Hamlet BioPharma Announces the Completion of the Alpha1H Phase II Study in Non-Muscle Invasive Bladder Cancer

Hamlet BioPharma, the pharmaceutical company, specializing in the development of drugs for cancer and infections, announces the completion of the successful Phase II clinical trial of the company's drug candidate Alpha1H in patients with cancer in the urinary bladder. The final clinical study report based on extensive analyses of clinical and laboratory data highlights the potent treatment effects. All primary and secondary endpoints of safety and efficacy were reached. The final clinical report has been completed and submitted to the FDA (Food and Drug Administration, USA).

"The final clinical report's consistent efficacy outcomes and favorable safety profile are highly encouraging. The strength of the data provides compelling evidence of Alpha1H's potential to become a much-needed proactive treatment option, and we look forward to advancing it in our regulatory discussions. We are committed to bringing this innovative therapy to patients as quickly and safely as possible. These results mark a major milestone for Hamlet BioPharma and for people with cancer in the urinary bladder. The study was made possible through close collaboration with leading universities and medical centers, including Lund University, Sweden, Motol University Hospital, Czechia and Linnane Pharma AB, whose combined expertise ensured robust design, execution, and analysis," said Catharina Svanborg, MD, PhD and CEO Hamlet BioPharma.

Summary from the Clinical Study Report

- **Efficacy was formally confirmed – 80% of tumors responded to Alpha1H, with 59% average tumor size reduction in the high-dose group**
- **Molecular and cellular secondary endpoints**
  Alpha1H reaches tumor tissue, triggers **tumor cell apoptosis**, and causes rapid **shedding of tumor cells into the urine**.

- **Durable effect shown across repeated treatment cycles**
  Patients who received a second round of instillations maintained clinical benefit, showing continued **tumor cell death and reduction** — demonstrating the treatment's **lasting efficacy**, even with repeated dosing.

- **BCG-like immune activation confirmed – but faster**
  Cytokine profiling shows Alpha1H activates a **broad immune response overlapping with BCG**, the current standard of care. However, Alpha1H triggers this response **more rapidly and without lasting side effects**.

- **Suppression of cancer genes and pathways**
  Advanced RNA sequencing revealed Alpha1H **downregulated over 700 of ~800 cancer-related genes**, including key oncogenes like **RAS** and **GJA1**. This provides a mechanistic explanation for its unique tumor-killing profile.

- **Strong safety profile confirmed over longer follow-up – no serious side effects**
  No drug-related serious adverse events occurred, even after **higher or repeated dosing**. Mild local side effects were **comparable to placebo**, and no systemic effects were observed, consistent with Alpha1H's **local mechanism of action**.

Why This Matters

Clinical Value

The results reinforce Alpha1H as a potential breakthrough therapy for NMIBC patients. Unlike current treatments that are often given after surgery, Alpha1H is used before surgery to reduce tumor burden, potentially allowing for less invasive procedures and improved outcomes. Importantly, Alpha1H achieved these effects without the toxic side effects associated with chemotherapy or systemic immunotherapy.

Differentiated Mechanism and Positioning

Alpha1H works through a unique mechanism: it enters tumor cells, causes programmed cell death (apoptosis), and activates the body's own immune response. Unlike BCG, which is limited by supply issues and safety concerns, Alpha1H is a well-tolerated, synthetic compound with strong stability and safety – even after repeated dosing. It acts locally in the bladder, without systemic exposure, making it easier to deliver and better suited for broader clinical use.

Commercial Opportunity
Each year, more than 500,000 patients globally are diagnosed with non-muscle invasive bladder cancer. Many do not respond to BCG or other interventions and experience relapses. With Fast Track designation from the FDA and patent protection in key markets, Alpha1H is well positioned to meet this urgent unmet need. The global NMIBC market is estimated at over USD 3 billion[1] annually. If approved, Alpha1H could serve as a neoadjuvant treatment, an add-on to standard of care, or a standalone therapy – representing a strong commercial opportunity. The results from the final clinical report will also strengthen our position in our dialogue with potential partners.

About the Study

The Phase II/III trial was designed to evaluate the efficacy and safety of Alpha1H in about 60 subjects. Participants were randomized to receive either Alpha1H or placebo of care over about one month. The primary endpoints were Adverse Events, Characteristics of papillary tumors, Quantification of cell shedding in urine and the secondary endpoints included Induction of apoptosis, Histopathology scoring, Tumor response to Alpha1H by gene expression analysis, Proteomic analysis of immune markers in urine. Safety was assessed for all patients, who received treatment with investigational product or placebo.

These achievements were made possible by close collaborations with leading universities and medical centers. The trial brought together leading researchers and clinicians from Lund University in Sweden, Motol University Hospital in Czechia and Linnane Pharma AB in Sweden. By combining expertise across disciplines and geographies, the partnership ensured rigorous study design, high-quality data collection, and robust analysis. This collaborative approach not only advanced the development of Alpha1H but also contributed valuable insights to the broader scientific community working to improve outcomes for patients with bladder cancer.

Next Steps

Hamlet BioPharma is engaged with FDA to discuss submission requirements and timelines for a Phase III study. The clinical study data and other progress is regularly published in international, peer-reviewed journals.

About Alpha1H

The drug candidate Alpha1H kills tumor cells quickly and selectively and shows strong anti-cancer effects in animal models of and patients with bladder cancer. Hamlet BioPharma announced that the drug candidate Alpha1H showed potent treatment effects in patients with cancer of the urinary bladder. The extensive data analysis of the complete study material, which includes safety, clinical data and advanced molecular and tissue analyses has now been completed and final clinical report prepared for regulatory purposes.

About Hamlet BioPharma

Hamlet BioPharma is an innovative biotechnology company that develops scientific discoveries into drugs for the treatment of cancer and infections. The goal is to address unmet medical needs in large patient groups in need of improved cancer treatments or alternatives to antibiotics. The company is leveraging highly innovative scientific discoveries and an extensive IP portfolio, to take these innovative drugs through mechanistic and preclinical phases, through the development of drug production technology to the clinic. Three projects in clinical development are in Phase II trials.

The company is listed on Spotlight Stockmarket, ticker HAMLET.

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[1] Transparency Market Research; http://www.transparencymarket-research.com/non-muscle-invasive-bladder-cancer-market.html