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CatalYm Presents Long-Term Phase 1/2a Data Confirming Sustained Responses with Visugromab in CPI-Refractory Tumors at ESMO 2025

- **Median duration of response exceeded 32 months in non-squamous non-small cell lung cancer (nsqNSCLC), 28 months in urothelial cancer (UC) and 19 months in hepatocellular carcinoma (HCC), with more than half of responses ongoing at the data cut-off**
- **Majority of responders experienced deeper and longer-lasting responses when compared to prior anti-PD-1/PD-(L)1 treatment**
- **GDF-15 blockade re-sensitized tumors to immunotherapy and demonstrated favorable safety and tolerability in heavily pretreated patients**
- **Visugromab mitigated cachexia in affected patients, supporting dual benefit in tumor control and weight gain**
- **The data is presented today by Principal Investigator Prof. Dr. Ignacio Melero in the proffered paper session "Investigational Immunotherapy" at the ESMO Congress 2025**

Munich, Germany and San Francisco, USA, October 20, 2025 – CatalYm, a world leader in neutralizing GDF-15 in cancer and cachexia, today announced updated long-term data from its ongoing GDFATHER-1/2a trial (NCT04725474) at the European Society of Medical Oncology (ESMO) Congress 2025. The data provide further evidence that Growth Differentiation Factor-15 (GDF-15) blockade by visugromab can reverse resistance to PD-(L)1 treatment in patients with advanced solid tumors and deliver durable responses in patients who have relapsed or progressed on prior checkpoint inhibitor treatment.

Visugromab is a humanized monoclonal antibody designed to neutralize the tumor-derived cytokine GDF-15, which plays a key role in immune suppression and resistance to therapy. The updated dataset highlights visugromab's potential to reinvigorate immune responses in difficult-to-treat tumor types and patient populations with limited treatment alternatives.

"The durability of responses we are seeing with visugromab in this heavily pretreated, late-stage population is particularly remarkable," said **Prof. Dr. Ignacio Melero, Co-Director of Immunology and Immunotherapy at CIMA, Universidad de Navarra, and Principal Investigator** of the trial. "To observe ongoing responses extending beyond two and sometimes even three years in patients who had progressed on prior checkpoint inhibition is both encouraging and remarkable in this setting. These data underscore the potential of GDF-15 blockade to establish immune sensitivity in resistant tumors."

Key trial results

- Out of 199 patients enrolled, 77 patients with either non-squamous NSCLC (n=22), urothelial cancer (n=27) or hepatocellular carcinoma (n=28) received visugromab in combination with nivolumab, all with progression on prior anti-PD-(L)1 therapy.
- Confirmed objective response rates (RECIST 1.1) were 18.2% (4/22) in non-squamous NSCLC, 18.5% (5/27) in urothelial cancer, and 14.3% (4/28) in hepatocellular carcinoma, including 5 complete responses and multiple deep partial responses across cohorts.
- Median duration of response reached 32.2 months in non-squamous NSCLC, 28.8 months in urothelial cancer, and 19.4 months in hepatocellular carcinoma. At data cut-off, 53.8% (7 of 13) of responses were ongoing across all three cohorts.
- In 76.9% (10/13) of responders, the duration of response on visugromab plus nivolumab exceeded that of their prior checkpoint inhibitor treatment; 61.5% of responders also achieved a deeper response than previously recorded.
- The combination was well tolerated, with treatment-related adverse events (TRAEs) reported in 58.4% of patients. Most TRAEs were Grade 1 or 2 and manageable. Grade ≥3 TRAEs occurred in 13% of patients and included expected immune-related events.
- In cachectic patients, treatment was associated with clinically meaningful weight gain, indicating potential quality-of-life benefit.

“Our long-term follow-up data suggest that GDF-15 blockade with visugromab may offer meaningful and sustained benefit to patients who progress or do not respond to immunotherapy,” said **Sujata Rao, MD, Chief Medical Officer at CatalYm**. “The duration and depth of responses we continue to observe support further development of visugromab in earlier treatment lines, where maintaining immune sensitivity is critical.”

“The growing body of clinical data for visugromab confirms our conviction that GDF-15 neutralization provides a novel strategy to overcome immune resistance and support immune reactivation,” said **Scott Clarke, Chief Executive Officer at CatalYm**. “With several Phase 2b trials now underway, we are focused on translating this approach into improved outcomes across different patient populations and tumor types.”

GDFATHER-1/2a (NCT04725474) is a multicenter, open-label Phase 1/2a trial evaluating visugromab in combination with an anti-PD-1 inhibitor in patients with advanced solid tumors. Phase 1 dose escalation comprised one cycle of monotherapy followed by combination treatment, while Phase 2a focused on expansion cohorts e.g. in non-squamous NSCLC, urothelial cancer, and hepatocellular carcinoma that had progressed on prior anti-PD-(L)1 therapy. Patients received visugromab at the recommended Phase 2 dose plus nivolumab every two weeks. Key endpoints included objective response rate, duration of response, and translational markers of immune activation.

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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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