



Pioneering mRNA Cell Therapy for Autoimmunity

October 2024



Forward-Looking Statements



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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) with *deep and durable responses* observed in randomized, double-blind, placebo-controlled Phase 2b trial 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

- EoP2 meeting with FDA to discuss MG Phase 3 plan expected by end of 2024
- Additional Phase 2b MG data expected by end of 2024
- IND filing for Phase 2 pediatric basket trial expected by end of 2024

DESCARTES-15

- Next-generation mRNA CAR-T candidate
- Dosing underway in first-in-human Phase 1 dose escalation trial

PRO FORMA CASH RESOURCES

- **Strong balance sheet with approximately \$213.3 million***
- Expected to support continued clinical development of Descartes-08 in MG through the completion of Phase 3

* Includes approximately \$88.9 million of cash, cash equivalents, and restricted cash as of June 30, 2024, and net proceeds from PIPE financing in July 2024.

GMP, Good manufacturing practices

CAR, Chimeric antigen receptor

EoP2, End of Phase 2

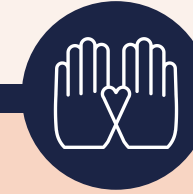
FDA, Food and Drug Administration

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

Wholly-owned pipeline targets autoimmune disease



Asset	Indications	Discovery/Preclinical	Phase 1	Phase 2	Pivotal
Descartes-08 Autologous mRNA CAR-T	Myasthenia Gravis (MG)	[Progress bar spanning Discovery/Preclinical, Phase 1, and Phase 2]			
	Systemic Lupus Erythematosus (SLE)	[Progress bar spanning Discovery/Preclinical and Phase 1]			
	Pediatric Autoimmune Diseases*	[Progress bar spanning Discovery/Preclinical]			
Descartes-15 Autologous mRNA CAR-T	Autoimmune Diseases**	[Progress bar spanning Discovery/Preclinical and Phase 1]			

* IND for pediatric basket trial expected by year-end 2024, includes juvenile SLE, juvenile MG and other conditions.

** Dosing in Phase 1 dose escalation trial in myeloma underway.

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

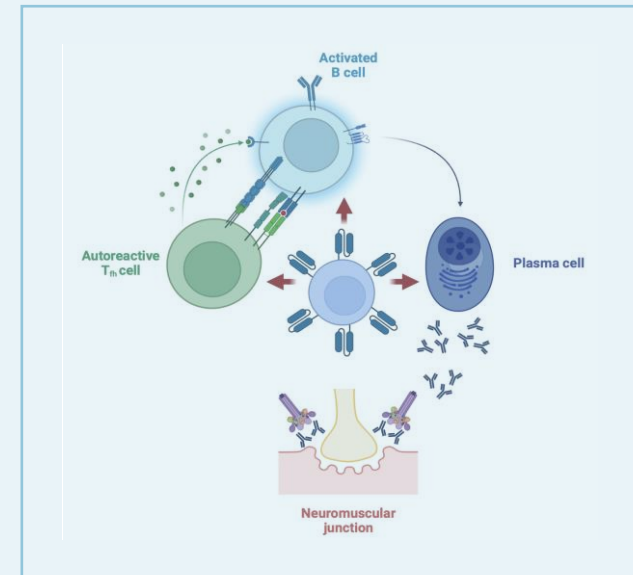


Typical lot processed for infusion within ~3 weeks



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



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



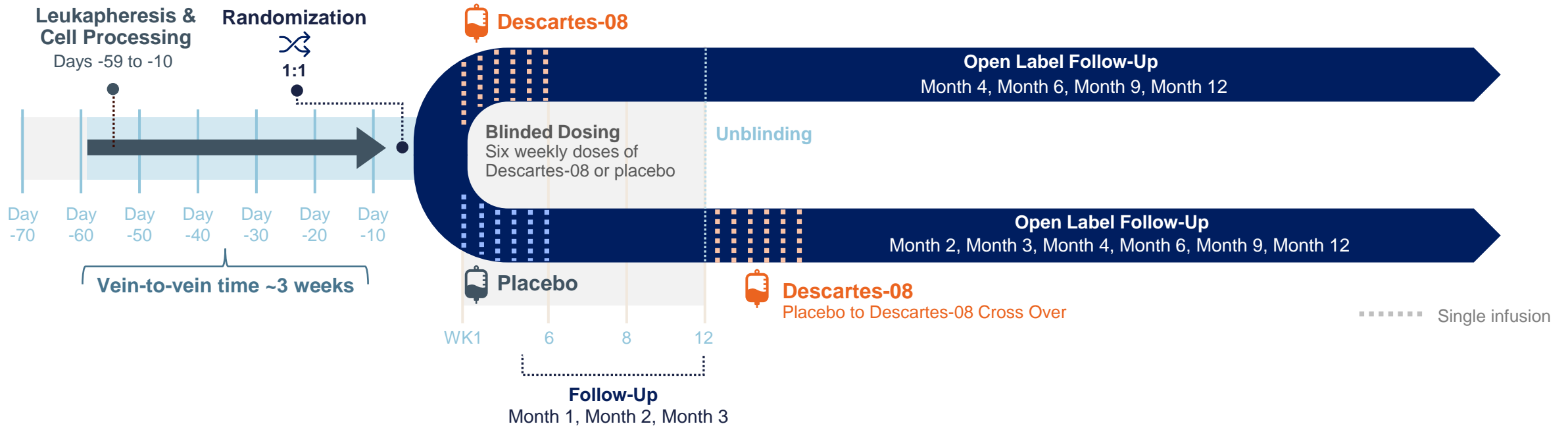
Facial



Current treatments require chronic or frequent administration and have limited durability



Phase 2b trial: double-blind, placebo-controlled clinical trial of Descartes-08 in patients with myasthenia gravis



INCLUSION CRITERIA

- Non-MuSK-MG
- MGFA Class II-IV
- MG-ADL ≥ 6
- Severe disease despite stable doses of immunosuppressants

PRIMARY ENDPOINT

- Proportion of patients with MG Composite improvement of ≥ 5 -points at Month 3, relative to placebo
- Predefined primary efficacy dataset

SECONDARY OBJECTIVES

- Safety and tolerability from predefined safety dataset
- Quantify clinical effect of Descartes-08 over 1 year
- QMG, MG QoL 15R, MG-ADL (change from baseline to Month 3)
- Compare effect of Descartes-08 versus placebo on MG scales (change from baseline to Month 3) in patients who cross over from placebo to Descartes-08

MGFA, Myasthenia Gravis Foundation of America
MG-ADL, Myasthenia Gravis Activities of Daily Living scale

MG QMG, Quantitative MG Scores
MG QoL 15R, MG Quality of Life 15-revised

Descartes-08 in MG Phase 2b Topline Results



Met primary endpoint



Responders observed to have ~3x greater improvements than clinically meaningful*



Deep, durable responses observed in patients treated with Descartes-08



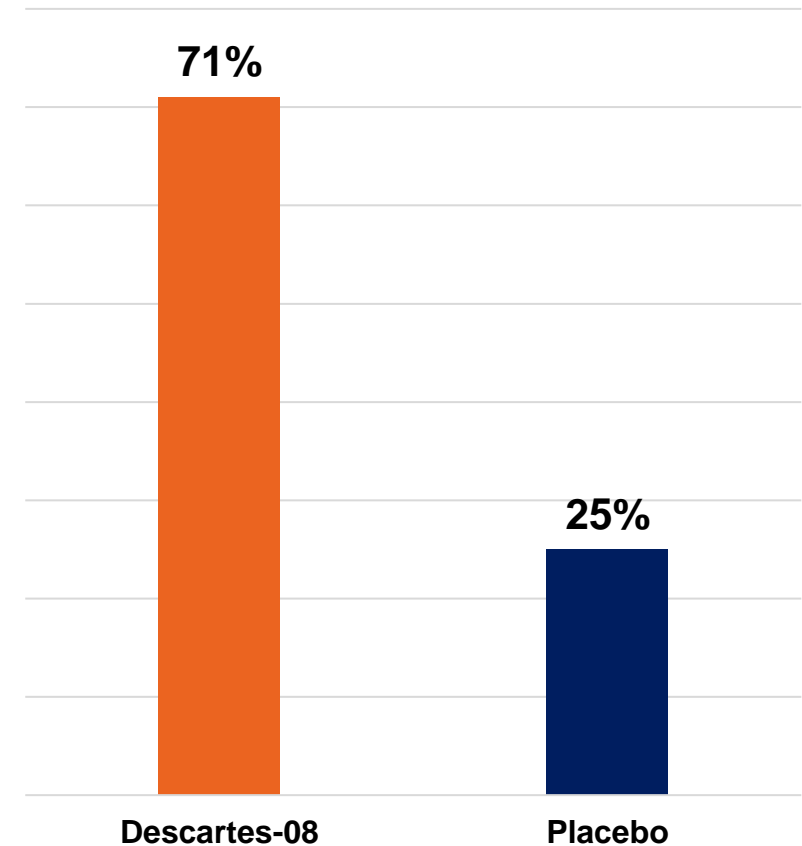
Safety profile continues to support outpatient administration



Data support advancement to Phase 3

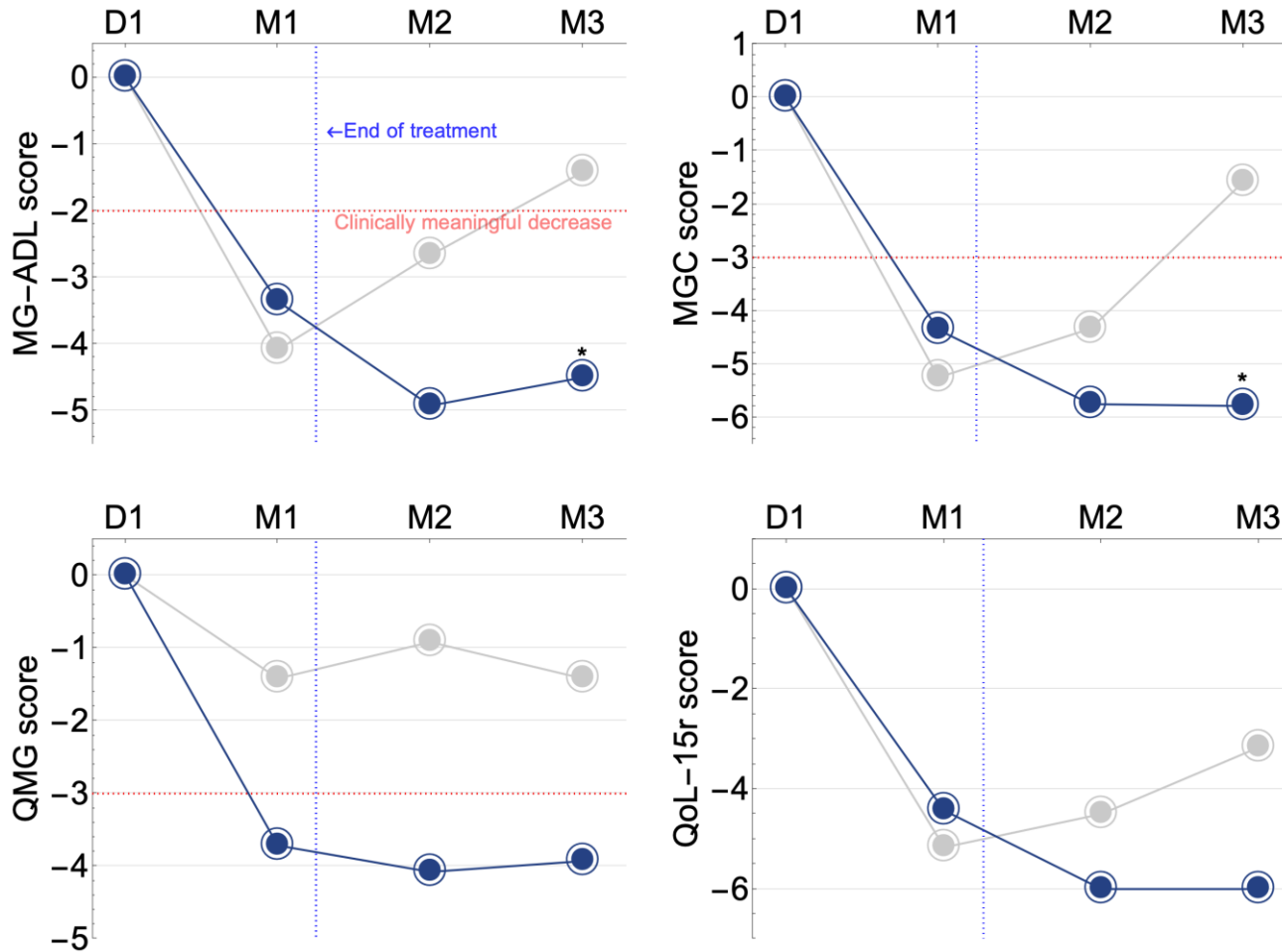
*Clinically meaningful response: three-point reduction in MG Composite score from baseline.

Proportion of MG Composite Responders (≥5-Point Reduction) at Month 3



p-value:0.018

Statistically significant improvements observed in Descartes-08 patients at Month 3 assessment



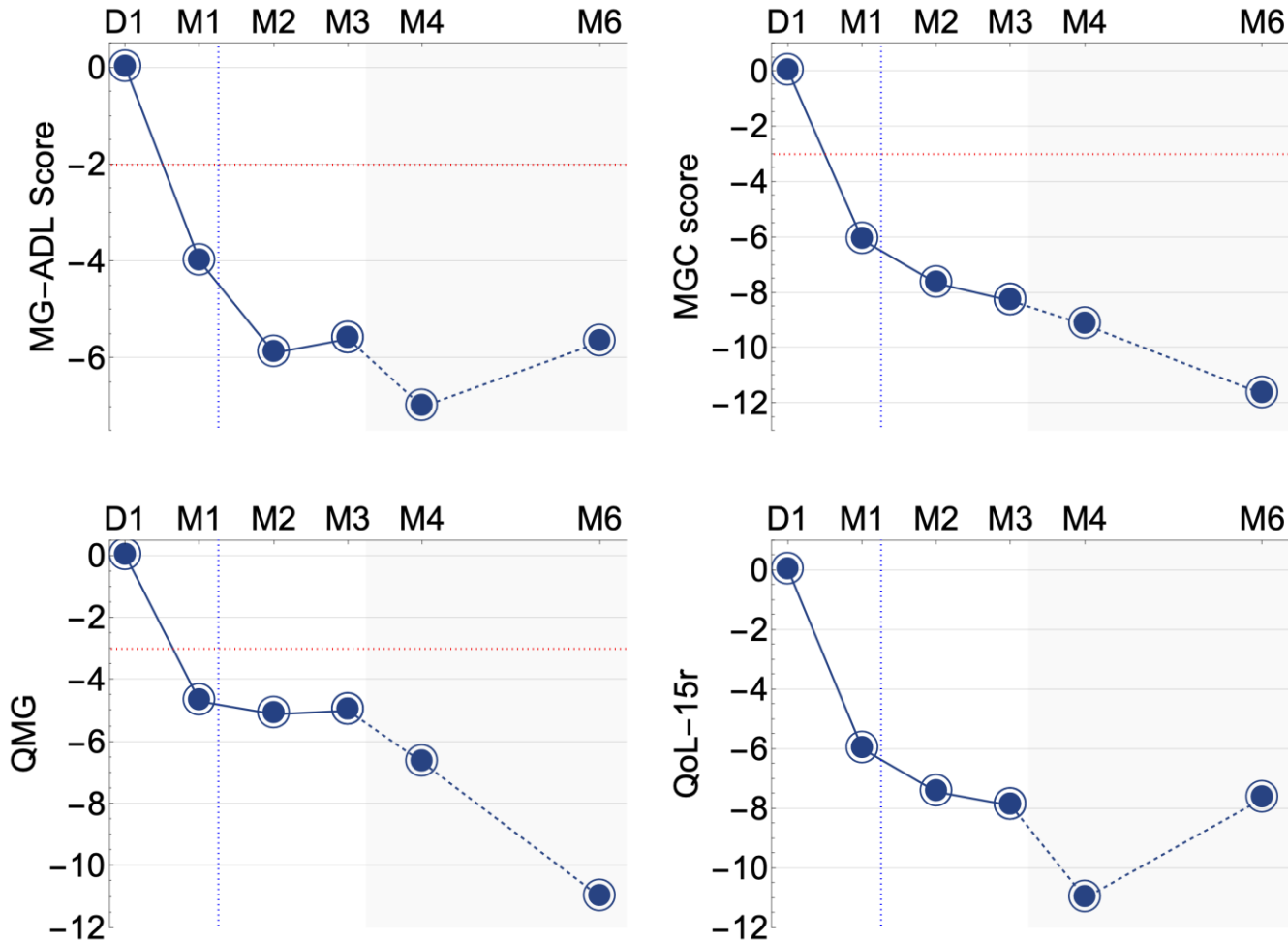
Mean decrease from Baseline in the prespecified primary efficacy population (n=26).
 $p < 0.05$ by Mann-Whitney U test at Month 3 in MGC and MG-ADL | LRP4+, low-density lipoprotein receptor-related protein 4

- **Non-responders (n=4)**

- 1 LRP4+ MG non-responder at Month 3 onward
- 1 additional non-responder at Month 3 onward
- 1 responded during open label follow-up
- 1 has not reached 1st open label follow-up

- **Placebo response generally in line with expectations**

Deep and durable responses observed in Descartes-08 responders through Month 6



- **Results consistent with Phase 2a open-label trial findings**

Mean decrease from Baseline in MGC Responders (participants who achieved a ≥ 5 -point reduction in MGC at Month 3, n=10. Month 4 n=5, Month 6 n=3.

Observed safety results support outpatient administration and in line with Phase 2a observations



	Descartes-08 (n=19)			Placebo (n=17)		
	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3
Headache	6 (32%)	4 (21%)		2 (12%)	3 (18%)	
Chills	7 (37%)	4 (21%)		1 (6%)		
Nausea	2 (11%)	5 (26%)		2 (12%)	2 (12%)	
Fever	6 (32%)	3 (17%)	1 (6%)			
Fatigue	5 (26%)	1 (5%)		1 (6%)		
Myalgia	3 (16%)	3 (16%)		1 (6%)		
Infusion related reaction	1 (5%)	2 (11%)	1 (6%)	1 (6%)		
Muscle weakness	1 (5%)	1 (5%)		1 (6%)		
Arthralgia		1 (5%)		1 (6%)	1 (6%)	
Tachycardia	3 (16%)					
Herpes simplex reactivation	2 (11%)		1 (6%)			
Dysgeusia	3 (16%)					
Diarrhea	1 (5%)				1 (6%)	
Sweating	1 (5%)			1 (6%)		
Limb edema	1 (5%)	1 (5%)				
Flushing	2 (11%)					
Dyspnea	1 (5%)	1 (5%)				
Insomnia	2 (11%)					
Vomiting	2 (11%)					
Tremor	2 (11%)					

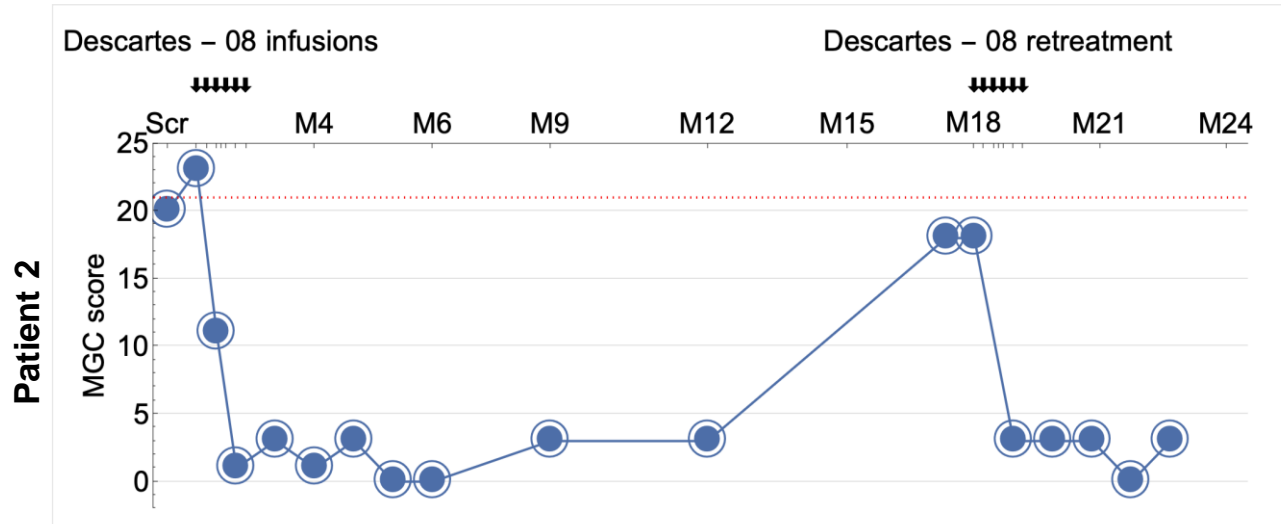
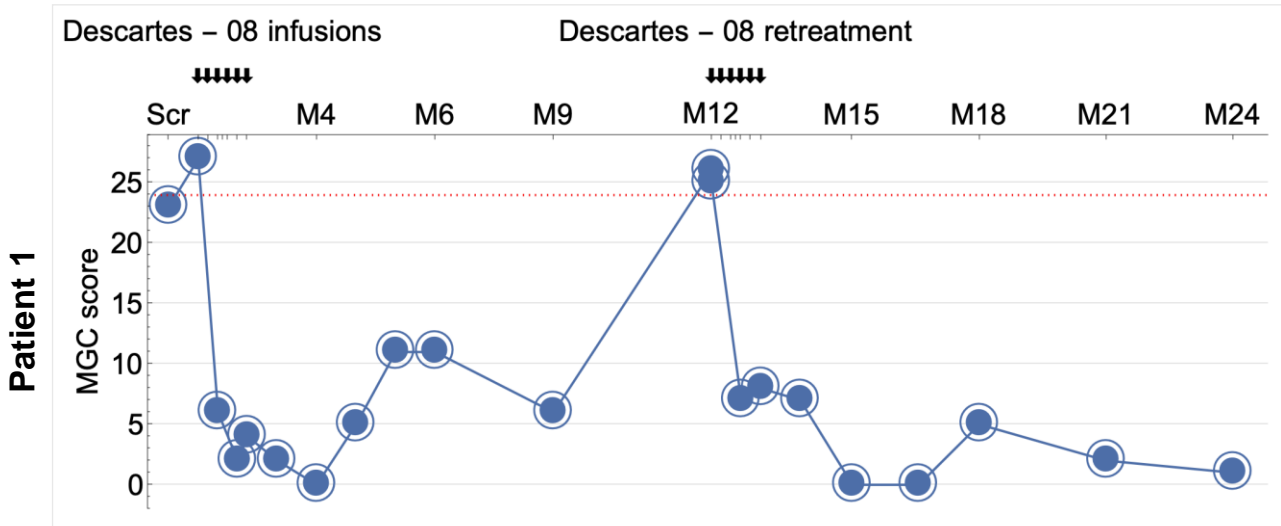
- **No cytokine release syndrome**
- **No neurotoxicity or ICANS**
- **Most AEs were transient or mild**

Safety dataset comprises all subjects who received at least one dose of Descartes-08 (n=19) or placebo (n=17).

All Grade 1–2 adverse events deemed possibly, probably or definitely related to the study drug with a cumulative incidence $\geq 10\%$ 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 update: Descartes-08 retreatment led to sustained clinically meaningful responses



- Retreated patients experienced rapid improvement in clinical scores and maintained minimal symptom expression for up to one year after receiving second treatment cycle

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

Planned next steps for Descartes-08 in MG



EoP2 meeting with FDA
expected **by year-end**



Initiate Phase 3
clinical trial

**RMAT designation to support efficient development
plan in collaboration with FDA**

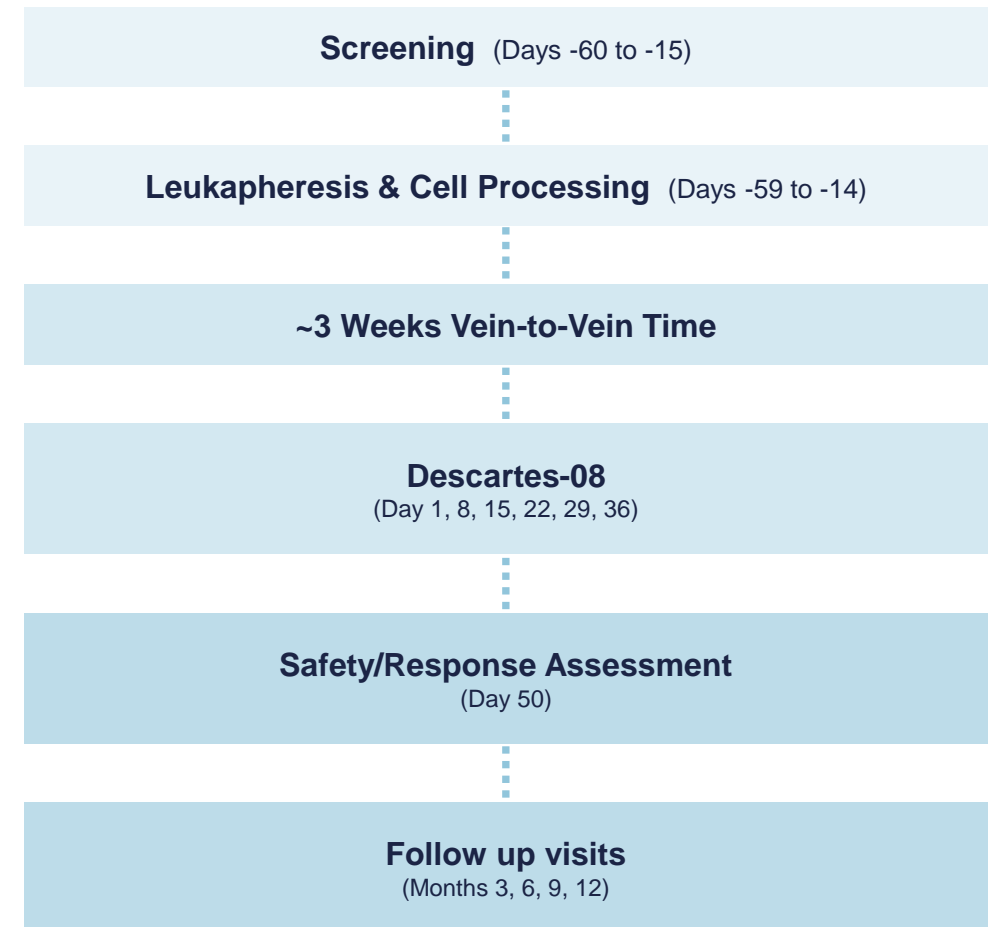
Exploring potential of Descartes-08 in Systemic Lupus Erythematosus (SLE)

IND CLEARED, FIRST PATIENT DOSED IN 1H 2024

PHASE 2 TRIAL ONGOING

- Open-label trial 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)

IND, Investigational New Drug Application



Intend to leverage the potential of Descartes-08 across multiple clinical programs



MG

- EoP2 FDA meeting expected by end of 2024
- Potential initiation of Phase 3 trial following FDA meeting

1

SLE

- Open-label Phase 2 trial
- First patient dosed

2

Potential New Indications

- Pediatric autoimmune diseases
- Neurological and rheumatological autoimmune diseases

3

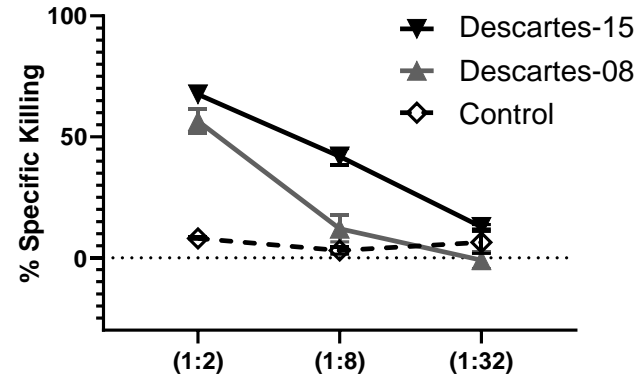
Leveraging clinical proof-of-concept of Descartes-08 in MG to expand autoimmune pipeline

Descartes-15, a next generation anti-BCMA mRNA CAR-T with >10x potency observed in preclinical studies

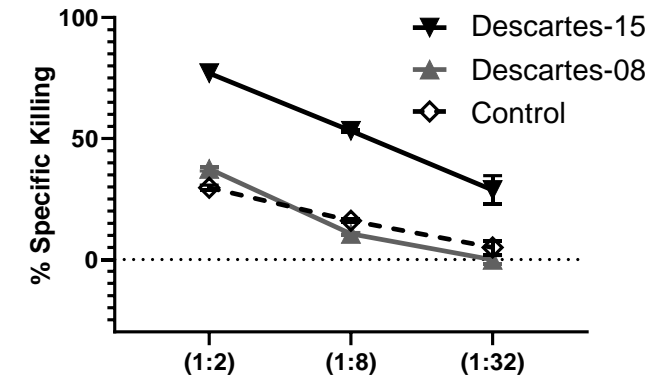
Descartes-15 is an anti-BCMA mRNA CAR-T with potential disruptive features:

- Engineered for maximum potency and CAR stability, even in the presence of target-driven suppression of CAR
- Clinical strategy expected to leverage safety and clinical activity data from Descartes-08

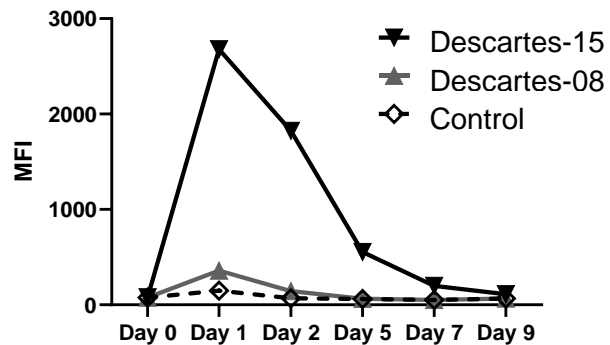
Potent killing (single target exposure)



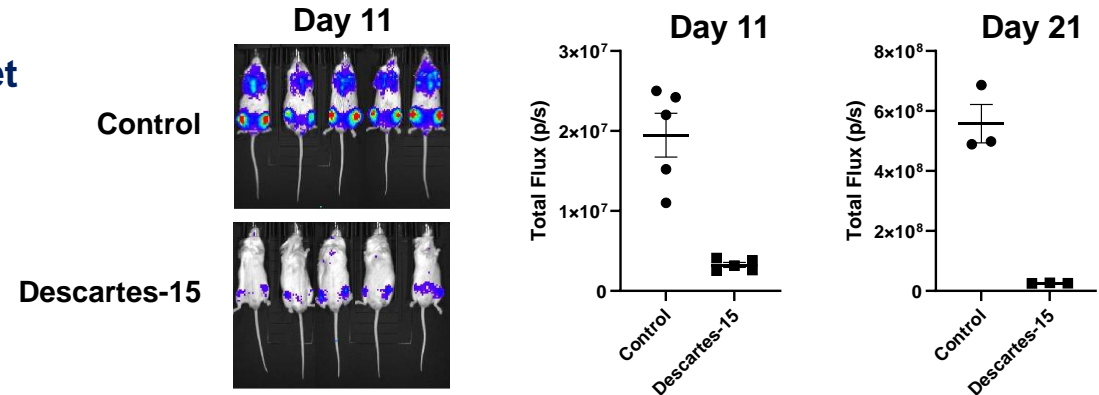
Persistent killing (multiple exposures)



Superior CAR expression



Efficient killing of BCMA+ target cells*



*MM1-S disseminated myeloma model in NSG mice infused with either control T-cells or Descartes-15.

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

Maturing pipeline offers potential for multiple catalysts



Descartes-08 in MG

EoP2 meeting with FDA expected by **end of 2024**; potential initiation of Phase 3 trial to follow

Descartes-08 in SLE

Phase 2 open-label trial ongoing, with first patient dosed in **1H 2024**

Descartes-08 Pediatric Basket Trial

Plan to file IND for Phase 2 pediatric basket trial in neurological and rheumatological autoimmune indications in **2H 2024**

Descartes-15

Phase 1 first-in-human trial ongoing, with first patient dosed in **2H 2024**

**STRONG FINANCIAL
POSITION:**

**Expected to
Support Pipeline
Through Key
Milestones**

\$213.3M*

In cash, cash equivalents and restricted cash

**<60 FULL TIME
EMPLOYEES**

Based in Gaithersburg, MD
and Frederick, MD

23.9M

Basic shares outstanding as of 9/25/24

33.3M

Fully diluted shares outstanding**

*Includes cash, cash equivalents, and restricted cash of approximately \$88.9 million as of June 30, 2024, plus net proceeds from the \$130.0 million PIPE financing announced in July 2024.

** Further includes Series A Non-Voting Convertible Preferred Stock and Series B Non-Voting Convertible Preferred Stock that remain subject to beneficial ownership limitations that are convertible into shares of common stock and includes outstanding options, RSUs and warrants.

PIPE, Private investment in public equity

Key Takeaways



Pioneering mRNA Cell Therapies

Pipeline designed to expand the reach of cell therapy to autoimmunity



Maturing Pipeline with Expected Near-term Catalysts

Clinically differentiated platform with EoP2 meeting for Descartes-08 in MG planned by year-end



Experienced Leadership Team

Focused on disciplined investment and creating value for stockholders and patients



Strong Balance Sheet to Support Maturing Pipeline

Current pro forma cash expected to support Descartes-08 through the completion of Phase 3

Our team | Management



Carsten Brunn, PhD
PRESIDENT AND CEO



Blaine Davis, PhD
CHIEF FINANCIAL OFFICER



Metin Kurtoğlu, MD, PhD
CHIEF TECHNOLOGY OFFICER



Miloš Miljković, MD
CHIEF MEDICAL OFFICER



Chris Jewell, PhD
CHIEF SCIENTIFIC OFFICER



Jessica Keliher
CHIEF PEOPLE OFFICER



Emily English, PhD
SENIOR VICE PRESIDENT,
HEAD OF MANUFACTURING OPERATIONS

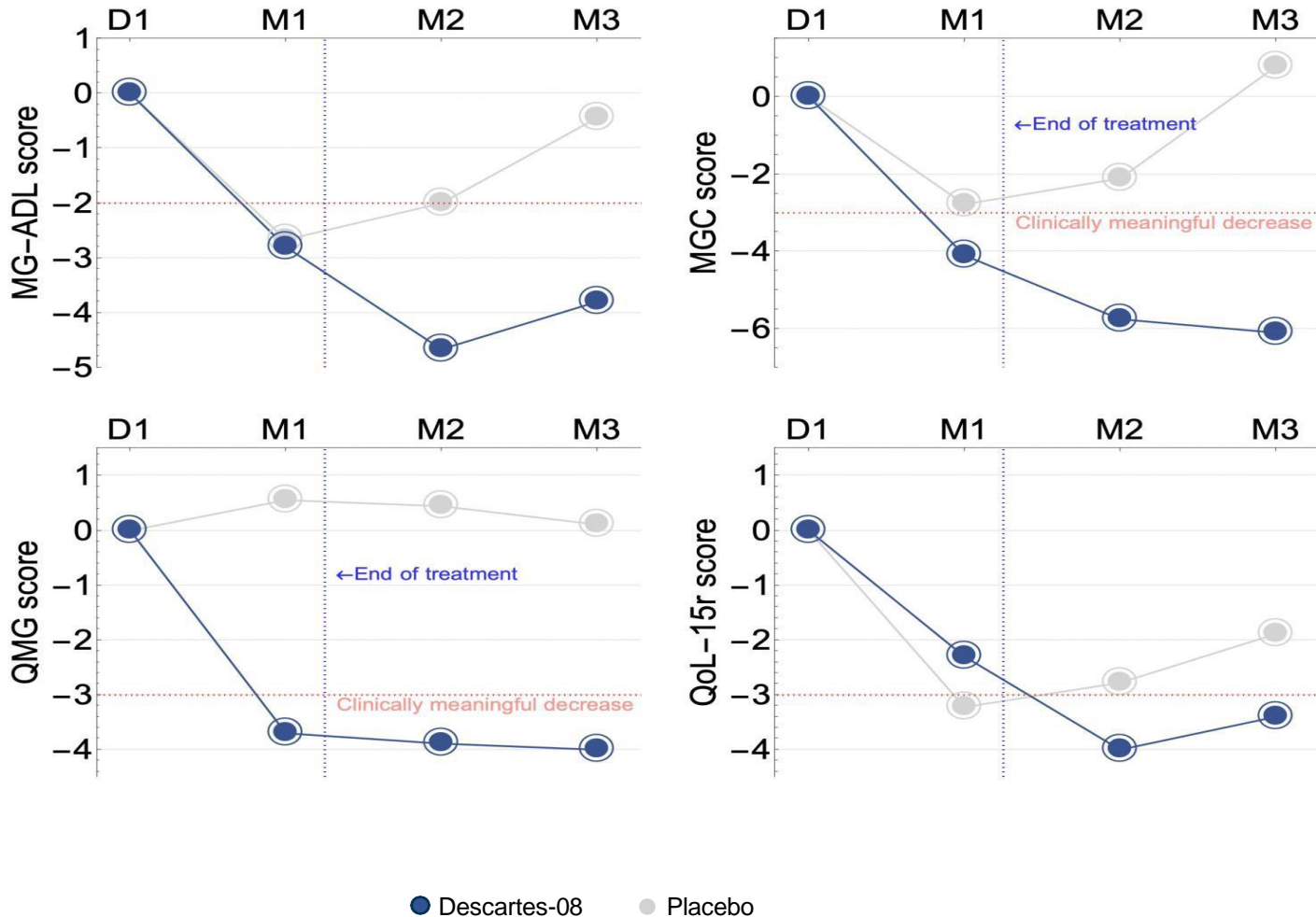


Matthew Bartholomae
GENERAL COUNSEL, SECRETARY



Appendix

Descartes-08 demonstrated improvement across important measures of disease activity in AChR Ab⁺ MG subjects

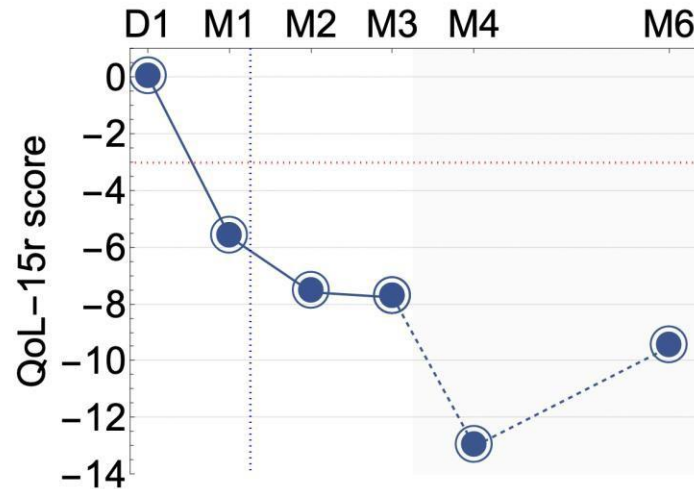
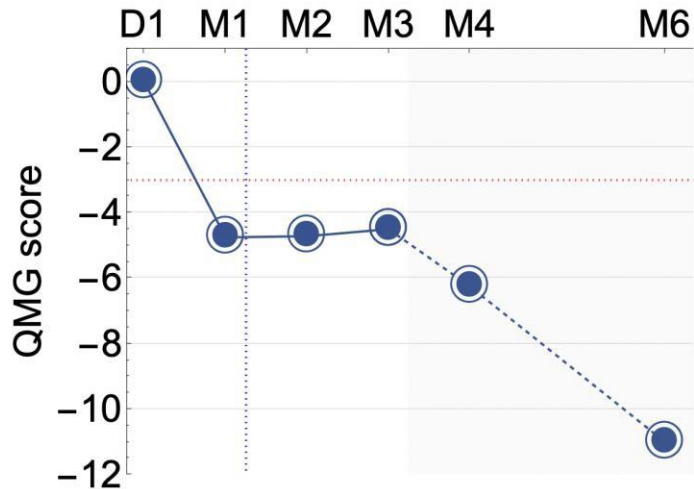
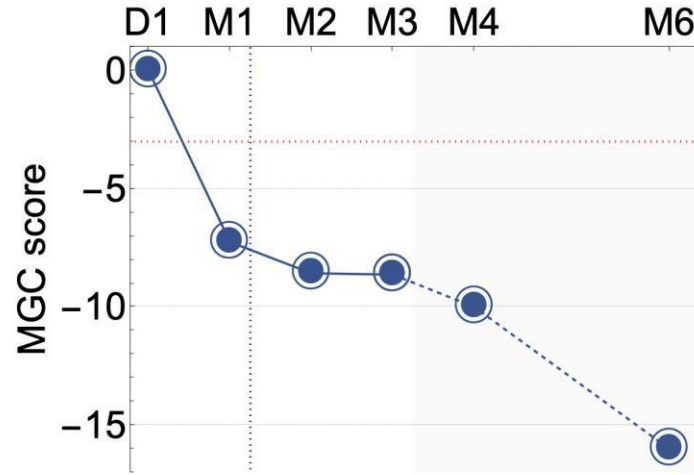
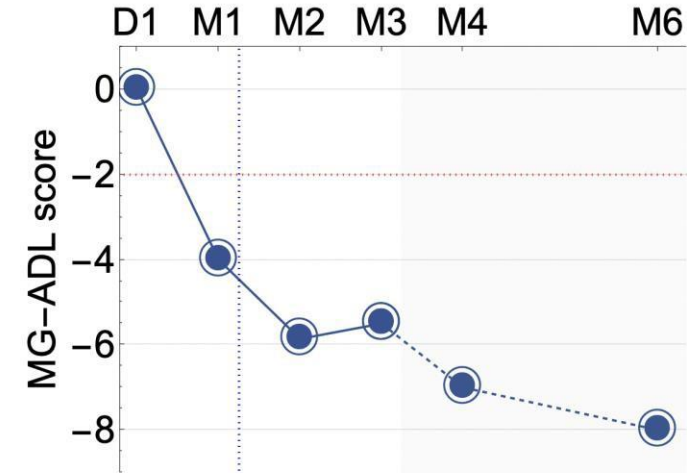


Improvements from baseline in participants with AChR Ab⁺ MG receiving Descartes-08 (n=10) versus placebo (n=9).

* p<0.05, ** p<0.01 by Mann Whitney U test.

- Statistically significant improvement in Descartes-08 compared to placebo at Month 3 seen across MGC (p=0.002), MG-ADL (p=0.012) and QMG (p=0.029).
- Placebo responses in AChR Ab⁺ subjects were consistent with Phase 2/3 published literature.

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



- Deepest responses seen in participants with no prior exposure to complement or FcRn inhibitors.

Mean change from baseline in in patients with no prior biologics (Months 1-3 n=8, Month 4 n=4, Month 6 n=2).

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

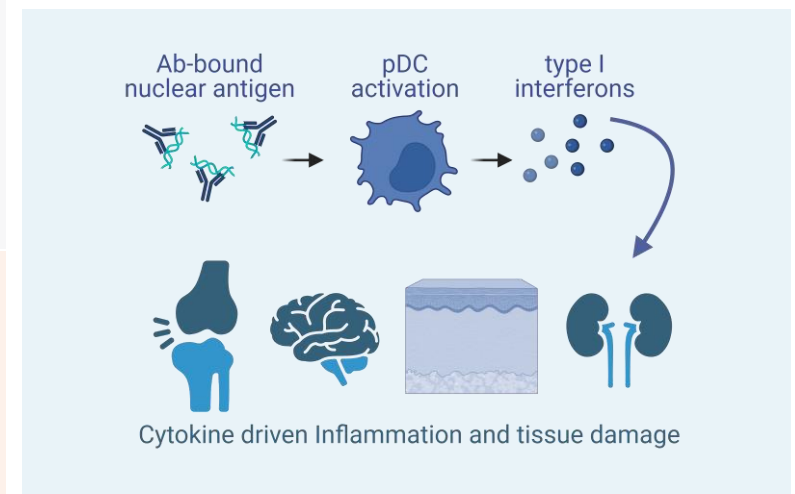
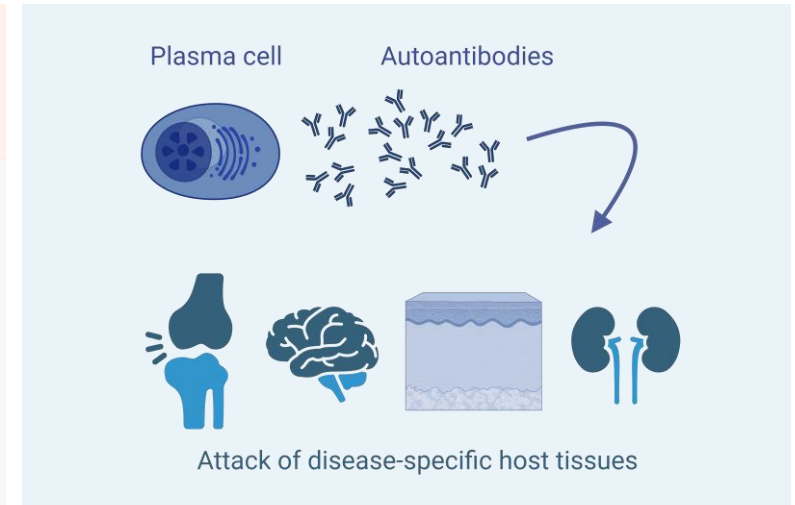
- PCs, plasmablasts and proliferating B cells targeted by Descartes-08 represent a tiny fraction of B cells
- These cells are entirely responsible for secreting pathogenic autoantibodies
- During autoimmunity, autoantibodies attack host tissue and drive inflammation

PLASMACYTOID DENDRITIC CELLS (pDCs)

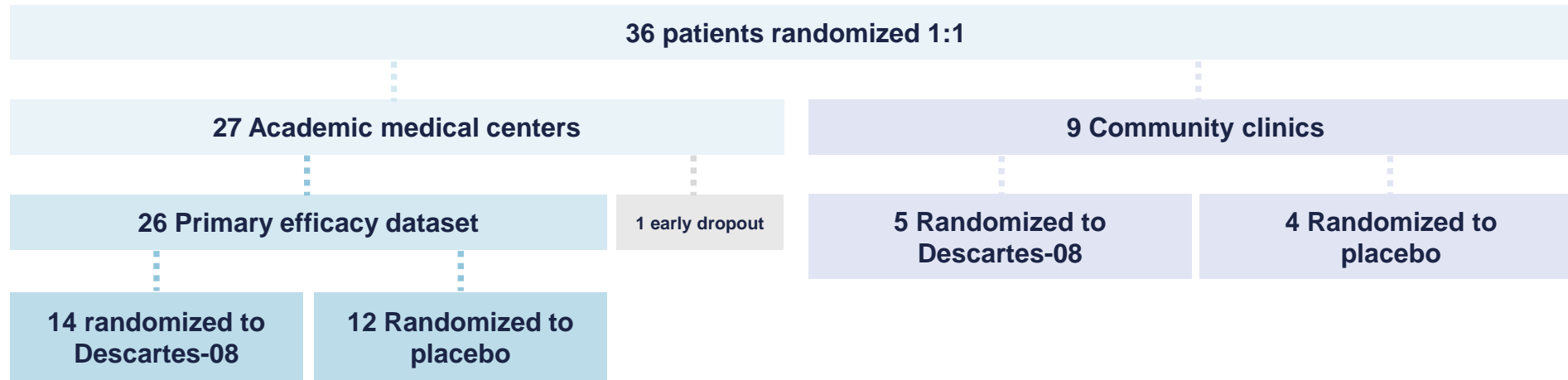
- pDCs, which Descartes-08 is designed to target, are a rare subset of antigen-presenting cells
- These cells secrete high levels of cytokines (i.e., type I interferons) that cause inflammation and tissue damage during many human autoimmune diseases
- pDCs are increased in patients with autoimmunity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



Phase 2b: 14 patients received Descartes-08 and 12 patients received placebo in the pre-specified primary efficacy dataset

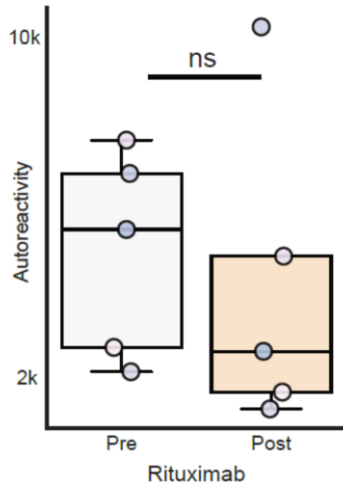


- Consistent with current IND, primary efficacy dataset includes modified ITT population enrolled at academic medical centers qualified for MG Composite assessment with at least one post-baseline follow-up.
- Safety dataset includes all participants at academic medical centers and community clinics who received at least one dose of Descartes-08 or placebo.

ITT, Intention to Treat

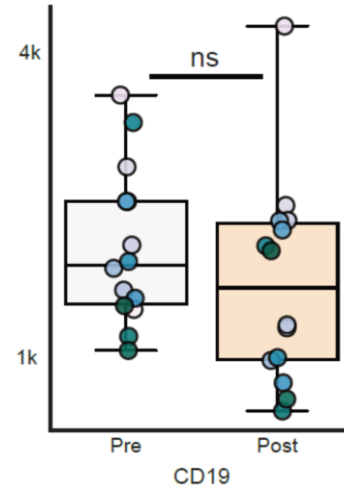
Clinical analyses of antigen-depletion therapies show BCMA-targeting with CAR-T may enable precision reset of autoantibody-producing PCs

Rituximab
(CD20+ cell depletion)



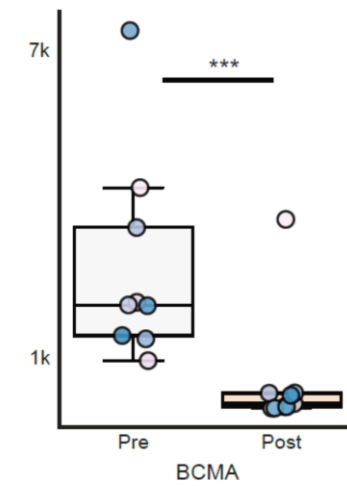
Minimal change in autoreactivity

Anti-CD19 CAR-T
(CD19+ cell depletion)



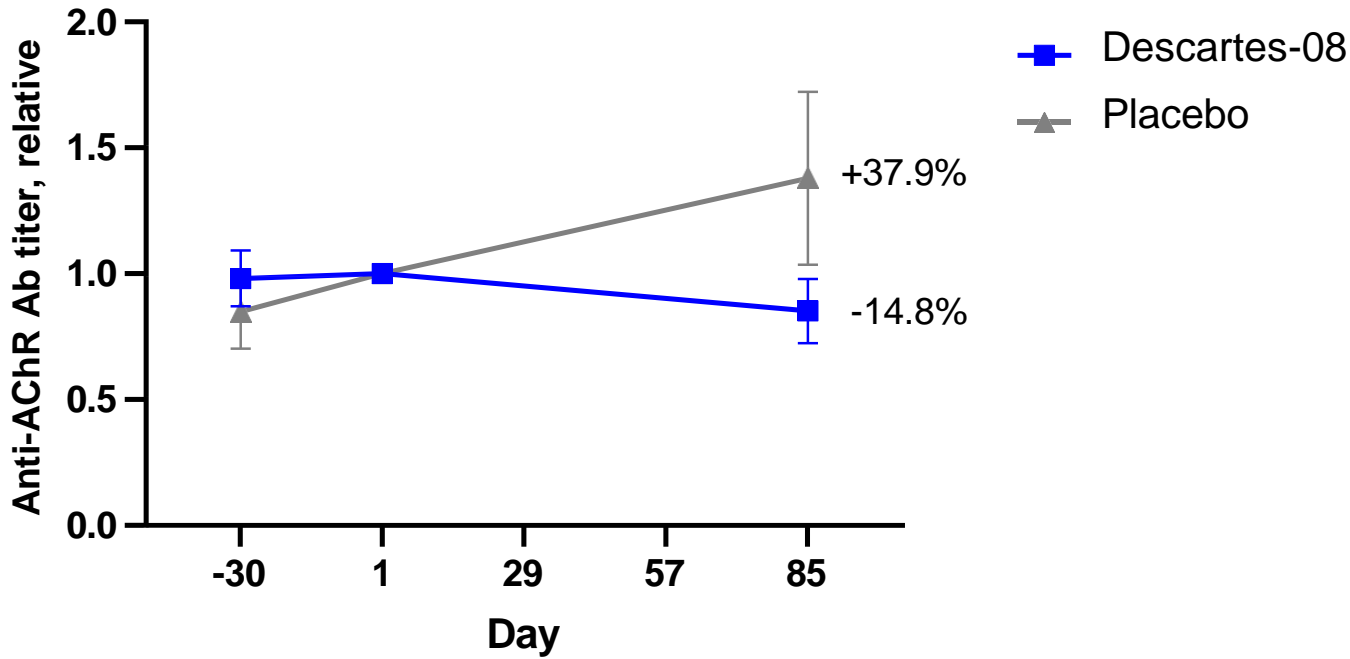
Minimal change in autoreactivity

Anti-BCMA CAR-T
(BCMA+ cell depletion)

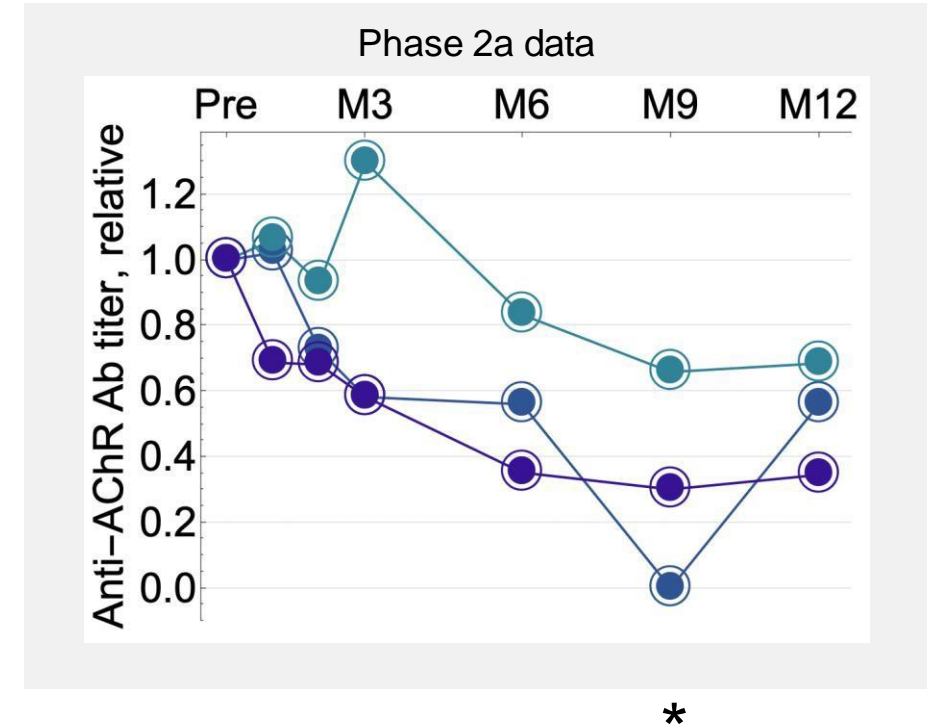


Nearly full reset of autoreactivity

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



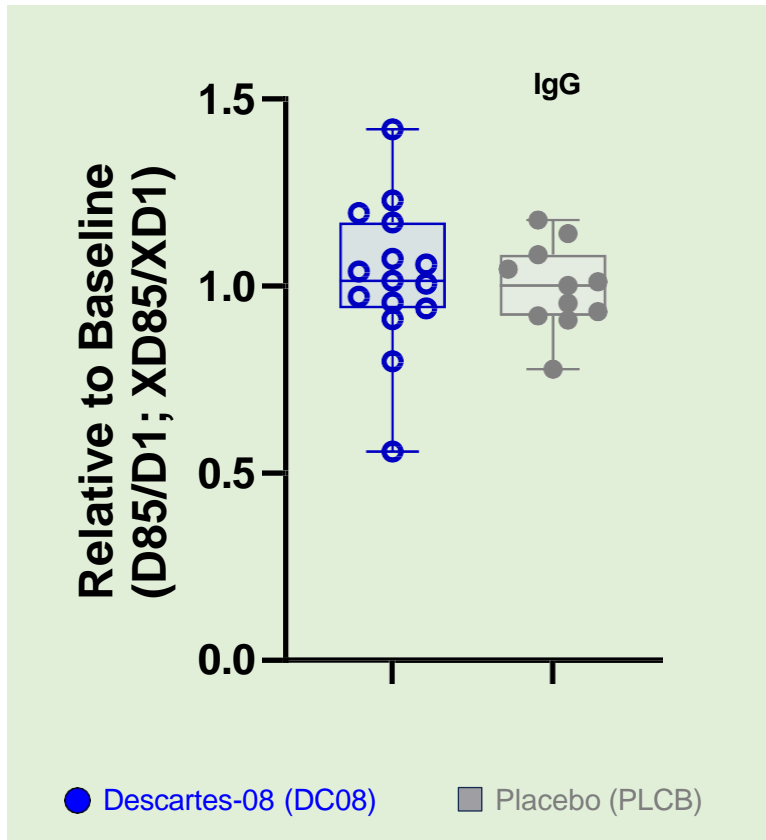
Average reduction (\pm SEM) in AChR antibody in participants with baseline levels above LLOQ randomized to Descartes-08 (n=12) vs. Placebo (n=9)



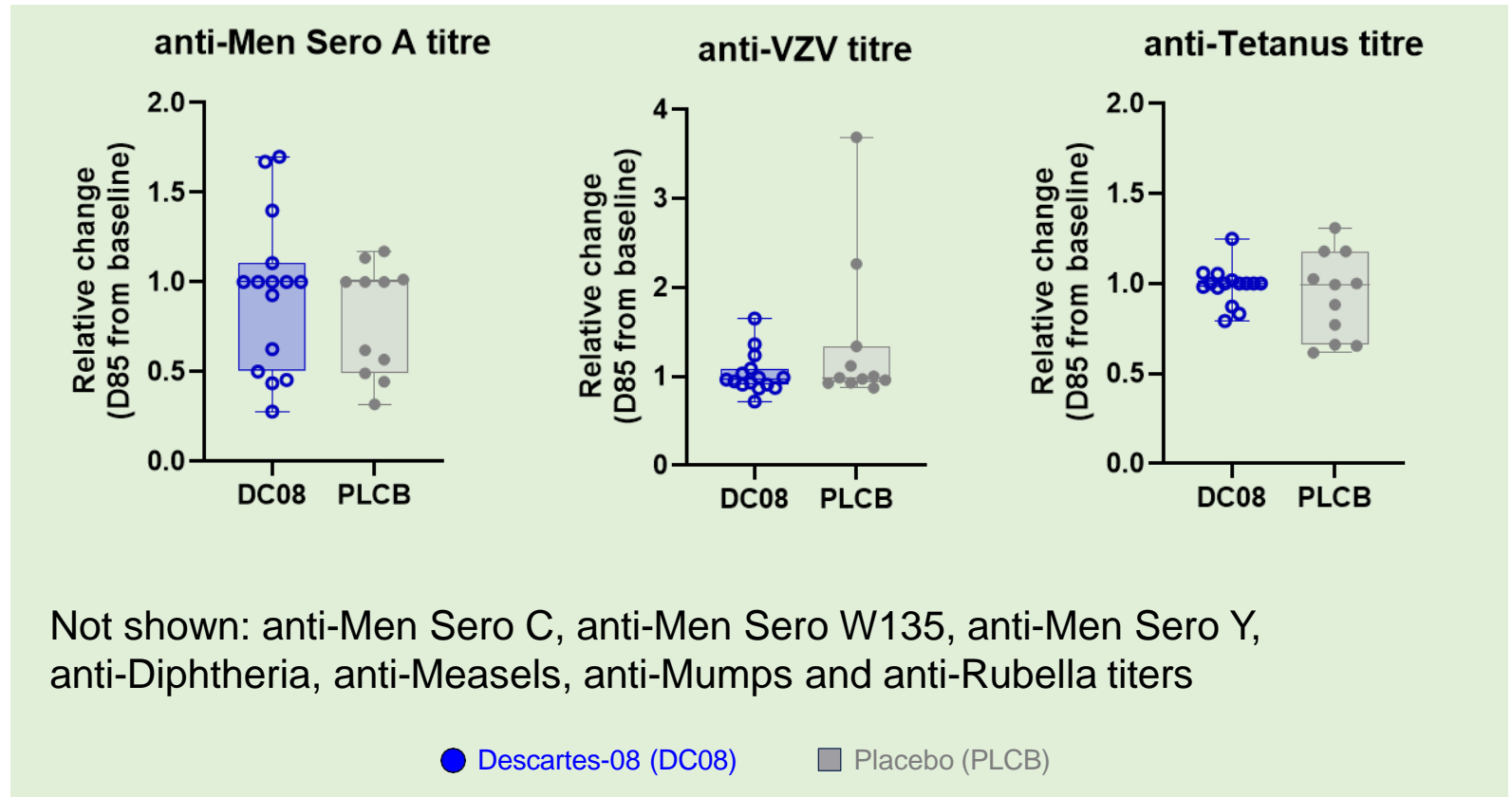
Individual Anti-AChR antibody titers in all participants receiving six once-weekly infusions in the Phase 2a trial with detectable baseline levels (n=3)

Descartes-08 does not deplete broader antibody repertoire or decrease vaccine titers for common viruses

No significant change in Ig at primary end point (D85) vs. Day 1¹



No significant change in common vaccine titers at primary end point (Day 85) relative to Day 1²



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

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