

**Durability of response following retreatment with Descartes-08,
an autologous BCMA-directed mRNA
CAR T-cell therapy, in generalized myasthenia gravis:
a case series with 12-month follow-up**

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September 29, 2026

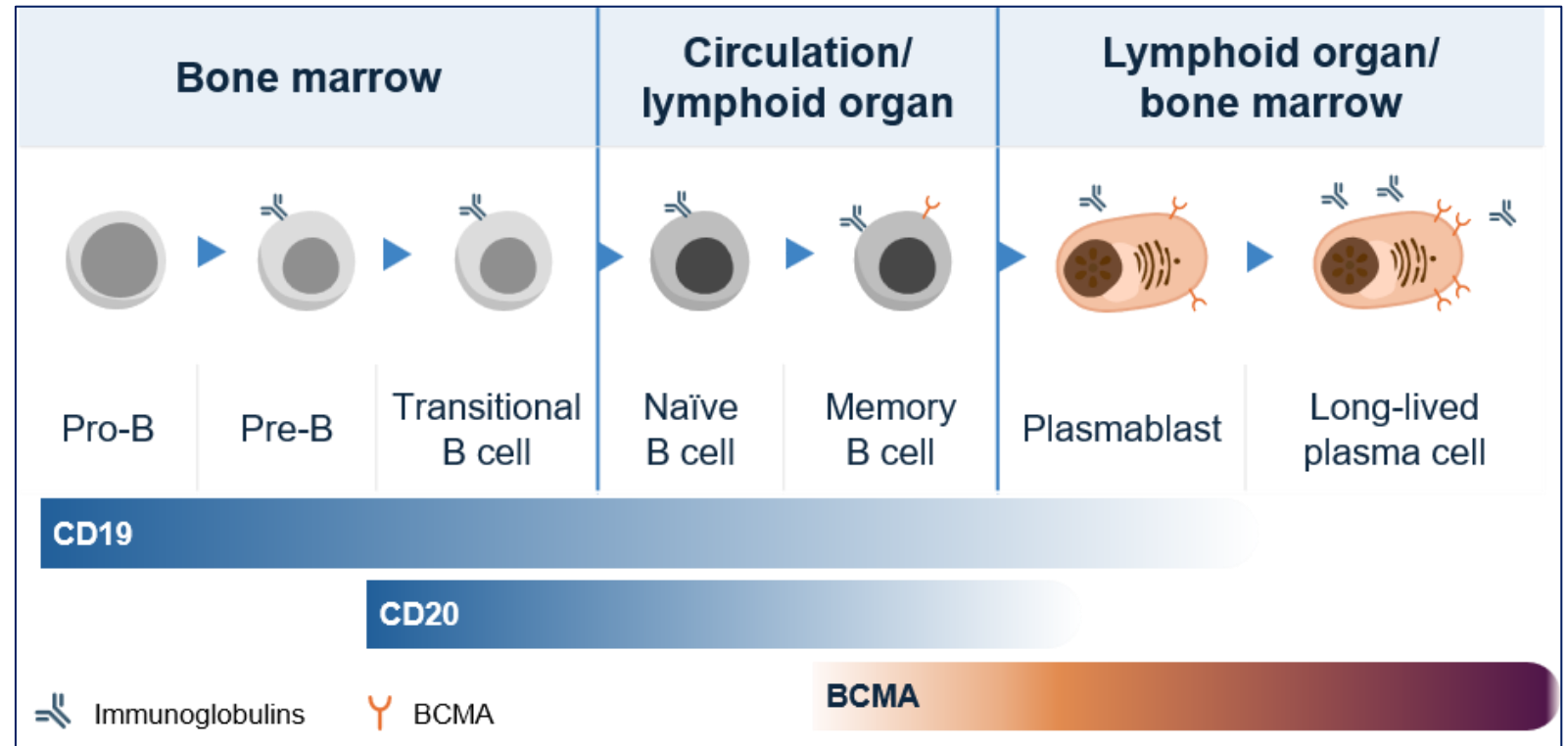
**2026 MGFA Scientific Session at AANEM
Orlando, FL, USA**

Disclosures

Commercial interest	Relationship(s)
Grants/research support	Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, Merck EMD Serono, Myasthenia Gravis Foundation of America (MGFA), Muscular Dystrophy Association, National Institutes of Health (NIH), NMD Pharma, Vertex Pharmaceuticals, UCB Bioscience, and Vor Biopharma (<i>paid to his institution</i>)
Speaker's bureau/honoraria	AcademicCME, AiCME, CheckRare CME, MedLive, PeerView CME, Physicians' Education Resource (PER, MJH) CME, and Rush Medical CME
Consulting fees	Alexion AstraZeneca Rare Disease, Amgen, argenx, Biohaven Ltd, Cartesian Therapeutics, CorEvitas, H. Lundbeck A/S, Japan Tobacco Company, Kyverna Therapeutics, Merck EMD Serono, NMD Pharma, Novartis Pharma, Regeneron Pharmaceuticals, Seismic Therapeutic, Toleranzia AB, UCB Bioscience, Vertex Pharma, and Vor Biopharma

Cells involved in myasthenia gravis pathogenesis express BCMA

- In anti-AChR–positive MG, pathogenic autoantibodies are produced by BCMA-expressing long-lived plasma cells.¹⁻⁴
- BCMA-directed cell therapy targets BCMA-expressing antibody-producing cells, addressing a key driver of MG pathology.⁵⁻⁷
- CD19/CD20 targeting depletes the broad B-cell lineage rather than only the downstream antibody-secreting cells, and sustained depletion may lead to B-cell aplasia, hypogammaglobulinemia, and an increased risk of infection.⁸⁻¹⁰

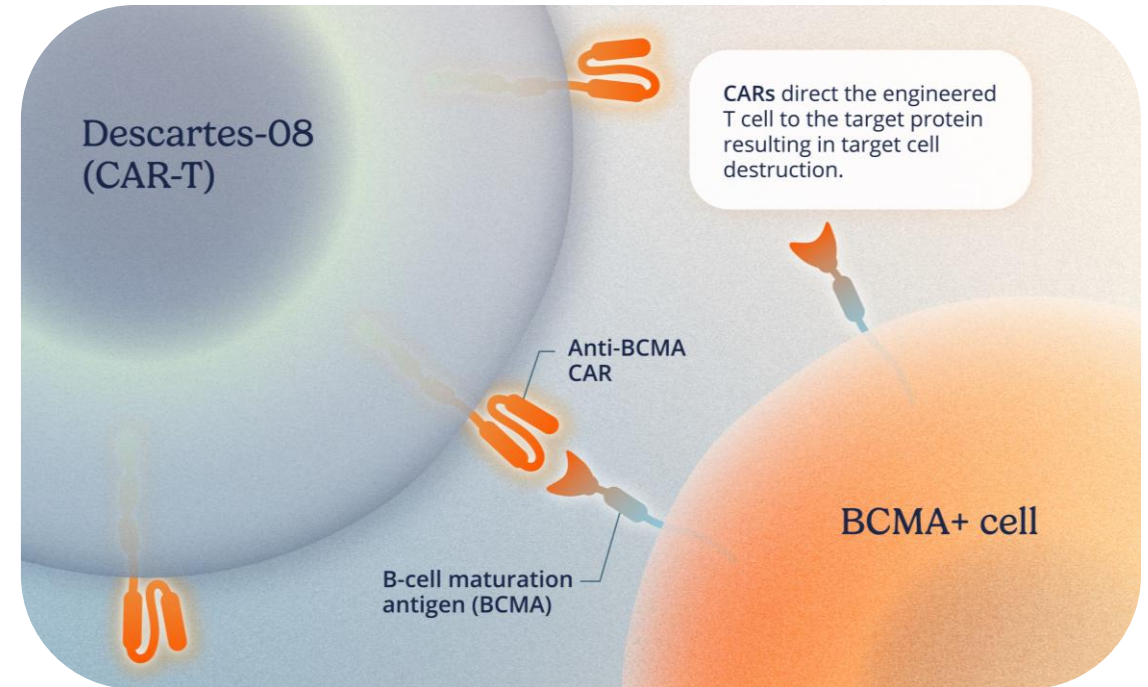
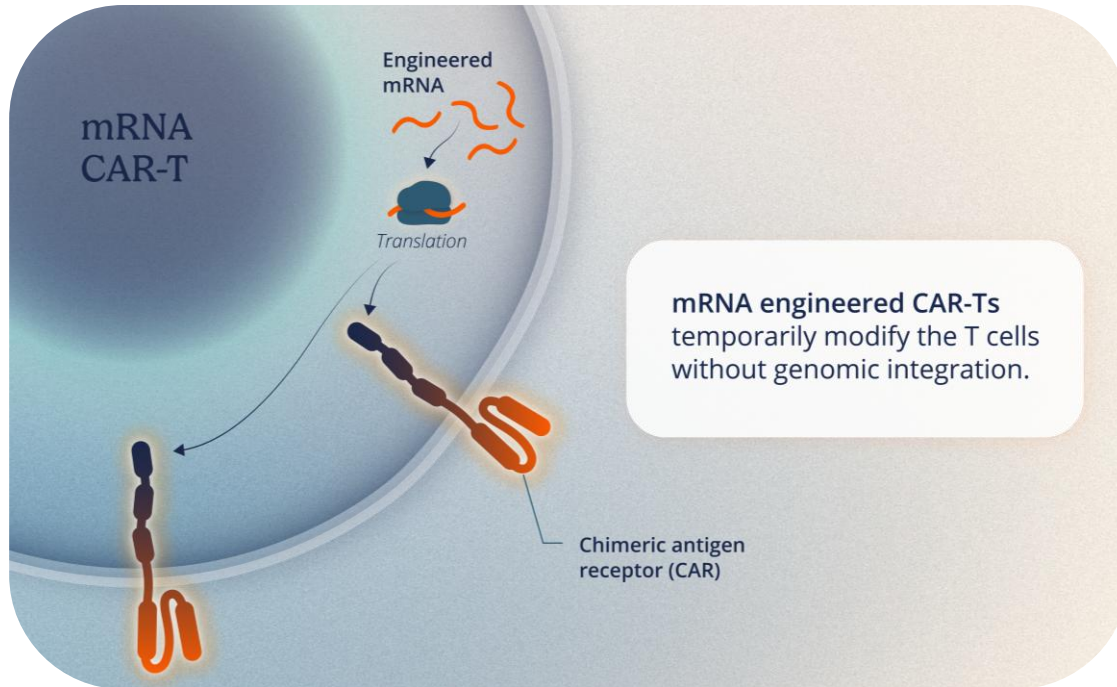


AChR, acetylcholine receptor; BCMA, B-cell maturation antigen; CD19/20, cluster of differentiation 19/20; MG, myasthenia gravis.

Figure adapted from English EP, et al. *Sci Transl Med*. 2024;16:eado2084, Chahin N, et al. *Ann Clin Transl Neurol*. 2025;12:2358–66, and Lee SWD, et al. *Nat Rev Drug Discov*. 2021;20(3):179–99.

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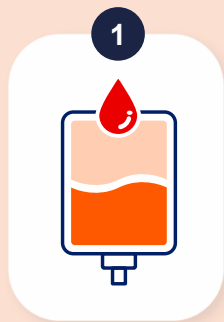
Cartesian mRNA cell therapy platform



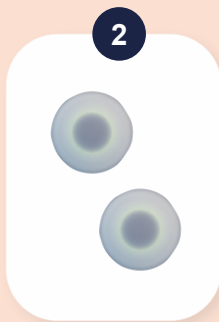
Descartes-08 is an investigational autologous, nonviral, BCMA-targeted, mRNA CAR T-cell product candidate designed to be dosed **in an outpatient setting without lymphodepleting chemotherapy**

mRNA cell therapy designed for outpatient delivery

The patient's T cells are isolated, expanded *ex vivo*, and engineered to become BCMA-directed CAR T cells^{1,2} so the therapeutic dose does not rely on *in vivo* proliferation.



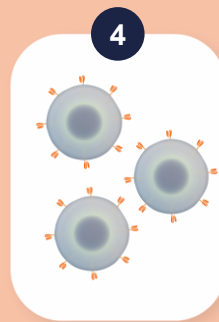
1
Cell collection/
Leukapheresis¹



2
Cell Selection¹
Isolation of CD8⁺ cells



3
Ex-vivo T-cell
Expansion¹



4
Transfection¹
Modification of the T cells
via mRNA transfection to
encode for BCMA CAR
(no virus involved)



5
Cryopreservation¹



6
Quality
Assessment



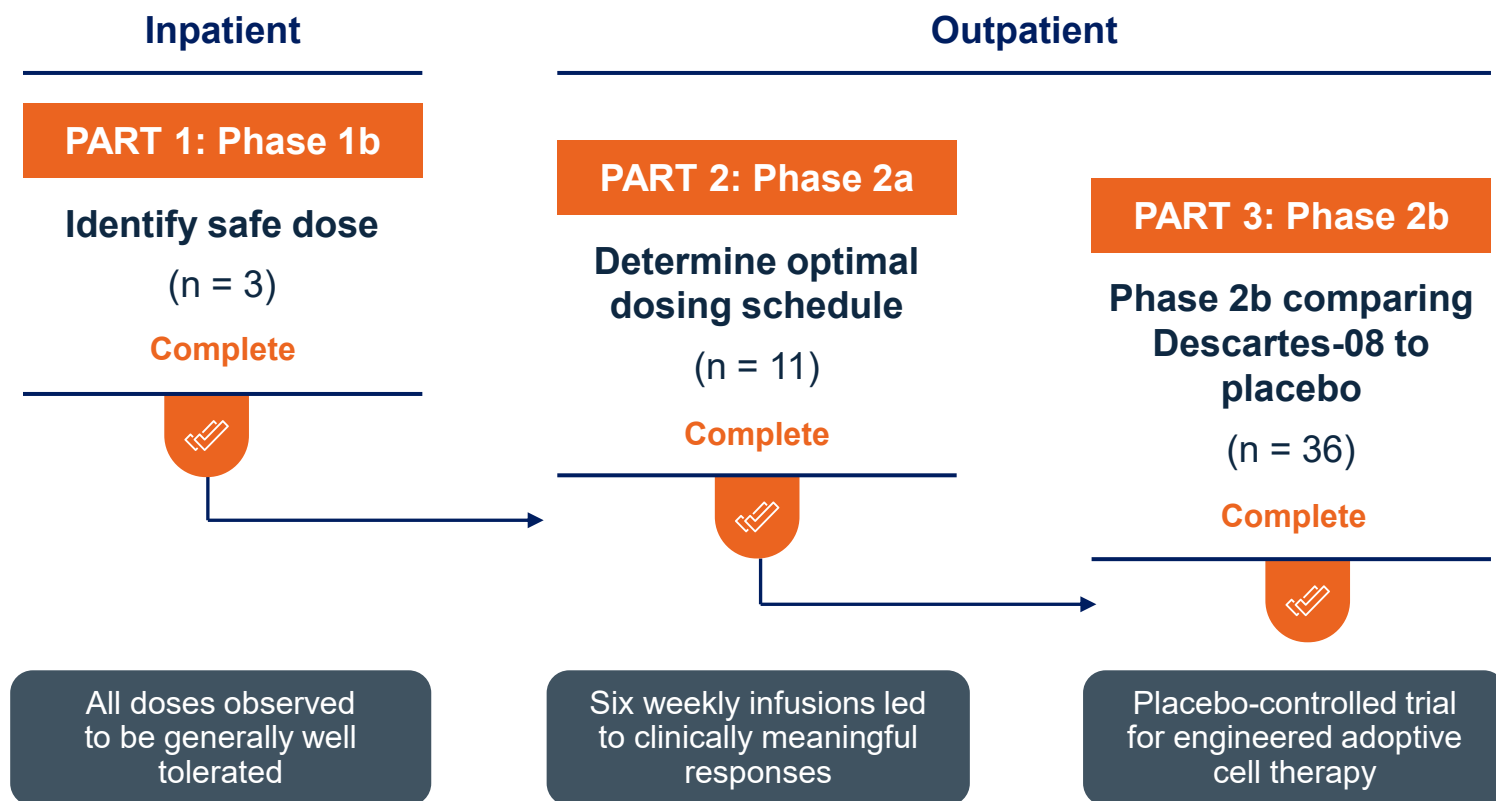
7
Infusion of
Descartes-08^{1, 2}

Descartes-08 has been administered in clinical trials at both academic centers and community clinics as six once-weekly outpatient infusions (~15 minutes each), with a 1-hour post-infusion observation period.¹

MG-001 Clinical Program Summary

3-Part Phase 1b/2 study of Descartes-08 in MG (NCT04146051)

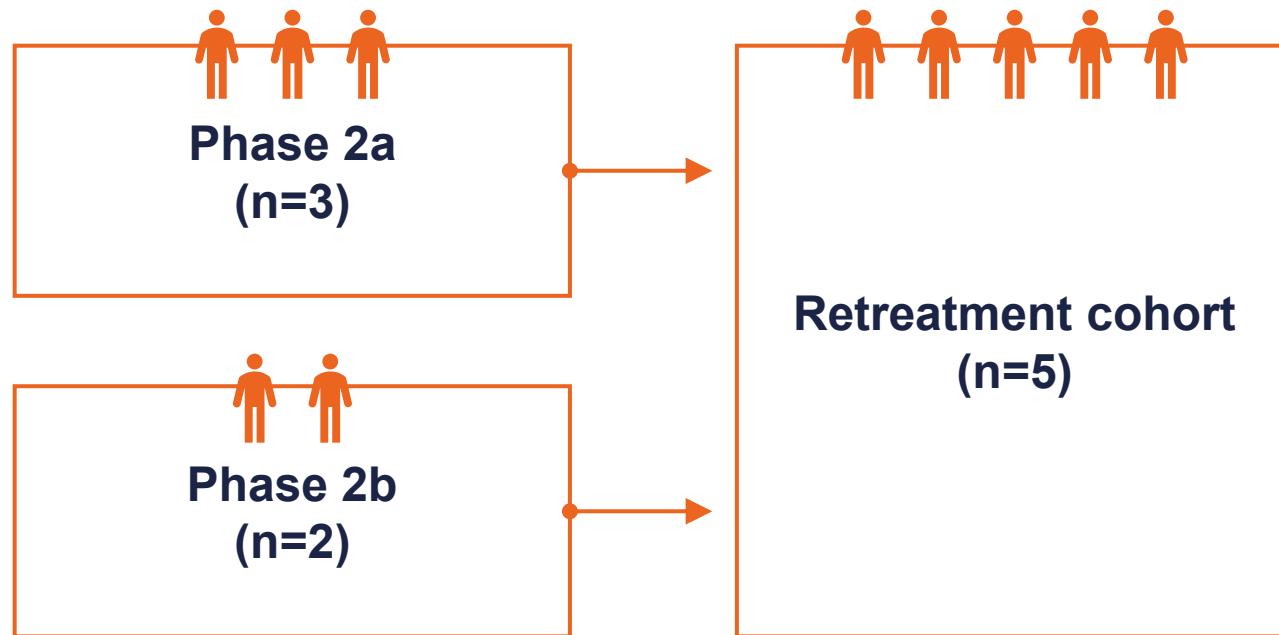
Across the MG-001 program, Descartes-08 demonstrated clinically meaningful and sustained improvements in MG clinical outcome measures¹⁻³



- In **Phase 2a**, clinical effect was observed with 6 once-weekly infusions, which was selected as the preferred treatment regimen
- The **Phase 2b** study demonstrated significant and sustained improvements in MG severity scores through 12 months following a single treatment course
- Descartes-08 was generally **well tolerated without evidence of CRS or ICANS**

Retreatment case series

MG-001 participants previously treated with Descartes-08



All participants had 12-month follow-ups for both initial treatment and retreatment

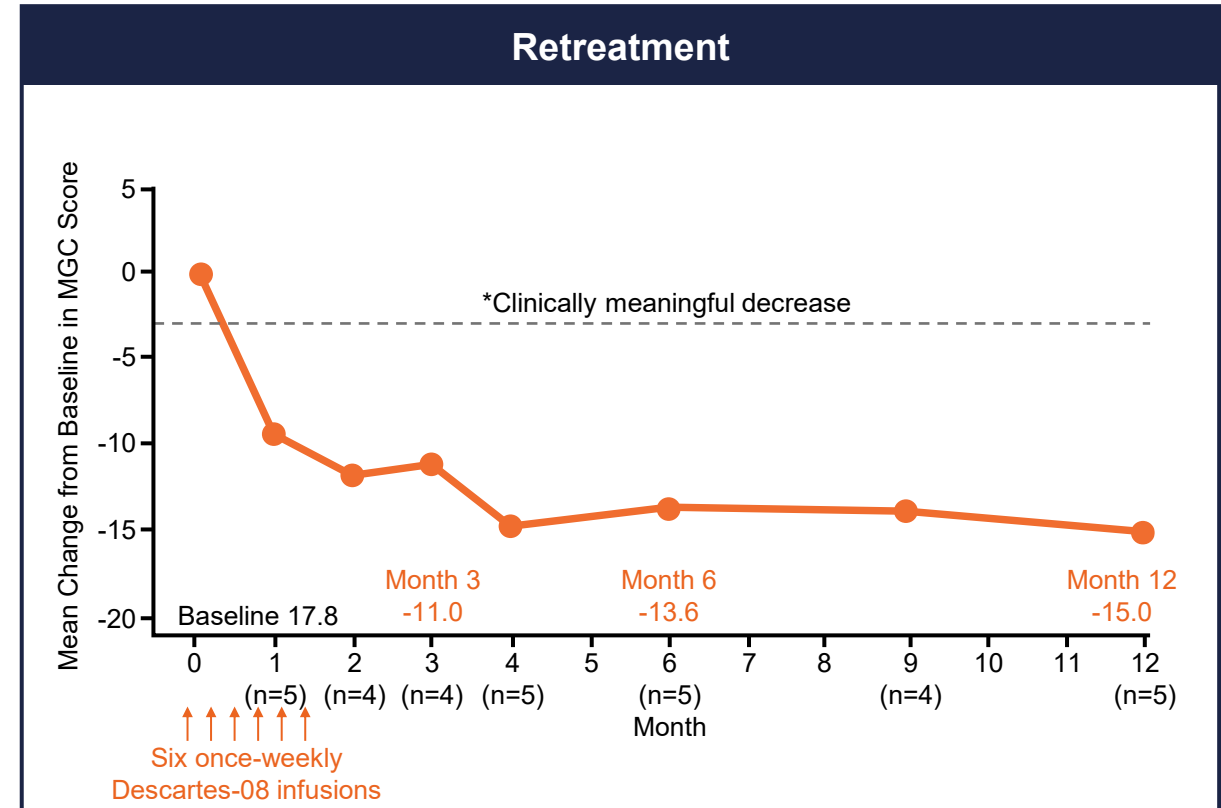
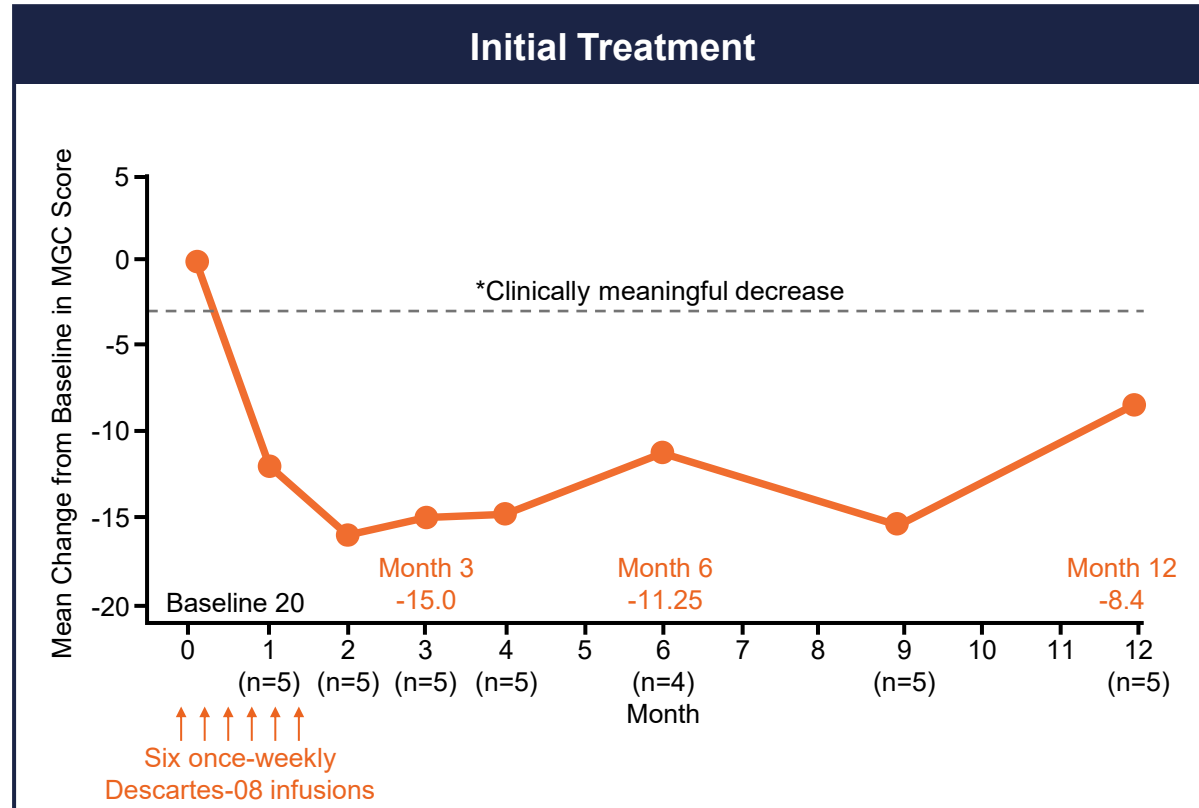
- The case series analyzed the efficacy, safety, and durability of response to Descartes-08 retreatment in participants with gMG who previously received a full treatment course in the Phase 2 portion of the MG-001 study and experienced recurrence of symptoms (MG-ADL ≥ 6)
- Retreatment consisted of 6 once-weekly Descartes-08 infusions
- Clinical outcomes were assessed by mean change in MGC and MG-ADL scores from baseline through Month 12 and compared with outcomes following the initial treatment course. Safety and tolerability were assessed across treatment courses

Retreatment case series:

Participant baseline characteristics

Characteristic	Participants (n=5)
Age, mean (SD)	58 (12) years
Age range	49–79
Women, n (%)	4 (80%)
AChR+ gMG, n (%)	4 (80%)
MG-ADL at baseline before initial treatment, mean (SD)	9.2 (3.1)
MG-ADL at baseline before retreatment, mean (SD)	9.6 (3.4)
Median interval between end of initial treatment course and first retreatment infusion	16.6 months (range 11.7–22.6)

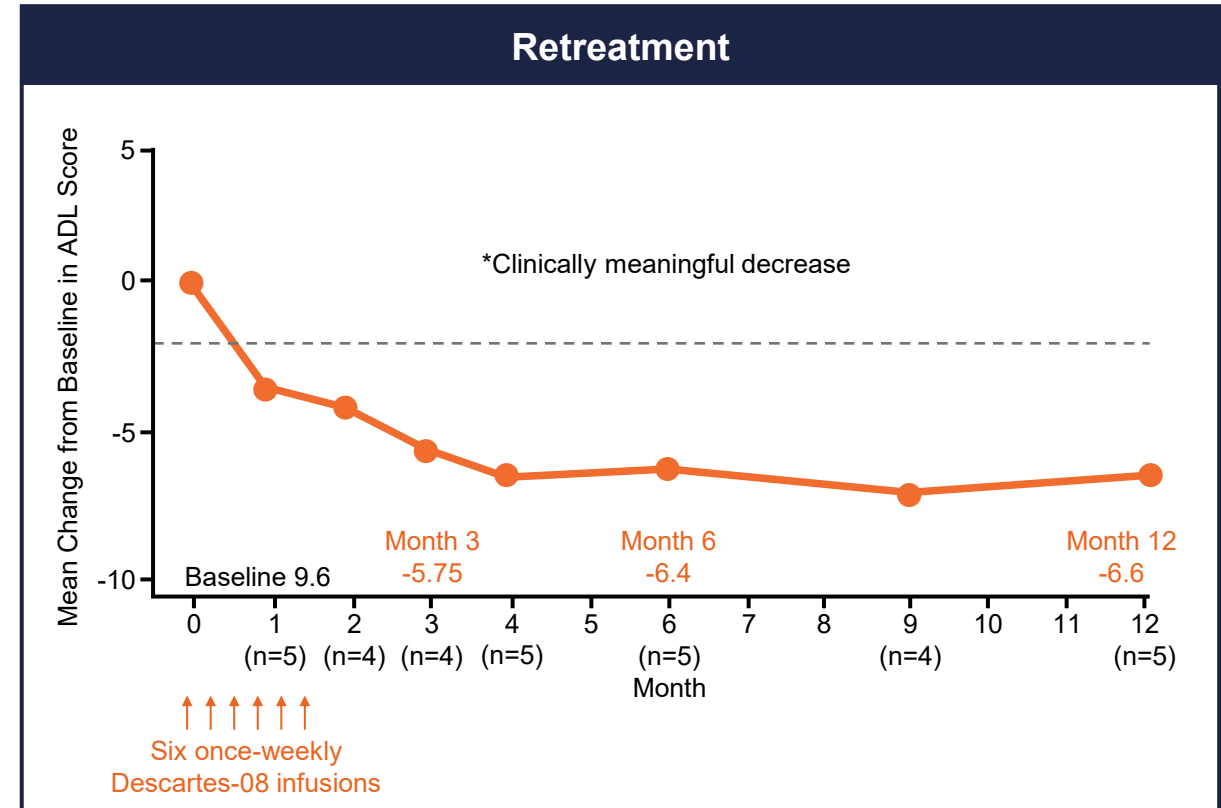
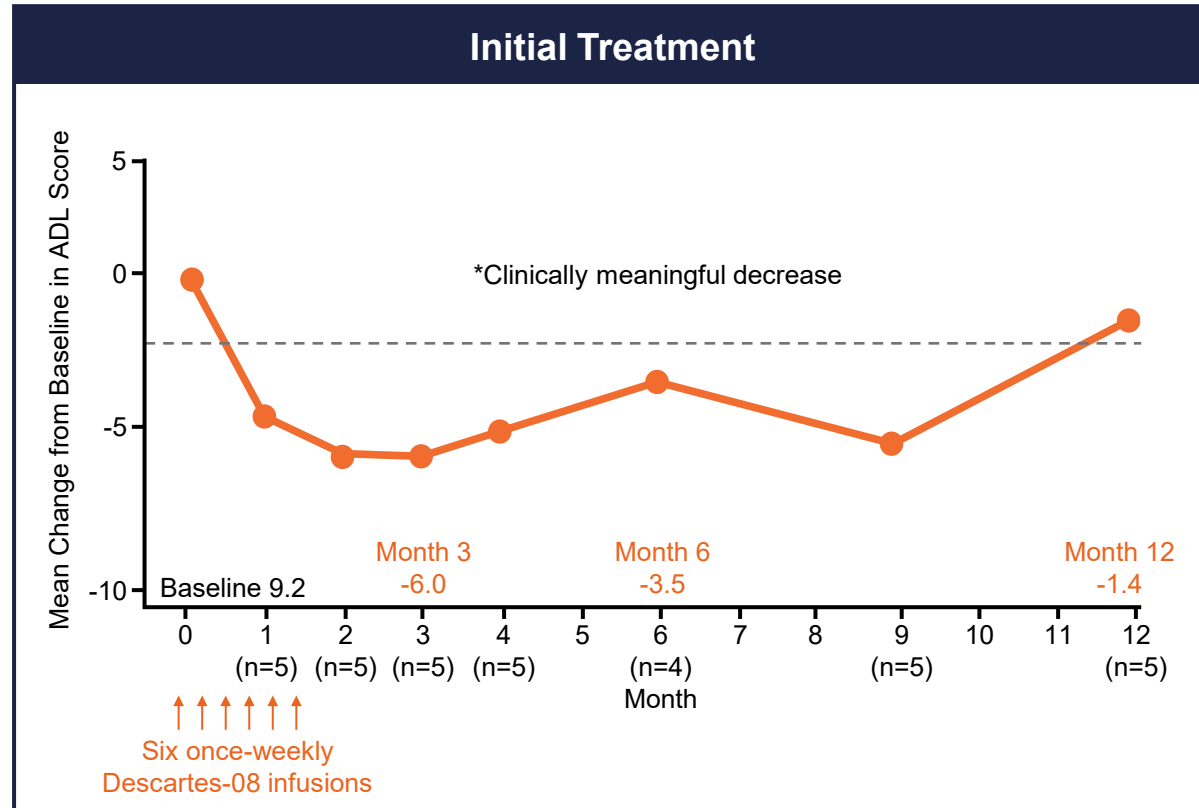
Results: Descartes-08 demonstrated improvement in mean change from baseline in MGC following initial treatment and retreatment



- Retreatment with Descartes-08 led to improvement in mean change from baseline in MGC, with responses sustained through 12 months
- Mean change in MGC from retreatment baseline was –15 points
- The reduction in mean MGC score from baseline following retreatment was consistent with, and potentially greater than, that observed following initial treatment

*Clinically meaningful decrease was defined as a ≥ 3 -point change in MGC score
MGC, Myasthenia Gravis Composite.

Results: Descartes-08 demonstrated improvement in mean change from baseline in MG-ADL following initial treatment and retreatment



- Retreatment with Descartes-08 led to improvement in mean MG-ADL score from baseline, with responses sustained through 12 months
- Mean change in MG-ADL from retreatment baseline was -6.6 points
- The reduction in mean MG-ADL score from baseline following retreatment was consistent with, and potentially greater than, that observed following initial treatment

Safety Summary

Retreatment safety profile was consistent with initial treatment, with no new or cumulative safety signals observed

Initial Treatment vs Retreatment (n=5)
6 once-weekly infusions per treatment course

Safety Event	Initial Treatment	Retreatment
SAEs#	1	0
Infusion-related reaction (IRR)*	16/30 infusions	17/30 infusions
Grade 1	10	12
Grade 2	6	5
TEAEs in >1 participant		
Tachycardia	1	5^
CRS	0	0
ICANS	0	0
Cytopenias+	0	0
Hypogammaglobulinemia	0	0

#Participant had an infected port not related to Descartes-08
*IRR is an infusion-related reaction developing within 24 hours and resolving spontaneously or with supportive care within 48 hours of Descartes-08 administration, manifesting as fever, chills, rigors, myalgia, arthralgia, nausea, vomiting, and/or headache
^All occurred in the same participant with 4 of 5 events occurring in combination with infusion reaction
+Cytopenia group term defined as anemia, thrombocytopenia, or neutropenia

Case #1 (Phase 2a)

MG History: 52-year-old Caucasian Woman

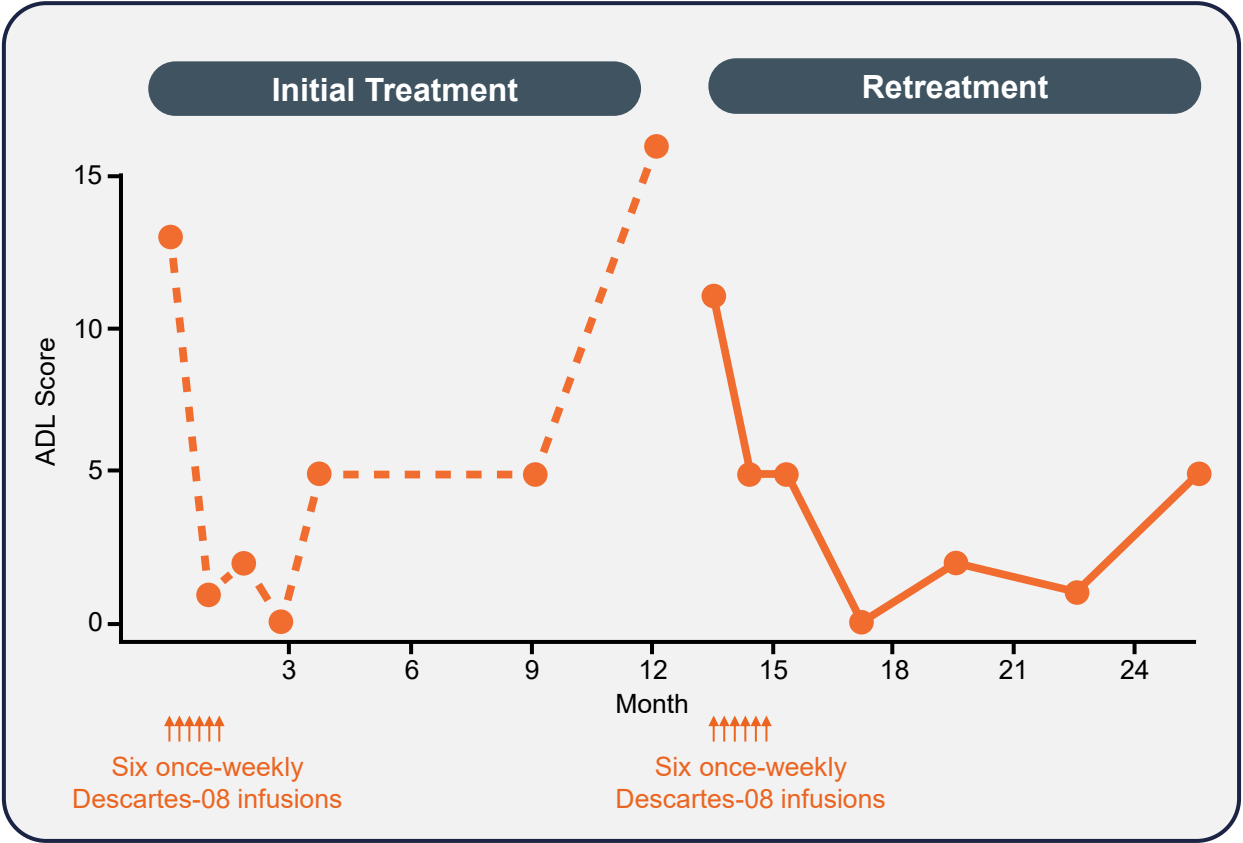
- 16-year history of AChR+ gMG, MGFA Class IIa at screening
- Prior therapies include prednisone, pyridostigmine, eculizumab, MMF, PLEX, IVIG, thymectomy
- Disease course has been complicated by MC requiring intubation
- Receiving pyridostigmine and azathioprine at time of initial treatment

At Retreatment

Timing: 11.7 months after completion of initial treatment course

Ongoing Medications:

- Pyridostigmine
- Azathioprine



Participant experienced a clinically meaningful reduction in MG-ADL through 12 months after retreatment

Case #2 (Phase 2a)

MG History: 67-year-old Caucasian Man

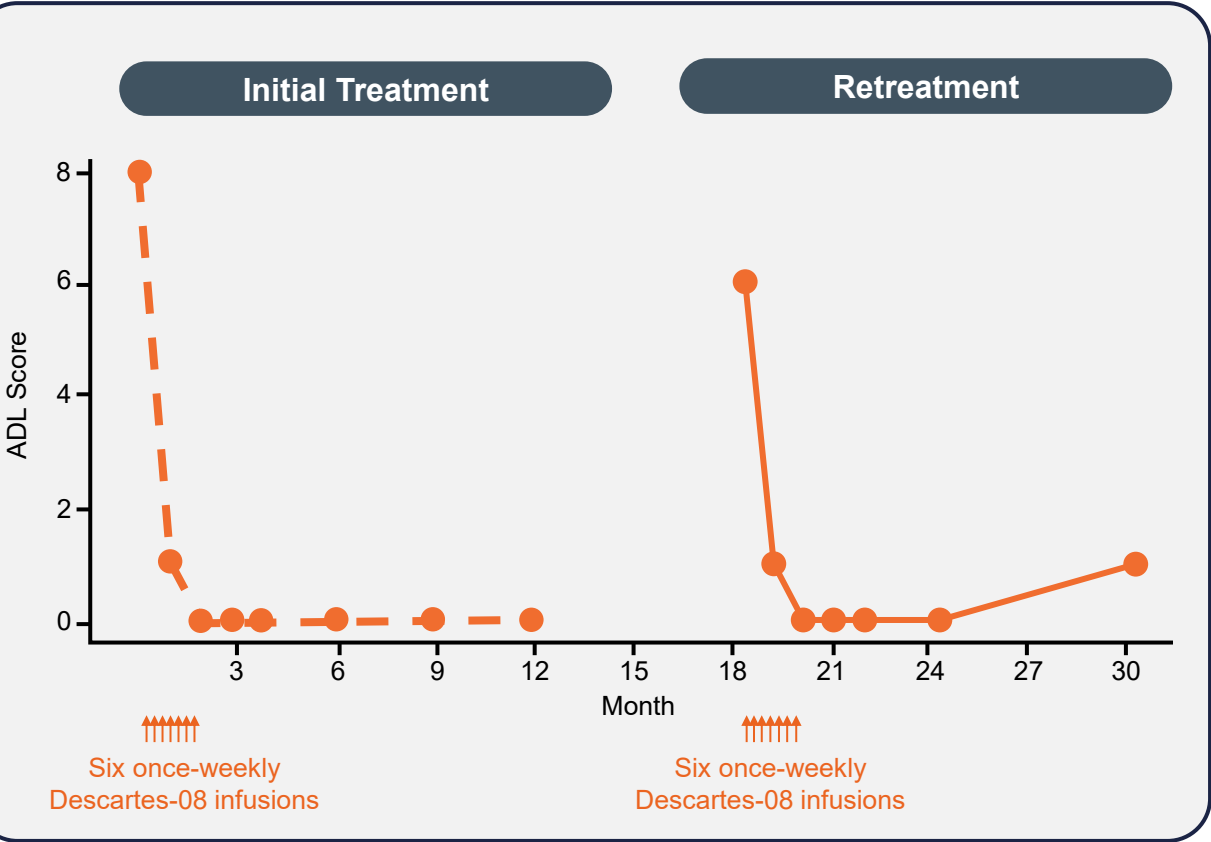
- 10-year history of seronegative gMG, MGFA Class IIa at screening
- Prior therapies include IVIG, PLEX, MMF, prednisone, azathioprine, MTX
- Receiving prednisone and pyridostigmine at time of initial treatment

At Retreatment

Timing: 19.9 months after completion of initial treatment course

Ongoing Medications:

- Prednisone
- Pyridostigmine



Participant experienced a reproducible reduction in MG-ADL with MSE achieved in initial treatment and retreatment

Minimum symptom expression was defined as an MG-ADL score of 0 or 1

ADL, Activities of Daily Living; gMG, generalized myasthenia gravis; IVIG, intravenous immunoglobulin; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MMF, mycophenolate mofetil; MSE, minimal symptom expression; MTX, methotrexate; PLEX, plasma exchange.

Conclusion



Among participants with gMG who initially responded to Descartes-08 and later experienced recurrence of symptoms (MG-ADL ≥ 6), retreatment with Descartes-08 led to improvements in MG severity scores



Clinical benefit following retreatment was sustained through Month 12 in multiple participants



Retreatment was generally well tolerated with a safety profile consistent with initial treatment

- No new or cumulative safety signals were observed
- No CRS, ICANS, cytopenias, or hypogammaglobulinemia were observed



These findings support the potential for retreatment with Descartes-08, if needed following recurrence of MG symptoms, with clinical benefit observed and no new safety concerns



The ongoing Phase 3 AURORA trial (NCT06799247) is evaluating the efficacy, safety, and durability of Descartes-08 in adults with gMG