CatalYm Expands Visugromab Development Based on Positive Early Phase 2 Data in Two Indications and Adds Confirmatory Response-Predictive Biomarker Cohort

MUNICH, December 14, 2022 – CatalYm today announced three major expansions of its ongoing Phase 2 visugromab clinical development program. Based on initial positive patient responses, the company is advancing two potential lead indication cohorts into the second stage of the Simon-2-stage design ahead of schedule. Additionally, CatalYm is expanding its visugromab Phase 2 development program to include a new confirmatory cohort exploring the response-predictive biomarkers identified in the Phase 1.

The Phase 2 study is evaluating visugromab in advanced-stage cancer patients that are relapsed or refractory to prior anti-PD-1/-PD-L1 treatment in a selected group of solid tumor indications. Based on early emerging responses in several major solid tumor indications, Catalym will enlarge the Phase 2 by expanding two cohorts as foreseen in the Phase 2 protocol. The persuasive responses seen in the study to date enable the expansion earlier than anticipated and before the original cohorts were fully enrolled. Combined with the clinical data generated in the Phase 1, these data further support the significant potential of visugromab in this PD-1 refractory solid tumor patient population.

In addition, CatalYm expanded its Phase 2 study with a newly established, tumor-agnostic, fully biomarker-selected cohort. This cohort aims to assess the prediction accuracy of response for two potential biomarkers in a total of 25 cancer patients treated with the GDF-15-targeting antibody visugromab in combination with the anti-PD1 antibody nivolumab in patients that are relapsed/refractory to prior anti-PD1/PD-L1 treatment. The two biomarkers were identified as part of the company's stringent Phase 1 biomarker program where triple-biopsies were mandatory and evaluated regarding molecular and immunohistochemical parameters of significance. The company recently presented mature results from this Phase 1 dose escalation study at the 2022 ESMO congress.

"Our first indication-specific cohorts reaching the trigger for stage-2 enrolment before having completed enrolment of stage 1 is a clearly positive signal for the clinical potential of visugromab in advanced-stage, anti-PD1/PD-L1 relapsed/refractory cancer patients. In light of the highly promising phase 1 biomarker data, we now also added a fully biomarker-selected cohort to our program, to ideally confirm these early

findings. This progress in the development of visugromab is exciting to see." **stated Prof. Dr. Eugen Leo, Chief Medical Officer at CatalYm. "**Identifying biomarkers that predict treatment outcomes is a critical endeavor in modern cancer medicine. The ability to identify the patients that will benefit most is a highly valuable additional asset for the future development of visugromab."

Dr. Phil L'Huillier, Chief Executive Officer at CatalYm added: "We have set up this Phase 2 program to confirm the potential clinical benefit of targeting GDF-15 in specific solid tumor indications. The new biomarker cohort and the first Simon-2-stage expansions will help us to gather valuable information for the future development of visugromab and should bring us significantly closer to registration trials. We are highly encouraged by the clear development opportunities unfolding in front of us which have also been validated through our recent oversubscribed Series C funding. Our path toward rapidly bringing this novel IO therapy to cancer patients is clear."

Recruitment for the biomarker expansion cohort has been initiated in Spain, Germany and Switzerland as part of the ongoing multi-center, open-label, **GDFATHER-2** trial (NCT04725474). The Phase 2 part of the study, originally commenced in February 2022, is evaluating the treatment of GDF-15 neutralizing antibody, visugromab, in combination with the anti-PD-1 checkpoint inhibitor nivolumab in advanced stage cancer patients that are relapsed or refractory to prior anti-PD-1/-PD-L1 treatment. The study is planned to enroll up to 164 participants aged 18 years or older in up to 7 cohorts at major clinical centers across Europe and the United States. The biomarker-selected cohort will include broad tissue analyses, incorporating protein- and RNA-levels as well as analysis of the patient's tumor immunogram which will be correlated with clinical outcomes. An initial data update from the first cohorts of the study is expected in mid 2023. CatalYm recently completed a €50 million Series C funding round to support the continued late-stage development of the program.

About CatalYm

CatalYm has identified GDF-15 as a central regulator of the immune system in the tumor microenvironment. We are pioneering the reversal of GDF-15-mediated immunosuppression to induce a potent antitumoral immune reaction in non-responsive tumors. CatalYm's lead program visugromab is poised to demonstrate clinical proof-of-concept in multiple solid tumor indications which will expand the treatment horizon for current and future immunotherapies.

About the GDFATHER-2 Trials

The **GDFATHER-2** trials (**GDF**-15 **A**ntibody-media**T**ed **H**uman **E**ffector cell **R**elocation Phase 2) (NCT04725474) are ongoing first-in-human Phase 2a cohorts investigating the effect of visugromab (CTL-002) as monotherapy and/or in combination with a PD-1 checkpoint inhibitor in patients with various advanced-stage, relapse/refractory solid tumors and the new biomarker-selected cohort. The study consists of two segments with a total of up to seven cohorts, enrolling up to 164 patients in Simon-2-stage designs to confirm a certain response rate within each tumor type. Five cohorts are within tumor types with anti-PD1/-L1 label, recruiting patients that either were refractory to or relapsed post prior anti-PD1/-L1 treatment. One cohort entails treatment of an anti-PD1/-L1 naïve tumor type in an indication

without anti-PD1/-L1 approval and one tumor-agnostic cohort evaluates patient-selection based on two novel predictive biomarkers. Main data read-outs from initial Phase 2a parts are expected by mid 2023. Additional cohorts and trials are in preparation.

About Visugromab (CTL-002)

Visugromab, formerly known as CTL-002, is a humanized, monoclonal antibody designed to neutralize the tumor-produced Growth Differentiation Factor-15 (GDF-15). GDF-15 secretion by the tumor has been shown to prevent T cell migration into the tumor and suppresses T cell function and the adaptive immune response in the tumor microenvironment. This enables the tumor to evade the immune system and become resistant to standard of care and current immunotherapy approaches such as checkpoint inhibitors. Visugromab counteracts these immuno-suppressive mechanisms by neutralizing GDF-15, enhancing the infiltration of immune cells into the tumor, improving both priming of T cells by dendritic cells and tumor killing by T cells and NK cells.

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