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Pressrelease

Strong anti-tumor effects detected in Alpha1H treated patients, for a combination of clinical and molecular endpoints

Hamlet BioPharma, the pharmaceutical company with a strong portfolio of projects for the treatment of cancer and infections, announces the results for the investigational drug Alpha1H, in patients with bladder cancer. The analysis of the combined data set from two clinical study parts has now been completed and submitted for publication. Treatment resulted in a significant reduction in tumor size in 82% of tumors treated with the higher and 45% of tumors treated with the lower dose of Alpha1H. Hamlet BioPharma is now proceeding with the third part of the clinical trial to optimize the design of further clinical trials in dialogue with the FDA (US Food and Drug Administration).

Facts about bladder cancer

The prevalence of bladder cancer is about 1/4000, making this the fourth most common malignancy in the United States and fifth in Europe¹. More than 80% of patients with early bladder cancer recur after complete surgical removal of the first tumor and 15% patients develop muscle invasive disease². As a result of disease progression, bladder cancer has considerable impact on day-to-day functioning, impairing the overall quality of life of affected individuals presenting persistent challenges throughout their treatment and during the surveillance process. There is therefore an urgent need to develop a safe and effective treatment that could prevent recurrence and stop disease progression.

Analysis of our investigational drug Alpha1H

Hamlet BioPharma develops the investigational drug Alpha1H, which rapidly kills bladder cancer cells and other tumor cells and has potent therapeutic effects in animal models of bladder cancer. Clinical effects in patients with bladder cancer have been demonstrated in a

¹ Source: Antoni, S. *et al.* Bladder cancer incidence and mortality: a global overview and recent trends. *Eur. Urol.* **71**, 96–108 (2017).

² Source: van Rhijn, B. W. *et al.* Recurrence and progression of disease in non–muscle invasive bladder cancer: from epidemiology to treatment strategy. *Eur. Urol.* **56**, 430–442 (2009).

randomized, placebo-controlled study of patients with non-muscle invasive bladder cancer. In a second part of the clinical study, patients were treated with increasing concentrations of Alpha1H and the effects were defined, compared to a placebo group.

The combined data analysis from the two clinical study parts has now been completed, including extensive laboratory analyses of patient samples. The results, which have been submitted for publication are summarized below.

1. Reduction in tumor size

Treatment resulted in a complete or partial response in 82% of the tumors treated with 8.5 mM and in 45% treated with 1.7 mM of Alpha1H.

2. Changes in the tumor

- Treatment resulted in tumor fragmentation and release of fragments and cells into the urine. This effect increased markedly with the higher dose of Alpha1H.
- The tumor cells died by apoptosis, after taking up Alpha1H.
- Tissues left in the patient after treatment had lost their tumor characteristics and become more “healthy-like”, as shown by total gene expression analysis.

Clinical use of Alpha1H

A novel neoadjuvant therapy holds the promise of improving the standard of care for multiple reasons.

- First, it could lead to an enhanced tumor response to subsequent treatment, facilitating more effective surgical removal.
- Second, this approach might reduce the recurrence rate by targeting residual cancer cells that could otherwise lead to tumor regrowth post-surgery.
- Third, by down-staging tumors, the therapy could limit the extent of cancer spread into deeper layers of the bladder wall, potentially enabling less invasive surgical interventions.

The investigational drug, Alpha1H, has the potential to be an effective neoadjuvant therapy for several key reasons.

- There is limited or even no toxicity associated with the administration of Alpha1H; nonclinical studies of Alpha1H all found no evidence of symptoms or signs or effects on body weight or organ weights, gross pathology or histopathology.
- An ongoing clinical trial evaluating the safety and efficacy of Alpha1H in Adult Patients with Non-Muscle Invasive Bladder Cancer Awaiting Transurethral Surgery (Study HP002-001), has found that Alpha1H is safe and well tolerated in this patient population.
- Clinical data, from this trial, suggests that Alpha1H instillations result in dose-dependent effects on both tumor size and cell shedding.

Hamlet BioPharma is now proceeding with the third part of the clinical trial to optimize the design of further clinical trials in dialogue with the FDA. Overall, an effective neoadjuvant therapy could significantly enhance treatment approaches, improving outcomes and quality of life for patients with this condition.

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