Poster 1130

Efficacy and safety of autologous BCMA-directed mRNA CAR T-cell therapy in generalized myasthenia gravis: Results from a phase 2b randomized placebo-controlled trial

2025 Neuromuscular Study Group Annual Scientific Meeting, September 26, 2025, Stresa, Italy

T. Vu[1], H.D. Tekce[2], M. Rivner[3], S. Shroff[4], T. Ragole[5], B. Myers[6], M. Pasnoor[7], G. Small[8], K. Gwathmey[9], C. Karam[10], M. Vullaganti[11], A. Peltier[12], G. Sahagian[13], M.H. Feinberg[14], A. Slansky[15], C. Barnett-Tapia[16], M. Badruddoja[17], Z. Siddiqi[18], H. Kamboh[19], M. Kurtoglu[19], C.M. Jewell[19], M.D. Miljkovic[19], T. Mozaffar[20], J.F. Howard[21] for the MG-001 Study Team

[1]University of South Florida, Tampa, FL, USA; [2]Istanbul University, Istanbul, Turkey; [3]Augusta University, Augusta, GA, USA; [4]Houston Methodist Hospital, Houston, TX, USA; [5]University of Colorado, Aurora, CO, USA; [6]Dent Neurologic Institute, Amherst, NY, USA; [7]University of Kansas Medical Center, Kansas City, KS, USA; [8]Allegheny General Hospital, Pittsburgh, PA, USA; [9]Virginia Commonwealth University, Richmond, VA, USA; [10]University of Pennsylvania, Philadelphia, PA, USA; [11]Tufts University, Boston, MA, USA; [12]Vanderbilt University, Nashville, TN, USA; [13]Profound Research, San Diego, CA, USA; [14]SFM Research, Boca Raton, FL, USA; [15]Neurology Associates, P.A., Maitland, FL, USA; [16]Toronto General Hospital, Toronto, Canada; [17]Center for Neurosciences, Tucson, AZ, USA; [18]University of Alberta, Edmonton, Canada; [19]Cartesian Therapeutics, Frederick, MD, USA; [20]University of California, Irvine, CA, USA; [21]University of North Carolina, Chapel Hill, NC, USA.

Key takeaways

A single course of six once-weekly infusions of Descartes-08 administered in the outpatient setting resulted in **robust and durable clinical responses** through 12 months

Descartes-08 was well tolerated, with no reported cases of cytokine release syndrome, neurotoxicity, immune suppression, or clinically significant cytopenias

The pivotal **phase 3 AURORA trial (NCT06799247) is currently enrolling** to further evaluate the safety and efficacy of Descartes-08 in generalized myasthenia gravis (gMG)

Introduction

Myasthenia gravis (MG) is an autoimmune condition characterized by chronic weakness and muscle fatigue.[1,2]

MG is driven by the secretion of autoantibodies from pathogenic B-cell maturation antigen (BCMA)-expressing plasma cells,[3-5] which cause tissue destruction and reduce the functionality of defined antigens at the neuromuscular junction, including acetylcholine receptors (AChR).[2,6]

Modulation of targets upstream of autoantibody production, such as pathogenic BCMA-expressing plasma cells, has the potential to improve therapeutic durability and tolerability for patients with MG compared with existing therapies that broadly suppress the immune system.

Descartes-08 is an autologous, BCMA-targeted, chimeric antigen receptor (CAR) T-cell product administered in the outpatient setting.[5]

In a phase 1b/2a open-label study in patients with gMG, a single course of six once-weekly infusions of Descartes-08 resulted in robust and durable clinical responses through 12 months of follow-up with a favorable safety profile.[5]

Objective

Assess the efficacy of Descartes-08 versus placebo in adults with gMG using the MG Composite (MGC) score at Month 3.

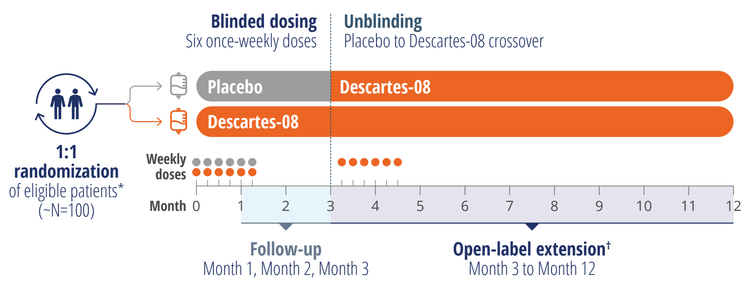
Methods

Study design

A phase 2b, double-blind, placebo-controlled trial of Descartes-08 in adults with gMG.

Patients eligible for inclusion were randomized 1:1 to receive either six once-weekly intravenous infusions of Descartes-08 or placebo with a 12-month follow-up period post infusion (Figure 1).

Figure 1. Study design



*Patients underwent leukopheresis for Descartes-08 manufacturing purposes ahead of randomization. Patients eligible for inclusion were those with MG-ADL score ≥6, MGFA Class II–IV, and non-MuSK+ gMG. Permitted concomitant medications were pyridostigmine, corticosteroids (≤40 mg prednisone daily or equivalent), azathioprine, mycophenolate mofetil, and complement inhibitors, provided a stable dose at least 8 weeks prior to first infusion. †During open-label extension, follow-up for patients randomized to the placebo to Descartes-08 crossover treatment cohort occurred at Months 3, 4, 6, 9 and 12 post infusion; follow-up for those randomized to the Descartes-08 cohort occurred at Months 4, 6, 9, and 12. gMG, generalized myasthenia gravis; MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK+, muscle-specific tyrosine kinase antibody positive.

Study endpoints

Primary endpoint:

The proportion of patients achieving a ≥5-point decrease in MGC at Month 3 compared with baseline.

Secondary endpoints:

Safety and tolerability of Descartes-08 in patients with gMG.

Mean change from baseline in MGC and MG-Activities of Daily Living (MG-ADL) scores at each post infusion visit.

Statistical analyses

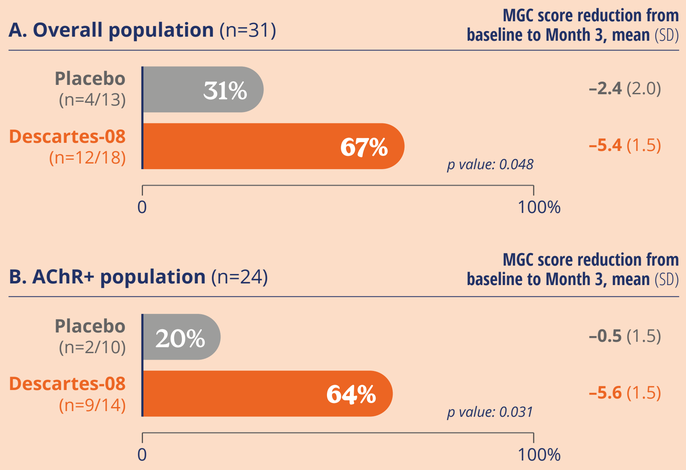
Analyses were performed on the overall patient population, which comprised per-protocol and modified intention-to-treat patients (those enrolled at academic centers with at least one follow-up).

A pre-specified subgroup analysis was performed to assess the efficacy and durability of Descartes-08 in patients positive for autoantibodies against AChR (AChR+).

Two independent samples testing for equality of proportions was used for the primary endpoint; Mann–Whitney U test and descriptive statistics were used for the secondary endpoints.

Efficacy

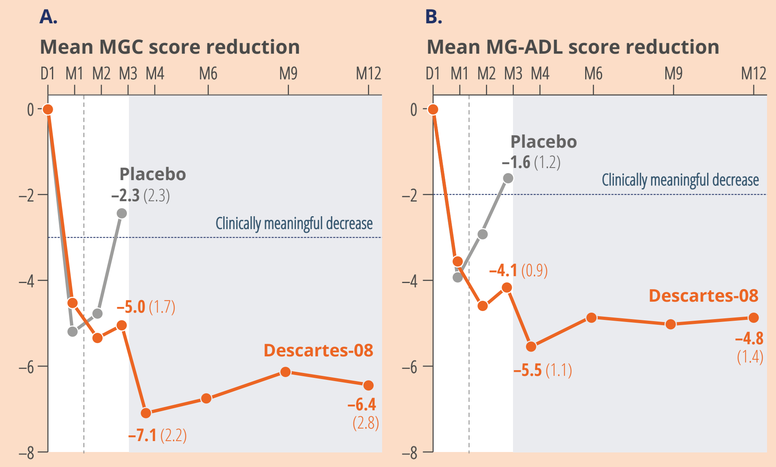
Figure 2. The proportion of MGC score responders (≥5-point score reduction) was **significantly higher in the Descartes-08 cohort** versus placebo at Month 3 in both the overall (A) and AChR+ (B) populations



Per-protocol population . AChR+, positive for autoantibodies against the acetylcholine receptor; MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGC, Myasthenia Gravis Composite; SD, standard deviation.

The mean reduction in MG-ADL score at Month 3 was **higher for the Descartes-08 treatment cohort** versus placebo for both the overall (–4.0 versus –1.7) and AChR+ (–3.4 versus –0.9) patient populations.

Figure 3. Mean reduction in MGC (A) and MG-ADL (B) scores was greater with Descartes-08 versus placebo at Month 3, with further deepening at Month 4, which was maintained through Month 12



mITT population: Descartes-08, n=15 D1 to M3, and n=12 M4 to M12 (three patients lost to follow-up); placebo, n=11 D1 to M3. Dashed line shows end of infusion; shaded area represents open-label follow-up period. Clinically meaningful decrease was defined as a ≥2-point reduction in MG-ADL score. Minimum symptom expression was defined as an MG-ADL score of 0 or 1. D, day; M, month; MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGC, Myasthenia Gravis Composite; mITT, modified intention-to-treat.

83% of participants treated with Descartes-08 reaching Month 12 maintained **clinically meaningful response.**

33% of patients achieved **minimum symptom expression** at Month 6, which was sustained through Month 12.

Safety

Descartes-08 demonstrated a well tolerated safety profile.

Table 1. The most commonly observed treatment-emergent adverse events through Month 3 for the Descartes-08 treatment cohort were **chills, headache, fever,** and **nausea,** which typically resolved 24 hours post infusion

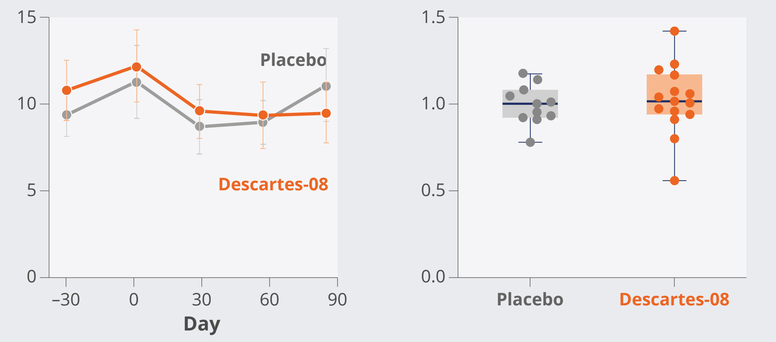
	Placebo (n=16)		Descartes-08 (n=20)		
AE, % (n)	Grade 1	Grade 2	Grade 1	Grade 2	Grade 3
Chills			40 (8)	20 (4)	
Headache	13 (2)	19 (3)	35 (7)	20 (4)	
Fever			35 (7)	20 (4)	5 (1)
Nausea	6 (1)	13 (2)	15 (3)	30 (6)	
Myalgia			20 (4)	10 (2)	
Fatigue	6 (1)		20 (4)	5 (1)	
Infusion-related reaction	6 (1)		5 (1)	10 (2)	5 (1)
Tachycardia			15 (3)		
Dysgeusia			15 (3)		
Vomiting			10 (2)	5 (1)	

AEs with a cumulative incidence of ≥15%. Total AEs reported through Month 3 for placebo-treated patients and through Month 12 for Descartes-08-treated patients. Safety dataset comprises all subjects who received at least one dose of Descartes-08 or placebo. AE, adverse event.

There were **no reports** of cytokine release syndrome or immune effector cell–associated neurotoxicity syndrome.

There were **no AEs reported after Month 3** post infusion.

Figure 4. There were **no observed changes** in circulating CD19⁺ B cells up to 90 days post infusion (A) or in IgG levels at Day 85 versus Day 1 (B)



For panel A, data at each time point represent mean±SEM for all patients (n=35). For panel B, data are individual values, median, range and IQR (n=26). D, day; IQR, interquartile range; SEM, standard error of the mean.

At Month 3, there were **no differences in vaccine titers in either the Descartes-08 or the placebo** treatment cohort relative to baseline (Supplementary Figure).

Patients

Demographics, baseline disease characteristics, and prior and ongoing treatments were comparable between treatment cohorts.

Table 2. Patient characteristics and demographics

		Placebo (n=16)	Descartes-08 (n=20)
	Female, **%** (n)	**62.5** (10)	**55.0** (11)
	Age, years, **mean** (SD)	**57.8** (14.4)	**59.4** (14.7)
	Median duration of disease, **years** (range)	**5** (1–23)	**6** (0–26)
MGFA class at screening, % (n)	Class II	**25.0** (4)	**25.0** (5)
	Class III	**68.8** (11)	**70.0** (14)
	Class IV	**6.3** (1)	**5.0** (1)
MG antibody status, % (n)	AChR+	**75.0** (12)	**80.0** (16)
	LRP4+	**0** (0)	**5.0** (1)
	Sero-negative	**25.0** (4)	**15.0** (3)
	MGC score, median (min, max)	**17.5** (8, 33)	**16.5** (7, 28)
	MG-ADL score, median (min, max)	**9.5** (6, 16)	**9.0** (5, 16)
Clinical characteristics, % (n)	Diagnosis of thymoma*	**31.3** (5)	**10.0** (2)
	Previous thymectomy	**50.0** (8)	**30.0** (6)
	Previous MG crisis requiring MV	**0**	**15.0** (3)

*p<0.05. AChR+, positive for autoantibodies against the acetylcholine receptor; LRP4+, autoantibodies against the lipoprotein-4 receptor; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGC, Myasthenia Gravis Composite; MGFA, Myasthenia Gravis Foundation of America; MV, mechanical ventilation; SD, standard deviation.

Table 3. Prior and ongoing treatments

		Placebo (n=16)	Descartes-08 (n=20)
Previous MG therapies (SoC), % (n)	IVIG	**87.5** (14)	**70.0** (14)
	Pyridostigmine	**75.0** (12)	**55.0** (11)
	Other immunosuppressants	**75.0** (12)	**40.0** (8)
	Prednisone	**37.5** (6)	**40.0** (8)
	FcRn antagonist	**37.5** (6)	**30.0** (6)
	Plasma exchange	**50.0** (8)	**20.0** (4)
	Complement inhibitor	**37.5** (6)	**15.0** (3)
MG ongoing therapy, % (n)	Pyridostigmine	**62.5** (10)	**80.0** (16)
	Prednisone	**50.0** (8)	**50.0** (10)
	Azathioprine	**18.8** (3)	**30.0** (6)
	Mycophenolate mofetil	**43.8** (7)	**20.0** (4)
	Complement inhibitor	**18.8** (3)	**15.0** (3)

FcRn, fragment crystallizable receptor neonatal; IVIG, intravenous immunoglobulin; MG, myasthenia gravis; SoC, standard of care.

Acknowledgments: This study was funded by Cartesian Therapeutics. Medical writing and editorial support was provided by Laura Graham, PhD, and Nick Gibbs of Ogilvy Health and Eva Rybak, PharmD, of Cartesian Therapeutics.

References: 1. McCallion J, *et al. BMC Neurol.* 2024;24:61; 2. Koneczny I, *et al. Cells.* 2019;8:671; 3. Zografou C, *et al. Front Immunol.* 2021;12:686466; 4. Jin W, *et al. Cell Discov.* 2021;7:85; 5. Granit V, *et al. Lancet Neurol.* 2023;22:578–90; 6. Kohler S, *et al. J Neuroimmunol.* 2013;264:114–9.

Please use this QR code to download a PDF of the poster, supplementary material, and author disclosures

Poster 1130

Efficacy and safety of autologous BCMA-directed mRNA CAR T-cell therapy in generalized myasthenia gravis: Results from a phase 2b randomized placebo-controlled trial

2025 Neuromuscular Study Group Annual Scientific Meeting, September 26, 2025, Stresa, Italy

T. Vu[1], H.D. Tekce[2], M. Rivner[3], S. Shroff[4], T. Ragole[5], B. Myers[6], M. Pasnoor[7], G. Small[8], K. Gwathmey[9], C. Karam[10], M. Vullaganti[11], A. Peltier[12], G. Sahagian[13], M.H. Feinberg[14], A. Slansky[15], C. Barnett-Tapia[16], M. Badruddoja[17], Z. Siddiqi[18], H. Kamboh[19], M. Kurtoglu[19], C.M. Jewell[19], M.D. Miljkovic[19], T. Mozaffar[20], J.F. Howard[21] for the MG-001 Study Team

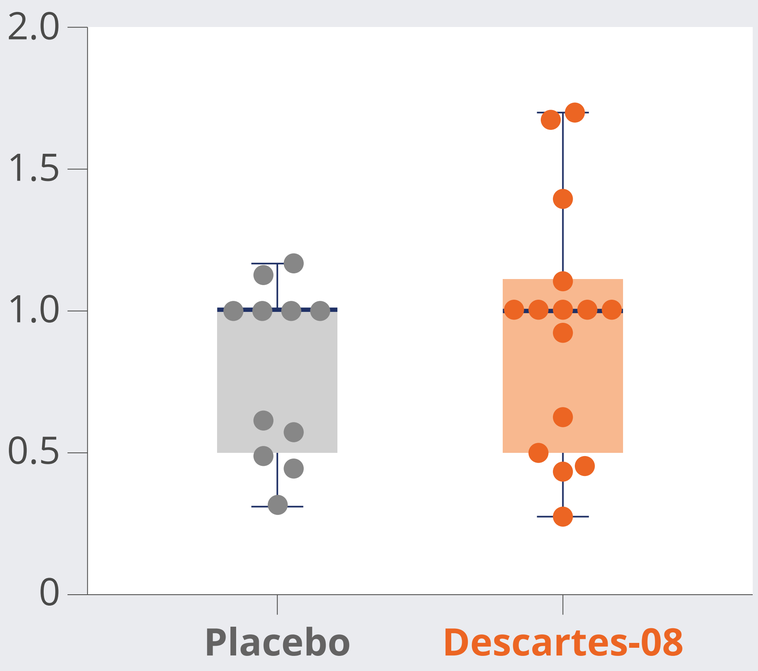
[1]University of South Florida, Tampa, FL, USA; [2]Istanbul University, Istanbul, Turkey; [3]Augusta University, Augusta, GA, USA; [4]Houston Methodist Hospital, Houston, TX, USA; [5]University of Colorado, Aurora, CO, USA; [6]Dent Neurologic Institute, Amherst, NY, USA; [7]University of Kansas Medical Center, Kansas City, KS, USA; [8]Allegheny General Hospital, Pittsburgh, PA, USA; [9]Virginia Commonwealth University, Richmond, VA, USA; [10]University of Pennsylvania, Philadelphia, PA, USA; [11]Tufts University, Boston, MA, USA; [12]Vanderbilt University, Nashville, TN, USA; [13]Profound Research, San Diego, CA, USA; [14]SFM Research, Boca Raton, FL, USA; [15]Neurology Associates, P.A., Maitland, FL, USA; [16]Toronto General Hospital, Toronto, Canada; [17]Center for Neurosciences, Tucson, AZ, USA; [18]University of Alberta, Edmonton, Canada; [19]Cartesian Therapeutics, Frederick, MD, USA; [20]University of California, Irvine, CA, USA; [21]University of North Carolina, Chapel Hill, NC, USA.

Supplementary figure

There was **no significant change from baseline in common vaccine titers** at primary end point (Day 85) for patients treated with Descartes-08 or placebo

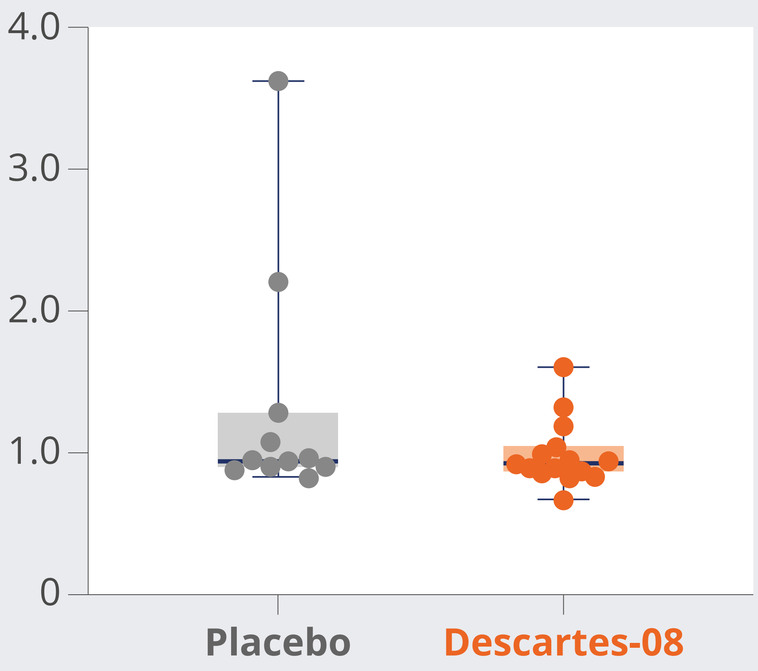
Anti-men Sero A titer

Relative change
(D85 from baseline)



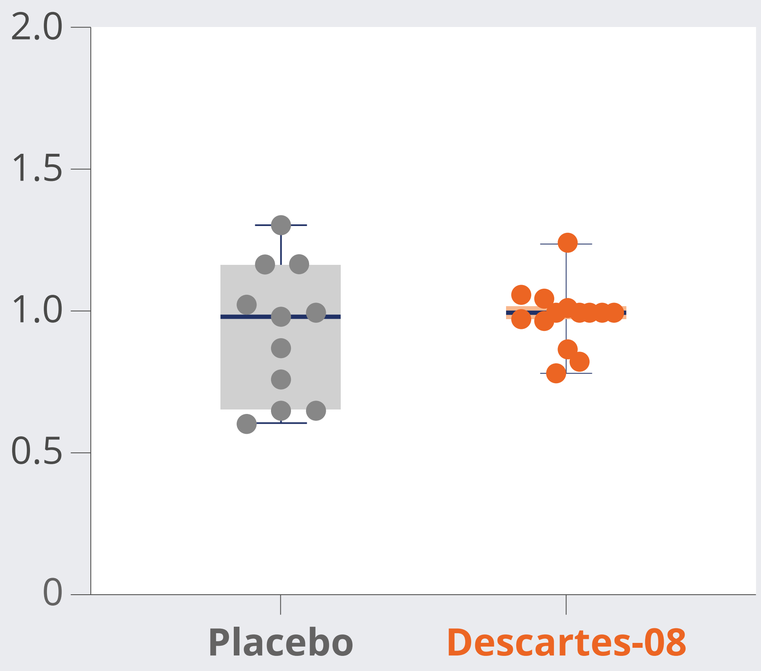
Anti-VZV titer

Relative change
(D85 from baseline)



Anti-tetanus titer

Relative change
(D85 from baseline)



Data indicate change in vaccine 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. Additional analyses demonstrated no differences between Descartes-08 and placebo for anti-men sero C, anti-men sero W135, anti-men sero Y, anti-diphtheria, anti-measles, anti-mumps, and anti-rubella titers (data not shown). D, day; Men, meningococcal; sero, serotype; VZV, varicella zoster.

Acknowledgments: Medical writing and editorial support was provided by Laura Graham, PhD, and Nick Gibbs of Ogilvy Health and Eva Rybak, PharmD, of Cartesian Therapeutics.

Disclosures: This study was funded by Cartesian Therapeutics. **HK, MK, CMJ,** and **MDM** are employed by, and may hold stocks in, Cartesian Therapeutics. **TV:** associations with and fees received from Alexion/AstraZeneca Rare Disease, Amgen, argenx, Cartesian Therapeutics, COUR, CSL Behring, Dianthus Therapeutics, EMD Serono, ImmunAbs, Immunovant, Johnson & Johnson, NMD Pharma, Regeneron, and UCB. **HDT:** fees from Alexion and UCB. **MR:** fees and/or grant support from Alexion, Amylyx, Apellis Pharma, argenx, Biohaven Pharmaceuticals, Inc., Cartesian Therapeutics, Catalyst Pharmaceuticals, Cytokinetics, Inc., Grifols, Healey Center, Janssen Research and Development, Mallinckrodt ARD, Inc., MedicinNova, Inc., Millennium Pharma, Momenta Pharmaceuticals, Inc., NMD Pharma, Orion Pharma, PTC Therapeutics, Inc., Seelos Therapeutics, Inc., Seikagaku Corporation, UCB, and Viela Bio. **SS:** fees from AstraZeneca, argenx, and UCB. **TR:** fees and/or grant support from Alexion, Annexon Biosciences, argenx, 2024 American Journal of Managed Care – Institute for Value-Based Medicine, and UCB. **BM:** fees from argenx and AstraZeneca. **MP:** fees from Alexion, Amgen, Annexon, argenx, BVBA, Catalyst, CSL Behring, Grifols, Immunovant, Janssen, Momenta, Octapharma Pharmaceuticals, Takeda, and TerumoBCT. **GS:** fees received from Alexion. **KG:** fees received from Alexion, Amgen, argenx, Novartis, and UCB. **CK:** fees and/or grant support from Acceleron: Alpine, Alexion, Alnylam, Amgen, Amicus, Annexon, argenx, AstraZeneca, Corino, Biogen, CSL Behring, Genentech, Genzyme, Ionis, J&J, Neuroderm, Novo Nordisk, Octapharma, Pfizer, Sanofi, UCB, Takeda, Vertex, and Zai lab. **GS:** fees and/or grant support from Alexion, argenx, Cartesian Therapeutics, Immunovant, NMD, Regeneron, and UCB. **MHF:** fees from argenx. **CBT:** fees and/or grant support from Alexion, argenx, Janssen, MGNet, Muscular Dystrophy Canada, Novartis, UCB, and the US Department of Defense. **TM:** fees and/or grant support from Alexion, Amicus, AnnJi, argenx, Arvinas, Ask Bio, Astellas Gene Therapeutics, AvroBio, BioCryst, Cabaletta, Cartesian Therapeutics, Fate Therapeutics, Grifols, Horizon Therapeutics, Immunovant, Maze Therapeutics, Merck, ML-Bio, Myositis Association, National Insititutes of Health, Neuromuscular Disease Foundation, NKarta, Poseida, Ra Pharmaceuticals, Regeneron, Shionogi, Momenta (now Janssen), Sanofi, Spark Therapeutics, UCB, and Valerion. **JFH:** fees and/or grant support from Academic CME, Ad Scientiam, Alexion/AstraZeneca Rare Disease, argenx, Biohaven Pharmaceuticals, Inc., Biologix Pharma, Cartesian Therapeutics, Centers for Disease Control and Prevention, MedScape CME, Merck EMB Serono, MGFA, Muscular Dystrophy Association, National Institutes of Health, NMD Pharma, Novartis, PeerView CME, Physicians' Education Resource CME, PlatformQ CME, Regeneron, Sanofi, TG Therapeutics, Toleranzia AB, and UCB. **MV, AP, AS, MB,** and **ZS** have nothing to disclose.