

First Clinical Evaluation of an Allogeneic CD19-Directed CAR T-Cell Therapy in Progressive Multiple Sclerosis: Initial Results From the Phase 1 TG-Azercel-101 Study

Daniel Ontaneda¹, Rana Zabad², Jennifer Graves³, Tirisham Gyang⁴, Rebecca S. Farber⁵, Lisa Stropp⁶, Andrew Goodman⁷, Ahmed Z. Obeidat⁸, Koby Mok⁹, Hari Miskin⁹, Jackie Parker⁹, Peter Sportelli⁹, Matthew Lunning²

¹Cleveland Clinic Mellen Center for MS, Cleveland, United States, ²University of Nebraska Medical Center, Omaha, United States, ³University of California San Diego, Department of Neurosciences, San Diego, United States, ⁴Ohio State University, Wexner Medical Center, Columbus, United States, ⁵Columbia University, Neurology, New York, United States, ⁶University of Michigan, Ann Arbor, United States, ⁷University of Rochester, Rochester, United States, ⁸Medical College of Wisconsin, Milwaukee, United States, ⁹TG Therapeutics, Morrisville, United States

Presented at the 10th Joint ACTRIMS-ECTRIMS Meeting | 21–23 October 2026 | Toronto, Canada

Disclosures

Dr. Ontaneda has received research support from the National Institutes of Health, National Multiple Sclerosis Society, Patient-Centered Outcomes Research Institute, Race to Erase MS Foundation, Genentech, Genzyme, Bristol Myers Squibb, and Novartis, and consulting fees from Ardanza Biopharma, Biogen Idec, Bristol Myers Squibb, Contineum Therapeutics, Convelo, Genentech/Roche, Novartis, and Sanofi.

This study is sponsored by TG Therapeutics, Inc.

Progressive MS: Unmet Need

Current State of Treatment in Progressive MS



- Disability can accumulate independent of relapse activity (PIRA)^{1,2}



- Limited approved treatment options for progressive MS^{3,4}



Putative Rationale for CAR T-Cell Treatment



- Deep B-cell depletion across peripheral and tissue compartments, including the CSF



- Immune reset

1. Kappos L, et al. JAMA Neurol. 2020;77:1132–1140.

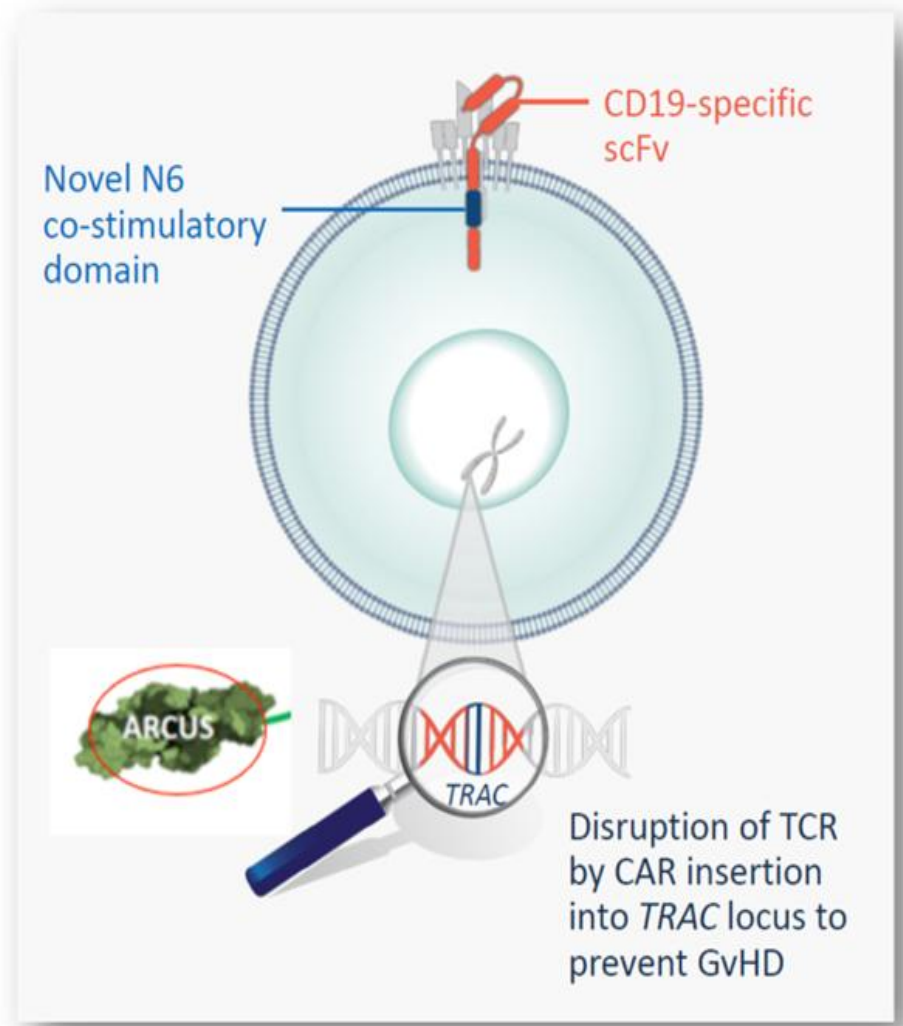
2. Müller J, et al. JAMA Neurol. 2023;80:1232–1245.

3. Fox R, et al. N Engl J Med. 2025;392:1883–1892.

4. Chataway J, et al. Lancet Neurol. 2024;23:277–301.

Azer-cel: Allogeneic Anti-CD19 CAR T-Cell Therapy

Azercabtagene zapreleucel



“Off-the-Shelf” CAR T¹

- Healthy donor-derived, manufactured and banked
- Available without patient-specific manufacturing

CAR T Engineering²

- ARCUS-mediated CAR insertion at the TRAC locus
- TCR disruption designed to reduce GvHD risk

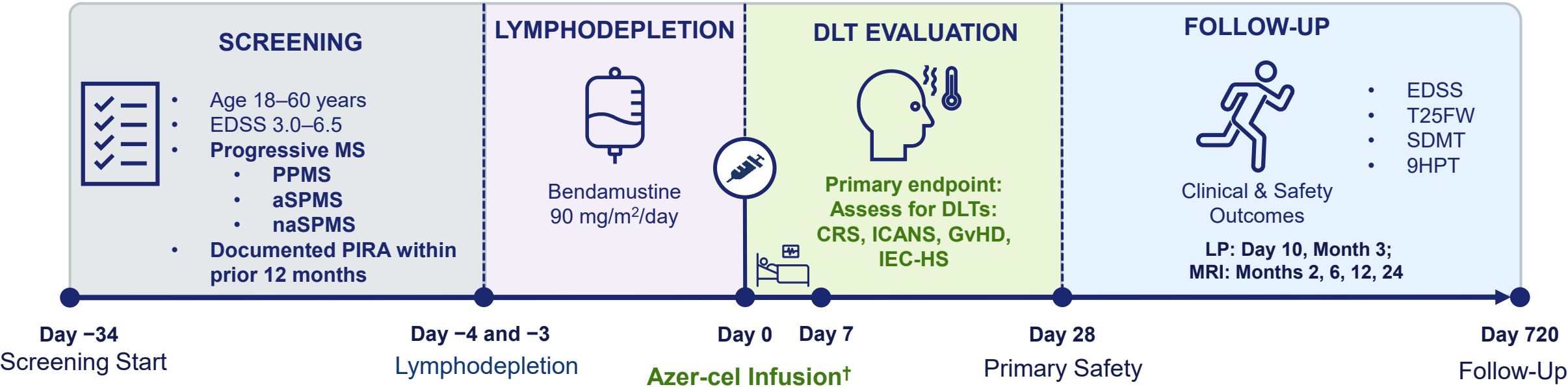
Prior Clinical Experience

- 130+ patients have been treated with azer-cel in oncology³
- FMC63 CD19 binding domain used in approved CAR T products⁴

ARCUS, gene-editing nuclease; CAR, chimeric antigen receptor; GvHD, graft-versus-host disease; scFv, single-chain variable fragment; TCR, T-cell receptor; TRAC, TCR alpha constant locus.
1. Depil S, et al. Nat Rev Drug Discov. 2020;19:185–199. 2. MacLeod DT, et al. Mol Ther. 2017;25:949–961; Shah BD, et al. Blood. 2021;138(Suppl 1):302. 3. Blunt DN, et al. J Clin Oncol. 2026;44(16_suppl):7012; Imugene Ltd. Annual Report 2026:5. 4. He C, et al. Sci Immunol. 2023;8:eadf1426; YESCARTA (axicabtagene ciloleucel) US prescribing information, section 12.6.

TG-Azercel-101 Study Design

Phase 1, open-label, dose-escalation study in progressive MS*



Dose Level	Azercel Dose
DL1	30 × 10 ⁶ cells
DL2	70 × 10 ⁶ cells
DL3	140 × 10 ⁶ cells
DL4	210 × 10 ⁶ cells
DL5	350 × 10 ⁶ cells
DL6	500 × 10 ⁶ cells

EDSS, Expanded Disability Status Scale; aSPMS, active secondary progressive MS; naSPMS, non-active secondary progressive MS; T25FW, Timed 25-Foot Walk; SDMT, Symbol Digit Modalities Test; 9HPT, 9-Hole Peg Test.

† Low-dose IL-2 evaluated in select expansion cohorts

* The protocol also permits enrollment of patients with MG, CIDP, and NMOSD

Baseline Characteristics

All 26 participants had PIRA in the prior 12 months; all had prior anti-CD20 therapy

Baseline Characteristic	Participants (N = 26)
Age, years, median (range)	51.5 (36–59)
Female, n (%)	13 (50%)
PPMS / naSPMS / aSPMS, n (%)	9 (35%) / 10 (38%) / 7 (27%)
Years since MS diagnosis, median (IQR)	8.6 (4.7–18.7)
Baseline EDSS , median (IQR)	6.0 (6.0–6.5)
PIRA in prior 12 months, n (%)	26 (100%)
Number of prior MS treatments, median (IQR)	3 (2–4)
Prior anti-CD20 therapy, n (%)	26 (100%)

Data maturity: median follow-up 4.9 months (range 0.1–15.0); data cutoff 3 Sep 2026. One participant discontinued early.

aSPMS, active secondary progressive MS; IQR, interquartile range; naSPMS, non-active secondary progressive MS; PIRA, progression independent of relapse activity; PPMS, primary progressive MS.

Primary and Secondary Safety Endpoints

No DLTs, Grade ≥ 3 CRS, Grade ≥ 2 ICANS, GvHD, or IEC-HS in 26 participants

Safety Outcome	Participants, n/N (%)
DLT	None
CRS, any grade	2/26 (7.7%)
• Grade 1	1/26 (3.8%)
• Grade 2	1/26 (3.8%)
• Grade ≥ 3	None
ICANS, any grade	2/26 (7.7%)
• Grade 1	2/26 (7.7%)
• Grade ≥ 2	None
IEC-HS, any grade	None
GvHD, any grade	None
Grade ≥ 3 TEAEs	11/26 (42.3%)
SAEs	4/26 (15.4%)
Grade ≥ 3 infections	None

CRS, ICANS, and IEC-HS graded per ASTCT criteria.

CRS, cytokine release syndrome; DLT, dose-limiting toxicity; GvHD, graft-versus-host disease; ICANS, immune effector cell-associated neurotoxicity syndrome; IEC-HS, immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Safety Endpoints by Dose Level

No apparent dose-related trend in CAR T-associated toxicities, supporting ongoing dose escalation

Safety Outcome	DL1 30 × 10 ⁶ cells	DL2 70 × 10 ⁶ cells	DL3 140 × 10 ⁶ cells	DL4 210 × 10 ⁶ cells	DL5 350 × 10 ⁶ cells	DL6 500 × 10 ⁶ cells	Total (N)
Participants, n	1	3	9	8	4	1	26
CRS: G1 / G2 / ≥G3	0/0/0	0/0/0	0/1/0	1/0/0	0/0/0	0/0/0	1/1/0
ICANS: G1 / G2 / ≥G3	0/0/0	1/0/0	1/0/0	0/0/0	0/0/0	0/0/0	2/0/0
IEC-HS	0	0	0	0	0	0	0
GvHD	0	0	0	0	0	0	0
Grade ≥3 TEAEs	1	2	3	4	1	0	11
SAEs	1	1	1	1	0	0	4
Grade ≥3 infections	0	0	0	0	0	0	0

CRS, ICANS, and IEC-HS graded per ASTCT criteria.

CRS, cytokine release syndrome; DL, dose level; G, grade; GvHD, graft-versus-host disease; ICANS, immune effector cell-associated neurotoxicity syndrome; IEC-HS, immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

PK/PD: Azer-cel Exposure and B-Cell Depletion

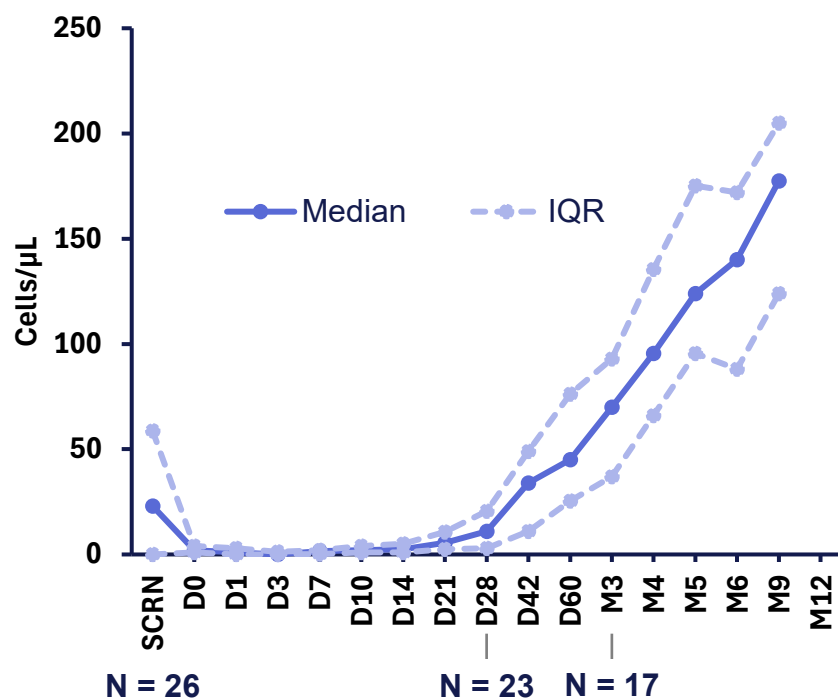
PK: Azer-cel detected in 24/24 evaluable participants, peaking at Day 1–3 across dose levels

PD: CD19+ B-cell depletion in blood and CSF

A. Peripheral Blood CD19+ B Cells

25/26 (96%) reached <10 CD19+ B cells/μL

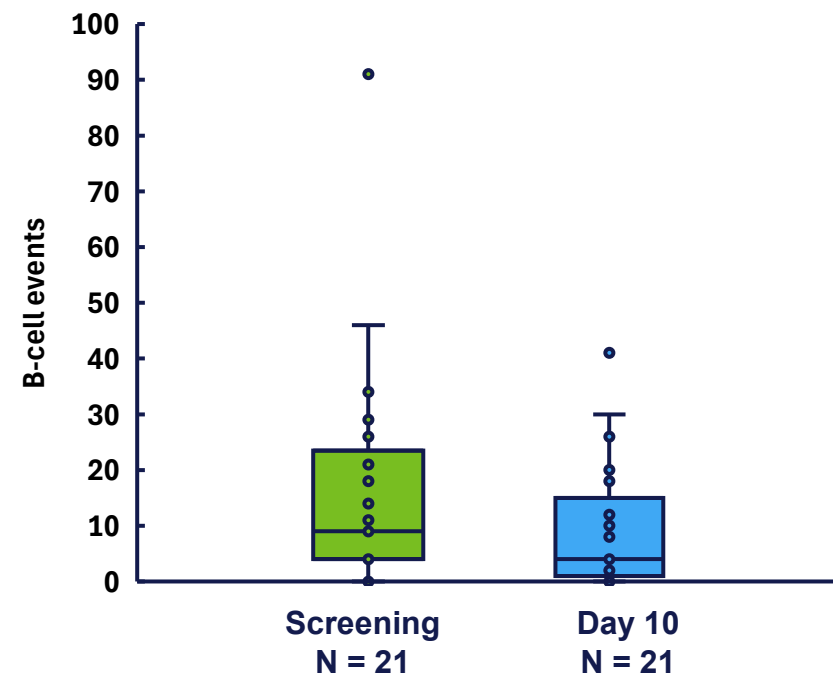
Median B-cell recovery began by Day 28



B. CSF CD19+ B Cells

Median: 9 → 4 CD19+ B-cell events

Median within-participant change: -52.3%



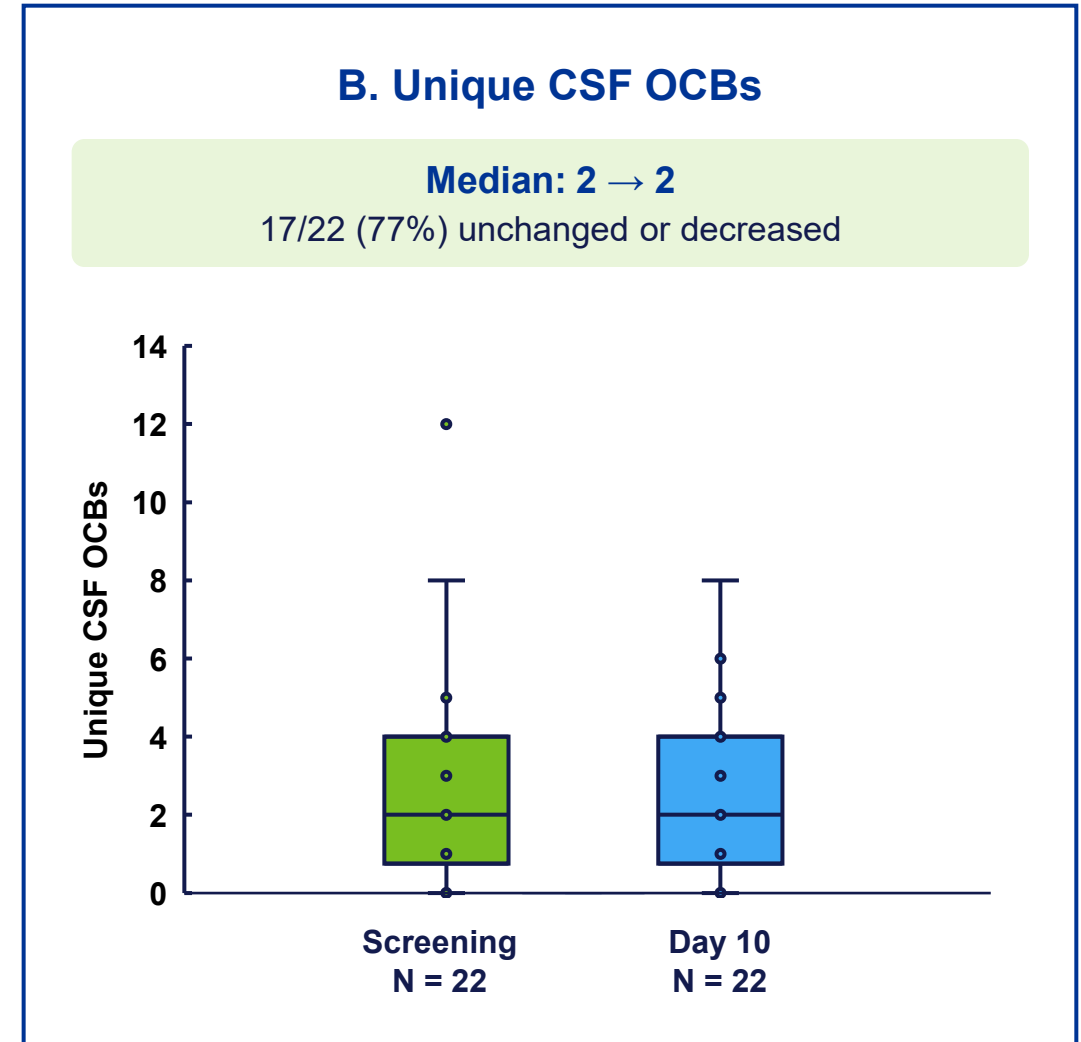
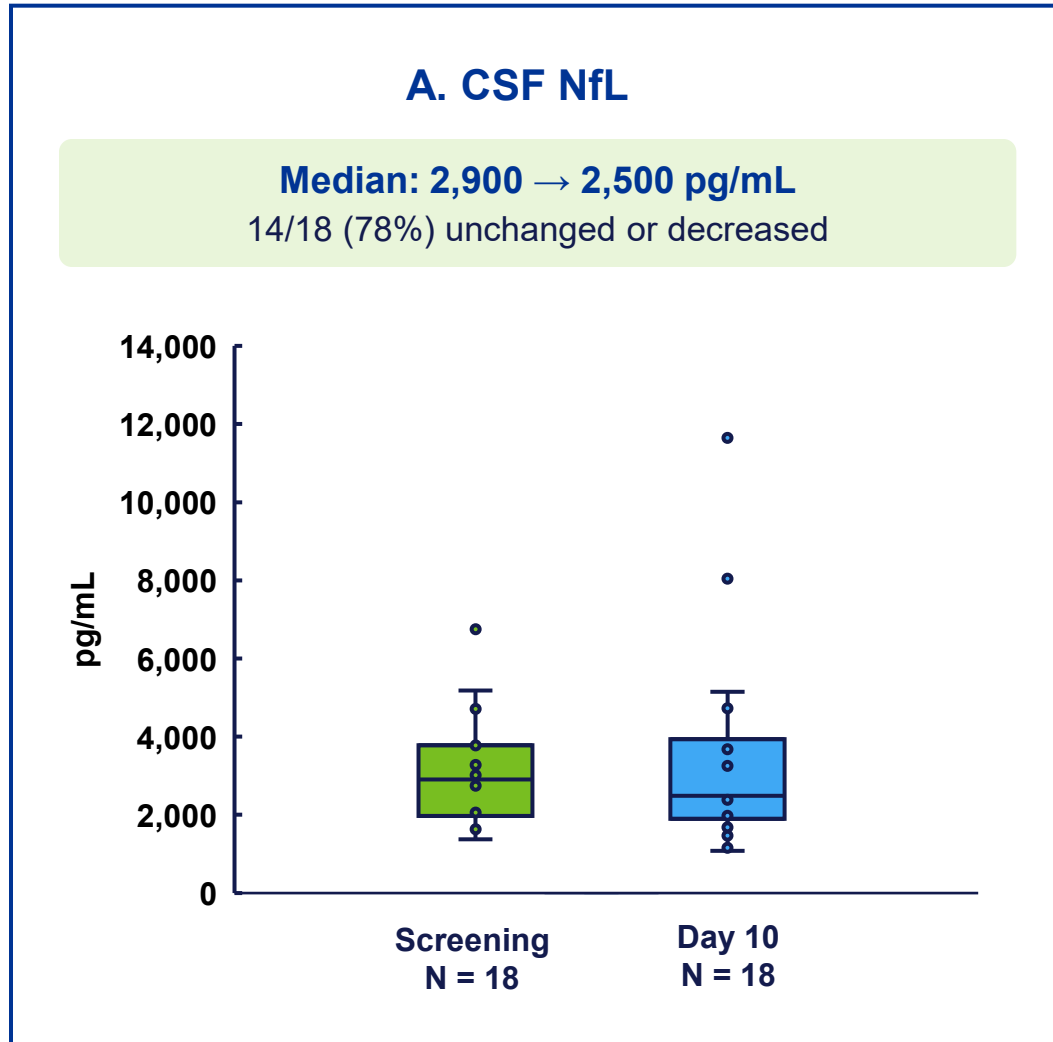
A: Solid line represents median blood CD19+ B-cell counts over time; N = participants with available data at the timepoint shown directly above each value (SCRN, D28, M3).

B: CSF CD19+ B-cell events are absolute CD19+ events acquired by flow cytometry per CSF sample. Boxes show median and IQR; whiskers extend to the most extreme values within 1.5 × IQR; outliers shown individually.

CSF, cerebrospinal fluid; D, day; IQR, interquartile range; M, month; PD, pharmacodynamics; PK, pharmacokinetics; SCRN, screening.

Early CSF Biomarkers Through Day 10

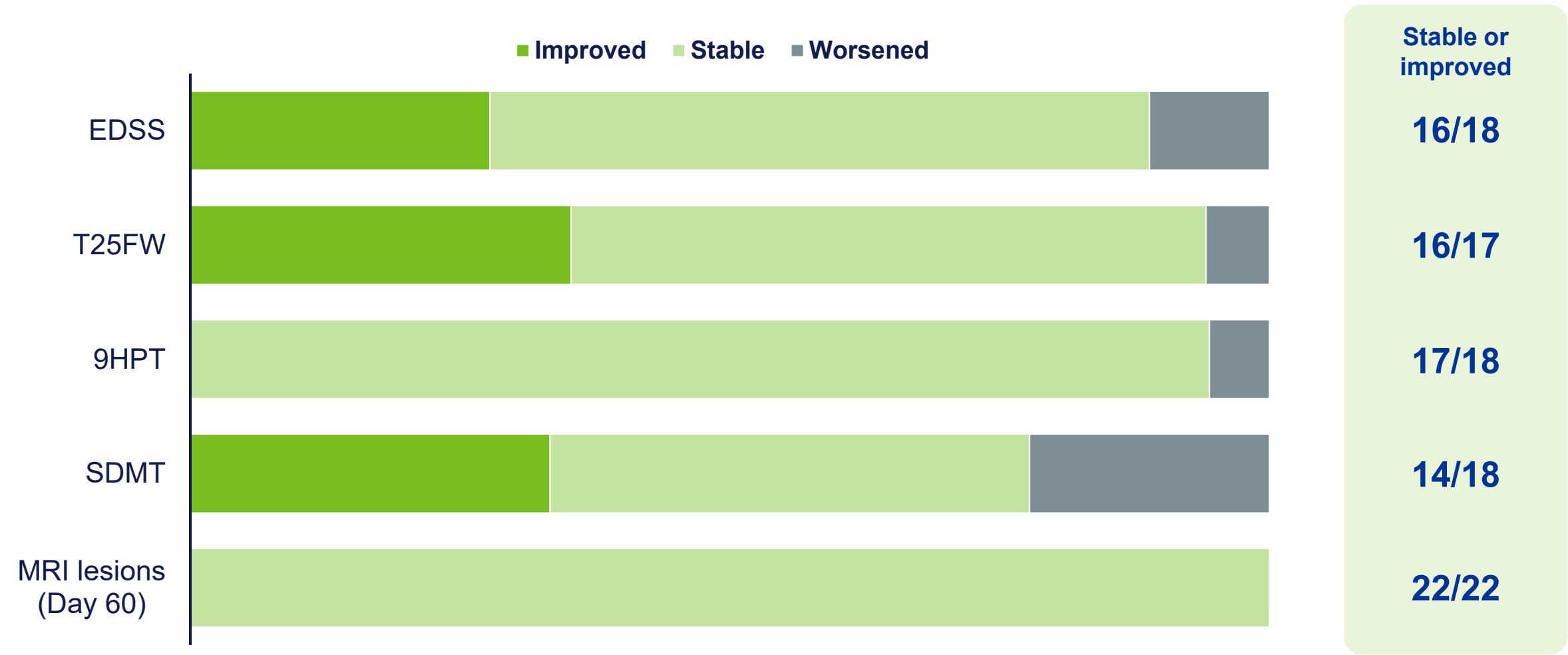
No median increase in neuroaxonal injury or intrathecal IgG synthesis at Day 10



Unchanged or decreased: NfL <20% increase from baseline; unique CSF OCB count unchanged or decreased.
Boxes show median and IQR; whiskers extend to the most extreme values within $1.5 \times$ IQR; outliers shown individually.

Clinical Outcomes at Day 90 and MRI at Day 60

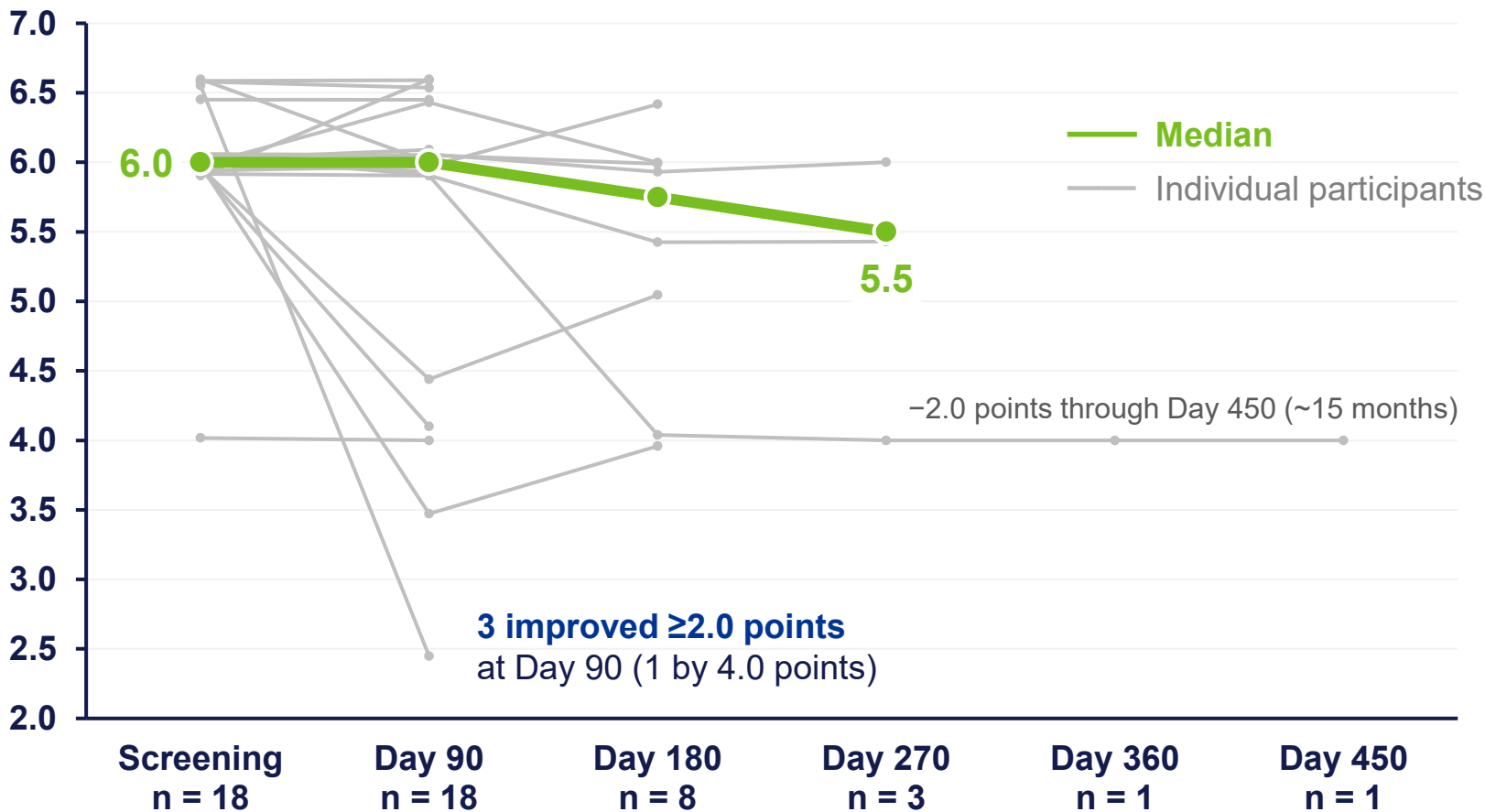
Most evaluable participants were stable or improved across clinical and MRI measures



Improved/worsened: EDSS ≥ 1.0 -point decrease/increase from baseline (≥ 0.5 if baseline EDSS ≥ 6.0); T25FW/9HPT $\geq 20\%$ decrease/increase in completion time; SDMT ≥ 4 -point increase/decrease. Stable: neither improved nor worsened. MRI lesions: gadolinium-enhancing (Gd+) T1 and new/enlarging T2 lesions.

Change in EDSS Following Azer-cel

Most participants stable or improved through Day 180



EDSS stable or improved

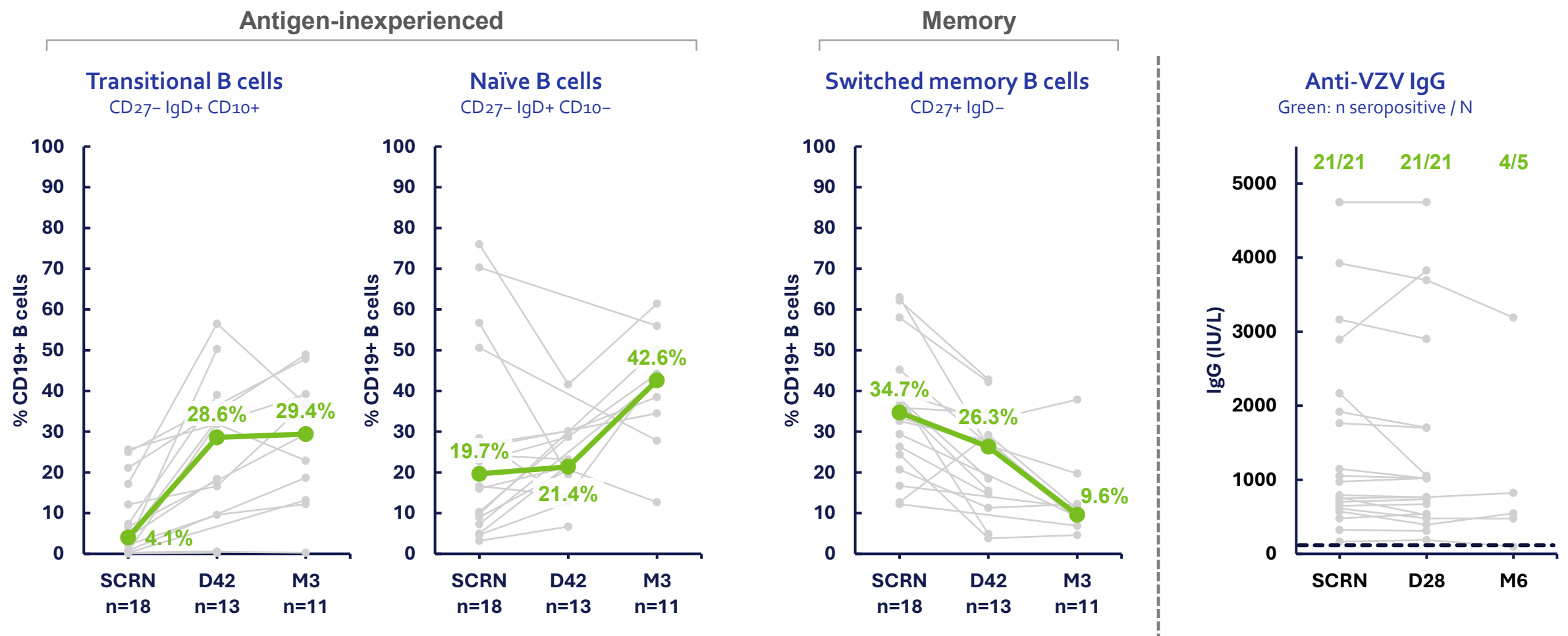
Day 90
16/18

Day 180
7/8

Day 270
3/3

One Day 90 EDSS responder subsequently discontinued the study to initiate another MS disease-modifying therapy. EDSS, Expanded Disability Status Scale; n, participants assessed at each timepoint.

B-Cell Reconstitution Is Enriched for Transitional and Naïve Phenotypes With Fewer Switched Memory B Cells; VZV Humoral Immunity Is Preserved



Paired participant data. B-cell panels: peripheral-blood flow cytometry, % of quantifiable CD19+ B cells at screening, Day 42, and Month 3; green line and labels, median; n, participants with data at each timepoint. Anti-VZV IgG panel: screening, Day 28, and Month 6; dashed line, assay-specific seropositivity cutoff. D, day; IgG, immunoglobulin G; IU, international units; M, month; SCRN, screening; VZV, varicella zoster virus.

Conclusions

- TG-Azercel-101 is the **first reported clinical evaluation of an allogeneic CD19-directed CAR T-cell therapy in progressive MS.**
- Azer-cel demonstrated an **encouraging safety profile to date.** No DLTs or high-grade CAR T-associated toxicities were observed across dose levels, including no Grade ≥ 3 CRS, Grade ≥ 2 ICANS, GvHD, or IEC-HS.
- Azer-cel produced **peripheral B-cell depletion** (25/26 participants < 10 CD19+ cells/ μ L) and an **early signal of B-cell reduction in the CSF.**
- **Clinical outcomes were predominantly stable or improved through Day 90.** EDSS was stable or improved in 16/18 participants at Day 90 and 7/8 at Day 180.
- **B-cell reconstitution was enriched for transitional and naïve phenotypes with fewer switched memory B cells,** consistent with an immune reset; **VZV humoral immunity was preserved.**
- These early findings are limited by small numbers and short follow-up; dose escalation and longer-term follow-up are ongoing.

Acknowledgements

Study TG-Azercel-101 requires a multidisciplinary effort. We would like to thank our **neurology, hematology-oncology, and cellular therapy investigators, coordinators, nurses, laboratory, and study teams** for their key contributions.

And most importantly, we are deeply grateful to **the patients and their families** for their participation.