissue, reduced tumor volume and prolonged survival of treated animals as compared to the controls.

Hamlet Pharma is currently exploring partnerships to develop Alfa1H-based treatments for new cancer indications, especially in the area of brain tumors. Specifically, new therapeutic technologies will be required to evaluate the safety and efficacy of Alpha1H as an intra-tumoral infusion in patients with recurrent malignant gliomas. In preparation for clinical development, it is important to show that Alfa1H is as effective and non-toxic properties as HAMLET in experimental brain



tumor therapy. Due to the successful development of the production and regulatory portfolio of HAMLET for the bladder cancer study, many critical steps have already been initiated.

**For more information, contact**

Catharina Svanborg, Chairman and founder of Hamlet Pharma, +46-709 42 65 49  
[Catharina.svanborg@med.lu.se](mailto:Catharina.svanborg@med.lu.se)

Mats Persson, CEO Hamlet Pharma, +46 705 17 67 57  
[mats.persson@hamletpharma.com](mailto:mats.persson@hamletpharma.com)

*Hamlet Pharma company listed on AktieTorget, is a company engaged in drug development based on a tumoricidal protein-lipid complex, HAMLET, formed by two natural and harmless molecules found in breast milk. The development aims to develop drugs that primarily will be used for the treatment and prevention of cancer. HAMLET effectively kills tumor cells but have also proven to be safe in the proof-of-concept studies done on humans. The substance has demonstrated therapeutic effect on skin papillomas in a placebo-controlled clinical trial and causes shedding of dead cancer cells by injection into the bladder in patients with bladder cancer. Hamlet Pharma intends to initiate a phase II study with Alpha1H in patients with bladder cancer, a difficult and costly cancer form. HAMLET is a registered trademark of Hamlet Pharma.*