Chimerix Announces Successful Launch of ONC201 Phase 3 ACTION Study at Society for Neuro-Oncology Conference and Provides Operational Update

December 8, 2022

– Natural Disease History study indicates median overall survival in recurrent H3 K27M-mutant diffuse glioma of 5.1 months compared to 13.7 months in the prior ONC201 Phase 2 efficacy analysis –

– Two external analyses presented at SNO concluded that glioma patients who received ONC201 experienced a meaningful survival benefit –

– Company to focus on Phase 3 ACTION study as potential first approval for ONC201 following interactions with U.S. Food and Drug Administration –

– Following TEMBEXA transition, planned workforce reduction of ~25% sharpens focus of organization to oncology pipeline and execution of Phase 3 ACTION study –

DURHAM, N.C., Dec. 08, 2022 (GLOBE NEWSWIRE) -- Chimerix (NASDAQ:CMRX), a biopharmaceutical company whose mission is to develop medicines that meaningfully improve and extend the lives of patients facing deadly diseases, today provided an operational update and announced the successful launch of the ONC201 Phase 3 ACTION study at the recent Society for Neuro Oncology (SNO) Conference, which took place November 16-20, 2022 in Tampa, Florida.

“We are very excited to announce the timely opening of enrollment for the ACTION study at SNO. Physicians have already initiated the referral process to ensure recently diagnosed patients have the potential to enroll in the study. We have also recently concluded the analysis from our Company-sponsored Natural Disease History study, which collected data from glioma patients with similar disease characteristics as those included in the Phase 2 efficacy analysis. These data support a potentially meaningful overall survival (OS) advantage for ONC201 in the recurrent setting. Additionally, two analyses presented by external parties at the SNO conference reported meaningful OS advantages for ONC201-treated patients in frontline and recurrent settings relative to external controls derived from clinical trials, institutional experiences, and real-world evidence. Collectively, these data support the robust ONC201 Phase 2 results and further reinforce our confidence in the probability of success of the ACTION study and the ongoing imperative of advancing this agent for patients as soon as possible,” said Mike Sherman, Chief Executive Officer of Chimerix.

“Following recent interactions with FDA, we believe the best path to approval for ONC201 is successful execution of the randomized controlled ACTION study and we are focusing resources appropriately. Additionally, as we near completion of the transition of TEMBEXA® to Emergent BioSolutions, we are reducing the size of the organization by approximately 25% in order to focus our development capability and capital allocation to our oncology pipeline. We are thankful for the commitment of these talented employees who have contributed so much to the Company. We will be working closely with those affected to support them in this transition. Importantly, we are confident that the steps we are taking today will help position Chimerix for continued success as we advance our ACTION study,” continued Mr. Sherman.

Company-Sponsored Natural Disease History Study Supports Poor Prognosis of Recurrent H3 K27M-mutant Glioma

Data from the recently completed Natural Disease History study across eleven sites in patients who did not receive ONC201 confirmed poor overall survival for patients with H3 K27M-mutant glioma, consistent with what was expected based on prior literature and expert consensus. Chimerix limited the number of sites contributing to this analysis, as it was not likely to be a critical element of a potential regulatory submission.

Overall Survival Cohort. In relapsed patients who did not receive ONC201, the median overall survival following first disease progression was 5.1 months[i]. This is in contrast to the previously reported ONC201 Phase 2 data set which showed a median OS of 13.7 months from the start of ONC201 treatment following disease progression. Rates of survival at 12 and 24 months in the ONC201 Phase 2 analysis were more than double the rates observed in this analysis of patients who did not receive ONC201.

Objective Response Cohort. The Company also evaluated objective response by RANO-HGG criteria in patients who received therapies other than ONC201 but met similar selection criteria used for the Phase 2 analysis of ONC201 designed to isolate single agent responses. In the two patients who were evaluable, neither achieved an objective response. The low number of patients who qualified was primarily due to the high prevalence of ONC201, bevacizumab and radiotherapy use during that period of relapse, which would confound an objective response determination.

The company plans to present a more comprehensive analysis of the Natural Disease History study at a future scientific conference.

Two External Presentations at SNO Report an OS Advantage in Patients Who Received ONC201

Overall survival analyses indicating superior outcomes for patients who received ONC201, either prior to or after disease progression, compared to patients who never received ONC201, were reported at SNO by a team of academic investigators who evaluated clinical trials and institutional experiences in the United States and Europe. For patients who received ONC201 prior to disease progression, the same treatment setting being evaluated in the Phase 3 ACTION study, the median OS for patients who received ONC201 was 26.3 months (n=35). This was compared to 12 months for patients who did not receive ONC201 (n=274, p<0.0001). In the recurrent setting, patients treated with ONC201 (n=37) had a median overall survival of 16.2 months compared to 8.1 months for those not treated with ONC201 (n=99, p=0.05). Authors concluded that ONC201 efficacy was enriched in patients treated prior to recurrence.[i]

Separately, a poster presentation at SNO from xCures evaluated real world outcomes and treatment patterns among patients with DMG, which also

concluded ONC201 meaningfully extends OS in patients with DMG.[ii]

About the Phase 3 ACTION Study

The ACTION trial enrolls patients shortly after they have completed front-line radiation therapy that is the standard of care. The study is designed to enroll 450 patients randomized 1:1:1 to receive ONC201 at one of two dosing frequencies or placebo. Participants will be randomized to receive 625mg of ONC201 once per week (the Phase 2 dosing regimen), 625mg twice per week on two consecutive days or placebo. The dose will be scaled by body weight for patients <52.5kg. OS will be assessed for efficacy at three alpha-allocated timepoints: two interim assessments by the Independent Data Monitoring Committee (IDMC) at 164 events and 246 events, respectively, and a final assessment at 327 events. The final progression-free survival (PFS) analysis will be performed after 286 events, with progression assessed using RANO HGG criteria by blinded independent central review (BICR). Secondary endpoints include corticosteroid response, performance status response, change from baseline in quality of life (QoL) assessments and change from baseline in neurologic function as assessed by the Neurologic Assessment in Neuro-Oncology (NANO) scale.

About Chimerix

Chimerix is a biopharmaceutical company with a mission to develop medicines that meaningfully improve and extend the lives of patients facing deadly diseases. The Company's most advanced clinical-stage development program, ONC201, is in development for H3 K27M-mutant glioma.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks and uncertainties that could cause actual results to differ materially from those projected. Forward-looking statements include those relating to, among other things, the initiation and probability of success of the Phase 3 ACTION study. Among the factors and risks that could cause actual results to differ materially from those indicated in the forward-looking statements are risks related to the timing and completion of the Phase 3 ACTION study of ONC201; risks that positive results observed in prior studies may not be repeated or observed in future clinical studies, risks that the benefits from our planned workforce reduction may not be realized; and additional risks set forth in the Company's filings with the Securities and Exchange Commission. These forward-looking statements represent the Company's judgment as of the date of this release. The Company disclaims, however, any intent or obligation to update these forward-looking statements.

CONTACTS:

Michelle LaSpaluto
919 972-7115
ir@chimerix.com

Will O'Connor
Stern Investor Relations
212-362-1200
will@sternir.com

Nick Lamplough / Dan Moore / Tanner Kaufman
Joele Frank, Wilkinson Brimmer Katcher
(212) 355-4449

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[i] The median OS was 5.1 months for both patients with H3 K27M-mutant and/or diffuse midline glioma (N=43) and the subgroup of patients with H3 K27M-mutant diffuse glioma excluding DIPG, CSF dissemination, spinal or leptomeningeal disease (N=12).

[ii] Sunjong Ji, B.S. et al, "Clinical efficacy and predictive biomarkers of ONC201 in H3 K27M-mutant diffuse midline glioma, SNO 2022

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