

Table S1. NAC PK (25 &amp; 40mg/kg/dose) for individual participants

| ID-NAC dose                                   | GA<br>(wks)   | Birth<br>Weight<br>(gm) | t <sub>1/2</sub> (hrs)<br>HT vs NT |              | Vd (L/kg)<br>HT vs NT |                | CL (mL/hr/kg)<br>HT vs NT |             | NAC C <sub>min</sub> <sub>ss</sub><br>(mcg/mL)<br>HT vs NT |              | NAC C <sub>max</sub> <sub>ss</sub><br>(mcg/mL)<br>HT vs NT |                | NAC CSF<br>(mcg/mL) | AUC<br>HT vs NT |              |
|---|---------------|-------------------------|------------------------------------|--------------|-----------------------|----------------|---------------------------|-------------|--|--------------|--|----------------|---------------------|-----------------|--------------|
| NAC 25mg/kg                                   |               |                         |                                    |              |                       |                |                           |             |  |              |  |                |                     |                 |              |
| NVD-1-25                                      | 37.8          | 3125                    | 3.6                                | 1.9          | 1.26                  | 1.46           | 78                        | 173         | 5.7  | 0.5          | 58.0   | 41.6           | 0.74                | 296             | 143          |
| NVD-2-25                                      | 41.0          | 3430                    | 4.2                                | 2.3          | 0.41                  | 0.48           | 68                        | 142         | 7.5  | 1.0          | 55.3   | 34.4           |                     | 277             | 151          |
| NVD-3-25                                      | 37.3          | 3615                    | 8.3                                | 3.8          | 0.65                  | 0.59           | 54                        | 107         | 21.6   | 4.6          | 59.1   | 41.7           |                     | 266             | 201          |
| NVD-4-25-ECMO                                 | 36.0          | 3180                    | 6.1                                | 5.8          | 0.78                  | 0.42           | 89                        | 51          | 10.5   | 17.3         | 41.5   | 72.7           |                     | 188             | 365          |
| NVD-5-25                                      | 37.0          | 2130                    | 6.6                                | 4.5          | 0.57                  | 0.73           | 59                        | 112         | 16.6   | 5.7          | 58.4   | 36.5           |                     | 285             | 185          |
| NVD-6-25-ECMO                                 | 37.9          | 2645                    | 4.5                                | 5.8          | 0.76                  | 1.13           | 117                       | 133         | 3.0  | 1.9          | 77.5   | 22.5           |                     | 437             | 144          |
| NVD-7-25                                      | 36.0          | 3560                    | 5.3                                | 3.3          | 0.41                  | 0.48           | 54                        | 101         | 16.3   | 4.4          | 79.3   | 54.9           |                     | 389             | 235          |
| NVD-8-25                                      | 40.4          | 3380                    | 4.4                                | 3.7          | 0.47                  | 0.64           | 73                        | 121         | 8.8  | 4.1          | 57.4   | 39.8           |                     | 284             | 182          |
| NVD-9-25                                      | 37.0          | 2370                    | 5.7                                | 5.2          | 0.48                  | 0.52           | 58                        | 69          | 4.2  | 3.0          | 52.8   | 48.8           |                     | 312             | 273          |
| NVD-10-25                                     | 41.1          | 3380                    | 8.1                                | 4.0          | 0.49                  | 0.63           | 42                        | 111         | 28.0   | 5.1          | 78.3   | 41.7           |                     | 359             | 183          |
| NVD-12-25                                     | 36.9          | 3440                    | 6.0                                | 5.0          | 1.36                  | 0.82           | 130                       | 114         | 2.0  | 1.6          | 22.5   | 29.5           |                     | 138             | 174          |
| NVD-13-25                                     | 39.7          | 3824                    | 4.0                                | 5.7          | 0.40                  | 0.77           | 69                        | 94          | 1.5  | 2.6          | 56.5   | 33.1           |                     | 310             | 196          |
| NVD-14-25                                     | 40.0          | 3581                    | 3.9                                | 3.9          | 0.47                  | 0.56           | 83                        | 99          | 1.2  | 1.0          | 47.5   | 39.2           |                     | 259             | 223          |
| NVD-15-25                                     | 39.1          | 3430                    | 5.8                                | 3.2          | 0.56                  | 0.32           | 67                        | 68          | 3.7  | 0.7          | 45.4   | 64.3           |                     | 263             | 334          |
| NVD-16-25                                     | 36.7          | 3080                    | 5.8                                | 3.7          | 0.49                  | 0.49           | 58                        | 92          | 14.9   | 5.5          | 63.0   | 52.0           |                     | 316             | 221          |
| NVD-24-25                                     | 37.6          | 3050                    | 5.8                                | 4.7          | 0.40                  | 1.30           | 48                        | 190         | 17.4   | 3.5          | 72.7   | 20.4           | 1.32                | 368             | 100          |
| NVD-25-25                                     | 38.0          | 2910                    | 4.9                                | 5.1          | 0.33                  | 0.73           | 47                        | 100         | 15.1   | 7.4          | 82.8   | 37.8           |                     | 387             | 188          |
| NVD-28-25                                     | 37.9          | 3645                    | 11.2                               | 4.8          | 0.76                  | 1.03           | 47                        | 149         | 29.8   | 4.7          | 62.5   | 26.6           | 9.76                | 274             | 104          |
| Mean (SD) NAC 25mg/kg                         | 38.1<br>(1.6) | 3210<br>(456)           | 5.8<br>(1.9)                       | 4.2<br>(1.1) | 0.63<br>(0.29)        | 0.73<br>(0.31) | 68<br>(23)                | 113<br>(35) | 11.5<br>(8.9)  | 4.1<br>(3.8) | 59.5<br>(15.2)   | 41.0<br>(13.7) |                     | 389<br>(102)    | 238<br>(86)  |
| <i>p value*</i><br><i>HT vs NT NAC25mg/kg</i> |               |                         | 0.0050*                            |              | 0.1415                |                | 0.0006*                   |             | 0.0017*  |              | 0.0030*  |                |                     |                 |              |
| NAC 40mg/kg                                   |               |                         |                                    |              |                       |                |                           |             |  |              |  |                |                     |                 |              |
| NVD-17-40                                     | 39            | 3325                    | 7.1                                | 3.8          | 0.78                  | 0.77           | 77                        | 144         | 21.8   | 5.6          | 70.5   | 51.4           |                     | 341             | 241          |
| NVD-18-40                                     | 38.3          | 3380                    | 3.8                                | 3.5          | 0.55                  | 0.68           | 101                       | 132         | 7.8  | 5.2          | 69   | 54.6           |                     | 344             | 268          |
| NVD-19-40                                     | 40.2          | 3238                    | 3.6                                | 2.3          | 0.40                  | 0.71           | 78                        | 213         | 9.1  | 1.3          | 93   | 47.5           | 0.52                | 453             | 180          |
| NVD-20-40                                     | 38.9          | 3495                    | 4.2                                | 4.3          | 0.40                  | 0.67           | 66                        | 107         | 14.4   | 9.8          | 105.6  | 67.2           |                     | 497             | 295          |
| NVD-21-40                                     | 40.4          | 3470                    | 3.9                                | 6.2          | 0.43                  | 0.63           | 77                        | 71          | 11.4   | 21.4         | 96.3   | 82.4           | 1.60                | 418             | 409          |
| NVD-22-40                                     | 38.3          | 3745                    | 6.3                                | 5.5          | 0.42                  | 0.93           | 46                        | 117         | 33.6   | 10.4         | 127  | 47.4           |                     | 619             | 275          |
| NVD-27-40                                     | 39.0          | 4005                    | 4.8                                | 4.5          | 0.39                  | 0.68           | 56                        | 105         | 19.6   | 9.5          | 112.5  | 60.1           |                     | 571             | 319          |
| NVD-29-40                                     | 36.0          | 2445                    | 4.5                                | 3.1          | 0.41                  | 0.59           | 63                        | 135         | 16.2   | 4.5          | 103.3  | 69.2           |                     | 534             | 221          |
| NVD-30-40                                     | 39.0          | 3930                    | 6.2                                | 2.8          | 0.61                  | 0.69           | 69                        | 173         | 21.4   | 2.6          | 82.5   | 56.5           |                     | 426             | 183          |
| Mean (SD) NAC 40mg/kg                         | 38.8<br>(1.3) | 3110<br>(1137)          | 4.9<br>(1.3)                       | 4.0<br>(1.3) | 0.49<br>(0.13)        | 0.70<br>(0.1)  | 70<br>(16)                | 133<br>(41) | 17.3<br>(8.0)  | 7.8<br>(6.0) | 95.5<br>(19.2)   | 59.6<br>(11.6) |                     | 573<br>(160)    | 325<br>(111) |
| <i>p value* HT vs NT</i><br><i>NAC40mg/kg</i> |               |                         | 0.15                               |              | 0.0026*               |                | 0.0018*                   |             | 0.0208*  |              | 0.001*   |                |                     |                 |              |
| <i>p value NAC 25 vs 40mg/kg</i>              |               |                         |                                    |              |                       |                |                           |             | 0.12   | 0.07         | 0.0018   | 0.0018         |                     |                 |              |

Table S2. 1,25(OH)<sub>2</sub>D (0.05mcg/kg/dose) PK for individual participants

| ID             | GA<br>(wks) | Birth<br>Weight<br>(gm) | t <sub>1/2</sub> (hrs)<br>HT vs NT |       | Vd (L/kg)<br>HT vs NT |        | CL<br>(mL/hr/kg)<br>HT vs NT |        | C <sub>min</sub> <sub>ss</sub><br>(μmol/L)<br>HT vs NT |       | C <sub>max</sub> <sub>ss</sub><br>(μmol/L)<br>HT vs NT |         |
|----------------|-------------|-------------------------|------------------------------------|-------|-----------------------|--------|------------------------------|--------|--|-------|--|---------|
| NVD-1          | 37.8        | 3125                    | 29.8                               |       | 0.88                  |        | 20.5                         |        | 415  |       | 550  |         |
| NVD-2          | 41.0        | 3430                    | 57.3                               |       | 0.84                  |        | 10.2                         |        | 943  |       | 1,090  |         |
| NVD-3          | 37.3        | 3615                    | 15.6                               |       | 0.35                  |        | 19.2                         |        | 367  |       | 712  |         |
| NVD-4-<br>ECMO | 36.0        | 3180                    | 19.0                               |       | 0.84                  |        | 31.0                         |        | 264  |       | 408  |         |
| NVD-8          | 40.4        | 3380                    | 20.6                               | 13.3  | 0.64                  | 0.11   | 22.0                         | 6.0    | 377  | 1,260 | 564  | 2,352   |
| NVD-13         | 39.7        | 3824                    | 20.5                               | 23.3  | 0.36                  | 0.75   | 12.2                         | 22.4   | 379  | 211   | 571  | 307     |
| Mean           | 37.9        | 3197                    | 26.2                               | 18.3  | 0.65                  | 0.43   | 24.4                         | 14.1   | 458  | 737   | 648  | 1,330   |
| (SD)           | (1.4)       | (466)                   | (16.0)                             | (7.0) | (0.25)                | (0.45) | (15.5)                       | (11.8) | (242)  | (742) | (238)  | (1,445) |