

**Supplementary Table 1**

**High throughput identification and characterization of novel, species-selective**

**GPR35 agonists**

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| MRCT code | pEC <sub>50</sub> |       |     | E <sub>max</sub> (100μM) |       |     |
|-----------|-------------------|-------|-----|--------------------------|-------|-----|
|           | Human             | Mouse | Rat | Human                    | Mouse | Rat |
| 1007      | 4.3               | <4    | 5.5 | 58                       | 42    | 34  |
| 18030     | 4.8               | 5.2   | 6.1 | 189                      | 135   | 164 |
| 18036     | 5.9               | 6.8   | 6.4 | 79                       | 82    | 105 |
| 26822     | 5                 | 4.9   | 4.8 | 75                       | 94    | 41  |
| 39029     | <4                | 4.9   | 5.2 | 5                        | 67    | 34  |
| 41311     | 5.2               | <4    | <4  | 25                       | 0     | 1   |
| 42475     | 5.3               | 4.6   | 5.1 | 40                       | 60    | 60  |
| 42699     | <4                | 4.2   | 5.1 | 29                       | 103   | 85  |
| 50003     | 5                 | <4    | <4  | 19                       | 0     | 3   |
| 50351     | 4.7               | 5     | <4  | 71                       | 40    | 50  |
| 54454     | 7                 | 4.9   | 5.5 | 94                       | 62    | 41  |
| 59297     | 4.8               | 5.7   | 6.1 | 54                       | 66    | 51  |
| 59416     | 5.5               | 5.1   | 4.3 | 92                       | 74    | 51  |
| 59439     | 5.1               | 4.2   | 5   | 87                       | 47    | 86  |
| 59521     | 5.1               | <4    | <4  | 61                       | 18    | 23  |
| 59872*    | 6.8               | 6.5   | 5.3 | 67                       | 60    | 56  |
| 60030     | 5                 | <4    | <4  | 68                       | 50    | 44  |
| 60211     | 5.5               | <4    | 4.2 | 99                       | 38    | 46  |
| 104124    | 5.6               | <4    | <4  | 98                       | 9     | 14  |
| 121525    | 5.1               | <4    | <4  | 83                       | 6     | 4   |
| 122758    | 5.3               | <4    | <4  | 80                       | 15    | 29  |
| 126907    | <4                | 5.2   | 5.2 | 9                        | 39    | 30  |
| 127254    | 5.3               | 4.5   | <4  | 44                       | 46    | 38  |
| 132295    | 5.8               | 4.8   | 5   | 21                       | 29    | 42  |
| 141051    | 5.1               | 4.6   | 4.9 | 92                       | 82    | 62  |
| 149265    | <4                | 5.4   | 4   | 38                       | 23    | 70  |
| 177540    | 4.5               | 5.8   | 4.4 | 87                       | 76    | 60  |
| 179831    | 4.6               | <4    | 5.3 | 103                      | 23    | 127 |
| 192086    | <4                | 5.5   | 5.8 | 9                        | 48    | 10  |
| 192973    | 5.5               | 5.2   | 5.2 | 23                       | 33    | 44  |

**Supplementary Table 1** The potency and efficacy of a series of compounds repurchased following initial screening of the diversity library against human GPR35 was assessed in BRET-based GPR35- $\beta$ -arrestin-2 interactions assays using each of the human, rat and mouse orthologs of the receptor. Efficacy values are compared to zaprinast. \* One compound was insufficiently soluble to be assayed at 100  $\mu$ M and therefore efficacy values reflect function at 10  $\mu$ M. The chemical identity of any of these ligands is available on request.