

**Table S1. Efficacy endpoints at week 12 assessed by treatment policy estimand.**

|                  | 150 mg Q2W              |                     |                      | 450 mg Q4W              |                     |                      |
|------------------|-------------------------|---------------------|----------------------|-------------------------|---------------------|----------------------|
|                  | Tafolecimab<br>(n = 52) | Placebo<br>(n = 23) | ETD versus placebo   | Tafolecimab<br>(n = 48) | Placebo<br>(n = 25) | ETD versus placebo   |
| <b>LDL-C</b>     |                         |                     |                      |                         |                     |                      |
| Percent CFB (%)* | -55.7 (5.9)             | -1.1 (6.4)          | -54.6 (-66.5, -42.6) | -62.0 (5.7)             | -1.3 (6.5)          | -60.7 (-71.3, -50.0) |
| ≥50% reduction*  | 28 (53.8)               | 0                   | 54.1 (37.8, 70.3)    | 37 (77.1)               | 0                   | 75.4 (60.8, 90.1)    |
| <1.8 mmol/L*     | 25 (48.1)               | 1 (4.3)             | 44.5 (26.0, 63.1)    | 31 (64.6)               | 0                   | 62.2 (45.8, 78.6)    |

Data are least squares mean (standard error) for CFB, n (%) for LDL-C target attainment rates, least squares mean (97.5%CI) for ETD.

$P < 0.0001$  for all comparisons versus placebo.

\*controlled for type I error (pairwise  $\alpha = 0.025$ ).

CFB = change from baseline; ETD = estimated treatment difference; LDL-C = low density lipoprotein cholesterol; Q2W = every 2 weeks; Q4W = every 4 weeks.

**Table S2. Descriptive statistics for endpoints in lipids and unbound PCSK9 levels at week 12 and week 24.**

|  | Tafolecimab 150 mg<br>Q2W | Placebo 150 mg<br>Q2W | Tafolecimab 450 mg<br>Q4W | Placebo 450 mg<br>Q4W |
|--|---------------------------|-----------------------|---------------------------|-----------------------|
| <b>LDL-C</b>                               |                           |                       |                           |                       |
| Baseline, mmol/L                           | 4.25 (1.115)              | 4.27 (0.975)          | 4.21 (1.143)              | 4.32 (1.223)          |
| Percent CFB at week 12                     | -54.67 (17.257)           | 3.75 (18.622)         | -59.16 (17.585)           | 1.77 (21.660)         |
| Percent CFB at week 24                     | -49.61 (23.505)           | -49.81 (27.545)       | -56.00 (22.257)           | -52.64 (22.821)       |
| ≥50% reduction from<br>baseline to week 24 | 23 (50.0)                 | 14 (60.9)             | 35 (72.9)                 | 18 (78.3)             |
| <1.8 mmol/L at week 24                     | 21 (45.7)                 | 9 (39.1)              | 28 (58.3)                 | 12 (52.2)             |
| <b>Lipoprotein(a)</b>                      |                           |                       |                           |                       |
| Baseline, g/L                              | 0.29 (0.09–0.53)          | 0.32 (0.10–0.46)      | 0.19 (0.10–0.50)          | 0.28 (0.12–0.49)      |
| Percent CFB at week 12                     | -40.33 (24.545)           | 3.78 (34.134)         | -39.85 (26.531)           | -6.57 (21.080)        |
| Percent CFB at week 24                     | -38.60 (20.415)           | -37.02 (23.095)       | -40.61 (26.175)           | -29.83 (31.649)       |
| <b>Apolipoprotein B</b>                    |                           |                       |                           |                       |
| Baseline, g/L                              | 1.20 (0.297)              | 1.21 (0.267)          | 1.19 (0.305)              | 1.23 (0.308)          |
| Percent CFB at week 12                     | -51.09 (18.069)           | 8.96 (46.148)         | -56.02 (16.855)           | -0.39 (16.411)        |
| Percent CFB at week 24                     | -47.79 (23.730)           | -49.50 (24.392)       | -51.79 (22.453)           | -52.54 (19.906)       |
| <b>non-HDL-C</b>                           |                           |                       |                           |                       |
| Baseline, mmol/L                           | 4.65 (1.284)              | 4.72 (1.104)          | 4.60 (1.332)              | 4.75 (1.369)          |
| Percent CFB at week 12                     | -55.53 (18.933)           | 3.02 (18.931)         | -59.74 (19.096)           | 0.32 (20.167)         |
| Percent CFB at week 24                     | -50.14 (23.515)           | -51.32 (28.399)       | -56.49 (23.990)           | -53.47 (25.402)       |
| <b>HDL-C</b>                               |                           |                       |                           |                       |
| Baseline, mmol/L                           | 1.21 (0.254)              | 1.17 (0.190)          | 1.25 (0.283)              | 1.23 (0.269)          |
| Percent CFB at week 12                     | 2.17 (14.795)             | 6.28 (12.742)         | 0.91 (12.919)             | 3.29 (11.662)         |
| Percent CFB at week 24                     | 7.93 (17.917)             | 4.42 (12.875)         | 4.10 (12.884)             | 4.89 (11.887)         |
| <b>Triglycerides</b>                       |                           |                       |                           |                       |
| Baseline, mmol/L                           | 1.48 (0.941)              | 1.66 (1.182)          | 1.59 (1.126)              | 1.54 (0.926)          |
| Percent CFB at week 12                     | -5.01 (48.027)            | 0.53 (38.718)         | -3.48 (44.278)            | 13.81 (57.704)        |
| Percent CFB at week 24                     | -10.53 (32.209)           | -17.47 (30.444)       | -14.68 (28.449)           | -3.80 (45.644)        |
| <b>Total cholesterol</b>                   |                           |                       |                           |                       |
| Baseline, mmol/L                           | 5.86 (1.350)              | 5.88 (1.157)          | 5.85 (1.332)              | 5.97 (1.407)          |
| Percent CFB at week 12                     | -43.16 (15.301)           | 3.91 (15.075)         | -45.94 (14.647)           | 0.52 (17.050)         |
| Percent CFB at week 24                     | -38.04 (19.740)           | -39.54 (23.466)       | -43.12 (18.969)           | -40.99 (21.191)       |
| <b>vLDL-C</b>                              |                           |                       |                           |                       |
| Baseline, mmol/L                           | 0.67 (0.419)              | 0.69 (0.352)          | 0.68 (0.379)              | 0.70 (0.413)          |
| Percent CFB at week 12                     | -5.35 (44.176)            | -3.87 (25.124)        | -6.88 (35.142)            | 12.96 (59.628)        |
| Percent CFB at week 24                     | -10.35 (32.659)           | -11.68 (33.710)       | -14.06 (30.884)           | -7.09 (48.238)        |
| <b>Unbound PCSK9</b>                       |                           |                       |                           |                       |
| Baseline, ng/mL                            | 707.28 (231.053)          | 795.74 (218.566)      | 785.03 (234.146)          | 708.71 (250.906)      |
| Percent CFB at week 12                     | -68.76 (40.991)           | 4.41 (44.781)         | -79.63 (44.632)           | 21.11 (37.123)        |
| Percent CFB at week 24                     | -55.15 (89.597)           | -66.19 (42.814)       | -81.62 (28.973)           | -62.78 (75.411)       |

Data are mean (standard interquartile range) for baseline lipoprotein(a), n (%) for LDL-C target attainment rates and mean (standard deviation) for the rest. Analysis on endpoints at week 12 and week 24 included only participants with lipids measurement at respective visit. N = 52, 23, 48 and 25 at baseline, n = 44, 22, 48 and 24 at week 12, n = 46, 23, 48 and 23 at week 24, for tafolecimab 150 mg, placebo 150 mg, tafolecimab 450 mg and placebo 450 mg, respectively.

CFB = change from baseline; LDL-C = low density lipoprotein cholesterol; HDL-C = high density lipoprotein cholesterol; non-HDL-C = non-high density lipoprotein cholesterol; Q2W = every 2 weeks; Q4W = every 4 weeks; vLDL-C = very low density lipoprotein cholesterol.

**Table S3. Most commonly-reported treatment-emergent adverse events (≥5% in any group) in participants receiving tafolecimab during the 12-week double-blind treatment period and 24-week treatment period.**

| MedDRA system organ class<br>Preferred term, n (%) | 12-week double-blind<br>treatment     |                                       | 24-week treatment                     |                                       |
|--|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
|  | Tafolecimab<br>150 mg Q2W<br>(n = 52) | Tafolecimab<br>450 mg Q4W<br>(n = 48) | Tafolecimab<br>150 mg Q2W<br>(n = 52) | Tafolecimab<br>450 mg Q4W<br>(n = 48) |
| Any TEAE   | 36 (69.2)                             | 23 (47.9)                             | 39 (75.0)                             | 32 (66.7)                             |
| Infections and infestations                        | 13 (25.0)                             | 6 (12.5)                              | 16 (30.8)                             | 11 (22.9)                             |
| Upper respiratory tract infection                  | 11 (21.2)                             | 2 (4.2)                               | 13 (25.0)                             | 4 (8.3)                               |
| Urinary tract infection                            | 1 (1.9)                               | 2 (4.2)                               | 2 (3.8)                               | 3 (6.3)                               |
| Investigations                                     | 11 (21.2)                             | 5 (10.4)                              | 14 (26.9)                             | 8 (16.7)                              |
| Blood creatine phosphokinase increased             | 3 (5.8)                               | 3 (6.3)                               | 4 (7.7)                               | 5 (10.4)                              |
| Alanine aminotransferase increased                 | 4 (7.7)                               | 0                                     | 6 (11.5)                              | 1 (2.1)                               |
| Aspartate aminotransferase increased               | 4 (7.7)                               | 0                                     | 5 (9.6)                               | 0                                     |
| Musculoskeletal and connective tissue disorders    | 8 (15.4)                              | 4 (8.3)                               | 9 (17.3)                              | 6 (12.5)                              |
| Myalgia  | 3 (5.8)                               | 0                                     | 3 (5.8)                               | 0                                     |
| Skin and subcutaneous tissue disorders             | 5 (9.6)                               | 2 (4.2)                               | 6 (11.5)                              | 2 (4.2)                               |
| Dermatitis allergic                                | 2 (3.8)                               | 0                                     | 3 (5.8)                               | 1 (2.1)                               |
| Metabolism and nutrition disorders                 | 0                                     | 2 (4.2)                               | 5 (9.6)                               | 3 (6.3)                               |
| Hyperuricaemia                                     | 0                                     | 0                                     | 3 (5.8)                               | 1 (2.1)                               |
| Vascular disorders                                 | 4 (7.7)                               | 0                                     | 4 (7.7)                               | 1 (2.1)                               |
| Hypertension                                       | 4 (7.7)                               | 0                                     | 4 (7.7)                               | 1 (2.1)                               |
| Hepatobiliary disorders                            | 2 (3.8)                               | 1 (2.1)                               | 3 (5.8)                               | 1 (2.1)                               |
| Hepatic function abnormal                          | 2 (3.8)                               | 1 (2.1)                               | 3 (5.8)                               | 1 (2.1)                               |

By MedDRA (version 24.0) system organ class and preferred term.

Q2W = every 2 weeks; Q4W = every 4 weeks.