Presentation at the AANEM Annual Meeting, October 29 – November 1, 2025,
San Francisco, California

Top-line results for MaGic, a phase 2 trial of claseprubart (DNTH103), an active C1s inhibitor, in generalized myasthenia gravis

MAGIC

Pushpa Narayanaswami,* Sankalp Gokhale, Caitlin M Briggs, Uzma Siddiqui, Simrat Randhawa, Matt I Truman, Luke Hickey, Shahar Shelly, Stojan Peric, Tuan Vu, John Vissing

*Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA, United States

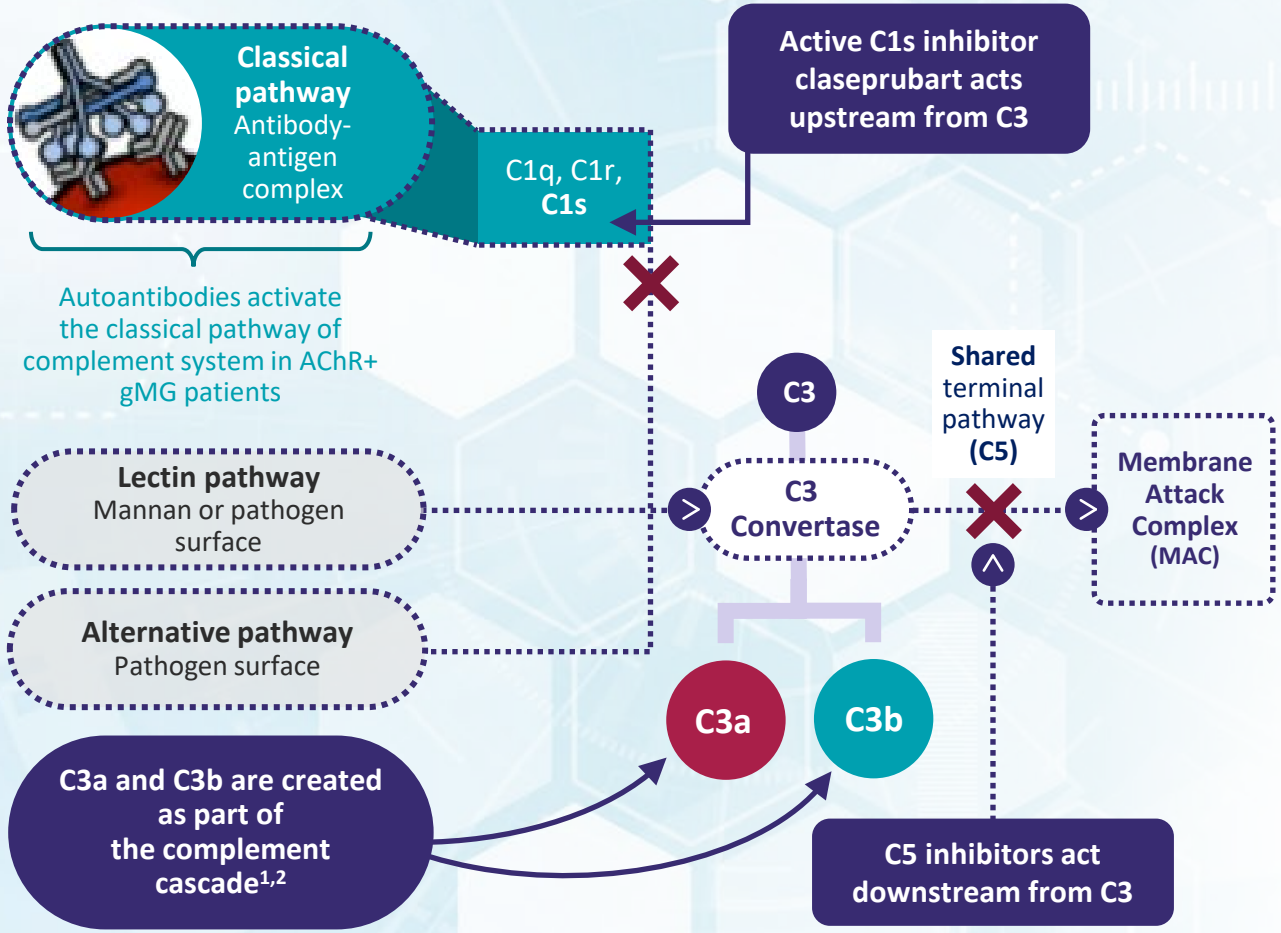
Claseprubart is an investigational agent that is not approved as a therapy in any indication in any jurisdiction worldwide.

Disclosures

- **Pushpa Narayanaswami** has received research support from AHRQ, PCORI, NIH, Alexion. She has served as advisor/consultant for Alexion/ Astra-Zeneca, Argenx, Amgen, Cartesian, CVS, Dianthus Therapeutics, EMD-Serono, GSK, Immuneabs, Immunovant, Johnson & Johnson, Novartis, UCB, Viridian. She serves on Data Monitoring Boards for Sanofi (ended), Argenx, NMD-pharma. She receives royalties from Springer Nature.

Introduction

- **Claseprubart** (DNTH103) targets the classical complement pathway through **active C1s (aC1s)** inhibition.
- **Claseprubart** is the **first aC1s inhibitor** evaluated in **generalized myasthenia gravis (gMG)**.
- Unlike **C5 inhibition**, which blocks **all complement pathways** (classical, lectin, and alternative) downstream, **claseprubart aC1s inhibition specifically targets the classical pathway upstream**, offering a more focused approach, with the potential to reduce the activity of upstream components, including C3a and C3b
- **Claseprubart preserves lectin and alternative complement activity,** which may address MG disease pathology while reducing the risk of severe encapsulated bacterial infections seen with broad C5 inhibition.



MaGic Trial: https://clinicaltrials.gov/study/NCT06282159

MaGic is a global Ph. 2 trial in AChR+ gMG patients

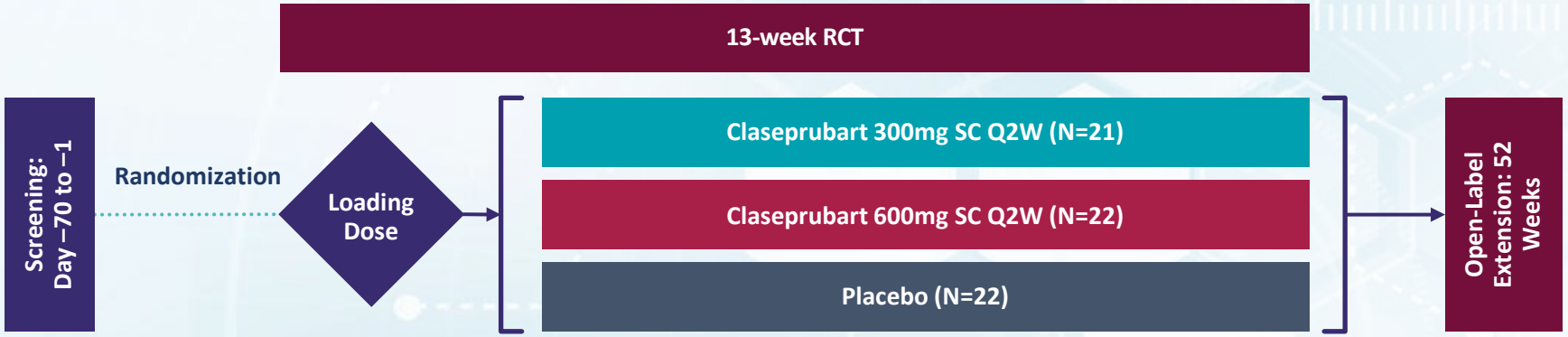
A global, multicenter, randomized, double-blind, placebo-controlled study to evaluate the safety, efficacy, and PK/PD of claseprubart administered SC following initial loading dose

Highlights

- **Design:** ~60 male and female subjects randomized to receive either claseprubart or placebo for 13 weeks
- **Inclusion:** ≥18 years old with AChR antibody+ gMG
- **Dosing:** 15 or 20mg/kg IV loading dose followed by 300mg or 600mg SC Q2W starting Day 7

Endpoints

- **Primary:** Safety
- **Secondary/exploratory:** Efficacy (MG-ADL, QMG MSE, MGC, MG-QoL-15r)



MAGIC

Trial enrollment exceeded target, with 65 participants enrolled

MaGic Trial: https://clinicaltrials.gov/study/NCT06282159

AChR, acetylcholine receptor; gMG, generalized myasthenia gravis; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis score; MGC, Myasthenia Gravis Composite score); Q2W, once every 2 weeks; QoL15r, Quality of Life scale; RCT, randomized, controlled trial; SC, subcutaneous

Participant baseline characteristics were generally well balanced across arms

AChR+ gMG participants	Placebo (N=22)	Claseprubart 300mg Q2W (N=21)	Claseprubart 600mg Q2W (N=22)
Age, mean (SD), years	52.2 (16.5)	57.1 (13.7)	55.3 (12.0)
Male, n (%)	13 (59%)	14 (67%)	10 (45%)
Weight, mean (SD), pounds	195.0 (48.0)	192.5 (35.5)	179.0 (35.4)
Duration of disease, median (range), years	7.7 (0.4–21.2)	3.0 (0.5–22.1)	7.6 (1.0–37.3)
MG-ADL score at baseline, mean (SD)	8.5 (2.9)	8.2 (2.2)	8.4 (2.6)
QMG score at baseline, mean (SD)	14.2 (5.8)	12.2 (2.7)	12.2 (3.6)
MG Composite score at baseline, mean (SD)	15.0 (7.8)	16.3 (4.5)	16.0 (5.3)
MG-QoL-15r score at baseline, mean (SD)	14.3 (7.0)	15.4 (6.6)	14.9 (5.9)
MGFA class at screening, n (%)			
II	7 (32%)	11 (52%)	12 (55%)
III	12 (55%)	10 (48%)	9 (41%)
IVa	3 (14%)	0 (0%)	1 (5%)
Prior thymectomy, n (%)	8 (36%)	6 (29%)	7 (32%)
Baseline corticosteroid use, n (%)	19 (86%)	17 (81%)	20 (91%)
Number of ISTs at baseline, n (%)			
1	11 (50%)	10 (48%)	12 (55%)
>1	11 (50%)	11 (52%)	10 (45%)
FcRn use in prior 24 months, n (%)	0 (0%)	1 (5%)	0 (0%)
Prior complement use, n (%)	0 (0%)	0 (0%)	0 (0%)

gMG, generalized myasthenia gravis; SD, standard deviation; MG-ADL, Myasthenia Gravis Activities of Daily Living scale; QMG, Quantitative Myasthenia Gravis score; MGFA, Myasthenia Gravis Foundation of America clinical classification; IST, immunosuppressive therapy; MGC, Myasthenia Gravis Composite; MG-QOL-15r, Myasthenia Gravis quality of life 15 revised.

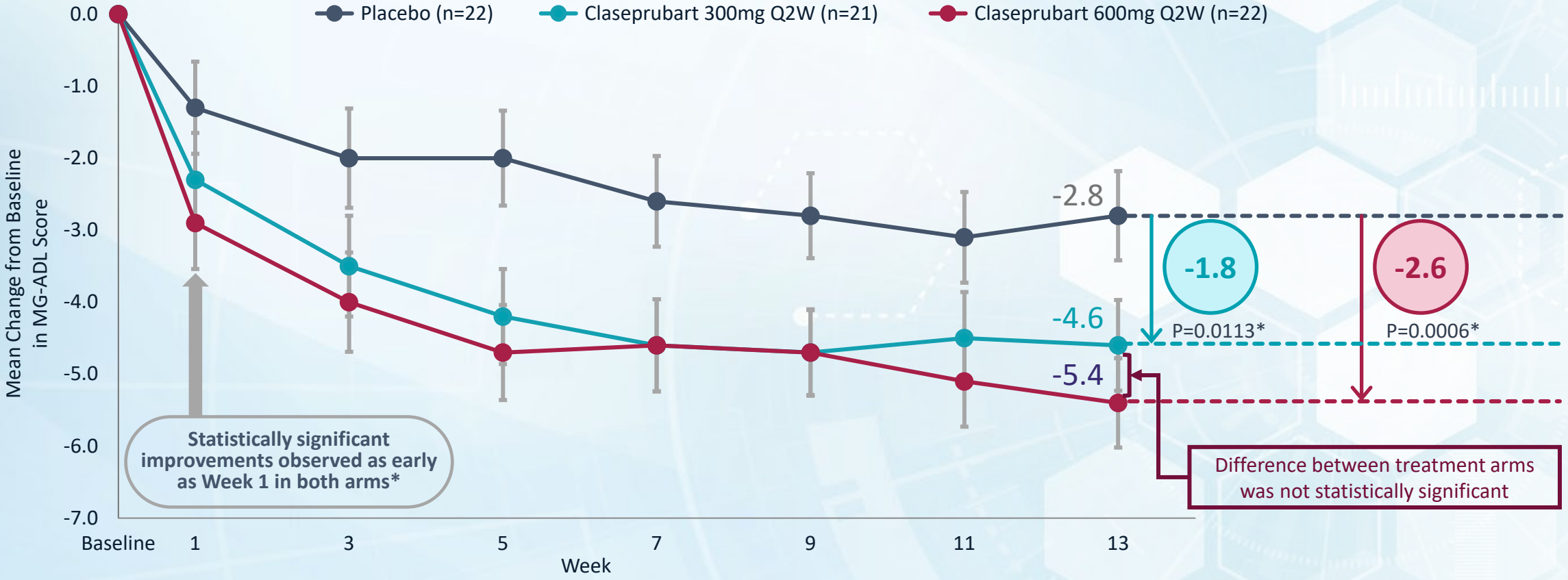
Claseprubart was generally well tolerated, with a favorable, potentially differentiated safety profile in Phase 2

	Placebo (N=22)	Claseprubart 300mg Q2W (n=21)	Claseprubart 600mg Q2W (n=22)
Clinical adverse events (AEs)[1]	11 (50.0%)	13 (61.9%)	15 (68.2%)
Related serious AEs	1 (4.5%)	0 (0%)	0 (0%)
RCT discontinuation due to related AE	0 (0%)	0 (0%)	0 (0%)
Infections	10 (45.5%)	5 (23.8%)	6 (27.3%)
Related serious infections	1 (4.5%)	0 (0%)	0 (0%)
Injection site reactions[2]	0 (0%)	2 (9.5%)	2 (9.1%)
Newly positive for anti-nuclear antibodies (ANA)[3]	0 (0%)	1 (5.9%)	8 (36.4%)
Rashes	0 (0%)	0 (0%)	0 (0%)
Arthralgia	1 (4.5%)	1 (4.8%)	0 (0%)

Comparable clinical safety profile to placebo with remarkably benign administration, no infection signal and no symptoms indicative of autoimmune activation

(1) Excludes events in the investigations System Organ Class (MedDRA).
(2) All injection site reactions were mild to moderate.
(3) Represents participants who were ANA negative at baseline and tested positive at ≥1:320 at any point during RCT (percentages calculated from n=17 for 300mg arm and n=22 for 600mg arm). An ANA titer of ≥1:320 was an exclusion criterion for the clinical trial protocol. At end of RCT (Week 13), 2 of the 8 patients in 600mg arm tested negative for ANA, 2 of the 8 patients in 600mg arm remained positive but at <1:320.

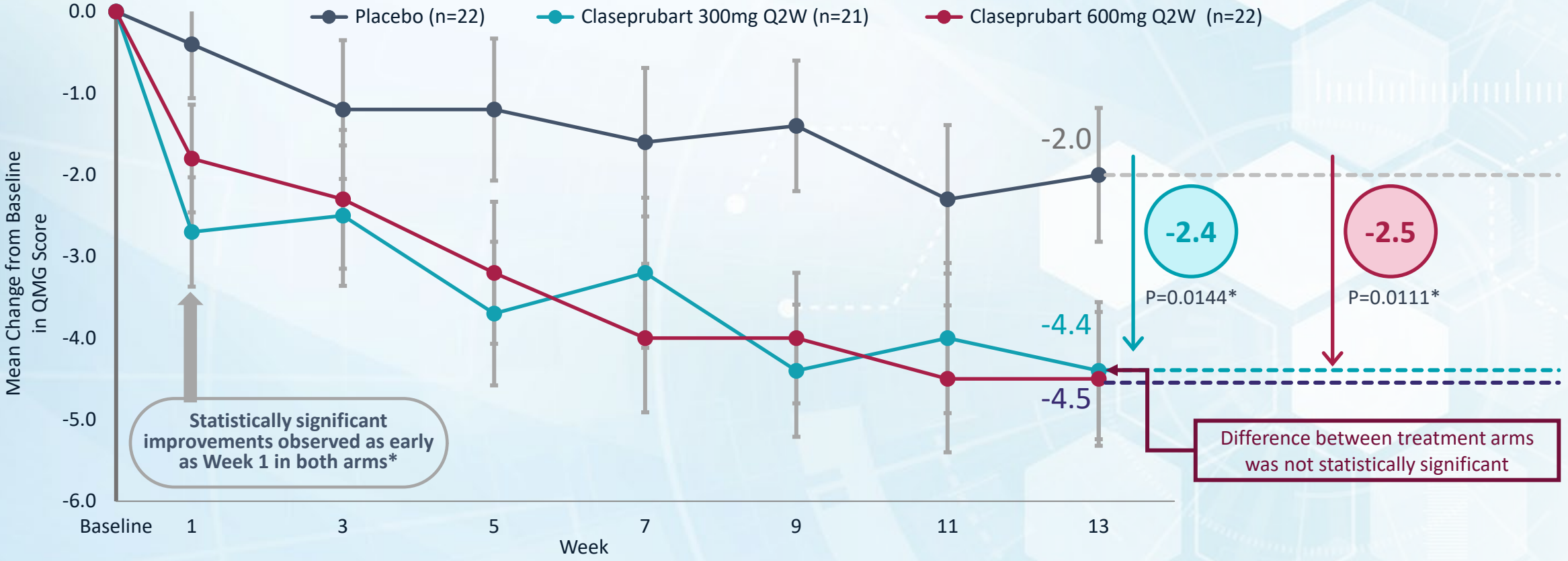
Claseprubart arms demonstrated rapid, sustained, and clinically meaningful improvements in MG-ADL score



MG-ADL improvements for participants treated with claseprubart were rapid, sustained, clinically meaningful and statistically significant as early as Week 1

The change from baseline in MG-ADL was analyzed using a mixed effect model for repeated measures (MMRM) with treatment group, visit, treatment by visit interaction, stratification factors, and baseline measure included. Bars represent standard error of the mean.
*One-sided p-values are presented for comparisons of claseprubart vs placebo, with any p-value below 0.1 considered nominally statistically significant.

Claseprubart arms demonstrated rapid, sustained, and clinically meaningful improvements in QMG score

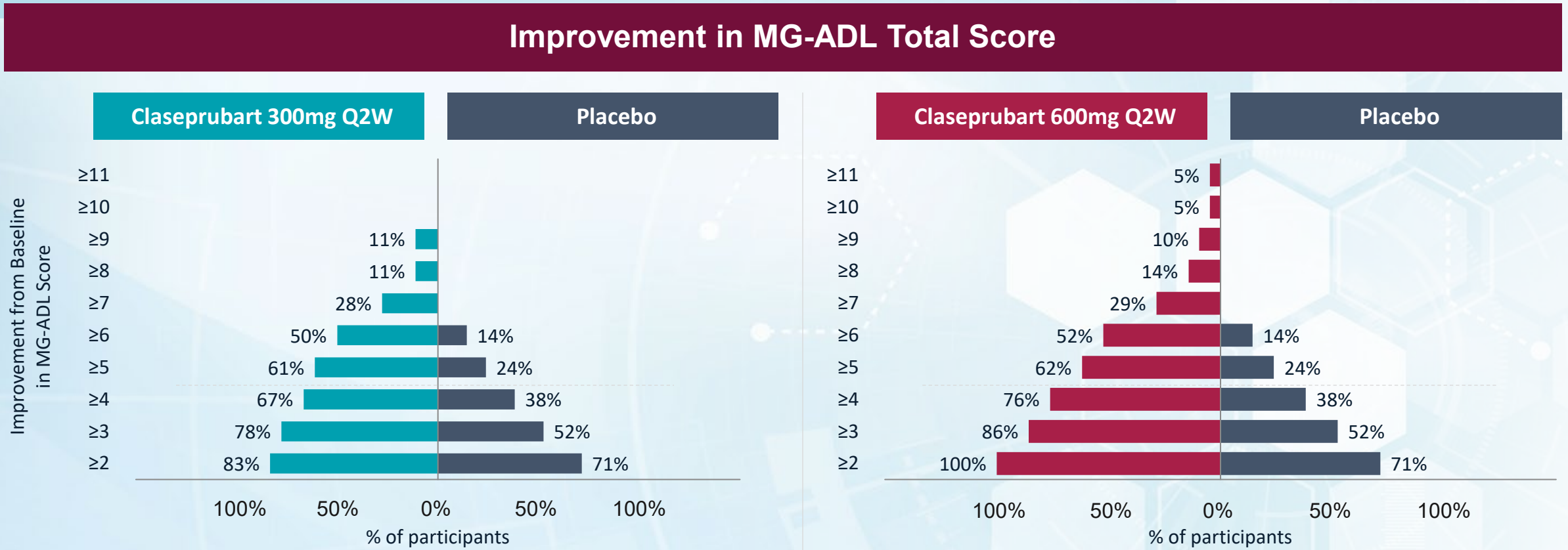


QMG improvements for participants treated with claseprubart were rapid, sustained, clinically meaningful and statistically significant as early as Week 1

The change from baseline in QMG was analyzed using a mixed effect model for repeated measures (MMRM) with treatment group, visit, treatment by visit interaction, stratification factors, and baseline measure included. Bars represent standard error of the mean.

*One-sided p-values are presented for comparisons of claseprubart vs placebo, with any p-value below 0.1 considered nominally statistically significant.

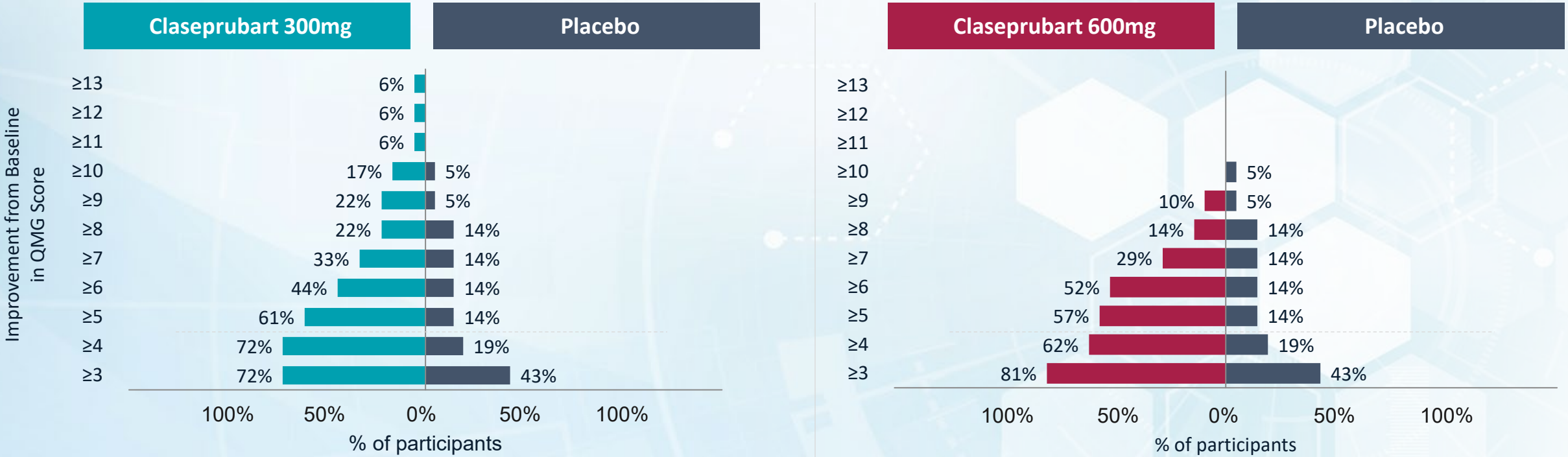
>60% of participants on claseprubart 300mg and 600mg achieved ≥5 point improvement in MG-ADL



Participants across both treatment arms achieved robust improvements in MG-ADL at Week 13

>60% of participants on claseprubart 300mg achieved ≥5 point improvement in QMG

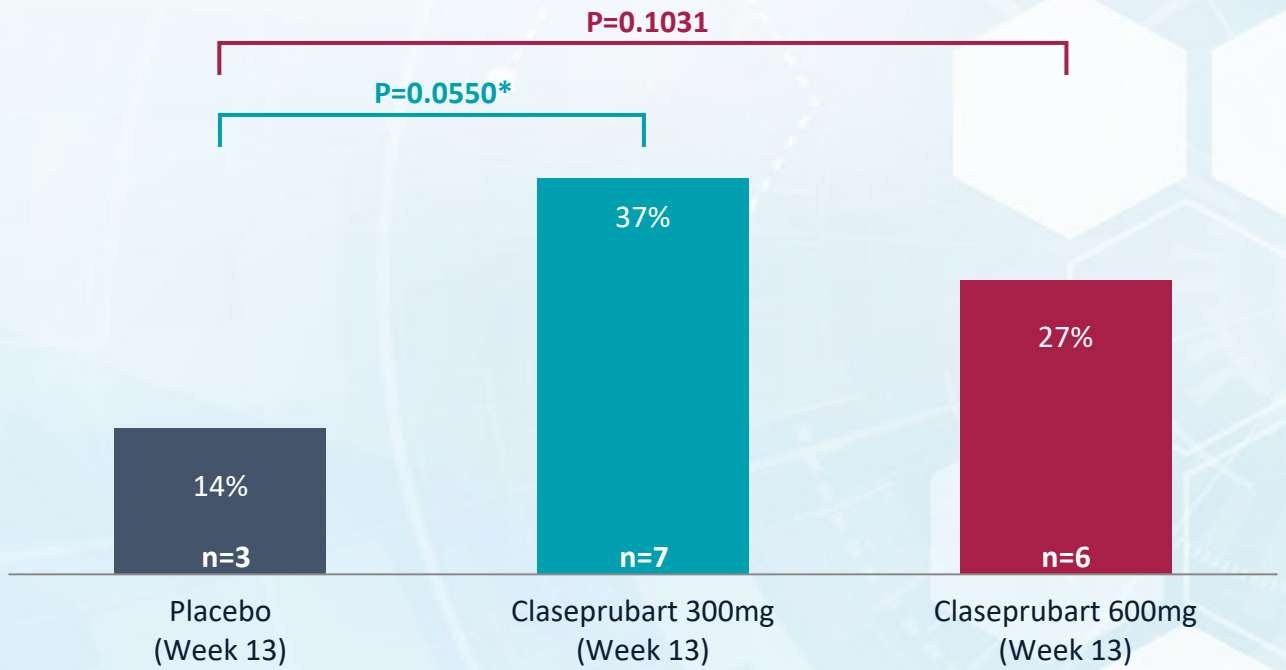
Improvement in QMG Total Score



Participants across both treatment arms achieved robust improvements in QMG at Week 13

37% of 300mg claseprubart-treated participants achieved Minimal Symptom Expression on MG-ADL at Week 13

Minimal Symptom Expression (MSE)
% of Participants Achieving MG-ADL Score of 0 or 1 at Week 13



The proportion of participants who achieve MSE was analyzed using a logistic regression with terms for treatment group, stratification factors, and baseline MG-ADL included.
*One-sided p-values are presented for comparisons of claseprubart vs placebo, with any p-value below 0.1 considered nominally statistically significant.

Across key efficacy measures, claseprubart demonstrated equally robust and clinically meaningful responses

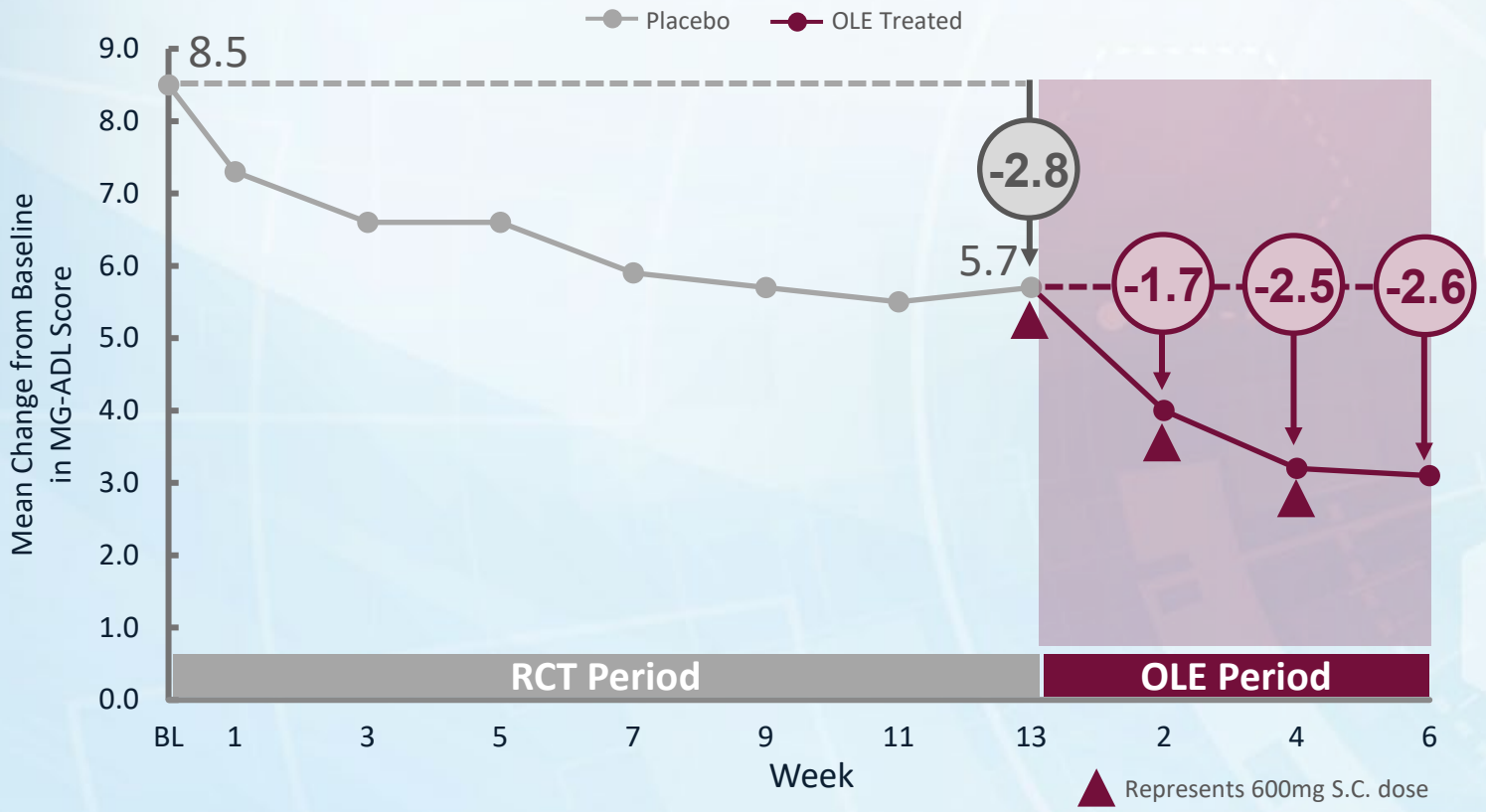
	Placebo	Claseprubart 300mg Q2W		Claseprubart 600mg Q2W	
		Absolute	Placebo-adjusted	Absolute	Placebo-adjusted
MG-ADL mean change from baseline at Week 13	-2.8	-4.6	-1.8 *(P=0.0113)**	-5.4	-2.6 *(P=0.0006)**
QMG mean change from baseline at Week 13	-2.0	-4.4	-2.4 *(P=0.0144)**	-4.5	-2.5 *(P=0.0111)**
MSE at Week 13	14%	37%	23% *(P=0.0550)**	27%	13% *(P=0.1031)*
MGC mean change from baseline at Week 13	-3.1	-8.7	-5.6 *(P=0.0008)**	-8.6	-5.5 *(P=0.0008)**
MG-QoL-15r mean change from baseline at Week 13	-3.9	-6.1	-2.2 *(P=0.0414)**	-5.4	-1.5 *(P=0.1122)*

Claseprubart 300mg Q2W treatment arm achieved statistical significance vs. placebo across all five key efficacy measures

*One-sided p-values are presented for comparisons of claseprubart vs placebo, with any p-value below 0.1 considered nominally statistically significant.

Early response of placebo cohort after switching to claseprubart favors Q4W regimen in Phase 3

Mean Change in MG-ADL Score from RCT Baseline to OLE Week 6



OLE Data Support 300mg Q4W Dosing in Future Phase 3 Study

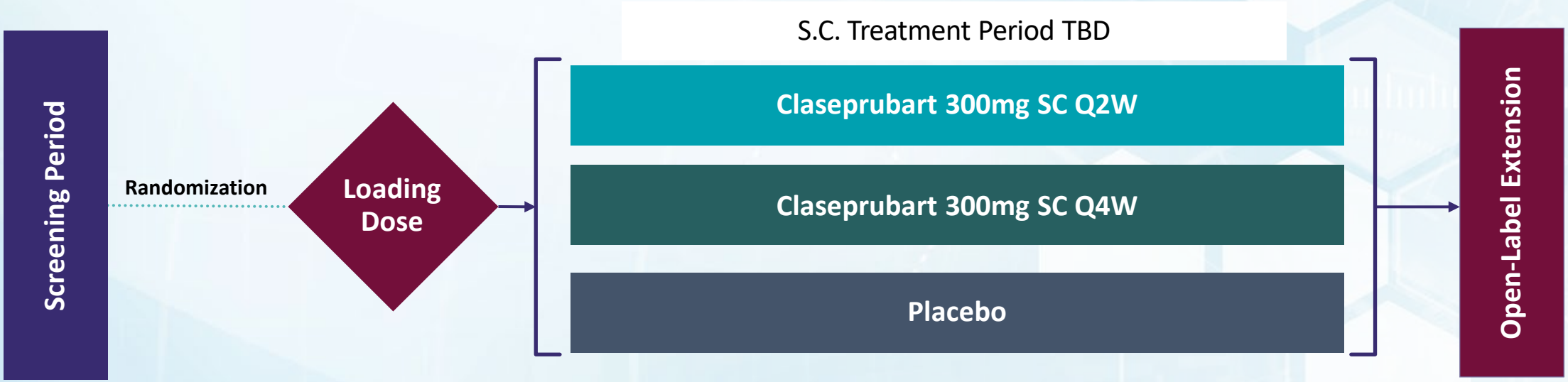
- Placebo patients entering OLE receive claseprubart 600mg Q2W with no loading dose
- Robust reduction in MG-ADL is achieved by OLE Week 4, and is stable in subsequent weeks
- PK of ~65 µg/mL, observed at OLE week 4, is substantially lower than 300mg Q2W steady state PK of 100–120 µg/mL
- Following two 600mg Q2W doses, maximum reduction in MG-ADL is achieved by Week 4 in the OLE, and is stable in subsequent weeks
- Growing evidence that lower levels of complement inhibition (<90%) may be sufficient for efficacy in gMG[1]

The change from RCT baseline in MG-ADL was analyzed using a mixed effect model for repeated measures (MMRM) with randomized treatment group, visit, randomized treatment by visit interaction, stratification factors, and baseline measure included. All patients received claseprubart in OLE.
gMG, generalized myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; OLE, open-label extension; PK, pharmacokinetics; Q2W, once every 2 weeks; Q4W, once every 4 weeks; RCT, randomized, controlled trial

1. https://newsroom.regeneron.com/node/31216/pdf

Phase 3 Trial Design Pending Regulatory Feedback

Evaluate 300mg Q4W based on early PK/PD data from Phase 2 OLE

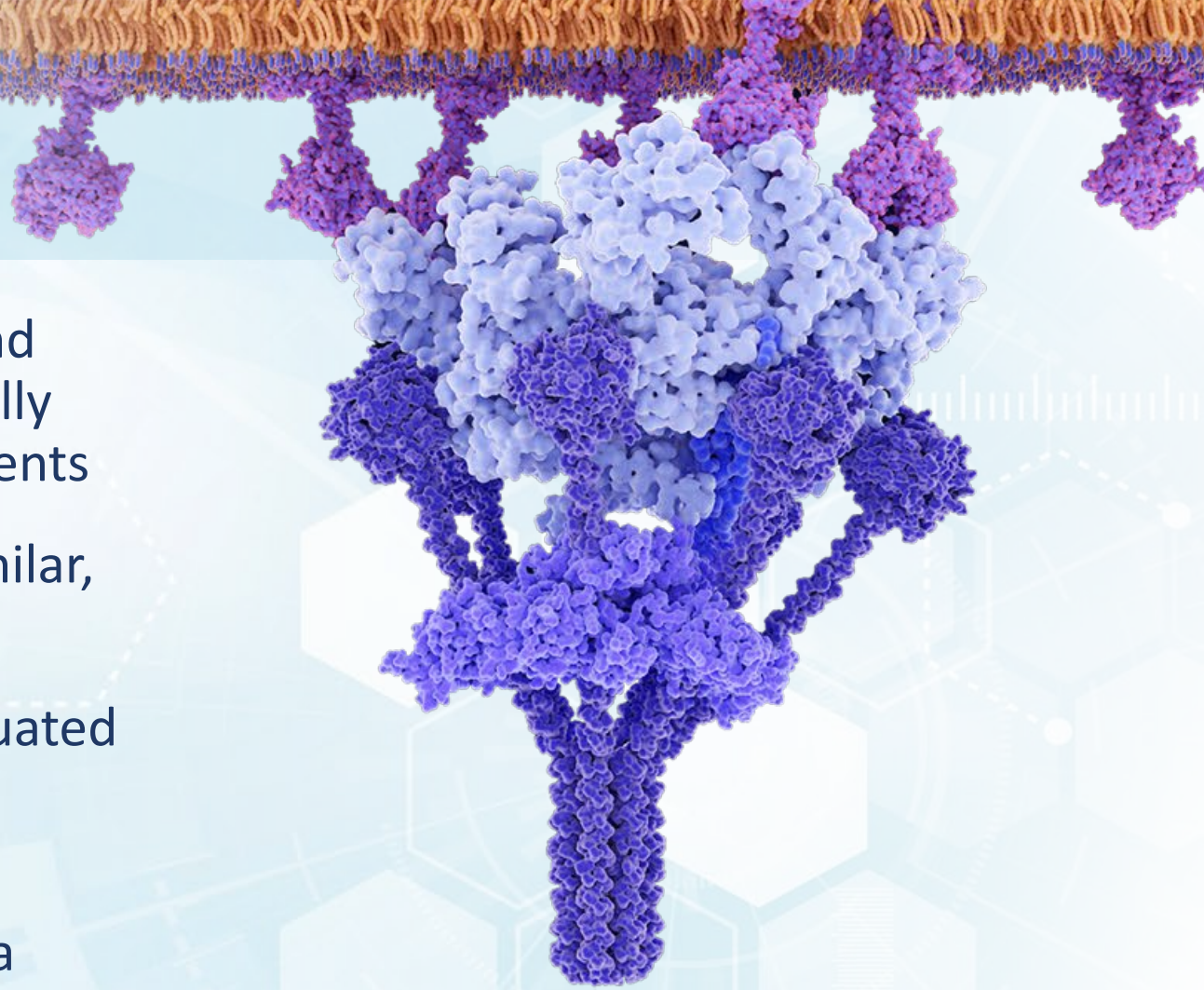


- **Primary Endpoint:** Change from Baseline to Week [Treatment Period TBD] in Myasthenia Gravis Activities of Daily Living (MG-ADL) scale score
- **Key Inclusion criteria:**
  - Adult males and females, between the ages of 18 - 80 years of age at screening.
  - Myasthenia Gravis Activities of Daily Living (MG-ADL) 6 or more, both at screening and confirmed prior to randomization.
  - Quantitative Myasthenia Gravis assessment score: TBD

Potential to further enhance best-in-class convenience with Q4W dosing

PD, pharmacodynamics; PK, pharmacokinetics; Q2W, once every other week; Q4W, once every 4 weeks; SC, subcutaneous; TBD, to be determined

Conclusions



- Claseprubart treatment was well tolerated and resulted in clinically meaningful and statistically significant improvements across key assessments
- The benefit/risk profile of both doses was similar, supporting research focus on the lower dose
- Claseprubart 300 Q2W and Q4W will be evaluated in an upcoming Phase 3 gMG trial
- Claseprubart has the potential to deliver meaningful benefit to AChr+ gMG patients via infrequent self administered SC injections and a reduced risk of encapsulated bacterial infections versus C5 inhibitors

AChR, acetylcholine receptor; gMG, generalized myasthenia gravis; Q2W, once every other week; Q4W, once every 4 weeks; SC, subcutaneous

THANK YOU TO ALL OUR PATIENT PARTICIPANTS

MaGic Principal Investigators

Ana Azanjac-Arsic

Cynthia Bodkin

Urszula Chyrchel-Paszkiewicz

Gordana Djordjevic

Dori, Amir

Erik Ensrud

Marc Feinberg

Laura Fionda

Folkens, Eric

Miriam Freimer

Nils Gilhus

Raghav Govindarajan

Mariusz Grudniak

Kelly Gwathmey

Ali Habib

Petr Hon

Andreea Illinca

Raffaele Iorio

Arnaldo Isa

Gustavo Jose

Zita Jovin

Agnieszka Kulaga

Hani Kushlaf

Susana del Valle Liwacki

Lopez, Pablo

Michelangelo Maestri Tassoni

Lorenzo Maggi

Peter McAllister

Aleksandra Nadaj-Pakleza

Pushpa Narayanaswami

Thy Nguyen

Michael Nicolle

Fatima Pagani Cassara

Mamatha Pasnoor

Stojan Peric

Dragana Petrovska Cvetkovska

Maria Philip

Nicolai Preisler

Roberto Daniel Rey

Lukasz Rzepinski

Ahmad Sabouni

Francesco Sacca

Sabrina Sacconi

Amit Sachdev

Radi Shahien

Aziz Shaibani

Shahar Shelly

Sheetal Shroff

Kumaraswamy Sivakumar

Agnieszka Slowik

Marek Smilowski

Guilhem Sole

Adnan Subei

Dario Tavolini

Anneke J van der Kooi

Tuan Vu

James Winkley