Guselkumab improves health-related quality of life as measured by PROMIS-29 in participants with moderately to severely active Crohn's disease: Phase 3 GRAVITI study

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Key Takeaways

- **Among participants with moderately to severely active CD, GUS SC induction and maintenance therapy sustained clinically meaningful improvements in HRQoL through Week 48 as measured by the PROMIS-29, which included assessments of:**
  - **Anxiety**
  - **Depression**
  - **Fatigue**
  - **Pain interference**
  - **Sleep disturbance**
  - **Physical function**
  - **Social participation**
  - **Pain intensity**

Background

- Crohn's disease (CD) symptoms are associated with impaired health-related quality of life (HRQoL)
- Guselkumab (GUS) is a selective dual-acting interleukin (IL)-23p19 subunit inhibitor that potently blocks IL-23 and binds to CD64, a receptor on cells that produce IL-23[1]
- GRAVITI (NCT05197049) is a 48-week, randomized, double-blind, placebo (PBO)-controlled treat-through trial assessing the efficacy and safety of subcutaneous (SC) GUS induction and maintenance in participants with moderately to severely active CD[2]

Objective

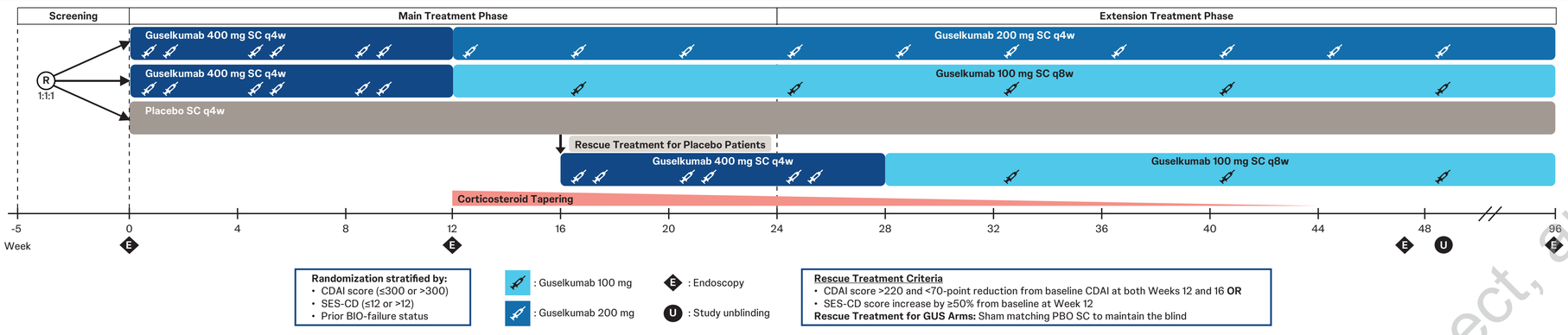
- **To report the effect of GUS SC induction and maintenance therapy on HRQoL through Week 48 in GRAVITI participants as measured by the 29-item Patient-Reported Outcomes Measurement Information System (PROMIS-29)**

Methods

Phase 3, Double-blind, Treat-through Design: GRAVITI

Key eligibility criteria

- *Moderately to severely active CD (CDAI score 220–450 AND either mean daily SF count ≥4 OR AP score ≥2) and SES-CD score ≥6 (or ≥4 for isolated ileal disease)*
- *Inadequate response/intolerance to oral corticosteroids, 6-MP/AZA/MTX, or biologic therapies[a]*



[a]Biologic therapies: TNF antagonists or vedolizumab. ***6-MP****=6-mercaptopurine;* ***AP****=abdominal pain;* ***AZA****=azathioprine;* ***BIO****=biologic;* ***CDAI****=Crohn's disease activity index;* ***MTX****=methotrexate;* ***q4w****=every four weeks;* ***q8w****=every eight weeks;* ***SES-CD****=simple endoscopic score for Crohn's disease;* ***SF****=stool frequency;* ***TNF****=tumor necrosis factor.*

- The raw score of each domain is converted into a standardized T-score with a general population mean of 50 and standard deviation of 10
- Physical component summary (PCS) and mental component summary (MCS) scores are derived from physical and mental domain T-scores, respectively
- Depending on the domain/score, improvement of ≥3 to ≥9 points from induction baseline was identified as clinically meaningful[3]

Results

Baseline Demographics and Disease Characteristics

Full analysis set	Placebo (N=117)	Guselkumab 400 mg SC q4w → 100 mg SC q8w (N=115)	Guselkumab 400 mg SC q4w → 200 mg SC q4w (N=115)	Total (N=347)
Demographics				
Age in years, mean (SD)	36.0 (12.71)	37.4 (13.32)	39.1 (12.56)	37.5 (12.89)
Male, n (%)	67 (57.3%)	66 (57.4%)	70 (60.9%)	203 (58.5%)
Characteristics				
CD duration in years, mean (SD)	7.0 (7.75)	9.2 (9.08)	7.9 (7.13)	8.0 (8.05)
CDAI score, mean (SD)	293.0 (49.09)	300.4 (54.32)	297.3 (54.69)	296.9 (52.68)
SES-CD score, mean (SD)	12.0 (6.89)	12.2 (6.85)	11.8 (7.12)	12.0 (6.94)
Endoscopic disease severity (SES-CD score), n (%)				
Moderate (7–16)	61 (52.1%)	64 (55.7%)	49 (42.6%)	174 (50.1%)
Severe (>16)	25 (21.4%)	26 (22.6%)	27 (23.5%)	78 (22.5%)
Involved GI areas by central reader, n (%)				
Colon only	40 (34.2%)	41 (35.7%)	40 (34.8%)	121 (34.9%)
Ileum only	22 (18.8%)	25 (21.7%)	27 (23.5%)	74 (21.3%)
Ileum and Colon	55 (47.0%)	49 (42.6%)	48 (41.7%)	152 (43.8%)
CRP in mg/L, median (IQR)	7.9 (2.1; 14.7)	5.2 (1.7; 13.3)	5.7 (1.7; 16.1)	5.8 (1.8; 14.9)
Fecal calprotectin in µg/g,[a] median (IQR)	712.0 (243.0; 1724.0)	610.0 (226.0; 1554.0)	600.5 (235.0; 1650.0)	643.0 (235.0; 1650.0)

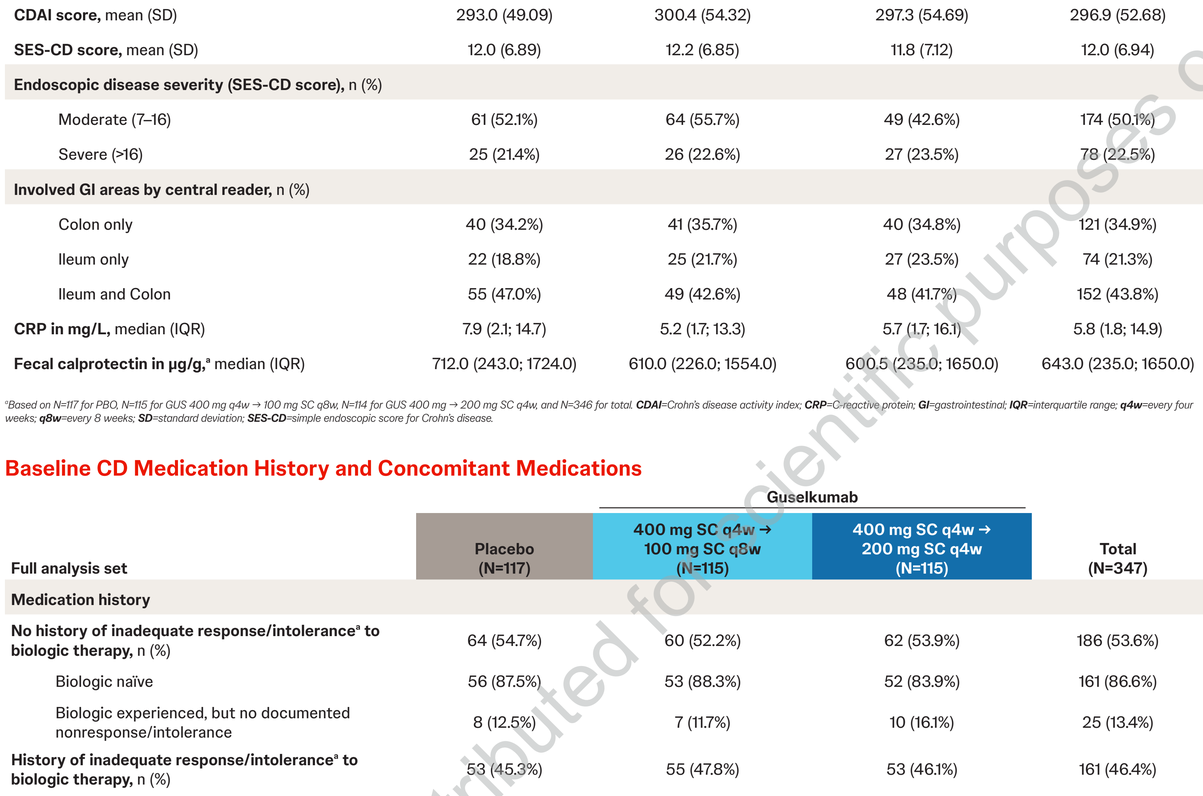
[a]Based on N=117 for PBO, N=115 for GUS 400 mg q4w → 100 mg SC q8w, N=114 for GUS 400 mg → 200 mg SC q4w, and N=346 for total. ***CDAI****=Crohn's disease activity index;* ***CRP****=C-reactive protein;* ***GI****=gastrointestinal;* ***IQR****=interquartile range;* ***q4w****=every four weeks;* ***q8w****=every eight weeks;* ***SD****=standard deviation;* ***SES-CD****=simple endoscopic score for Crohn's disease.*

Baseline CD Medication History and Concomitant Medications

Full analysis set	Placebo (N=117)	Guselkumab 400 mg SC q4w → 100 mg SC q8w (N=115)	Guselkumab 400 mg SC q4w → 200 mg SC q4w (N=115)	Total (N=347)
Medication history				
No history of inadequate response/intolerance[a] to biologic therapy, n (%)	64 (54.7%)	60 (52.2%)	62 (53.9%)	186 (53.6%)
Biologic naïve	56 (87.5%)	53 (88.3%)	52 (83.9%)	161 (86.6%)
Biologic experienced, but no documented nonresponse/intolerance	8 (12.5%)	7 (11.7%)	10 (16.1%)	25 (13.4%)
History of inadequate response/intolerance[a] to biologic therapy, n (%)	53 (45.3%)	55 (47.8%)	53 (46.1%)	161 (46.4%)
At least one anti-TNF	50 (94.3%)	51 (92.7%)	52 (98.1%)	153 (95.0%)
Two or more anti-TNFs	11 (20.8%)	12 (21.8%)	13 (24.5%)	36 (22.4%)
Vedolizumab	8 (15.1%)	13 (23.6%)	6 (11.3%)	27 (16.8%)
Concomitant medications				
Participants with ≥1 CD medication at baseline, n (%)	79 (67.5%)	74 (64.3%)	84 (73.0%)	237 (68.3%)
6-mercaptopurine/Azathioprine/Methotrexate	33 (28.2%)	29 (25.2%)	37 (32.2%)	99 (28.5%)
Oral corticosteroids	33 (28.2%)	32 (27.8%)	38 (33.0%)	103 (29.7%)

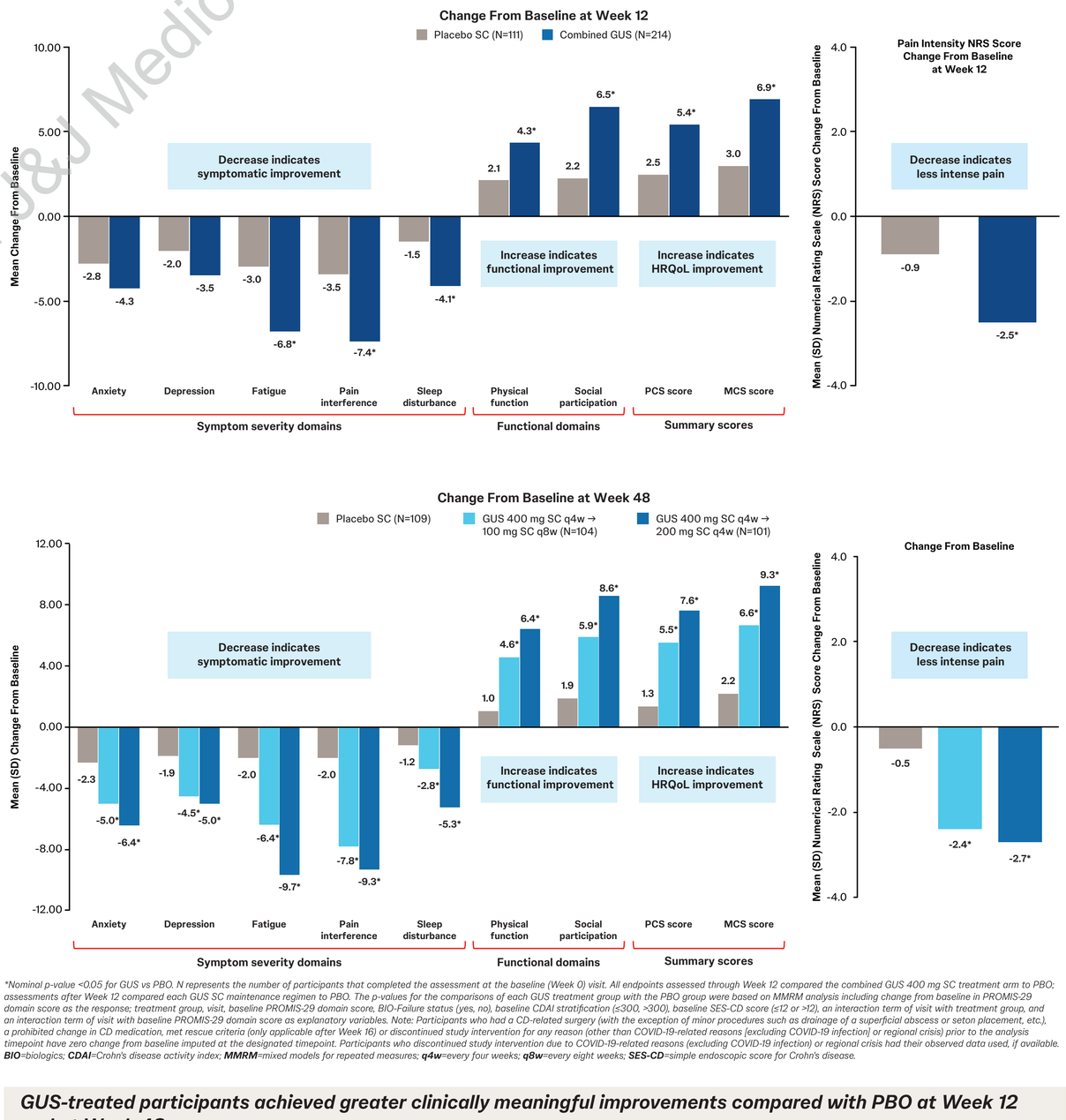
[a]Primary nonresponse, secondary nonresponse, or intolerance. ***q4w****=every four weeks;* ***q8w****=every eight weeks;* ***TNF****=tumor necrosis factor.*

Baseline mean PROMIS-29 scores indicated impaired HRQoL



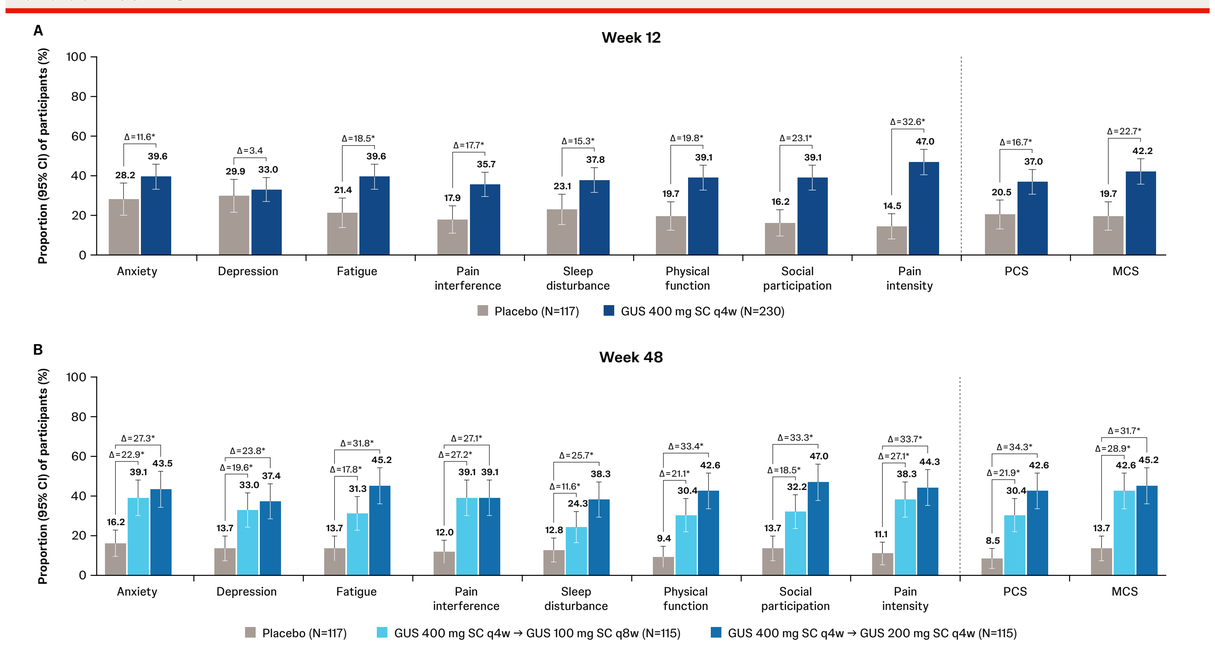
[a]Scores higher or lower than the mean trend towards more severe symptoms, worse function, or worse HRQoL, as indicated in light blue boxes. N represents the number of participants that completed the assessment at the baseline (Week 0) visit. ***q4w****=every four weeks;* ***q8w****=every eight weeks;* ***SD****=standard deviation.*

GUS-treated participants achieved greater improvements from baseline in PROMIS-29 scores at Week 12 and Week 48 compared with PBO



Nominal p-value <0.05 for GUS vs PBO. N represents the number of participants that completed the assessment at the baseline (Week 0) visit. All endpoints assessed through Week 12 compared the combined GUS 400 mg SC treatment arm to PBO; assessments after Week 12 compared each GUS SC maintenance regimen to PBO. The p-values for the comparisons of each GUS treatment group with the PBO group were based on MMRM analysis including change from baseline in PROMIS-29 domain score as the response; treatment group, visit, baseline PROMIS-29 domain score, BIO-Failure status (yes, no), baseline CDAI stratification (≤300, >300), baseline SES-CD score (≤12 or >12), an interaction term of visit with treatment group, and an interaction term of visit with baseline PROMIS-29 domain score as explanatory variables. Note: Participants who had a CD-related surgery (with the exception of minor procedures such as drainage of a superficial abscess or seton placement, etc.), a prohibited change in CD medication, met rescue criteria (only applicable after Week 16) or discontinued study intervention for any reason (other than COVID-19-related reasons [excluding COVID-19 infection] or regional crisis) prior to the analysis timepoint have zero change from baseline imputed at the designated timepoint. Participants who discontinued study intervention due to COVID-19-related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available.* ***BIO**=biologics;* ***CDAI****=Crohn's disease activity index;* ***MMRM****=mixed models for repeated measures;* ***q4w****=every four weeks;* ***q8w****=every eight weeks;* ***SES-CD****=simple endoscopic score for Crohn's disease.*

GUS-treated participants achieved greater clinically meaningful improvements compared with PBO at Week 12 and at Week 48



Nominal p-value <0.05 for GUS vs PBO. Clinically meaningful improvement was according to previously defined thresholds for each domain and the MCS and PCS (pain intensity ≥3; anxiety, depression, sleep disturbance, and physical function ≥5; fatigue, social participation, PCS, and MCS ≥7; pain interference ≥9).[3] Participants who had a CD-related surgery, a prohibited change in concomitant CD medication, met rescue criteria (only applicable after Week 16) or discontinued study intervention for any reason (other than COVID-19-related reasons [excluding COVID-19 infection] or regional crisis) prior to the analysis timepoint were considered not to have achieved the binary endpoint from that timepoint onwards. Participants who had discontinued study agent due to COVID-19-related reasons (excluding COVID-19 infection) or regional crisis had their observed data used, if available, to determine responder status from that timepoint onwards. Note: The confidence intervals for the proportion of subjects meeting the endpoint in each treatment group were based on the normal approximation confidence limits. The treatment differences (Δ), confidence intervals, and p-values were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator. The stratification factors were baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), and BIO-Failure status at baseline (yes or no).* ***BIO**=biologics;* ***CDAI****=Crohn's disease activity index;* ***CI****=confidence interval;* ***q4w****=every four weeks;* ***q8w****=every eight weeks;* ***SES-CD****=simple endoscopic score for Crohn's disease.*

PRESENTED BY: A. Hart at the 20th Congress of European Crohn's and Colitis Organization (ECCO), February 19–22, 2025, Berlin, Germany. **REFERENCES: 1.** Atreya R, et al. *J Crohns Colitis*. 2024;18(suppl):S470. **2.** Panaccione R, et al. *Am J Gastro*. 2024;119(10S):p S740-S741. **3.** Sands BE, et al. *Value Health*. 2024;27(9):1225-1234. **ACKNOWLEDGMENTS:** Medical writing support was provided by Jackie L. Johnson, PhD of Certara under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298-1304). Sponsored by Janssen Research & Development, LLC, a Johnson & Johnson Company. **DISCLOSURES: BES:** reports consulting fees from AbbVie, Adiso Therapeutics, Agomab, Alimentiv, Amgen, AnaptysBio, Arena Pharmaceuticals, Artugen Therapeutics, Astra Zeneca, Biolojic Design, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Calibr, Celgene, Celltrion, ClostraBio, Equillium, Enthera, Envied Biosciences, Evommune, Ferring, Fresenius Kabi, Fiat, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Imhotex, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Kaleido, Kallyope, Merck, Microba, Mobius Care, Morphic Therapeutics, MRM Health, Nexus Therapeutics, Nimbus Discovery, Odyssey Therapeutics, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Rasayana Therapeutics, Recludix Therapeutics, Reistone Biopharma, Sanofi, Spyre Therapeutics, Sun Pharma, Surrozen, Target RWE, Teva, TLL Pharmaceutical, Tr1X, Union Therapeutics, and Ventyx Biosciences; consulting and speaking fees from Abivax; consulting and speaking fees and other support from Lilly; research grants, consulting and speaking fees and other support from Bristol Myers Squibb, Janssen, Pfizer, and Takeda; research grants and consulting fees from Theravance Biopharma; and stock/stock options from Ventyx Biopharma. **SD:** reports consultancy fees from AbbVie, Alimentiv, Allergan, Amgen, AstraZeneca, Athos, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Enthera, Ferring, Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity, Takeda, TiGenix, UCB, and Vifor; and reports lecture fees from AbbVie, Amgen, Ferring, Gilead, Janssen, Mylan, Pfizer, and Takeda. **QC:** received grant support from Janssen Pharmaceutical K.K, and Takeda Pharmaceutical Co. Ltd; and consulting fees from Janssen Pharmaceutical K.K. **FS:** served as a clinical investigator and consultant for AbbVie, Amgen, Celltrion, Ferring, Janssen, Pfizer, Sandoz, and Takeda. **JK:** served as a clinical investigator and consultant for Janssen. **CH, MO, ZY, EM,** and **NAT:** are employees of and may own stock in Johnson & Johnson. **AH:** served as a clinical investigator and consultant for Janssen.