CatalYm Presents Positive Phase 2a Outcome for Visugromab in Advanced NSCLC and Urothelial Cancer at the ESMO Immuno-Oncology Congress 2023

- Visugromab demonstrated potent and durable clinical efficacy as well as excellent tolerability in combination with nivolumab in advanced-stage/last-line non-small cell lung cancer (NSCLC) and urothelial cancer patients (UC) in the GDFATHER-Phase 2a trial, supporting further clinical development
- Observed Objective Response Rates (ORR) as per RECIST were 14.8% in both UC and NSCLC and 21.1% in non-squamous NSCLC, all in predominantly third to fourth line patients that were anti-PD-1/PD-L1 relapsed/refractory as per strict criteria
- Substantial Duration of Response (DoR) in last-line was observed with mean DoR surpassing 11 months for non-sq NSCLC and 10 months for UC, with 6/8 responses still ongoing and DoR further expanding
- Data confirm that GDF-15 represents a key resistance factor for checkpoint-inhibition based on evidence that GDF-15 blockade by visugromab in checkpoint-inhibitor (CPI)-relapsed/refractory patients can reconstitute, deepen and prolong anti-tumor activity significantly

Munich, Germany, December 6, 2023 – CatalYm announced that maturing Phase 2a results from its ongoing GDFATHER-2 trial (**GDF**-15 **A**ntibody-media**T**ed **H**uman **E**ffector Cell **R**elocation Phase 2) (NCT04725474) were presented today in an oral presentation at the European Society for Medical Oncology (ESMO) Immuno-Oncology Congress 2023 in Geneva, Switzerland. The data highlight that treatment with a combination of CatalYm's lead candidate visugromab and nivolumab achieves compelling anti-tumoral activity in (as per strict criteria) anti-PD-1/PD-L1 relapsed/refractory non-small cell lung cancer (NSCLC) and urothelial cancer (UC) patients while retaining 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 presentation by International Coordinating Investigator Prof. Ignacio Melero, MD, PhD, Co-Director of Immunology and Immunotherapy (CIMA) at the Universidad de Navarra, Pamplona/Spain, expands the clinical data for visugromab significantly and highlights the benefits that neutralizing GDF-15 can provide for patients with metastatic solid tumors.

"These data, in particular the clinical efficacy and durability of responses observed with visugromab/nivolumab in non-squamous NSCLC and UC are truly exceptional for advanced-stage/last-line, anti-PD-1/PD-L1 relapsed/refractory solid tumor disease treated with an I/O combination therapy. It underscores visugromab's potential for reversing immunotherapy-refractoriness and restoring CPI activity back to levels that are at or near CPI-naïve disease," said **Professor Eugen Leo, Chief Medical Officer at CatalYm**. "The impressive duration of response, still expanding with 6/8 responses ongoing, is indicative of restoration of a lasting immunologic tumor control in advanced solid tumor patients that had previously exhausted

available standard of care and are relapsed/refractory to prior anti-PD-1/PD-1 treatment as defined by strict criteria."

The matured results from the NSCLC and UC Phase 2a cohorts included a total of 27 patients in each indication. The Objective Response Rate (ORR) as per RECIST criteria in both the NSCLC and the UC cohorts was 14.8% (4/27, respectively), and 21.1% (4/19) in non-squamous NSCLC. The mean Duration of Response (DoR) has surpassed 11 months in non-NSCLC and 10 months in UC and is further expanding with 6/8 subjects in response continuing on study treatment. Non-sq NSCLC and UC both had been predicted as major GDF-15 immunosuppressed tumor types by a proprietary translational research analysis involving several thousand tumor samples (data unpublished), and the clinical results are in line with this. Interestingly, responses were observed in both PD-L1 positive and negative tumors, but all three patients in the urothelial tumor cohort with PD-L1 levels of Tumor Proportion Score (TPS) >5 responded to treatment, including one complete response (in fourth line of treatment) and two partial responses (PR), all ongoing. The ORR rates and the emerging and still maturing DoR favorably compare to existing historical data of various PD-1 mono- (with reported ORR of 0-5% in as per strict criteria anti-PD-1/PD-L1 r/r patients) or various I/O combo-retreatment regimens in similar third and fourth line populations. Further biomarker correlative analyses are ongoing and are an integral part of future trials in preparation.

Regarding safety, the majority of Treatment-Emergent Adverse Events (TEAE) reported were mild to moderate, with just 5.2% of patients (9/174) experiencing TEAE of Grade > 3, demonstrating a good overall tolerability and safety of the combination in heavily pretreated patients. As of December 2023, for only 1/174 (0.6%) subjects treated/exposed, a single Serious Adverse Reaction (SAR) > Grade 3 was reported that was assessed as per investigator judgement as at least possibly Treatment-Related Adverse Event (TRAE).

"We continue to make important progress in our Phase 2 evaluation of visugromab, further demonstrating the potential of GDF-15 neutralizing approaches as a critical component for treatment success in a broad range of anti-cancer regimens," said **Phil L'Huillier, Managing Director and Chief Executing Officer at CatalYm**. "The next stage is to expand our clinical evaluation in 2024 to further maximize the value of GDF-15-targeting therapies for patients both in advanced and earlier stages of their disease. There is a huge unmet medical need not only in CPI-relapsed/refractory solid tumors but also in newly diagnosed metastatic solid tumor disease, where despite all encouraging recent advances, a cure or at least true long-term-remission/-disease control are still far out of reach for the vast majority of patients, who ultimately will die from their disease. We want to improve patient's lives and outcome with a well tolerable immunotherapy concept that we see emerge here."

The Phase 2a GDFATHER-2 program was initiated in March 2022. The ongoing study consists of two segments with up to seven cohorts, expected to enroll a total of over 200 patients in various cohorts. Based on the matured Phase 2a results, CatalYm plans to launch randomized, controlled studies in several major cancer indications in combination with

checkpoint inhibitors and standard-of-care in early lines of treatment in the first half of 2024.

Presentation Details

Title: Definitive results for NSCLC and bladder cancer cohorts in the phase 1/2a trial of visugromab (CTL-002) in advanced/metastatic anti-PD/PD-L1 relapsed/refractory solid tumors (GDFATHER-1 trial)
Presenter: Dr. Ignacio Melero, Co-Director of the Department of Immunology and Immunotherapy Researcher at the Universidad de Navarra, Spain
Abstract number: 318
Date and time: Wednesday, December 6th, 2:15-2:25pm CET

About the GDFATHER-2 Trials
The GDFATHER-2a trial (**GDF**-15 **A**ntibody-media**T**ed **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 already in Phase 1 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 2 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.

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