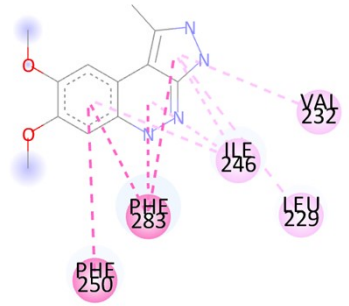
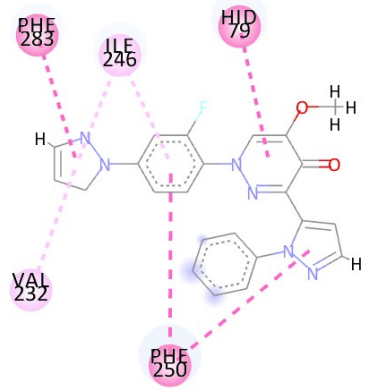
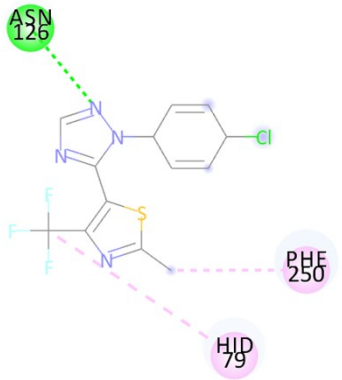
Electronic Supplementary Material (ESI) for RSC Advances.
This journal is © The Royal Society of Chemistry 2021

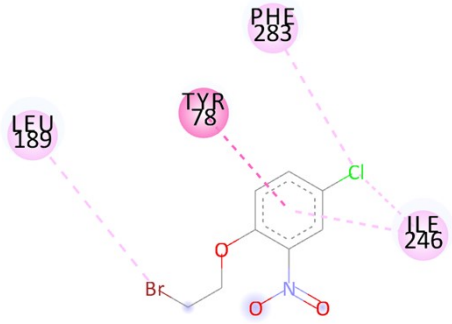
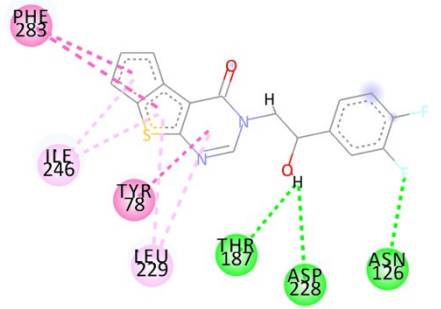
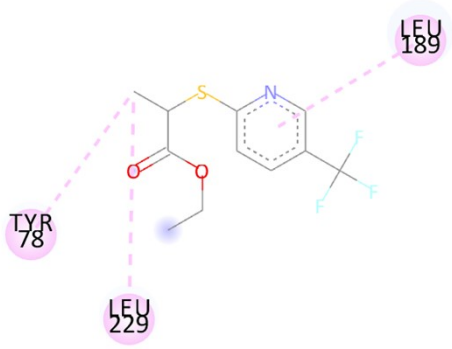
Table S1. Physicochemical properties of the hits that fit the criteria of the CNS active drug.

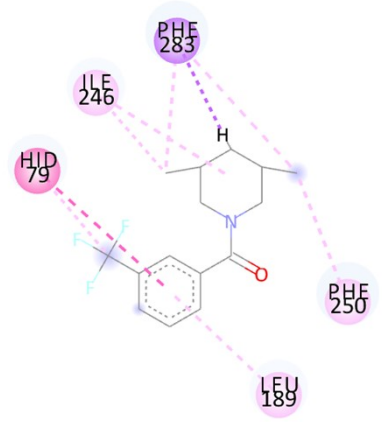
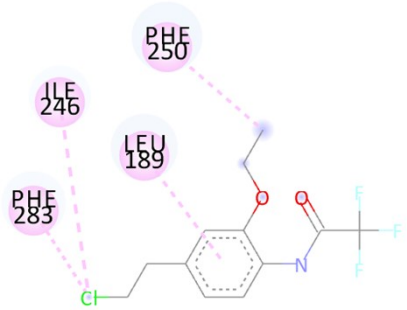
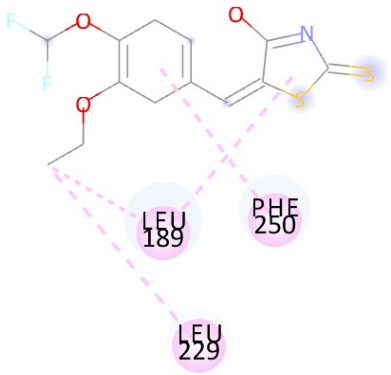
Ligand	M.wt	Log P	No. of HBA	No. of HBD	PSA	LogBB	CNS active drug	No. of RB	PFS
Zinc01397213	344.7	3.9	4.0	0	42.5	0.5	2	0	48.0
Zinc02156284	280.5	2.9	1.7	0	47.5	0	1	4	48.0
Zinc42657360	348.3	3.2	5.7	1	57.6	0	0	4	55.3
Zinc43638301	279.2	3.4	3.0	0	36.9	0.3	1	4	56.0
Zinc47464611	285.3	3.9	3.0	0	27.0	0.4	2	1	55.7
Zinc71439134	295.6	3.8	3.2	1	43.5	0.4	1	4	56.9
Zinc71759377	331.3	2.6	3.7	1	55.9	0	1	6	56.6
Zinc72553806	310.3	2.9	4.5	1	36.0	0.6	2	4	56.3
Zinc72878277	284.3	4.0	4.0	2	43.9	0.4	2	6	56.0
Zinc79055898	327.3	4.2	4.0	0	41.0	0	1	6	55.9
Zinc82446000	296.4	2.9	5.2	0	52.5	0	1	4	48.4
Zinc82779572	250.2	2.8	2.0	2	35.4	0.3	1	4	48.0
Zinc82779574	250.2	2.7	2.0	2	36.3	0.3	1	4	48.0
Zinc82779590	268.2	3.0	2.0	2	36.2	0.4	2	4	48.0

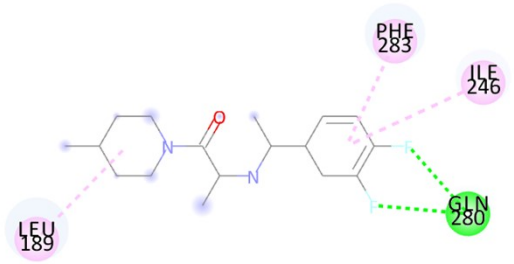
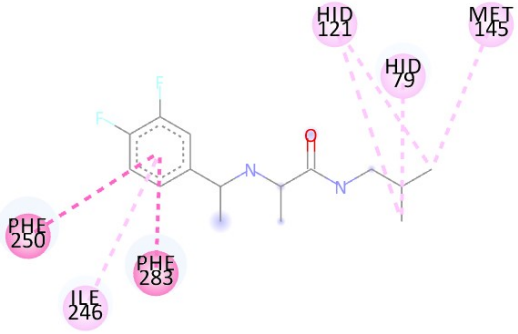
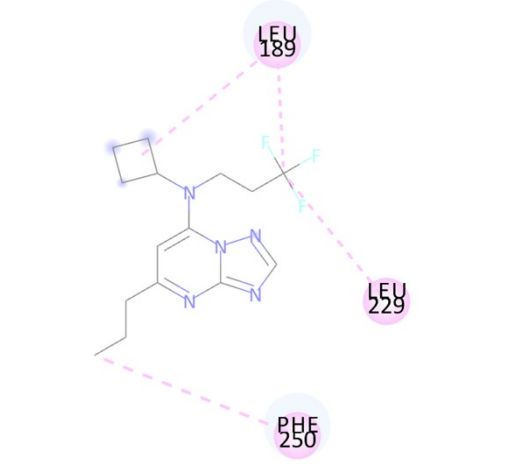
*M.wt: Molecular weight, Log P: Octanol/Water partition coefficient, No. of HBA: Number of hydrogen bond acceptor, No. of HBD: Number of hydrogen bond donor, PSA: Polar surface area, LogBB: Blood/Brain partition coefficient, No. of RB: Number of rotatable bond, PFS: Pharmacophore fit score.

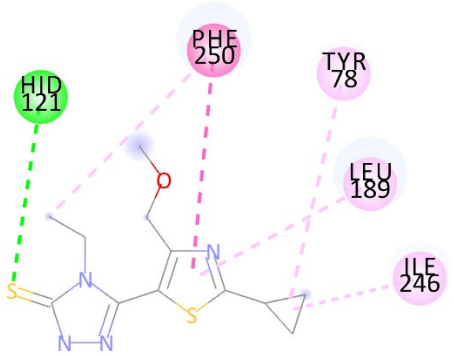
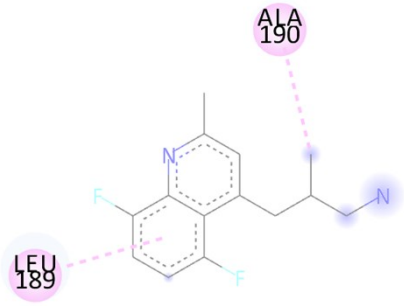
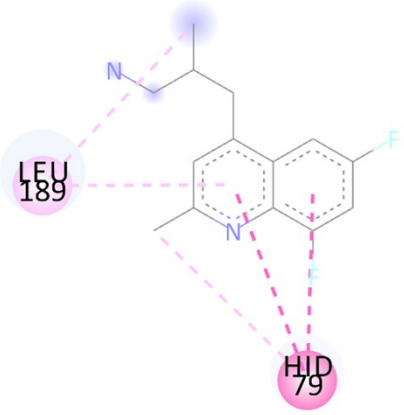
Table S2. Amino acids involved in the interactions between PDE10A and the ligands

Ligand	Hydrophobic Interactions	Hydrogen Bond Interactions	π-Stacking Interactions	2D Image
Co-crystallised ligand (JY4)	LEU229, VAL232 and ILE246	-	PHE250 with dimethoxybenzene PHE283 with pyrazole, tetrahydropyridazine and dimethoxybenzene	
TAK063 (standard)	VAL232 and ILE246	-	HID79 with pyridazine PHE250 with fluorobenzene and pyrazole PHE283 and pyrazole	
Zinc01397213	HID79 and PHE250	ASN126 N of triazole	-	

Zinc02156284	LEU189, ILE246 and PHE283	-	TYR78 with chlorobenzene	
Zinc42657360	LEU229 and ILE246	THR187 and ASP228 with OH ASN126 with fluorine	TYR78 with pyrimidine PHE283 with cyclopentathiophene	
Zinc43638301	TYR78, LEU189 and LEU229	-	-	

Zinc47464611	HID79, LEU189, ILE246, PHE250 and PHE283	-	HID79 with trifluoromethyl benzene	
Zinc71439134	LEU189, ILE246, PHE250 and PHE283	-	-	
Zinc71759377	LEU189, LEU229 and PHE250	-	-	

Zinc72553806	LEU189, ILE246 and PHE283	GLN280 with fluorine	-	
Zinc72878277	HID79, HID121, MET145 and ILE246	-	PHE250 and PHE283 with difluorobenzene	
Zinc79055898	LEU189, LEU229 and PHE250	-	-	

Zinc82446000	TYR78, LEU189 and ILE246	HID121 with sulphur	PHE250 with thiazole	
Zinc82779572	LEU189 and ALA190	-	-	
Zinc82779574	HID79 and LEU189	-	HID79 with quinoline	

Zinc82779590	TYR78, HID79, PHE250, MET267 and PHE283	TYR247 and GLN280 with fluorine	-