UNDER EMBARGO UNTIL JUNE 2, 2024, 11:30 AM CDT / 6:30 PM CET

CatalYm Reports Impressive and Lasting Responses Including Multiple Complete Responses in Heavily Pretreated, Late- to Last-Line Metastatic NSCLC, Urothelial and Hepatocellular Cancer Patients Treated with Visugromab/Nivolumab Combination

- The results include data from three main study cohorts: In the non-squamous non-small cell lung cancer (NSCLC) cohort, an Objective Response Rate (ORR) for NSCLC of 19.0% (4/21), with 2 Partial Responses (PR) and 2 Complete Responses (CR) was observed. In the UC cohort, the ORR was 19.2% (5/26), with 4 PRs and 1 CR. In HCC, data from the first 20 patients showed an ORR of 20.0% (4/20), with 3 PRs and 1 CR in the early readouts.
- Exceptional Duration of Response (DoR) was observed with mean and median surpassing 15 months for NSCLC and 14 months for UC cohorts at data cut-off, with 77% of all responses still ongoing.
- All responses are confirmed as per RECIST 1.1, with the 4 CRs all ongoing; 3 of the 4 CRs had not experienced a CR with any prior systemic treatment, including initial/prior anti-PD-(L)1 treatment.
- 53.3% of all responders (PR and CR) experienced a response level/depth as per RECIST 1.1 that had not been achieved on prior/initial anti-PD-(L)1 treatment, indicative of deep, lasting immune-mediated tumor control that has not been experienced with prior/initial anti-PD-(L)1 treatment.
- The data were presented by the International Coordinating Investigator, Ignacio Melero, MD, PhD, in an oral presentation at the ASCO Annual Meeting 2024.

Munich, Germany, June 2, 2024 – CatalYm today announced positive new follow-up results from its ongoing "GDFATHER" Phase 1/2a trial (**GDF**-15 **A**ntibody-media**T**ed **H**uman **E**ffector Cell **R**elocation Phase 1/2a) (NCT04725474) in an oral presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting 2024 in Chicago. Featuring matured data from the non-small cell lung cancer (NSCLC) and urothelial cancer (UC) cohorts, as well as novel, early data for the hepatocellular carcinoma (HCC) cohort and an additional biomarker cohort, the presentation highlighted that treatment with a combination of CatalYm's lead candidate, visugromab, combined with the anti-PD-1 antibody nivolumab achieves compelling deep and durable anti-tumoral activity in anti-PD-1/PD-L1 relapsed/refractory patients as defined by strict criteria. The combination of visugromab and nivolumab further demonstrates an excellent safety and tolerability profile. Visugromab is a monoclonal antibody designed to neutralize the tumor-produced Growth Differentiation Factor-15 (GDF-15), a central mediator of immune resistance to cancer therapies.

The oral presentation by International Coordinating Investigator Prof. Ignacio Melero, MD, PhD, Co-Director of Immunology and Immunotherapy (CIMA) at the Universidad de

Navarra, Pamplona/Spain, provides further evidence for the potential of visugromab to improve the clinical response depth and duration for patients with advanced, metastatic tumors.

"These recent data continue to impress us with the significant ability to generate deep partial and complete responses with enormous durability in heavily pretreated patients that have failed their approved therapies including prior anti-PD-(L)1 treatment as defined by strict criteria," **said Prof. Dr. Eugen Leo, Chief Medical Officer at CatalYm**. "Remarkably, more than half of all responders experienced a response level/depth as per RECIST 1.1 (up to lasting CR) that had not been achieved on their prior/initial anti-PD-(L)1 treatment. This demonstrates that GDF-15 blockade by visugromab can induce a remission depth and durability, and long-term immunologic tumor control that other cancer immunotherapies could not induce. Visugromab may have the potential to bring us a major step closer to finally providing deep long-term tumor control and potentially cure for metastatic solid tumor patients with non-squamous NSCLC, UC, and HCC."

Summary of Key Clinical Results:

- The matured results from the Phase 2a indication-specific cohorts for NSCLC, UC, and all HCC so far treated show the following Objective Response Rates (ORR):
  - non-squamous NSCLC: ORR of 19.0% (4/21), with 2 partial responses (PR) and 2 complete responses (CR)
  - UC: ORR of 19.2% (5/26), with 4 PR and 1 CR
  - HCC: ORR of 20.0% (4/20), with 3 PR and 1 CR in the primary early readout
- The DoR results indicate that visugromab may have a significant impact on deepening and prolonging responses to checkpoint inhibitor (CPI) therapy:
  - non-squamous NSCLC and UC: mean DoR surpassed 15 and 14 months, respectively, with 7/9 responses ongoing
  - HCC: data still maturing with 12 patients ongoing on study treatment at data cut-off in the newly initiated cohort
- Overall, in a total of 90 patients with the above indications treated in various cohorts (including a biomarker-oriented cohort with varying tumor types), an ORR of 16.7% across all three main tumor types is currently observed, with data partly maturing further.
- In totality, 8/15 RECIST 1.1 responders (53.3%) experienced a response level/depth (PR, CR) that had not been achieved with their initial CPI therapy:
  - Complete responses (CRs): Among the 4 patients who achieved CR, 3 had no prior CR on any treatment regimen, including previous CPI treatments.
  - Partial responses (PRs): 5/11 patients who achieved PR had no RECIST 1.1 response at all on prior CPI treatments.
- The combination of visugromab with nivolumab showed excellent overall tolerability, with a safety profile very similar to nivolumab treatment alone:
  - most Treatment-Emergent Adverse Events (TEAEs) were mild to moderate
  - only 8.1% of patients experienced severe TEAEs (Grade ≥ 3)

- Patient sample analyses strongly support the involvement of GDF-15 in the creation of an immunosuppressed tumor microenvironment and highlight the therapeutic potential of GDF-15 neutralization in these indications:
    - Elevated serum levels of GDF-15 were shown to correlate inversely with intratumoral T cell numbers and their proliferation in samples of patients with non-squamous NSCLC, UC, and HCC.
    - Blockade of GDF-15 by visugromab, in combination with nivolumab treatment, resulted in the rise of serum interferon-γ levels, a critical cytokine for the stimulation of an immune response, in NSCLC and UC patients.
    - Blockade of GDF-15 by visugromab, in combination with nivolumab treatment, resulted in the rise of serum interferon-γ inducible chemokines CXCL9 and CXCL10 which remained significantly elevated over the monitoring period of six weeks.
- Additional preclinical studies indicated that GDF-15 was significantly elevated by standard cancer treatments, specifically e.g. platinum-based chemotherapies, checkpoint inhibitor treatment, and respective combinations. This is another layer of support for the significant role of GDF-15 in the development of immune resistance to these treatment regimens and reason to develop visugromab in the first- and second-line settings where these agents are in standard use.

"We have designed a broad Phase 2b development plan to thoroughly investigate where visugromab can have its biggest impact for patients. These new results further confirm that neutralizing GDF-15 may be a critical strategy in overcoming cancer therapy resistance by breaking immunosuppressive barriers that currently limit therapeutic outcomes," **said Phil L'Huillier, Managing Director and Chief Executing Officer at CatalYm**. "Validated by the strong clinical and preclinical data on visugromab's mechanism of action and GDF-15's relevance in therapeutic resistance to date, we will now investigate the clinical benefit of visugromab in first- and second-line treatment and there in combination with standard-of-care that has been shown to increase GDF-15 levels further on top of the tumoral production of GDF-15. It is our goal to significantly improve patient responses and establish a new benchmark in cancer care."

The Phase 2a GDFATHER-2 program was initiated in March 2022. The ongoing study consists of two segments with up to seven cohorts and is expected to enroll over 200 patients in various cohorts. An evaluation of potential response-predictive biomarker(s) is ongoing. Based on a previous positive readout presented at the ESMO IO Congress in 12/2023, CatalYm is in preparations to launch randomized, controlled studies in several major cancer indications in combination with checkpoint inhibitors and standard-of-care in first- and second-line treatment in the first half of 2025.

Presentation Details

Title: Effects of neutralization of tumor-derived immunosuppressant GDF-15 on anti-PD-1 activity in anti-PD-(L)1 relapsed/refractory non-squamous NSCLC, urothelial, and hepatocellular cancer

Presenter: Dr. Ignacio Melero Bermejo, MD | Clinica Universidad de Navarra
Abstract Number: 2513
Date and time: Sunday, June 2, 2024, from 11:30 AM – 1:00 PM CDT

About the GDFATHER-2 Trials
The GDFATHER-2 trial (**GDF**-15 **A**ntibody-mediaTed **H**uman **E**ffector cell **R**elocation Phase 2) (NCT04725474) is the Phase 2a part of the ongoing Phase 1/2a trial with several cohorts investigating the effect of visugromab (CTL-002) in combination with a PD-1 checkpoint inhibitor in patients in various advanced-stage/last-line and by strict criteria anti-PD1/PD-L1 relapsed/refractory solid tumor types. The study can enroll up to 200 patients and has extensive biomarker-evaluations integrated to assess for potential responder patient population identification or similar.

About Visugromab (CTL-002)
Visugromab is a monoclonal antibody that neutralizes the tumor-derived Growth Differentiation Factor-15 (GDF-15), a locally acting immunosuppressant fostering immunotherapy resistance. Neutralizing GDF-15 with visugromab reverses key cancer resistance mechanisms to reinstate an efficient anti-tumor response by reenabling immune cell activation and tumor infiltration. Visugromab has demonstrated a good safety profile and potent and durable anti-tumor efficacy in combination with anti-PD-1 treatment in advanced cancer patients The antibody is currently being investigated in ongoing Phase 2a studies in multiple solid tumor indications.

About CatalYm
CatalYm has identified GDF-15 as a key cancer therapy resistance mechanism and is developing it as safe and efficacious immune therapy for solid tumors. GDF-15, an immunosuppressant important for feto-maternal tolerance, is hijacked by cancer cells to evade immune system attack. Visugromab, CatalYm's lead antibody, has 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. CatalYm is now advancing to Phase 2b studies to confirm visugromab as a new class of cancer immunotherapy in a broad range of anti-cancer regimens.

Contact
CatalYm GmbH
Dr. Phil L'Huilier, CEO
info@catalym.com

Media Inquiries
Trophic Communications
Dr. Stephanie May or Dr. Alison Opalko
Phone: +49 171 185 56 82 or +49 151 54041130
catalym@trophic.eu