

A first-in-human Phase 1, multicenter, open-label study of CB-011, a next-generation CRISPR-genome edited allogeneic anti-BCMA immune-cloaked CAR-T cell therapy, in patients with relapsed/refractory multiple myeloma (CaMMouflage trial)

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Introduction

- Current therapeutic options have inherent challenges for patients with r/r MM**
- **Bispecifics:** treatment burden from frequent dosing over several months
 - **Autologous CAR-T cell therapy:** need for apheresis or bridging therapy, constrained manufacturing capacity, long manufacturing timelines, manufacturing failures, and variable quality

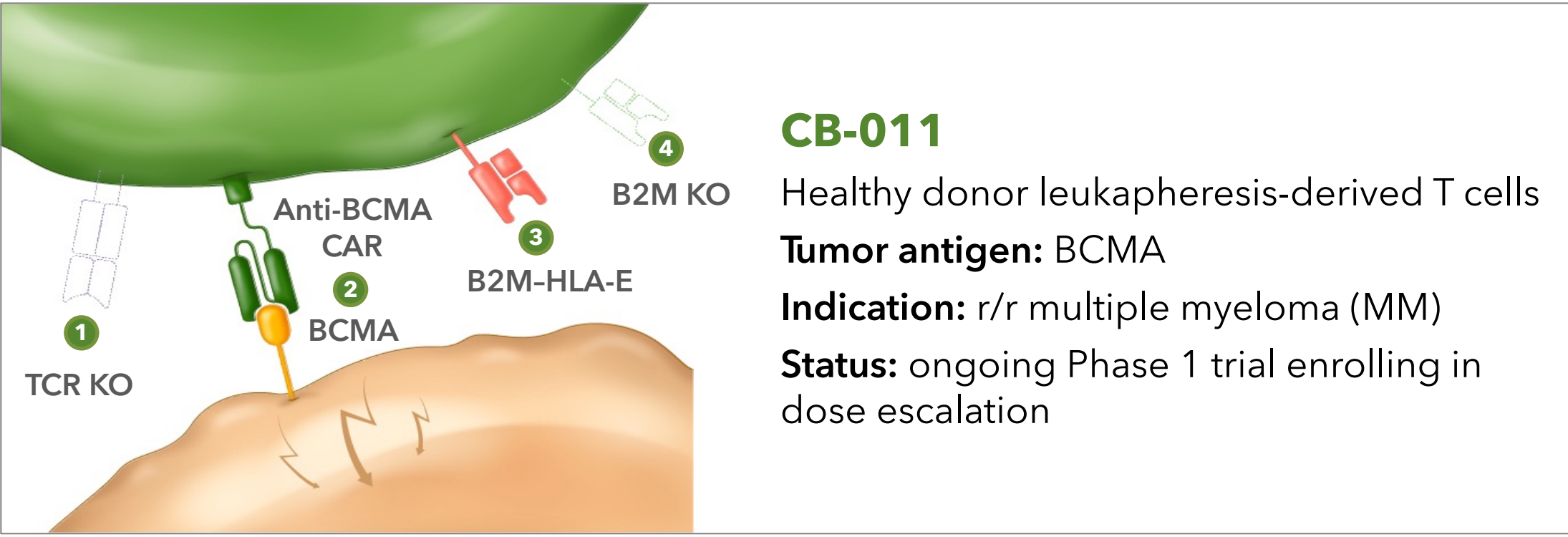
There is a significant unmet need for an off-the-shelf CAR-T cell therapy as a readily available treatment option for patients with r/r MM

- Allogeneic CAR-T cell therapies may offer a significant benefit to patients who are:**
- Refractory to or relapsed on prior systemic anti-cancer therapies
 - Ineligible for autologous CAR-T cell therapies
 - At risk for manufacturing failure
 - Facing issues with access to autologous CAR-T therapy
 - At risk of disease progression while on bridging therapy or awaiting long manufacturing timelines for autologous CAR-T cell therapies

r/r: relapsed refractory; **MM:** multiple myeloma; **CAR-T:** chimeric antigen receptor T cell therapy

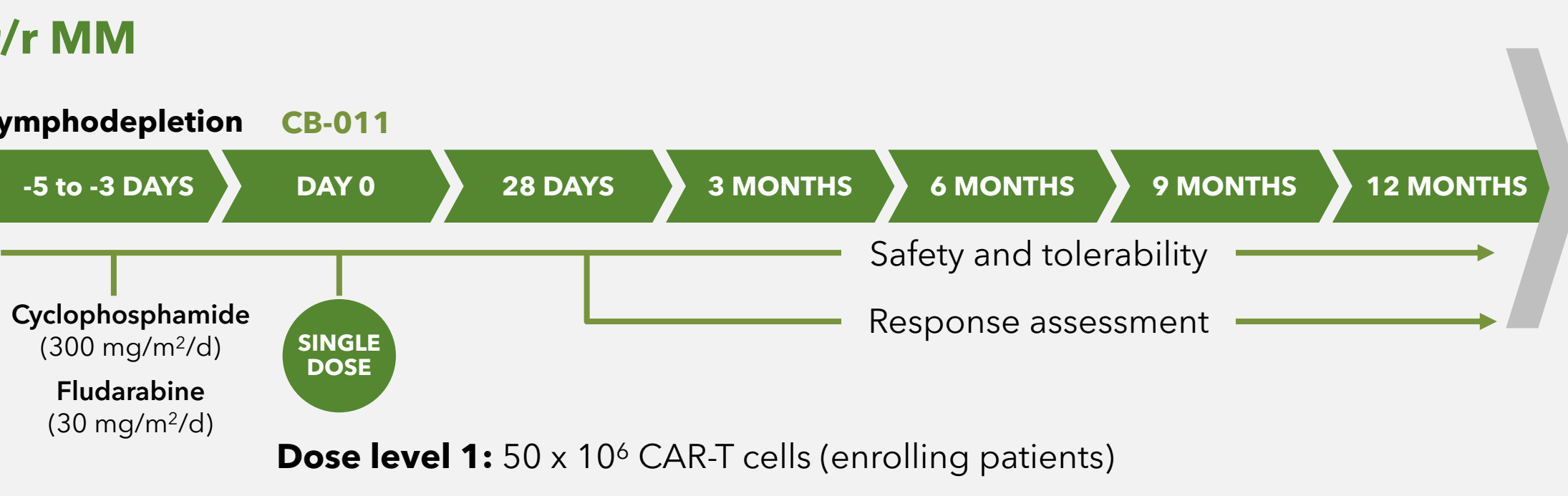
CB-011: anti-BCMA allogeneic CAR-T cell therapy with immune cloaking to blunt rejection

KEY ATTRIBUTES	CB-011	Conventional allogeneic anti-BCMA CAR-Ts
Cas12a chrDNA editing for enhanced genomic integrity <ul style="list-style-type: none">▪ Reduced off-target editing and enhanced insertion rates	✔	✘
1 TRAC gene knockout (KO) <ul style="list-style-type: none">▪ Eliminates TCR expression, reduces GvHD risk	✔	Varies
2 Humanized anti-BCMA CAR site-specifically inserted into TRAC gene <ul style="list-style-type: none">▪ Eliminates random integration, targets tumor antigen	✔	Varies
3 B2M-HLA-E-peptide fusion site-specifically inserted into B2M gene <ul style="list-style-type: none">▪ Blunts NK cell-mediated rejection	✔	✘
4 B2M gene KO <ul style="list-style-type: none">▪ Reduces HLA class I presentation and T cell-mediated rejection	✔	✘



CaMMouflage Phase 1 trial design

Part A: 3+3 dose escalation to determine safety, MTD, RP2D
Part B: dose expansion to determine tumor response



NCT#05722418 on clinicaltrials.gov

MTD: maximum tolerated dose; **RP2D:** recommended Phase 2 dose

CaMMouflage key trial endpoints

- Primary endpoints**
- **Dose escalation (part A):**
 - Incidence of AEs and SAEs¹, incidence of AEs defined as a DLT²
 - **Dose expansion (part B):**
 - Objective response rate (sCR, CR, VGPR, PR)
- Secondary endpoints**
- **Dose escalation (part A):**
 - Objective response rate, MRD negativity
 - Evaluate duration of CB-011 persistence, incidence of anti-CB-011 antibodies, presence of CAR+ T cells in the peripheral blood and bone marrow, soluble BCMA levels
 - **Dose expansion (part B):**
 - Duration of response, MRD negativity rate, clinical benefit rate, progression-free survival, overall survival
 - Incidence of AEs and SAEs¹

¹CTCAE v5.0 and CRS, ICANS, GvHD grading criteria
²DLT assessment period is 28 days following CB-011 infusion

AE: adverse event; **SAE:** serious adverse event; **DLT:** dose-limiting toxicity; **sCR:** stringent complete response; **CR:** complete response; **VGPR:** very good partial response; **PR:** partial response

CaMMouflage key inclusion criteria

- Documented diagnosis of multiple myeloma based on IMWG 2016 criteria
- Measurable disease at screening with:
 - Serum M-protein 1.0 g/dL or urine M-protein 200 mg/24h or
 - Light chain MM without measurable disease in the serum or the urine: serum immunoglobulin free light chain ≥ 10 mg/dL and abnormal serum immunoglobulin kappa lambda free light chain ratio
- Received ≥ 3 MM prior lines of therapy (must include a PI, an IMiD, and anti-CD38 monoclonal antibody)
- Documented evidence of PD on or within 12 months of last line of therapy. Patients with documented evidence of PD within the previous 6 months and who are refractory or non-responsive to their most recent line of therapy are eligible
- ECOG grade 0 or 1
- Prior BCMA-directed therapy allowed (except CAR-T) and if ≥ 3 months from last dose of BMCA-targeted therapy

IMiD: immunomodulatory drug; **PI:** proteasome inhibitor; **ECOG:** Eastern Cooperative Oncology Group; **IMWG:** International Myeloma Working Group

CaMMouflage key inclusion criteria

- Hematology**
- Hemoglobin > 8.0 g/dL
 - Platelets ≥ 50 x 10⁹/L
 - Absolute neutrophil count ≥ 0.75 x 10⁹/L
- Chemistry**
- AST and ALT ≤ 3.0 x upper limit of normal (ULN)
 - Creatinine clearance ≥ 40 mL/min/1.73 m²
 - Total bilirubin ≤ 2.0 x ULN
 - Corrected serum calcium ≤ 12.5 mg/dL or free ionized calcium ≤ 6.5 mg/dL

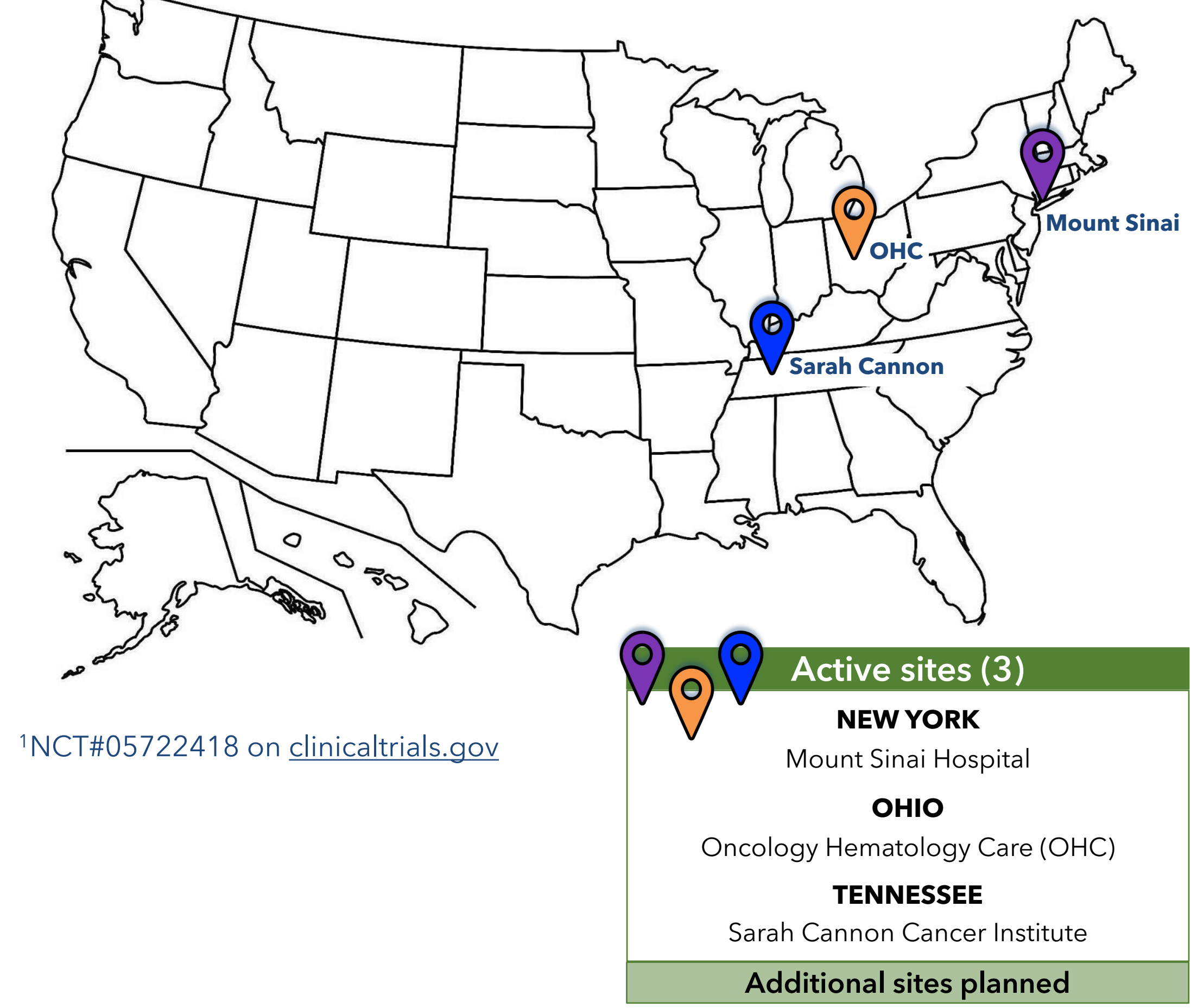
ULN: upper limit of normal; **AST:** aspartate aminotransferase; **ALT:** alanine transaminase

CaMMouflage key exclusion criteria

- Prior treatment with CAR-T cell therapy directed at any target
- Monoclonal antibody for treatment of MM within 21 days; BiTE/ADC within 90 days; IMiD within 7 days; PI or chemo within 14 days; XRT within 14 days
- AlloSCT within 6 months prior to LDC
 - AlloSCT > 6 months prior without GvHD and immunosuppressive therapy can enroll
- Auto SCT < 12 weeks prior to LDC
- Known active or prior history of CNS involvement
- Seropositive for HIV; active HBV/HCV infection
- Plasma-cell leukemia, WM, POEMS, clinically significant AL
- Malignancy within 2 years (unless treated with curative intent and NED > 2 years; adequately treated non-malignant skin cancers)
- Clinically significant organ dysfunction

BiTE: bispecific T cell engager, **ADC:** antibody drug conjugate; **GvHD:** graft-vs-host disease; **CNS:** central nervous system; **LDC:** lymphodepleting chemotherapy; **POEMS:** polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder; **WM:** Waldenstrom macroglobulinemia; **AL:** amyloidosis; **HIV:** human immunodeficiency virus; **HBV:** hepatitis B virus; **HCV:** hepatitis C virus; **NED:** no evidence of disease

CaMMouflage trial participating sites¹



CB-011CaMMouflage trial summary

- Allogeneic CAR-T cell therapy is an investigational treatment that may address the unmet needs of r/r MM patients
- CB-011 is an **allogeneic anti-BCMA CAR-T cell therapy** engineered using Cas12a chrDNA technology. CB-011 is the first allogeneic CAR-T cell therapy in the clinic, to our knowledge, that is engineered to improve antitumor activity through an immune cloaking strategy with a B2M knockout and insertion of a B2M-HLA-E fusion protein to blunt immune-mediated rejection, and it is derived from healthy donor T cells
- CB-011 has been granted FDA Fast Track Designation for r/r MM
- CaMMouflage is a Phase 1 first-in-human trial investigating the safety and efficacy of CB-011 as a single infusion in patients with r/r MM at clinical sites across the United States

Patient enrollment is ongoing in the dose escalation phase of the CaMMouflage trial

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