Supplementary Table 1  Mean plasma exposure parameters $C_{\text{max}}$ and AUC (0–24 h, 48 h or 96 after single or repeated subcutaneous (RTR5001, RTR4955 or RTR3649) or intravenous administration (RTR2996) to female minipigs, female NHPs or humans at different dose levels. Similar study durations and same route of administrations per LNA SSO were compared for the different non-rodent species (except for RTR3649, where NHPs were dosed intravenously over 5 min while minipig and human subjects were dosed subcutaneously).

|               | Day 1 | Day 15 | Day 16 |
|---------------|-------|--------|--------|
| **minipig**   |       |        |        |
| dose [mg/kg]  |       |        |        |
| Mean AUC(0-24h) [µg•h)/mL] |  |  |  |
| Mean Cmax [µg/mL] | | | |
| **RTR5001**  |       |        |        |
| dose [mg/kg]  | 6     | 20     | 6      | 20    |
| Mean AUC(0-24h) [µg•h)/mL] | 25.3 ± 4.3 | 120.0 ± 26.9 | 23.6 ± 4.1 | 111.1 ± 21.9 |
| Mean Cmax [µg/mL] | 3.8 ± 1.2 | 15.1 ± 1.5 | 3.3 ± 1.0 | 15.6 ± 3.5 |
| **RTR4955**  |       |        |        |
| dose [mg/kg]  | 8     | 24     | 8      | 24    |
| Mean AUC(0-24h) [µg•h)/mL] | 66.6 ± 7.0 | 231.3 ± 21.0 | 99.3 ± 11.7 | 443.5 ± 68.6 |
| Mean Cmax [µg/mL] | 7.2 ± 0.5 | 25.8 ± 8.2 | 13.1 ± 3.2 | 65.8 ± 2.5 |
| **RTR3649**  |       |        |        |
| dose [mg/kg]  | 3     | 12     | 48     |       |
| Mean AUC(0-72h) [µg•h)/mL] | 22.4 ± 4.3 | 119.3 ± 13.1 | 749 ± 56.8 | 199 ± 9.5 |
| Mean Cmax [µg/mL] | 2.7 ± 0.5 | 8.0 ± 1.2 | 56.5 ± 7.3 | 12.6 ± 0.3 |
| **RTR2996**  |       |        |        |
| dose [mg/kg]  | 5     | 15     | 45     | 45    |
| Mean AUC(0-24h) [µg•h)/mL] | 98.4 ± 14.7 | 524.3 ± 301.6 | 1103.6 ± 198.1 | 129.0 ± 20.4 |
| Mean Cmax [µg/mL] | 64.1 ± 7.2 | 239.7 ± 148.8 | 541.2 ± 358.8 | 74.9 ± 9.6 |
| **Human**    |       |        |        |
| dose [mg/kg]  |       |        |        |
| Mean AUC(0-24h) [µg•h)/mL] |  |  |  |
| Mean Cmax [µg/mL] | | | |
| **RTR5001**  |       |        |        |
| dose [mg/kg]  | 6     | 20     | 6      | 20    |
| Mean AUC(0-24h) [µg•h)/mL] | 35.8 ± 20.7 | 77.3 ± 65.9 | 312.6 ± 126.7 | 44.1 ± 20.3 |
| Mean Cmax [µg/mL] | 19.9 ± 12.4 | 30.6 ± 26.6 | 83.7 ± 29.8 | 23.4 ± 13.2 |
| **RTR4955**  |       |        |        |
| dose [mg/kg]  | 8     | 24     | 8      | 24    |
| Mean AUC(0-24h) [µg•h)/mL] |  | no samples collected |  |  |
| Mean Cmax [µg/mL] | | | |
| **RTR3649**  |       |        |        |
| dose [mg/kg]  | 3     | 12     | 48     |       |
| Mean AUC(0-96h) [µg•h)/mL] | | |  | |
| Mean Cmax [µg/mL] |  | |  | |
| **RTR2996**  |       |        |        |
| dose [mg/kg]  | 5     | 15     | 45     | 45    |
| Mean AUC(0-24h) [µg•h)/mL] |  |  |  |
| Mean Cmax [µg/mL] |  |  |  |