

Treatment of Sjögren's Disease by Blocking FcRn: Clinical and Translational Data From RHO, a Phase 2 Randomized, Placebo-Controlled, Double-Blind, Proof-of-Concept Study With Efgartigimod

<u>Isabelle Peene</u>, ¹ Gwenny M. Verstappen, ² Joke Deprez, ¹ Frans G.M. Kroese, ² Suzanne Arends,² Andrew Kelly,³ Lana Vandersarren,³ Edward Bowen,⁴ Julie Jacobs,³ Paul Meyvisch,³ Dirk Elewaut,^{1,*} Hendrika Bootsma^{2,*}

¹Ghent University Hospital and Unit Molecular Immunology and Inflammation, VIB Center for Inflammation Research, Ghent University, Ghent, Belgium; ²University of Groningen, University Medical Center Groningen, Groningen, the Netherlands; ³argenx, Ghent, Belgium; ⁴IQVIA, Durham, NC, USA *Co-senior authors

BACKGROUND METHODS

Sjögren's Disease (SjD)

- O SjD is a chronic and progressive, systemic, autoimmune disease¹
- SjD is characterized by lymphocytic infiltration and immune-mediated dysfunction of exocrine glands, with possible extraglandular manifestations^{1–4}
- O IgG autoantibodies targeting Ro52, Ro60, and La antigens contribute to disease pathology^{5,6}

Efgartigimod Blocks FcRn and Reduces IgG Levels

- Efgartigimod is a human IgG1 antibody Fc fragment that has been engineered for increased affinity to FcRn compared to endogenous IgG and is uniquely composed of the only part of the IgG antibody that normally binds FcRn^{7,8}
- O By blocking FcRn, efgartigimod selectively reduces IgG antibodies and pathogenic autoantibodies, and does so without:^{7,9–11}
- Impacting antibody production (including other Ig antibodies) or other parts of the immune system
- Decreasing albumin levels
- Increasing LDL cholesterol levels



FIGURE 1 RHO: A Randomized, Double-Blinded, Placebo-Controlled, Phase 2, Multicenter Study

Key Inclusion Criteria

 ACR/EULAR 2016 criteria fo SjD who met criteria ≤7 years

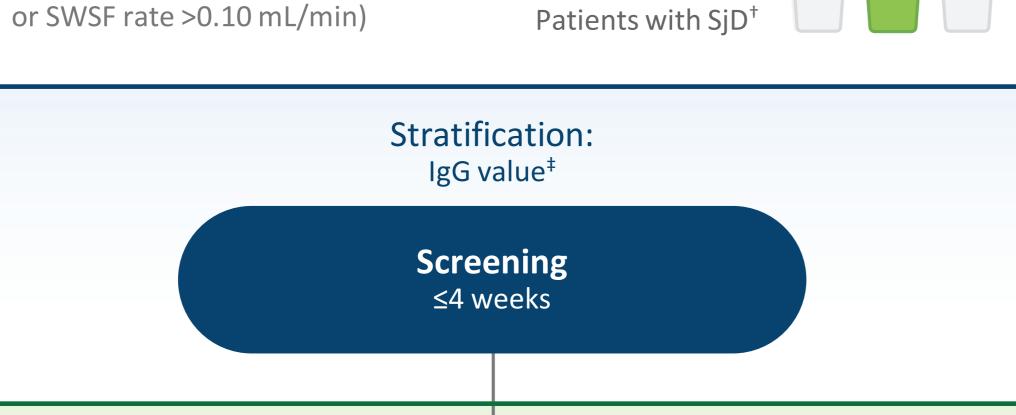
before screening* • ESSDAI ≥5

(UWSF rate >0 mL/min and/

Anti-Ro/SS-A positive

Presence of residual salivary flow

Study Population



PHASE 2 STAGE: 24-Week Treatment Period 24-week placebo-controlled **Efgartigimod IV** Placebo 10 mg/kg once weekly

Follow-Up Rollover ingle-arm OLE study (RHO+) Safety follow-up 48-week treatment period 56 days after last dose (weekly or biweekly dosing depending on response

Objective

To evaluate the efficacy and safety of intravenous efgartigimod in adults with SjD

Primary

Select

≥3 out of 5 items) at Week 24 Proportion of responders to cSTAR (score ≥5)

Proportion of responders to CRESS§ (response on

at Week 24 Effect on disease activity (ESSDAI, ClinESSDAI, ESSPRI) Safety, evaluated by the incidence and severity of AEs

*Patients with secondary Sjögren's syndrome overlap syndromes where another confirmed autoimmune rheumatic or systemic inflammatory condition (eg, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, inflammatory bowel disease) is the primary diagnosis were excluded. †3 patients did not meet eligibility criteria and were (i) discontinued within the first weeks after randomization, and (ii) removed from the efficacy analysis. [‡]>16.0 g/L or ≤16 g/L. [§]CRESS response thresholds: ClinESSDAI (score of <5 points); ESSPRI (decrease of ≥1 point or ≥15% from baseline); tear gland function (increase of ≥5 mm from baseline in Schirmer's test or decrease of ≥2 points from baseline in OSS); UWSF/SGUS (increase of ≥25% in UWSF or decrease of ≥25% in the SGUS Hocevar score, or if UWSF was 0 mL/min at baseline, any increase from baseline); RF/IgG (RF decrease of ≥25% from baseline or IgG reduction of ≥10%). ClinicalTrials.gov Identifier: NCT05817669. https://clinicaltrials.gov/study/NCT05817669. Accessed April 2025.

RESULTS

TABLE 1 Participant Demographics and **Baseline Characteristics**

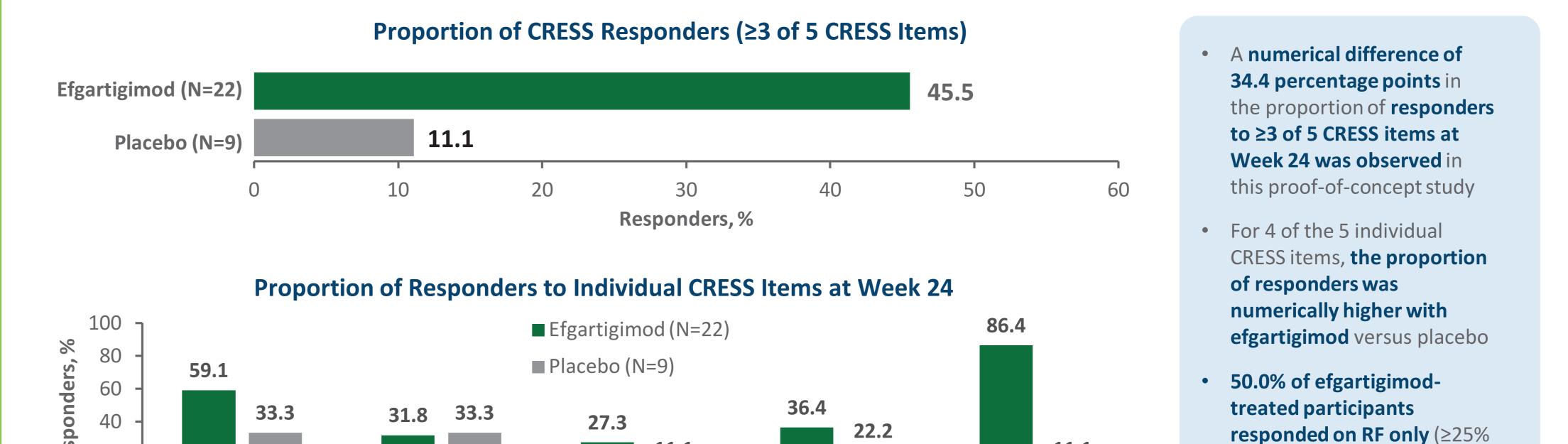
	Efgartigimod (N=23)	Placebo (N=11)		
Age, years, median (Q1, Q3)	49 (39, 64)	58 (45, 69)		
Sex, female, n (%)	22 (95.7)	11 (100.0)		
Time since diagnosis, years, median (Q1, Q3)	3 (1, 6)	6 (3, 7)		
Race, n (%)				
White	22 (95.7)	11 (100.0)		
Unknown	1 (4.3)	0		
ESSDAI total score, median (Q1, Q3)	12 (8, 15)	17 (8, 19)		
ClinESSDAI total score, median (Q1, Q3)	13 (9, 17)	18 (9, 21)		
ESSPRI score, median (Q1, Q3)	6.7 (5.8, 7.7)	5.0 (4.7, 6.3)		
Schirmer <5 mm/5 min in ≥1 eye, n (%)	18 (78.3)	9 (81.8)		
UWSF, mL/min, median (Q1, Q3)	0.12 (0.05, 0.17)	0.10 (0.07, 0.15)		
IgG, g/L, median (Q1, Q3)	17.32 (10.91, 22.20)	17.75 (10.77, 18.76)		
RF, IU/mL, median (Q1, Q3)	51.0 (21.0, 89.0)	59.0 (37.0, 176.0)		

TABLE 2 Summary of Safety

	PYFU=12.62)*		PYFU=5) [™]	
Number of administrations, median (Q1, Q3)	22 (20, 24)		22 (2, 23)	
	n (%)	m (ER)	n (%)	m (ER)
≥1 AE	20 (87.0)	81 (6.4)	7 (63.6)	23 (4.6)
≥1 SAE [‡]	1 (4.3)	1 (0.1)	0	0
≥1 grade ≥3 AE	0	0	0	0
≥1 AE leading to study drug discontinuation	1 (4.3)	1 (0.1)	0	0
≥1 AESI (infection)§	15 (65.2)	25 (2.0)	5 (45.5)	7 (1.4)
≥1 injection- and infusion-related reaction	3 (13.0)	5 (0.4)	1 (9.1)	1 (0.2)
≥1 fatal AE	0	0	0	0
Most common AEs (occurring in >10% of participants)				
Headache	4 (17.4)	6	1 (9.1)	1
Nasopharyngitis	4 (17.4)	5	1 (9.1)	1
Influenza	3 (13.0)	3	0	0
Upper respiratory tract infection	3 (13.0)	3	2 (18.2)	2
Urinary tract infection	3 (13.0)	3	1 (9.1)	1

*18 participants from the efgartigimod arm completed study treatment. †7 participants from the placebo arm completed study treatment. [‡]Grade 2 SAE of vasospasm, which the investigator and sponsor considered not related to efgartigimod. §Efgartigimod treatment leads to reduced IgG levels; as low IgG levels are associated with increased infection risks, events in the MedDRA System Organ Class Infections and Infestations are considered AESIs in this study.

FIGURE 2 Proportion of Responders to Individual CRESS Items at Week 24



reduction), compared with

0% in the placebo group

*Total ClinESSDAI score <5 points from baseline. [†]Total ESSPRI score decrease of ≥1 point or ≥15% from baseline. [‡]Increase in Schirmer's test ≥5 mm or a decrease in OSS ≥2 points from baseline or stable. §Increase in UWSF ≥25%, or any increase if baseline is 0, or decrease in SGUS ≥25%. Decrease in RF ≥25% or decrease in IgG ≥10%; 50.0% of participants in the efgartigimod group had a ≥25% decrease from baseline in RF compared with 0% in the placebo group

FIGURE 3 Proportion of Responders and Clinically Meaningful ESSDAI Improvements

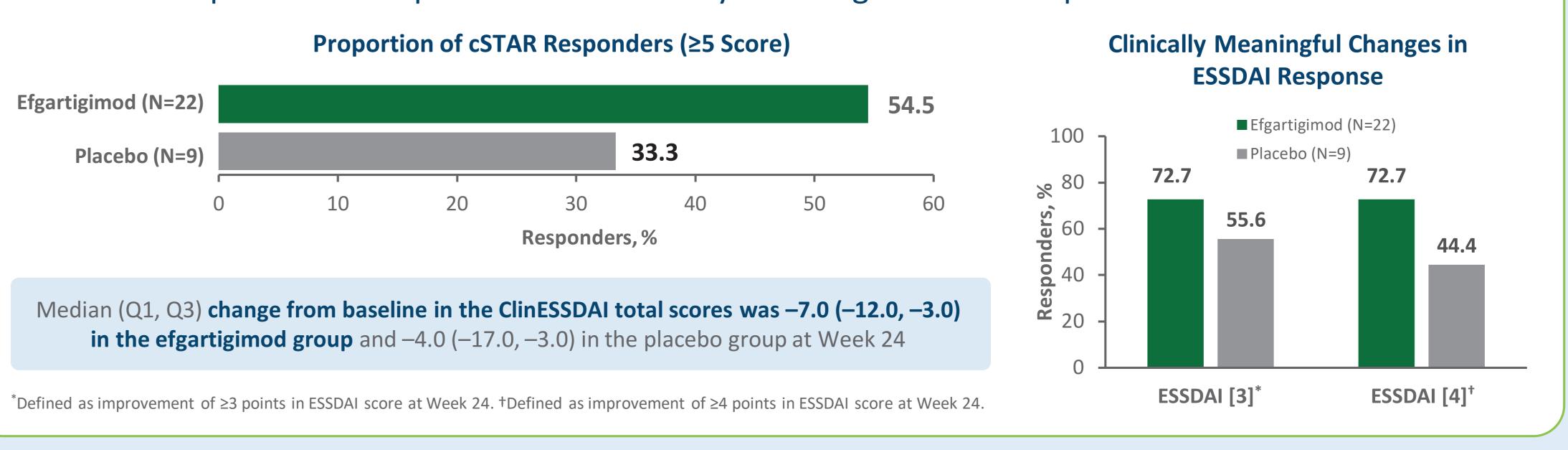
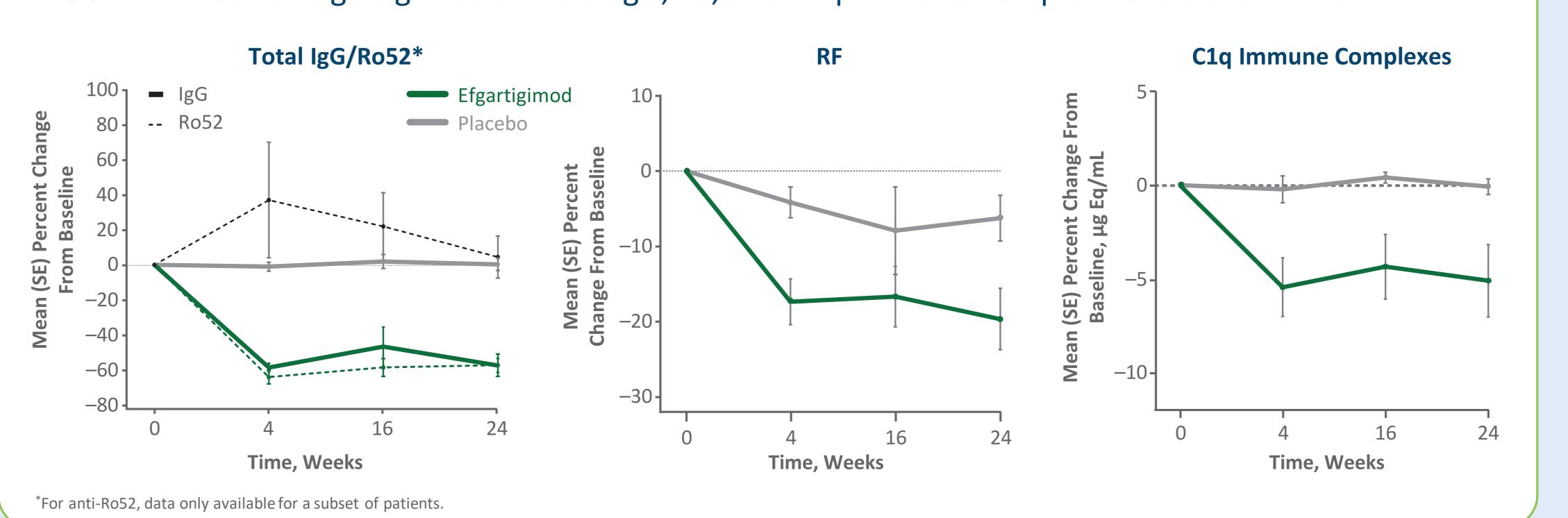


FIGURE 4 Effect Of Efgartigimod on Total IgG, RF, and C1q Immune Complex Levels Over Time



KEY TAKEAWAYS



Results from this proof-of-concept study suggest an improved outcome with efgartigimod treatment compared with placebo for the primary endpoint and secondary endpoints



Treatment with efgartigimod led to a rapid and sustained reduction in total IgG, disease-relevant autoantibodies, and RF



Efgartigimod was safe and well tolerated, with no new safety signals observed



The phase 3 UNITY trial (NCT06684847) is currently underway to assess the efficacy and safety of efgartigimod PH20 SC (administered by prefilled syringe) in patients with SjD with ClinESSDAI ≥6

PRESENTED AT THE AMERICAN COLLEGE OF RHEUMATOLOGY (ACR) CONVERGENCE 2025; OCTOBER 24–29, 2025; CHICAGO, IL, USA

Previously presented at Virginia Society of Rheumatology (VSR) Annual Meeting; Williamsburg, VA, USA.

ABBREVIATIONS

ACR, American College of Rheumatology; AE, adverse event; AESI, adverse events of special interest; C1q, complement component 1q; ClinESSDAI, Clinical EULAR Sjögren's Syndrome Disease Activity Index; CRESS, Composite of Relevant Endpoints for Sjögren's Syndrome; cSTAR, candidate Sjögren's Tool for Assessing Response; ER, event rate (number of events/PYFU); ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; EULAR, European Alliance of Associations for Rheumatology; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; IgG, immunoglobulin G; IV, intravenous; IU, international units; LDL, low-density lipoprotein; m, number of events; MedDRA, Medical Dictionary for Regulatory Activities; N, number of participants; OLE, open-label extension; OSS, ocular staining score; PH20, recombinant human hyaluronidase PH20; PYFU, participant years of follow-up; Q, quartile; R, randomization; RF, rheumatoid factor; SAE, serious adverse event; SC, subcutaneous; SE, standard error; SGUS, salivary gland ultrasound; SjD, Sjögren's disease; SS-A, anti-Sjögren's syndrome-related antigen; SWSF, stimulated whole salivary flow; UWSF, unstimulated whole salivary flow.

DISCLOSURES AND ACKNOWLEDGMENTS

IP: consultant for argenx and BMS; GMV: consultant for argenx; FGMK: consultant for argenx; SA: consultant for argenx, BMS, and Novartis; AK: employee and stockholder of argenx; JR: employee and stockholder of argenx; LV: employee and stockholder of argenx; EB: employee of IQVIA; JJ: employee and stockholder of argenx; PM: employee and stockholder of argenx; JD: nothing to declare; DE: nothing to declare; HB: nothing to declare. The RHO trial is funded by argenx. Medical writing support was provided by Jason Vuong, BPharm, CMPP, of Envision Ignite, an Envision Medical Communications Agency, part of Envision Pharma Group, and funded by argenx.

REFERENCES

1. Negrini S, et al. Clin Exp Med. 2022;22:9–25. 2. Roszkowska AM, et al. Genes (Basel). 2021;12:365. 3. Zhang H, et al. *Medicine (Baltimore)*. 2015;94:e387. **4**. Vílchez-Oya F, et al. *Front Immunol*. 2022;13:1003054. **5**. Kelly AL, et al. J Clin Med. 2022;11:5227. 6. Veenbergen S, et al. J Transl Autoimmun. 2022;5:100138. 7. Ulrichts P, et al. J Clin Invest. 2018;128:4372–86. 8. Vaccaro C, et al. Nat Biotechnol. 2005;23:1283–8. 9. Howard JF, Jr., et al. Lancet Neurol. 2021;20:526–36. **10**. Guptill JT, et al. *Autoimmunity*. 2022;55:620–31. **11**. argenx, data on file. **12**. Roopenian DC, Akilesh S. Nat Rev Immunol. 2007;7:715–25. 13. Ward ES, Ober RJ. Trends Pharmacol Sci. 2018;39:892–904.



