Table e-1: Primary and secondary cognitive and clinical outcomes in low-dose 300 mg SC cohort at Week 73 (placebo vs. crenezumab, mITT population)

ADAS-Cog12									
MMSE range	n (placebo)	n (crenezumab)	Placebo LSM (SE)	Crenezumab LSM (SE)	Difference (SE)	95% CI	p-value	Reduction*	Effect size† (SD)
18–26	45	88	7.85 (1.13)	7.81 (0.81)	0.04 (1.40)	–2.73, 2.81	0.977	0.5%	0.00 (8.15)
20–26	31	62	5.97 (1.36)	5.96 (0.97)	0.01 (1.67)	–3.33, 3.35	0.995	0.2%	0.00 (8.12)
22–26‡	22	41	4.14 (1.71)	5.65 (1.22)	–1.52 (2.10)	–5.79, 2.75	0.476	–37.0%	–0.18 (8.29)
18–19	14	26	11.83 (1.88)	12.29 (1.36)	–0.46 (2.33)	–5.16, 4.24	0.843	–3.9%	–0.06 (7.38)
18–21	23	47	10.95 (1.49)	9.65 (1.07)	1.31 (1.83)	–2.34, 4.95	0.478	11.9%	0.17 (7.89)
CDR-SB									

MMSE range	n (placebo)	n (crenezumab)	Placebo LSM (SE)	Crenezumab LSM (SE)	Difference (SE)	95% CI	p-value	Reduction*	Effect size† (SD)
18–26	47	88	2.70 (0.36)	2.01 (0.26)	0.69 (0.45)	–0.20, 1.57	0.128	25.4%	0.26 (2.63)
20–26	33	62	2.18 (0.43)	1.47 (0.31)	0.71 (0.53)	–0.34, 1.75	0.181	32.6%	0.27 (2.59)
22–26‡	23	41	1.20 (0.49)	1.34 (0.35)	–0.14 (0.61)	–1.35, 1.07	0.819	–12.0%	–0.06 (2.40)
18–19	14	26	3.89 (0.64)	3.32 (0.47)	0.57 (0.79)	–1.03, 2.17	0.475	14.7%	0.23 (2.54)
18–21	24	47	4.01 (0.50)	2.62 (0.37)	1.39 (0.62)	0.16, 2.63	0.028	34.7%	0.51 (2.71)
ADCS-ADL									
MMSE range	n (placebo)	n (crenezumab)	Placebo LSM (SE)	Crenezumab LSM (SE)	Difference (SE)	95% CI	p-value	Reduction*	Effect size† (SD)

18–26	47	88	–10.1 (3.38)	–12.4 (2.52)	–1.42 (1.91)	–5.20, 2.37	0.461	16.8%	–0.13 (11.3)
20–26	33	63	–12.0 (2.29)	–10.4 (1.71)	–2.78 (2.14)	–7.02, 1.46	0.196	35.6%	–0.26 (10.5)
22–26‡	23	41	–4.31 (1.85)	–3.21 (1.33)	–1.10 (2.28)	–5.66, 3.46	0.632	25.5%	–0.12 (8.98)
18–19	14	25	–10.1 (3.38)	–12.4 (2.52)	2.31 (4.25)	–6.33, 10.95	0.590	–23.0%	0.17 (13.5)
18–21	24	47	–12.0 (2.29)	–10.4 (1.71)	–1.63 (2.86)	–7.33, 4.08	0.571	13.6%	–0.13 (12.5)

*Percentage reduction relative to placebo. †Standardized effect size. ‡Exploratory post hoc analysis.

Abbreviations: ADAS-Cog12 = 12-point Alzheimer's Disease Assessment Scale-Cognitive Subscale; ADCS-ADL = Alzheimer's Disease Cooperative Study–Activities of Daily Living; CDR-SB = Clinical Dementia Rating-Sum of Boxes; LSM = least squares mean; mITT = modified intent-to-treat; MMSE = Mini-Mental State Exam; SC = subcutaneous; SE = standard error.

Table e-2: Primary, secondary, and exploratory clinical outcomes in high-dose 15 mg/kg IV cohort at Week 73 stratified by MMSE score (placebo vs. crenezumab; mITT population)

ADAS-Cog12									
MMSE range	n (placebo)	n (crenezumab)	Placebo LSM (SE)	Crenezumab LSM (SE)	Difference (SE)	95% CI	p-value	Reduction*	Effect size† (SD)
18–26	64	122	10.56 (1.09)	8.79 (0.79)	1.78 (1.35)	–0.89, 4.44	0.190	16.8%	0.20 (9.08)
19–26	56	105	10.18 (1.15)	8.07 (0.84)	2.12 (1.42)	–0.69, 4.93	0.139	20.8%	0.24 (8.89)
20–26	47	93	9.43 (1.20)	7.18 (0.85)	2.24 (1.47)	–0.66, 5.15	0.128	23.8%	0.27 (8.44)
21–26	39	83	9.22 (1.30)	6.96 (0.90)	2.26 (1.58)	–0.88, 5.39	0.157	24.5%	0.27 (8.40)
22–26	33	70	9.70 (1.33)	6.26 (0.91)	3.44 (1.61)	0.24, 6.64	0.036	35.4%	0.44 (7.80)

23–26	24	60	7.92 (1.44)	5.51 (0.91)	2.40 (1.70)	–0.99, 5.79	0.163	30.3%	0.33 (7.18)
24–26	16	45	7.41 (1.77)	4.58 (1.06)	2.83 (2.07)	–1.31, 6.97	0.176	38.2%	0.39 (7.25)
25–26	11	30	6.88 (2.13)	3.51 (1.31)	3.37 (2.50)	–1.68, 8.43	0.185	49.0%	0.47 (7.21)
26–26	6	19	7.37 (2.92)	3.47 (1.65)	3.90 (3.40)	–3.15, 10.96	0.263	53.0%	0.55 (7.14)
CDR–SB									
MMSE range	n (placebo)	n (crenezumab)	Placebo LSM (SE)	Crenezumab LSM (SE)	Difference (SE)	95% CI	p-value	Reduction*	Effect size† (SD)
18–26	67	126	2.57 (0.35)	2.49 (0.25)	0.08 (0.43)	–0.77, 0.92	0.853	3.1%	0.03 (2.94)
19–26	58	108	2.65 (0.38)	2.43 (0.28)	0.22 (0.47)	–0.71, 1.15	0.641	8.3%	0.07 (3.02)

20–26	48	96	2.18 (0.40)	2.21 (0.28)	–0.02 (0.49)	–1.00, 0.96	0.964	–1.0%	–0.01 (2.91)
21–26	40	85	2.26 (0.45)	2.16 (0.31)	0.10 (0.54)	–0.97, 1.18	0.848	4.6%	0.04 (2.98)
22–26	34	71	2.24 (0.45)	1.80 (0.31)	0.44 (0.55)	–0.65, 1.52	0.423	19.6%	0.16 (2.75)
23–26	24	60	1.88 (0.45)	1.48 (0.28)	0.40 (0.53)	–0.65, 1.45	0.449	21.4%	0.18 (2.25)
24–26	16	45	1.87 (0.45)	1.02 (0.27)	0.85 (0.52)	–0.21, 1.91	0.114	45.4%	0.46 (1.85)
25–26	11	30	1.95 (0.44)	0.71 (0.27)	1.24 (0.52)	(0.19, 2.29)	0.022	63.6%	0.83 (1.50)
26–26	6	19	1.83 (0.65)	0.83 (0.36)	1.00 (0.75)	–0.55, 2.54	0.196	54.4%	0.64 (1.56)
ADCS-ADL									

MMSE range	n (placebo)	n (crenezumab)	Placebo LSM (SE)	Crenezumab LSM (SE)	Difference (SE)	95% CI	p-value	Reduction*	Effect size† (SD)
18–26	68	125	−9.04 (1.44)	−9.55 (1.06)	0.51 (1.79)	−3.02, 4.04	0.775	−5.7%	0.04 (12.3)
19–26	58	107	−7.76 (1.45)	−8.70 (1.07)	0.93 (1.80)	−2.63, 4.50	0.605	−12.0%	0.08 (11.4)
20–26	48	95	−5.96 (1.57)	−8.14 (1.12)	2.18 (1.93)	−1.64, 6.00	0.260	−37.0%	0.19 (11.2)
21–26	40	84	−5.78 (1.68)	−7.35 (1.17)	1.57 (2.05)	−2.48, 5.63	0.444	−27.2%	0.14 (11.0)
22–26	34	70	−6.21 (1.71)	−6.34 (1.20)	0.12 (2.10)	−4.04, 4.29	0.953	−2.0%	0.01 (10.3)
23–26	24	59	−4.52 (1.79)	−5.02 (1.14)	0.50 (2.13)	−3.73, 4.74	0.814	−11.1%	0.06 (8.90)

24–26	16	44	−3.43 (1.99)	−3.67 (1.21)	0.24 (2.34)	–4.46, 4.93	0.920	–6.9%	0.03 (8.16)
25–26	11	29	−3.60 (2.46)	−3.09 (1.56)	–0.51 (2.92)	–6.43, 5.41	0.862	14.2%	–0.06 (8.42)
26–26	6	18	−4.59 (3.85)	−2.64 (2.28)	–1.95 (4.50)	–11.2, 7.32	0.669	42.4%	–0.20 (9.64)

*Percentage reduction relative to placebo. †Standardized effect size.

Abbreviations: ADAS-Cog12 = 12-point Alzheimer's Disease Assessment Scale-Cognitive Subscale; ADCS-ADL = Alzheimer's Disease Cooperative Study–Activities of Daily Living; CDR-SB = Clinical Dementia Rating-Sum of Boxes; LSM = least squares mean; mITT = modified intent-to-treat; MMSE = Mini-Mental State Exam; SE = standard error.

Table e-3: Summary of ARIA events

	300 mg SC q2wk (low dose)		15 mg/kg IV q4wk (high dose)*		All patients	
	Placebo (n = 62)	Crenezumab (n = 122)	Placebo (n = 82)	Crenezumab (n = 165)	Placebo (n = 144)	Crenezumab (n = 300)
Any ARIA-E, n	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	1 (0.3%)
Symptomatic, n	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Asymptomatic, n	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	1 (0.3%)
Superficial siderosis, n	1 (1.6%)	1 (0.8%)	1 (1.2%)	0 (0%)	2 (1.4%)	1 (0.3%)
Macrohemorrhage, n	0 (0%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	1 (0.3%)
New ARIA-H, n	10 (16.1%)	16 (13.1%)	11 (13.4%)	15 (9.1%)	21 (14.6%)	31 (10.3%)
Symptomatic, n	1 (1.6%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	0 (0%)
1 microhemorrhage, n	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2–4 microhemorrhages, n	1 (1.6%)	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	0 (0%)
Asymptomatic, n	9 (14.5%)	16 (13.1%)	11 (13.4%)	15 (9.1%)	20 (13.9%)	31 (10.3%)
1 microhemorrhage, n	2 (3.2%)	0 (0%)	0 (0%)	3 (1.8%)	2 (1.4%)	3 (1.0%)
2–4 microhemorrhages, n	7 (11.3%)	16 (13.1%)	11 (13.4%)	12 (7.3%)	18 (12.5%)	28 (9.3%)

*Safety population; does not include SRI cohort.

Abbreviations: ARIA-E = Amyloid-related imaging abnormalities: vasogenic edema or effusions; ARIA-H = Amyloid-related imaging abnormalities: microhemorrhage and siderosis; q2wk = every 2 weeks; q4wk = every 4 weeks; SC = subcutaneous.