Cartesian® THERAPEUTICS

# Bringing mRNA cell therapy to patients with autoimmunity

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American Society of Gene and Cell Therapy
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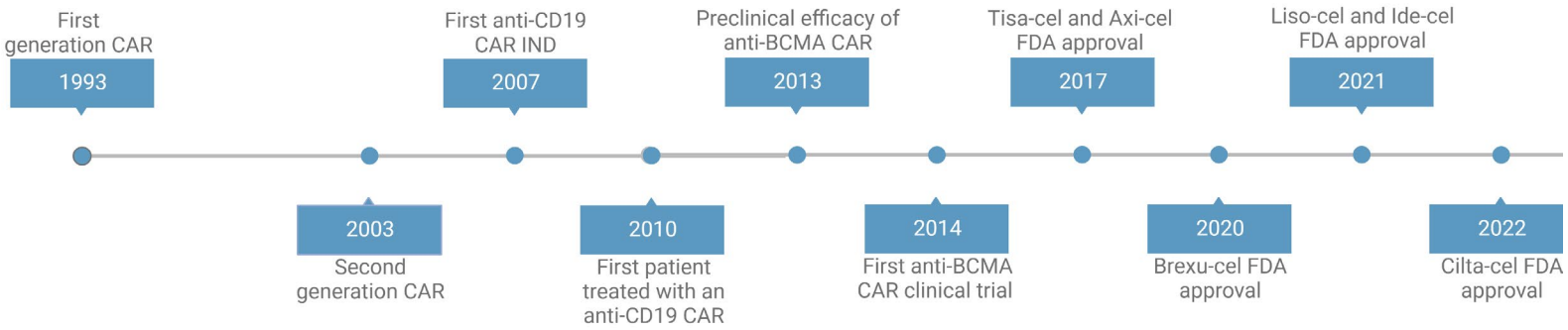
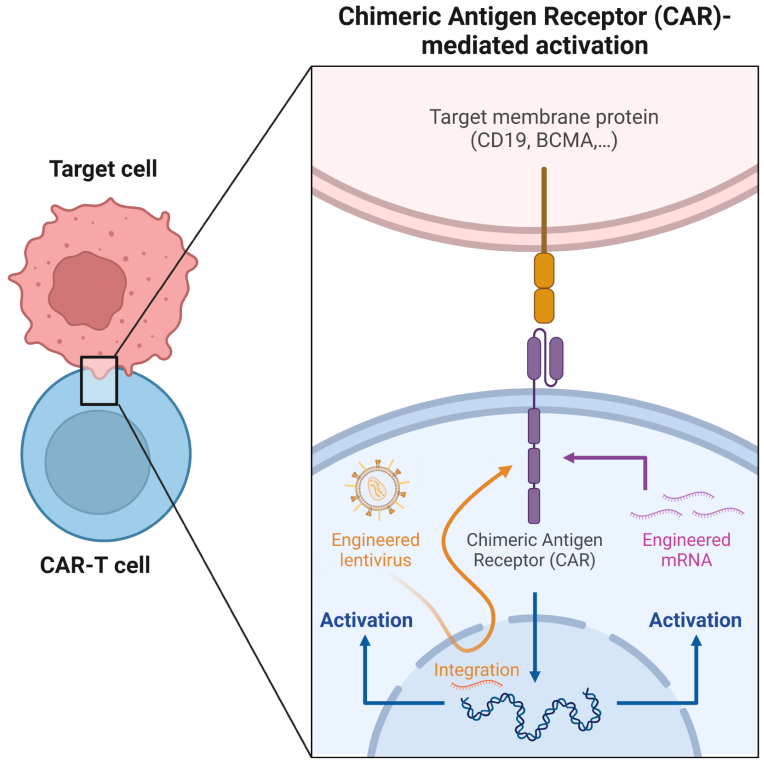
# Disclosures

- CM Jewell is employed by and holds an equity position with Cartesian Therapeutics
- CM Jewell is the Fischell Institute Professor of Translational Engineering and MPower Professor at the University of Maryland – College Park
- CM Jewell is a Research Biologist with the Baltimore VA Medical Center
- The views presented here do not reflect the views of the University of Maryland or the United States government
- CM Jewell holds an equity position with Barinthus Biotherapeutics plc
- CM Jewell is a co-founder and holds an equity position with Nodal Therapeutics. Inc.

# The selectivity of chimeric antigen-specific (CAR) T cell therapy offers transformative potential for diverse indications beyond oncology

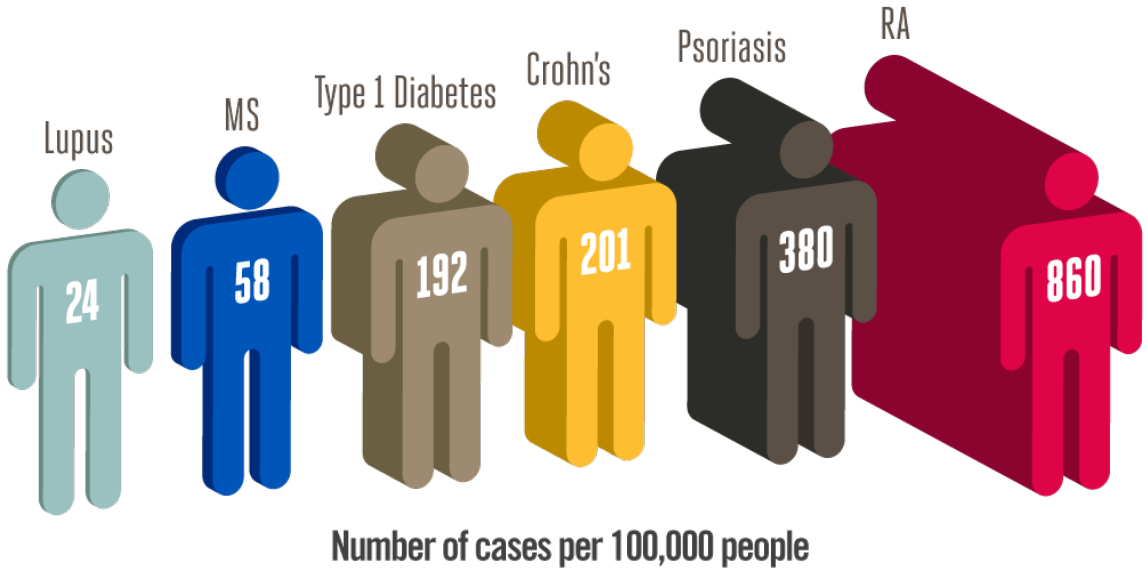


# Autoimmune diseases impact an estimated 300M+ people

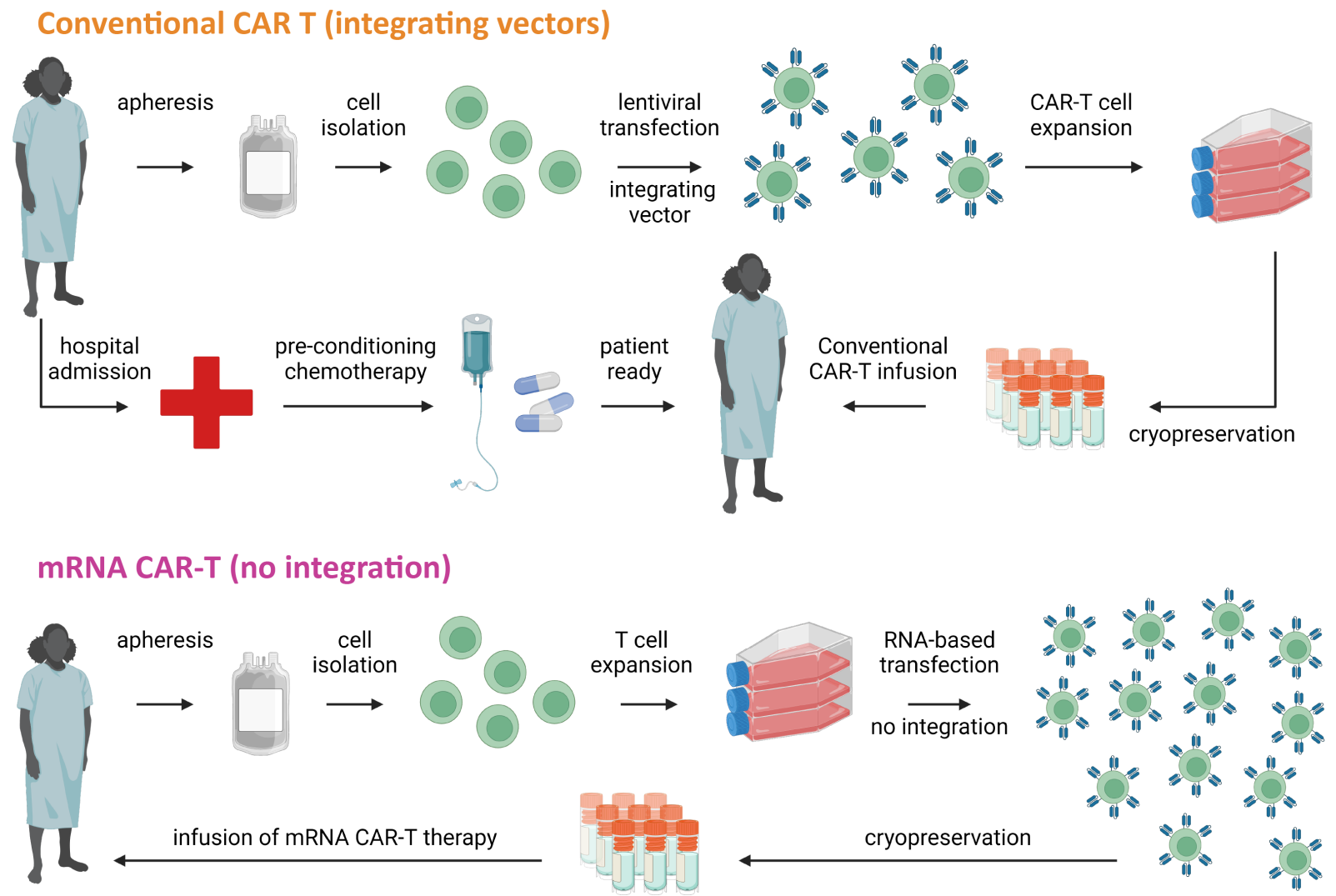
- **Diverse pathologies but common features**
  - Autoimmunity - characterized by attack against self
  - 100+ autoimmune disorders
  - Many poorly defined

- **Persistent treatment challenges:**
  - No cures
    → varying severities and co-morbidities
  - Require life-long treatment
    → often poor compliance and patient QOL
  - Multi-faceted side effects




Source: NIH.gov, National MS Society, RheumatoidArthritis.net, Organdonor.gov, NIH.gov

# Integrating vector CAR-T and RNA-based CAR-T create different patient experiences



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

## Cartesian THERAPEUTICS mRNA Cell Therapy

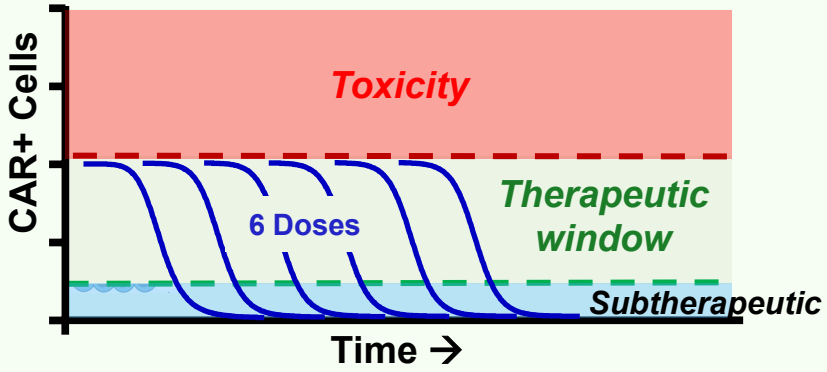
**No Lymphodepleting Chemotherapy Required**
No requirement for cell proliferation → no expected need for pre-treatment chemotherapy → no Grade 3-4 cytopenias

**Administered Outpatient**
Reduced patient burden and lower indirect cost

**Delivered at Therapeutic Levels**
Expectation for cells to be administered at therapeutic, but sub-toxic doses

**Controllable PK/PD**
mRNA does not replicate → predictable half-life with more controllable PK/PD defined by the dose

**Transient Cell Modification**
Does not carry risk of genomic integration




## Conventional DNA Cell Therapy

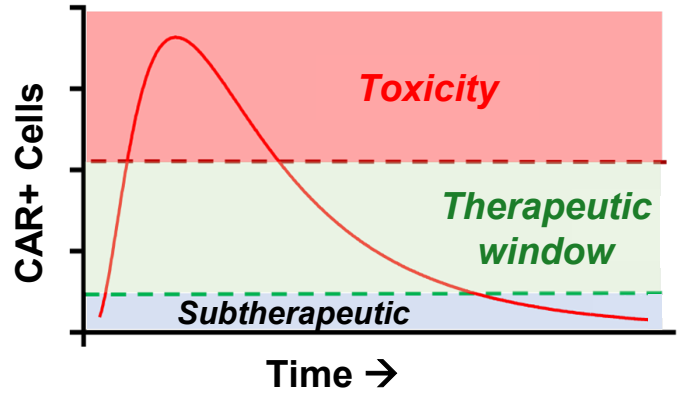
**Requires Lymphodepleting Chemotherapy**
Associated with high rates of toxicity, including cytokine release syndrome

**Requires Inpatient Administration**
High patient burden resulting in higher indirect costs

**Administered at Subtherapeutic Levels**
Cells proliferate rapidly beyond therapeutic window

**Uncontrollable PK/PD**
Effector function of cell therapy engineered with DNA amplifies exponentially with cell replication

**Permanent Cell Modification**
Associated with insertional mutagenesis leading to potential secondary malignancies



# Wholly-owned pipeline targets autoimmune disease

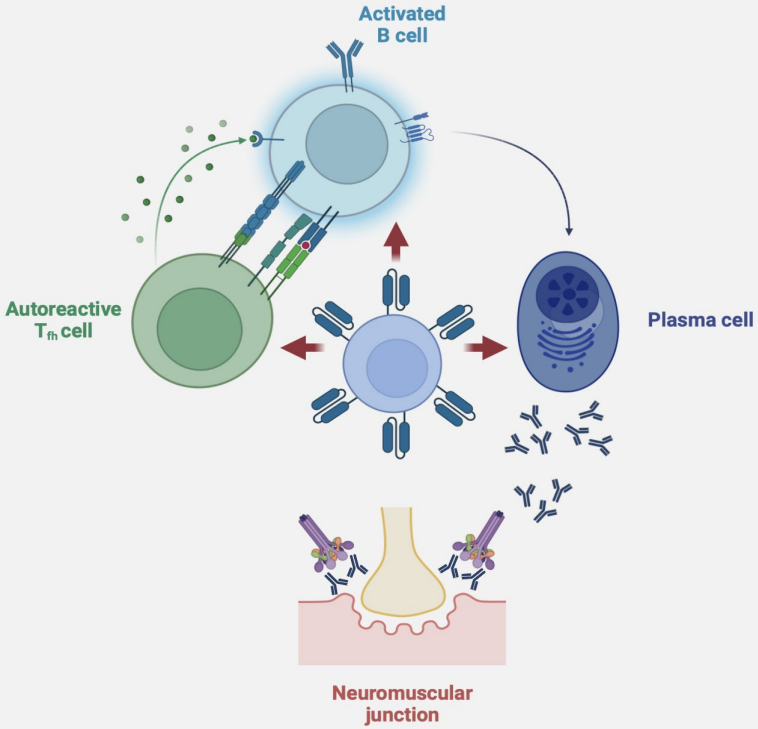
| Asset | Indications | Discovery/Preclinical | Phase 1 | Phase 2 | Pivotal |
|---|---|---|---|---|---|
| **Descartes-08 Autologous mRNA CAR-T** | Myasthenia Gravis | | | | |
| | SLE, other Autoimmune Diseases | | | | |
| **Descartes-15 Autologous mRNA CAR-T** | Autoimmune Diseases* | | | | |
| **Descartes-33 Allogeneic mRNA MSC** | Autoimmune Diseases | | | | |
| ***In situ* LN transfection** | Undisclosed | | | | |

SLE, Systemic Lupus Erythematosus
mRNA MSC, Mesenchymal Stem Cells transfected with mRNA

* Phase 1 dose escalation study in myeloma underway
LN, Lymph node

# Descartes-08 is believed to be the first mRNA CAR-T 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 ~3 weeks**
- **Positive Phase 2a data** in myasthenia gravis underscores potential for deep and durable responses
- Granted **U.S. FDA orphan designation** for generalized myasthenia gravis



# Descartes-08 is designed for dual action, precisely targeting two key BCMA+ cell populations involved in a spectrum of autoimmune diseases

Descartes-08 is designed to target BCMA, a surface antigen expressed on ***plasma cells/plasmablasts*** and ***plasmacytoid dendritic cells***

## PLASMA CELLS (PCs) AND PLASMABLASTS

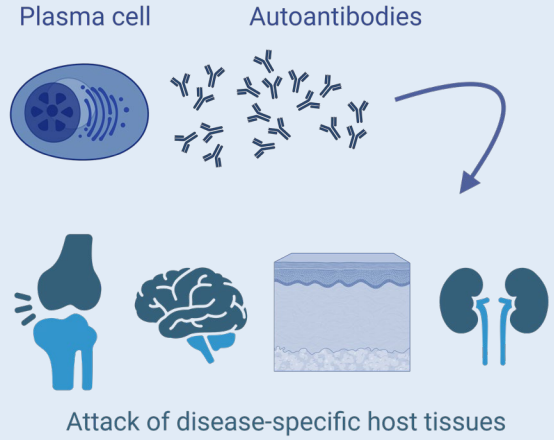
- PCs, plasmablasts and proliferating B cells targeted by Descartes-08 represent a tiny fraction of B cells
- These cells are entirely responsible for secreting pathogenic autoantibodies
- During autoimmunity, autoantibodies attack host tissue and drive inflammation

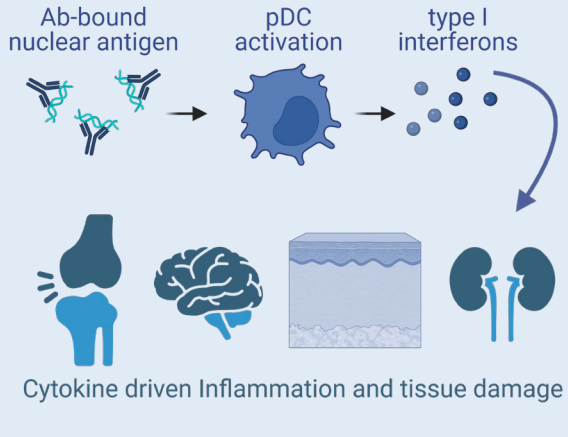
## PLASMACYTOID DENDRITIC CELLS (pDCs)

- pDCs, which Descartes-08 is designed to target, are a rare subset of antigen-presenting cells
- These cells secrete high levels of cytokines (i.e., type I interferons) that cause inflammation and tissue damage during many human autoimmune diseases
- pDCs are increased in patients with autoimmunity (e.g., SLE) and interfere with optimal treatment

Several autoimmune disease segments involve pathogenic contributions from ***both PCs/plasmablasts*** and ***pDCs***, including rheumatology, nephrology, neurology, and others

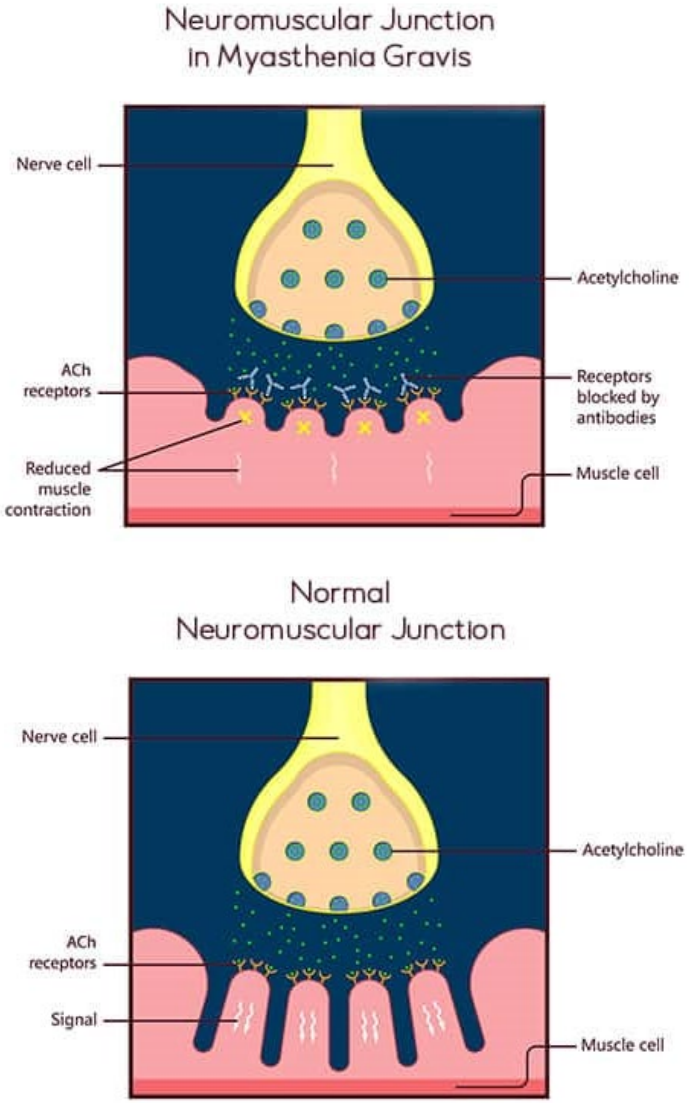
Selectively deleting PCs/plasmablasts and pDCs, if successful, may create a differentiated cell therapy platform



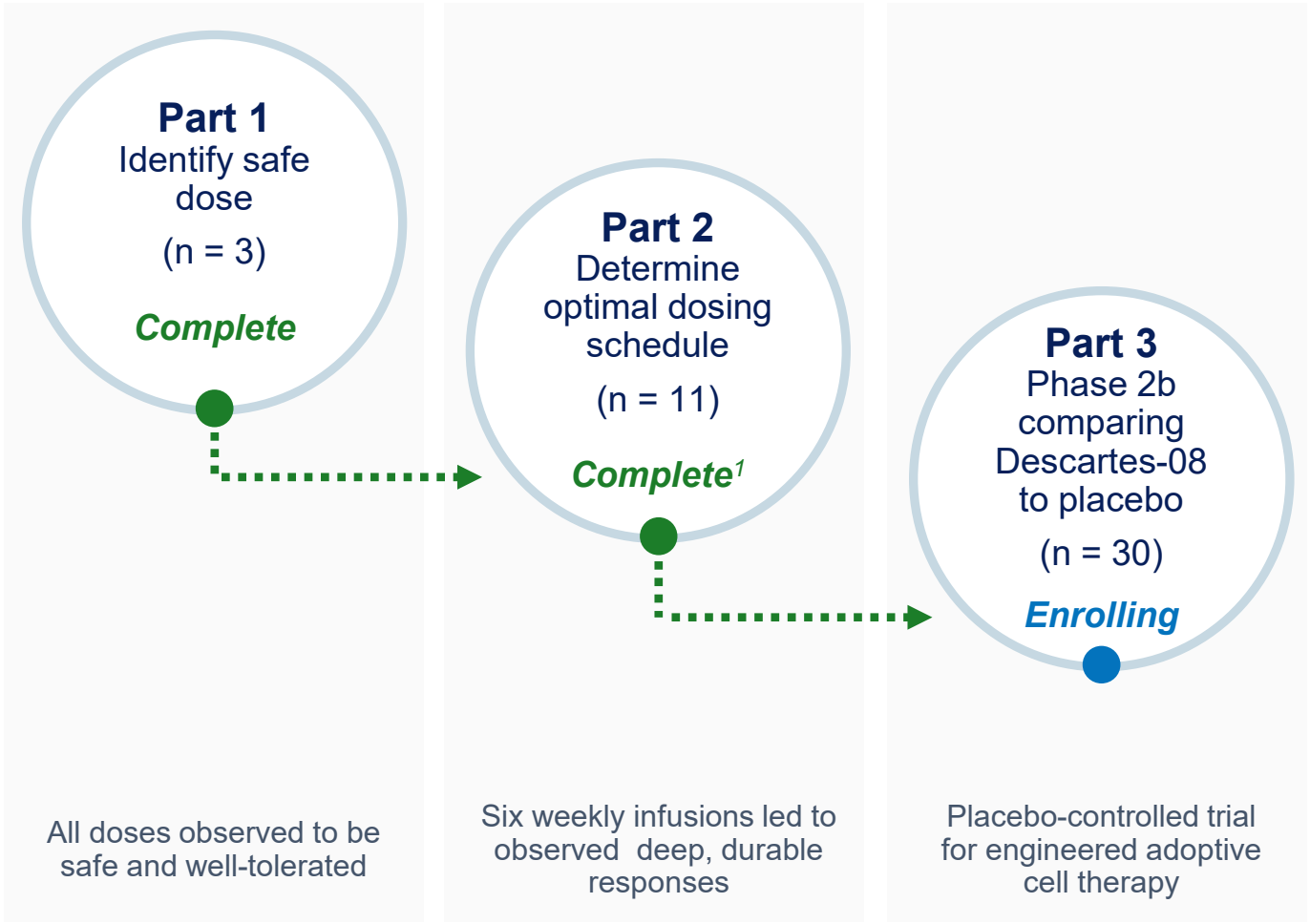



# Initial indication for Descartes-08: Myasthenia gravis

- Affects **over 120,000 patients** in US and EU
- Characterized by debilitating weakness: limbs, respiratory, ocular, facial muscles
- **Standard of care** includes **chronic use of immunosuppressants**, which are **often toxic:**
  - Progressive disease that is fatal in 1/3 of patients without immunosuppressants
- Newer agents include **complement inhibitors and anti-FcRn mAbs**, which must be **administered chronically** to maintain responses
- **Pathogenesis is similar across many autoimmune diseases;** involves attack on self by both T cells and B/plasma cells



# Phase 2 study of Descartes-08 in MG (NCT04146051)




## Patient eligibility

- MG-ADL ≥ 6
- MGFA Class II-IV
- Stable medication dosing ≥ 8 wks prior to infusion
- 4-week washout for biologics
- IVIg and plasma exchange not allowed after starting Descartes-08

Patients on immunosuppression or complement inhibitors expected to be able to continue their treatment while receiving Descartes-08

Cell manufacturing platform tolerates most standard immunosuppressive therapies

[1] Continues to enroll patients with MuSK MG and subjects who are otherwise not eligible for Part 3
MG-ADL, Myasthenia Gravis Activities of Daily Living scale
MGFA, Myasthenia Gravis Foundation of America

# Phase 1/2a study population comprises patients with significant disease

THE LANCET Neurology

**Volume 22, Issue 7**, July 2023, Pages 578-590

- Baseline MG-ADL mean score of 10
- 79% were MGFA Class III-IV at screening
- All patients presented with disease that was not controlled with standard of care therapies

| | |
|---|---|
| **Mean age, years (SD)** | 52 (18) |
| Female | 10 (71%) |
| Male | 4 (29%) |
| **Mean weight, kg (SD)** | 84 (21) |
| **Mean BMI, kg/m$^2$ (SD)** | 31.6 (8.1) |
| **Race and ethnicity** | |
| White, non-Hispanic | 11 (79%) |
| White, Hispanic | 1 (7%) |
| Asian | 2 (14%) |
| **MGFA class at screening** | |
| II | 3 (21%) |
| III | 10 (71%) |
| IV | 1 (7%) |
| **Median age of disease onset, years (range)** | 40 (14-79) |
| **Median duration of disease, years (range)** | 14 (3-27) |
| **Myasthenia gravis antibody status** | |
| Anti-AChR antibody | 11 (79%) |
| Anti-MuSK antibody | 2 (14%) |
| Seronegative (for AChR, MuSK, and LRP4 antibodies) | 1 (7%) |
| **Mean baseline scores (SD)** | |
| QMG | 15.3 (4.1) |
| MG-ADL | 10.0 (3.2) |
| MGC | 21.9 (5.7) |
| MG-QoL-15r | 19.9 (5.8) |

| | |
|---|---|
| **Previous myasthenia gravis therapies (standard of care)** | |
| Pyridostigmine | 14 (100%) |
| Prednisone | 14 (100%) |
| Other immunosuppressants | 14 (100%) |
| Eculizumab | 2 (14%) |
| Rituximab | 2 (14%) |
| **Previous intravenous immunoglobin** | 12 (86%) |
| **Previous plasma exchange** | 8 (57%) |
| **Diagnosis of thymoma** | 0 |
| **Previous thymectomy** | 6 (43%) |
| **Previous myasthenia gravis crisis requiring intubation** | 4 (29%) |
| **Myasthenia gravis ongoing therapy** | |
| Pyridostigmine | 11 (79%) |
| Prednisone | 10 (71%) |
| Azathioprine | 1 (7%) |
| Mycophenolate mofetil | 1 (7%) |

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# Descartes-08 was observed to be safe and well-tolerated in MG

THE LANCET Neurology

**Volume 22, Issue 7**, July 2023, Pages 578-590

**KEY OBSERVATIONS:**

- No dose-limiting toxicities
- No cytokine release syndrome
- No neurotoxicity
- No pre-treatment chemotherapy and related cytopenias
- Outpatient treatment

| | Grade* | Part 1 (n=3) | Part 2: all groups (n=11) | Part 2: group 1 (n=3) | Part 2: group 2 (n=7) | Part 2: group 3 (n=1) |
|---|---|---|---|---|---|---|
| Hand numbness | 2 | 1 (33%) | 0 | 0 | 0 | 0 |
| Headache | 1 | 1 (33%) | 5 (45%) | 1 (33%) | 3 (43%) | 1 (100%) |
| Muscle soreness | 1 | 1 (33%) | 1 (9%) | 0 | 1 (14%) | 0 |
| Nausea | 1 | 1 (33%) | 4 (36%) | 2 (67%) | 2 (29%) | 0 |
| Rash | 3 | 0 | 1 (9%) | 1 (33%) | 0 | 0 |
| Itchy throat | 1 | 0 | 2 (18%) | 0 | 1 (14%) | 1 (100%) |
| Vomiting | 1 | 0 | 3 (27%) | 2 (67%) | 1 (14%) | 0 |
| Weakness | 1 | 0 | 2 (18%) | 2 (67%) | 0 | 0 |
| Line infiltration | 1 | 0 | 1 (9%) | 1 (33%) | 0 | 0 |
| Fever | 1 | 0 | 4 (36%) | 1 (33%) | 3 (43%) | 0 |
| Shortness of breath[1] | 1 | 0 | 2 (18%) | 1 (33%) | 1 (14%) | 0 |
| Chills | 1 | 0 | 2 (18%) | 1 (33%) | 1 (14%) | 0 |
| Diarrhoea | 1 | 0 | 1 (9%) | 1 (33%) | 1 (14%) | 0 |
| Gum inflammation | 1 | 0 | 1 (9%) | 0 | 1 (14%) | 0 |
| Teeth sensitivity | 1 | 0 | 1 (9%) | 0 | 1 (14%) | 0 |
| Night sweats | 1 | 0 | 1 (9%) | 0 | 1 (14%) | 0 |
| Restless leg | 1 | 0 | 1 (9%) | 0 | 1 (14%) | 0 |
| Light-headedness | 1 | 0 | 1 (9%) | 0 | 1 (14%) | 0 |

*There were no adverse events of grade 3 or higher reported in part 1, and no grade 2 or grade 4 events reported in part 2, where grade 1 is mild, grade 2 is moderate, grade 3 is severe, and grade 4 is life-threatening.

[1]Not associated with hypoxia

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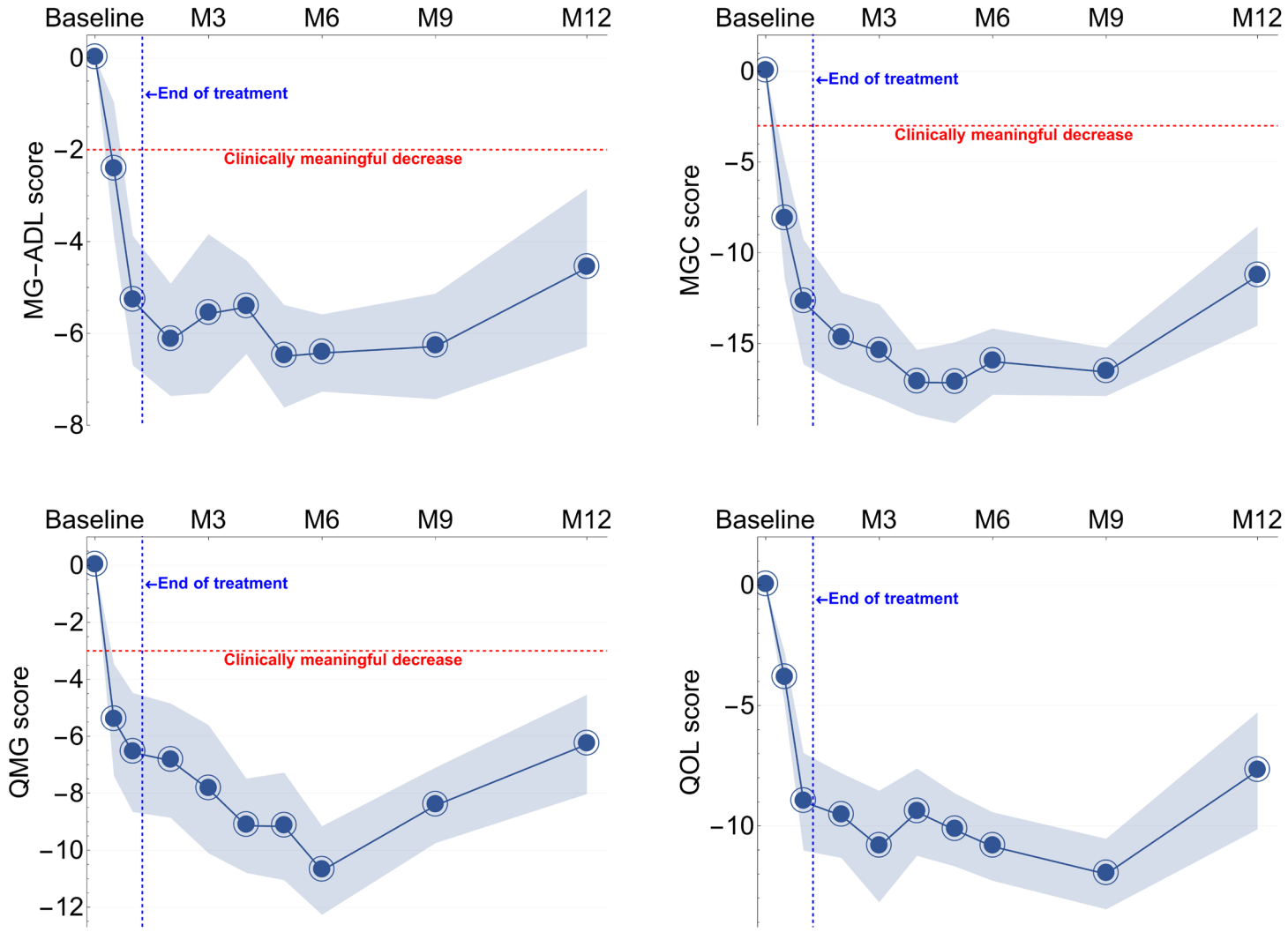
# Descartes-08 observed to induce deep and durable clinical improvement in MG

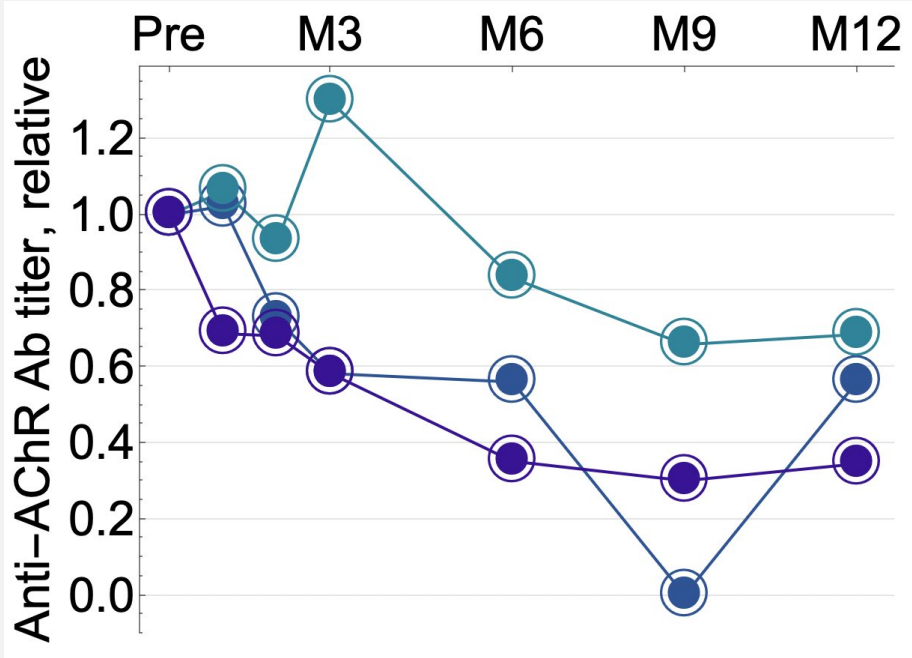
- **Notable magnitude and duration of response** across all 4 standard MG severity scales
- Responses appear **to *deepen after completing treatment*** at Week 6
- **Positive** twelve-month follow-up data from Phase 2a study reinforce prior findings published in *Lancet Neurology*




Manuscript submitted for peer review; pre-print available at medRxiv.org
Efficacy dataset includes all MG patients completing the 6-dose once-weekly regimen (n=7). Data are mean score improvement (point) and standard error (light blue shading). Note that QOL scale does not have an agreed-upon threshold for clinically meaningful disease improvement; MG-ADL, MGC and QMG scales are validated, quantitated, standardized instruments of disease severity and have been acceptable endpoints for registration studies.

# Descartes-08: Durable depletion of autoantibodies consistent with observed clinical responses and MoA

- All three participants with detectable AChR antibody levels at baseline experienced autoantibody reductions by Month 6
- Reductions deepened further by Month 9, and were maintained at Month 12

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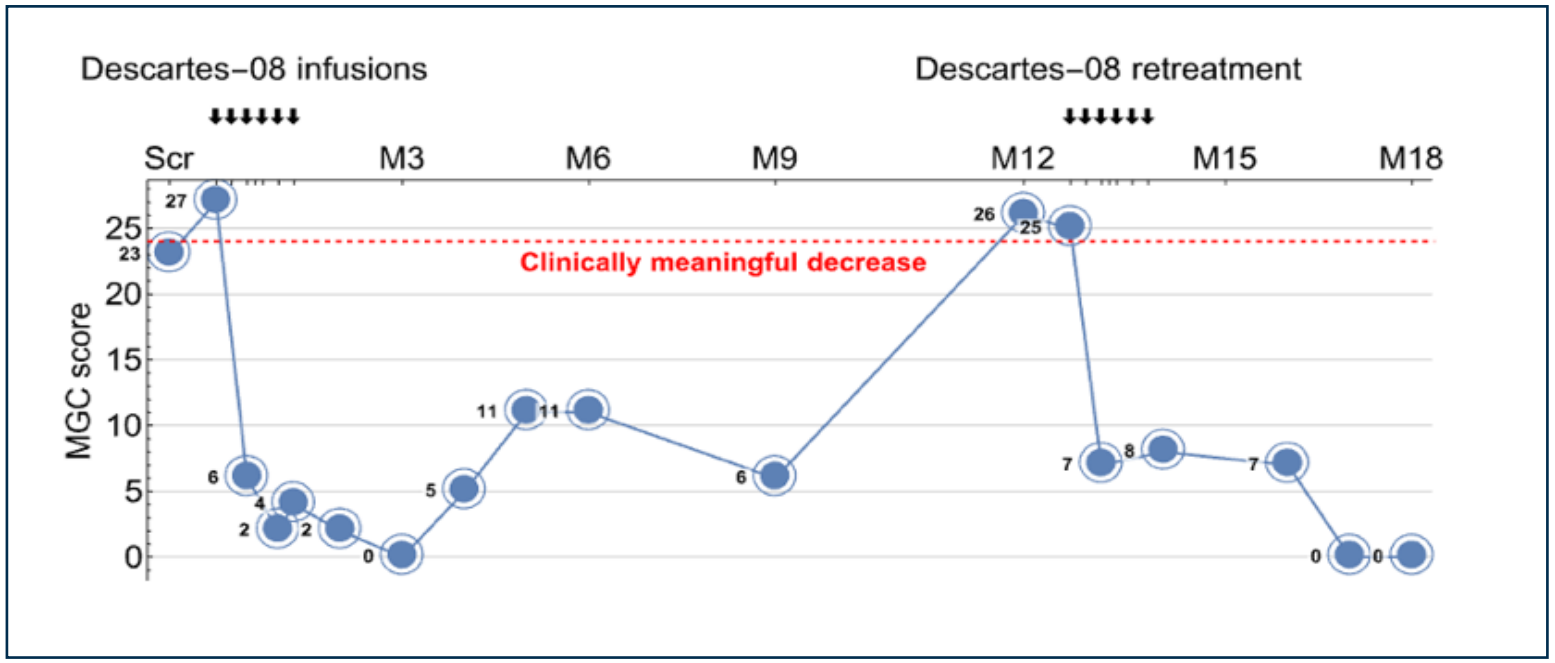
Manuscript submitted for peer review; pre-print available at medRxiv.org

Anti-acetylcholine receptor, AChR MoA, Mechanism of action

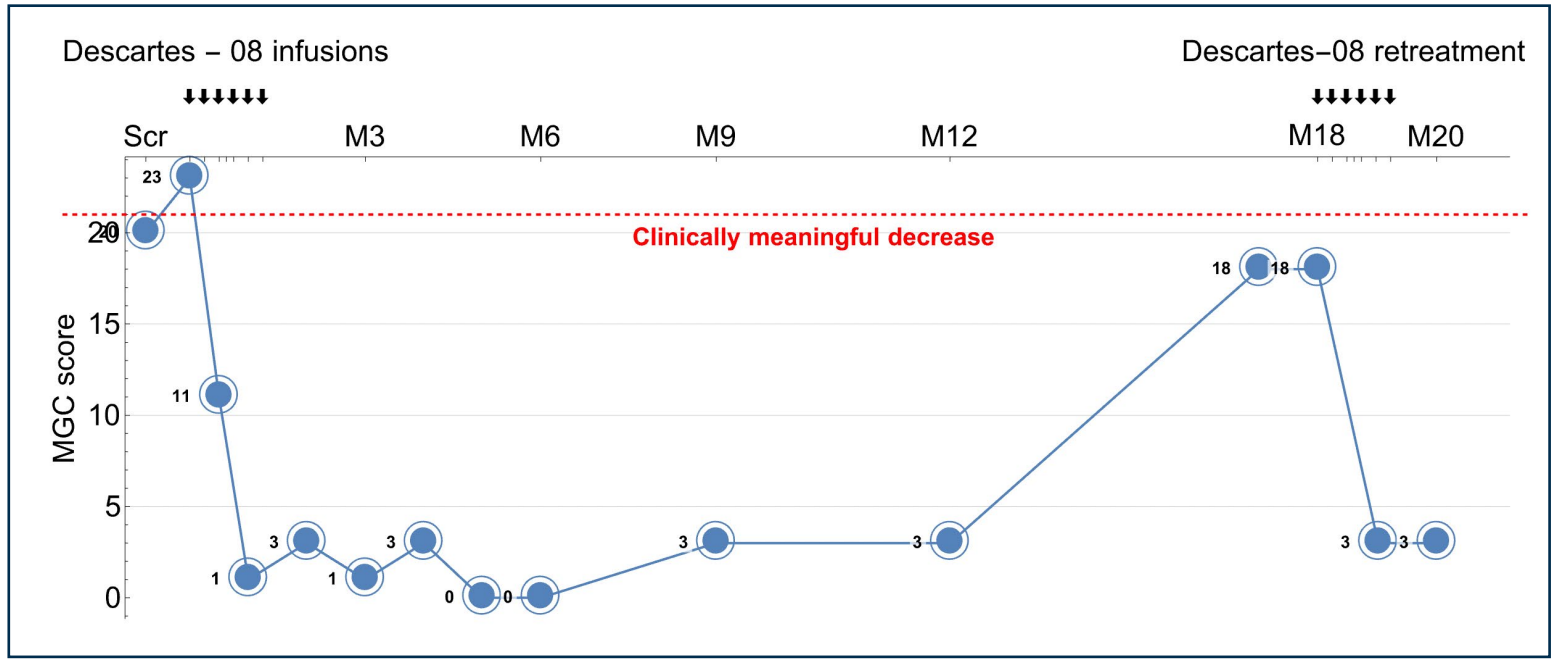
# Descartes-08 retreatment led to a rapid decrease in MG-specific clinical scores

- Retreated patients experienced rapid improvement in clinical scores and minimal symptom expression

Patient 1




Patient 2




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

# Phase 2b randomized, placebo-controlled, double-masked study of Descartes-08 in MG

**Plan to treat ~30 patients**

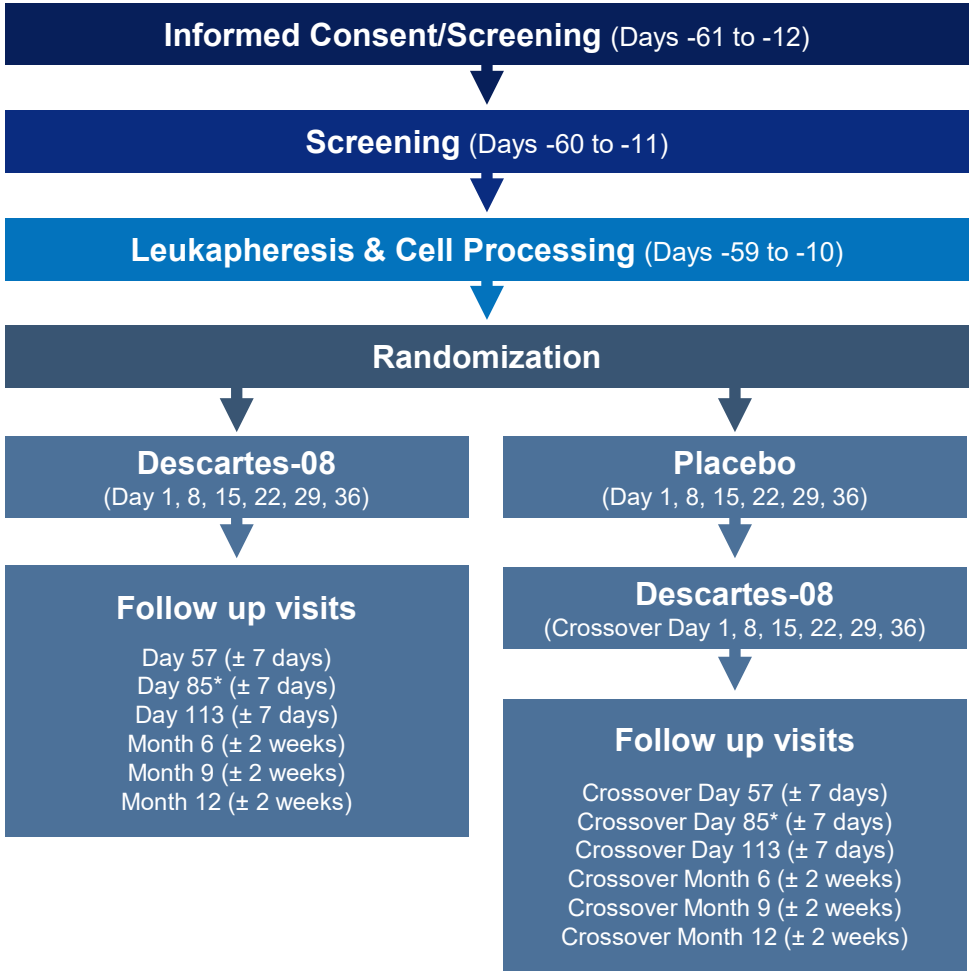
**PRIMARY ENDPOINT**

- Proportion of **MG Composite** responders (**≥5-point** reduction) at Day 85

**SECONDARY OBJECTIVES**

- Safety and tolerability
- Quantify clinical effect of Descartes-08 over 1 year
- QMG, MG QoL 15R, MG ADL, and MG PIS (change from baseline to Day 85)
- Compare effect of Descartes-08 versus placebo on MG scales (change from baseline to Day 85) in patients who cross over from placebo to Descartes-08

**Enrollment underway, with top-line results expected in mid-2024**




MG QMG, Quantitative MG Scores
MG QOL15R, MG Quality of Life 15-revised

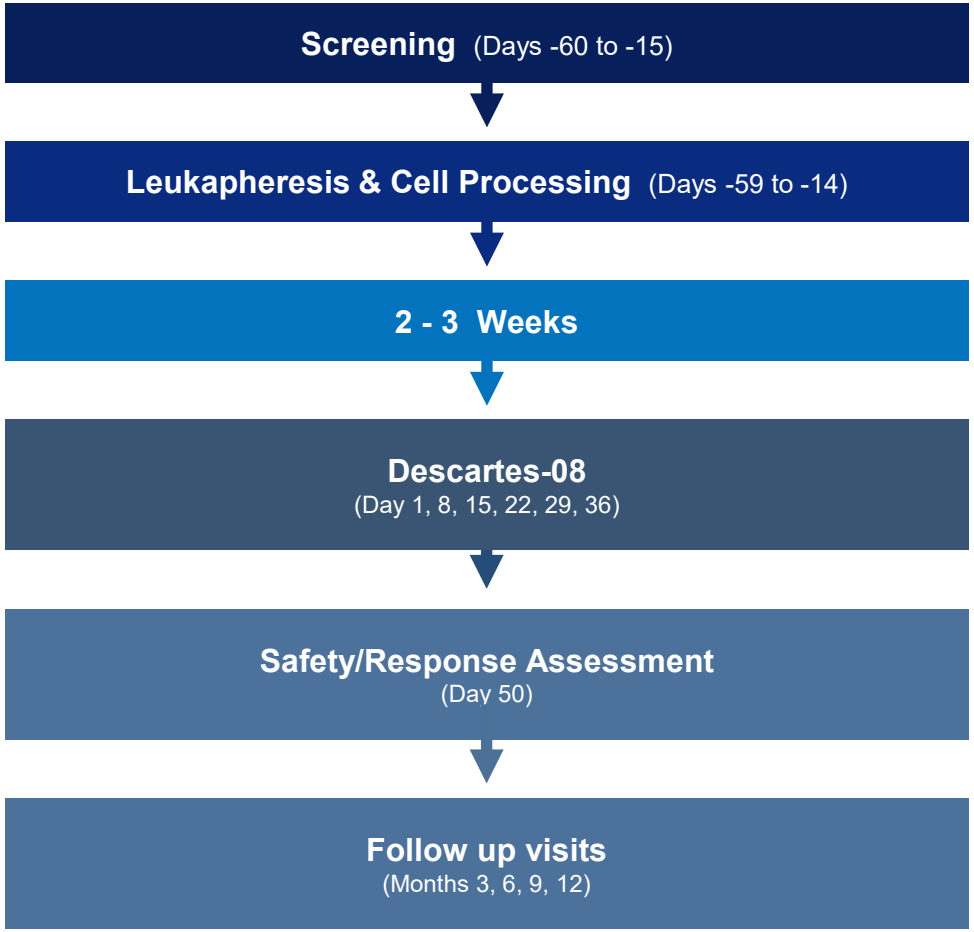
MG ADL, MG Activities of Daily Living
MG PIS, MG Post-intervention Status

# Exploring potential of Descartes-08 in Systemic Lupus Erythematosus (SLE)

**IND CLEARED**

**PHASE 2 STUDY ON TRACK FOR 1H 2024**

- Open-label study in up to 30 adults with moderate to severe multi-refractory SLE and no CNS involvement
- Designed to assess safety, tolerability, and manufacturing feasibility of Descartes-08 in patients with SLE
- Secondary objectives include standard measures of clinical activity in SLE:
  - Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K)
  - Physician Global Assessment (PGA)
  - Systemic Lupus Erythematosus Responder Index (SRI)
  - British Isles Lupus Assessment Group (BILAG)–based Composite Lupus Assessment (BICLA)



# Clinical-stage company pioneering mRNA cell therapies designed to expand the reach of cell therapy to autoimmunity

- Pipeline of mRNA cell therapies designed to be dosed more reliably and safely in an outpatient setting **without lymphodepletion**
- Descartes-08: Potential first-in-class mRNA CAR T-cell (CAR-T) demonstrated **deep and durable clinical responses** in Phase 2a study in patients with myasthenia gravis (MG)
- **Wholly-owned GMP manufacturing** designed to enable rapid optimization of processes in iterative manner

## MULTIPLE ANTICIPATED NEAR-TERM CATALYSTS

### DESCARTES-08

- Phase 2b topline data in MG expected mid-2024
- Initiation of Phase 2 study in SLE expected in 1H 2024
- Initiation of studies in additional autoimmune indications expected in 2H 2024

### DESCARTES-15

- Next-generation mRNA CAR-T candidate
- IND cleared, with first-in-human Phase 1 planning activities underway

## PRO FORMA CASH RESOURCES*

**$118.3M as of end of 2023; expected to fund currently planned operations into 2H26**

Expected to provide for continued clinical development of Descartes-08 in MG through Phase 3 and multiple additional clinical programs

*Reflects the receipt of $40M through two delayed settlement payments previously announced as part of the November 2023 financing, which occurred in January 2024 and February 2024
CAR, Chimeric antigen receptor
SLE, Systemic Lupus Erythematosus

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# Pioneering mRNA Cell Therapy for Autoimmunity