Cabaletta Bio®

CAR T Cell Therapy in Myositis: A Potential Emerging Treatment Option

MED-2026-IIM-PPT-004
March 2026

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Words such as, but not limited to, "look forward to," "believe," "expect," "anticipate," "estimate," "intend," "plan," "would," "should" and "could," and similar expressions or words, identify forward-looking statements.

Various risks, uncertainties and assumptions could cause actual results to differ materially from those anticipated or implied in our forward-looking statements. Such risks and uncertainties include, but are not limited to, risks related to the success, cost, and timing of our development activities and clinical trials, risks related to our ability to demonstrate sufficient evidence of safety, efficacy and tolerability in our clinical trials, the risk that the results observed with the similarly-designed construct, including, but not limited to, dosing regimen, are not indicative of the results we seek to achieve with rese-cel, the risk that signs of biologic activity or persistence may not inform long-term results, risks related to clinical trial site activation or enrollment rates that are lower than expected, risks that modifications to trial design or approach may not have the intended benefits and that the trial design may need to be further modified; our ability to protect and maintain our intellectual property position, risks related to our relationships with third parties, uncertainties related to regulatory agencies' evaluation of regulatory filings and other information related to our product candidates, our ability to retain and recognize the intended incentives conferred by any regulatory designations, risks related to regulatory filings and potential clearance, the risk that any one or more of our product candidates will not be successfully developed and commercialized, the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies, risks related to volatile market and economic conditions and our ability to fund operations and continue as a going concern. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, you are cautioned not to place undue reliance on these forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ materially from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent annual report on Form 10-K and quarterly report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in our other filings with the Securities and Exchange Commission. Certain information contained in this Presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this Presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. The Company is the owner of various trademarks, trade names and service marks. Certain other trademarks, trade names and service marks appearing in this Presentation are the property of third parties. Solely for convenience, the trademarks and trade names in this Presentation are referred to without the ® and TM symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

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Speaker	Disclosures
David J. Chang, MD, MPH, FACR Chief Medical Officer Cabaletta Bio Symposium Chair	DJC is an employee of Cabaletta Bio
Hector Chinoy, PhD FRCP BMBS MSc BMedSci Professor of Rheumatology & Neuromuscular Disease / Honorary Consultant Rheumatologist Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, United Kingdom Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, United Kingdom	HC has received grant support from Pfizer; advisory board member for Astra Zeneca, Pfizer, Argenx, J&J; Data and Science Monitoring Board chair for Horizon Therapeutics; speaker fees from Cabaletta Bio.

Learning Objectives

- Review key lessons of CAR T cell therapy from hematology and in autoimmune diseases
- Describe the rationale for deep B cell depletion, particularly by targeting CD19, in the treatment of myositis
- Describe late-stage clinical study designs and review the latest results from RESET-Myositis®

CAR, chimeric antigen receptor; CD, cluster of differentiation.

Symposium Presenters

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Symposium Chair

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University of Manchester

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Overview of CAR T in Autoimmune Diseases

David J. Chang

What are Chimeric Antigen Receptor (CAR) T Cells?

Engineered T cells that combine the targeting ability of antibodies with the cell-killing machinery of T cells[1]

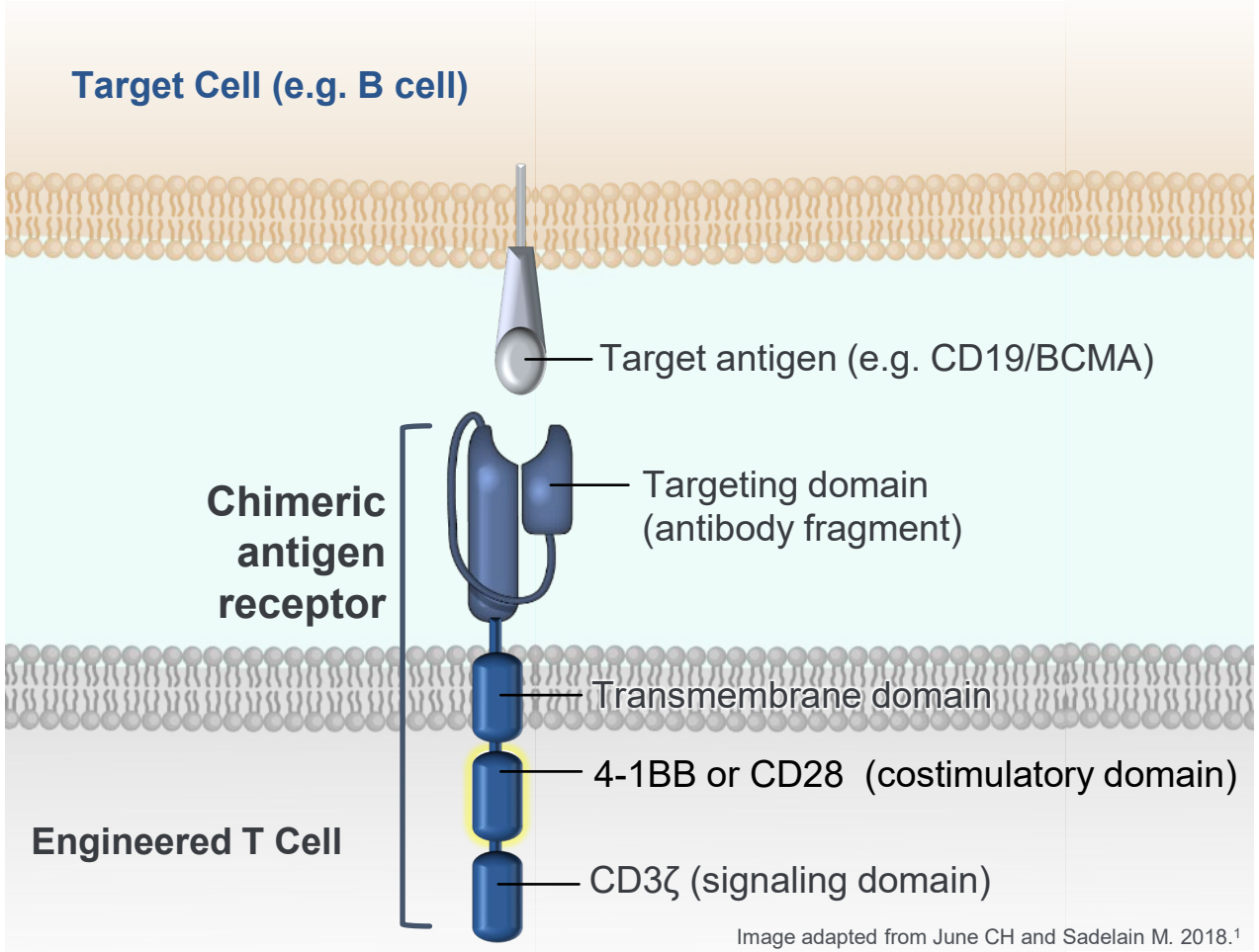


Image adapted from June CH and Sadelain M. 2018.[1]

Seven CAR T therapies have been FDA-approved in oncology since 2017[2–4]

CAR T cells bind to their target antigen, killing the associated cell[1,5]

- The binding results in activation of bystander immune and non-immune cells
- This activation may result in a significant release of a range of cytokines

BCMA, B cell maturation antigen; CAR, chimeric antigen receptor; CD, cluster of differentiation; FDA, U.S. Food and Drug Administration.

1. June CH, Sadelain M. *N Engl J Med*. 2018;379:64-73. 2. Holzinger A, Abken H. *Pharmacology*. 2022;107(9-10):446–463. 3. National Cancer Institute: CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. Available at www.cancer.gov/about-cancer/treatment/research/car-t-cells (accessed October 2025). 4. U.S. Food and Drug Administration. (2024 November 8). *FDA approves obecabtagene autoleucel for adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia* [Press release]. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-obecabtagene-autoleucel-adults-relapsed-or-refractory-b-cell-precursor-acute (accessed October 2025). 5. Shimabukuro-Vornhagen A, et al. *J Immunother Cancer*. 2018;6(1):56.

CD19-CAR T Therapy: Lessons From Oncology

Efficacy

COMPLETE remission rate:
40%–67%[1–5]

LONG-TERM remission rate:
30%–59%[6–7]

Safety

Known AEs include[8–10]

- CRS and ICANS
- Prolonged B cell aplasia
- Infections
- Insertional oncogenesis
- Secondary malignancies

Familiarity with managing AEs has enabled potential outpatient CAR T administration in oncology[11,12]

Risk factors in oncology[13–17]

Target-cell burden	→ CRS, ICANS
CAR T persistence	→ Prolonged B cell aplasia
Prolonged aplasia	→ Infection risk
Mutational load	→ Malignancy/relapse

AE risk may be reduced in autoimmune patients[18]

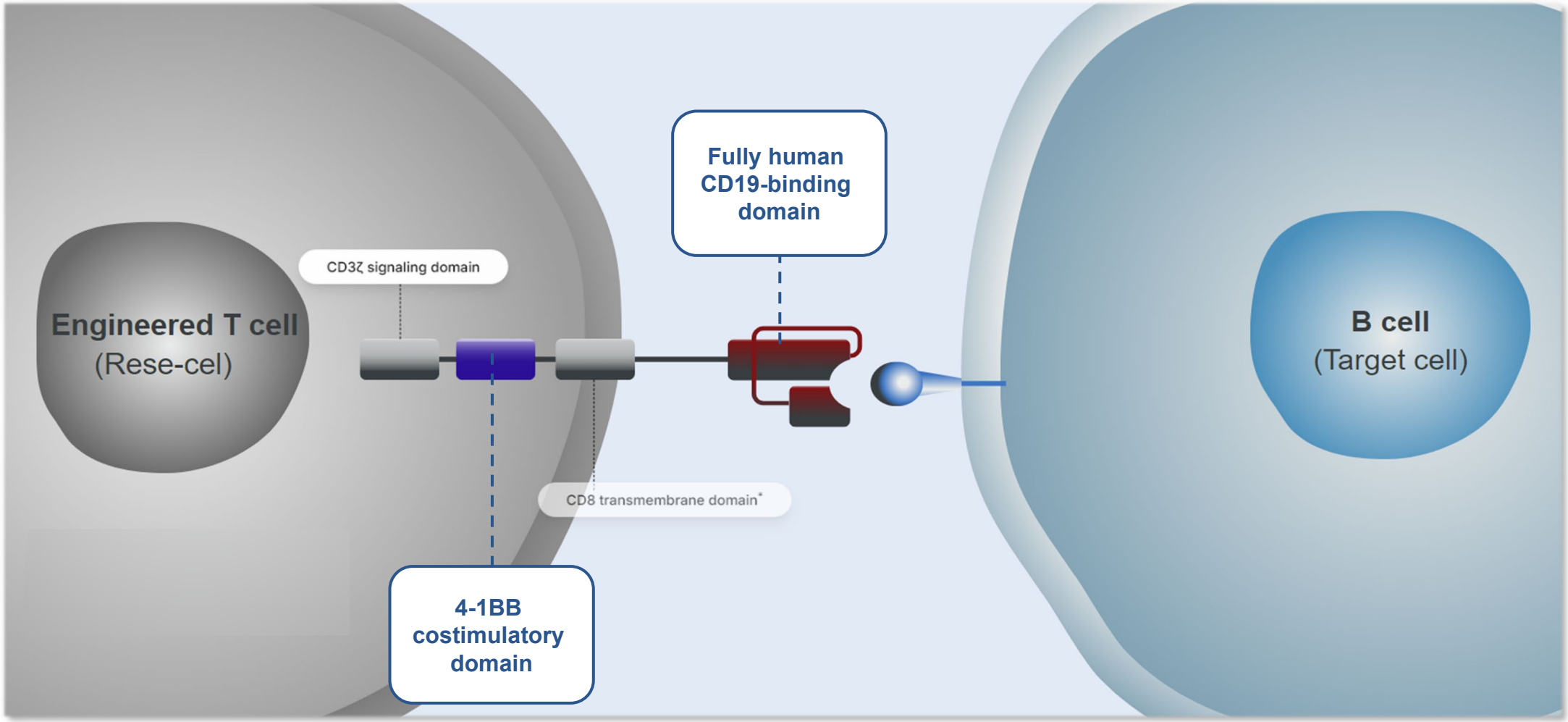
University of Erlangen study of CD19-CAR T-treated SLE patients reported less severe AEs than B-cell non-Hodgkin lymphoma patients despite similar CD19-CAR T-cell expansion

AE, adverse event; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

1. Maude SL, et al. *N Engl J Med*. 2018;378(5):439–448. 2. Schuster SJ, et al. *N Engl J Med*. 2019;380(1):45–56. 3. Locke FL, et al. *Lancet Oncol*. 2019;20(1):31–42. 4. Abramson JS, et al. *Lancet*. 2020;396(10254):839–852. 5. Wang M, et al. *N Engl J Med*. 2020;382(14):1331–1342. 6. Schuster SJ, et al. *Lancet Oncol*. 2021;22(10):1403–1415. 7. Neelapu SS, et al. *Blood*. 2023;141(19):2307–2315. 8. Breyanzi. Prescribing information; 2025. Available at: www.fda.gov/media/145711/download (accessed October 2025). 9. Yescarta. Prescribing information; 2024. Available at: www.fda.gov/media/108377/download (accessed October 2025). 10. Kymriah. Prescribing information; 2025. Available at: www.fda.gov/media/107296/download (accessed October 2025). 11. Zhang Y, et al. *J Clin Med*. 2023;12(19):6124. 12. Furqan F, et al. *Blood Adv*. 2024;8(16):4320–4329. 13. Baker DJ, et al. *Nature*. 2023;619(7971):707–715. 14. Baker DJ, June CH. *Cell*. 2022;185(24):4471–4473. 15. Li YR, et al. *Trends Pharmacol Sci*. 2024;45(9):839–857. 16. Schett G, et al. *Nat Rev Rheumatol*. 2024;20(9):531–544. 17. Blache U, et al. *RMD Open*. 2023;9(4):e002907. 18. Müller F, et al. *Blood*. 2025;146(9):1088–1095.

Rese-cel: Designed for Patients with Autoimmune Disease[1]

Fully human CD19-binding domain and 4-1BB costimulatory domain



*Same construct as used in tisagenlecleucel, a CAR T therapy approved in oncology.[2]

CAR, chimeric antigen receptor; CD, cluster of differentiation; rese-cel, resecabtagene autoleucel.

1. Peng BJ, et al. *Mol Ther Methods Clin Dev*. 2024;32(2):101267. 2. Schuster SJ, et al. *N Engl J Med*. 2019;380(1):45–56.

Autologous CAR T Cell Therapy: Rese-cel Manufacturing[1]

Leveraging a patient's own T cells presents the possibility of removing or reducing preconditioning

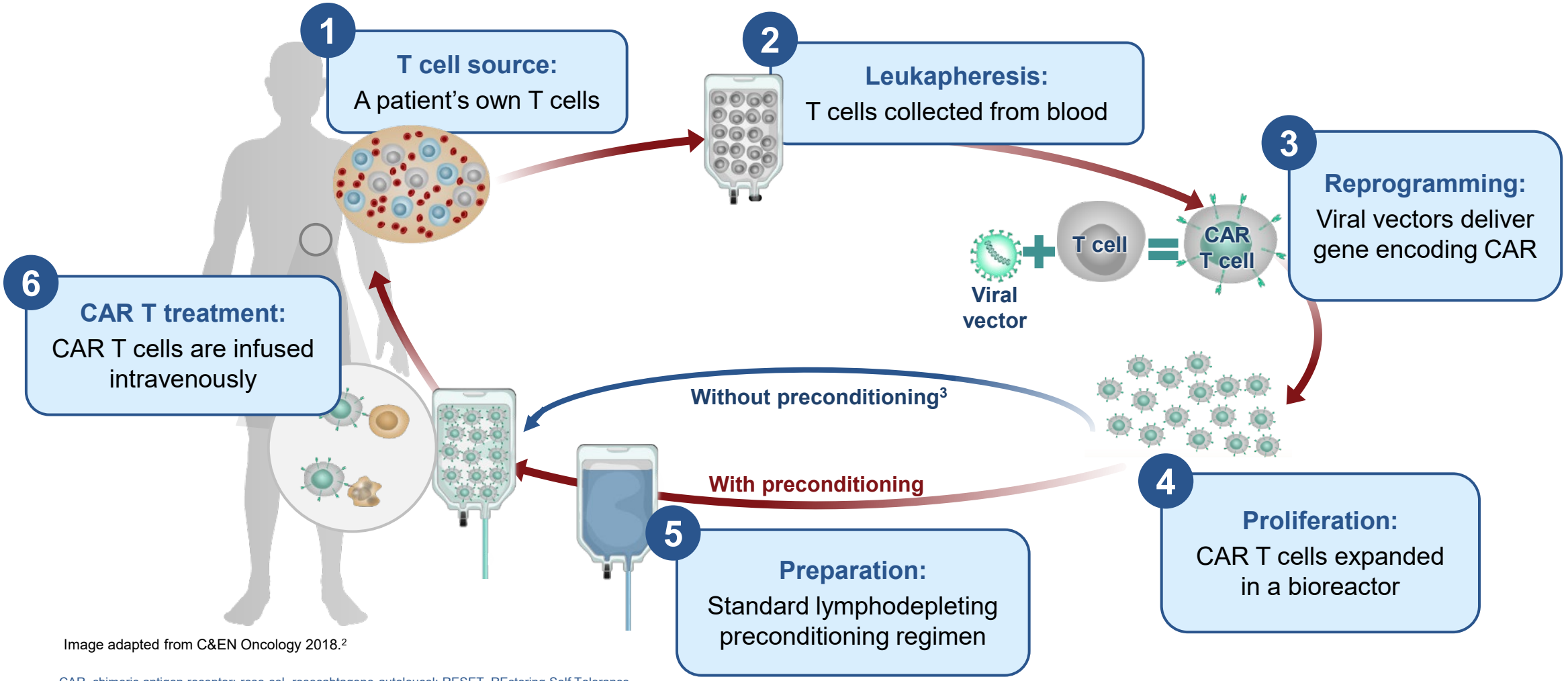


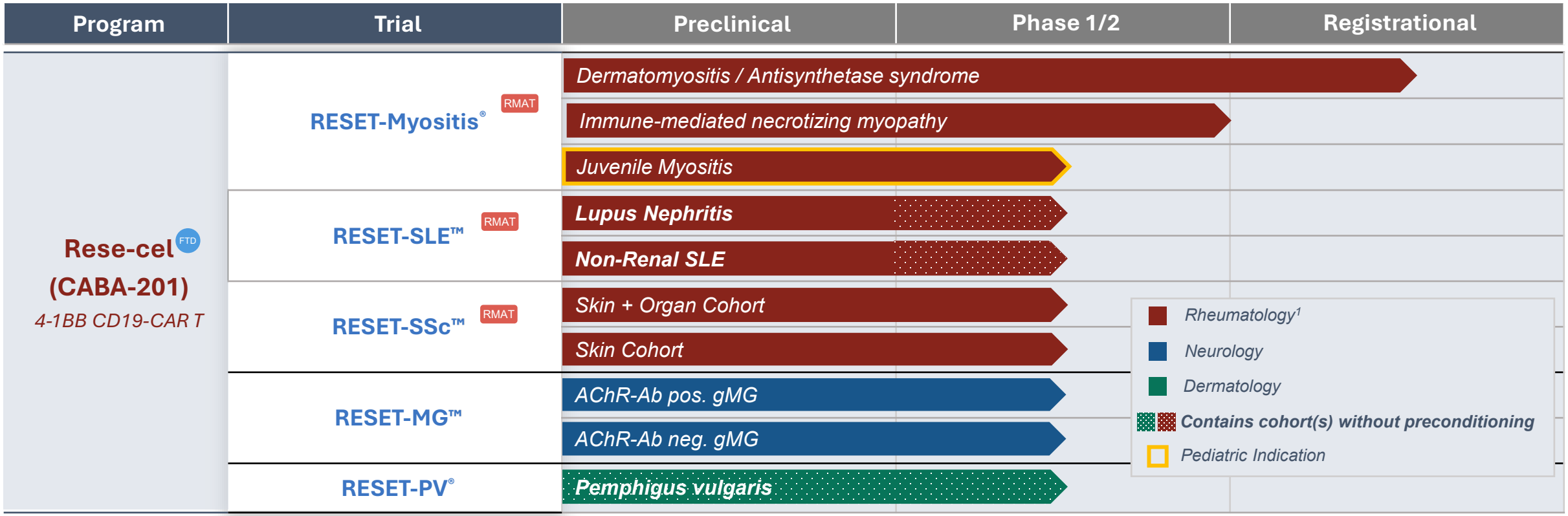
Image adapted from C&EN Oncology 2018.[2]

CAR, chimeric antigen receptor; rese-cel, resecabtagene autoleucel; RESET, REstoring Self Tolerance.

1. Peng BJ, et al. *Mol Ther Methods Clin Dev*. 2024;32(2):101267. 2. C&EN Oncology. 2024. Available at: https://cen.acs.org/pharmaceuticals/oncology/Controlling-CAR-T-scientists-plan/96/i19 (accessed October 2025). 3. NCT04422912. Available at: https://clinicaltrials.gov/study/NCT04422912 (accessed October 2025).

RESET™ Clinical Program for Rese-cel, a CD19-Directed CAR T

Disease-specific cohorts in RESET clinical program are designed to evolve directly into registrational studies



RESET™ – **RE**storing **SE**lf-**T**olerance; Ab – Antibody; AChR – Acetylcholine receptor; gMG – Generalized myasthenia gravis; PV – Pemphigus vulgaris; SLE – Systemic lupus erythematosus; SSc – Systemic sclerosis

1. Myositis patients can also be treated by neurologists or dermatologists; lupus nephritis patients can also be treated by nephrologists.

● FDA Fast Track Designation received in dermatomyositis, SLE and lupus nephritis, systemic sclerosis, generalized myasthenia gravis and multiple sclerosis.

■ FDA Regenerative Medicine Advanced Therapy (RMAT) received in myositis, SLE, LN and systemic sclerosis.

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CAR T in Autoimmune Disease: Focus on Myositis

Hector Chinoy

Myositis: A Disease of Significant Unmet Need

Affects ~80K U.S. patients and ~85K patients in Europe; high mortality and limited treatment options[1–10]

High disease burden: disability & mortality

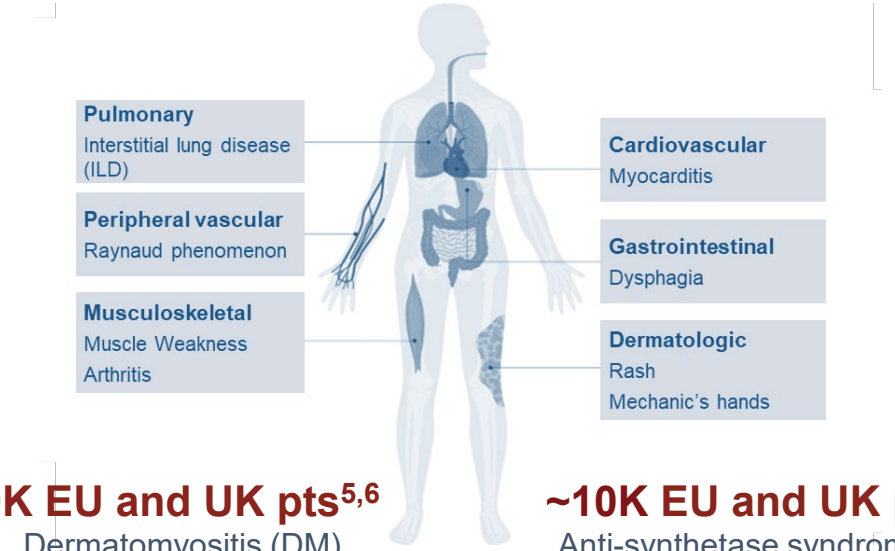
- Moderate to severe disability (40% to 65%)[2]
- Assisted walking devices (18% to 38%)[2]
- The **risk of mortality is ~3 times higher** than the general population, primarily due to cancer and lung & cardiac complications[3]
  - ~20% mortality <5 years with standard immunosuppressive treatment[4]

High unmet medical need

- Mainstay of therapy is glucocorticoids with immunomodulators[1]
  - Only FDA-approved therapy is IVIg in adult dermatomyositis[1]

Potential manifestations & subtype prevalence in Europe

Key myositis subtypes based on underlying immune mechanisms & clinical characteristics[1]



~59K EU and UK pts[5,6]
Dermatomyositis (DM)

~10K EU and UK pts[5,7,11]
Anti-synthetase syndrome (ASyS)

~16K EU and UK pts[5]
Immune-mediated necrotizing myopathy (IMNM)

FDA, U.S. Food and Drug Adminisration; IVIg, intravenous immunoglobulin

1. Lundberg IE, et al. *Nat Rev Dis Primers.* 2021;7(1):86. 2. Opinc AH, et al. *Rheumatol Int.* 2019;39(7):1213-1220. 3. Marie I. *Curr Rheumatol Rep.* 2012;14(3):275-285. 4. Schiopu E, et al *Arthritis Res Ther.* 2012;14(1):R22. 5. Khoo T, et al. *Nat Rev Rheumatol.* 2023;19(11):695–712. 6. Kronzer VL, et al. *Arthritis Care Res (Hoboken).* 2023;75(2):348–355. 7. Coffey C, et al. *Arthritis Rheumatol.* 2021;73 (Suppl 9). Abstr. No. 1022. 8. Dahal K, et al. *Ann Med Surg (Lond).* 2022;82:104571. 9. Papadopoulou C, et al. *Nat Rev Rheumatol.* 2023;19(6):343–362. 10. Shelly S, et al. *Muscle Nerve.* 2022;65(5):541–546. 11. . Orphanet: Antisynthetase syndrome. Available at: https://www.orpha.net/en/disease/detail/81 (accessed June 2025).

Myositis Classification Is Based on Autoantibodies and Clinical Features

Subtypes have distinct underlying immune mechanisms and clinical characteristics

	DM[1]	ASyS[1]	IMNM
Myositis clinical features	Symmetric proximal weakness	Symmetric proximal muscle weakness	Severe symmetric proximal muscle weakness with very high CK; prominent muscle atrophy likely due to necrotized muscle with permanent damage[1,2]
Extramuscular features	At least one of the associated conditions (ILD, dysphagia, dysphonia, malignancy, vasculitis)	ILD; cutaneous features such as mechanic's hands, arthritis, Raynaud's syndrome; fever	Primarily muscle-predominant, limited systemic involvement[1,2]
Key autoantibodies	Anti-Mi-2, anti-MDA5, anti-TIF1, anti-NXP2	Anti–tRNA synthetase (e.g. Jo-1, PL-7)	Anti-SRP and anti-HMGCR[1,2]
Muscle biopsy	Perifascicular atrophy with complement-mediated microangiopathy	Perimysial and perifascicular inflammation	Widespread myofiber necrosis with minimal lymphocytic infiltrate, macrophage and complement-rich[1,3]

ASyS, anti-synthetase syndrome; CK, creatine kinase; DM, dermatomyositis; HMGCR, 3-hydroxy-3-methylglutaryl-coenzyme A reductase; ILD, interstitial lung disease; IMNM, immune-mediated necrotizing myopathy; MDA5, melanoma differentiation-associated gene 5; NXP, nuclear matrix protein; SRP, signal recognition particle; TIF, transcriptional intermediary factor; tRNA, transfer ribonucleic acid.

1. Paik JJ, et al. *Rheumatology (Oxford).* 2025;64(6):3288–3302. 2. Weeding E, Tiniakou E. *Curr Treatm Opt Rheumatol.* 2021;7(2):150–160. 3. Preuße C, et al. *Am J Pathol.* 2012;181(6):2161–2171.

B Cells Play a Central Role in Autoimmune Diseases

Current therapeutic options often result in incomplete B cell depletion in tissues and lymphoid organs[1]

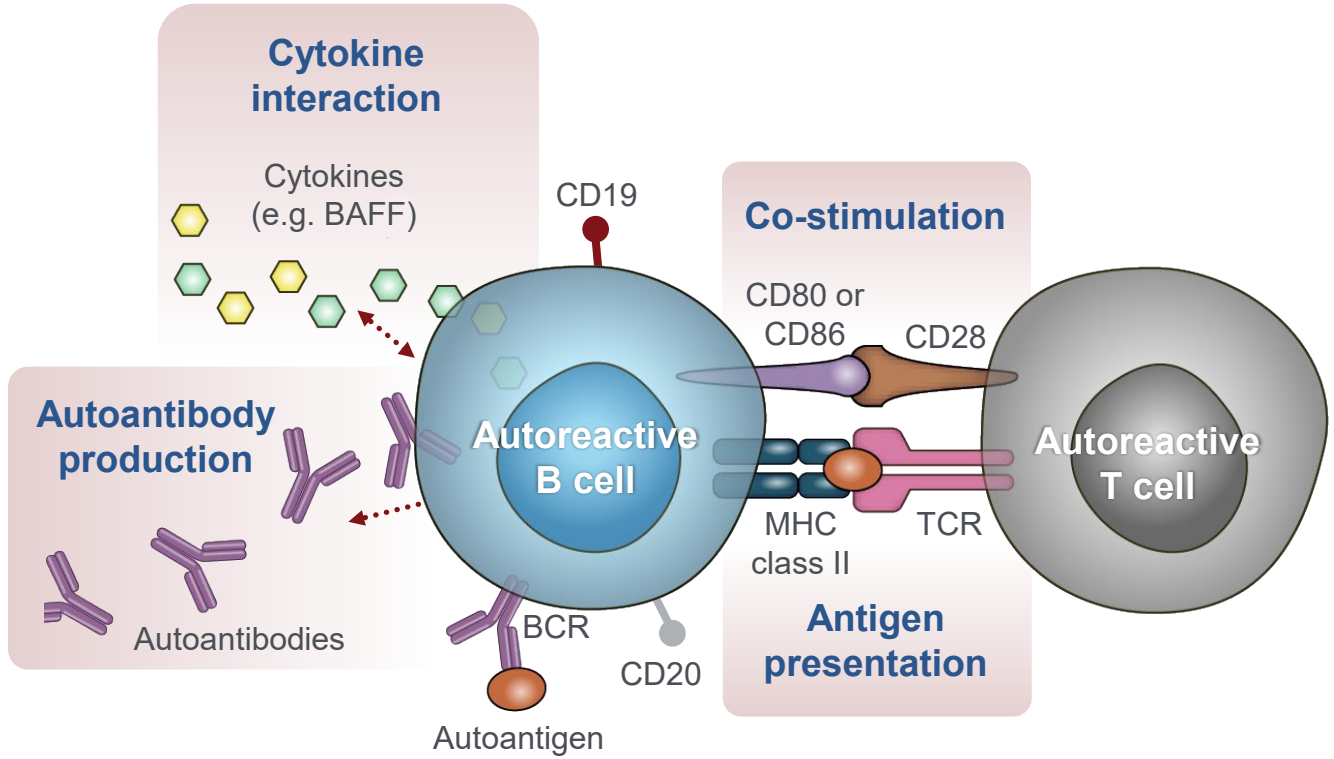


Image adapted from Rubin SJS, et al. 2019[2]

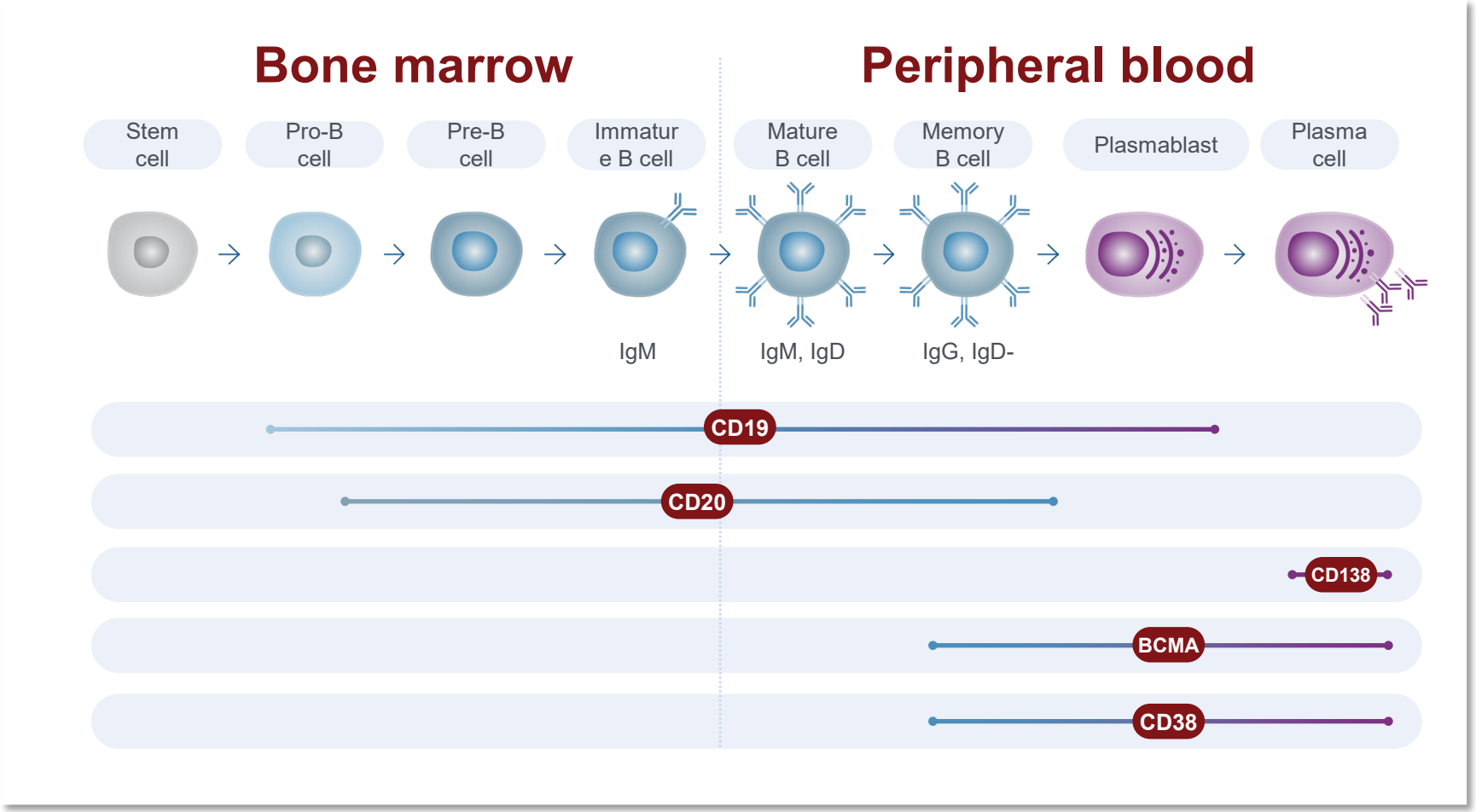
- B cells contribute to autoimmunity through a variety of mechanisms[2,3]
- B cells display profound and multifaceted autoreactivity that extends beyond the bloodstream into inflamed tissues[1]
- B cell-directed therapies are important tools in the treatment of autoimmune diseases[3]
- Failure to achieve long-standing remission with mAb-based therapy may be due to incomplete B cell depletion[1,4–6]

BAFF, B cell activating factor; BCR, B cell receptor; CD, cluster of differentiation; mAb, monoclonal antibody; MHC, major histocompatibility complex; TCR, T cell receptor.

1. Schett G, et al. *Ann Rheum Dis*. 2024;83(11):1409–1420. 2. Rubin SJS, et al. *Nat Rev Rheumatol.* 2019;15(5):303–315. 3. Barnas JL, et al. *Curr Opin Immunol.* 2019;61:92–99. 4. Tur C, et al. *Ann Rheum Dis.* 2025;84(1):106–114. 5. Bucci L, et al. *Nat Med.* 2024;30(6):1593–1601. 6. Gonzalez T, et al. *Ann Rheum Dis.* 2024;83(1):945. Abstr. No. POS1062.

B Cells Play a Central Role in Autoimmune Diseases

CD19 is expressed early in the development of B cells and throughout most of the B cell lifecycle[1]



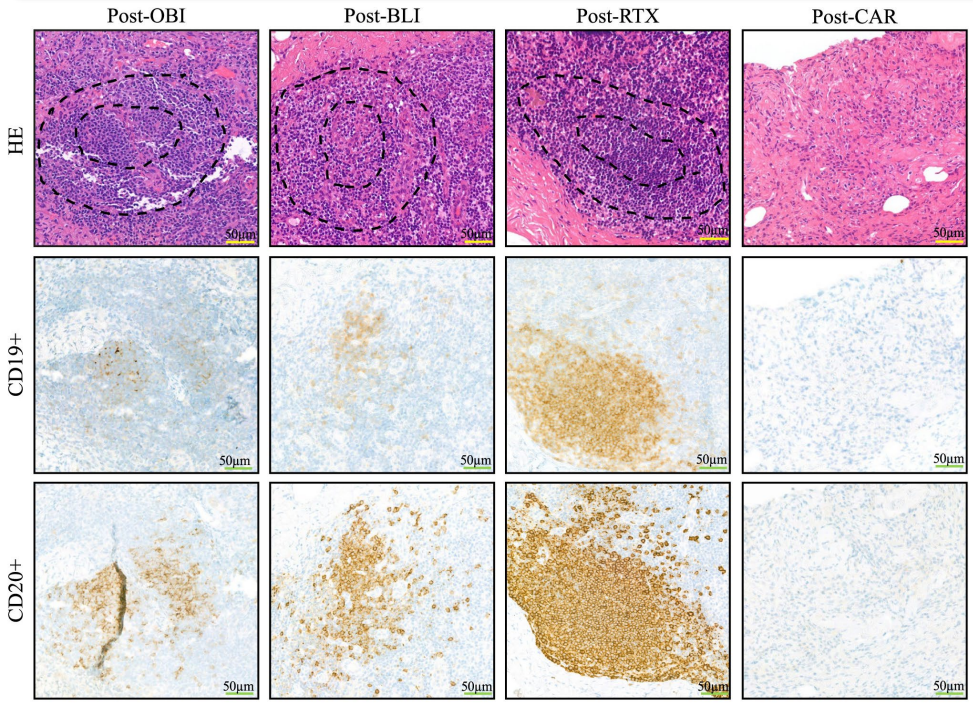
1. Lejeune M, et al. *Front Immunol*. 2020;11:762.
Imagine adapted from Lejeune M, et al. *Front Immunol*. 2020;11:762.

Incomplete B Cell Depletion Limits Durable Remission

- mAb-based therapy may result in incomplete B cell depletion, during which tissue-resident B cells escape[1]
- **A true "immune system reset" may therefore not be achieved with current therapies[1]**

- An academic study in autoimmune diseases has shown CD19-CAR T therapy achieves deeper depletion than with antibody-based therapies[2]
- To date, multiple bispecific T cell engager therapies have demonstrated an inability to fully deplete tissue-resident B cells[2–4]

Representative images of lymph node biopsies from OBI-, BLI-, RTX-, and CAR-treated patients[2]



HE, haematoxylin and eosin-stained biopsy
CD19+ / CD20+, immunohistochemistry pictures of CD19+ and CD20+ B cells within biopsy

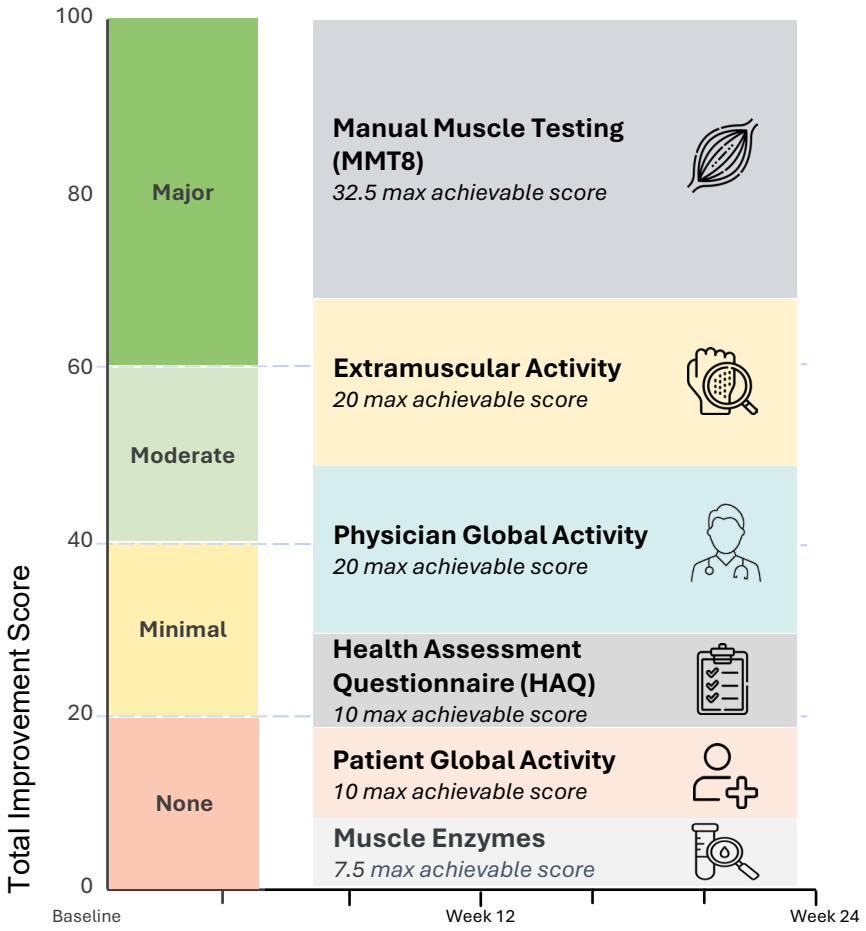
BLI, blinatumomab; CAR, chimeric antigen receptor; CD, cluster of differentiation; mAb, monoclonal antibody; OBI, obinutuzumab; RTX, rituximab.

1. Schett G, et al. *Ann Rheum Dis*. 2024:ard-2024-225727. 2. Tur C, et al. *Ann Rheum Dis*. 2025:S0003-4967(25)04174-3. doi: 10.1016/j.ard.2025.06.2120. Online ahead of print. 3. Bucci L, et al. *Nat Med*. 2024;30(6):1593–1601. 4. Gonzalez et al. *Ann Rheum Dis*. 2024;83(1):945 [EULAR 2024 abstract POS1062].

TIS: Myositis Outcomes Captured Through Validated Composite Endpoint

A composite tool measuring a patient's relative improvement from their baseline

Total improvement score (TIS) components

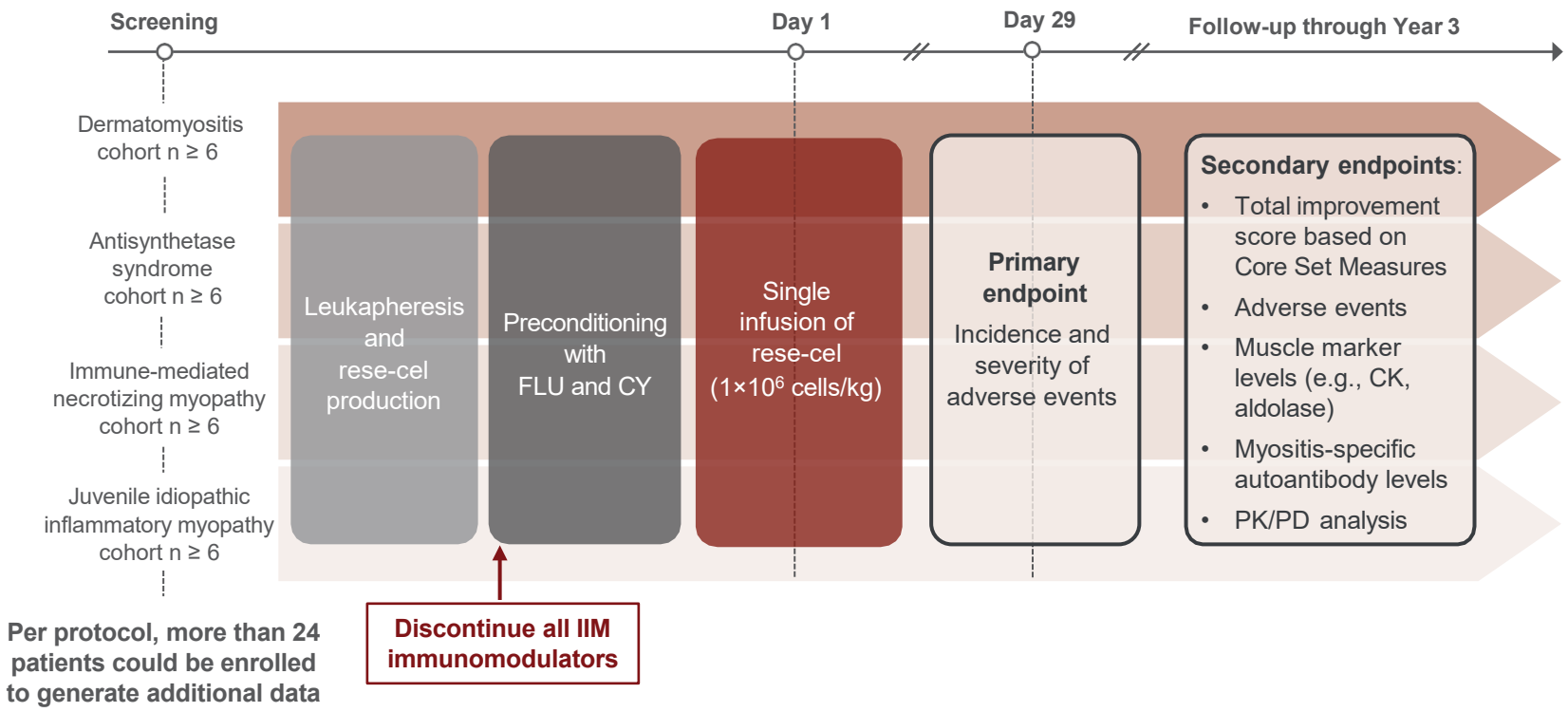


- TIS developed via conjoint analysis based continuous model using **absolute percentage change** in 6 core set measures (CSM): MMT8, Extramuscular Activity, Physician Global Activity, Health Assessment Questionnaire, Patient Global Activity, and Muscle Enzymes
- TIS is the sum of improvement scores in the 6 CSMs, with **ceiling of potential effect likely higher in DM and ASyS than in IMNM given minimal extramuscular involvement**

ASyS, antisynthetase syndrome; DM, dermatomyositis; IMNM, immune-mediated necrotizing myopathy.
Aggarwal R, et al. *NEJM*. 2022;387(14):1264–1278.

RESET *Myositis*® : Phase 1/2 Study Design[1,2]

Enrolling patients with moderate to severe disease that is refractory to standard of care



Key Inclusion Criteria[1,2]

- A definite or probable clinical diagnosis of IIM (2017 EULAR/ACR classification criteria)
- **For adult IIM cohorts**: Age ≥18 and ≤75 with a diagnosis of **dermatomyositis, antisynthetase syndrome, or immune-mediated necrotizing myopathy** based on presence of serum myositis-specific antibodies (MSA)
- **For JIIM cohort:** Age ≥6 and ≤17 with presence of at least one MSA or myositis-associated antibody (MAA)

Key Exclusion Criteria[1,2]

- Cancer-associated myositis or malignancy within the last 5 years
- Significant lung or cardiac impairment
- Previous CAR T cell therapy and/or HSCT
- Treatment with B cell-depleting agent within prior ~6 months

ACR, American College of Rheumatology; CAR, chimeric antigen receptor; CK, creatine kinase; CY, cyclophosphamide; EULAR, European Alliance of Associations for Rheumatology; FLU, fludarabine; HSCT, hematopoietic stem cell transplant; IIM, idiopathic inflammatory myopathy; JIIM, juvenile idiopathic inflammatory myopathy; MAA, myositis-associated antibody; MSA, myositis-specific antibodies; PK/PD, pharmacokinetic/pharmacodynamic; rese-cel, resecabtagene autoleucel; RESET, REstoring SElf-Tolerance.

1. Cabaletta Bio – Data on File. 2. NCT06154252. Available online at: www.clinicaltrials.gov/study/NCT06154252 (accessed October 2025).

Baseline Characteristics: First 13 Patients in RESET Myositis® *

All patients had active, refractory disease despite multiple immunomodulatory agents, including IVIg and B cell-targeting therapies

	DM N=4	ASyS N=2	IMNM N=6	JIIM N=1
Mean age, years (min, max)	~58 (45, 72)	~44 (39, 48)	~55 (33, 64)	14
Female, n (%)	3 (75)	1 (50)	1 (17)	1 (100)
Years since diagnosis, mean (min, max)	3.0 (2.0, 3.6)	9.2 (3.6, 14.8)	4.5 (1.4, 8.8)	8.5
Myositis-specific autoantibody	50% TIF1-γ 25% NXP, 25% SAE	100% Jo-1	67% HMGCR 33% SRP	NXP-2
Baseline disease activity†				
Mean MMT-8	109.6	129.5	122.0	134.0
Median CK, U/L	40.0	311.5	2214.5	176.0
Mean CDASI-A	26	N/A	N/A	N/A
Prior RTX‡	75%	100%	50%	100%
Prior IVIg‡	100%	100%	83%	100%
Therapies at Screening				
Systemic GCs	75%	100%	67%	0
≤2 IMs	50%	50%	100%	0
≥3 IMs	50%	50%	0%	100%

*As of 11 Sep 2025.
†Baseline disease activity = activity before preconditioning; ‡Reflects any exposure to RTX and IVIg prior or at time of study entry. RTX is not allowed within approximately 6 months of Screening.
ASyS, antisynthetase syndrome; CDASI-A, Cutaneous Dermatomyositis Disease Area and Severity Index – Activity; CK, creatine kinase; DM, dermatomyositis; GC, glucocorticoid; HMGCR, 3-hydroxy-3-methylglutaryl-coenzyme A reductase; IM, immunomodulatory medication; IMNM, immune-mediated necrotizing myopathy; IVIg, intravenous immunoglobulin; JIIM, juvenile idiopathic inflammatory myopathy; MMT-8, manual muscle testing 8; NXP, nuclear matrix protein; N/A, not applicable; RESET, REstoring SElf-Tolerance; RTX, rituximab; SAE, small ubiquitin-like modifier activating enzyme; SRP, signal recognition particle; TIF1, transcription intermediary factor 1; U/L, units per liter.
Cabaletta Bio – Data on File.

RESET *Myositis*® : Incidence of Relevant and Related Serious Adverse Events*

Mild CRS (Grade 1) in 4 of 13 patients and no ICANS in any patients

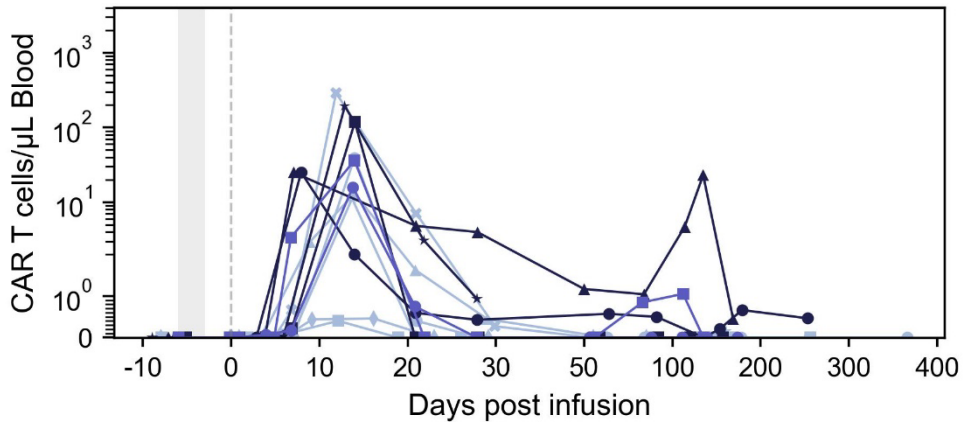
Cohort	DM				ASyS		IMNM						JIIM
Patient	DM-1	DM-2	DM-3	DM-4	ASyS-1	ASyS-2	IMNM-1	IMNM-2	IMNM-3	IMNM-4	IMNM-5	IMNM-6	JIIM-1
CRS†	None	Grade 1	None	None	Grade 1	Grade 1	None	None	Grade 1	None	None	None	None
ICANS†	None	None	None	None	None	None	None	None	None	None	None	None	None
Serious infections‡	None	None	None	None	None	None	None	None	None	None	None	None	None
Related SAEs (Grade)§ (excluding CRS and ICANS)	None	None	None	None	None	None	None	None	None	None	None	None	Febrile Neutropenia (2)

*As of 11 Sep 2025; primary endpoint of the Phase 1/2 study is incidence and severity of adverse events through Day 29. Serious infections and related SAEs are reported to latest follow-up.
†Graded per ASTCT Consensus Grading Criteria.
‡Coded in System Organ Class of Infections and Infestations and meets seriousness criteria.
§As assessed per US Food and Drug Administration guidelines.
ASTCT, American Society for Transplantation and Cellular Therapy; ASyS, antisynthetase syndrome; CRS, cytokine release syndrome; DM, dermatomyositis; ICANS, immune effector cell-associated neurotoxicity syndrome; IMNM, immune-mediated necrotizing myopathy; JIIM, juvenile idiopathic inflammatory myopathy; RESET, REstoring SElf-Tolerance; SAE, serious adverse event.
Cabaletta Bio: Data on File.

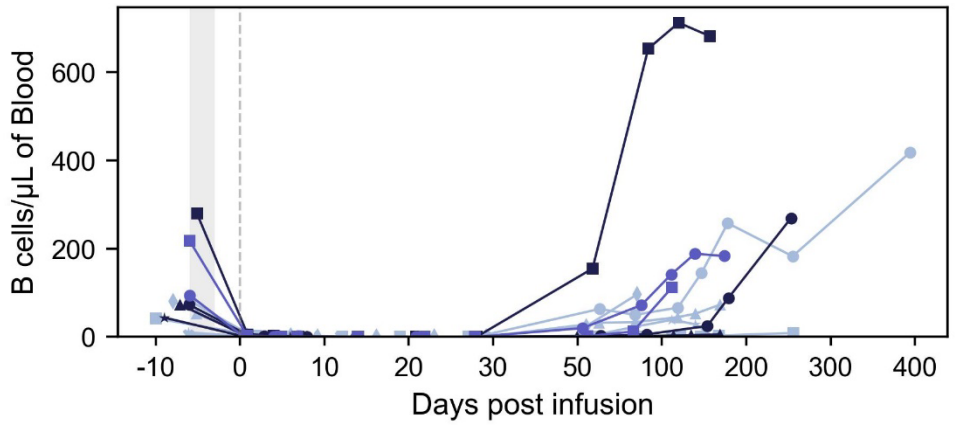
RESET *Myositis*® : Rese-cel Expansion and B Cell Kinetics*

Peak rese-cel expansion and complete and transient peripheral B cell depletion occurred within 1 to 2 weeks post-infusion in all patients

Rese-cel Pharmacokinetics



B Cell Kinetics



IMNM-1
IMNM-2
IMNM-3
IMNM-4
IMNM-5
IMNM-6
DM-1
DM-2
DM-3†
DM-4
ASyS-1
ASyS-2

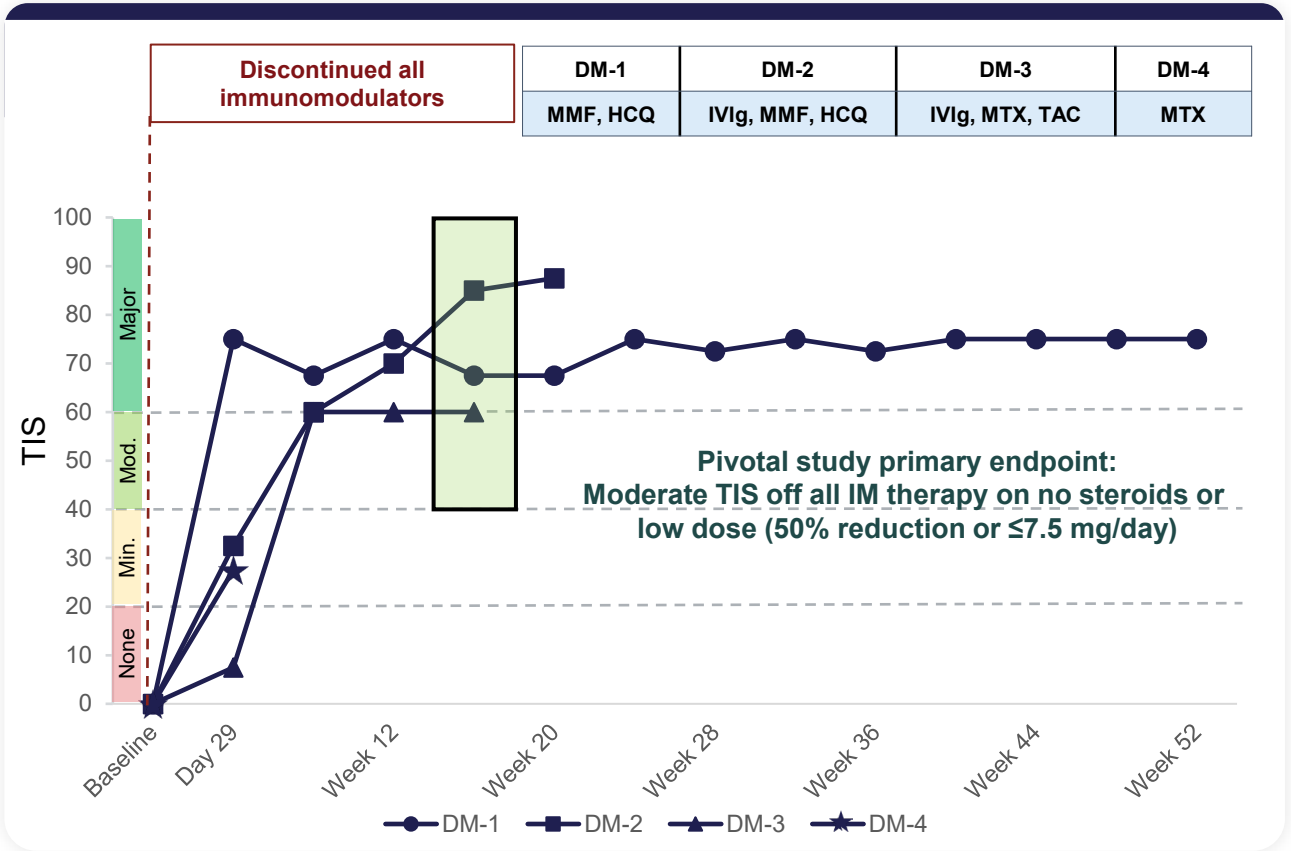
Peripheral B cells began repopulating 2–3 months after rese-cel infusion with transitional naïve cells, indicating B cell reset in patients with sufficient follow-up data

*All data is as of 11 Sep 2025, except DM-3 which includes Week 24 data as of 08 Oct 2025.
†DM-3 rese-cel PK at Week 20 was artifactually elevated due to low circulating lymphocyte counts.
ASyS, antisynthetase syndrome; DM, dermatomyositis; IMNM, immune-mediated necrotizing myopathy; rese-cel, resecabtagene autoleuce; RESET, REstoring SElf-Tolerance.
Cabaletta Bio: Data on File.

RESET *Myositis*®: Efficacy Data in DM Patients Following Rese-cel Infusion*

3 of 3 patients with DM and sufficient follow-up achieved at least moderate TIS response at Week 16 following rese-cel infusion

Assessment at Week 16	DM Patients (baseline autoantibody)			
	DM-1 (SAE)	**DM-2** (None detected†)	**DM-3** (TIF1-γ)	**DM-4** (TIF1-γ)
IM-free	✓	✓	✓	✓‡
Low dose or no GC	✓	✓	✓	✓‡
TIS Response	Major	Major	Major	N/A§
Complete and transient B cell depletion	✓	✓	✓	✓‡
Antibody trend¶	↓	N/A	↓	N/A§
Meets pivotal primary endpoint	✓	✓	✓	N/A§



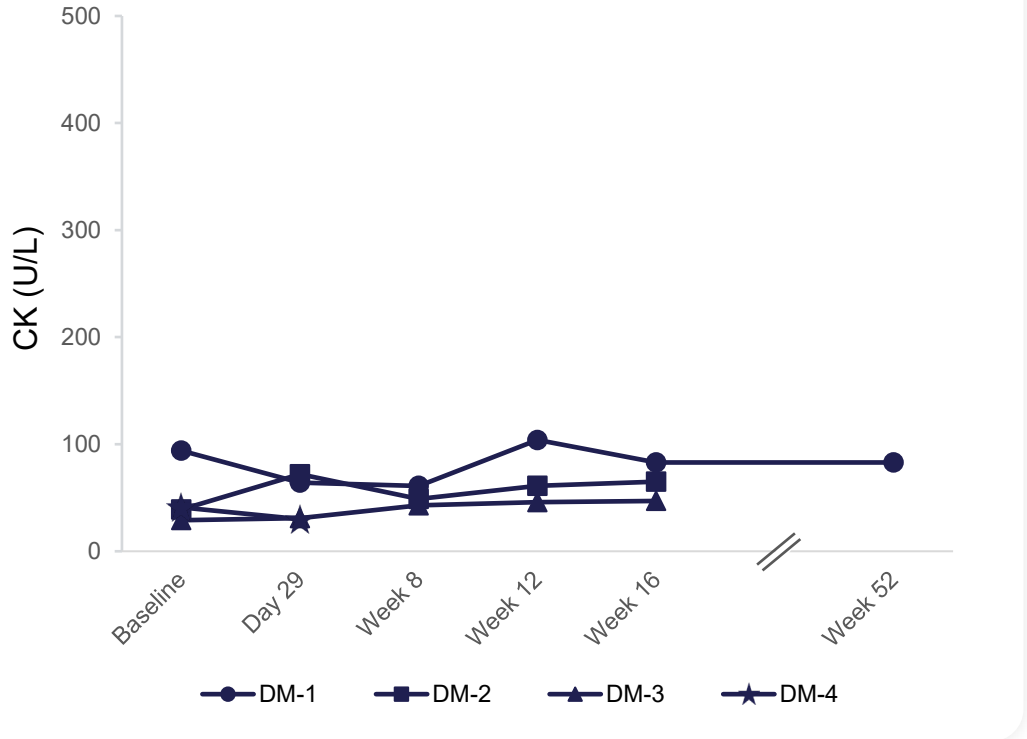
After discontinuation of all IM medications, 3 of 3 DM patients achieved the 16-week primary endpoint for the upcoming pivotal study of at least moderate TIS response

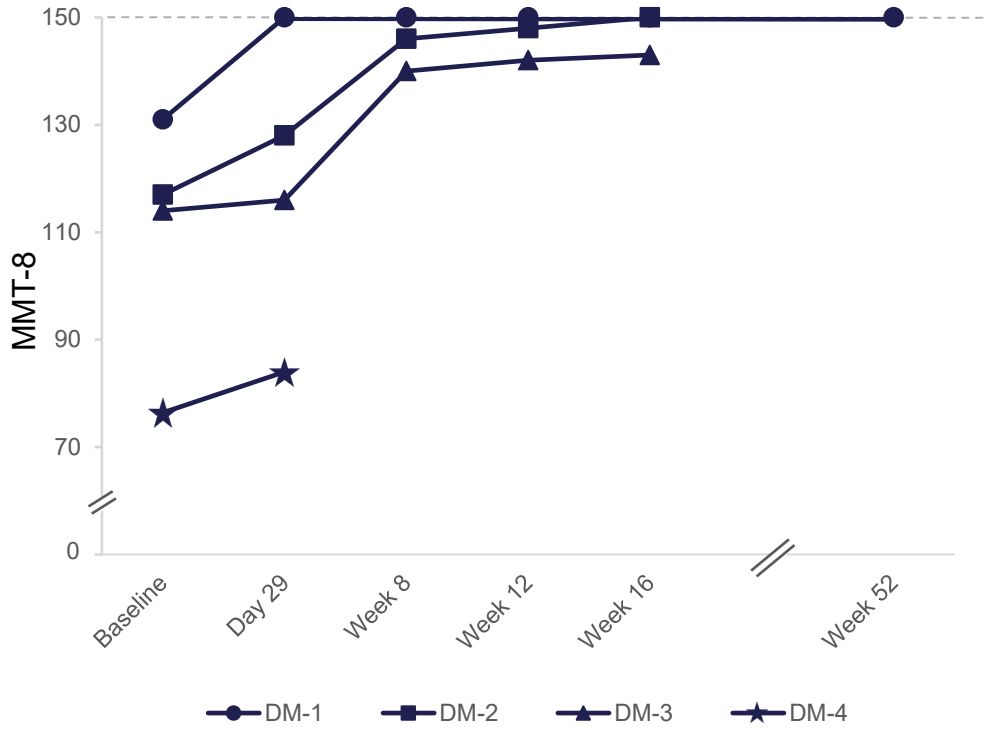
*As of 11 Sep 2025.
†Historical NXP-2 autoantibody, but none detected at Pre-preconditioning (Baseline) visit. ‡At latest follow-up (Day 29). §Insufficient follow-up. ¶Reflects trend from baseline to latest timepoint.
DM, dermatomyositis; GC, glucocorticoid; HCQ, hydroxychloroquine; IM, immunomodulatory medication; IVIg, intravenous immunoglobulin; mg, milligrams; MMF, mycophenolate mofetil; MTX, methotrexate; N/A, not available; NXP, nuclear matrix protein; rese-cel, resecabtagene autoleucel; RESET, REstoring SElf-Tolerance; SAE, small ubiquitin-like modifier activating enzyme; TAC, tacrolimus; TIF1-γ, transcription intermediary factor 1 gamma; TIS, total improvement score.
Cabaletta Bio: Data on File.

RESET *Myositis*®: Efficacy Data in DM Patients Following Rese-cel Infusion*

All patients with DM show improvement in muscle strength on MMT-8 following rese-cel and normal CK levels

Discontinued all immunomodulators at baseline





Clinical responses to rese-cel among DM patients show potential for achieving drug-free remission in patients with refractory myositis

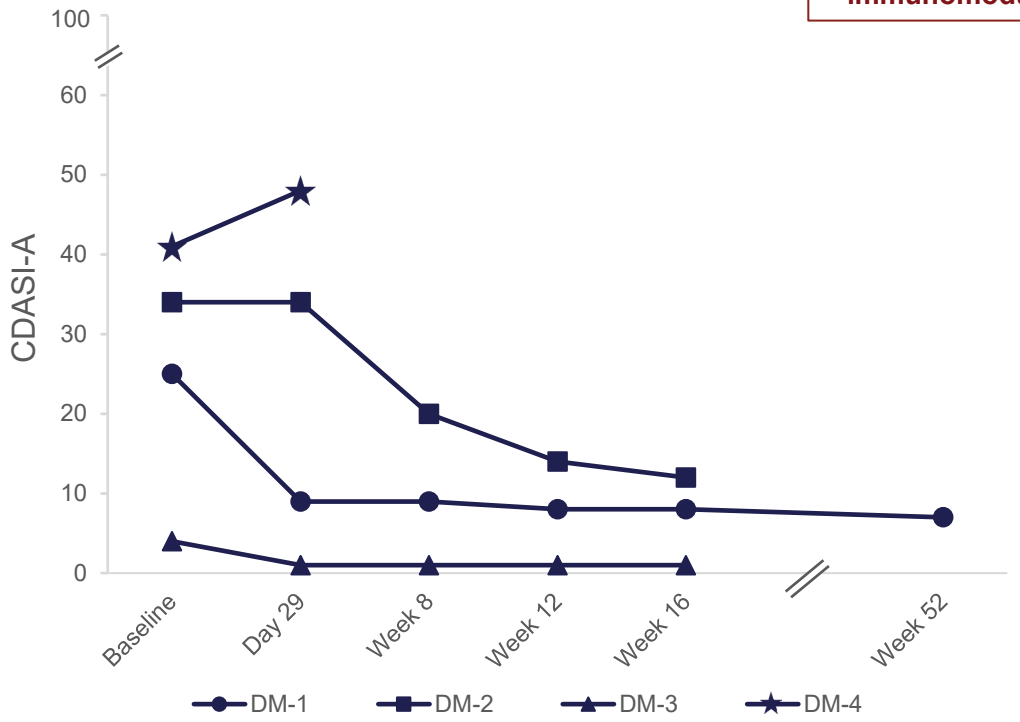
*As of 11 Sep 2025.
†DM-4 MMT-8 measurements were normalized to a total score of 150; not all muscle groups could be evaluated.
CK, creatine kinase; DM, dermatomyositis; MMT-8, manual muscle testing 8; rese-cel, resecabtagene autoleucel; RESET, REstoring SElf-Tolerance; TIS, total improvement score; U/L, units per liter.
Cabaletta Bio: Data on File.

RESET *Myositis*®: Efficacy in DM Patients Following Rese-cel Infusion*

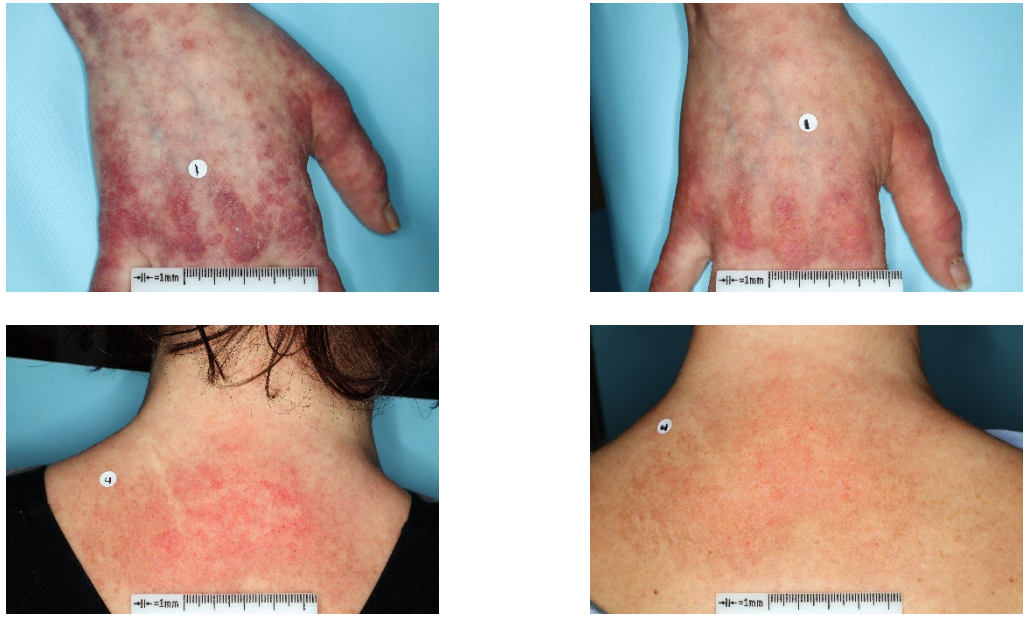
Early clinical responses in DM skin manifestations have been observed off immunomodulators

CDASI-A (N=4)

Discontinued all immunomodulators at baseline



Skin images (DM-2)†



Baseline **Week 12**

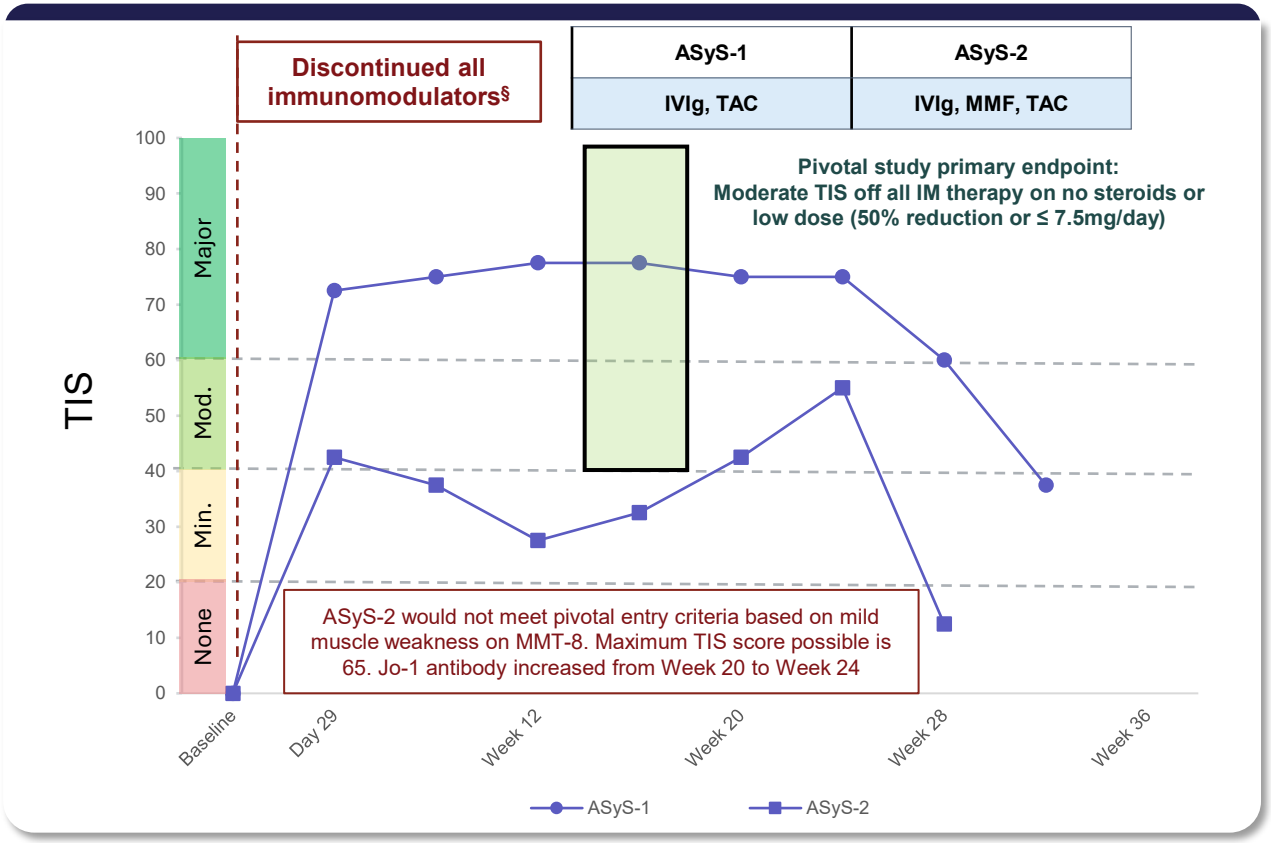
First known adult DM patients dosed with CAR T demonstrated early and clinically visible CDASI-A response off immunomodulators

*As of 11 Sep 2025.
†Participant provided consent to optional clinical photography.
CAR, chimeric antigen receptor; CDASI-A, Cutaneous Dermatomyositis Disease Area and Severity Index – Activity; DM, dermatomyositis; rese-cel, resecabtagene autoleucel; RESET, REstoring SElf-Tolerance.
Cabaletta Bio: Data on file.

RESET *Myositis*®: Efficacy in ASyS Patients Following Rese-cel Infusion[1*]

1 of 2 patients with ASyS achieved at least moderate TIS response at Week 16 following rese-cel infusion

Assessment at Week 16	ASyS (baseline autoantibody)	
	ASyS-1 (Jo-1)	ASyS-2 (Jo-1)
IM-free	✓	✓
Low dose or no GC	✓	✓
TIS response	Major	Minimal
Complete and transient B cells depletion	✓	✓
Antibody trend†	↓‡	↓→‡
Meets pivotal primary endpoint	✓	✗



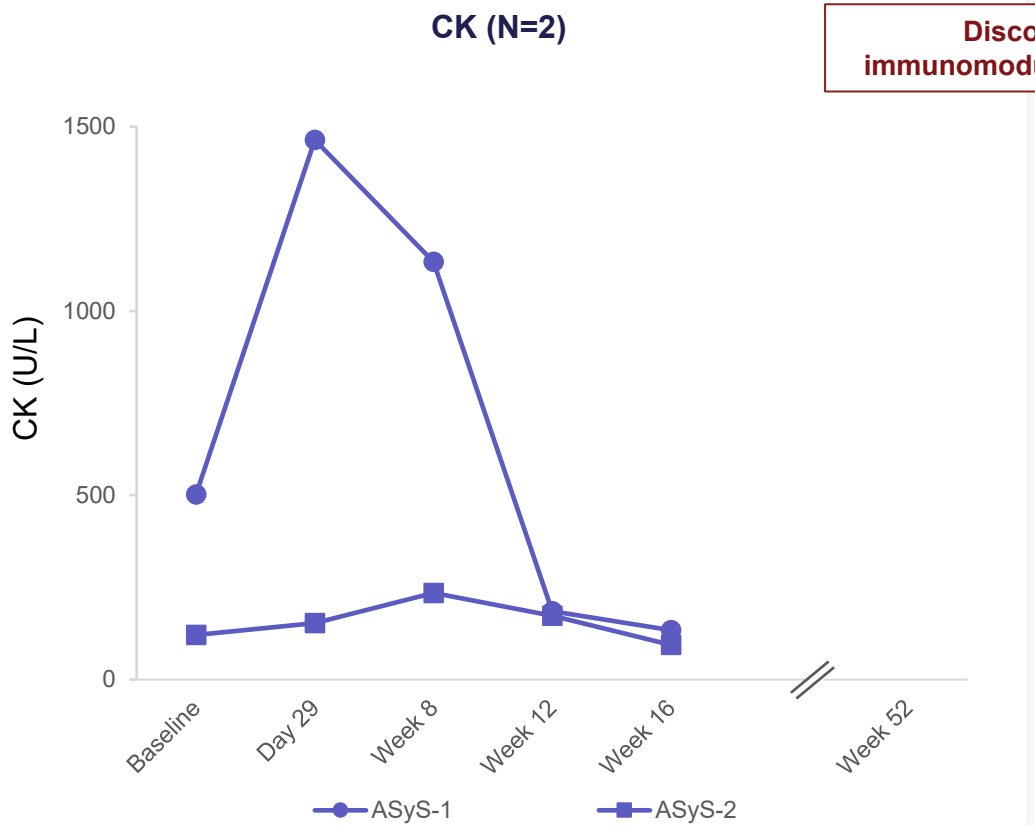
Responses to rese-cel among some ASyS patients may be time-limited by the recurrence or persistence of pathogenic autoantibodies[2–4] from CD19-negative long-lived plasma cells despite complete B cell depletion

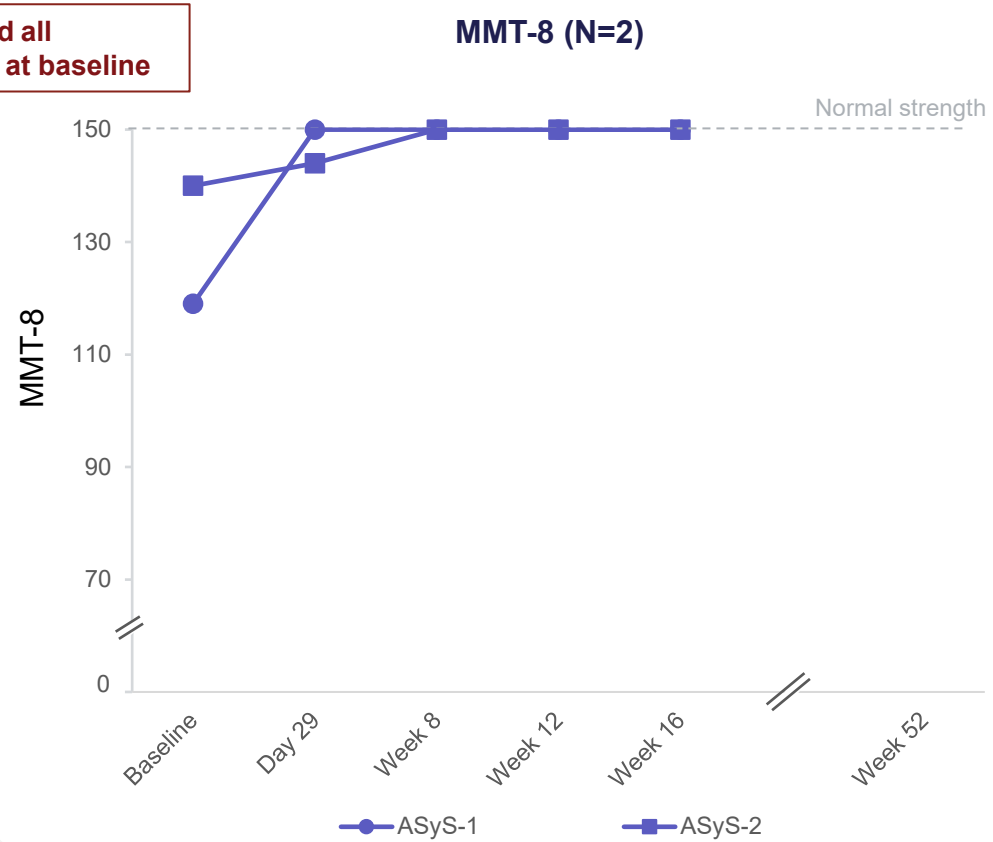
*As of 11 Sep 2025.
†Reflects trend from baseline to latest timepoint antibody; results are available (Week 24 for both patients). In ASyS-2, Jo-1 antibody level trended up from Week 20 to Week 24 but was lower than baseline. ‡Based on the research-based, qualified, quantitative Luminex assay. §ASyS-1 to minimal response at latest follow-up (Week 32); treated with GC bursts and obinutuzumab; ASyS-2 to no response at latest follow-up (Week 28); treated with GC burst.
ASyS, antisynthetase syndrome; GC, glucocorticoid; IM, immunomodulatory medication; IVIg, intravenous immunoglobulin; mg, milligrams; MMF, mycophenolate mofetil; N/A, not available; rese-cel, resecabtagene autoleucel; RESET, REstoring SElf-Tolerance; TAC, tacrolimus; TIS, total improvement score.
1. Cabaletta Bio: Data on File. 2. Pinal-Fernandez I, et al. *Ann Rheum Dis*. 2024;83(11):1549–1560. 3. Galindo-Feria AS, et al. *Best Pract Res Clin Rheumatol*. 2022;36(2):101767. 4. Müller, F, et al. *Nat Med*. 2025:31(6):1793–1797.

RESET *Myositis*®: Efficacy in ASyS Patients Following Rese-cel Infusion*

Patients with ASyS achieve improvements in CK levels and normalization of MMT-8 following rese-cel by Week 16

Discontinued all immunomodulators at baseline





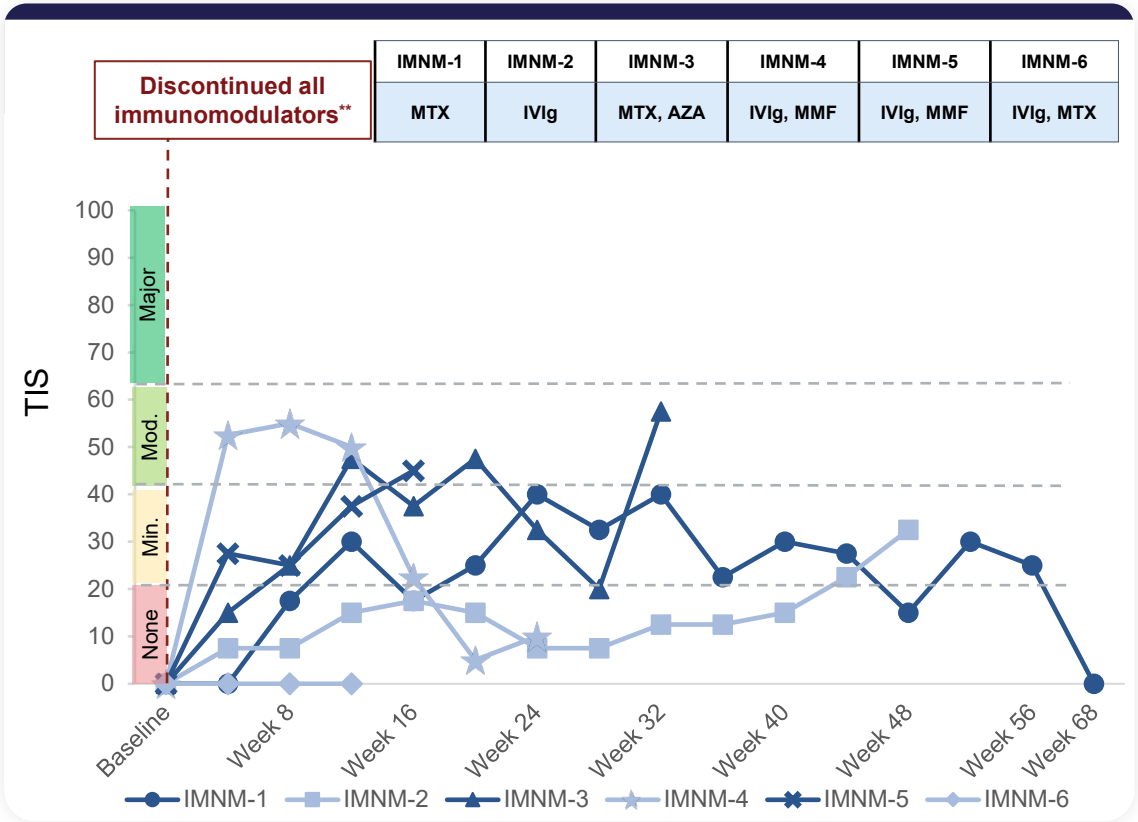
*As of 11 Sep 2025.
ASyS, antisynthetase syndrome; CK, creatine kinase; MMT-8, manual muscle testing 8; rese-cel, resecabtagene autoleucel; RESET, REstoring SElf-Tolerance; U/L, units per liter.
Cabaletta Bio: Data on File.

RESET *Myositis*®: Efficacy in IMNM Patients Following Rese-cel Infusion*

Minimal to moderate TIS response in patients whose antibodies decreased; lower and/or less consistent responses in patients without autoantibody decrease

Assessment at Week 24†	IMNM (baseline autoantibody)					
	IMNM-1 (SRP)	IMNM-2 (HMGCR)	**IMNM-3** (SRP)	IMNM-4 (HMGCR)	**IMNM-5** (HMGCR)	IMNM-6 (HMGCR)
IM-free	✓	–	✓	–	✓‡	–
Low dose or no GC	✓	–	✓	–	✓‡	–
TIS Response	Moderate	None	Minimal	None	Moderate‡	None‡
Complete and transient B cell depletion	✓	✓	✓	✓	✓‡	✓‡
Antibody trend§	↓→¶	→	↓¶	→	↓	→

Patients with antibodies decreased are in dark blue



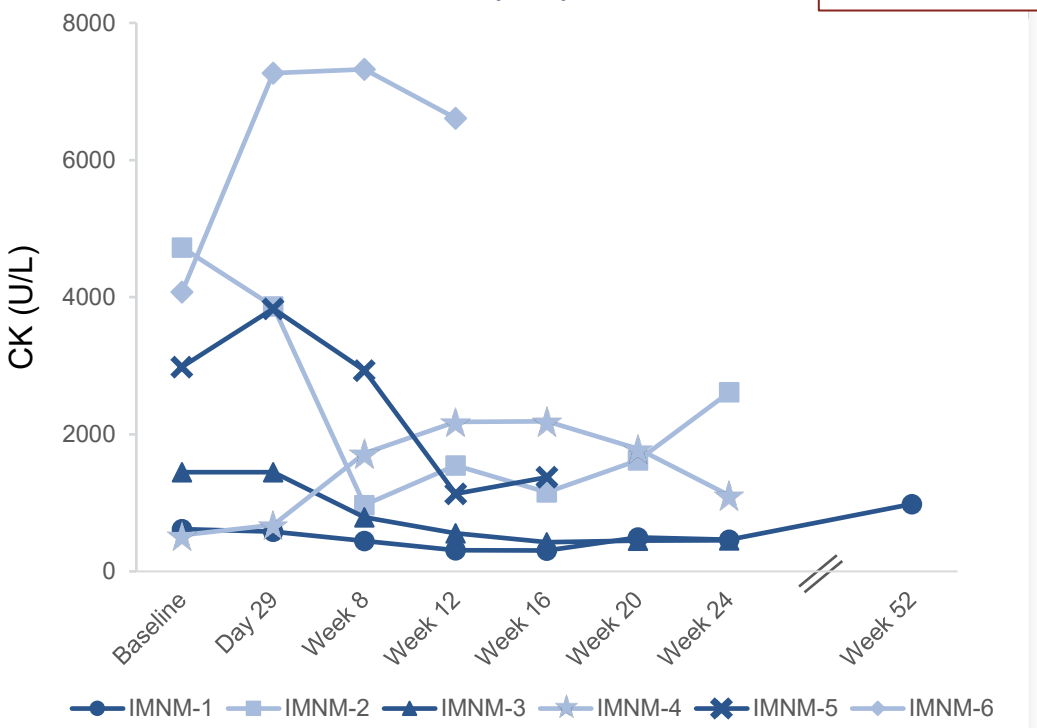
Modest and/or less consistent response in IMNM patients may be due to persistence of pathogenic autoantibodies[2–4] from CD19-negative long-lived plasma cells despite complete B cell depletion. Additional patients are being evaluated in the Phase 1/2 study using modified entry criteria

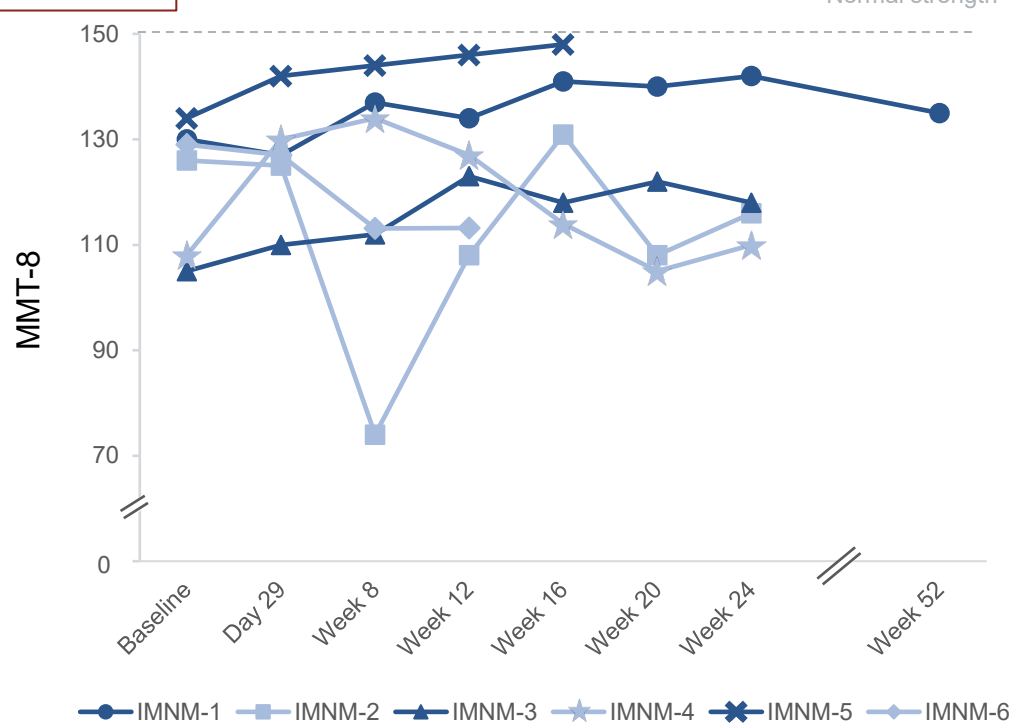
*As of 11 Sep, 2025.
† The primary endpoint for the upcoming sub-study in IMNM is minimal TIS off all IM therapies and on low dose steroids (50% reduction or ≤7.5 mg/day) at Week 24; Week 52 will be evaluated as a secondary endpoint.
‡At latest follow-up (IMNM-5: Week 16 and IMNM-6: Week 12). §Reflects trend from baseline to latest timepoint or timepoint prior to initiating confounding rescue medication. In IMNM-1, SRP antibody level trended up Week 36 to Week 52 but was lower than baseline.
¶Based on the research-based, qualified, quantitative Luminex assay.
**IMNM-1 started IVIg after Week 68; IMNM-2 received GC between Weeks 4 and 8 and started IVIg after Week 12; IMNM-4 received GC burst after Week 12 and started IVIg and RTX at Week 24; IMNM-6 started MTX, IVIg, PEX, DARA after Day 29.
DARA, daratumumab; GC, glucocorticoids; HMGCR, 3-hydroxy-3-methylglutaryl-coenzyme A reductase; IM, immunomodulatory medication; IMNM, immune-mediated necrotizing myopathy; IVIg, intravenous immunoglobulin; MMF, mycophenolate mofetil; MTX, methotrexate; N/A, not available; PEX, plasma exchange; rese-cel, resecabtagene autoleucel; SRP, signal recognition particle; TIS, total improvement score.
1. Cabaletta Bio: Data on File. 2. Pinal-Fernandez I, et al. Ann Rheum Dis. 2024;83(11):1549–1560. 3. Galindo-Feria AS, et al. Best Pract Res Clin Rheumatol. 2022;36(2):101767. 4. Müller, F, et al. Nat Med. 2025:31(6):1793–1797.

RESET *Myositis*®: Efficacy in IMNM Patients Following Rese-cel Infusion*

CK and MMT-8 in patients with IMNM following rese-cel infusion

Discontinued all immunomodulators at baseline





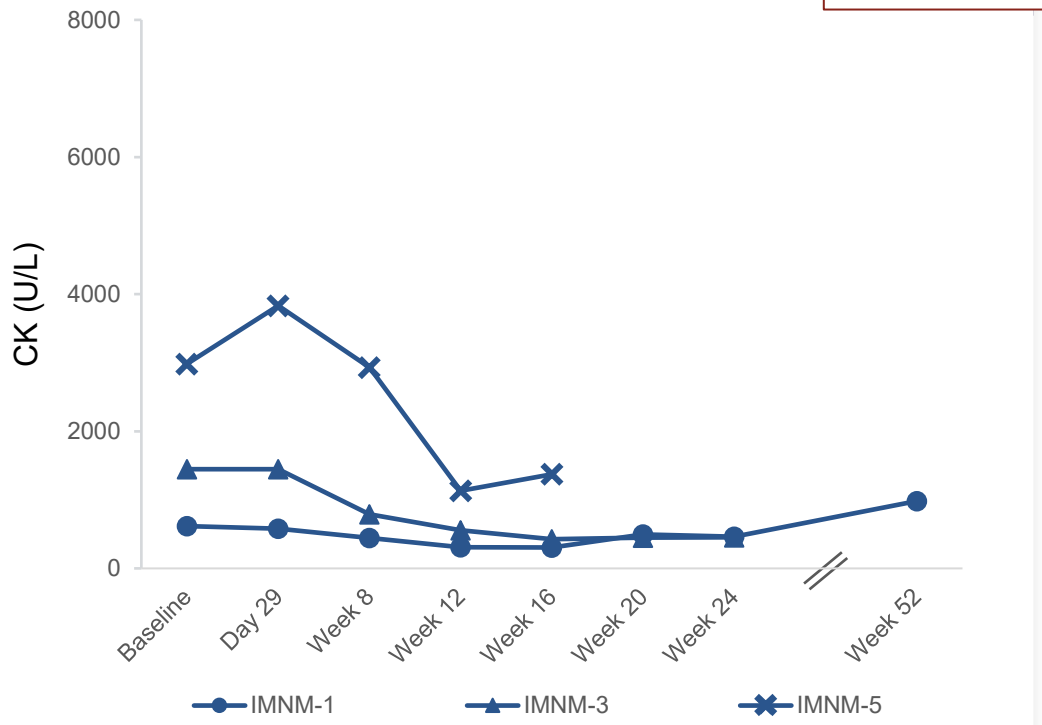
Patients with antibodies decreased are in dark blue

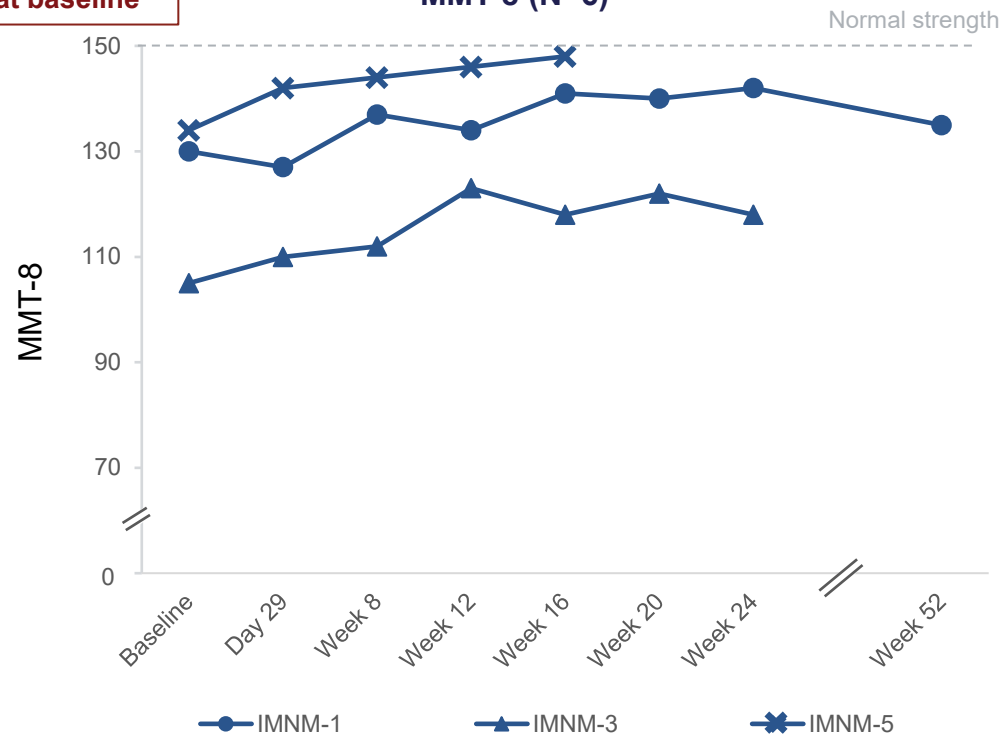
*As of 11 Sep, 2025.
†IMNM-2 Week 16 and IMNM-6 Weeks 8 and 12 MMT-8 measurements were normalized to a total score of 150; not all muscle groups could be evaluated.
CK, creatine kinase; IMNM, immune-mediated necrotizing myopathy; MMT-8, manual muscle testing 8; rese-cel, resecabtagene autoleucel; TIS, total improvement score; U/L, units per liter.
Cabaletta Bio: Data on File.

RESET *Myositis*®: Efficacy in IMNM Patients with Autoantibody Decreases Following Rese-cel Infusion*

Improvement in CK and MMT-8 seen in three patients with IMNM, who also experienced reduction in autoantibody levels

Discontinued all immunomodulators at baseline





Patients with antibodies decreased are in dark blue

*As of 11 Sep, 2025.
CK, creatine kinase; IMNM, immune-mediated necrotizing myopathy; MMT-8, manual muscle testing 8; rese-cel, resecabtagene autoleucel; TIS, total improvement score; U/L, units per liter.
Cabaletta Bio: Data on File.

Summary from Clinical and Translational Data: RESET Myositis®

- Rese-cel was generally well tolerated across 13 IIM patients treated to date, including one patient with JIIM
  - Grade 1 CRS in 4 of 13 patients
  - No ICANS in any of the 13 patients
- B cells were completely and transiently depleted in peripheral blood within 1-2 weeks following rese-cel infusion
- The persistence or recurrence of autoantibodies suggests CD19-negative long-lived plasma cells may be the primary source of pathogenic autoantibodies in a subset of ASyS and IMNM patients with limited durability or response
- After discontinuing IM medications, patients demonstrated compelling clinical responses following rese-cel infusion
  - DM: 3 of 3 patients with sufficient follow-up achieved IM-free moderate TIS response or greater at Week 16
  - ASyS: 1 of 2 patients achieved IM-free moderate TIS response or greater at Week 16
    - In the setting of persistence or recurrence of autoantibodies, responses were not durable
  - IMNM: 2 of 4 patients with sufficient follow-up achieved IM-free TIS response at Week 24
    - Antibodies persist in 3 of 6 patients who either did not achieve or maintain response

Based on these data, Cabaletta Bio has initiated a pivotal cohort in DM & ASyS:
~17 patients with 16-week primary endpoint of moderate TIS off IM & on no steroids or low dose†

*As of 11 Sep, 2025.
†Low dose steroids is defined as 50% reduction from baseline or ≤7.5 mg/day
ASyS, antisynthetase syndrome; CRS, cytokine release syndrome; DM, dermatomyositis; ICANS, immune effector cell-associated neurotoxicity syndrome; IIM, idiopathic inflammatory myopathy; IM, immunomodulatory medication; IMNM, immune-mediated necrotizing myopathy; JIIM, juvenile idiopathic inflammatory myopathy; rese-cel, resecabtagene autoleucel; RESET, REstoring SElf-Tolerance; TIS, total improvement score.
Cabaletta Bio: Data on File.

Cabaletta Bio®

Question & Answer Session