



Alpha1H Investigational new drug

Demonstrable strong anti-tumor effects in non-muscle invasive bladder cancer (NMIBC)

- Alpha1H is a synthetic peptide-oleate complex with broad tumoricidal activity and low toxicity.
- Received FDA Fast Track designation.
- Deep understanding of underlying biology.
- Indicated as a neoadjuvant therapy in NMIBC, demonstrating strong therapeutic efficacy in a randomized, placebo-controlled study, without any notable drug-related side effects.

High Unmet Need

- **Bladder cancer:** a global concern with high mortality and financial burden. It affects 390,000 globally and causes 150,000 deaths yearly, with 70% being non-muscle invasive. Over 80% of early-stage patients experience recurrence after initial tumor removal.
- BCG and Mitomycin C are widely used for intravesical chemotherapy of newly diagnosed bladder cancer. Both are associated with side effects and tumor recurrence.
- Most expensive cancer indication in the US, due to high recurrence rates and associated treatment costs and extensive suffering.
- Unmet need for effective, less invasive treatments.
- The bladder cancer market is forecast to reach 5.6 billion USD in 2028.

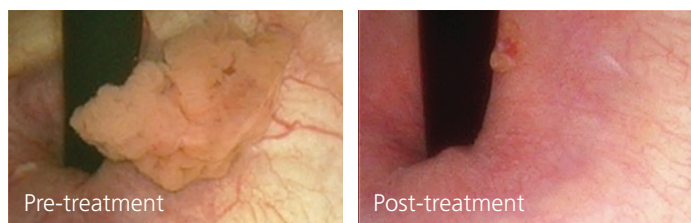
Alpha1H Highlights

- **First-in-class:** Innovative solution targeting early-stage bladder cancer, addressing gaps in non-invasive treatment options.
- Improves treatment response and surgical outcomes, reducing recurrence by targeting residual cancer cells to inhibit regrowth post-surgery.
- Downstaging tumors to limit the extent of cancer spread into deeper layers of the bladder wall.
- Significantly improves outcomes and quality of life for patients.
- Excellent safety profile provides opportunities for combination treatments and portfolio expansion, leveraging existing commercial infrastructure.

Clinical Outcomes

Efficacy and Safety

- Complete or partial response in 82% of patients receiving 8.5mM and 45% at 1.7mM of alpha1-oleate.
- A significant, dose-dependent reduction in tumor size and tumor number was observed compared to placebo.
- Alpha1H is rapidly internalized by tumor tissue in a dose-dependent manner after intra-vesical instillation.
- Triggers a rapid cell shedding increase compared to pre-instillation samples in all treated patients and all visits.
- No drug related safety concerns.

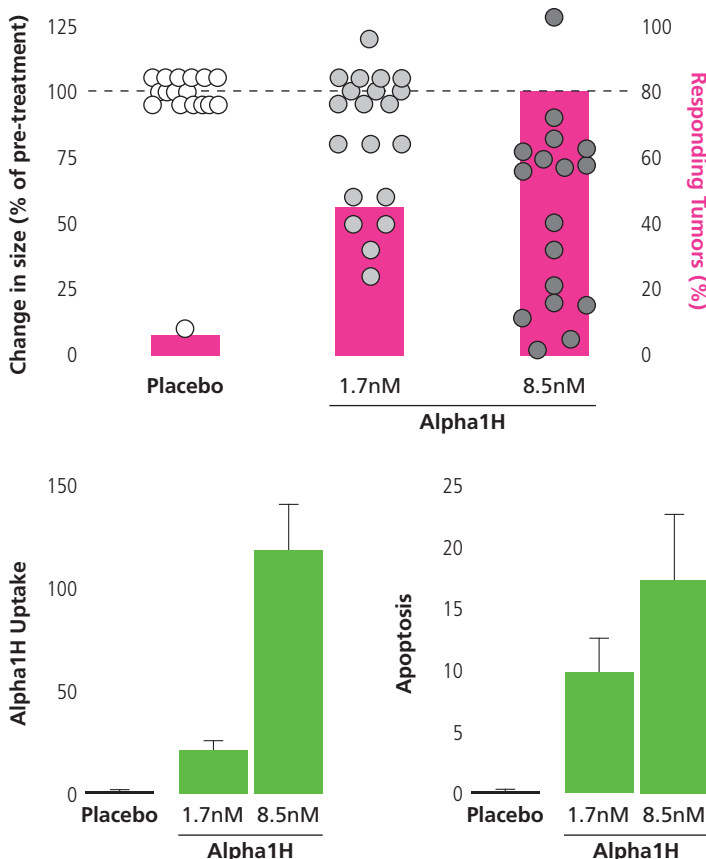


Reduction in tumor size after intra-vesical Alpha1H instillations were evaluated using cystoscopy, comparing pre-treatment to post-treatment images. Individual tumor sizes are shown.

Current Stage

- Part I** A placebo-controlled study: Completed
- Part II** A dose-escalation study: Completed
- Part III** Repeated treatment protocol: Ongoing

Dose-Dependent Reduction in Tumor Number and Size

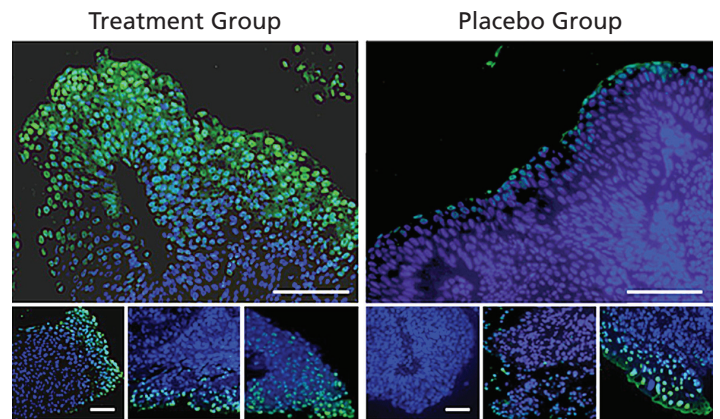




Clinical Outcomes

Alpha1H – Clinical Anti-tumor Effect

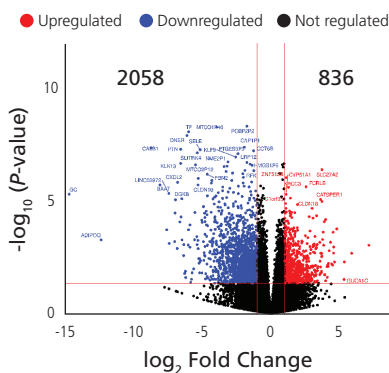
- Due to its structural flexibility, Alpha-lactalbumin forms complexes with oleic acid.
- The complexes effectively kill many different tumor cell types through an apoptosis-like mechanism.
- Figure shows increased apoptotic response (green staining) of tumor tissue in Alpha1H treated patients, compared to placebo.



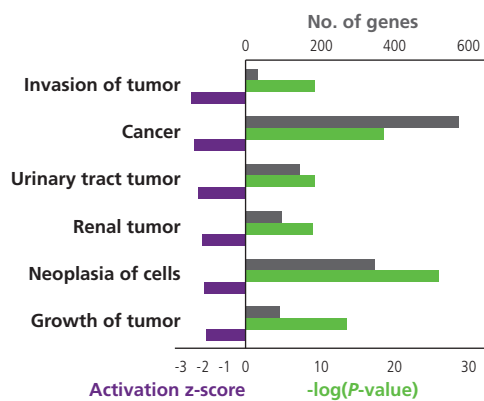
Brisuda et al., 2021, Nature Communications

Alpha1H reprograms gene expression towards health in tumor biopsies

Inhibition of cancer genes (blue) (Alpha1H 8.5 mM vs Placebo)



Diseases and Biofunctions



Reprogramming of gene expression in Alpha1H treated patients

Cancer-related genes accounted for 82% of the significantly regulated genes and 14% were bladder cancer-related. The expression of genes involved in tumor invasion, neoplasia, tumor growth, and urinary tract tumors was strongly inhibited.

GMP drug manufacturing

- Manufacturing carried out by GMP certified multinational drug production corporations.
- Large-scale peptide synthesis by the Polypeptide group; followed by Alpha1H production by Rechon Life Sciences.
- Well-defined storage conditions and stability.

Strong IP Portfolio

- Hamlet owns 15 patent families including 8 families for cancer therapy.
- USA, EU, Asia patents valid until 2038 guarantee lasting protection and innovation potential.

Pipeline and R&D

- Alpha1H in NMIBC (Ph2) and brain (pre-clinical).
- IL-1RA against bacterial infections and pain (Ph2).
- Promising assets with proven efficacy in animal models relevant to human disease.

Hamlet BioPharma

An innovative pharmaceutical company with a broad and strong portfolio of projects for the treatment of cancer and infections.

Hamlet is looking to out-license Alpha1H to a pharmaceutical company, to take on clinical development and commercialisation.

Hamlet BioPharma has developed a strong discovery and drug development platform and is continuing the development of its pre-clinical assets.

Further Information



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