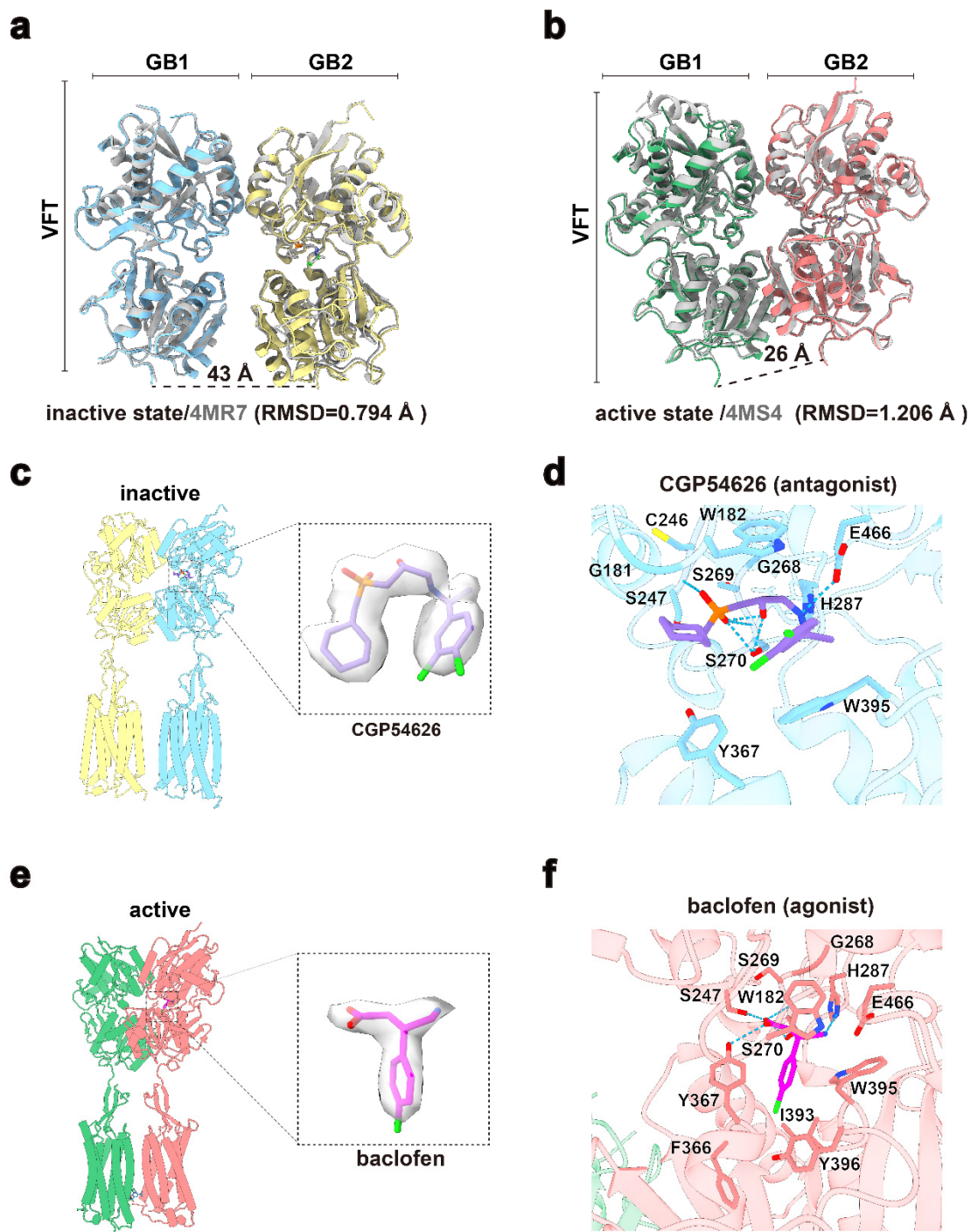


## Supplementary information, Figure S7



**Fig. S7 Structural comparisons of the VFT and ligand binding site. a** Superimposition of VFT domain from inactive structure of full-length GABA<sub>B</sub> receptor and crystal structure of CGP54626-bound soluble VFT domain (grey; PDB code: 4MR7). **b** Superimposition of VFT domain from active structure of full-length GABA<sub>B</sub>

receptor and crystal structure of baclofen-bound soluble VFT domain (grey; PDB code: 4MS4). **c-d** Cryo-EM density (**c**) and the binding pocket analysis (**d**) of CGP54626 in inactive state. Detailed interaction of CGP54626 in the orthosteric binding site, in agreement with the reported crystal structure of CGP54626-bound GABA<sub>B</sub> VFT. **e-f** Cryo-EM density (**e**) and the binding pocket analysis (**f**) of baclofen in active state. Detailed interaction of baclofen in the orthosteric binding site is in agreement with the reported crystal structure of baclofen-bound GABA<sub>B</sub> VFT.