**Table 02.** Basic physicochemical properties of the experimental compounds

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Compounds** | **Formula** | **MW  g/mol** | **Num.  heavy  atoms** | **Num.  arom.  Heavy  atoms** | **Fraction  Csp3** | **Num.  rotatable  bonds** | **Num.  H-bond  acceptors** | **Num.  H-bond  donors** | **Molar  Refractivity** |
|  |  |  |  |  |  |  |  |  |  |
| CMP1 | C27H26N6O4 | 498.53 | 37 | 23 | 0.22 | 9 | 7 | 1 | 141.04 |
| CMP2 | C25H22N2O5S2 | 494.58 | 34 | 23 | 0.08 | 10 | 5 | 1 | 133.18 |
| CMP3 | C22H19N3O5S | 437.47 | 31 | 20 | 0.18 | 8 | 7 | 1 | 115.7 |
| CMP4 | C25H23N3O5 | 445.47 | 33 | 22 | 0.16 | 8 | 6 | 1 | 124.61 |
| CMP5 | C22H24N4O4 | 408.45 | 30 | 17 | 0.23 | 8 | 5 | 2 | 114.83 |
| CMP6 | C20H20N4O4 | 380.4 | 28 | 17 | 0.15 | 8 | 5 | 2 | 104.9 |
| CMP7 | C22H13BrN4O | 429.27 | 28 | 22 | 0 | 2 | 5 | 1 | 114.37 |
| CMP8 | C22H13N5O3 | 395.37 | 30 | 22 | 0 | 3 | 7 | 1 | 115.49 |
| CMP9 | C22H13ClN4O | 384.82 | 28 | 22 | 0 | 2 | 5 | 14 | 111.68 |
| CMP10 | C27H27N3O4S | 489.59 | 35 | 18 | 0.22 | 10 | 4 | 1 | 146.8 |
| CMP11 | C22H18ClN3O3S2 | 471.98 | 31 | 21 | 0.14 | 8 | 4 | 1 | 125.85 |
| CMP12 | C23H16N4O2 | 380.40 | 29 | 22 | 0.04 | 3 | 6 | 1 | 113.16 |
| CMP13 | C32H21ClN4O5 | 576.99 | 42 | 24 | 0.12 | 5 | 6 | 1 | 165.27 |
| CMP14 | C23H23N5O4 | 433.46 | 32 | 21 | 0.22 | 8 | 6 | 1 | 119.81 |
| CMP15 | C19H18N4O4 | 366.37 | 27 | 17 | 0.11 | 8 | 5 | 3 | 100 |
| CMP16 | C24H21N3O5 | 431.44 | 32 | 22 | 0.12 | 8 | 6 | 1 | 119.64 |
| JBJ-125 | C29H26FN5O3S | 543.61 | 39 | 23 | 0.21 | 7 | 6 | 3 | 159.07 |
| osimertinib | C28H33N7O2 | 499.61 | 37 | 21 | 0.25 | 11 | 5 | 2 | 150.43 |

**Table 03.** Lipophilicity of the selected compounds.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Compounds** | **TPSA (Å²)** | **Log  Po/w (iLOGP)** | **Log  Po/w  (XLOGP3)** | **Log  Po/w  (WLOGP)** | **Log  Po/w  (MLOGP)** | **Log  Po/w  (SILICOS-IT)** | **Consensus Log  Po/w** |
| CMP1 | 111.47 | 3.99 | 4.14 | 3.02 | 2.88 | 2.79 | 3.36 |
| CMP2 | 121.56 | 3.25 | 5.05 | 6.27 | 2.57 | 3.85 | 4.2 |
| CMP3 | 132.76 | 3.26 | 4.46 | 4.42 | 1.83 | 4.36 | 3.67 |
| CMP4 | 91.16 | 3.3 | 2.75 | 3.51 | 2.26 | 3.71 | 3.1 |
| CMP5 | 94.48 | 3.25 | 2.91 | 3.18 | 1.84 | 2.92 | 2.82 |
| CMP6 | 94.48 | 3.08 | 2.18 | 2.56 | 1.39 | 1.86 | 2.22 |
| CMP7 | 70.73 | 2.89 | 4.96 | 4.95 | 3 | 5.79 | 4.32 |
| CMP8 | 116.55 | 2.51 | 4.1 | 4.1 | 2.31 | 2.94 | 3.19 |
| CMP9 | 70.73 | 3.13 | 4.9 | 4.84 | 2.89 | 5.75 | 4.3 |
| CMP10 | 103.2 | 4.12 | 4.22 | 3.33 | 2.61 | 4.71 | 3.8 |
| CMP11 | 126.24 | 3.66 | 4.07 | 4.68 | 3.06 | 5.64 | 4.16 |
| CMP12 | 79.96 | 3.26 | 4.24 | 4.2 | 2.08 | 5.17 | 3.79 |
| CMP13 | 124.66 | 3.04 | 5.45 | 4.53 | 2.88 | 3.21 | 3.82 |
| CMP14 | 99.75 | 3.64 | 2.39 | 2.97 | 2.31 | 2.16 | 2.69 |
| CMP15 | 105.34 | 2.18 | 2.34 | 2.55 | 0.76 | 2.38 | 2.04 |
| CMP16 | 91.16 | 3.54 | 2.37 | 3.2 | 2.05 | 3.18 | 2.87 |
| JBJ-125 | 126.04 | 3.21 | 3.76 | 3.01 | 2.48 | 4.67 | 3.42 |
| osimertinib | 87.55 | 3.51 | 3.72 | 4.32 | 1.71 | 2.95 | 3.24 |

**Table 04. Water solubility properties of compounds**.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Compounds** | **Log S  (ESOL)** | **LogS  Solubility  mg/ml** | **LogS  Solubility  mol/l** | **Class** | **Ali  log S** | **Ali Solubility  mg/ml** | **Ali Solubility  mol/l** | **Ali  Class** | **SILICOS-IT  Log S** | **Solubility  mg/ml** | **Solubility  mol/l** | **SILICOS-IT  Class** |
| **CMP1** | -5.41 | 1.96e-03 | 3.93e-06 | Moderately  soluble | -6.19 | 3.23E-04 | 6.48E-07 | Poorly  soluble | -7.82 | 7.63e-06 | 1.53e-08 | Poorly  soluble |
| **CMP2** | -5.93 | 5.83E-04 | 1.18E-06 | Moderately  soluble | -7.34 | 2.24e-05 | 4.53e-08 | Poorly soluble | -8.58 | 1.30E-06 | 2.63E-09 | Poorly  soluble |
| **CMP3** | -5.31 | 2.14e-03 | 4.88e-06 | Moderately  soluble | -6.97 | 4.72e-05 | 1.08E-07 | Poorly soluble | -8.04 | 3.95e-06 | 9.04e-09 | Poorly  soluble |
| **CMP4** | -4.3 | 2.23E-02 | 5.01E-05 | Moderately  soluble | -4.32 | 2.14E-02 | 4.79e-05 | Moderately  soluble | -8.11 | 3.44E-06 | 7.73E-09 | Poorly  soluble |
| **CMP5** | -4.1 | 3.27e-02 | 8.00e-05 | Moderately  soluble | -4.55 | 1.14E-02 | 2.79E-05 | Moderately  soluble | -6.78 | 6.83e-05 | 1.67E-07 | Poorly  soluble |
| **CMP6** | -3.49 | 1.22e-01 | 3.21E-04 | Soluble | -3.8 | 6.06E-02 | 1.59E-04 | Soluble | -6.03 | 3.58e-04 | 9.42E-07 | Poorly  soluble |
| **CMP7** | -6.08 | 3.61e-04 | 8.40E-07 | Poorly soluble | -6.18 | 2.81e-04 | 6.55E-07 | Poorly soluble | -8.93 | 5.01e-07 | 1.17e-09 | Poorly  soluble |
| **CMP8** | -5.22 | 2.39E-03 | 6.04E-06 | Moderately  soluble | -6.25 | 2.21e-04 | 5.58e-07 | Poorly soluble | -7.49 | 1.28e-05 | 3.23E-08 | Poorly  soluble |
| **CMP9** | -5.76 | 6.65E-04 | 1.73E-06 | Moderately  soluble | -6.12 | 2.91E-04 | 7.56e-07 | Poorly soluble | -8.74 | 7.07E-07 | 1.84E-09 | Poorly  soluble |
| **CMP10** | -5.25 | 2.72E-03 | 5.56e-06 | Moderately  soluble | -6.1 | 3.91E-04 | 7.99e-07 | Poorly soluble | -7.99 | 5.03e-06 | 1.03E-08 | Poorly  soluble |
| **CMP11** | -5.3 | 2.35E-03 | 4.97E-06 | Moderately  soluble | -6.43 | 1.77e-04 | 3.75E-07 | Poorly soluble | -8.23 | 2.78E-06 | 5.89E-09 | Poorly  soluble |
| **CMP12** | -5.23 | 2.22e-03 | 5.85E-06 | Moderately  soluble | -5.63 | 8.91E-04 | 2.34E-06 | Moderately  soluble | -8.25 | 2.13E-06 | 5.60e-09 | Poorly  soluble |
| **CMP13** | -6.94 | 6.57E-05 | 1.14e-07 | Poorly soluble | -6.94 | 6.57E-05 | 1.14E-07 | Poorly soluble | -9.83 | 8.55E-08 | 1.48E-10 | Poorly  soluble |
| **CMP14** | -3.99 | 4.43e-02 | 1.02E-04 | Soluble | -4.13 | 3.24e-02 | 7.48E-05 | Moderately  soluble | -6.45 | 1.56E-04 | 3.59E-07 | Poorly  soluble |
| **CMP15** | -3.52 | 1.10E-01 | 2.99E-04 | Soluble | -4.19 | 2.36E-02 | 6.43e-05 | Moderately  soluble | -6.47 | 1.23e-04 | 3.35E-07 | Poorly  soluble |
| **CMP16** | -3.99 | 4.43E-02 | 1.03E-04 | Soluble | -3.92 | 5.13E-02 | 1.19e-04 | Soluble | -7.74 | 7.87E-06 | 1.82E-08 | Poorly  soluble |
| **JBJ-125** | -5.55 | 1.52E-03 | 2.80e-06 | Moderately  soluble | -6.1 | 4.32E-04 | 7.95e-07 | Poorly soluble | -8.64 | 1.24E-06 | 2.28E-09 | Poorly  soluble |
| **osimertinib** | -4.98 | 5.29E-03 | 1.06E-05 | Moderately  soluble | -5.25 | 2.81e-03 | 5.62e-06 | Moderately  soluble | -8.23 | 2.96E-06 | 5.93e-09 | Poorly  soluble |

**Table 05.** Predicted metabolism properties of compounds.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Compounds** | **GI**  **absorption** | **BBB permeant** | **P-gp substrate** | **CYP1A2 inhibitor** | **CYP2C19 inhibitor** | **CYP2C9 inhibitor** | **CYP2D6 inhibitor** | **CYP3A4 inhibitor** | **Log Kp(skin permeation)cm/s** |
| CMP1 | High | No | Yes | No | Yes | Yes | Yes | Yes | -6.4 |
| CMP2 | Low | No | No | No | Yes | yes | Yes | Yes | -5.73 |
| CMP3 | Low | No | No | No | Yes | yes | No | Yes | -8.04 |
| CMP4 | High | No | Yes | No | yes | yes | yes | yes | -7.06 |
| CMP5 | High | No | No | No | No | Yes | yes | Yes | -6.73 |
| CMP6 | High | No | Yes | No | No | Yes | yes | Yes | -7.07 |
| CMP7 | High | No | No | Yes | Yes | Yes | No | No | -5.4 |
| CMP8 | High | No | No | No | No | yes | No | No | -5.8 |
| CMP9 | High | No | No | Yes | Yes | Yes | No | No | -5.17 |
| CMP10 | High | No | Yes | No | yes | yes | yes | yes | -6.29 |
| CMP11 | Low | No | No | Yes | Yes | Yes | yes | yes | -6.29 |
| CMP12 | High | No | No | Yes | No | Yes | No | yes | -5.61 |
| CMP13 | Low | No | yes | yes | yes | yes | No | No | -5.95 |
| CMP14 | High | No | Yes | No | No | Yes | No | Yes | -7.25 |
| CMP15 | High | No | Yes | yes | No | Yes | Yes | yes | -6.87 |
| CMP16 | High | No | Yes | yes | Yes | yes | Yes | yes | -7.25 |
| JBJ-125 | High | No | Yes | No | Yes | yes | Yes | yes | -6.95 |
| osimertinib | High | No | Yes | No | yes | yes | yes | yes | -6.71 |