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CatalYm Presents Phase 2 Data in Neoadjuvant Bladder Cancer Demonstrating Substantial Increase of Anti-Tumor Activity for Visugromab in Combination with PD-1 Inhibitor at ESMO

- **Visugromab combined with PD-1 inhibitor, nivolumab, more than quadrupled the rate of pathological Complete Response (pCR; 33.3% vs. 7.1%) and substantially increased Major Pathologic Response (MPR; 66.7% vs. 21.4%) rate compared to nivolumab alone**
- **Combination achieved a fourfold increase in radiologic Objective Response Rate (rORR) (60% vs. 14.3%)**
- **Visugromab + nivolumab showed good tolerability in line with expected checkpoint inhibitor safety profile and all previous and ongoing visugromab studies**
- **In the visugromab treatment arm, more patients retained their bladders after tumor resection compared to the nivolumab control arm**
- **The data was presented today by the trial's Principal Investigator, Prof. Dr. Andrea Necchi, as an oral late-breaker at the ESMO Congress 2025**

Munich, Germany and San Francisco, USA, October 17, 2025 – CatalYm, a world-leader in neutralizing GDF-15 in cancer and cachexia, today presented compelling primary results from the Phase 2 GDFATHER-NEO trial in an oral late-breaking session at the European Society of Medical Oncology (ESMO) Congress 2025. The data demonstrated that Growth Differentiation Factor-15 (GDF-15) blockade by visugromab enhanced the efficacy of PD-1 inhibition by nivolumab as a neoadjuvant therapy in muscle-invasive bladder cancer (MIBC), with a similar safety profile compared to nivolumab plus placebo. Visugromab is a humanized, monoclonal antibody designed to neutralize the tumor-derived cytokine GDF-15 which plays a central role in immune suppression and anti-PD-(L)1 treatment resistance.

Prof. Dr. Andrea Necchi, Director of Genitourinary Medical Oncology at IRCCS San Raffaele Hospital and Principal Investigator of the trial, presented the late-breaking data, underscoring the potential of the visugromab combination as a new treatment option in this indication, where standard chemotherapy is hindered by limited activity and significant off-target toxicity.

"The impact seen in this checkpoint naive setting demonstrates the activity of visogromab with a PD-1 inhibitor in an earlier line of treatment and builds on the benefit seen in patients with refractory disease," said **Sujata Rao, MD, Chief Medical Officer at CatalYm**.

"MIBC still has a poor 5-year survival rate of around 50%. As many patients are diagnosed at an older age and/or with existing comorbidities, a significant number are not eligible for aggressive standard-of-care neoadjuvant chemotherapy, and a proportion refuse to undergo radical cystectomy after neoadjuvant therapy. Previous combinations of chemotherapy with

anti-PD-(L)1 therapy have shown limited or non-additive clinical benefit with regards to the pathological response. There is a clear need for efficient new treatment regimens endowed with minimal side effects to improve patient outcomes," said **Prof. Dr. Andrea Necchi, Director of Genitourinary Medical Oncology at IRCCS San Raffaele Hospital and Principal Investigator of the trial**. "These early results for the novel visugromab/anti-PD-1 combination are promising, demonstrating enhanced anti-tumor activity. Moreover, its good safety and tolerability profile suggest that even more vulnerable or frail patients may potentially benefit from this new treatment approach."

The multicenter, single-blinded Phase 2 GDFather-NEO trial (NCT06059547) investigates visugromab plus nivolumab vs. nivolumab plus placebo, in cisplatin-ineligible/refusing patients with newly diagnosed MIBC that had not spread to the lymph nodes or distant organs. The combination was administered every four weeks for three cycles. Radical cystectomy or re-transurethral resection of the bladder tumor (re-TURBT) was performed 4-8 weeks after the last dose. Key endpoints of the trial are pathological complete response (pCR)[1], major pathologic response (MPR)[2] and radiologic objective response rate (rORR)[3].

Key trial results

- Out of 31 patients enrolled with a median age of 76 years, 29 were efficacy-evaluable (n=15 in the nivolumab + visugromab (N+V) arm, n=14 in the nivolumab + placebo (N+P) arm) at the data cut-off on September 29, 2025.
- Efficacy analysis demonstrated substantially higher pCR (33.3% vs. 7.1%) and MPR (66.7% vs. 21.4%) in the N+V arm compared to the N+P arm.
- The rORR (as per RECIST v1.1 criteria) was approximately four times higher in the N+V combination with 60.0% (7 complete responses, 2 partial responses), compared to 14.3% (0 complete responses, 2 partial responses) in the N+P arm.
- The visugromab combination performed superior across all clinical tumor stages, and dominantly in PD-L1-positive patients (CPS≥10%)[4].
- More participants in the visugromab combination arm were eligible to receive the bladder-sparing re-TURBT surgery approach (n=6 in the N+V arm vs. n=3 in the N+P arm).
- Based on early safety and tolerability assessment, the N+V combination demonstrated good tolerability, in line with the expected safety profile of nivolumab monotherapy.
- Most Treatment-Related Adverse Events (TRAEs) were mild to moderate, with some Grade 3 clinical and laboratory events as expected in this population. No differences in type, severity or frequency of events were observed between the two trial arms.
- Baseline serum GDF-15 levels and immune cell profile were comparable between the N+V and N+P arms.

[1] pCR is achieved when there is no residual cancer (ypT0) in the surgically removed bladder tissue after neoadjuvant therapy

[2] MPR (ypT≤1) in the primary tumor after neoadjuvant therapy is achieved when the tumor's remaining size is significantly reduced, without invasion of the muscle layer

[3] rORR refers to the proportion of trial participants whose tumors show a significant reduction in size or complete disappearance, as determined by medical imaging (radiology) after a specific treatment

[4] Combined Positive Score, a method for measuring PD-L1 protein expression on cancer cells, lymphocytes, and macrophages in a tumor sample, ranging from 0% to 100%.

"Our latest data update indicates that we are on the right path with our GDF-15 neutralizing approach as a powerful new regimen in cancer treatment," said **Scott Clarke, Chief Executive Officer at CatalYm**. "These results extend our clinical findings into earlier lines of therapy and demonstrate proof-of-concept for visugromab in another hard-to-treat tumor indication. We are committed to rapidly advancing our targeted Phase 2b program, an important next step on our mission to improve the outcomes for a broad range of cancer patients in need."

The Phase 2 GDFATHER-NEO trial is still ongoing with biomarker analysis of blood and tumor microenvironment focused on treatment-induced changes specific to visugromab therapy as well as a final safety assessment. CatalYm is conducting a broad Phase 2b clinical program with randomized trials in 1L and 2L non-small cell lung cancer, 2L hepatocellular carcinoma and cachexia underway.

About Visugromab
Visugromab is a monoclonal antibody that neutralizes Growth Differentiation Factor-15 (GDF-15), a locally acting immunosuppressant produced by tumors which fosters resistance to therapy and drives cachexia in people with cancer. Neutralizing GDF-15 with visugromab reverses key cancer resistance mechanisms and induces an efficient anti-tumor response by enabling immune cell activation, proliferation and induction of interferon-γ. In addition, visugromab also mitigates cancer cachexia, a severe condition affecting a significant number of advanced cancer patients by inhibiting the activation of the GFRAL pathway in the brainstem, a key driver of weight loss and appetite suppression in cancer patients.

About CatalYm
CatalYm is developing visugromab, a first-in-class anti-GDF-15 antibody, in solid tumors and cachexia. In its first-in-human Phase 1/2a study, visugromab demonstrated durable anti-tumor efficacy with long-lasting objective responses in relapsed and refractory metastatic solid tumor patients in combination with anti-PD-1 treatment. In addition, data from the same study demonstrated that visugromab can significantly counteract the effects of cachexia in these patients. This data was published in *Nature* and presented at the International Conference on Sarcopenia, Cachexia & Wasting Disorders. CatalYm is now advancing visugromab into multiple Phase 2b studies including first-line metastatic NSCLC (NCT07098988) and cachexia (NCT07112196).

Founded in 2016 and based in Munich, Germany and San Francisco, USA, CatalYm is backed by leading international investors including Canaan Partners, Bioqube Ventures, Forbion, Omega Funds, Gilde Healthcare, Jeito Capital, Novartis Venture Fund, Vesalius, Brandon Capital, Bayern Kapital, BioGeneration Ventures, and Coparion.

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