

**Supplementary Table 5: Aqueous kinetic solubility, Caco-2 permeability, plasma protein binding and hepatocyte stability of HC4, HC19, HC28 and GSK-157**

| HC #   | Aq Sol<br>( $\mu\text{M}$ ) | Caco-2                                |     | Plasma Protein Binding, % |      |       |      | Hepatocyte Cl ( $t_{1/2}$ min) |     |       |     |
|--------|-----------------------------|---------------------------------------|-----|---------------------------|------|-------|------|--------------------------------|-----|-------|-----|
|        |                             | $P_{app}$<br>( $\times 10^{-6}$ cm/s) |     | Human                     | Rat  | Mouse | Dog  | Human                          | Rat | Mouse | Dog |
|        |                             | A-B                                   | B-A |                           |      |       |      |                                |     |       |     |
| HC04   | 31                          | 15                                    | 30  | 99.3                      | 97.6 | 98.3  | 98.6 | 245                            | 9.3 | 69    | 187 |
| HC19   | 48                          | 14                                    | 46  | 98.1                      | 96.7 | 97.2  | 97.1 | 118                            | 34  | 69    | 877 |
| HC28   | 10                          | 22                                    | 51  | 99.7                      | 99.3 | 99.4  | 99.8 | 310                            | 14  | 63    | 493 |
| GSK157 | 27                          | NT                                    | NT  | 99.5                      | 99.6 | 97.8  | 94.6 | NT                             | NT  | NT    | NT  |

NT = Not Tested