Supplementary Materials:

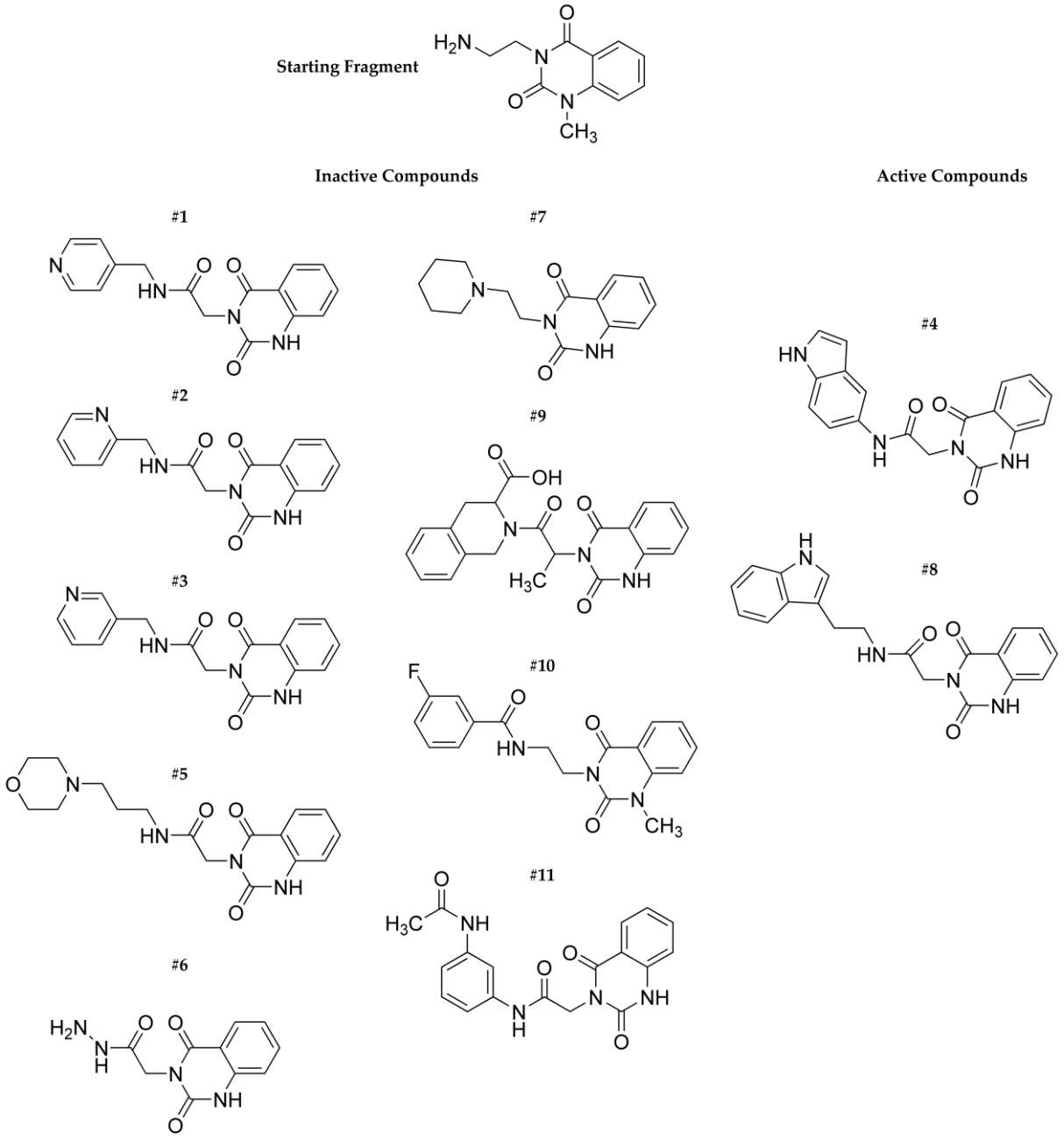


Figure S1. Scaffold and compounds selected by similarity-based search in the ChemBridge screening compounds database. Compounds were classified as active if they showed significant inhibition of *Lm*USP activity at 500 μM. The compounds can be identified by their respective ChemBridge ID numbers: #**1** (CID 9245967), #**2** (CID 9214059), #**3** (CID 9252929), #**4** (CID 9207718), #**5** (CID 9231249), #**6** (CID 9270353), #**7** (CID 9195974), #**8** (CID 9206277), #**9** (CID 9280745), #**10** (CID 9329111), #**11** (CID 9212920).

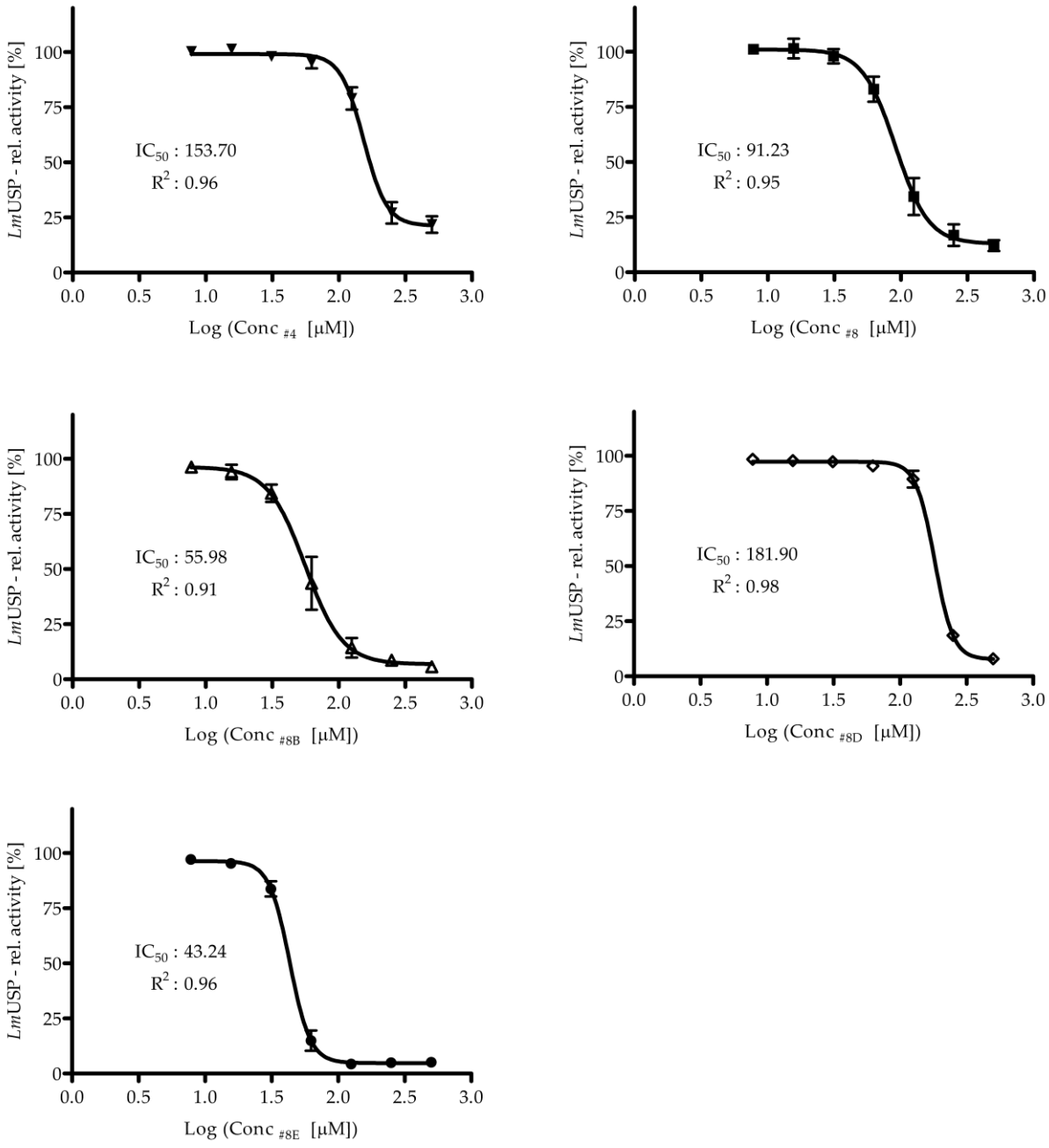


Figure S2. Nonlinear regression – sigmoidal dose-response curve for IC_{50} determination of compounds #**4**, #**8**, #**8B**, #**8D** and #**8E** bound to *Lm*USP. Error bars are given as standard deviations from at least 2 independent experiments.

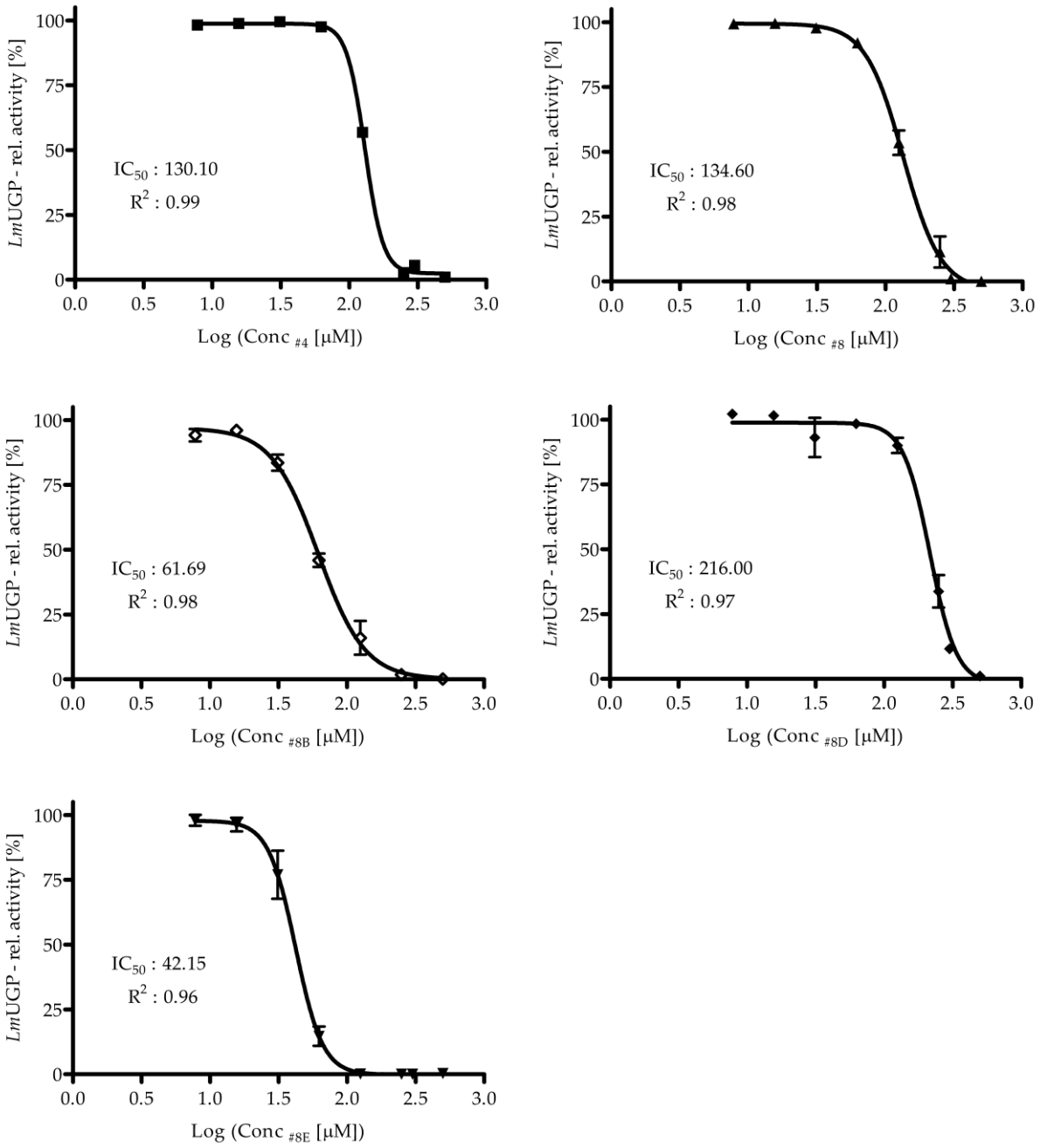
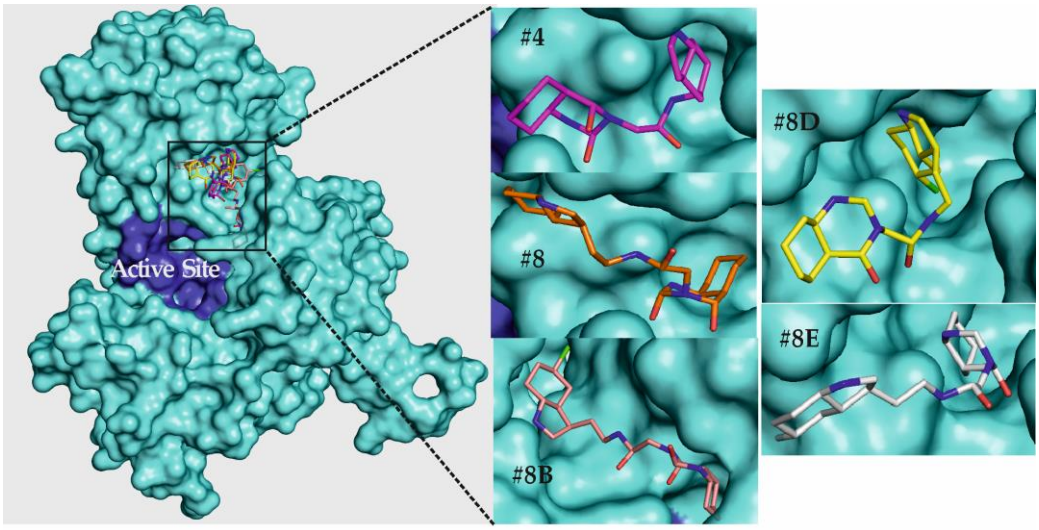
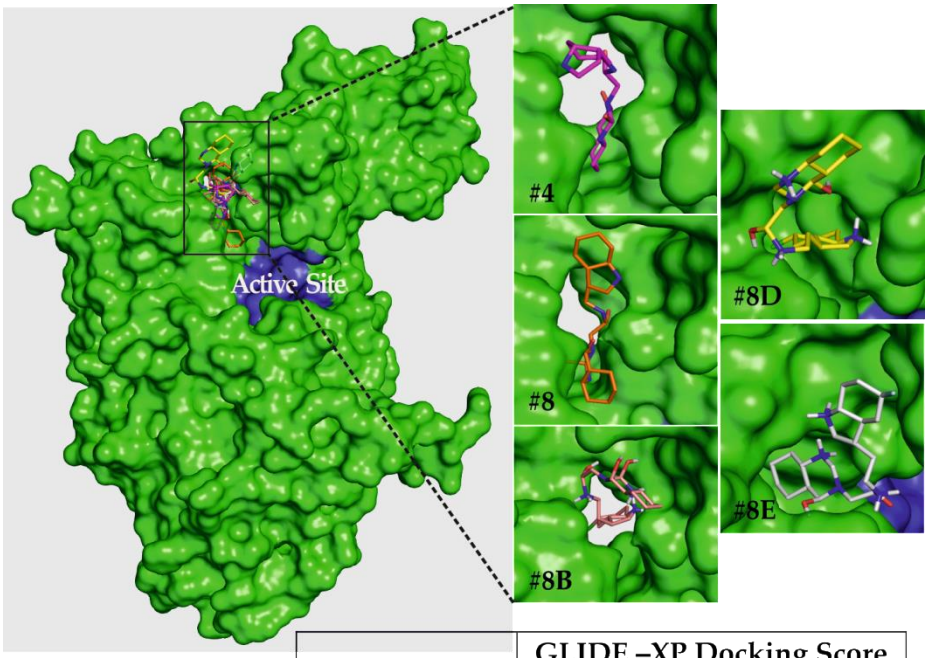


Figure S3. Nonlinear regression – sigmoidal dose-response curve for IC_{50} determination of compounds #**4**, #**8**, #**8B**, #**8D** and #**8E** bound to *Lm*UGP. Error bars are given as standard deviations from at least 2 independent experiments.



Compound	GLIDE –XP Docking Score (kcal/mol)
#4	-9.647
#8	-8.186
#8B	-10.638
#8D	-7.428
#8E	-10.099

Figure S4. Surface representation of *Lm*UGP in cyan with the active site colored in blue. The docked ligands (**#4**, **#8**, **#8B**, **#8D**, and **#8E**) at the allosteric site are shown in stick representation. The table shows the corresponding docking scores.



Compound	GLIDE –XP Docking Score (kcal/mol)
#4	-9.960
#8	-8.183
#8B	-9.065
#8D	-9.358
#8E	-9.761

Figure S5. Surface representation of *Lm*USP in green with the active site colored in blue. The docked ligands (**#4**, **#8**, **#8B**, **#8D,** and **#8E**) at site 1 are shown in stick representation. The table shows the corresponding docking scores.

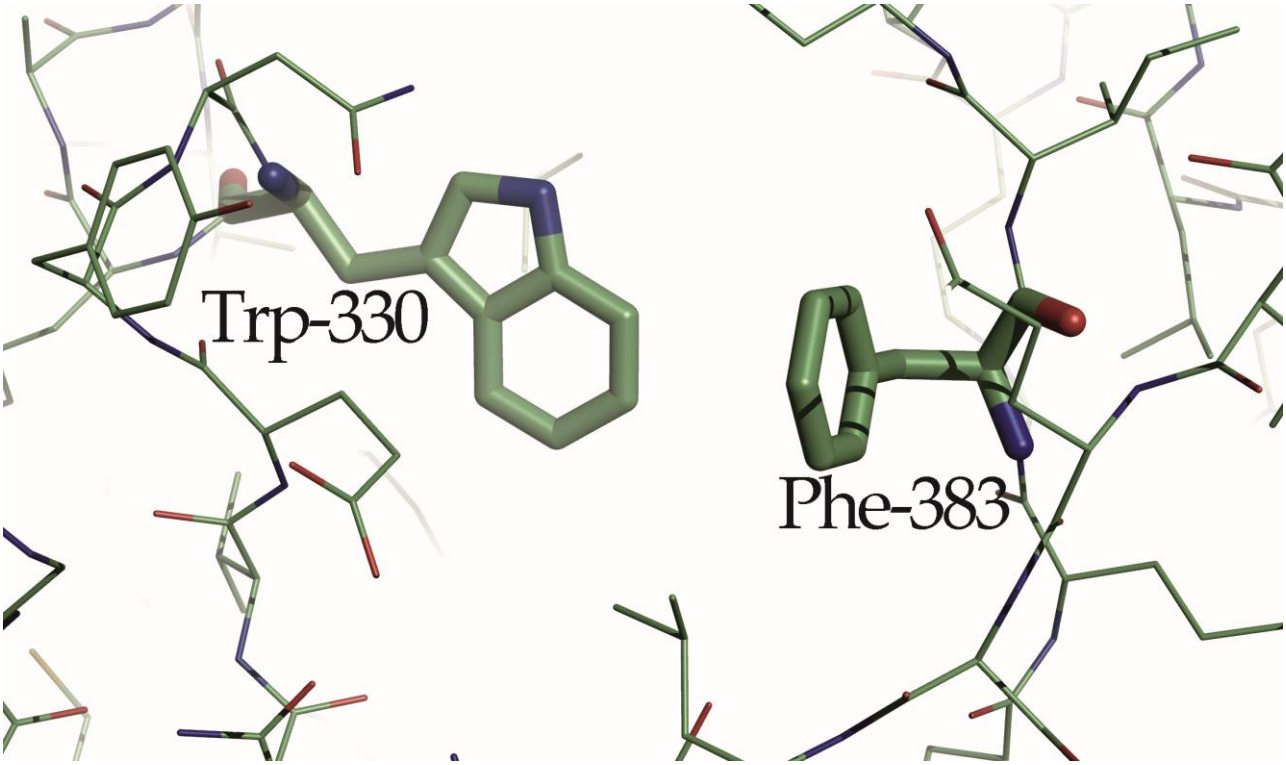


Figure S6. Phenylalanine 383 (Wild type) and Tryptophan 330 (introduced by point mutation) hypothesized to favor catalytically active conformation via π- interaction. Mutation was introduced using the 'Mutagenesis' feature in Pymol.

Table S1. Structure and estimated K_D values of hits from the BLI based fragment binding study.

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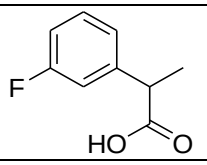
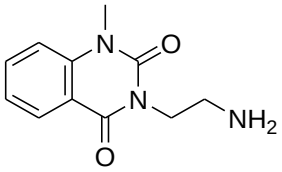
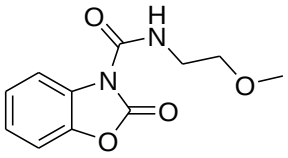
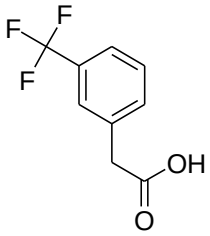
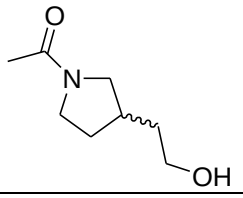
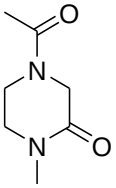
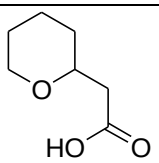
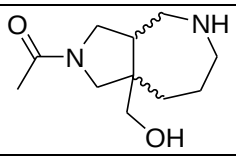
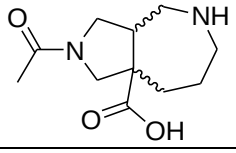
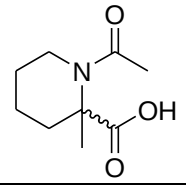
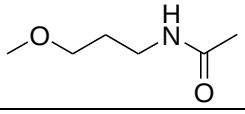
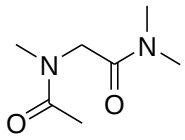
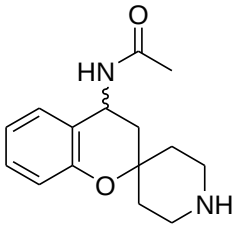
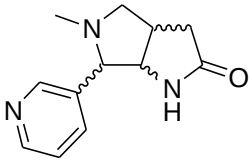
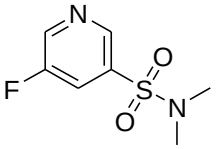
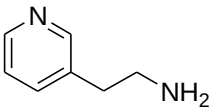
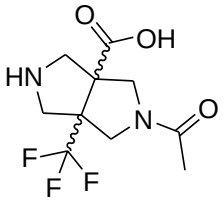
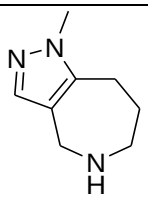
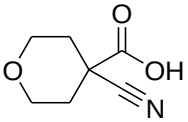
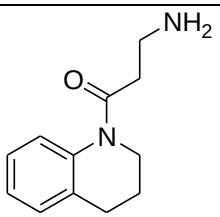
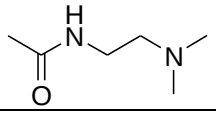
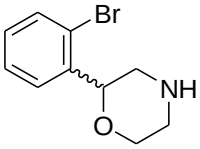
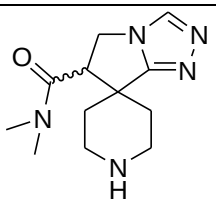
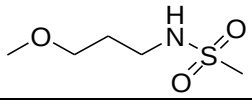
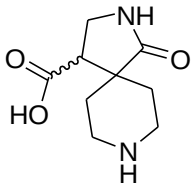
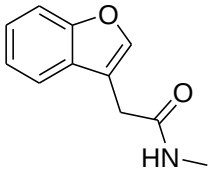
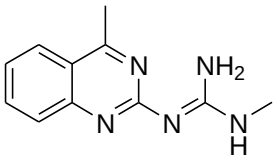
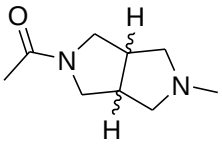
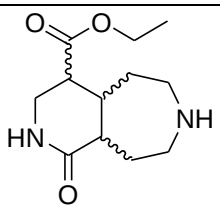
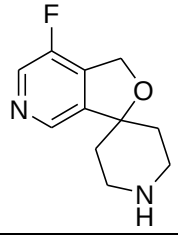
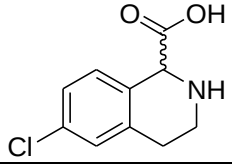
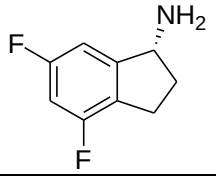
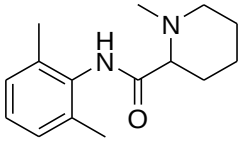
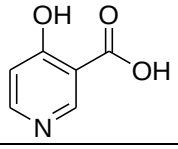
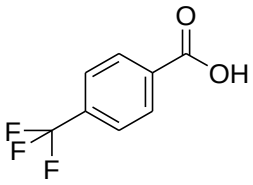
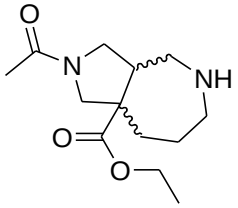
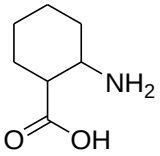
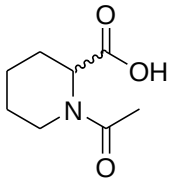
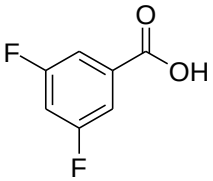
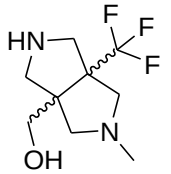
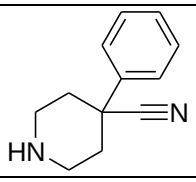
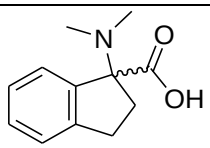
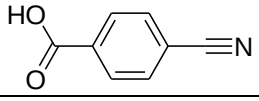
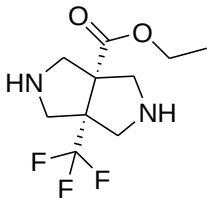
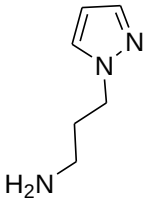
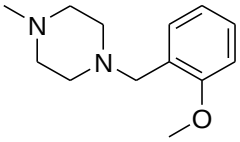
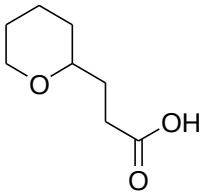
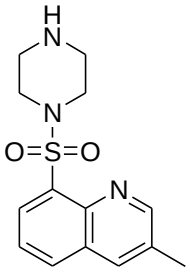
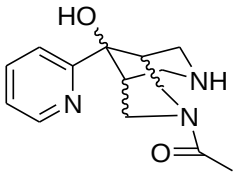
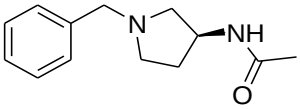
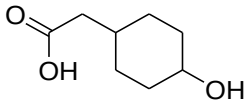
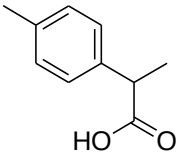
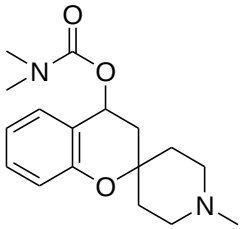
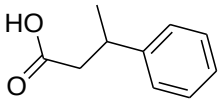
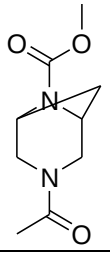
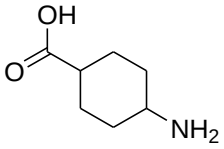
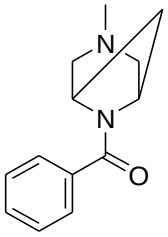
DDD01305586		60.1
DDD00808259		67.6
DDD00102262		72.6
DDD00095351		83.3
DDD00957472		105
DDD00957473		120
DDD01305716		120
DDD01085540		135
DDD01085543		137

DDD01008789		140
DDD00805740		156
DDD00957469		156
DDD01085499		156
DDD01085562		157
DDD01012352		161
DDD00771428		163
DDD01085542		167
DDD00103423		173
DDD01008838		173
DDD01008805		176

DDD00770978		181
DDD01008822		185
DDD01269650		194
DDD00805744		204
DDD01269623		207
DDD00771029		210
DDD00103338		212
DDD00957468		220
DDD01269624		220
DDD01008885		221
DDD01008890		223

DDD00808270		247
DDD00203536		247
DDD00121991		250
DDD00327080		251
DDD01085541		251
DDD01305698		256
DDD01008830		264
DDD00771485		267
DDD01085545		270
DDD01008781		274

DDD01008895		283
DDD00923236		286
DDD01085465		295
DDD00321558		296
DDD01024717		297
DDD01305646		318
DDD00362117		320
DDD01085520		328
DDD01008813		355
DDD01305629		388
DDD01305746		391

DDD01085515		395
DDD00910832		432
DDD01512351		452
DDD01305686		457
DDD01512353		481