BACKGROUND

- Globlastoma multiforme (GBM) is the most common and most aggressive primary brain tumor
- More than 300,000 new cases are diagnosed globally with over 250,000 deaths each year
- Patients with recurrent GBM have a poor prognosis, with limited treatment options and a median survival of less than 1 year
- While prior attempts to treat GBM with chimeric antigen receptor (CAR) T-cells have been limited by tumor heterogeneity, chlorotoxin (CLTX)-directed CAR T-cells in mice demonstrated broad anti-tumor activity and prolonged survival with no off-tumor toxicity or antigen escape
- CLTX, a 36-amino acid peptide identified in scorpion venom, selectively binds to malignant glioma cells through matrix metalloproteinase-2 (MMP2) and clinical administration of CLTX-based biologics has been well-tolerated in patients
- CHM 1101 is the first CAR T to utilize CLTX as its tumor targeting domain for autologous CAR T-cell therapy
- The following was observed in an ongoing single-center first-in-human phase 1 study of CHM 1101 in patients with recurrent GBM:
  - Safety: no dose-limiting toxicities; one cerebral edema possibly attributed to CHM 1101
  - Efficacy: 75% disease control rate with survival up to 15.5 months
- Clinical Trial NCT05627323 is a phase 1b, multi-center study of CHM 1101 in adult subjects with MMP2+ recurrent or progressive GBM after standard therapy

PRECLINICAL ANTI-GBM ACTIVITY

- Tumor control by CLTX-CAR T-cells led to prolonged survival
- CLTX-CAR T-cells exhibited no observable off-target effector activity or toxicity to normal tissues (data not shown)

MMP2 BIOMARKER

- Direct correlation between CLTX binding and MMP2 localization in GBM tumor tissue
- MMP2 is required for anti-tumor activity of CLTX-CAR T-cells (CHM 1101) in GBM

THE PATIENT JOURNEY

- After leukapheresis and tumor resection, CHM 1101 is administered across 3 once-weekly (Days 0, 7, and 14) intracranial (intraventricular) infusions
- After disease assessment at Day 28, additional weekly doses of CHM 1101 may be administered in the absence of disease progression or unacceptable toxicity

STUDY DESIGN AND ENDPOINTS

OBJECTIVES:

- PFS
- OS
- ORR (RANO)
- Safety & feasibility
- RP2D
- Cellular kinetics

PART A - DOSE CONFIRMATION

- Recurrent/progressive glioblastoma
- 440 x 10^6/3-6 patients

PART B - DOSE EXPANSION

- Recurrent/progressive glioblastoma
- 440 x 10^6/12-26 patients

CHLOROTOXIN DEVELOPMENT

- fluorescein CLTX (Tumor Paint), crosses BBB and differentiates GBM from normal tissue in surgery
- Radiolabeled CLTX (131I-TM-601) is safe, feasible and shows signs of antitumor activity

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DISCLOSURES

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REFERENCES


KEY PATIENT ELIGIBILITY

- Age 18 years and older
- Eastern Cooperative Oncology Group (ECOG) status of 0 or 1
- Life expectancy ≤12 weeks
- Histologically confirmed diagnosis of grade 4 GBM, a grade 2 or 3 malignant glioma with radiographic progression consistent with a grade 4 GBM (IDH wild type), grade 4 diffuse astrocytoma (IDH mutant), or a unifocal relapse of GBM
- Relapsed disease: radiographic evidence of recurrence/progression of measurable disease after standard therapy and ≥ 12 weeks after completion of front-line radiation therapy
- MMP2+ tumor expression confirmed by IHC (≥20% moderate/high MMP2 score (2+ or 3+))
- Adequate baseline organ function and venous access for leukapheresis