PHASE 1B MULTICENTER STUDY TO EVALUATE CHM 1101 IN PATIENTS WITH RECURRENT OR PROGRESSIVE GBM

POSTER
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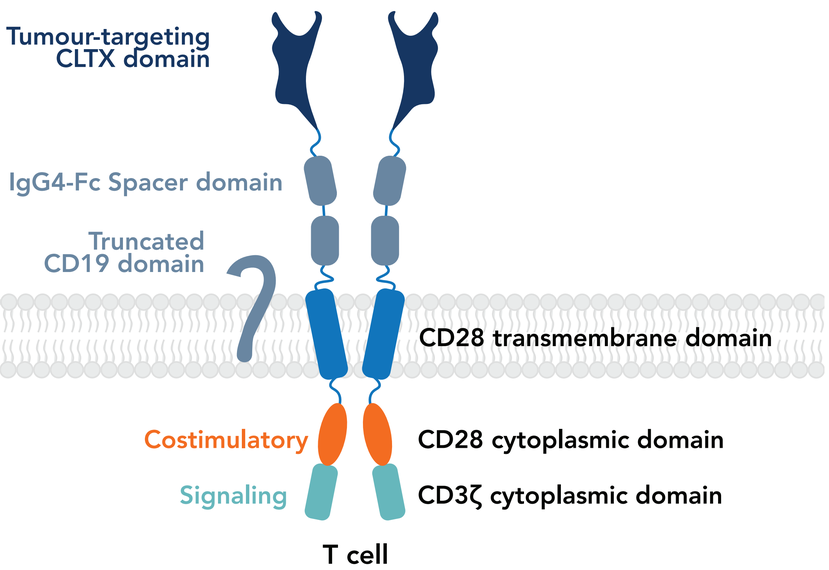
BACKGROUND

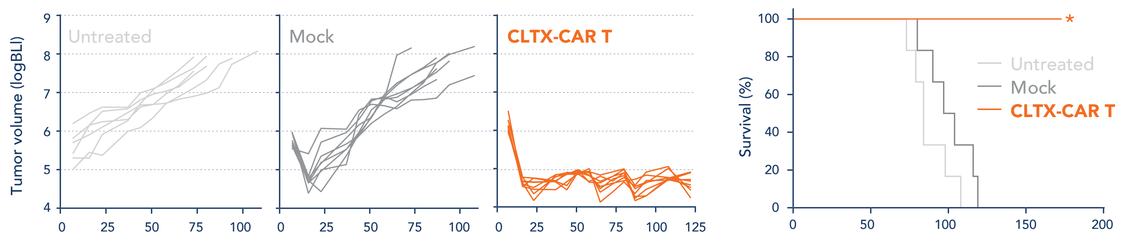
- Glioblastoma multiforme (GBM) is the most common and most aggressive primary brain tumor
  - More than 300,000 new cases are diagnosed globally with over 250,000 deaths each year[1]
  - Patients with recurrent GBM have a poor prognosis, with limited treatment options and a median survival of less than 1 year[2]
- 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 **(Figure 3)**[3]
- CLTX, a 36–amino acid peptide identified in scorpion venom[4], selectively binds to malignant glioma cells through matrix metalloproteinase-2 (MMP2) and clinical administration of CLTX-based biologics has been well-tolerated in patients **(Figure 4)**[5-8]
- CHM 1101 is the first CAR T to utilize CLTX as its tumor targeting domain for autologous CAR T-cell therapy **(Figure 1)**
- The following was observed in an ongoing single-center first-in-human phase 1 study of CHM 1101 in patients with recurrent GBM[8]
  - 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 **(Figure 2)**

FIGURE 1. CHM 1101 WAS DESIGNED FOR CLINICAL SAFETY & EFFICACY



PRECLINICAL ANTI-GBM ACTIVITY

FIGURE 3. CHM 1101 (CLTX-CAR T-CELLS) DEMONSTRATE ROBUST ANTI-TUMOR ACTIVITY AND IMPROVED SURVIVAL IN VIVO[3]

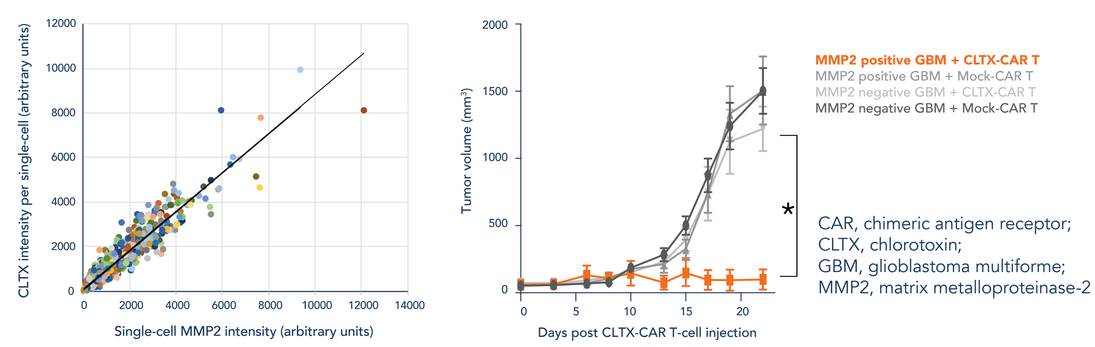


- In immunodeficient mice with established GBM tumors, mice treated with CLTX-CAR T-cells experienced dramatic and prolonged tumor control, while untreated mice and those treated with a Mock CAR T-cell product showed uncontrolled tumor growth
- Tumor control by CLTX-CAR T-cells led to prolonged survival
- CLTX-CAR T-cells exhibited no observable off-target effector activity or toxicity to normal tissues (data not shown)

BLI, bioluminescent intensity; CAR, chimeric antigen receptor; CLTX, chlorotoxin; GBM, glioblastoma multiforme; ICT, intracerebrotumoral; IVT, intracerebroventricular

MMP2 BIOMARKER

FIGURE 4. CHM 1101 (CLTX-CAR T-CELLS) REQUIRES MMP2 FOR ANTI-GBM ACTIVITY

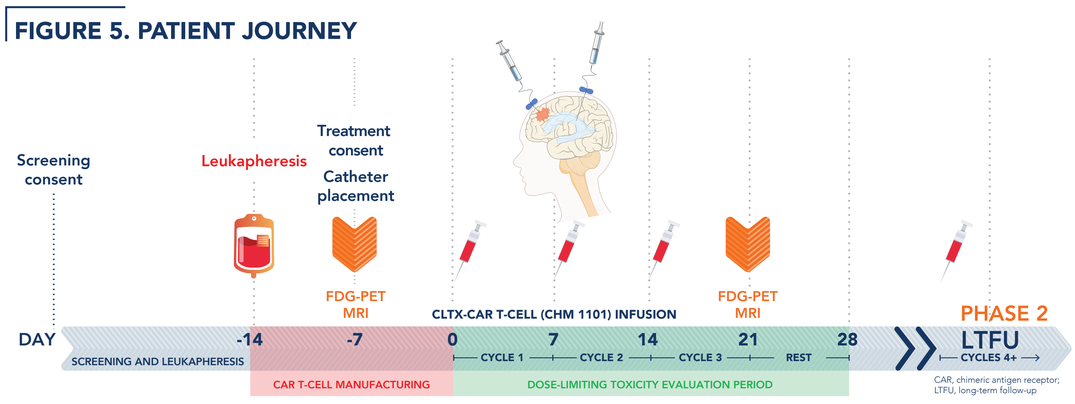


CAR, chimeric antigen receptor; CLTX, chlorotoxin; GBM, glioblastoma multiforme; MMP2, matrix metalloproteinase-2

- Direct correlation between CLTX binding and MMP2 localization in GBM tumor tissue (left)[9]
- MMP2 is required for anti-tumor activity of CLTX-CAR T-cells (CHM 1101) in GBM (right)[3]

THE PATIENT JOURNEY

FIGURE 5. PATIENT JOURNEY

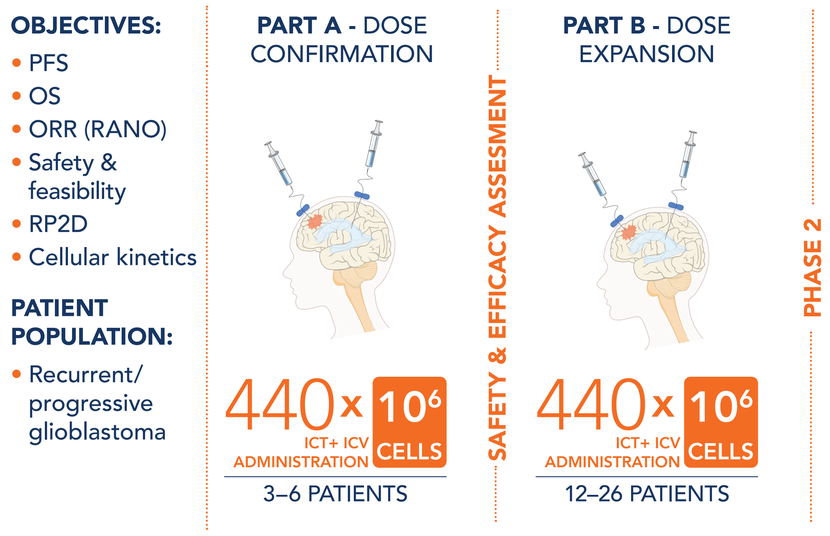


CAR, chimeric antigen receptor; LTFU, long-term follow-up

- After leukapheresis and tumor resection, CHM 1101 is administered across 3 once-weekly (Days 0, 7, and 14) intracranial (intracavitary and 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

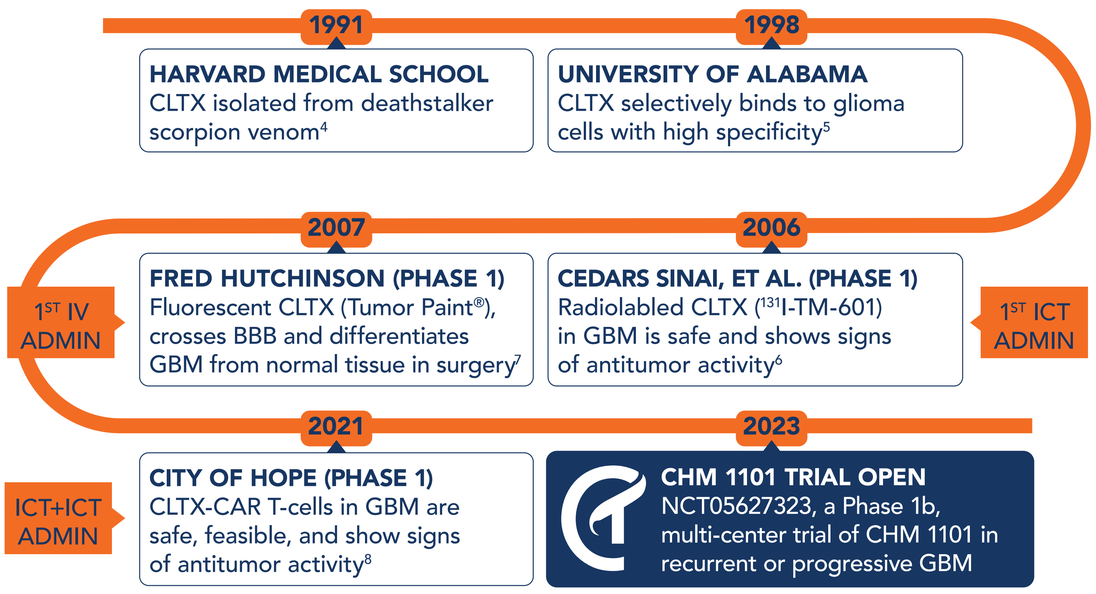
FIGURE 2. CHM 1101 STUDY DESIGN AND KEY ENDPOINTS



ICT, intracerebrotumoral; IVT, intracerebroventricular; ORR, objective response rate (RANO); OS, overall survival; PFS, progression-free survival; RANO, Response Assessment in Neuro-Oncology; RP2D, recommended Phase 2 dose

CHLOROTOXIN DEVELOPMENT

FIGURE 6. TIMELINE FOR DEVELOPMENT OF CLTX THERAPIES IN GBM



BBB, blood-brain-barrier; CAR, chimeric antigen receptor; CLTX, chlorotoxin; GBM, glioblastoma multiforme; ICT, intracerebrotumoral; IV, intravenous; IVT, intracerebroventricular

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 a 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

REGISTRATION

The study is sponsored by Chimeric Therapeutics, Ltd., and is registered at ClinicalTrials.gov (NCT05627323)

STATUS

The study opened to accrual in 2023 and is currently enrolling patients from sites in the United States

Refer to ClinicalTrials.gov for the most up to date list of activated sites

For questions or comments, please email: clinicaltrials@chimerictherapeutics.com

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DISCLOSURES

BB: consulting, advisory role, and research support from Chimeric Therapeutics; research funding from NIH, patent EP3411393B1 granted. **AA:** employment at Chimeric Therapeutics. **CH:** employment and equity ownership in Chimeric Therapeutics. **SHA:** employment and equity ownership in Chimeric Therapeutics. **JBL:** employment and equity ownership in Chimeric Therapeutics.

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