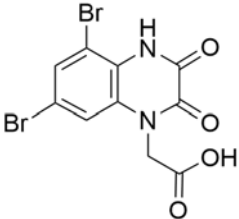
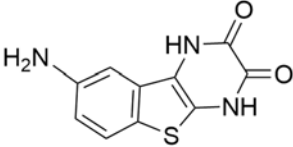
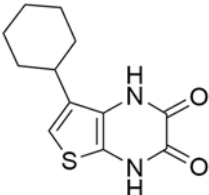
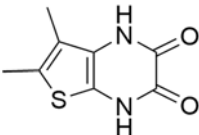
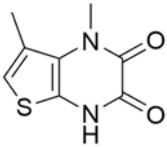
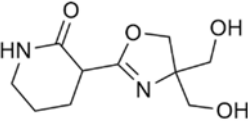
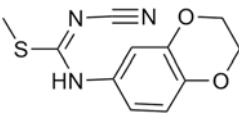
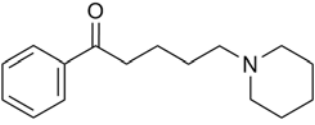
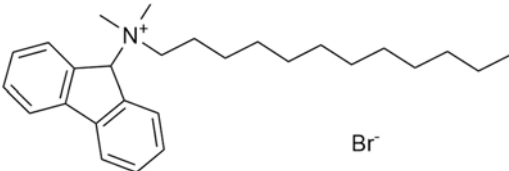
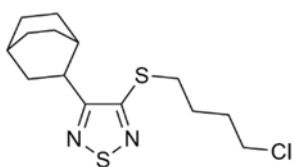


**Supplementary Table S1. Hits from primary screening.**

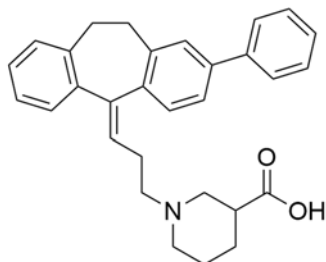
| Compound     | Structure  | Activity<br>(% positive control) |
|--------------|--|----------------------------------|
| WNN0002-F006 |     | 73                               |
| WNN0003-B006 |     | 54                               |
| WNN0003-F007 |    | 51                               |
| WNN0003-G011 |   | 54                               |
| WNN0004-D007 |   | 57                               |
| WNN0027-E003 |   | 53                               |
| WNN0027-G008 |   | 56                               |
| WNN0028-D009 |   | 56                               |
| WNN0048-A002 |  | 215                              |

WNN0056-B006



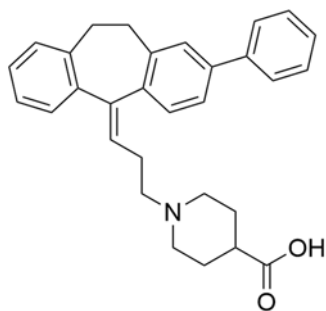
76

WNN0063-E008



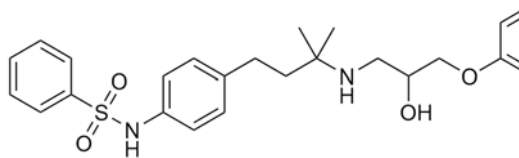
68

WNN0063-E009



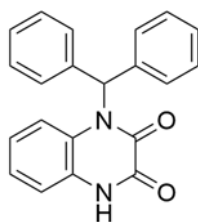
130

WNN0109-C011



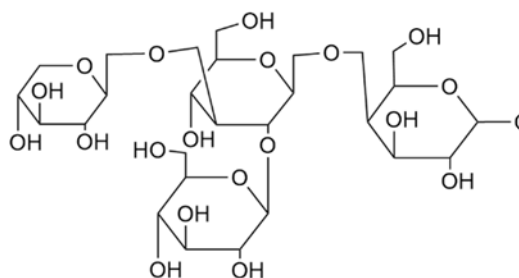
85

WNN0119-H005



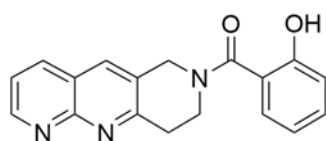
82

WNN0148-E005



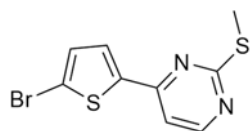
129

WNN0195-H002



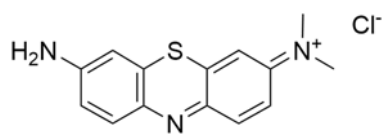
65

WNN0196-B004



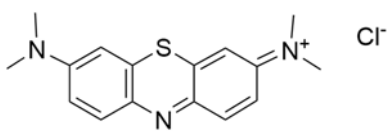
78

WNN0314-F004



50

WNN0314-G003



51

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**Supplementary Table S2. Binding of europium-labelled H3 B1-22R to RXFP3 in competition with various small molecules agonists.**

| Compound                     | <i>p</i> Ki        |
|------------------------------|--------------------|
| H3 B1-22R (RXFP3 antagonist) | 7.59 ± 0.06 (n=12) |
| <i>R</i> -WNN0109-C011       | 4.50 ± 0.16 (n=3)  |
| <i>S</i> -WNN0109-C011       | 4.04 ± 0.16 (n=3)  |
| (±)WNN0109-C011              | 4.38 ± 0.10 (n=3)  |