

Supporting Information 2

Database Mining of ZINC15 Natural Compounds Reveals Potential Thyroid Receptor β Agonists for Non-Alcoholic Fatty Liver Disease

Management: An *in silico* Study

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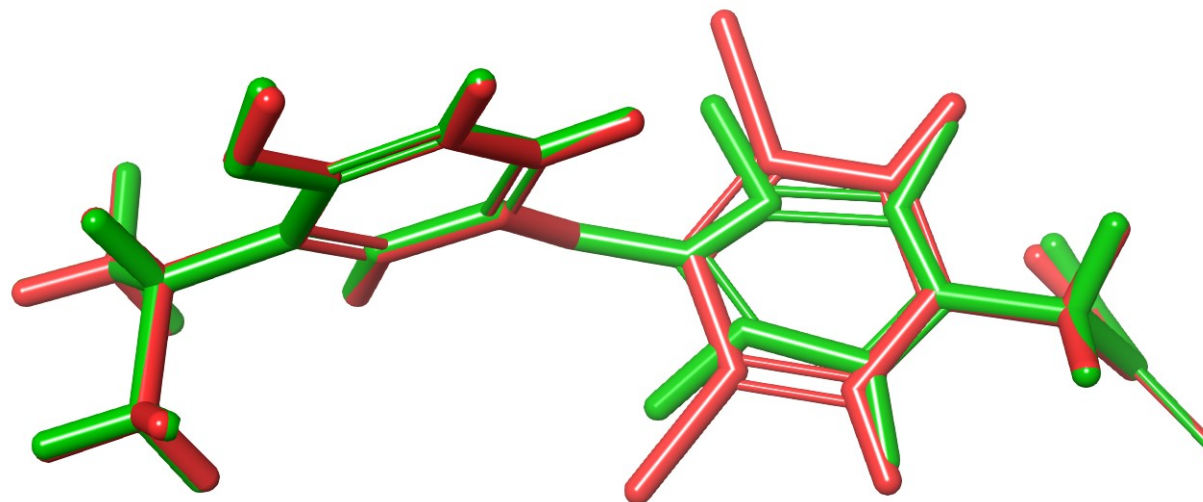


Figure S1. Validation image obtained by redocking the cognate ligand. RMSD: 0.0024 Å

Table S1. Docking scores (kcal/mol) and amino acid interactions afforded by the top ranking 78 compounds obtained following the induced fit docking towards THR- β receptor.

Compound number	ZINC ID	Docking score kcal/mol	Amino acid interactions	Interactions that are identical with cognate ligand	Interactions that are identical with resmetirom
			H-bond: Arg316(WB), Arg320, Asn331, Gly344, Gly332(WB),Ala279(WB)	H-Bond: Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276,	H-Bond: Arg316(WB), Arg320, Gly344

1	33832220	-19.89	Salt Bridge: Arg320, Arg282 Hydrophobic: Leu341, Leu346, Phe269, Phe272, Ile275, Ile276, Ala317, Met310	Leu341, Leu346, Met310, Phe269, Phe272	Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272
2	100038257	-19.78	H-bond: Gly344, Arg282, Gly332(WB), Arg320(WB), Thr329(WB), Ala279(WB), Arg316(WB) Salt Bridge: Arg320, Arg282 Hydrophobic: Leu330, Ala317, Ile275, Met310, Leu341, Leu346, Phe269, Phe272	H-Bond: Ala279(WB), Arg282, Arg316(WB) Hydrophobic: Ala317, Ile275, Phe269, Phe272	H-Bond: Ala279(WB), Arg316(WB), Gly344, Thr329(WB) Hydrophobic: Ala317, Ile275, Leu330, Phe269, Phe272
3	2151572	-19.62	H-bond: Asn331, Arg316(WB), Arg282, Ala279(WB), Gly332(WB) Salt Bridge: Arg320 Hydrophobic: Leu330, Met334, Ile280, Ala279, Ile276, Ile275, Phe269	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ile275, Ile276, Phe269	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ile275, Ile276, Leu330, Phe269
4	36190184	-19.06	H-bond: Arg282, Asn331, Gly332(WB), Arg316(WB), Ala279(WB) Salt Bridge: Arg282, Arg320 Hydrophobic: Leu330, Leu328, Ala317, Met310, Phe439, Met442	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Met310	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Leu330, Met310
			H-bond: Asn331, Arg282,	H-Bond: Ala279(WB), Arg282,	H-Bond: Ala279(WB),

5	2093734	-18.99	Arg316(WB), Ala279(WB), Gly332(WB) Salt Bridge: Arg282, Arg320 Hydrophobic: Ala317, Met313, Met310, Met442, Phe439	Arg316(WB), Arg320 Hydrophobic: Ala317, Met310, Met313	Arg316(WB), Arg320 Hydrophobic: Ala317, Met310, Met313
6	217900411	-18.87	H-bond: Asn331, Arg320(WB), Ala279(WB), Arg316(WB) Salt Bridge: Arg320, Arg282 Pi-pi: Phe272 Hydrophobic: Ala317, Met313, Met310, Leu341, Leu346, Phe269	H-Bond: Ala279(WB), Arg282, Arg316(WB) Hydrophobic: Ala317, Leu341, Leu346, Met310, Met313, Phe269	H-Bond: Ala279(WB), Arg316(WB) Hydrophobic: Ala317, Leu341, Leu346, Met310, Met313, Phe269
7	8437239	-18.52	H-bond: Asn331, Arg282, Arg316(WB), Gly332(WB), Ala279(WB) Salt Bridge: Arg282, Arg320 Hydrophobic: Ile276, Ile275, Phe272, Phe269, Leu346, Leu341, Met310, Ala317	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272
8	514287910	-18.28	H-bond: Asn331, Arg320, Ala279(WB), Gly332(WB), Arg316(WB) Salt Bridge: Arg320, Arg282 Hydrophobic: Ala279, Ile276, Ile275, Phe272, Phe269, Pro452, Phe455, Met310, Met313, Ala317	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Met310, Met313, Phe269, Phe272	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Met310, Met313, Phe269, Phe272

9	11766131	-18.11	H-bond: Arg282, Asn331, Gly332(WB), Arg316, Ala279 Salt Bridge: Arg320, Arg282 Pi-pi: Phe272 Hydrophobic: Ile275, Ile276, Phe269, Leu341, Leu346, Ala317, Met313, Met310	H-Bond: Ala279, Arg282, Arg316, Arg320 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe269	H-Bond: Ala279, Arg316, Arg320 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe269
10	8764797	-17.57	H-bond: Arg282, Asn331, Gly332(WB), Ala279(WB), Arg316(WB) Salt Bridge: Arg282, Arg320 Halogen Bond: Gly344(with Cl) Hydrophobic: Ile276i Ile275, Phe272, Leu346, Leu341, Met310, Met313, Ala317	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Leu341, Leu346, Met310, Met313, Phe272	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Leu341, Leu346, Met310, Met313, Phe272
11	33831074	-17.33	H-bond: Arg282, Asn331, Met313, Gly344, Phe272, Arg316(WB) Hydrophobic: Leu330, Ala279, Ile276, Ile275, Phe269, Leu346, Leu341	H-Bond: Arg282, Arg316(WB) Hydrophobic: Ile275, Ile276, Leu341, Leu346, Phe269	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ile275, Ile276, Leu330, Leu341, Leu346, Phe269
			H-bond: Arg320, Asn331, Gly332(WB), Arg316(WB),	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276,	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275,

12	248012330	-17.3	Ala279(WB) Salt Bridge: Arg320, Arg282 Hydrophobic: Ala317, Ile276, Ile275, Phe272,i Met313, Met310	Met310, Met313	Ile276, Met310, Met313
13	95919069	-17.29	H-bond: Arg320, Arg282, Asn331, Gly332(WB), His435 Salt Bridge: Arg282, Arg320 Hydrophobic: Ala317, Ala279, Met313, Met310, Ile276, Ile275, Phe272	H-Bond: Arg282, Arg320 Hydrophobic: Ala317, Ile275, Ile276, Met310, Met313, Phe272	H-Bond: Arg320 Hydrophobic: Ala317, Ile275, Ile276, Met310, Met313, Phe272
14	15271340	-17.09	H-bond: Gly344, Phe272, Ile275, Met313, Arg282, Arg316(WB) Hydrophobic: Met310, Ala279, Ile276, Phe269, Ala317	H-Bond: Arg282, Arg316(WB) Hydrophobic: Ala317, Ile276, Met310, Phe269	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ala317, Ile276, Met310, Phe269
15	123799	-16.82	H-bond: Asn331, Arg282, Arg316(WB), Thr329(WB), Ala279(WB), Gly332(WB) Salt Bridge: Arg320, Arg282 Pi-pi: Phe269 Hydrophobic: Ala317, Ile276, Ile275, Phe272, Leu341, Leu346, Met310,	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe272	H-Bond: Ala279(WB), Arg316(WB), Arg320, Thr329(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe272

			Met313		
16	9034032	-16.81	H-bond: Arg320, Asn331, Gly332(WB), Arg316(WB), Ala279(WB) Salt Bridge: Arg282, Arg320 Halogen Bond: Leu341(with Br), Leu346(with Br) Hydrophobic: Ala317, Met310, Ile276, Ile275, Phe272, Phe269	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272
17	2149076	-16.79	H-bond: Gly332(WB) Salt Bridge: Arg282, Arg320 Hydrophobic: Ala317, Ala279, Ile276, Ile275, Phe272, Phe269, Met310	H-Bond: Arg282, Arg320 Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272	H-Bond: Arg320 Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272
18	14710225	-16.7	H-bond: Arg282, Arg316, Asn331, His434, Arg316(WB), Ala279(WB), Arg320(WB), Gly332(WB), Thr329(WB) Hydrophobic: Ala317, Leu328, Ile354, Leu341, Met442, Leu346, Phe439, Phe269, Phe276	H-Bond: Ala279(WB), Arg282, Arg320(WB) Hydrophobic: Ala317, Leu341, Leu346, Phe269	H-Bond: Ala279(WB), Thr329(WB) Hydrophobic: Ala317, Leu341, Leu346, Phe269

19	13409813	-16.67	H-bond: Arg282, Asn331, Gly344, Arg316(WB), Ala279(WB), Gly332(WB) Salt Bridge: Arg282, Arg320 Hydrophobic: Leu330, Ala279, Ile276, Ile275, Phe272, Phe269, Leu341, Leu346	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ile275, Ile276, Leu341, Leu346, Phe269, Phe272	H-Bond: Ala279(WB), Arg316(WB), Arg320, Gly344 Hydrophobic: Ile275, Ile276, Leu330, Leu341, Leu346, Phe269, Phe272
20	85569228	-16.53	H-bond: Met131, Gly344, Arg316(WB) Pi-pi: Phe372 Hydrophobic: Ala317, Ala279, Ile276, Ile272, Phe269, Met310	H-Bond: Arg316(WB) Hydrophobic: Ala317, Ile276, Met310, Phe269	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ala317, Ile276, Met310, Phe269
21	20760824	-16.46	H-bond: Asn331, Arg320, Gly332(WB), Arg316(WB), Ala279(WB) Hydrophobic: Leu330, Ala317, Met310	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Met310	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Leu330, Met310
22	685935278	-16.4	H-bond: Asn331, Ala279(WB), Arg316(WB), Gly332(WB) Salt Bridge: Arg320, Arg282 Hydrophobic: Ile276, Ile275, Phe272, Ala317, Met310	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe272	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe272
23	2149604	-16.24	H-bond: Asn331, Arg282, Arg320, Gly332(WB), Thr329(WB) Salt Bridge: Arg282, Arg320	H-Bond: Arg282, Arg320 Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272	H-Bond: Arg320, Thr329(WB) Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272

			Hydrophobic: Ala317, Ala279, Ile276, Ile275, Phe272, Phe269, Met310		
24	4260476	-16.21	H-bond: Asn331, Gly332(WB), Arg316(WB), Ala279(WB) Salt Bridge: Arg320, Arg282 Pi-pi: Phe269 Hydrophobic: Phe272, Leu341, Leu346, Val349, Met310, Met313	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Leu341, Leu346, Met310, Met313, Phe272	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Leu341, Leu346, Met310, Met313, Phe272
25	95918854	-16.06	H-bond: Asn331, Arg282, Met313, Phe272, His435, Arg282(WB), Arg320(WB), Arg316(WB) Hydrophobic: Ala317, Ala279, Ile276, Phe269, Leu341, Leu346, Met310	H-Bond: Arg316(WB), Arg320(WB), His435 Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe269	H-Bond: Arg316(WB) Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe269
26	95919068	-15.96	H-bond: Asn331, Gly344, Arg320(WB), Arg316(WB), Ala279 Salt Bridge: Arg320, Arg282 Hydrophobic: Ile276, Ile275, Phe272, Phe269, Leu330, Met310, Met313, Ala317	H-Bond: Ala279, Arg282, Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Met310, Met313, Phe269, Phe272	H-Bond: Ala279, Arg316(WB), Gly344 Hydrophobic: Ala317, Ile275, Ile276, Leu330, Met310, Met313, Phe269, Phe272
27	14436067	-15.83	H-bond: Gly344, Arg316(WB) Hydrophobic: Ala317, Ala279, Ile276,	H-Bond: Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276,	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ala317, Ile275, Ile276, Met310, Met313, Phe269,

			Ile275, Phe272, Phe269, Met310, Met313	Met310, Met313, Phe269, Phe272	Phe272
28	2578411	-15.75	H-bond: Asn331, Arg320, Arg316(WB), Ala279(WB) Salt Bridge: Arg320, Arg282 Hydrophobic: Phe269, Leu346, Leu341, Met310, Met313, Ala317, Ile276, Ile275, Phe272	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe269, Phe272	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe269, Phe272
29	15249507	-15.65	H-bond: His435, Asn331, Arg282, Ala279(WB), Arg316(WB), Gly332(WB) Salt Bridge: Arg282, Arg320 Hydrophobic: Leu330, Ile276, Ile275, Phe272, Phe269, Leu341, Leu346, Phe439, Met442	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320, His435 Hydrophobic: Ile275, Ile276, Leu341, Leu346, Phe269, Phe272	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ile275, Ile276, Leu330, Leu341, Leu346, Phe269, Phe272
30	95918985	-15.6	H-bond: Met313, Arg282, Asn331, His435, Arg320(WB), Arg316(WB) Pi-pi: Phe455 Hydrophobic: Ala279, Ile275, Met310, Phe272, Phe269, Met442, Phe439, Ala317	H-Bond: Arg282, Arg316(WB), Arg320(WB), His435 Hydrophobic: Ala317, Ile275, Met310, Phe269, Phe272	H-Bond: Arg316(WB) Hydrophobic: Ala317, Ile275, Met310, Phe269, Phe272
			H-bond: Met313, Arg282, Arg320(WB), Ala279(WB), Asn331,	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320(WB)	H-Bond: Ala279(WB), Arg316(WB)

31	15112191	-15.57	Arg316(WB) Hydrophobic: Ile353, Met310, Ala317, Ile276, Ile275, Phe272, Phe269, Met442, Phe439	Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272	Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272
32	4098340	-15.55	H-bond: Gly344, Leu341, Asn331 Hydrophobic: Ala317 Ala279, Ile276i Ile275, Phe272, Phe269, Met310	H-Bond: N/A Hydrophobic: Ala317, Ile275, Met310, Phe269, Phe272	H-Bond: Gly344 Hydrophobic: Ala317, Ile275, Met310, Phe269, Phe272
33	85569243	-15.48	H-bond: Met313, Gly344, Arg316(WB), Asn331(WB) Hydrophobic: Met310, Ala317, Ala279, Ile276, Ile275, Phe272, Phe269	H-Bond: Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272
34	3589221	-15.42	H-bond: Arg282, Met313, Gly344, Arg320(WB), Arg316(WB) Hydrophobic: Ala279, Ile276, Ile275, Phe272, Phe269	H-Bond: Arg282, Arg316(WB), Arg320(WB) Hydrophobic: Ile275, Ile276, Phe269, Phe272	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ile275, Ile276, Phe269, Phe272
35	14585210	-15.39	H-bond: Arg282, Gly344, Met313, Arg316(WB), Arg320(WB), Asn331(WB) Hydrophobic: Ile276, Ile275, Phe269, Met310, Ala317, Leu330, Leu341	H-Bond: Arg282, Arg316(WB), Arg320(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Met310, Phe269	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ala317, Ile275, Ile276, Leu330, Leu341, Met310, Phe269
			H-bond: Ans331, Arg282, Arg316(WB), Gly332(WB), Ala279(WB)	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276,	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275,

36	1382	-15.17	Salt Bridge: Arg282, Arg320 Hydrophobic: Ala317, Ile276, Ile275, Phe272, Phe269, Leu346, Leu341, Met310	Leu346, Phe269, Phe272	Ile276, Leu346, Phe269, Phe272
37	14585193	-15.14	H-bond: Phe272, Met313, Ala279(WB), Arg320(WB), Asn331(WB), Arg316(WB) Hydrophobic: Ala317, Met310, Phe269, Ile275, Ile276 Leu341, Leu346	H-Bond: Ala279(WB), Arg316(WB), Arg320(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269	H-Bond: Ala279(WB), Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269
38	13377009	-15.06	H-bond: Gly344, Met313 Pi-pi: Phe272 Hydrophobic: Met310, Ala317, Ala279, Ile275, Phe269	H-Bond: N/A Hydrophobic: Ala317, Ile275, Met310, Phe269	H-Bond: Gly344 Hydrophobic: Ala317, Ile275, Met310, Phe269
39	1100099	-15.06	H-bond: Arg320, Arg316(WB), Ala279(WB), Gly332(WB) Salt Bridge: Arg282, Arg320 Hydrophobic: Ala279, Ile276, Ile275, Phe272, Phe269, Leu346, Leu341, Leu328, Leu330	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ile275, Ile276, Leu346, Phe269, Phe272	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ile275, Ile276, Leu330, Leu346, Phe269, Phe272
40	14645330	-14.92	H-bond: Ile275, Arg282, Met313, Arg320(WB)	H-Bond: Arg282, Arg320(WB) Hydrophobic: Ala317, Ile276, Leu341,	H-Bond: N/A Hydrophobic: Ala317, Ile276,

			Pi-pi: Phe272 Hydrophobic: Ala279, Ile276, Leu341, Met310, Ala317	Met310	Leu341, Met310
41	14437964	-14.75	H-bond: Met313, His435, Arg320(WB) Hydrophobic: Met310, Ala317, Phe269, Phe272, Ile275, Ile276, Ala279	H-Bond: Arg320(WB), His435 Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272	H-Bond: N/A Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272
42	6525270	-14.72	H-bond: Met313, Arg316(WB), Asn331(WB) Hydrophobic: Met310, Ala317, Ala279, Ile276, Ile275, Phe272, Phe269	H-Bond: Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272	H-Bond: Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272
43	5784821	-14.71	H-bond: Met313, Arg282, Ile272, Gly344, Arg320(WB), Arg316(WB) Hydrophobic: Ala279, Ile276, Phe272, Phe269, Leu346, Leu431, Ala317, Met310	H-Bond: Arg282, Arg316(WB), Arg320(WB) Hydrophobic: Ala317, Ile276, Leu346, Met310, Phe269, Phe272	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ala317, Ile276, Leu346, Met310, Phe269, Phe272
44	13462153	-14.7	H-bond: Asn331, Arg282, Arg320, Ala279(WB), Arg316(WB) Salt Bridge: Arg320, Arg282 Hydrophobic: Ala317, Leu330, Leu328, Met310, Met313	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320 Hydrophobic: Ala317, Met310, Met313	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Leu330, Met310, Met313
45	66470	-14.68	H-bond: Ile275 Hydrophobic: Phe269, Phe272, Ala279, Ala317, Met313, Met310, Leu341,	H-Bond: N/A Hydrophobic: Ala317, Leu341, Leu346, Met310, Met313, Phe269, Phe272	H-Bond: N/A Hydrophobic: Ala317, Leu341, Leu346, Met310, Met313, Phe269, Phe272

			Leu346		
46	2097398	-14.66	H-bond: Arg282, Asn331, Arg320(WB), Arg316(WB), Ala279(WB) Salt Bridge: Arg320, Arg282 Hydrophobic: Ile276, Ile275, Phe272, Phe269, Leu341, Leu346, Met310, Ala317	H-Bond: Ala279(WB), Arg282, Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272	H-Bond: Ala279(WB), Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272
47	59200522	-14.62	H-bond: Met313, Gly344, His435, Asn331(WB) Hydrophobic: Met310, Ala317, Leu341, Leu346, Ile276, Ala279	H-Bond: His435 Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310	H-Bond: Gly344 Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310
48	95912004	-14.62	H-bond: Met313, Ile275, Gly344, Asn331(WB), Arg316(WB) Hydrophobic: Ala279, Ile276, Phe272, Phe269, Leu346, Leu341, Met310	H-Bond: Arg316(WB) Hydrophobic: Ile276, Leu341, Leu346, Met310, Phe269, Phe272	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ile276, Leu341, Leu346, Met310, Phe269, Phe272
49	14811038	-14.56	H-bond: Met313, Asn331, Leu341 Pi-pi: Phe272 Hydrophobic: Ala279, Ile276, Ile275, Phe269, Met310, Ala317	H-Bond: N/A Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269	H-Bond: N/A Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269
50	95919173	-14.53	H-bond: Met313, Asn331, Ile275, Arg316(WB), Arg320(WB) Hydrophobic: Ala317, Ala279, Phe455, Phe272, Phe269, Leu341, Met310	H-Bond: Arg316(WB), Arg320(WB) Hydrophobic: Ala317, Leu341, Met310, Phe269, Phe272	H-Bond: Arg316(WB) Hydrophobic: Ala317, Leu341, Met310, Phe269, Phe272

51	6524405	-14.49	H-bond: His435, Met313, Ile275, Asn331(WB), Arg316(WB) Hydrophobic: Met310, Ala279, Ile276, Phe272, Phe269, Leu341, Leu346, Met442, Phe439	H-Bond: Arg316(WB), His435 Hydrophobic: Ile276, Leu341, Leu346, Met310, Phe269, Phe272	H-Bond: Arg316(WB) Hydrophobic: Ile276, Leu341, Leu346, Met310, Phe269, Phe272
52	14585197	-14.42	H-bond: Met313, Asn331, Ile275, Arg282(WB) Hydrophobic: Ala279, Ile276, Phe272, Phe269, Met310	H-Bond: N/A Hydrophobic: Ile276, Met310, Phe269, Phe272	H-Bond: N/A Hydrophobic: Ile276, Met310, Phe269, Phe272
53	14585200	-14.34	H-bond: Met313, Arg282, Asn331(WB), Arg316(WB), Ala279(WB), Arg320(WB) Hydrophobic: Ala317, Ile276, Ile275, Phe269, Leu341, Leu346, Met310	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269	H-Bond: Ala279(WB), Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269
54	4749	-14.21	H-bond: Asn331, Met313, Gly344 Hydrophobic: Ala317, Ala279, Ile276, Phe272, Phe269, Leu346, Leu341, Met310	H-Bond: N/A Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe269, Phe272	H-Bond: Gly344 Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe269, Phe272
55	95099475	-14.14	H-bond: Met313, Asn331, Ile275, Gly344, Arg316(WB) Hydrophobic: Ala279, Ile276, Phe269, Leu246, Leu341, Met310	H-Bond: Arg316(WB) Hydrophobic: Ile276, Leu341, Met310, Phe269	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ile276, Leu341, Met310, Phe269
			H-bond: Met313, Asn331, Arg320(WB)	H-Bond: Arg320(WB)	H-Bond: N/A

56	18188912	-14.13	Pi-pi: Phe272 Hydrophobic: Met310, Ala317, Ala279, Ile275, Leu346, Leu341, Phe269	Hydrophobic: Ala317, Ile275, Leu341, Leu346, Met310, Phe269	Hydrophobic: Ala317, Ile275, Leu341, Leu346, Met310, Phe269
57	39004853	-14.12	H-bond: Met313, Gly344, Arg320(WB) Hydrophobic: Ala279, Ile276, Ile275, Phe272, Phe269, Ala317, Met310	H-Bond: Arg320(WB) Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272	H-Bond: Gly344 Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe269, Phe272
58	95099479	-14.08	H-bond: Asn331, Ile275, Gly344, Arg316(WB), Arg320(WB) Hydrophobic: Ala317, Ala279, Ile276, Phe269, Met310, Met313	H-Bond: Arg316(WB), Arg320(WB) Hydrophobic: Ala317, Ile276, Met310, Met313, Phe269	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ala317, Ile276, Met310, Met313, Phe269
59	14585198	-14.08	H-bond: Phe272, Met313, Arg320(WB), Asn331(WB) Hydrophobic: Ala317, Ala279, Ile276, Ile275, Phe269, Leu341, Leu346, Met310	H-Bond: Arg320(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269	H-Bond: N/A Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269
60	14647563	-14.07	H-bond: Asn331, Met313, His435, Gly344 Hydrophobic: Ala317, Ala279, Ile276, Phe272, Phe269, Met310, Leu341, Leu346	H-Bond: His435 Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe269, Phe272	H-Bond: Gly344 Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe269, Phe272
61	85541368	-14.05	H-bond: Asn331, Gly344 Hydrophobic: Ala317, Ala279, Ile276, Ile275, Phe272, Phe269, Leu346, Leu341, Met310, Met313	H-Bond: N/A Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe269, Phe272	H-Bond: Gly344 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe269, Phe272
			H-bond: Arg282, Asn331,	H-Bond: Ala279(WB), Arg282,	H-Bond: Ala279(WB),

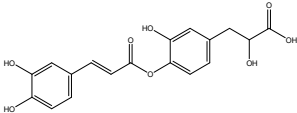
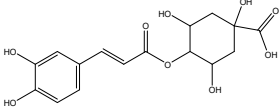
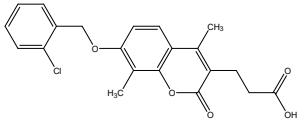
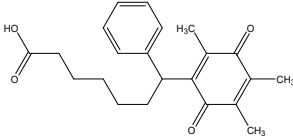
62	70454473	-13.82	Gly332(WB), Ala279(WB), Arg316(WB) Hydrophobic: Ala317, Met313, Met310, Phe272, Ile275, Ile276	Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Met310, Met313, Phe272	Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Met310, Met313, Phe272
63	14646151	-13.79	H-bond: Met313, Ile276, Gly344, Asn331(WB), Arg316(WB) Hydrophobic: Ala279, Ile276, Phe272, Phe269, Leu346, Leu341, Ala279, Ala317	H-Bond: Arg316(WB) Hydrophobic: Ala317, Ile276, Leu341, Leu346, Phe269, Phe272	H-Bond: Arg316(WB), Gly344 Hydrophobic: Ala317, Ile276, Leu341, Leu346, Phe269, Phe272
64	14759297	-13.78	H-bond: Met313, Gly344, Asn331(WB) Hydrophobic: Met310, Ala317, Ala279, Ile276, Ile275, Phe272, Phe269, Leu341, Leu346	H-Bond: N/A Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272	H-Bond: Gly344 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272
65	100018343	-13.73	H-bond: Met313, Asn331, Phe272, Gly344 Hydrophobic: Ala317, Ala279, Ile276, Ile275, Phe269, Met310, Leu341, Leu346	H-Bond: N/A Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269	H-Bond: Gly344 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269
66	13829483	-13.72	H-bond: Arg282, Arg316(WB), Ala279 Hydrophobic: Met310, Ala317, Ile276, Ile275, Phe272, Phe269, Leu341, Leu346	H-Bond: Ala279, Arg282, Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272	H-Bond: Ala279, Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272

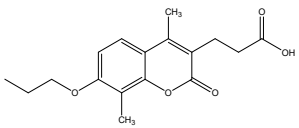
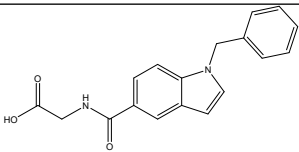
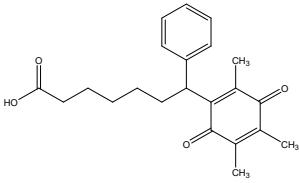
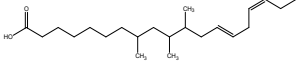
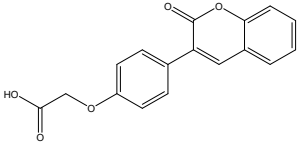
67	5732527	-13.7	H-bond: Met313, Asn331, Arg320(WB) Hydrophobic: Met310, Leu346, Phe269, Phe272, Ile275, Ile276, Leu330, Ala279 Ala317	H-Bond: Arg320(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu346, Met310, Phe269, Phe272	H-Bond: N/A Hydrophobic: Ala317, Ile275, Ile276, Leu330, Leu346, Met310, Phe269, Phe272
68	196431	-13.64	H-bond: Asn331, Gly332(WB), Arg320(WB), Ala279(WB), Arg316(WB) Salt Bridge: Arg282 Hydrophobic: Ala317, Met313, Met310, Leu341, Leu346, Phe269, Phe272, Ile275, Ile276	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe269, Phe272	H-Bond: Ala279(WB), Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe269, Phe272
69	14585208	-13.56	H-bond: Arg282, Asn331, Gly344, Arg320(WB) Hydrophobic: Ala317, Met313, Met310, Phe269, Phe272, Ile276, Ala279, Leu328, Leu330	H-Bond: Arg282, Arg320(WB) Hydrophobic: Ala317, Ile276, Met310, Met313, Phe269, Phe272	H-Bond: Gly344 Hydrophobic: Ala317, Ile276, Leu330, Met310, Met313, Phe269, Phe272
70	3874317	-13.5	H-bond: Met313, Ile275, Gly344, His435, Asn331(WB) Hydrophobic: Met310, Ala317, Ala279, Ile276, Phe269, Leu341, Leu346	H-Bond: His435 Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe269	H-Bond: Gly344 Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe269
71	3870337	-13.43	H-bond: Met313, Ile275, His435, Gly344 Hydrophobic: Ala317, Ala279, Ile276, Phe272, Leu341, Leu346, Phe269, Met310	H-Bond: His435 Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe269, Phe272	H-Bond: Gly344 Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe269, Phe272

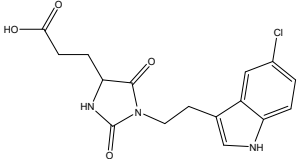
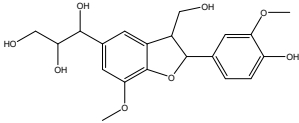
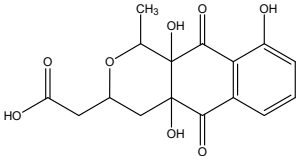
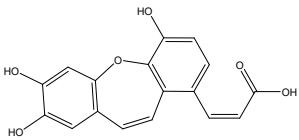
72	14638400	-13.34	H-bond: Met313, Asn331(WB) Hydrophobic: Met310, Ala317, Ala279, Ile276, Ile275, Phe272, Ala268, Leu341, Leu346	H-Bond: N/A Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe272	H-Bond: N/A Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe272
73	33833930	-13.27	H-bond: Met313, Asn331, His435, Gly344 Hydrophobic: Ile280, Ala279, Ile276, Ile275, Phe272, Phe269, Leu341, Leu346, Met310, Ala317	H-Bond: His435 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272	H-Bond: Gly344 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272
74	77031588	-13.19	H-bond: Arg282, Met313, His435, Arg316(WB), Ala279(WB), Arg320(WB), Asn331(WB) Hydrophobic: Ala317, Ile276, Ile275, Phe272, Phe439, Met442, Met310, Leu330	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320(WB), His435 Hydrophobic: Ala317, Ile275, Ile276, Met310, Phe272	H-Bond: Ala279(WB), Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu330, Met310, Phe272
75	95099473	-12.95	H-bond: Met313, Arg282, Arg320(WB), Pi-pi: Phe272 Hydrophobic: Ala317, Ala279, Ile276, Ile275, Leu346, Met310	H-Bond: Arg282, Arg316(WB), Arg320(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu346, Met310	H-Bond: Arg316(WB) Hydrophobic: Ala317, Ile275, Ile276, Leu346, Met310
76	14646005	-12.68	H-bond: Ile275 Hydrophobic: Ala317, Ala279, Ile276,	H-Bond: N/A Hydrophobic: Ala317, Ile276, Met310, Phe269, Phe272	H-Bond: N/A Hydrophobic: Ala317, Ile276, Met310, Phe269, Phe272

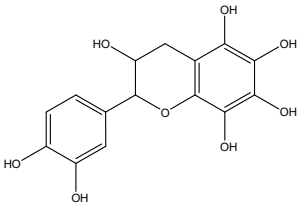
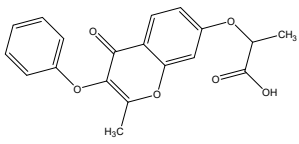
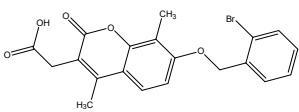
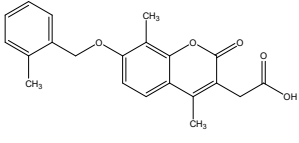
			Phe272, Phe269, Met310		
77	36434366	-12.57	H-bond: Asn331, Ile275 Hydrophobic: Ala317, Ala318, Ala279, Ile276, Phe272, Leu341, Leu346, Met310	H-Bond: N/A Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe272	H-Bond: N/A Hydrophobic: Ala317, Ile276, Leu341, Leu346, Met310, Phe272
78	685935930	-12.54	H-bond: Met313, His435 Hydrophobic: Met310, ala317, Ala279, Ile276, Ile275, Phe272, Phe269, Leu341, Leu346	H-Bond: His435 Hydrophobic: Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272	H-Bond: N/A Hydrophobic: Ile275, Ile276, Leu341, Leu346, Met310, Phe269, Phe272
	Resmetirom	-12.95	H-bond: Arg320, Gly344, Arg316(WB), Ala279(WB), Thr329(WB) Hydrophobic: Ala317, Ile276, Ile275, Phe272, Phe269, Leu346, Leu341, Met310, Met313, Leu330	H-Bond: Ala279(WB), Arg316(WB), Arg320 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe269, Phe272	N/A
	Cognate ligand	-13.041	H-bond: His435, Arg282, Arg320(WB), Arg316(WB), Ala279(WB) Hydrophobic: Ala317, Met313, Ile276, Ile275, Met310, Phe272, Leu341, Leu346, Phe269	N/A	H-Bond: Ala279(WB), Arg282, Arg316(WB), Arg320(WB), His435 Hydrophobic: Ala317, Ile275, Ile276, Leu341, Leu346, Met310, Met313, Phe269, Phe272

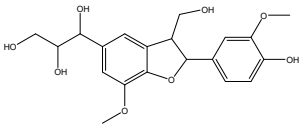
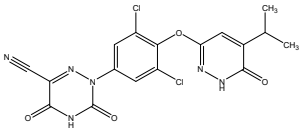
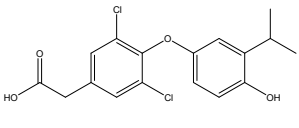
Table S2. Compounds that stand out with the highest affinity in molecular docking results

Compound number	ZINC ID	Compound structure	Docking score (kcal/mol)
1	33832220		-19.89
2	100038257		-19.78
3	2151572		-19.62
4	36190184		-19.06

5	2093734		-18.99
6	217900411		-18.87
7	8437239		-18.52
8	514287910		-18.28
9	11766131		-18.11

10	8764797		-17.57
11	33831074		-17.33
12	248012330		-17.3
13	95919069		-17.29
14	15271340		-17.09

			
15	123799		-16.82
16	9034032		-16.81
17	2149076		-16.79

18	14710225		-16.7
23	Resmetirom		-12.95
24	Cognate ligand		-13.041

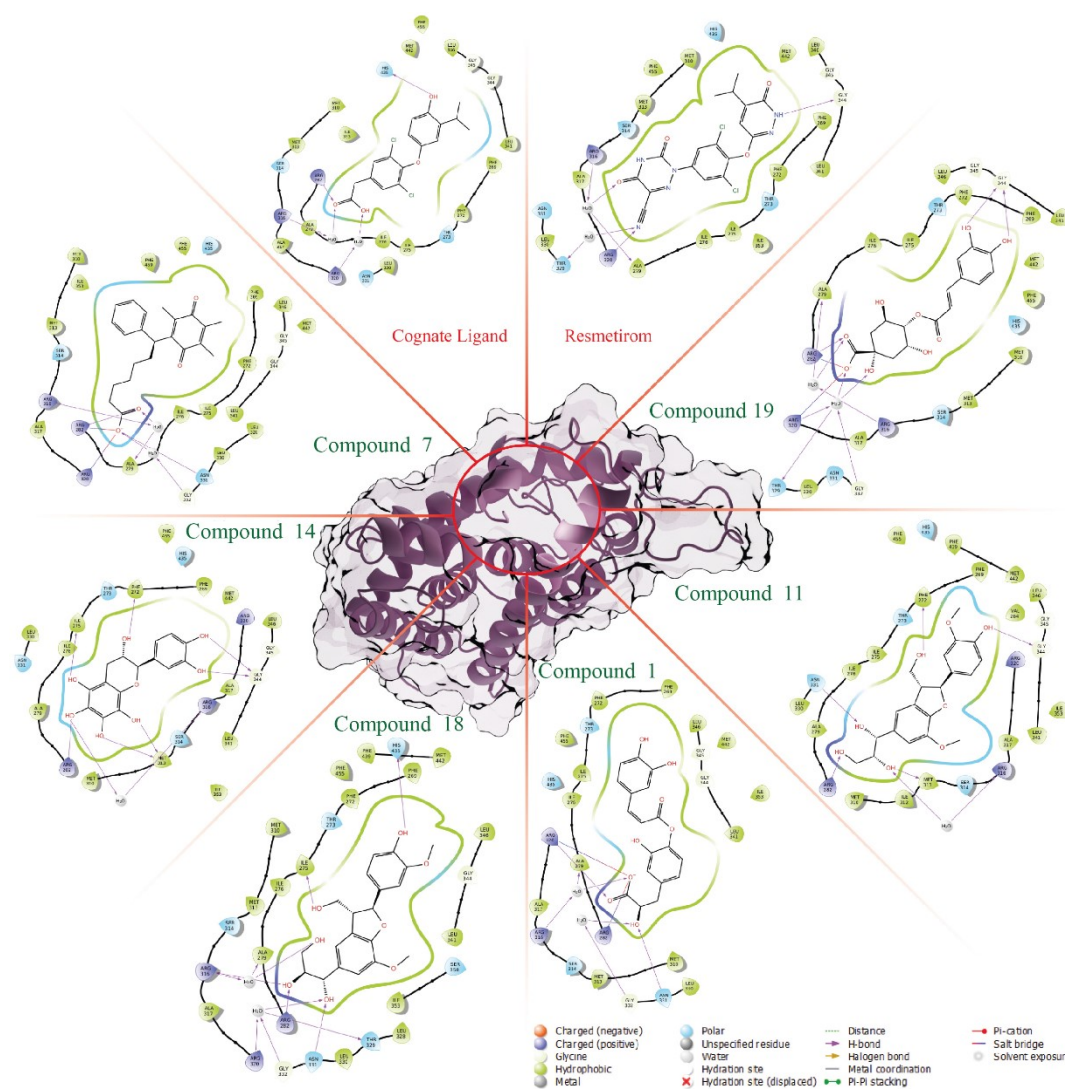
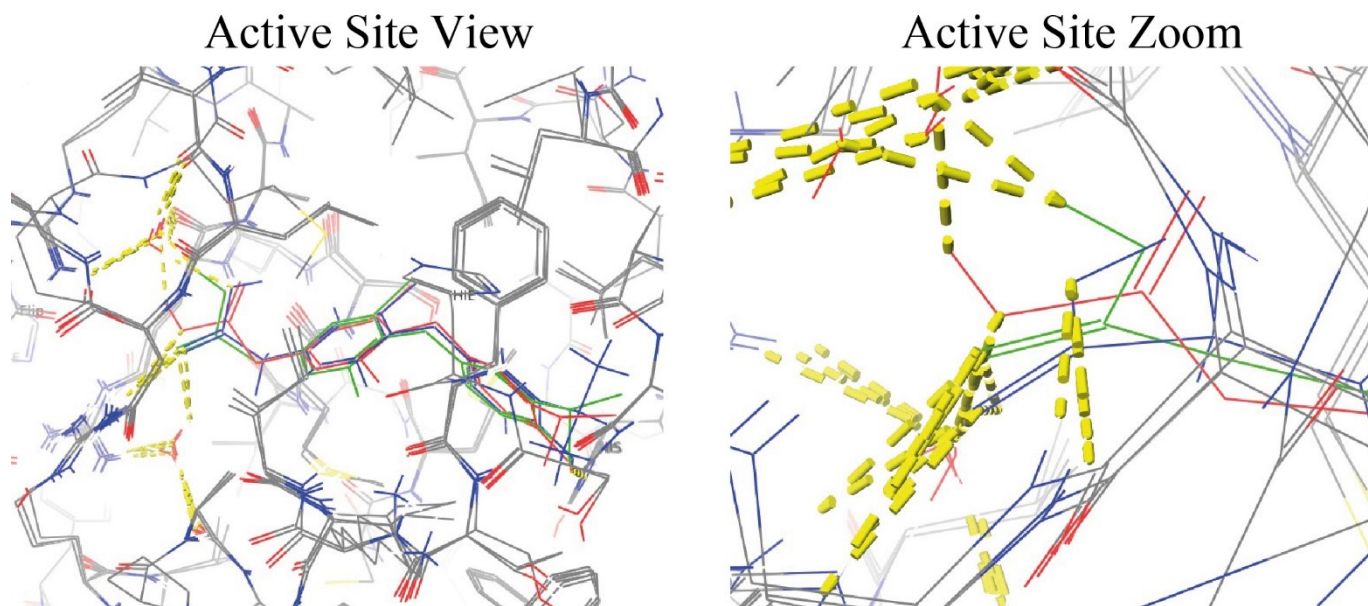


Figure S2. Binding modes of the compounds showing the highest binding affinity and reference compounds

Table S3. Differences in verification and binding energy with different force fields

Force Field	Docking Score (kcal/mol)	Reference Amino Acid Distance (Arg282 – Carbonyl Oxygen) Å
OPLS4	-13.041	1.59
OPLS2005	-12.641	N/A
Crystal Structure	-	1.14

Figure S3. Binding poses of the crystal structure (blue) with redocking binding poses with OPLS4(green) and OPLS2005(red) force field for the cognate ligand in PDB ID 1NAX



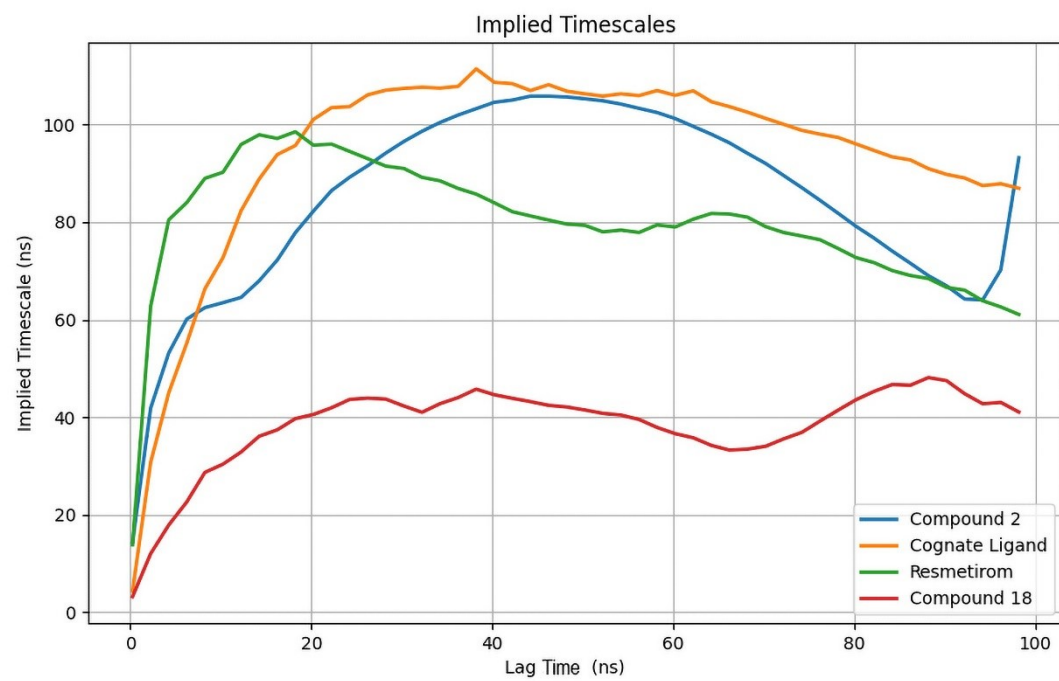
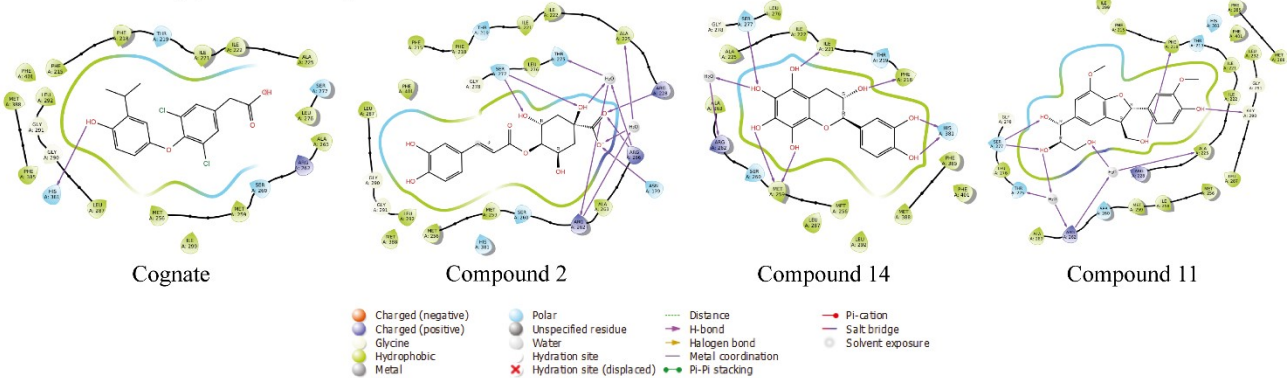


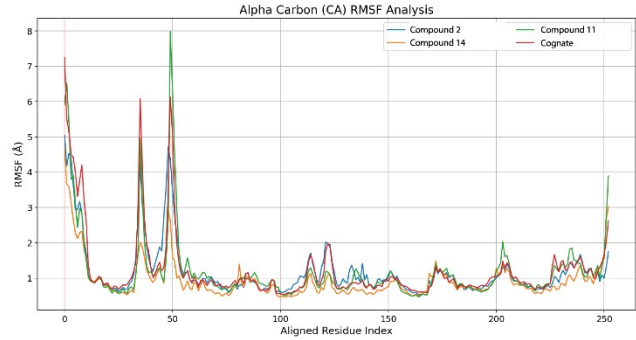
Figure S4. MSM graph showing the conformational transition states of the lead compounds.

Molecular Docking (2D Interactions)

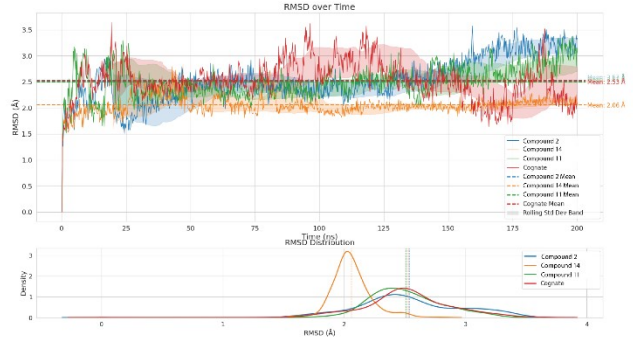


Molecular Dynamics

RMSF



RMSD



Protein Dynamics (PCA)

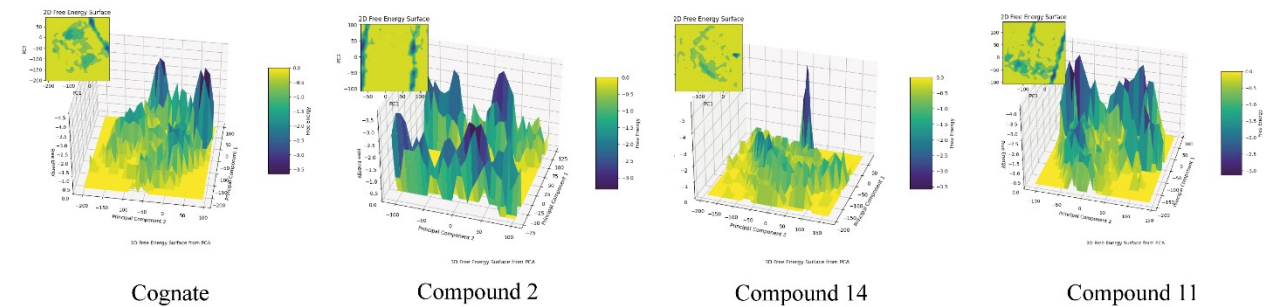


Figure S5. Molecular docking, molecular dynamics and PCA analysis results of the lead compounds on THR- α isoform.