

## Basic Results Summary

### **A study in healthy volunteers to evaluate the effect of repeated LPS skin challenges in a single individual**

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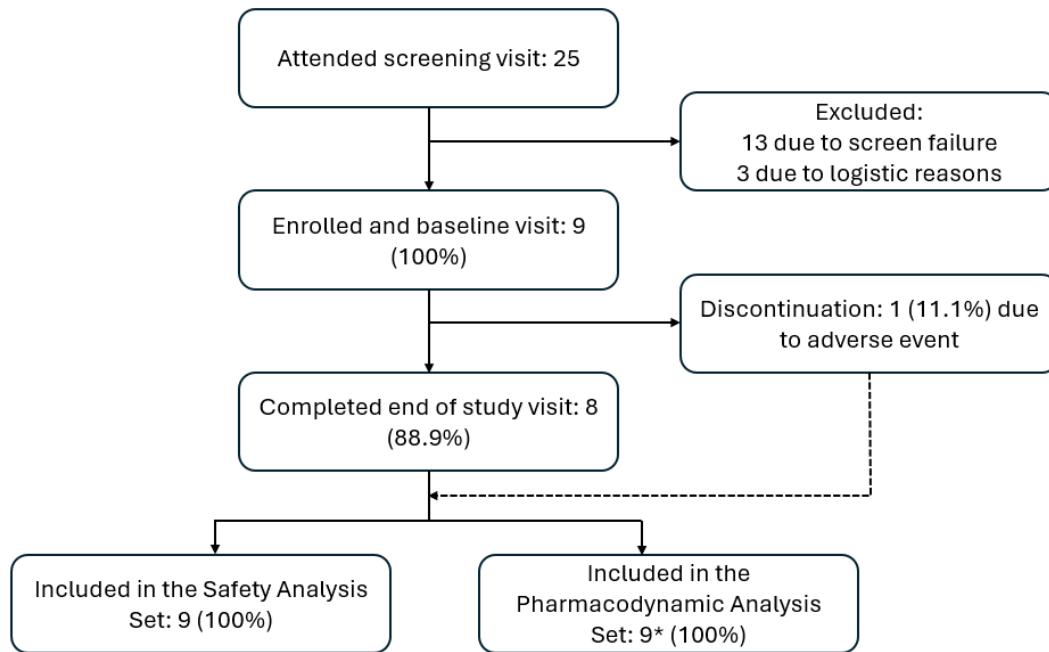
ISRCTN number: ISRCTN13536369

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## Participant flow



*\*One participant remained part of the PD population but is excluded from the PD summary and analysis due to an adverse event, unrelated to the lipopolysaccharide, leading to discontinuation.*

## Baseline characteristics

|                          | ENROLLED SUBJECTS<br>(N=9) |
|--------------------------|----------------------------|
| Age (years)              |                            |
| n                        | 9                          |
| Mean (SD)                | 23.8 (2.8)                 |
| Median                   | 25                         |
| Min, Max                 | 19, 27                     |
| Height (cm)              |                            |
| n                        | 9                          |
| Mean (SD)                | 180.86 (8.82)              |
| Median                   | 176.0                      |
| Min, Max                 | 167.5, 193.0               |
| Weight (kg)              |                            |
| n                        | 9                          |
| Mean (SD)                | 76.94 (13.21)              |
| Median                   | 79.40                      |
| Min, Max                 | 58.15, 93.85               |
| BMI (kg/m <sup>2</sup> ) |                            |
| n                        | 9                          |
| Mean (SD)                | 23.37 (2.42)               |
| Median                   | 22.8                       |
| Min, Max                 | 20.7, 26.9                 |
| Sex                      |                            |
| Female                   | 2 (22.2%)                  |
| Male                     | 7 (77.8%)                  |
| Race                     |                            |
| WHITE                    | 9 (100.0%)                 |

## Primary outcome measures

### 1. Safety

*NB: The NRS pain assessment was performed on Day 1 for the arm and on 1 area on the back, but was not evaluated in comparison to the other LPS challenge sets. As it was not included in the SAP listings and summaries, no output is available.*

#### 1.1. Treatment-emergent (serious) adverse events ((S)AEs).

Please refer to the section [Adverse events](#).

#### 1.2. Safety labs tests (acute phase proteins (CRP), leukocyte differentiation)

| Summary of C-Reactive Protein (CRP) Results |                                 |           |   |        |         |         |        |       |       |   |                      |         |         |        |        |       |
|---------------------------------------------|---------------------------------|-----------|---|--------|---------|---------|--------|-------|-------|---|----------------------|---------|---------|--------|--------|-------|
| Parameter (Unit)                            | Treatment                       | Visit     | N | Result |         |         |        |       |       | N | Change from baseline |         |         |        |        |       |
|                                             |                                 |           |   | mean   | SEM     | SD      | median | min*  | max   |   | mean                 | SEM     | SD      | median | min    | max   |
| High-Sensitivity C Reactive Protein (mg/L)  | LIPOPOLYSAC CHARIDE CHALLENGE 1 | DAY 1     | 9 | 0.5211 | 0.28862 | 0.86587 | 0.190  | 0.075 | 2.660 | 0 |                      |         |         |        |        |       |
|                                             |                                 | DAY 2     | 9 | 1.0283 | 0.39396 | 1.18187 | 0.580  | 0.075 | 3.850 | 9 | 0.5072               | 0.16191 | 0.48572 | 0.300  | 0.000  | 1.380 |
|                                             | LIPOPOLYSAC CHARIDE CHALLENGE 2 | DAY 1     | 8 | 0.6900 | 0.32282 | 0.91308 | 0.235  | 0.075 | 2.740 | 0 |                      |         |         |        |        |       |
|                                             |                                 | DAY 2     | 8 | 1.1419 | 0.78399 | 2.21746 | 0.225  | 0.075 | 6.570 | 8 | 0.4519               | 0.48317 | 1.36662 | -0.010 | -0.160 | 3.830 |
|                                             | LIPOPOLYSAC CHARIDE CHALLENGE 3 | DAY 1     | 8 | 1.0050 | 0.48893 | 1.38290 | 0.325  | 0.075 | 3.480 | 0 |                      |         |         |        |        |       |
|                                             |                                 | DAY 2     | 8 | 1.9256 | 1.09880 | 3.10788 | 0.480  | 0.075 | 8.300 | 8 | 0.9206               | 0.62353 | 1.76362 | 0.080  | -0.175 | 4.820 |
|                                             | NO_TRT                          | SCREENING | 9 | 0.5717 | 0.32771 | 0.98314 | 0.230  | 0.075 | 3.150 |   |                      |         |         |        |        |       |
|                                             |                                 | FOLLOW-UP | 9 | 1.0244 | 0.34144 | 1.02432 | 0.680  | 0.075 | 2.760 |   |                      |         |         |        |        |       |

NO\_TRT: No treatment

\*According to the SAP, safety and PD values below the Limit of Quantification (LOQ) are set to half of the LOQ for summary outputs. As the LOQ for High-Sensitivity C-Reactive Protein is 0.15, the corresponding value used here is 0.075.

| Summary of Leukocytes Results      |                                       |                        |                       |   |        |        |        |        |      |       |   |                      |        |        |        |       |      |
|------------------------------------|---------------------------------------|------------------------|-----------------------|---|--------|--------|--------|--------|------|-------|---|----------------------|--------|--------|--------|-------|------|
| Parameter<br>(Unit)                | Treatment                             | Visit                  | Analysis<br>Timepoint | N | Result |        |        |        |      |       | N | Change from baseline |        |        |        |       |      |
|                                    |                                       |                        |                       |   | mean   | SEM    | SD     | median | min  | max   |   | mean                 | SEM    | SD     | median | min   | max  |
| Leukocytes<br>(10 <sup>9</sup> /L) | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 1 | DAY 1                  | -00D00H36M            | 9 | 4.911  | 0.4361 | 1.3082 | 4.85   | 3.36 | 7.88  | 0 |                      |        |        |        |       |      |
|                                    |                                       |                        | 00D01H55M             | 9 | 5.084  | 0.4581 | 1.3743 | 4.87   | 3.35 | 7.82  | 9 | 0.173                | 0.1384 | 0.4153 | 0.23   | -0.58 | 0.65 |
|                                    |                                       |                        | 00D03H55M             | 9 | 8.962  | 1.0966 | 3.2899 | 8.07   | 4.88 | 14.96 | 9 | 4.051                | 0.7725 | 2.3174 | 4.21   | 0.99  | 7.16 |
|                                    |                                       |                        | 00D09H34M             | 9 | 7.233  | 0.5510 | 1.6530 | 6.62   | 5.63 | 10.02 | 9 | 2.322                | 0.2703 | 0.8109 | 2.13   | 1.35  | 4.05 |
|                                    |                                       | DAY 2                  | 00D23H36M             | 9 | 4.677  | 0.3882 | 1.1647 | 4.39   | 3.18 | 6.89  | 9 | -0.234               | 0.1353 | 0.4059 | -0.18  | -0.99 | 0.45 |
|                                    |                                       |                        |                       |   |        |        |        |        |      |       |   |                      |        |        |        |       |      |
|                                    |                                       |                        |                       |   |        |        |        |        |      |       |   |                      |        |        |        |       |      |
|                                    |                                       |                        |                       |   |        |        |        |        |      |       |   |                      |        |        |        |       |      |
|                                    | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 2 | DAY 1                  | -00D00H30M            | 8 | 4.704  | 0.3044 | 0.8610 | 4.79   | 2.86 | 5.68  | 0 |                      |        |        |        |       |      |
|                                    |                                       |                        | 00D01H58M             | 8 | 5.316  | 0.3261 | 0.9223 | 5.53   | 3.56 | 6.30  | 8 | 0.613                | 0.1713 | 0.4845 | 0.66   | -0.17 | 1.31 |
|                                    |                                       |                        | 00D03H58M             | 7 | 6.241  | 0.3022 | 0.7995 | 6.44   | 5.07 | 7.16  | 7 | 1.677                | 0.2313 | 0.6119 | 1.70   | 0.64  | 2.54 |
|                                    |                                       |                        | 00D09H43M             | 8 | 6.438  | 0.3285 | 0.9292 | 6.26   | 5.29 | 7.81  | 8 | 1.734                | 0.3485 | 0.9856 | 1.97   | -0.14 | 2.76 |
|                                    |                                       | DAY 2                  | 00D23H43M             | 8 | 4.725  | 0.3023 | 0.8549 | 4.91   | 3.05 | 5.96  | 8 | 0.021                | 0.0637 | 0.1801 | 0.01   | -0.18 | 0.28 |
|                                    |                                       |                        |                       |   |        |        |        |        |      |       |   |                      |        |        |        |       |      |
|                                    |                                       |                        |                       |   |        |        |        |        |      |       |   |                      |        |        |        |       |      |
|                                    |                                       |                        |                       |   |        |        |        |        |      |       |   |                      |        |        |        |       |      |
|                                    | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 3 | DAY 1                  | -00D00H30M            | 8 | 4.754  | 0.3725 | 1.0536 | 4.59   | 3.13 | 6.64  | 0 |                      |        |        |        |       |      |
|                                    |                                       |                        | 00D01H58M             | 8 | 5.186  | 0.5405 | 1.5288 | 4.84   | 3.21 | 8.40  | 8 | 0.433                | 0.2788 | 0.7885 | 0.13   | -0.41 | 1.76 |
|                                    |                                       |                        | 00D03H58M             | 8 | 6.528  | 0.7221 | 2.0425 | 6.12   | 4.12 | 10.01 | 8 | 1.774                | 0.5227 | 1.4785 | 1.23   | 0.46  | 4.82 |
|                                    |                                       |                        | 00D09H43M             | 8 | 6.459  | 0.3950 | 1.1172 | 6.18   | 5.01 | 8.37  | 8 | 1.705                | 0.2571 | 0.7273 | 1.64   | 0.80  | 2.92 |
|                                    |                                       | DAY 2                  | 00D23H43M             | 8 | 4.378  | 0.3743 | 1.0586 | 4.55   | 2.89 | 6.27  | 8 | -0.376               | 0.1721 | 0.4867 | -0.42  | -0.94 | 0.43 |
|                                    |                                       |                        |                       |   |        |        |        |        |      |       |   |                      |        |        |        |       |      |
|                                    |                                       |                        |                       |   |        |        |        |        |      |       |   |                      |        |        |        |       |      |
|                                    |                                       |                        |                       |   |        |        |        |        |      |       |   |                      |        |        |        |       |      |
|                                    | NO_TRT                                | SCREENING<br>FOLLOW-UP | SCR                   | 9 | 5.272  | 0.5698 | 1.7093 | 4.88   | 3.14 | 9.04  |   |                      |        |        |        |       |      |
|                                    |                                       |                        | 37D00H00M             | 9 | 5.719  | 0.7958 | 2.3873 | 4.84   | 3.69 | 9.90  |   |                      |        |        |        |       |      |

NO\_TRT: No treatment

| Summary of Lymphocytes Results      |                                       |                        |                       |   |        |        |        |        |      |      |   |                      |        |        |        |       |      |
|-------------------------------------|---------------------------------------|------------------------|-----------------------|---|--------|--------|--------|--------|------|------|---|----------------------|--------|--------|--------|-------|------|
| Parameter<br>(Unit)                 | Treatment                             | Visit                  | Analysis<br>Timepoint | N | Result |        |        |        |      |      | N | Change from baseline |        |        |        |       |      |
|                                     |                                       |                        |                       |   | mean   | SEM    | SD     | median | min  | max  |   | mean                 | SEM    | SD     | median | min   | max  |
| Lymphocytes<br>(10 <sup>9</sup> /L) | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 1 | DAY 1                  | -00D00H36M            | 9 | 1.822  | 0.1529 | 0.4588 | 1.81   | 1.12 | 2.54 | 0 |                      |        |        |        |       |      |
|                                     |                                       |                        | 00D01H55M             | 9 | 1.716  | 0.1266 | 0.3797 | 1.76   | 1.02 | 2.11 | 9 | -0.107               | 0.1010 | 0.3030 | -0.13  | -0.54 | 0.30 |
|                                     |                                       |                        | 00D03H55M             | 9 | 1.791  | 0.1499 | 0.4498 | 1.95   | 1.00 | 2.37 | 9 | -0.031               | 0.1150 | 0.3450 | 0.03   | -0.52 | 0.56 |
|                                     |                                       |                        | 00D09H34M             | 9 | 2.102  | 0.1451 | 0.4354 | 2.31   | 1.24 | 2.72 | 9 | 0.280                | 0.0746 | 0.2238 | 0.28   | -0.02 | 0.56 |
|                                     |                                       | DAY 2                  | 00D23H36M             | 9 | 1.533  | 0.1262 | 0.3786 | 1.44   | 1.03 | 2.19 | 9 | -0.289               | 0.0804 | 0.2412 | -0.35  | -0.57 | 0.17 |
|                                     |                                       |                        |                       |   |        |        |        |        |      |      |   |                      |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |      |   |                      |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |      |   |                      |        |        |        |       |      |
|                                     | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 2 | DAY 1                  | -00D00H30M            | 8 | 1.728  | 0.1581 | 0.4472 | 1.79   | 1.00 | 2.29 | 0 |                      |        |        |        |       |      |
|                                     |                                       |                        | 00D01H58M             | 8 | 1.709  | 0.1653 | 0.4676 | 1.64   | 1.17 | 2.66 | 8 | -0.019               | 0.1399 | 0.3957 | 0.08   | -0.57 | 0.45 |
|                                     |                                       |                        | 00D03H58M             | 7 | 1.884  | 0.1908 | 0.5048 | 1.90   | 1.13 | 2.78 | 7 | 0.084                | 0.1278 | 0.3381 | 0.13   | -0.35 | 0.49 |
|                                     |                                       |                        | 00D09H43M             | 8 | 1.936  | 0.1952 | 0.5522 | 1.97   | 1.08 | 2.92 | 8 | 0.209                | 0.1119 | 0.3166 | 0.18   | -0.23 | 0.63 |
|                                     |                                       | DAY 2                  | 00D23H43M             | 8 | 1.569  | 0.1337 | 0.3783 | 1.60   | 0.99 | 2.17 | 8 | -0.159               | 0.1174 | 0.3319 | -0.02  | -0.79 | 0.21 |
|                                     |                                       |                        |                       |   |        |        |        |        |      |      |   |                      |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |      |   |                      |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |      |   |                      |        |        |        |       |      |
|                                     | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 3 | DAY 1                  | -00D00H30M            | 8 | 1.628  | 0.0705 | 0.1994 | 1.62   | 1.41 | 1.97 | 0 |                      |        |        |        |       |      |
|                                     |                                       |                        | 00D01H58M             | 8 | 1.706  | 0.1318 | 0.3728 | 1.73   | 1.14 | 2.28 | 8 | 0.079                | 0.1353 | 0.3826 | 0.03   | -0.53 | 0.65 |
|                                     |                                       |                        | 00D03H58M             | 8 | 1.669  | 0.1151 | 0.3255 | 1.56   | 1.15 | 2.13 | 8 | 0.041                | 0.1328 | 0.3755 | 0.05   | -0.49 | 0.51 |
|                                     |                                       |                        | 00D09H43M             | 8 | 1.910  | 0.1332 | 0.3768 | 1.87   | 1.43 | 2.44 | 8 | 0.283                | 0.1323 | 0.3742 | 0.25   | -0.27 | 0.74 |
|                                     |                                       | DAY 2                  | 00D23H43M             | 8 | 1.496  | 0.0875 | 0.2475 | 1.55   | 1.06 | 1.81 | 8 | -0.131               | 0.0781 | 0.2208 | -0.11  | -0.42 | 0.23 |
|                                     |                                       |                        |                       |   |        |        |        |        |      |      |   |                      |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |      |   |                      |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |      |   |                      |        |        |        |       |      |
|                                     | NO_TRT                                | SCREENING<br>FOLLOW-UP | SCR                   | 9 | 1.798  | 0.1847 | 0.5542 | 1.70   | 1.06 | 2.65 |   |                      |        |        |        |       |      |
|                                     |                                       |                        | 37D00H00M             | 9 | 1.720  | 0.1714 | 0.5142 | 1.68   | 1.13 | 2.55 |   |                      |        |        |        |       |      |

NO\_TRT: No treatment

| Summary of Monocytes Results      |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|-----------------------------------|---------------------------------------|------------------------|-----------------------|--------|-------|--------|--------|--------|------|------|----------------------|--------|--------|--------|--------|-------|------|
| Parameter<br>(Unit)               | Treatment                             | Visit                  | Analysis<br>Timepoint | Result |       |        |        |        |      |      | Change from baseline |        |        |        |        |       |      |
|                                   |                                       |                        |                       | N      | mean  | SEM    | SD     | median | min  | max  | N                    | mean   | SEM    | SD     | median | min   | max  |
| Monocytes<br>(10 <sup>9</sup> /L) | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 1 | DAY 1                  | -00D00H36M            | 9      | 0.427 | 0.0437 | 0.1311 | 0.39   | 0.30 | 0.72 | 0                    |        |        |        |        |       |      |
|                                   |                                       |                        | 00D01H55M             | 9      | 0.418 | 0.0542 | 0.1627 | 0.39   | 0.20 | 0.75 | 9                    | -0.009 | 0.0250 | 0.0749 | 0.00   | -0.12 | 0.14 |
|                                   |                                       |                        | 00D03H55M             | 9      | 0.662 | 0.0854 | 0.2563 | 0.63   | 0.36 | 1.25 | 9                    | 0.236  | 0.0499 | 0.1496 | 0.29   | 0.04  | 0.53 |
|                                   |                                       |                        | 00D09H34M             | 9      | 0.556 | 0.0631 | 0.1894 | 0.58   | 0.29 | 0.92 | 9                    | 0.129  | 0.0286 | 0.0857 | 0.15   | -0.03 | 0.23 |
|                                   |                                       | DAY 2                  | 00D23H36M             | 9      | 0.377 | 0.0468 | 0.1405 | 0.34   | 0.24 | 0.70 | 9                    | -0.050 | 0.0134 | 0.0403 | -0.06  | -0.11 | 0.01 |
|                                   |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                                   |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                                   |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                                   | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 2 | DAY 1                  | -00D00H30M            | 8      | 0.389 | 0.0416 | 0.1178 | 0.36   | 0.23 | 0.56 | 0                    |        |        |        |        |       |      |
|                                   |                                       |                        | 00D01H58M             | 8      | 0.424 | 0.0477 | 0.1348 | 0.38   | 0.30 | 0.66 | 8                    | 0.035  | 0.0155 | 0.0438 | 0.02   | -0.01 | 0.12 |
|                                   |                                       |                        | 00D03H58M             | 7      | 0.473 | 0.0435 | 0.1150 | 0.45   | 0.35 | 0.69 | 7                    | 0.109  | 0.0273 | 0.0722 | 0.08   | 0.02  | 0.22 |
|                                   |                                       |                        | 00D09H43M             | 8      | 0.479 | 0.0388 | 0.1099 | 0.45   | 0.37 | 0.68 | 8                    | 0.090  | 0.0252 | 0.0713 | 0.07   | 0.01  | 0.19 |
|                                   |                                       | DAY 2                  | 00D23H43M             | 8      | 0.385 | 0.0231 | 0.0652 | 0.38   | 0.31 | 0.46 | 8                    | -0.004 | 0.0217 | 0.0614 | 0.01   | -0.10 | 0.08 |
|                                   |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                                   |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                                   |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                                   | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 3 | DAY 1                  | -00D00H30M            | 8      | 0.410 | 0.0423 | 0.1195 | 0.38   | 0.24 | 0.58 | 0                    |        |        |        |        |       |      |
|                                   |                                       |                        | 00D01H58M             | 8      | 0.446 | 0.0518 | 0.1465 | 0.43   | 0.25 | 0.67 | 8                    | 0.036  | 0.0271 | 0.0767 | 0.02   | -0.08 | 0.16 |
|                                   |                                       |                        | 00D03H58M             | 8      | 0.515 | 0.0756 | 0.2139 | 0.51   | 0.26 | 0.85 | 8                    | 0.105  | 0.0390 | 0.1102 | 0.08   | -0.03 | 0.27 |
|                                   |                                       |                        | 00D09H43M             | 8      | 0.496 | 0.0426 | 0.1206 | 0.53   | 0.30 | 0.62 | 8                    | 0.086  | 0.0237 | 0.0670 | 0.11   | -0.03 | 0.17 |
|                                   |                                       | DAY 2                  | 00D23H43M             | 8      | 0.376 | 0.0477 | 0.1348 | 0.36   | 0.20 | 0.57 | 8                    | -0.034 | 0.0293 | 0.0830 | -0.02  | -0.20 | 0.06 |
|                                   |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                                   |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                                   |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                                   | NO_TRT                                | SCREENING<br>FOLLOW-UP | SCR                   | 9      | 0.473 | 0.0661 | 0.1984 | 0.44   | 0.28 | 0.91 |                      |        |        |        |        |       |      |
|                                   |                                       |                        | 37D00H00M             | 9      | 0.478 | 0.0693 | 0.2080 | 0.41   | 0.26 | 0.94 |                      |        |        |        |        |       |      |

NO\_TRT: No treatment

| Summary of Neutrophils Results      |                                       |                        |                       |   |        |        |        |        |      |       |                      |        |        |        |        |       |      |
|-------------------------------------|---------------------------------------|------------------------|-----------------------|---|--------|--------|--------|--------|------|-------|----------------------|--------|--------|--------|--------|-------|------|
| Parameter<br>(Unit)                 | Treatment                             | Visit                  | Analysis<br>Timepoint | N | Result |        |        |        |      |       | Change from baseline |        |        |        |        |       |      |
|                                     |                                       |                        |                       |   | mean   | SEM    | SD     | median | min  | max   | N                    | mean   | SEM    | SD     | median | min   | max  |
| Neutrophils<br>(10 <sup>9</sup> /L) | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 1 | DAY 1                  | -00D00H36M            | 9 | 2.420  | 0.2757 | 0.8271 | 2.22   | 1.75 | 4.43  | 0                    |        |        |        |        |       |      |
|                                     |                                       |                        | 00D01H55M             | 9 | 2.737  | 0.3127 | 0.9380 | 2.29   | 1.85 | 4.67  | 9                    | 0.317  | 0.1265 | 0.3794 | 0.24   | -0.10 | 1.23 |
|                                     |                                       |                        | 00D03H55M             | 9 | 6.277  | 0.9761 | 2.9283 | 5.79   | 2.68 | 11.29 | 9                    | 3.857  | 0.7622 | 2.2865 | 3.57   | 0.87  | 6.97 |
|                                     |                                       |                        | 00D09H34M             | 9 | 4.322  | 0.4333 | 1.2999 | 3.90   | 2.67 | 6.40  | 9                    | 1.902  | 0.2748 | 0.8245 | 1.79   | 0.72  | 3.43 |
|                                     |                                       | DAY 2                  | 00D23H36M             | 9 | 2.531  | 0.2566 | 0.7698 | 2.43   | 1.75 | 4.11  | 9                    | 0.111  | 0.0780 | 0.2340 | 0.20   | -0.32 | 0.50 |
|                                     |                                       |                        |                       |   |        |        |        |        |      |       |                      |        |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |       |                      |        |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |       |                      |        |        |        |        |       |      |
|                                     | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 2 | DAY 1                  | -00D00H30M            | 8 | 2.403  | 0.2394 | 0.6770 | 2.28   | 1.51 | 3.68  | 0                    |        |        |        |        |       |      |
|                                     |                                       |                        | 00D01H58M             | 8 | 3.015  | 0.2087 | 0.5903 | 3.04   | 2.03 | 3.98  | 8                    | 0.612  | 0.1500 | 0.4242 | 0.49   | 0.04  | 1.41 |
|                                     |                                       |                        | 00D03H58M             | 7 | 3.693  | 0.2152 | 0.5694 | 3.75   | 2.97 | 4.40  | 7                    | 1.473  | 0.2390 | 0.6323 | 1.40   | 0.82  | 2.45 |
|                                     |                                       |                        | 00D09H43M             | 8 | 3.790  | 0.2057 | 0.5818 | 3.73   | 3.08 | 4.76  | 8                    | 1.388  | 0.3653 | 1.0333 | 1.55   | -0.45 | 2.81 |
|                                     |                                       | DAY 2                  | 00D23H43M             | 8 | 2.576  | 0.2822 | 0.7982 | 2.65   | 1.57 | 4.05  | 8                    | 0.174  | 0.1159 | 0.3277 | 0.19   | -0.38 | 0.67 |
|                                     |                                       |                        |                       |   |        |        |        |        |      |       |                      |        |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |       |                      |        |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |       |                      |        |        |        |        |       |      |
|                                     | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 3 | DAY 1                  | -00D00H30M            | 8 | 2.513  | 0.3273 | 0.9256 | 2.41   | 1.31 | 4.39  | 0                    |        |        |        |        |       |      |
|                                     |                                       |                        | 00D01H58M             | 8 | 2.856  | 0.4298 | 1.2155 | 2.71   | 1.64 | 5.56  | 8                    | 0.344  | 0.1507 | 0.4263 | 0.27   | -0.10 | 1.17 |
|                                     |                                       |                        | 00D03H58M             | 8 | 4.128  | 0.5979 | 1.6911 | 3.91   | 2.20 | 7.31  | 8                    | 1.615  | 0.4416 | 1.2491 | 1.27   | 0.39  | 4.37 |
|                                     |                                       |                        | 00D09H43M             | 8 | 3.854  | 0.3356 | 0.9492 | 3.75   | 2.49 | 5.60  | 8                    | 1.341  | 0.1733 | 0.4901 | 1.36   | 0.68  | 2.02 |
|                                     |                                       | DAY 2                  | 00D23H43M             | 8 | 2.330  | 0.2911 | 0.8233 | 2.40   | 1.26 | 3.81  | 8                    | -0.183 | 0.1537 | 0.4348 | -0.20  | -0.86 | 0.35 |
|                                     |                                       |                        |                       |   |        |        |        |        |      |       |                      |        |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |       |                      |        |        |        |        |       |      |
|                                     |                                       |                        |                       |   |        |        |        |        |      |       |                      |        |        |        |        |       |      |
|                                     | NO_TRT                                | SCREENING<br>FOLLOW-UP | SCR                   | 9 | 2.761  | 0.3344 | 1.0031 | 2.53   | 1.66 | 4.99  |                      |        |        |        |        |       |      |
|                                     |                                       |                        | 37D00H00M             | 9 | 3.326  | 0.5625 | 1.6876 | 2.75   | 1.81 | 6.35  |                      |        |        |        |        |       |      |

NO\_TRT: No treatment

## Summary of Basophils Results

| Parameter<br>(Unit)   | Treatment                             | Visit                  | Analysis<br>Timepoint | Result |       |        |        |        |      |      | Change from baseline |        |        |        |        |       |      |
|-----------------------|---------------------------------------|------------------------|-----------------------|--------|-------|--------|--------|--------|------|------|----------------------|--------|--------|--------|--------|-------|------|
|                       |                                       |                        |                       | N      | mean  | SEM    | SD     | median | min  | max  | N                    | mean   | SEM    | SD     | median | min   | max  |
| Basophils<br>(10^9/L) | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 1 | DAY 1                  | -00D00H36M            | 9      | 0.047 | 0.0058 | 0.0173 | 0.05   | 0.02 | 0.07 | 0                    |        |        |        |        |       |      |
|                       |                                       |                        | 00D01H55M             | 9      | 0.047 | 0.0062 | 0.0187 | 0.05   | 0.02 | 0.08 | 9                    | 0.000  | 0.0033 | 0.0100 | 0.00   | -0.01 | 0.01 |
|                       |                                       |                        | 00D03H55M             | 9      | 0.046 | 0.0058 | 0.0174 | 0.04   | 0.03 | 0.07 | 9                    | -0.001 | 0.0031 | 0.0093 | 0.00   | -0.02 | 0.01 |
|                       |                                       |                        | 00D09H34M             | 9      | 0.048 | 0.0072 | 0.0217 | 0.04   | 0.02 | 0.09 | 9                    | 0.001  | 0.0039 | 0.0117 | 0.00   | -0.02 | 0.02 |
|                       |                                       | DAY 2                  | 00D23H36M             | 9      | 0.040 | 0.0041 | 0.0122 | 0.04   | 0.02 | 0.06 | 9                    | -0.007 | 0.0037 | 0.0112 | 0.00   | -0.02 | 0.01 |
|                       |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                       |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                       |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                       | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 2 | DAY 1                  | -00D00H30M            | 8      | 0.033 | 0.0059 | 0.0167 | 0.03   | 0.01 | 0.06 | 0                    |        |        |        |        |       |      |
|                       |                                       |                        | 00D01H58M             | 8      | 0.039 | 0.0064 | 0.0181 | 0.04   | 0.02 | 0.07 | 8                    | 0.006  | 0.0018 | 0.0052 | 0.01   | 0.00  | 0.01 |
|                       |                                       |                        | 00D03H58M             | 7      | 0.049 | 0.0086 | 0.0227 | 0.05   | 0.02 | 0.08 | 7                    | 0.016  | 0.0020 | 0.0053 | 0.02   | 0.01  | 0.02 |
|                       |                                       |                        | 00D09H43M             | 8      | 0.041 | 0.0052 | 0.0146 | 0.04   | 0.03 | 0.07 | 8                    | 0.009  | 0.0040 | 0.0113 | 0.01   | 0.00  | 0.03 |
|                       |                                       | DAY 2                  | 00D23H43M             | 8      | 0.039 | 0.0052 | 0.0146 | 0.04   | 0.02 | 0.06 | 8                    | 0.006  | 0.0018 | 0.0052 | 0.01   | 0.00  | 0.01 |
|                       |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                       |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                       |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                       | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 3 | DAY 1                  | -00D00H30M            | 8      | 0.033 | 0.0037 | 0.0104 | 0.03   | 0.02 | 0.05 | 0                    |        |        |        |        |       |      |
|                       |                                       |                        | 00D01H58M             | 8      | 0.039 | 0.0052 | 0.0146 | 0.04   | 0.02 | 0.06 | 8                    | 0.006  | 0.0032 | 0.0092 | 0.00   | 0.00  | 0.02 |
|                       |                                       |                        | 00D03H58M             | 8      | 0.045 | 0.0057 | 0.0160 | 0.05   | 0.02 | 0.07 | 8                    | 0.013  | 0.0037 | 0.0104 | 0.01   | 0.00  | 0.03 |
|                       |                                       |                        | 00D09H43M             | 8      | 0.039 | 0.0048 | 0.0136 | 0.04   | 0.02 | 0.06 | 8                    | 0.006  | 0.0046 | 0.0130 | 0.01   | -0.01 | 0.02 |
|                       |                                       | DAY 2                  | 00D23H43M             | 8      | 0.036 | 0.0053 | 0.0151 | 0.04   | 0.01 | 0.05 | 8                    | 0.004  | 0.0038 | 0.0106 | 0.01   | -0.01 | 0.02 |
|                       |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                       |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                       |                                       |                        |                       |        |       |        |        |        |      |      |                      |        |        |        |        |       |      |
|                       | NO_TRT                                | SCREENING<br>FOLLOW-UP | SCR                   | 9      | 0.042 | 0.0066 | 0.0199 | 0.04   | 0.02 | 0.08 |                      |        |        |        |        |       |      |
|                       |                                       |                        | 37D00H00M             | 9      | 0.042 | 0.0057 | 0.0172 | 0.04   | 0.02 | 0.08 |                      |        |        |        |        |       |      |

NO\_TRT: No treatment.

| Summary of Eosinophils Results      |                                       |                        |                       |        |       |        |        |        |      |                      |   |        |        |        |        |       |      |
|-------------------------------------|---------------------------------------|------------------------|-----------------------|--------|-------|--------|--------|--------|------|----------------------|---|--------|--------|--------|--------|-------|------|
| Parameter<br>(Unit)                 | Treatment                             | Visit                  | Analysis<br>Timepoint | Result |       |        |        |        |      | Change from baseline |   |        |        |        |        |       |      |
|                                     |                                       |                        |                       | N      | mean  | SEM    | SD     | median | min  | max                  | N | mean   | SEM    | SD     | median | min   | max  |
| Eosinophils<br>(10 <sup>9</sup> /L) | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 1 | DAY 1                  | -00D00H36M            | 9      | 0.196 | 0.0320 | 0.0961 | 0.20   | 0.07 | 0.34                 | 0 |        |        |        |        |       |      |
|                                     |                                       |                        | 00D01H55M             | 9      | 0.168 | 0.0324 | 0.0971 | 0.14   | 0.03 | 0.33                 | 9 | -0.028 | 0.0121 | 0.0363 | -0.02  | -0.08 | 0.02 |
|                                     |                                       |                        | 00D03H55M             | 9      | 0.187 | 0.0369 | 0.1106 | 0.19   | 0.05 | 0.38                 | 9 | -0.009 | 0.0166 | 0.0499 | 0.00   | -0.11 | 0.07 |
|                                     |                                       |                        | 00D09H34M             | 9      | 0.206 | 0.0376 | 0.1127 | 0.24   | 0.05 | 0.38                 | 9 | 0.010  | 0.0149 | 0.0447 | 0.00   | -0.07 | 0.07 |
|                                     |                                       | DAY 2                  | 00D23H36M             | 9      | 0.196 | 0.0379 | 0.1136 | 0.20   | 0.04 | 0.42                 | 9 | 0.000  | 0.0181 | 0.0543 | -0.01  | -0.08 | 0.11 |
|                                     |                                       |                        |                       |        |       |        |        |        |      |                      |   |        |        |        |        |       |      |
|                                     |                                       |                        |                       |        |       |        |        |        |      |                      |   |        |        |        |        |       |      |
|                                     |                                       |                        |                       |        |       |        |        |        |      |                      |   |        |        |        |        |       |      |
|                                     | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 2 | DAY 1                  | -00D00H30M            | 8      | 0.153 | 0.0323 | 0.0915 | 0.15   | 0.05 | 0.31                 | 0 |        |        |        |        |       |      |
|                                     |                                       |                        | 00D01H58M             | 8      | 0.130 | 0.0266 | 0.0752 | 0.11   | 0.04 | 0.25                 | 8 | -0.023 | 0.0124 | 0.0349 | -0.02  | -0.07 | 0.03 |
|                                     |                                       |                        | 00D03H58M             | 7      | 0.143 | 0.0341 | 0.0901 | 0.10   | 0.06 | 0.31                 | 7 | -0.004 | 0.0107 | 0.0282 | 0.00   | -0.06 | 0.02 |
|                                     |                                       |                        | 00D09H43M             | 8      | 0.191 | 0.0406 | 0.1147 | 0.18   | 0.06 | 0.44                 | 8 | 0.039  | 0.0161 | 0.0455 | 0.04   | -0.03 | 0.13 |
|                                     |                                       | DAY 2                  | 00D23H43M             | 8      | 0.156 | 0.0343 | 0.0971 | 0.15   | 0.03 | 0.34                 | 8 | 0.004  | 0.0096 | 0.0272 | 0.01   | -0.03 | 0.04 |
|                                     |                                       |                        |                       |        |       |        |        |        |      |                      |   |        |        |        |        |       |      |
|                                     |                                       |                        |                       |        |       |        |        |        |      |                      |   |        |        |        |        |       |      |
|                                     |                                       |                        |                       |        |       |        |        |        |      |                      |   |        |        |        |        |       |      |
|                                     | LIPOPOLYSAC<br>CHARIDE<br>CHALLENGE 3 | DAY 1                  | -00D00H30M            | 8      | 0.171 | 0.0282 | 0.0799 | 0.19   | 0.05 | 0.25                 | 0 |        |        |        |        |       |      |
|                                     |                                       |                        | 00D01H58M             | 8      | 0.139 | 0.0218 | 0.0617 | 0.16   | 0.05 | 0.22                 | 8 | -0.033 | 0.0096 | 0.0271 | -0.03  | -0.08 | 0.00 |
|                                     |                                       |                        | 00D03H58M             | 8      | 0.171 | 0.0324 | 0.0916 | 0.17   | 0.03 | 0.28                 | 8 | 0.000  | 0.0141 | 0.0400 | 0.01   | -0.07 | 0.06 |
|                                     |                                       |                        | 00D09H43M             | 8      | 0.160 | 0.0237 | 0.0670 | 0.16   | 0.05 | 0.24                 | 8 | -0.011 | 0.0152 | 0.0429 | 0.00   | -0.09 | 0.04 |
|                                     |                                       | DAY 2                  | 00D23H43M             | 8      | 0.139 | 0.0232 | 0.0656 | 0.15   | 0.04 | 0.21                 | 8 | -0.033 | 0.0124 | 0.0349 | -0.04  | -0.09 | 0.01 |
|                                     |                                       |                        |                       |        |       |        |        |        |      |                      |   |        |        |        |        |       |      |
|                                     |                                       |                        |                       |        |       |        |        |        |      |                      |   |        |        |        |        |       |      |
|                                     |                                       |                        |                       |        |       |        |        |        |      |                      |   |        |        |        |        |       |      |
|                                     | NO_TRT                                | SCREENING<br>FOLLOW-UP | SCR                   | 9      | 0.198 | 0.0454 | 0.1363 | 0.19   | 0.06 | 0.42                 |   |        |        |        |        |       |      |
|                                     |                                       |                        | 37D00H00M             | 9      | 0.153 | 0.0336 | 0.1009 | 0.17   | 0.03 | 0.29                 |   |        |        |        |        |       |      |

NO\_TRT: No treatment

## 1.3. Vital signs (Heart rate, Blood pressure)

| Summary of Vital Signs                   |                                       |                        |            |        |       |      |       |        |     |     |                      |       |      |       |        |     |     |
|------------------------------------------|---------------------------------------|------------------------|------------|--------|-------|------|-------|--------|-----|-----|----------------------|-------|------|-------|--------|-----|-----|
| Parameter<br>(Unit)                      | Treatment                             | Visit                  | Timepoint  | Result |       |      |       |        |     |     | Change from baseline |       |      |       |        |     |     |
|                                          |                                       |                        |            | N      | mean  | SEM  | SD    | median | min | max | N                    | mean  | SEM  | SD    | median | min | max |
| Systolic<br>Blood<br>Pressure<br>(mmHg)  | LIPOPOLYSACC<br>HARIDE<br>CHALLENGE 1 | DAY 1                  | -00D00H57M | 9      | 121.8 | 3.61 | 10.84 | 122    | 104 | 139 | 0                    |       |      |       |        |     |     |
|                                          |                                       |                        | 00D01H53M  | 9      | 116.2 | 4.71 | 14.14 | 115    | 89  | 136 | 9                    | -5.6  | 2.37 | 7.11  | -7     | -15 | 10  |
|                                          |                                       |                        | 00D03H53M  | 9      | 121.7 | 2.73 | 8.20  | 123    | 111 | 133 | 9                    | -0.1  | 2.00 | 5.99  | 2      | -8  | 7   |
|                                          |                                       |                        | 00D09H33M  | 9      | 119.7 | 2.86 | 8.59  | 121    | 105 | 130 | 9                    | -2.1  | 1.59 | 4.76  | -1     | -10 | 5   |
|                                          |                                       | DAY 2                  | 00D23H36M  | 9      | 114.6 | 2.29 | 6.88  | 118    | 104 | 123 | 9                    | -7.2  | 2.13 | 6.38  | -6     | -21 | 1   |
|                                          | LIPOPOLYSACC<br>HARIDE<br>CHALLENGE 2 | DAY 1                  | -00D00H49M | 8      | 115.1 | 3.91 | 11.06 | 117    | 95  | 130 | 0                    |       |      |       |        |     |     |
|                                          |                                       | DAY 2                  | 00D09H42M  | 8      | 112.9 | 4.83 | 13.66 | 114    | 94  | 137 | 8                    | -2.3  | 2.08 | 5.87  | -2     | -13 | 7   |
|                                          |                                       |                        | 00D23H43M  | 8      | 111.1 | 4.74 | 13.40 | 112    | 94  | 135 | 8                    | -4.0  | 3.52 | 9.94  | -2     | -23 | 7   |
|                                          | LIPOPOLYSACC<br>HARIDE<br>CHALLENGE 3 | DAY 1                  | -00D00H49M | 8      | 112.9 | 4.57 | 12.93 | 112    | 95  | 133 | 0                    |       |      |       |        |     |     |
|                                          |                                       | DAY 2                  | 00D09H42M  | 8      | 118.6 | 5.61 | 15.86 | 118    | 96  | 143 | 8                    | 5.8   | 3.00 | 8.48  | 5      | -6  | 21  |
|                                          |                                       |                        | 00D23H41M  | 8      | 113.6 | 3.29 | 9.32  | 113    | 100 | 131 | 8                    | 0.8   | 2.58 | 7.29  | 2      | -16 | 7   |
|                                          | NO_TRT                                | SCREENING<br>FOLLOW-UP | SCR        | 9      | 118.1 | 3.40 | 10.19 | 118    | 103 | 137 |                      |       |      |       |        |     |     |
|                                          |                                       |                        | 37D00H00M  | 9      | 114.9 | 4.22 | 12.65 | 116    | 92  | 134 |                      |       |      |       |        |     |     |
| Diastolic<br>Blood<br>Pressure<br>(mmHg) | LIPOPOLYSACC<br>HARIDE<br>CHALLENGE 1 | DAY 1                  | -00D00H57M | 9      | 67.1  | 1.99 | 5.97  | 66     | 57  | 74  | 0                    |       |      |       |        |     |     |
|                                          |                                       |                        | 00D01H53M  | 9      | 66.4  | 3.07 | 9.22  | 67     | 49  | 80  | 9                    | -0.7  | 1.49 | 4.47  | -2     | -8  | 6   |
|                                          |                                       |                        | 00D03H53M  | 9      | 64.7  | 2.03 | 6.10  | 65     | 54  | 75  | 9                    | -2.4  | 1.46 | 4.39  | -1     | -10 | 2   |
|                                          |                                       |                        | 00D09H33M  | 9      | 65.9  | 1.76 | 5.28  | 65     | 56  | 73  | 9                    | -1.2  | 1.28 | 3.83  | -1     | -9  | 5   |
|                                          |                                       | DAY 2                  | 00D23H36M  | 9      | 63.4  | 2.11 | 6.33  | 62     | 52  | 76  | 9                    | -3.7  | 1.93 | 5.79  | -5     | -12 | 5   |
|                                          | LIPOPOLYSACC<br>HARIDE<br>CHALLENGE 2 | DAY 1                  | -00D00H49M | 8      | 62.4  | 2.57 | 7.27  | 62     | 51  | 73  | 0                    |       |      |       |        |     |     |
|                                          |                                       | DAY 2                  | 00D09H42M  | 8      | 59.1  | 1.61 | 4.55  | 59     | 54  | 68  | 8                    | -3.3  | 1.50 | 4.23  | -4     | -11 | 3   |
|                                          |                                       |                        | 00D23H43M  | 8      | 60.1  | 1.97 | 5.57  | 59     | 55  | 70  | 8                    | -2.3  | 2.01 | 5.68  | -2     | -12 | 5   |
|                                          | LIPOPOLYSACC<br>HARIDE<br>CHALLENGE 3 | DAY 1                  | -00D00H49M | 8      | 65.1  | 4.25 | 12.02 | 59     | 55  | 83  | 0                    |       |      |       |        |     |     |
|                                          |                                       | DAY 2                  | 00D09H42M  | 8      | 63.8  | 2.59 | 7.32  | 65     | 54  | 72  | 8                    | -1.4  | 2.83 | 8.00  | -2     | -11 | 13  |
|                                          |                                       |                        | 00D23H41M  | 8      | 62.3  | 3.03 | 8.56  | 63     | 50  | 76  | 8                    | -2.9  | 2.22 | 6.27  | -4     | -11 | 7   |
|                                          | NO_TRT                                | SCREENING<br>FOLLOW-UP | SCR        | 9      | 65.0  | 2.21 | 6.63  | 65     | 55  | 76  |                      |       |      |       |        |     |     |
|                                          |                                       |                        | 37D00H00M  | 9      | 62.1  | 2.46 | 7.37  | 59     | 55  | 75  |                      |       |      |       |        |     |     |
| Heart Rate<br>(beats/min)                | LIPOPOLYSACC<br>HARIDE<br>CHALLENGE 1 | DAY 1                  | -00D00H57M | 9      | 64.9  | 3.12 | 9.35  | 62     | 53  | 79  | 0                    |       |      |       |        |     |     |
|                                          |                                       |                        | 00D01H53M  | 9      | 53.8  | 2.17 | 6.50  | 56     | 44  | 62  | 9                    | -11.1 | 4.80 | 14.41 | -7     | -34 | 5   |
|                                          |                                       |                        | 00D03H53M  | 9      | 58.3  | 2.23 | 6.69  | 61     | 46  | 67  | 9                    | -6.6  | 4.03 | 12.09 | -3     | -31 | 8   |
|                                          |                                       |                        | 00D09H33M  | 9      | 60.8  | 1.92 | 5.76  | 62     | 53  | 69  | 9                    | -4.1  | 3.71 | 11.12 | 0      | -24 | 7   |
|                                          |                                       | DAY 2                  | 00D23H36M  | 9      | 61.1  | 3.78 | 11.34 | 65     | 44  | 73  | 9                    | -3.8  | 4.70 | 14.10 | -4     | -29 | 15  |
|                                          | LIPOPOLYSACC<br>HARIDE<br>CHALLENGE 2 | DAY 1                  | -00D00H49M | 8      | 58.0  | 2.91 | 8.23  | 58     | 48  | 67  | 0                    |       |      |       |        |     |     |
|                                          |                                       | DAY 2                  | 00D09H42M  | 8      | 62.9  | 3.23 | 9.14  | 65     | 50  | 75  | 8                    | 4.9   | 1.82 | 5.14  | 6      | -3  | 13  |
|                                          |                                       |                        | 00D23H43M  | 8      | 61.1  | 2.29 | 6.49  | 60     | 54  | 72  | 8                    | 3.1   | 2.64 | 7.45  | 4      | -10 | 15  |

## CHDR2336 Basic Results Summary

|                           |                    |            |           |       |       |       |       |      |      |      |      |       |       |     |      |     |  |
|---------------------------|--------------------|------------|-----------|-------|-------|-------|-------|------|------|------|------|-------|-------|-----|------|-----|--|
|                           | LIPOPOLYSACC DAY 1 | -00D00H49M | 8         | 63.0  | 2.92  | 8.25  | 64    | 48   | 74   | 0    |      |       |       |     |      |     |  |
|                           | HARIDE             | 00D09H42M  | 8         | 64.1  | 3.01  | 8.53  | 63    | 47   | 75   | 8    | 1.1  | 3.91  | 11.05 | -1  | -15  | 19  |  |
|                           | CHALLENGE 3 DAY 2  | 00D23H41M  | 8         | 56.8  | 2.45  | 6.92  | 59    | 42   | 62   | 8    | -6.3 | 3.93  | 11.12 | -8  | -20  | 13  |  |
|                           | NO_TRT             | SCREENING  | SCR       | 9     | 57.9  | 3.18  | 9.53  | 55   | 47   | 76   |      |       |       |     |      |     |  |
| Heart Rate<br>(beats/min) | NO_TRT             | FOLLOW-UP  | 37D00H00M | 9     | 59.3  | 3.46  | 10.37 | 63   | 47   | 76   |      |       |       |     |      |     |  |
| Temperatu<br>re (C)       | LIPOPOLYSACC DAY 1 | -00D00H56M | 9         | 36.58 | 0.085 | 0.254 | 36.6  | 36.2 | 37.0 | 0    |      |       |       |     |      |     |  |
|                           | HARIDE             | 00D01H54M  | 9         | 36.70 | 0.107 | 0.320 | 36.8  | 35.9 | 37.0 | 9    | 0.12 | 0.121 | 0.363 | 0.2 | -0.5 | 0.6 |  |
|                           | CHALLENGE 1        | 00D03H54M  | 9         | 36.89 | 0.115 | 0.344 | 36.9  | 36.3 | 37.5 | 9    | 0.31 | 0.105 | 0.314 | 0.3 | -0.1 | 0.8 |  |
|                           | DAY 2              | 00D23H36M  | 9         | 36.71 | 0.081 | 0.242 | 36.7  | 36.3 | 37.0 | 9    | 0.13 | 0.071 | 0.212 | 0.1 | -0.1 | 0.6 |  |
|                           | LIPOPOLYSACC DAY 1 | -00D00H48M | 8         | 36.66 | 0.098 | 0.277 | 36.7  | 36.3 | 37.1 | 0    |      |       |       |     |      |     |  |
|                           | HARIDE             | 00D01H57M  | 8         | 36.81 | 0.122 | 0.344 | 36.8  | 36.3 | 37.4 | 8    | 0.15 | 0.105 | 0.298 | 0.1 | -0.4 | 0.5 |  |
|                           | CHALLENGE 2        | 00D03H57M  | 8         | 36.66 | 0.100 | 0.283 | 36.7  | 36.2 | 37.2 | 8    | 0.00 | 0.060 | 0.169 | 0.0 | -0.2 | 0.2 |  |
|                           | DAY 2              | 00D23H43M  | 8         | 36.85 | 0.180 | 0.510 | 36.9  | 36.1 | 37.6 | 8    | 0.19 | 0.162 | 0.458 | 0.3 | -0.7 | 0.8 |  |
|                           | LIPOPOLYSACC DAY 1 | -00D00H48M | 8         | 36.59 | 0.149 | 0.422 | 36.5  | 36.1 | 37.3 | 0    |      |       |       |     |      |     |  |
|                           | HARIDE             | 00D01H57M  | 8         | 36.78 | 0.132 | 0.373 | 36.6  | 36.4 | 37.4 | 8    | 0.19 | 0.064 | 0.181 | 0.2 | -0.1 | 0.4 |  |
|                           | CHALLENGE 3        | 00D03H57M  | 8         | 36.84 | 0.122 | 0.346 | 36.9  | 36.3 | 37.3 | 8    | 0.25 | 0.057 | 0.160 | 0.3 | 0.0  | 0.5 |  |
|                           | DAY 2              | 00D23H42M  | 8         | 36.76 | 0.167 | 0.472 | 37.1  | 36.1 | 37.2 | 8    | 0.18 | 0.118 | 0.333 | 0.1 | -0.3 | 0.6 |  |
|                           | NO_TRT             | SCREENING  | SCR       | 9     | 36.62 | 0.068 | 0.205 | 36.6 | 36.4 | 37.1 |      |       |       |     |      |     |  |
|                           |                    | FOLLOW-UP  | 37D00H00M | 9     | 36.66 | 0.116 | 0.347 | 36.6 | 36.2 | 37.3 |      |       |       |     |      |     |  |

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NO\_TRT: No treatment

## 2. Dermal imaging/scoring

### 2.1. Perfusion by Laser Speckle Contrast Imaging (LSCI)

| Analysis results LSCI Flare-1 Mean (AU) |         |                       |                        |                            |        |       |
|-----------------------------------------|---------|-----------------------|------------------------|----------------------------|--------|-------|
| Effect/Contrast                         | P-value | First LSM of contrast | Second LSM of contrast | Estimate of the difference | 95% CI |       |
|                                         |         |                       |                        |                            | Lower  | Upper |
| Prevalue                                | 0.0003  |                       |                        |                            |        |       |
| LPS Challenge Day                       | 0.1523  |                       |                        |                            |        |       |
| Time                                    | <.0001  |                       |                        |                            |        |       |
| Day by time                             | 0.0157  |                       |                        |                            |        |       |
| LPS Day 15 - LPS Day 1                  | 0.2565  | 114.0                 | 118.8                  | -4.7                       | -13.3  | 3.9   |
| LPS Day 29 - LPS Day 1                  | 0.0547  | 110.9                 | 118.8                  | -7.9                       | -16.0  | 0.2   |
| LPS Day 29 - LPS Day 15                 | 0.3425  | 110.9                 | 114.0                  | -3.2                       | -10.2  | 3.8   |
| LPS Day 15 - LPS Day 1 at 10h           | 0.9799  | 121.0                 | 121.2                  | -0.1                       | -10.3  | 10.1  |
| LPS Day 29 - LPS Day 1 at 10h           | 0.5173  | 118.0                 | 121.2                  | -3.1                       | -12.9  | 6.6   |
| LPS Day 29 - LPS Day 15 at 10h          | 0.4671  | 118.0                 | 121.0                  | -3.0                       | -11.3  | 5.3   |
| LPS Day 15 - LPS Day 1 at 24h           | 0.9236  | 109.1                 | 108.7                  | 0.5                        | -9.7   | 10.7  |
| LPS Day 29 - LPS Day 1 at 24h           | 0.5354  | 105.7                 | 108.7                  | -3.0                       | -12.7  | 6.8   |
| LPS Day 29 - LPS Day 15 at 24h          | 0.4005  | 105.7                 | 109.1                  | -3.5                       | -11.8  | 4.8   |

| Treatment  | Time    | LSM   | 95% CI |       | LSM change from baseline | 95% CI |       |
|------------|---------|-------|--------|-------|--------------------------|--------|-------|
|            |         |       | Lower  | Upper |                          | Lower  | Upper |
| LPS Day 1  | Overall | 118.8 | 111.4  | 126.1 | 29.5                     | 22.1   | 36.8  |
|            | 2h      | 121.2 | 112.9  | 129.5 | 31.9                     | 23.6   | 40.2  |
|            | 4h      | 124.0 | 115.7  | 132.3 | 34.7                     | 26.4   | 43.0  |
|            | 10h     | 121.2 | 112.9  | 129.4 | 31.9                     | 23.6   | 40.1  |
|            | 24h     | 108.7 | 100.4  | 117.0 | 19.4                     | 11.1   | 27.7  |
| LPS Day 15 | Overall | 114.0 | 108.5  | 119.6 | 24.7                     | 19.2   | 30.3  |
|            | 2h      | 108.5 | 102.3  | 114.7 | 19.2                     | 13.0   | 25.4  |
|            | 4h      | 117.5 | 111.0  | 124.0 | 28.2                     | 21.7   | 34.7  |
|            | 10h     | 121.0 | 114.8  | 127.3 | 31.7                     | 25.5   | 38.0  |
|            | 24h     | 109.1 | 102.9  | 115.4 | 19.9                     | 13.6   | 26.1  |
| LPS Day 29 | Overall | 110.9 | 105.7  | 116.0 | 21.6                     | 16.4   | 26.7  |
|            | 2h      | 101.5 | 95.6   | 107.4 | 12.2                     | 6.3    | 18.1  |
|            | 4h      | 118.2 | 112.3  | 124.1 | 28.9                     | 23.0   | 34.8  |
|            | 10h     | 118.0 | 112.1  | 123.9 | 28.7                     | 22.9   | 34.6  |
|            | 24h     | 105.7 | 99.8   | 111.6 | 16.4                     | 10.5   | 22.3  |

| Analysis results LSCI Flare-1 Area (AU) |         |                          |                           |                               |        |       |
|-----------------------------------------|---------|--------------------------|---------------------------|-------------------------------|--------|-------|
| Effect/Contrast                         | P-value | First LSM<br>of contrast | Second LSM<br>of contrast | Estimate of<br>the difference | 95% CI |       |
|                                         |         |                          |                           |                               | Lower  | Upper |
| Prevalue                                | 0.9236  |                          |                           |                               |        |       |
| LPS Challenge Day                       | 0.6354  |                          |                           |                               |        |       |
| Time                                    | <.0001  |                          |                           |                               |        |       |
| Day by time                             | 0.0399  |                          |                           |                               |        |       |
| LPS Day 15 - LPS Day 1                  | 0.6615  | 209.9                    | 199.0                     | 10.9                          | -42.6  | 64.3  |
| LPS Day 29 - LPS Day 1                  | 0.7185  | 187.8                    | 199.0                     | -11.2                         | -76.1  | 53.7  |
| LPS Day 29 - LPS Day 15                 | 0.3619  | 187.8                    | 209.9                     | -22.1                         | -72.8  | 28.7  |
| LPS Day 15 - LPS Day 1 at 10h           | 0.1339  | 261.8                    | 216.5                     | 45.3                          | -15.1  | 105.7 |
| LPS Day 29 - LPS Day 1 at 10h           | 0.6833  | 231.1                    | 216.5                     | 14.6                          | -57.9  | 87.0  |
| LPS Day 29 - LPS Day 15 at 10h          | 0.3077  | 231.1                    | 261.8                     | -30.7                         | -91.2  | 29.8  |
| LPS Day 15 - LPS Day 1 at 24h           | 0.2049  | 183.7                    | 145.7                     | 38.0                          | -22.4  | 98.5  |
| LPS Day 29 - LPS Day 1 at 24h           | 0.9865  | 145.1                    | 145.7                     | -0.6                          | -73.0  | 71.8  |
| LPS Day 29 - LPS Day 15 at 24h          | 0.2023  | 145.1                    | 183.7                     | -38.6                         | -99.1  | 21.9  |

| Treatment  | Time    | LSM   | 95% CI |       | LSM change<br>from baseline | 95% CI |       |
|------------|---------|-------|--------|-------|-----------------------------|--------|-------|
|            |         |       | Lower  | Upper |                             | Lower  | Upper |
| LPS Day 1  | Overall | 199.0 | 147.5  | 250.6 | 154.6                       | 103.0  | 206.1 |
|            | 2h      | 207.5 | 153.5  | 261.6 | 163.1                       | 109.0  | 217.1 |
|            | 4h      | 226.4 | 172.3  | 280.4 | 181.9                       | 127.9  | 235.9 |
|            | 10h     | 216.5 | 162.5  | 270.6 | 172.1                       | 118.0  | 226.1 |
|            | 24h     | 145.7 | 91.7   | 199.8 | 101.3                       | 47.2   | 155.3 |
| LPS Day 15 | Overall | 209.9 | 182.8  | 237.0 | 165.4                       | 138.4  | 192.5 |
|            | 2h      | 166.6 | 132.7  | 200.6 | 122.2                       | 88.2   | 156.2 |
|            | 4h      | 227.4 | 191.4  | 263.4 | 182.9                       | 146.9  | 218.9 |
|            | 10h     | 261.8 | 227.9  | 295.8 | 217.4                       | 183.4  | 251.4 |
|            | 24h     | 183.7 | 149.7  | 217.7 | 139.3                       | 105.3  | 173.2 |
| LPS Day 29 | Overall | 187.8 | 143.9  | 231.7 | 143.4                       | 99.5   | 187.3 |
|            | 2h      | 153.6 | 103.9  | 203.3 | 109.1                       | 59.5   | 158.8 |
|            | 4h      | 221.5 | 171.8  | 271.2 | 177.0                       | 127.4  | 226.7 |
|            | 10h     | 231.1 | 181.4  | 280.8 | 186.7                       | 137.0  | 236.3 |
|            | 24h     | 145.1 | 95.4   | 194.8 | 100.7                       | 51.0   | 150.3 |

| Analysis results LSCI Mean Basal Flow (AU) |         |                          |                           |                               |        |       |
|--------------------------------------------|---------|--------------------------|---------------------------|-------------------------------|--------|-------|
| Effect/Contrast                            | P-value | First LSM<br>of contrast | Second LSM<br>of contrast | Estimate of<br>the difference | 95% CI |       |
|                                            |         |                          |                           |                               | Lower  | Upper |
| Prevalue                                   | 0.2150  |                          |                           |                               |        |       |
| LPS Challenge Day                          | 0.4913  |                          |                           |                               |        |       |
| Time                                       | <.0001  |                          |                           |                               |        |       |
| Day by time                                | 0.0898  |                          |                           |                               |        |       |
| LPS Day 15 - LPS Day 1                     | 0.5315  | 82.0                     | 85.4                      | -3.4                          | -15.2  | 8.3   |
| LPS Day 29 - LPS Day 1                     | 0.2429  | 78.6                     | 85.4                      | -6.8                          | -18.8  | 5.3   |
| LPS Day 29 - LPS Day 15                    | 0.4495  | 78.6                     | 82.0                      | -3.3                          | -12.6  | 5.9   |
| LPS Day 15 - LPS Day 1 at 10h              | 0.3958  | 95.4                     | 89.5                      | 6.0                           | -8.2   | 20.1  |
| LPS Day 29 - LPS Day 1 at 10h              | 0.9780  | 89.3                     | 89.5                      | -0.2                          | -14.9  | 14.5  |
| LPS Day 29 - LPS Day 15 at 10h             | 0.3103  | 89.3                     | 95.4                      | -6.2                          | -18.3  | 6.0   |
| LPS Day 15 - LPS Day 1 at 24h              | 0.6786  | 74.5                     | 71.6                      | 2.9                           | -11.3  | 17.1  |
| LPS Day 29 - LPS Day 1 at 24h              | 0.6330  | 68.1                     | 71.6                      | -3.5                          | -18.2  | 11.3  |
| LPS Day 29 - LPS Day 15 at 24h             | 0.2943  | 68.1                     | 74.5                      | -6.4                          | -18.5  | 5.8   |

| Treatment  | Time    | LSM  | 95% CI |       | LSM change<br>from baseline | 95% CI |       |
|------------|---------|------|--------|-------|-----------------------------|--------|-------|
|            |         |      | Lower  | Upper |                             | Lower  | Upper |
| LPS Day 1  | Overall | 85.4 | 74.6   | 96.3  | 30.6                        | 19.7   | 41.4  |
|            | 2h      | 87.6 | 75.6   | 99.6  | 32.8                        | 20.8   | 44.8  |
|            | 4h      | 93.0 | 81.0   | 105.0 | 38.2                        | 26.2   | 50.2  |
|            | 10h     | 89.5 | 77.5   | 101.4 | 34.6                        | 22.6   | 46.6  |
|            | 24h     | 71.6 | 59.6   | 83.5  | 16.7                        | 4.7    | 28.7  |
| LPS Day 15 | Overall | 82.0 | 75.5   | 88.5  | 27.1                        | 20.6   | 33.6  |
|            | 2h      | 71.9 | 63.8   | 80.0  | 17.1                        | 9.0    | 25.1  |
|            | 4h      | 86.1 | 78.0   | 94.2  | 31.3                        | 23.2   | 39.3  |
|            | 10h     | 95.4 | 87.4   | 103.5 | 40.6                        | 32.5   | 48.6  |
|            | 24h     | 74.5 | 66.4   | 82.5  | 19.6                        | 11.5   | 27.7  |
| LPS Day 29 | Overall | 78.6 | 70.9   | 86.4  | 23.8                        | 16.0   | 31.6  |
|            | 2h      | 70.4 | 60.9   | 80.0  | 15.6                        | 6.0    | 25.1  |
|            | 4h      | 86.9 | 77.3   | 96.4  | 32.0                        | 22.5   | 41.5  |
|            | 10h     | 89.3 | 79.7   | 98.8  | 34.4                        | 24.9   | 43.9  |
|            | 24h     | 68.1 | 58.5   | 77.6  | 13.2                        | 3.7    | 22.8  |

## 2.2. Erythema by Antera 3D camera

| Analysis results Skin Colour (AU) |         |                       |                        |                            |        |       |
|-----------------------------------|---------|-----------------------|------------------------|----------------------------|--------|-------|
| Effect/Contrast                   | P-value | First LSM of contrast | Second LSM of contrast | Estimate of the difference | 95% CI |       |
|                                   |         |                       |                        |                            | Lower  | Upper |
| Prevalue                          | 0.1102  |                       |                        |                            |        |       |
| LPS Challenge Day                 | 0.2305  |                       |                        |                            |        |       |
| Time                              | <.0001  |                       |                        |                            |        |       |
| Day by time                       | 0.3560  |                       |                        |                            |        |       |
| LPS Day 15 - LPS Day 1            | 0.6480  | 9.9                   | 10.1                   | -0.2                       | -1.3   | 0.8   |
| LPS Day 29 - LPS Day 1            | 0.0956  | 9.1                   | 10.1                   | -1.0                       | -2.2   | 0.2   |
| LPS Day 29 - LPS Day 15           | 0.1659  | 9.1                   | 9.9                    | -0.8                       | -1.9   | 0.4   |
| LPS Day 15 - LPS Day 1 at 10h     | 0.5442  | 10.9                  | 10.5                   | 0.4                        | -1.0   | 1.9   |
| LPS Day 29 - LPS Day 1 at 10h     | 0.6261  | 10.1                  | 10.5                   | -0.4                       | -1.9   | 1.2   |
| LPS Day 29 - LPS Day 15 at 10h    | 0.2459  | 10.1                  | 10.9                   | -0.8                       | -2.2   | 0.6   |
| LPS Day 15 - LPS Day 1 at 24h     | 0.9663  | 9.1                   | 9.1                    | 0.0                        | -1.4   | 1.5   |
| LPS Day 29 - LPS Day 1 at 24h     | 0.5786  | 8.6                   | 9.1                    | -0.4                       | -2.0   | 1.1   |
| LPS Day 29 - LPS Day 15 at 24h    | 0.5068  | 8.6                   | 9.1                    | -0.5                       | -1.8   | 0.9   |

| Treatment  | Time    | LSM  | 95% CI |       | LSM change from baseline | 95% CI |       |
|------------|---------|------|--------|-------|--------------------------|--------|-------|
|            |         |      | Lower  | Upper |                          | Lower  | Upper |
| LPS Day 1  | Overall | 10.1 | 9.2    | 11.0  | 3.0                      | 2.1    | 3.9   |
|            | 2h      | 10.3 | 9.2    | 11.5  | 3.2                      | 2.1    | 4.4   |
|            | 4h      | 10.6 | 9.5    | 11.8  | 3.5                      | 2.4    | 4.7   |
|            | 10h     | 10.5 | 9.3    | 11.6  | 3.4                      | 2.3    | 4.6   |
|            | 24h     | 9.1  | 7.9    | 10.2  | 2.0                      | 0.8    | 3.1   |
| LPS Day 15 | Overall | 9.9  | 9.1    | 10.7  | 2.8                      | 2.0    | 3.6   |
|            | 2h      | 9.0  | 8.1    | 10.0  | 1.9                      | 1.0    | 2.9   |
|            | 4h      | 10.5 | 9.6    | 11.4  | 3.4                      | 2.5    | 4.4   |
|            | 10h     | 10.9 | 10.0   | 11.8  | 3.8                      | 2.9    | 4.8   |
|            | 24h     | 9.1  | 8.2    | 10.0  | 2.0                      | 1.1    | 2.9   |
| LPS Day 29 | Overall | 9.1  | 8.2    | 10.0  | 2.0                      | 1.1    | 3.0   |
|            | 2h      | 8.3  | 7.3    | 9.4   | 1.3                      | 0.2    | 2.3   |
|            | 4h      | 9.3  | 8.2    | 10.4  | 2.2                      | 1.2    | 3.3   |
|            | 10h     | 10.1 | 9.0    | 11.2  | 3.0                      | 2.0    | 4.1   |
|            | 24h     | 8.6  | 7.6    | 9.7   | 1.5                      | 0.5    | 2.6   |

| Analysis results Haemoglobin Average Level (AU) |         |                       |                        |                            |        |       |
|-------------------------------------------------|---------|-----------------------|------------------------|----------------------------|--------|-------|
| Effect/Contrast                                 | P-value | First LSM of contrast | Second LSM of contrast | Estimate of the difference | 95% CI |       |
|                                                 |         |                       |                        |                            | Lower  | Upper |
| Prevalue                                        | 0.2827  |                       |                        |                            |        |       |
| LPS Challenge Day                               | 0.3393  |                       |                        |                            |        |       |
| Time                                            | <.0001  |                       |                        |                            |        |       |
| Day by time                                     | 0.3008  |                       |                        |                            |        |       |
| LPS Day 15 - LPS Day 1                          | 0.9341  | 22.8                  | 22.9                   | -0.1                       | -2.9   | 2.7   |
| LPS Day 29 - LPS Day 1                          | 0.1713  | 20.4                  | 22.9                   | -2.5                       | -6.1   | 1.2   |
| LPS Day 29 - LPS Day 15                         | 0.1706  | 20.4                  | 22.8                   | -2.4                       | -5.9   | 1.1   |
| LPS Day 15 - LPS Day 1 at 10h                   | 0.4113  | 25.7                  | 24.1                   | 1.5                        | -2.2   | 5.2   |
| LPS Day 29 - LPS Day 1 at 10h                   | 0.6966  | 23.3                  | 24.1                   | -0.8                       | -5.1   | 3.4   |
| LPS Day 29 - LPS Day 15 at 10h                  | 0.2522  | 23.3                  | 25.7                   | -2.3                       | -6.4   | 1.7   |
| LPS Day 15 - LPS Day 1 at 24h                   | 0.5694  | 20.9                  | 19.8                   | 1.0                        | -2.6   | 4.7   |
| LPS Day 29 - LPS Day 1 at 24h                   | 0.6648  | 18.9                  | 19.8                   | -0.9                       | -5.1   | 3.3   |
| LPS Day 29 - LPS Day 15 at 24h                  | 0.3354  | 18.9                  | 20.9                   | -1.9                       | -6.0   | 2.1   |

| Treatment  | Time    | LSM  | 95% CI |       | LSM change from baseline | 95% CI |       |
|------------|---------|------|--------|-------|--------------------------|--------|-------|
|            |         |      | Lower  | Upper |                          | Lower  | Upper |
| LPS Day 1  | Overall | 22.9 | 20.5   | 25.3  | 7.9                      | 5.5    | 10.3  |
|            | 2h      | 23.2 | 20.4   | 26.0  | 8.2                      | 5.3    | 11.0  |
|            | 4h      | 24.4 | 21.6   | 27.2  | 9.4                      | 6.5    | 12.2  |
|            | 10h     | 24.1 | 21.3   | 27.0  | 9.1                      | 6.3    | 12.0  |
|            | 24h     | 19.8 | 17.0   | 22.7  | 4.8                      | 2.0    | 7.6   |
| LPS Day 15 | Overall | 22.8 | 20.7   | 24.8  | 7.8                      | 5.7    | 9.8   |
|            | 2h      | 20.4 | 17.8   | 23.0  | 5.4                      | 2.8    | 8.0   |
|            | 4h      | 24.2 | 21.6   | 26.8  | 9.2                      | 6.6    | 11.8  |
|            | 10h     | 25.7 | 23.1   | 28.2  | 10.6                     | 8.1    | 13.2  |
|            | 24h     | 20.9 | 18.3   | 23.5  | 5.9                      | 3.3    | 8.4   |
| LPS Day 29 | Overall | 20.4 | 17.3   | 23.5  | 5.4                      | 2.3    | 8.5   |
|            | 2h      | 18.3 | 15.1   | 21.6  | 3.3                      | 0.0    | 6.6   |
|            | 4h      | 21.1 | 17.8   | 24.4  | 6.1                      | 2.8    | 9.4   |
|            | 10h     | 23.3 | 20.0   | 26.6  | 8.3                      | 5.0    | 11.6  |
|            | 24h     | 18.9 | 15.6   | 22.2  | 3.9                      | 0.6    | 7.2   |

### 2.3. Erythema grading score: Clinical Erythema Assessment (CEA)

| Frequency Clinical Erythema Assessment                                                                                                                                                                                                                                                                                             |      |          |              |         |          |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|--------------|---------|----------|
| Treatment and location                                                                                                                                                                                                                                                                                                             | Time | Clear    | Almost Clear | Mild    | Moderate |
| LPS Day 1: Site A                                                                                                                                                                                                                                                                                                                  | Pre  | 8 (100%) | 0 (0%)       | 0 (0%)  | 0 (0%)   |
|                                                                                                                                                                                                                                                                                                                                    | 10h  | 0 (0%)   | 2 (25%)      | 5 (63%) | 1 (13%)  |
|                                                                                                                                                                                                                                                                                                                                    | 24h  | 0 (%)    | 0 (%)        | 0 (%)   | 0 (%)    |
| LPS Day 1: Site B                                                                                                                                                                                                                                                                                                                  | Pre  | 8 (100%) | 0 (0%)       | 0 (0%)  | 0 (0%)   |
|                                                                                                                                                                                                                                                                                                                                    | 10h  | 0 (0%)   | 1 (13%)      | 6 (75%) | 1 (13%)  |
|                                                                                                                                                                                                                                                                                                                                    | 24h  | 1 (13%)  | 1 (13%)      | 6 (75%) | 0 (0%)   |
| LPS Day 1: Site G                                                                                                                                                                                                                                                                                                                  | Pre  | 8 (100%) | 0 (0%)       | 0 (0%)  | 0 (0%)   |
|                                                                                                                                                                                                                                                                                                                                    | 10h  | 0 (0%)   | 0 (0%)       | 5 (63%) | 3 (38%)  |
|                                                                                                                                                                                                                                                                                                                                    | 24h  | 0 (%)    | 0 (%)        | 0 (%)   | 0 (%)    |
| LPS Day 15: Site C                                                                                                                                                                                                                                                                                                                 | Pre  | 8 (100%) | 0 (0%)       | 0 (0%)  | 0 (0%)   |
|                                                                                                                                                                                                                                                                                                                                    | 10h  | 0 (0%)   | 4 (50%)      | 4 (50%) | 0 (0%)   |
|                                                                                                                                                                                                                                                                                                                                    | 24h  | 0 (%)    | 0 (%)        | 0 (%)   | 0 (%)    |
| LPS Day 15: Site D                                                                                                                                                                                                                                                                                                                 | Pre  | 8 (100%) | 0 (0%)       | 0 (0%)  | 0 (0%)   |
|                                                                                                                                                                                                                                                                                                                                    | 10h  | 0 (0%)   | 2 (25%)      | 6 (75%) | 0 (0%)   |
|                                                                                                                                                                                                                                                                                                                                    | 24h  | 0 (0%)   | 3 (38%)      | 4 (50%) | 1 (13%)  |
| LPS Day 29: Site E                                                                                                                                                                                                                                                                                                                 | Pre  | 8 (100%) | 0 (0%)       | 0 (0%)  | 0 (0%)   |
|                                                                                                                                                                                                                                                                                                                                    | 10h  | 0 (0%)   | 1 (13%)      | 6 (75%) | 1 (13%)  |
|                                                                                                                                                                                                                                                                                                                                    | 24h  | 0 (%)    | 0 (%)        | 0 (%)   | 0 (%)    |
| LPS Day 29: Site F                                                                                                                                                                                                                                                                                                                 | Pre  | 8 (100%) | 0 (0%)       | 0 (0%)  | 0 (0%)   |
|                                                                                                                                                                                                                                                                                                                                    | 10h  | 0 (0%)   | 2 (25%)      | 5 (63%) | 1 (13%)  |
|                                                                                                                                                                                                                                                                                                                                    | 24h  | 0 (0%)   | 4 (50%)      | 4 (50%) | 0 (0%)   |
| <b>A:Upper back/Left(L) Upper(D) B:Upper back/Right(L) Upper(D) C:Upper back/Left(L) Middle(D)</b><br><b>D:Upper back/Right(L) Middle(D) E:Upper back/Left(L) Bottom(D) F:Upper back/Right(L) Bottom(D)</b><br><b>G:Forearm/Right(L) Volar(D); L=Lateral; D=Directional</b><br><b>No scores taken at 24h for sites A,C,E and G</b> |      |          |              |         |          |

### 3. Blister exudate analysis

#### 3.1. Neutrophils and monocyte subsets

| Analysis results LOG Amount of CD16+ CD66+ Neutrophils (cells) |         |                          |                           |                               |        |         |
|----------------------------------------------------------------|---------|--------------------------|---------------------------|-------------------------------|--------|---------|
| Effect/Contrast                                                | P-value | Back Transformed         |                           |                               |        |         |
|                                                                |         | First LSM<br>of contrast | Second LSM<br>of contrast | Estimate of<br>the difference | 95% CI |         |
|                                                                |         |                          |                           |                               | Lower  | Upper   |
| LPS Challenge Day                                              | 0.6145  |                          |                           |                               |        |         |
| Time                                                           | 0.0008  |                          |                           |                               |        |         |
| Day by time                                                    | 0.1431  |                          |                           |                               |        |         |
| LPS Day 15 - LPS Day 1                                         | 0.4491  | 25.7                     | 52.2                      | -50.7%                        | -93.0% | 248.6%  |
| LPS Day 29 - LPS Day 1                                         | 0.3720  | 24.9                     | 52.2                      | -52.4%                        | -91.5% | 167.0%  |
| LPS Day 29 - LPS Day 15                                        | 0.9720  | 24.9                     | 25.7                      | -3.3%                         | -87.4% | 641.9%  |
| LPS Day 15 - LPS Day 1 at 10h                                  | 0.0803  | 38.5                     | 286.3                     | -86.6%                        | -98.6% | 30.4%   |
| LPS Day 29 - LPS Day 1 at 10h                                  | 0.1958  | 70.9                     | 286.3                     | -75.2%                        | -97.2% | 116.7%  |
| LPS Day 29 - LPS Day 15 at 10h                                 | 0.6228  | 70.9                     | 38.5                      | 84.4%                         | -85.5% | 2238.7% |
| LPS Day 15 - LPS Day 1 at 24h                                  | 0.5929  | 17.2                     | 9.5                       | 80.9%                         | -81.4% | 1655.8% |
| LPS Day 29 - LPS Day 1 at 24h                                  | 0.9270  | 8.7                      | 9.5                       | -8.4%                         | -87.0% | 546.0%  |
| LPS Day 29 - LPS Day 15 at 24h                                 | 0.5574  | 8.7                      | 17.2                      | -49.3%                        | -95.3% | 441.2%  |

| Back Transformed |         |       |        |        |
|------------------|---------|-------|--------|--------|
| Treatment        | Time    | LSM   | 95% CI |        |
|                  |         |       | Lower  | Upper  |
| LPS Day 1        | Overall | 52.2  | 14.8   | 183.9  |
|                  | 10h     | 286.3 | 73.1   | 1120.9 |
|                  | 24h     | 9.5   | 2.4    | 37.3   |
| LPS Day 15       | Overall | 25.7  | 4.6    | 144.1  |
|                  | 10h     | 38.5  | 5.4    | 274.1  |
|                  | 24h     | 17.2  | 2.4    | 122.7  |
| LPS Day 29       | Overall | 24.9  | 6.0    | 102.4  |
|                  | 10h     | 70.9  | 11.4   | 443.0  |
|                  | 24h     | 8.7   | 1.9    | 41.1   |

## Analysis results LOG Amount of classical monocytes (CD14+ CD16-) (cells)

| Effect/Contrast                | P-value | Back Transformed         |                           |                               |        |        |
|--------------------------------|---------|--------------------------|---------------------------|-------------------------------|--------|--------|
|                                |         | First LSM<br>of contrast | Second LSM<br>of contrast | Estimate of<br>the difference | 95% CI |        |
|                                |         |                          |                           |                               | Lower  | Upper  |
| LPS Challenge Day              | 0.1261  |                          |                           |                               |        |        |
| Time                           | 0.4437  |                          |                           |                               |        |        |
| Day by time                    | 0.1169  |                          |                           |                               |        |        |
| LPS Day 15 - LPS Day 1         | 0.0543  | 128.0                    | 279.4                     | -54.2%                        | -79.4% | 1.7%   |
| LPS Day 29 - LPS Day 1         | 0.1452  | 127.3                    | 279.4                     | -54.5%                        | -84.8% | 36.8%  |
| LPS Day 29 - LPS Day 15        | 0.9912  | 127.3                    | 128.0                     | -0.6%                         | -66.9% | 199.2% |
| LPS Day 15 - LPS Day 1 at 10h  | 0.0053  | 85.8                     | 566.5                     | -84.8%                        | -95.7% | -46.4% |
| LPS Day 29 - LPS Day 1 at 10h  | 0.1060  | 155.8                    | 566.5                     | -72.5%                        | -94.4% | 35.0%  |
| LPS Day 29 - LPS Day 15 at 10h | 0.4759  | 155.8                    | 85.8                      | 81.5%                         | -67.0% | 898.4% |
| LPS Day 15 - LPS Day 1 at 24h  | 0.5986  | 190.9                    | 137.8                     | 38.5%                         | -60.9% | 390.4% |
| LPS Day 29 - LPS Day 1 at 24h  | 0.6776  | 104.0                    | 137.8                     | -24.5%                        | -81.2% | 202.3% |
| LPS Day 29 - LPS Day 15 at 24h | 0.4175  | 104.0                    | 190.9                     | -45.5%                        | -88.1% | 149.7% |

| Treatment  | Time    | Back Transformed |        |        |  |
|------------|---------|------------------|--------|--------|--|
|            |         | LSM              | 95% CI |        |  |
|            |         |                  | Lower  | Upper  |  |
| LPS Day 1  | Overall | 279.4            | 150.1  | 520.0  |  |
|            | 10h     | 566.5            | 254.9  | 1259.3 |  |
|            | 24h     | 137.8            | 62.0   | 306.4  |  |
| LPS Day 15 | Overall | 128.0            | 68.2   | 240.2  |  |
|            | 10h     | 85.8             | 29.7   | 248.4  |  |
|            | 24h     | 190.9            | 66.0   | 552.4  |  |
| LPS Day 29 | Overall | 127.3            | 46.2   | 350.8  |  |
|            | 10h     | 155.8            | 36.6   | 662.8  |  |
|            | 24h     | 104.0            | 31.0   | 348.4  |  |

## Analysis results LOG Amount of intermediate monocytes (CD14+ CD16+) (cells)

| Effect/Contrast   | P-value | Back Transformed         |                           |                               |        |       |
|-------------------|---------|--------------------------|---------------------------|-------------------------------|--------|-------|
|                   |         | First LSM<br>of contrast | Second LSM<br>of contrast | Estimate of<br>the difference | 95% CI |       |
|                   |         |                          |                           |                               | Lower  | Upper |
| LPS Challenge Day | 0.4470  |                          |                           |                               |        |       |
| Time              | 0.9514  |                          |                           |                               |        |       |

|                                |        |      |      |        |        |         |
|--------------------------------|--------|------|------|--------|--------|---------|
| Day by time                    | 0.1328 |      |      |        |        |         |
| LPS Day 15 - LPS Day 1         | 0.3562 | 10.6 | 20.3 | -47.8% | -87.9% | 125.1%  |
| LPS Day 29 - LPS Day 1         | 0.2418 | 7.8  | 20.3 | -61.8% | -93.0% | 109.1%  |
| LPS Day 29 - LPS Day 15        | 0.7109 | 7.8  | 10.6 | -26.9% | -87.7% | 333.8%  |
| LPS Day 15 - LPS Day 1 at 10h  | 0.0406 | 5.1  | 35.6 | -85.7% | -97.8% | -8.6%   |
| LPS Day 29 - LPS Day 1 at 10h  | 0.1672 | 8.8  | 35.6 | -75.2% | -96.7% | 87.7%   |
| LPS Day 29 - LPS Day 15 at 10h | 0.5909 | 8.8  | 5.1  | 73.4%  | -78.7% | 1310.1% |
| LPS Day 15 - LPS Day 1 at 24h  | 0.4801 | 22.1 | 11.6 | 90.7%  | -70.2% | 1119.4% |
| LPS Day 29 - LPS Day 1 at 24h  | 0.5698 | 6.8  | 11.6 | -41.2% | -91.3% | 298.1%  |
| LPS Day 29 - LPS Day 15 at 24h | 0.2316 | 6.8  | 22.1 | -69.2% | -95.8% | 125.3%  |

|            |         | Back Transformed |        |       |
|------------|---------|------------------|--------|-------|
|            |         | LSM              | 95% CI |       |
| Treatment  | Time    |                  | Lower  | Upper |
| LPS Day 1  | Overall | 20.3             | 7.1    | 58.0  |
|            | 10h     | 35.6             | 9.6    | 132.0 |
|            | 24h     | 11.6             | 3.1    | 42.9  |
| LPS Day 15 | Overall | 10.6             | 3.1    | 35.8  |
|            | 10h     | 5.1              | 1.2    | 21.6  |
|            | 24h     | 22.1             | 5.2    | 93.9  |
| LPS Day 29 | Overall | 7.8              | 1.7    | 35.7  |
|            | 10h     | 8.8              | 1.6    | 47.5  |
|            | 24h     | 6.8              | 1.4    | 32.1  |

| Analysis results LOG Amount of non classical monocytes (CD14- CD16+) (cells) |         |                       |                        |                            |        |        |
|------------------------------------------------------------------------------|---------|-----------------------|------------------------|----------------------------|--------|--------|
|                                                                              |         | Back Transformed      |                        |                            | 95% CI |        |
| Effect/Contrast                                                              | P-value | First LSM of contrast | Second LSM of contrast | Estimate of the difference | Lower  | Upper  |
| LPS Challenge Day                                                            | 0.1363  |                       |                        |                            |        |        |
| Time                                                                         | 0.0254  |                       |                        |                            |        |        |
| Day by time                                                                  | 0.2579  |                       |                        |                            |        |        |
| LPS Day 15 - LPS Day 1                                                       | 0.1023  | 6.2                   | 16.4                   | -62.2%                     | -88.6% | 24.8%  |
| LPS Day 29 - LPS Day 1                                                       | 0.0758  | 5.9                   | 16.4                   | -64.1%                     | -88.6% | 12.9%  |
| LPS Day 29 - LPS Day 15                                                      | 0.9346  | 5.9                   | 6.2                    | -4.9%                      | -73.6% | 243.2% |

|                                |        |     |      |        |        |        |
|--------------------------------|--------|-----|------|--------|--------|--------|
| LPS Day 15 - LPS Day 1 at 10h  | 0.0194 | 6.3 | 44.6 | -85.9% | -97.2% | -29.2% |
| LPS Day 29 - LPS Day 1 at 10h  | 0.0452 | 9.3 | 44.6 | -79.1% | -95.5% | -3.6%  |
| LPS Day 29 - LPS Day 15 at 10h | 0.5993 | 9.3 | 6.3  | 48.6%  | -68.1% | 592.7% |
| LPS Day 15 - LPS Day 1 at 24h  | 0.9849 | 6.1 | 6.0  | 1.5%   | -79.8% | 411.3% |
| LPS Day 29 - LPS Day 1 at 24h  | 0.5033 | 3.7 | 6.0  | -38.2% | -85.7% | 167.4% |
| LPS Day 29 - LPS Day 15 at 24h | 0.4920 | 3.7 | 6.1  | -39.1% | -86.1% | 166.3% |

|            |         | Back Transformed |        |       |
|------------|---------|------------------|--------|-------|
| Treatment  | Time    | LSM              | 95% CI |       |
|            |         |                  | Lower  | Upper |
| LPS Day 1  | Overall | 16.4             | 7.3    | 36.8  |
|            | 10h     | 44.6             | 13.5   | 147.2 |
|            | 24h     | 6.0              | 1.8    | 19.9  |
| LPS Day 15 | Overall | 6.2              | 2.2    | 17.4  |
|            | 10h     | 6.3              | 1.9    | 21.2  |
|            | 24h     | 6.1              | 1.8    | 20.7  |
| LPS Day 29 | Overall | 5.9              | 2.3    | 15.4  |
|            | 10h     | 9.3              | 3.2    | 27.6  |
|            | 24h     | 3.7              | 1.4    | 10.0  |

## Adverse events

| Summary of Number of Subjects with TEAEs by Treatment SOC and PT |                                            |             |                                            |             |                                            |             |                       |             |
|------------------------------------------------------------------|--------------------------------------------|-------------|--------------------------------------------|-------------|--------------------------------------------|-------------|-----------------------|-------------|
| System Organ Class/<br>Preferred Term                            | LIPOPOLYSACCHARIDE<br>CHALLENGE 1<br>(N=9) |             | LIPOPOLYSACCHARIDE<br>CHALLENGE 2<br>(N=8) |             | LIPOPOLYSACCHARIDE<br>CHALLENGE 3<br>(N=8) |             | All Subjects<br>(N=9) |             |
|                                                                  | Subjects<br>N (%)                          | Events<br>N | Subjects<br>N (%)                          | Events<br>N | Subjects<br>N (%)                          | Events<br>N | Subjects<br>N (%)     | Events<br>N |
| ANY EVENTS                                                       | 3 ( 33.3%)                                 | 6           | 3 ( 37.5%)                                 | 3           | 3 ( 37.5%)                                 | 3           | 6 ( 66.7%)            | 12          |
| GENERAL DISORDERS AND<br>ADMINISTRATION SITE<br>CONDITIONS       | 1 ( 11.1%)                                 | 1           | 0                                          | 0           | 0                                          | 0           | 1 ( 11.1%)            | 1           |
| INFLUENZA LIKE ILLNESS                                           | 1 ( 11.1%)                                 | 1           | 0                                          | 0           | 0                                          | 0           | 1 ( 11.1%)            | 1           |
| INFECTIONS AND<br>INFESTATIONS                                   | 1 ( 11.1%)                                 | 1           | 2 ( 25.0%)                                 | 2           | 1 ( 12.5%)                                 | 1           | 3 ( 33.3%)            | 4           |
| HERPES ZOSTER                                                    | 1 ( 11.1%)                                 | 1           | 0                                          | 0           | 0                                          | 0           | 1 ( 11.1%)            | 1           |
| NASOPHARYNGITIS                                                  | 0                                          | 0           | 2 ( 25.0%)                                 | 2           | 1 ( 12.5%)                                 | 1           | 2 ( 22.2%)            | 3           |
| MUSCULOSKELETAL AND<br>CONNECTIVE TISSUE<br>DISORDERS            | 1 ( 11.1%)                                 | 1           | 0                                          | 0           | 0                                          | 0           | 1 ( 11.1%)            | 1           |
| MYALGIA                                                          | 1 ( 11.1%)                                 | 1           | 0                                          | 0           | 0                                          | 0           | 1 ( 11.1%)            | 1           |
| NERVOUS SYSTEM DISORDERS                                         | 0                                          | 0           | 1 ( 12.5%)                                 | 1           | 1 ( 12.5%)                                 | 1           | 2 ( 22.2%)            | 2           |
| HEADACHE                                                         | 0                                          | 0           | 1 ( 12.5%)                                 | 1           | 0                                          | 0           | 1 ( 11.1%)            | 1           |
| PRESYNCOPE                                                       | 0                                          | 0           | 0                                          | 0           | 1 ( 12.5%)                                 | 1           | 1 ( 11.1%)            | 1           |
| RESPIRATORY, THORACIC AND<br>MEDIASTINAL DISORDERS               | 1 ( 11.1%)                                 | 2           | 0                                          | 0           | 0                                          | 0           | 1 ( 11.1%)            | 2           |
| HAEMOPTYSIS                                                      | 1 ( 11.1%)                                 | 1           | 0                                          | 0           | 0                                          | 0           | 1 ( 11.1%)            | 1           |
| OROPHARYNGEAL PAIN                                               | 1 ( 11.1%)                                 | 1           | 0                                          | 0           | 0                                          | 0           | 1 ( 11.1%)            | 1           |
| SKIN AND SUBCUTANEOUS<br>TISSUE DISORDERS                        | 1 ( 11.1%)                                 | 1           | 0                                          | 0           | 1 ( 12.5%)                                 | 1           | 2 ( 22.2%)            | 2           |
| PRURITUS                                                         | 1 ( 11.1%)                                 | 1           | 0                                          | 0           | 0                                          | 0           | 1 ( 11.1%)            | 1           |
| SENSITIVE SKIN                                                   | 0                                          | 0           | 0                                          | 0           | 1 ( 12.5%)                                 | 1           | 1 ( 11.1%)            | 1           |

SOC: System Organ Class, PT: Preferred Term, TEAE: Treatment Emergent Adverse Event