Cartesian® therapeutics

# Updated Data from Phase 2b Trial of Descartes-08 in Myasthenia Gravis

December 3, 2024

# Forward-looking statements

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# Call participants

Carsten Brunn, PhD
PRESIDENT AND CEO

Miloš Miljković, MD
CHIEF MEDICAL OFFICER

Blaine Davis
CHIEF FINANCIAL OFFICER

James F. Howard Jr., MD
PROFESSOR OF NEUROLOGY, MEDICINE, AND ALLIED HEALTH
**UNIVERSITY OF NORTH CAROLINA SCHOOL OF MEDICINE**

# Deep and durable response maintained over 12 months in participants treated with Descartes-08

**Deepening responses observed over time**

**Durable responses observed over time**

**Deepest responses observed in participants without exposure to prior biologic therapy**

**Safety profile continues to support outpatient administration**

## Planned Phase 3 AURORA study design finalized following meeting with U.S. FDA

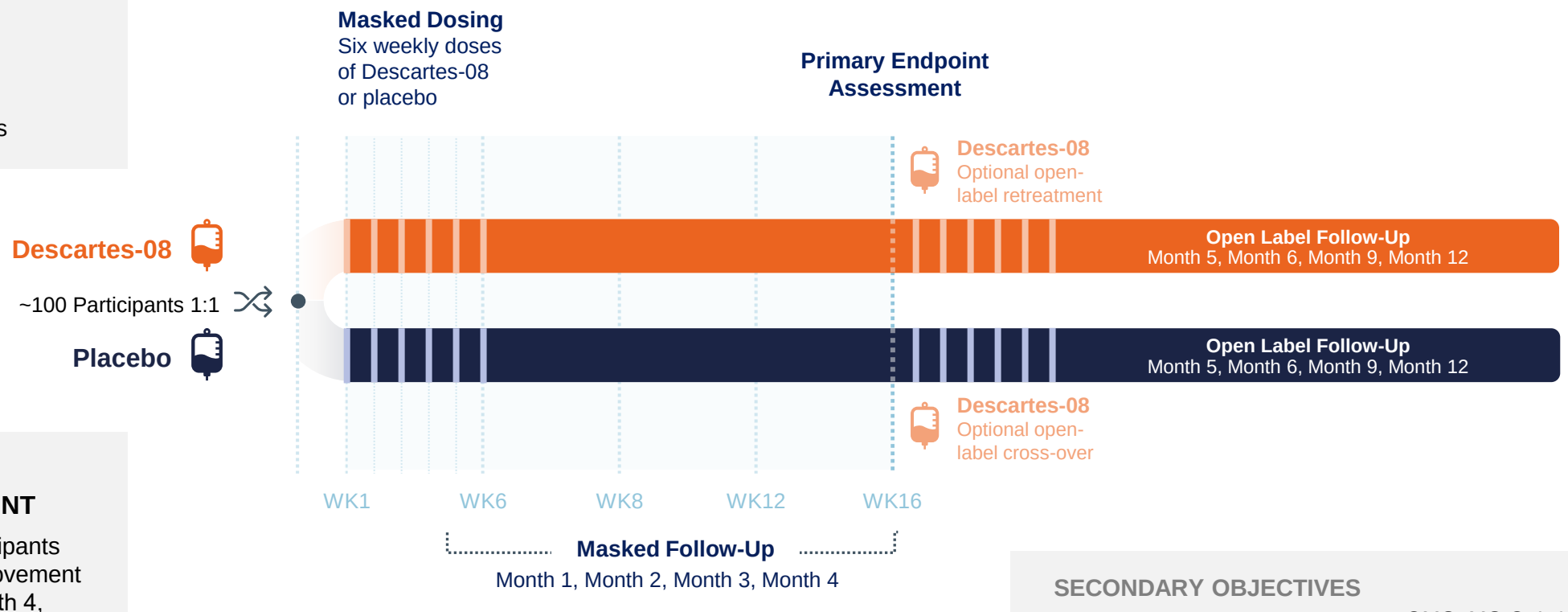
- Primary endpoint to assess MG-ADL improvement of ≥3 points at Month 4 relative to placebo
- Expected to commence in 1H25

MG-ADL, Myasthenia Gravis Activities of Daily Living scale
U.S. FDA, United States Food and Drug Administration

# AURORA: Randomized double-blind, placebo-controlled Phase 3 trial of Descartes-08 in AChR Ab+ gMG

## INCLUSION CRITERIA

- AChR Ab+
- MGFA Class II-IV
- MG-ADL ≥6
- On stable doses of immunosuppressants




## PRIMARY ENDPOINT

- Proportion of participants with MG-ADL improvement of ≥3 points at Month 4, relative to placebo

## SECONDARY OBJECTIVES

- Proportion of participants with MGC improvement of ≥4 points at Month 4
- Safety and tolerability
- QMG, MG QoL 15R, MG-ADL (change from baseline to Month 4)
- Quantify clinical effect of Descartes-08 over 1 year

gMG, Generalized myasthenia gravis
MGFA, Myasthenia Gravis Foundation of America
MGC, Myasthenia Gravis Composite

MG QMG, Quantitative MG Scores
MG QoL 15R, MG Quality of Life 15-revised
AChR Ab+, Acetylcholine receptor autoantibody positive



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# Myasthenia gravis is a rare, progressive autoimmune disease with significant unmet need

**>120,000**

**Patients in the U.S. and EU**

**Significant unmet need remains**

**Characterized by debilitating fatigue and muscle weakness**

Limbs

Respiratory

Ocular

Facial

**Current treatments require chronic or frequent administration and have limited durability**



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# Cartesian's mRNA approach is designed to expand the reach of potent cell therapy products to address autoimmunity

## No Lymphodepletion

No associated cytopenia, secondary malignancies, or other chemotherapy toxicities

## Administered Outpatient

Convenient dosing schedule

## Delivered at Therapeutic Levels

Administered at therapeutic doses without uncontrollable proliferation

## Transient Cell Modification

Does not carry risk of genomic integration



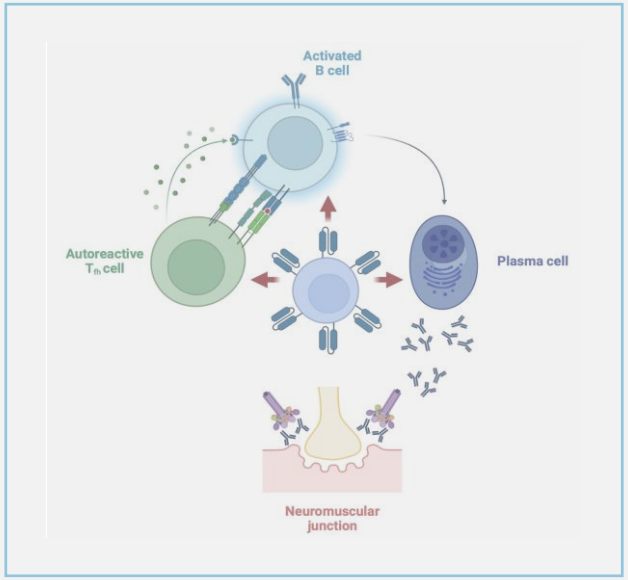
Cartesian therapeutics

# Descartes-08 is an mRNA CAR T-cell therapy in clinical development for autoimmune disease

**Engineered by transfection of autologous CD8+ T cells with mRNA encoding anti-BCMA CAR**

Typical lot **processed for infusion within as little as ~3 weeks**

Granted **U.S. FDA orphan and RMAT designations** for generalized myasthenia gravis, and **RPDD** for juvenile dermatomyositis



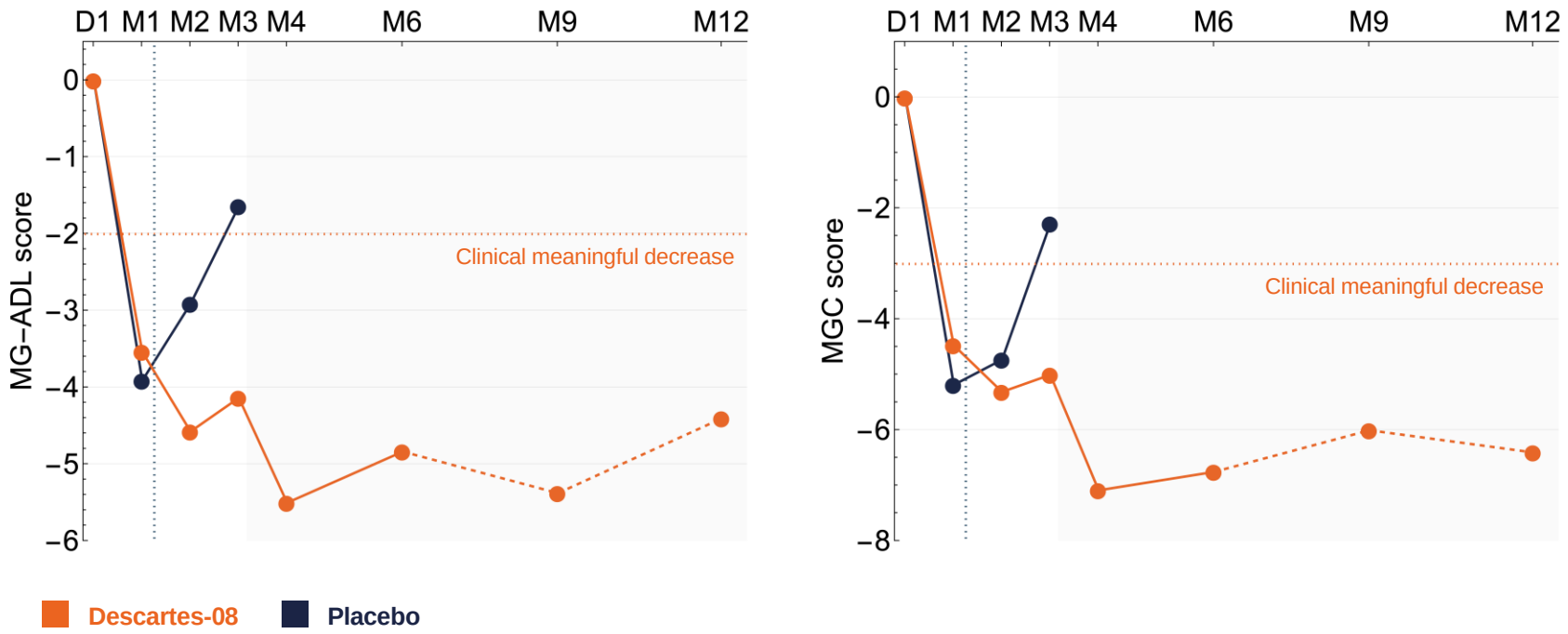



RMAT, Regenerative Medicine Advanced Therapy
RPDD, Rare Pediatric Disease Designation

BCMA, B-cell maturation antigen
CAR, Chimeric antigen receptor

# Deepening responses observed in participants treated with Descartes-08

## Primary Efficacy Dataset




Month 3 (n=14), Month 4 (n=12*), Month 6 (n=12), Month 9 (n=8), Month 12 (n=5)
**Two participants lost to follow-up*

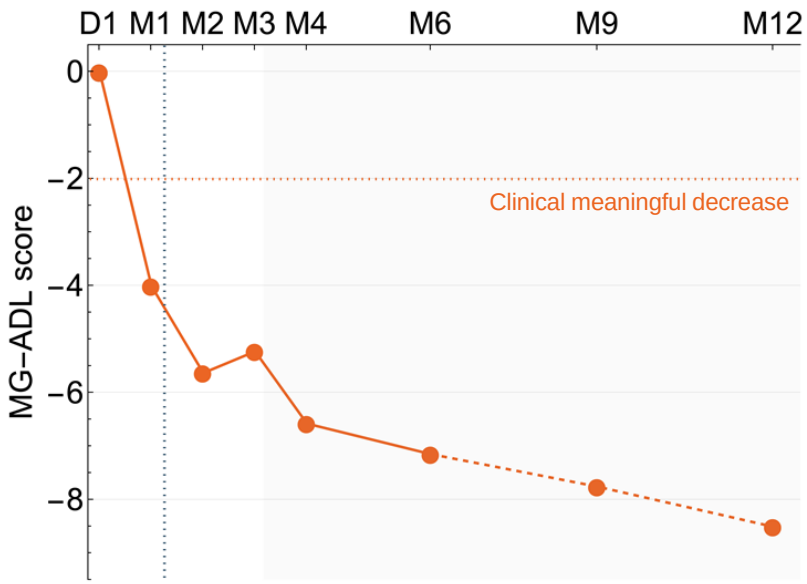
- Average MG-ADL reduction of 5.5 (±1.1) points at Month 4
- 33% of participants achieved minimum symptom expression at Month 6
- 80% of participants reaching Month 12 maintained clinically meaningful response

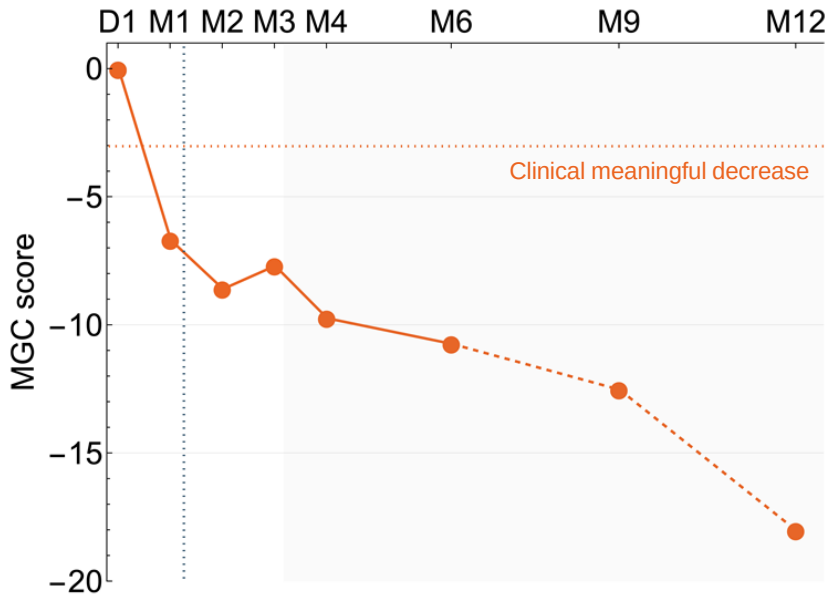


Minimum symptom expression: MG-ADL 0-1

# Deepest responses observed in participants with no prior exposure to complement or FcRn inhibitors

## Primary Efficacy Dataset (No Prior Biologics)




**Descartes-08**

Month 3 (n=9), Month 4 (n=7*), Month 6 (n=7), Month 9 (n=4), Month 12 (n=2)
**Two participants lost to follow-up*

- Average MG-ADL reduction of 6.6 (±1.5) points at Month 4
- 57% of participants achieved minimum symptom expression at Month 6
- 100% of participants reaching Month 12 maintained clinically meaningful response



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# Safety profile continues to support outpatient administration

| | Descartes-08 (n=20) | | | Placebo (n=16) | | |
|---|---|---|---|---|---|---|
| | Grade 1 | Grade 2 | Grade 3 | Grade 1 | Grade 2 | Grade 3 |
| **Headache** | 7 (35%) | 4 (20%) | | 2 (13%) | 3 (19%) | |
| **Chills** | 8 (40%) | 4 (20%) | | | | |
| **Nausea** | 3 (15%) | 6 (30%) | | 1 (6%) | 2 (13%) | |
| **Fever** | 7 (35%) | 4 (20%) | 1 (5%) | | | |
| **Fatigue** | 4 (20%) | 1 (5%) | | 1 (6%) | | |
| **Myalgia** | 4 (20%) | 2 (10%) | | | | |
| **Infusion related reaction** | 1 (5%) | 2 (10%) | 1 (5%) | 1 (6%) | | |
| **Muscle weakness** | 1 (5%) | 1 (5%) | | 1 (6%) | | |
| **Arthralgia** | 1 (5%) | 1 (5%) | | | 1 (6%) | |
| **Tachycardia** | 3 (15%) | | | | | |
| **Upper respiratory infection** | | 1 (5%) | | | 1 (6%) | |
| **Herpes simplex reactivation** | 1 (5%) | | 1 (5%) | | | |
| **Dysgeusia** | 3 (15%) | | | | | |
| **Diarrhea** | 1 (5%) | | | | 1 (6%) | |
| **Sweating** | 1 (5%) | | | 1 (6%) | | |
| **Limb edema** | 1 (5%) | 1 (5%) | | | | |
| **Flushing** | 2 (10%) | | | | | |
| **Dyspnea** | 1 (5%) | 1 (5%) | | | | |
| **Insomnia** | 2 (10%) | | | | | |
| **Vomiting** | 2 (10%) | 1 (5%) | | | | |
| **Tremor** | 2 (10%) | | | | | |

- **No new type of AEs reported**
- **No hypogammaglobulinemia or increased infections reported**
- **No difference in vaccine titers between Descartes-08 and placebo**

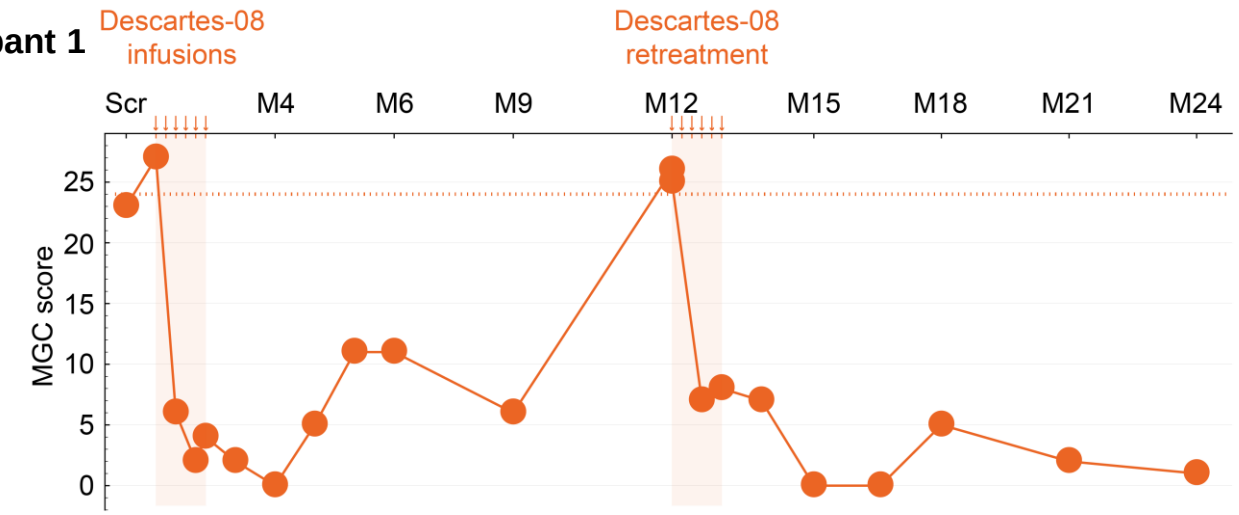
Safety dataset comprises all subjects who received at least one dose of Descartes-08 (n=20) or placebo (n=16).

All Grade 1–2 adverse events deemed possibly, probably or definitely related to the study drug with a cumulative incidence ≥10% and all Grade 3 adverse events deemed possibly, probably or definitely related to the study drug are reported. There were no Grade 4 adverse events

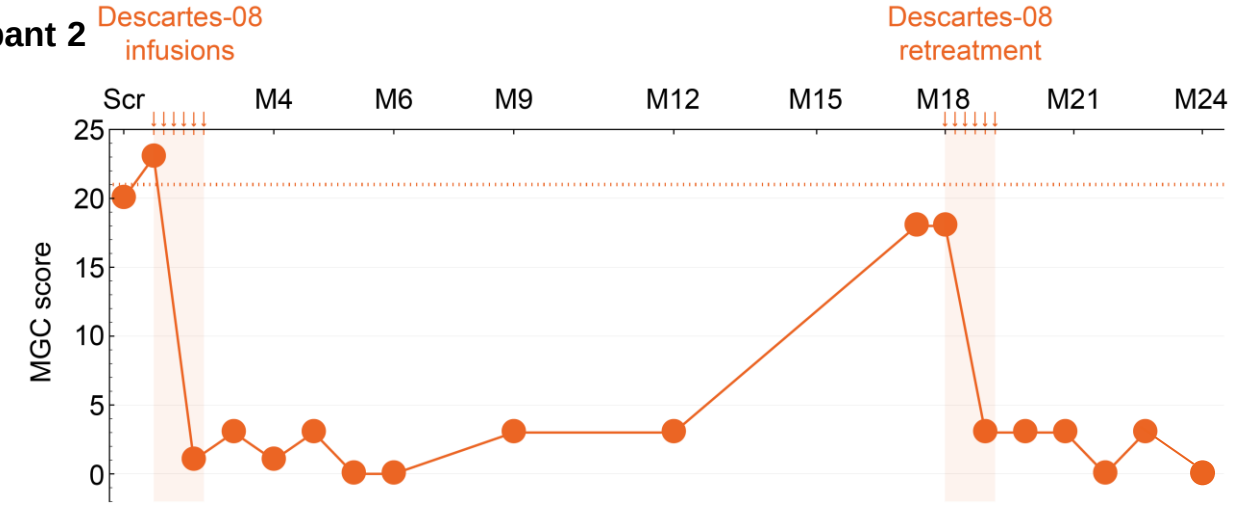
AE, Adverse event

# Phase 2a trial update: Descartes-08 retreatment continues to elicit deep and durable responses

**Participant 1**




**Participant 2**




- Three participants retreated to date, two of whom maintain minimum symptom expression 2 years after initial treatment
- Third participant achieved 4-point reduction in MG-ADL and 6-point reduction in MGC at the most recent, Month 2 follow-up of retreatment

Manuscript submitted for peer review; pre-print available at medRxiv.org.



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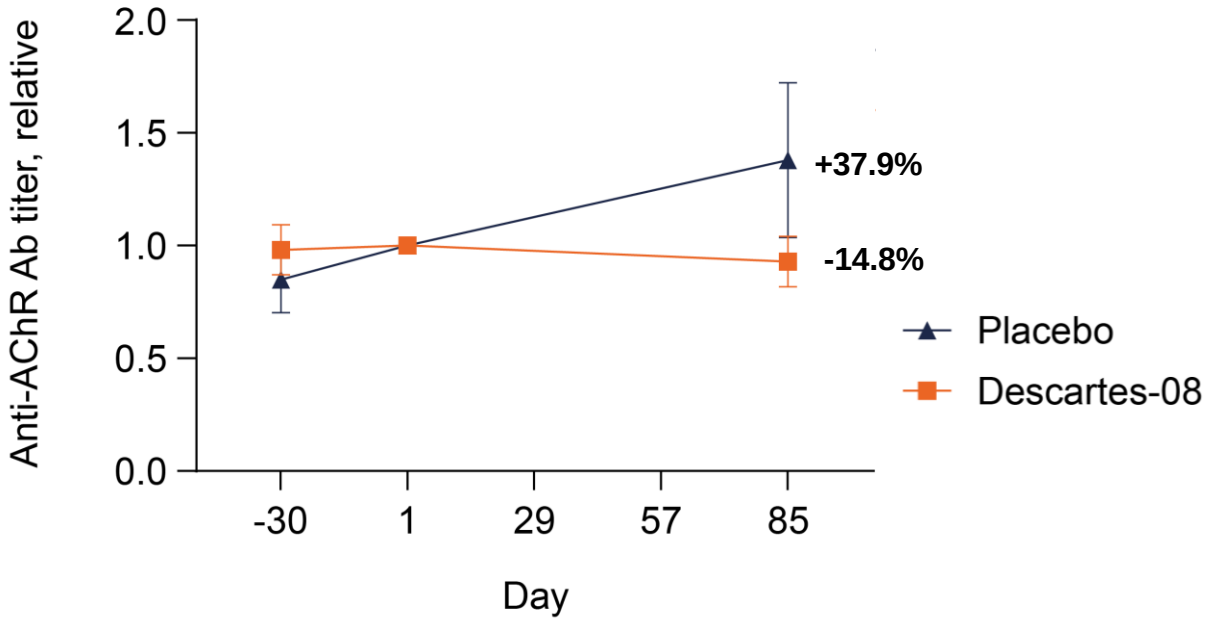
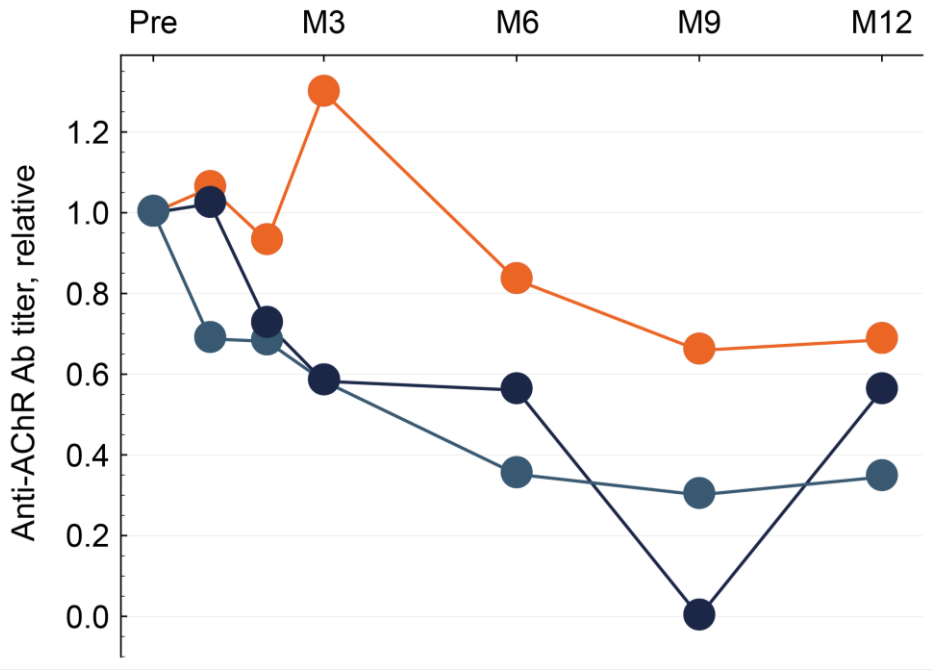
# Approximately 15% reduction in AChR antibody titer at Month 3 is in line with Phase 2a data




Average reduction (±SEM) in AChR antibody in participants with baseline levels above LLOQ randomized to Descartes-08 (n=12) vs. Placebo (n=9).

## Phase 2a data




Individual Anti-AChR antibody titers in all participants receiving six once-weekly infusions in the Phase 2a trial with detectable baseline levels (n=3).

SEM, Standard error of the mean
LLOQ, Lower limit of quantification



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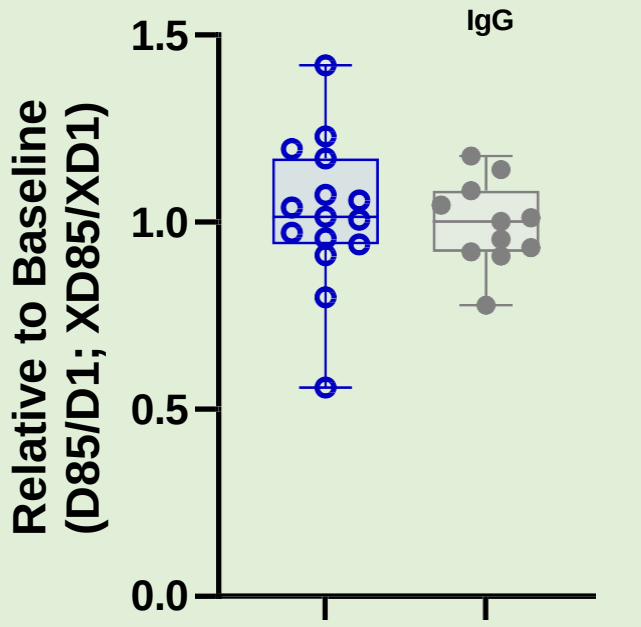
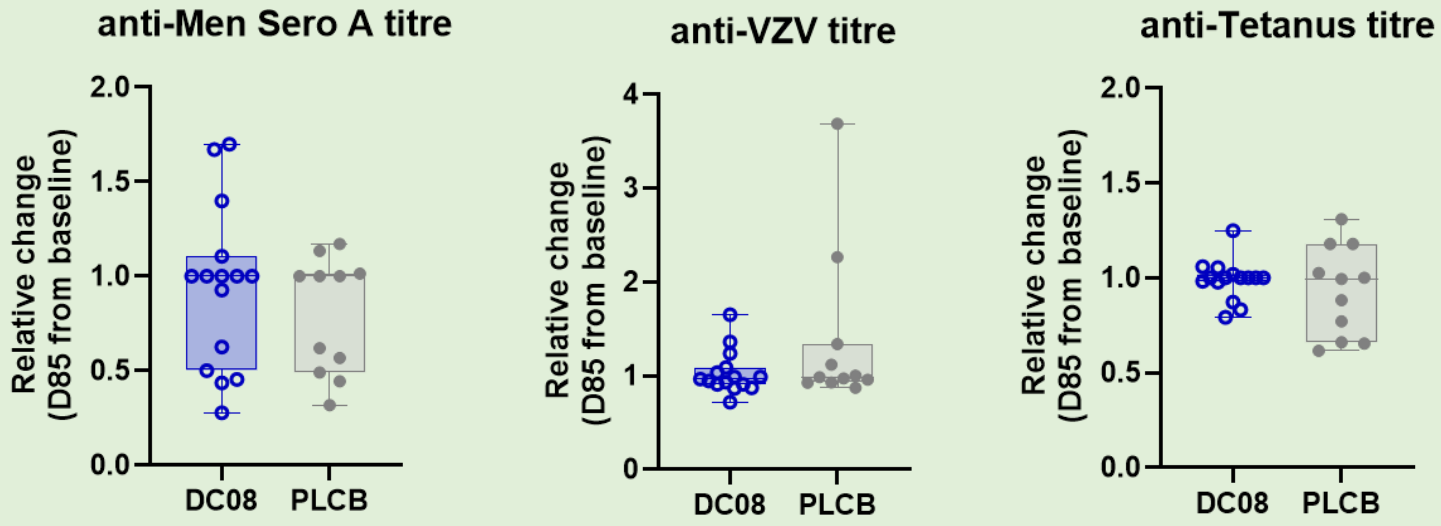
# Descartes-08 observed not to deplete broader antibody repertoire or decrease vaccine titers for common viruses

## No significance change in Ig at primary end point (D85) vs. Day 1[1]




Descartes-08 (DC08) Placebo (PLCB)

## No significant change in common vaccine titers at primary end point (Day 85) relative to Day 1[2]




Not shown: anti-Men Sero C, anti-Men Sero W135, anti-Men Sero Y, anti-Diphtheria, anti-Measels, anti-Mumps and anti-Rubella titers

Descartes-08 (DC08) Placebo (PLCB)

1. Data indicate change in Ig levels for each participant in the miTT group (n = 26) at Day 85 relative to Day 1. Data are individual values, median, range and IQR.
2. Data indicate change in vaccines titers for each participant in the mITT group (n=26) at Day 85 relative to Day 1. Data are individual values, median, range and IQR.

Ig, Immunoglobulin
VZV, Varicella zoster virus
mITT, Modified intent-to-treat



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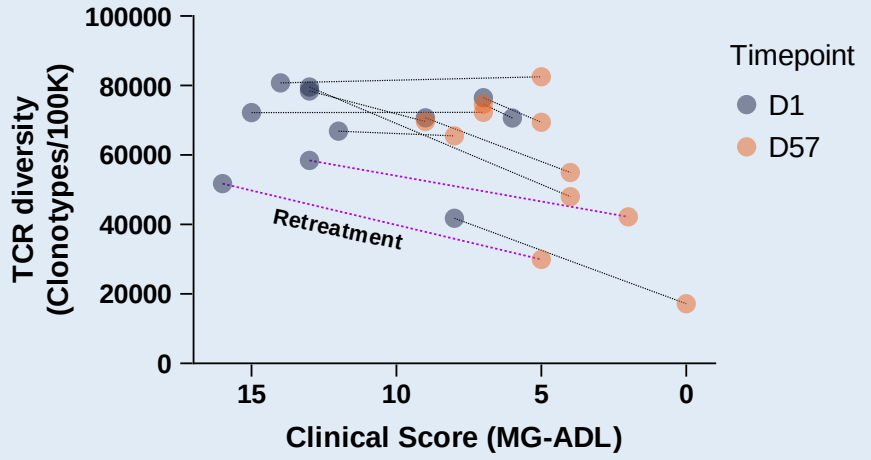
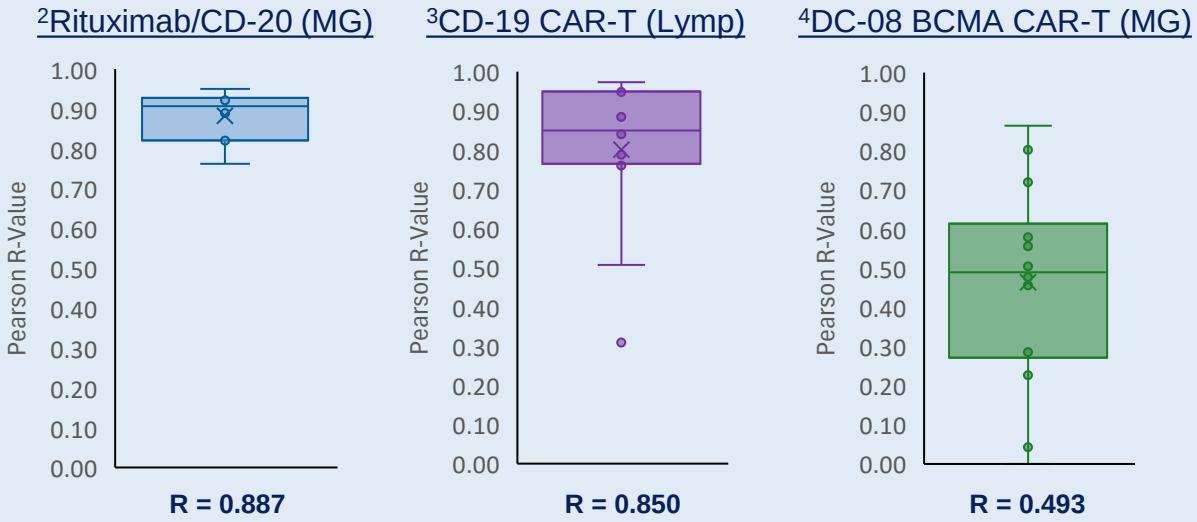
# Descartes-08 focuses the T-cell repertoire and selectively alters the autoreactome, showing clear biological activity

## Descartes-08 focuses the T-cell repertoire in a manner that correlates with clinical effect




p=0.048 (Wilcoxon signed rank test) TCR Diversity D57 vs D1

## Descartes-08 selectively alters the self-reactive branch of the antibody repertoire (i.e., autoreactome[1])




Data show Clinical Score and TCR Sequencing TCR Diversity (Downsampled Rearrangements) in Phase 2a samples analyzed at Adaptive Biotechnologies (R06 dataset). For certain subjects where TCR sequencing sample data was unavailable, D1 data was imputed from Screen, and D57 data was imputed from D85. Samples from one re-treated patient were analyzed as indicated. P-value is provided for Wilcoxon matched-pairs signed rank test on all primary-treatment data pairs from D1 vs D57.

[1]Bodansky et al., *Journal of Clinical Investigation* **2024**, doi: 10.1101/2023.12.19.23300188.

Serum analysis of [2]Myasthenia gravis patients receiving Rituximab targeting CD20+ B cells, [3]lymphoma patients receiving conventional CD19 DNA CAR-T, or [4]gMG patients following infusion with DC-08. Data compare D85 to D1 for MG open label cohort (N=13).



TCR, T-cell receptor

# Wholly owned, in-house manufacturing

~30,000 sq. ft. state-of-the-art cGMP facility

Facility located in Frederick, MD

## FUTURE GROWTH

Clinical and commercial manufacturing scale capabilities support maturing pipeline and future growth

## QUICK TO ADAPT

Flexibility to quickly adapt to changes in processes or needs

## WHOLLY OWNED

Ownership of quality control and production timelines

## COST EFFICIENT

Potential cost efficiency

cGMP, Current good manufacturing practice

# Deep and durable response maintained over 12 months in participants treated with Descartes-08

**Deepening responses observed over time**

**Durable responses observed over time**

**Deepest responses observed in participants without exposure to prior biologic therapy**

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# Q&A