**Supplemental Table S1.** Baseline-adjusted pharmacokinetic parameters (mean ± SD)

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|  | **TX-004HR** | **Placebo** **(n=17)** |
| **4 µg (n=18)** | **10 µg (n=19)** | **25 µg (n=18)** |
| **Estradiol** |  |  |  |  |
| Day 1 |  |  |  |  |
| AUC, pg\*h/mL |  -0.4 ± 46.3 |  19.5 ± 22.8 |  130.4 ± 111.9d |  8.8 ± 32.3 |
| Cmax, pg/mL |  2.6 ± 2.2 |  6.0 ± 4.4b |  26.2 ± 18.2e |  2.1 ± 3.5 |
| Cavg, pg/mL | -0.01 ± 1.9 |  0.8 ± 1.0 |  5.4 ± 4.7d |  0.4 ± 1.4 |
| Cmin, pg/mL |  -0.7 ± 1.8 |  -0.5 ± 1.0 | -0.1 ± 0.6a | -0.6 ± 0.7 |
| Day 14 |  |  |  |  |
| AUC, pg\*h/mL |  3.4 ± 16.3 |  5.7 ± 29.3 |  84.6 ± 62.7e |  -3.7 ± 30.7 |
| Cmax, pg/mL |  1.3 ± 1.1 |  3.0 ± 1.7b | 12.1 ± 7.3e |  1.0 ± 1.8 |
| Cavg, pg/mL |  0.1 ± 0.7 |  0.2 ± 1.2 |  3.5 ± 2.6e |  -0.2 ± 1.3 |
| Cmin, pg/mL | -0.3 ± 0.7 | -0.8 ± 1.1 |  0.7 ± 1.1c |  -1.1 ± 1.6 |
| **Estrone** |  |  |  |  |
| Day 1 |  |  |  |  |
| AUC, pg\*h/mL | -64.1 ± 81.8 | -25.4 ± 63.8 |  17.5 ± 89.6 |  3.1 ± 120.8 |
| Cmax, pg/mL |  0.4 ± 3.1 |  3.2 ± 3.0 |  5.1 ± 4.8 |  6.3 ± 12.8 |
| Cavg, pg/mL | -2.3 ± 2.3 | -1.1 ± 2.7 |  0.7 ± 3.7 |  0.1 ± 5.0 |
| Cmin, pg/mL | -3.7 ± 1.9 | -3.3 ± 3.9 | -1.8 ± 3.9 | -2.9 ± 4.3 |
| Day 14 |  |  |  |  |
| AUC, pg\*h/mL |  -41.3 ± 78.0 |  -22.6 ± 141.8 |  27.0 ± 115.3 |  -38.0 ± 91.1 |
| Cmax, pg/mL |  0.7 ± 3.5 |  3.7 ± 8.8 | 5.6 ± 4.8 |  3.4 ± 5.7 |
| Cavg, pg/mL | -1.7 ± 3.3 | -0.9 ± 5.9 | 1.1 ± 4.8 | -1.6 ± 3.8 |
| Cmin, pg/mL | -3.1 ± 2.9 | -2.9 ± 5.6 | -0.8 ± 4.8a | -5.1 ± 5.4 |
| **Estrone conjugates** |  |  |  |  |
| Day 1 |  |  |  |  |
| AUC, pg\*h/mL | -510.1 ± 2123 | 192.1 ± 821b |  883.8 ± 7001 | -807.7 ± 1127 |
| Cmax, pg/mL |  35.4 ± 89.1 |  90.2 ± 65.2b |  198.6 ± 301.5a |  27.1 ± 49.7 |
| Cavg, pg/mL | -21.8 ± 88.4 |  8.0 ± 34.2b |  36.8 ± 291.7 | -33.7 ± 47.0 |
| Cmin, pg/mL | -59.4 ± 93.2 |  -30.5 ± 53.1a | -55.4 ± 266 | -80.1 ± 75.5 |
| Day 14 |  |  |  |  |
| AUC, pg\*h/mL | -606.2 ± 2897 |  3364 ± 7934 |  1688 ± 7209 |  -189 ± 2157 |
| Cmax, pg/mL |  48.2 ± 132.6 |  277.8 ± 493.6 |  236.1 ± 372.4 |  67.1 ± 121.8 |
| Cavg, pg/mL |  -25.3 ± 120.7 |  140.2 ± 330.6 |  70.3 ± 300.4 |  -7.9 ± 89.9 |
| Cmin, pg/mL |  -66.5 ± 115.5 |  37.7 ± 211.2 | -39.8 ± 287 | -62.0 ± 84.0 |
| a*P*<0.05; b*P*<0.01; c*P*<0.001; d*P*=0.0001; e*P*<0.0001 vs placebo using t-tests. |