**Supplemental Table 1: Exposure to Daprodustat’s Three Major Circulating Human Metabolites in the Mouse Carcinogenicity Study**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Mouse | Sex | Week 26 Composite | | | | | |
| 2.0 mg/kg/day M2 | | 2.5 mg/kg day M3 | | 1.3 mg/kg/day M13 | |
| Daprodustat Dose | AUC0-24 | Cmax | AUC0-24 | Cmax | AUC0-24 | Cmax |
| mg/kg/day | µg.h/mL | µg/mL | µg.h/mL | µg/mL | µg.h/mL | µg/mL |
| 0.2a | M | 1.24 | 3.39 | 1.46 | 4.06 | 1.08 | 2.37 |
| F | 1.95 | 3.60 | 2.02 | 3.89 | 1.48 | 2.58 |
| 0.8 | M | NM | NM | NM | NM | NM | NM |
| F |
| 0.8a | M | 1.53 | 3.79 | 1.86 | 4.56 | 1.37 | 2.71 |
| F | 1.87 | 4.61 | 1.95 | 5.50 | 1.42 | 3.12 |
| 3a | M | 1.50 | 4.00 | 1.79 | 4.70 | 1.29 | 2.83 |
| F | 1.86 | 3.83 | 1.98 | 4.57 | 1.40 | 2.57 |

a = Included once daily subcutaneous administration of a cocktail solution containing the 3 major circulating human metabolites of daprodustat (M2, M3 and M13 at 2.0, 2.5 and 1.3 mg/kg/day, respectively). Gender-averaged exposures achieved for metabolites in Week 26 yielded margins of 1.61-fold, 1.43-fold and 1.75-fold for AUC, and; 52.3-fold, 58.5-fold and 68.5-fold for Cmax for M2, M3 and M13, respectively, over respective predicted human metabolite exposures for 24 mg QD at steady-state (data not presented).

NM = Not measured. Metabolites were not dosed to this group.