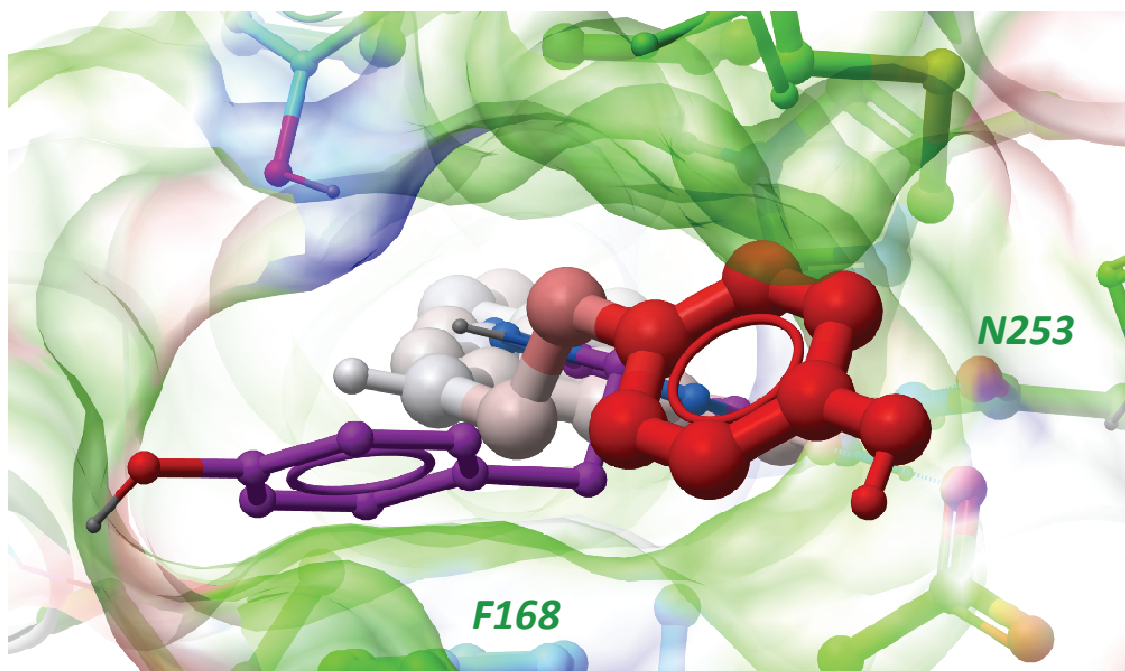


## Supplementary Material

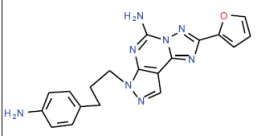
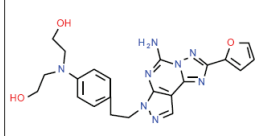
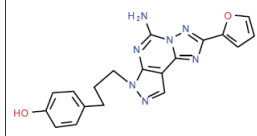
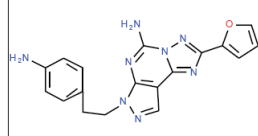
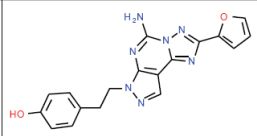
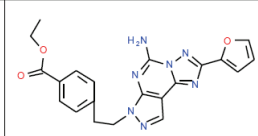
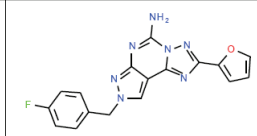
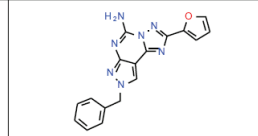
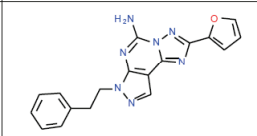
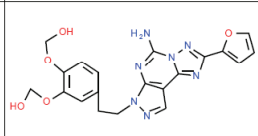
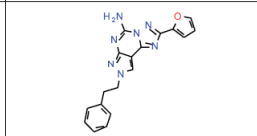
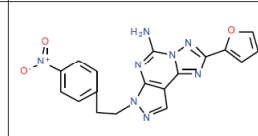
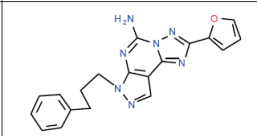
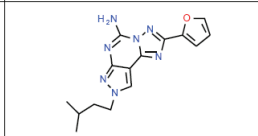
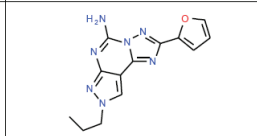
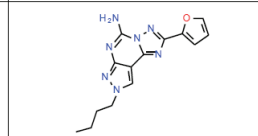
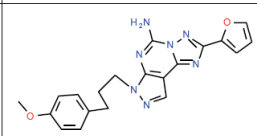
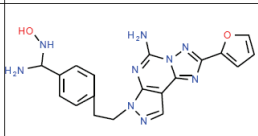
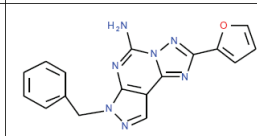
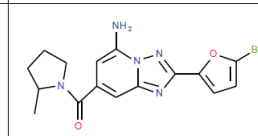
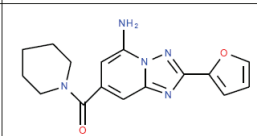
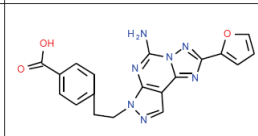
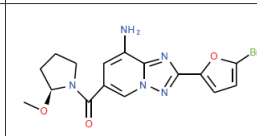
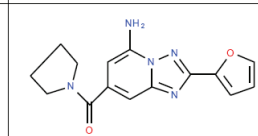
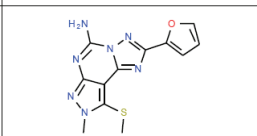
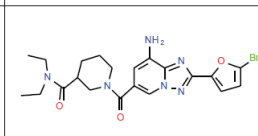
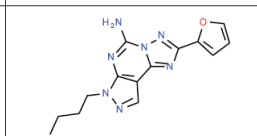
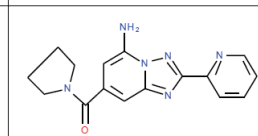
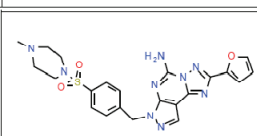
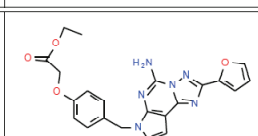
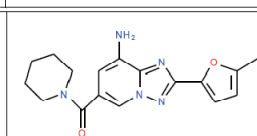
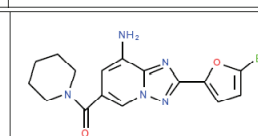
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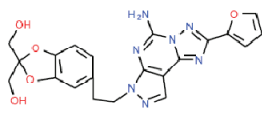
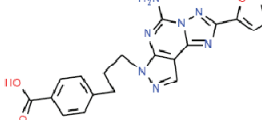
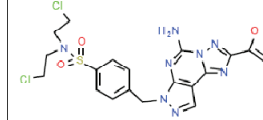
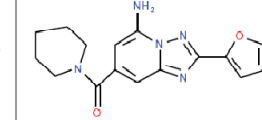
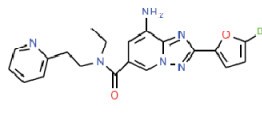
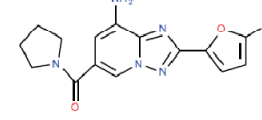
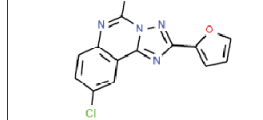
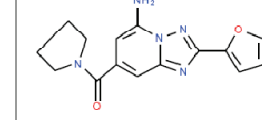
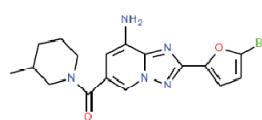
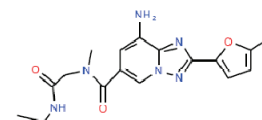
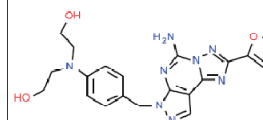
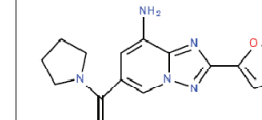
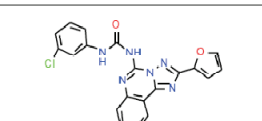
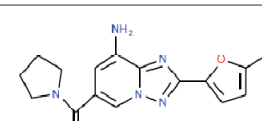
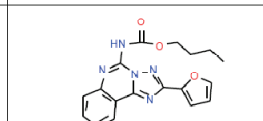
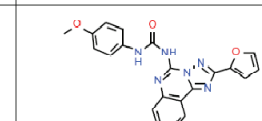
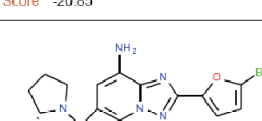
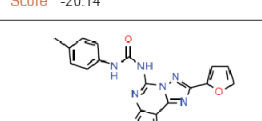
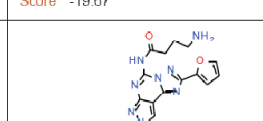
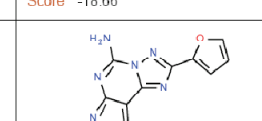
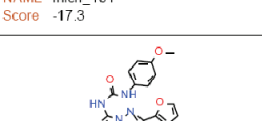
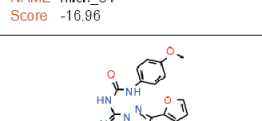
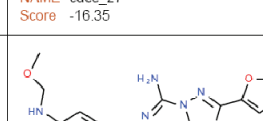
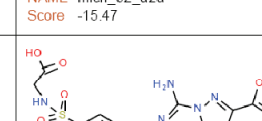
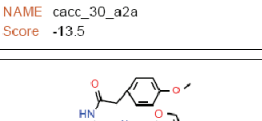
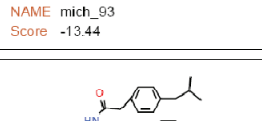
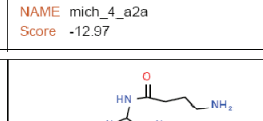
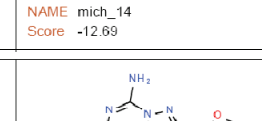
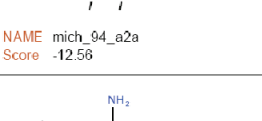
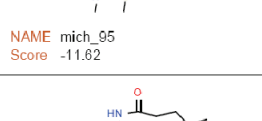
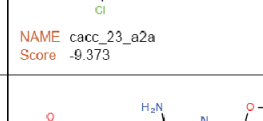
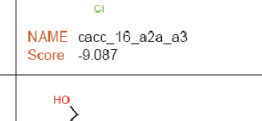
1. Figure SM1
2. Table SM1
3. A zip file with 64 models of A2a ligands presented in Table SM1.



**Figure SM1.** An extracellular view on alternative (magenta) best scoring conformation of ZMA ligand docked by ICM into the crystal structure of AA2AR. The ligand conformation from 3EML PDB file is colored according to its B-factor, where red represent B-factor > 100 Å<sup>2</sup>. Phenoxy moiety of ZMA is in foreground. The pocket of the receptor is shown as transparent skin, colored according to surface properties (green - hydrophobic, blue - donor, red - acceptor of hydrogen bonds.)

**Table SM1.** AA2AR binding ligands from ref. (Cacciari et al, [Purinergic Signal.](#) 2007 3(3):183-93) and (Michaelan et al *J. Chem. Inf. Model.*, 2008, 48 (2), 350-363). Predicted ICM binding score in mod2upu model is shown for each ligand. Corresponding binding poses can be found in the pdb files attached.

 <p>NAME cacc_13_a2a Score -46.79</p>	 <p>NAME mich_5_a2a Score -45.43</p>	 <p>NAME cacc_9_a2a Score -44.52</p>	 <p>NAME mich_2_a2a Score -43.58</p>
 <p>NAME cacc_8_a2a Score -43.46</p>	 <p>NAME mich_6_a2a Score -42.73</p>	 <p>NAME cacc_3_a2a Score -42.63</p>	 <p>NAME mich_89_a2a Score -41.7</p>
 <p>NAME cacc_6_a2a Score -41.11</p>	 <p>NAME mich_17_a2a Score -41.06</p>	 <p>NAME cacc_14_a2a Score -40.76</p>	 <p>NAME mich_3_a2a Score -40.46</p>
 <p>NAME cacc_7_a2a Score -40.3</p>	 <p>NAME cacc_26_a2a Score -40.1</p>	 <p>NAME mich_88_a2a Score -39.51</p>	 <p>NAME cacc_5_a2a Score -39.31</p>
 <p>NAME cacc_10_a2a Score -39.1</p>	 <p>NAME mich_8_a2a Score -39.07</p>	 <p>NAME mich_16_a2a Score -38.76</p>	 <p>NAME mich_111_a2a Score -37.65</p>
 <p>NAME mich_124 Score -37.52</p>	 <p>NAME mich_9_a2a Score -37.28</p>	 <p>NAME mich_100_a2a Score -36.74</p>	 <p>NAME mich_123_a2a Score -36.25</p>
 <p>NAME mich_91_a2a Score -35.59</p>	 <p>NAME mich_99 Score -35.09</p>	 <p>NAME cacc_4_a2a Score -34.93</p>	 <p>NAME mich_122 Score -34.23</p>
 <p>NAME mich_12_a2a Score -33.26</p>	 <p>NAME mich_7_a2a Score -33.04</p>	 <p>NAME mich_108 Score -32.86</p>	 <p>NAME mich_98 Score -32.3</p>

 <p>NAME mich_19_a2a Score -31.93</p>	 <p>NAME cacc_11_a2a Score -31.6</p>	 <p>NAME mich_13_a2a Score -31.34</p>	 <p>NAME mich_112_a2a Score -26.41</p>
 <p>NAME mich_104 Score -25.74</p>	 <p>NAME mich_97 Score -25.02</p>	 <p>NAME cacc_2_a2a Score -24.91</p>	 <p>NAME mich_110_a2a Score -24.79</p>
 <p>NAME mich_103_a2a Score -24.62</p>	 <p>NAME mich_102 Score -24.3</p>	 <p>NAME mich_1_a2a Score -24.27</p>	 <p>NAME mich_106 Score -23.69</p>
 <p>NAME mich_87_a2a Score -20.85</p>	 <p>NAME mich_107 Score -20.14</p>	 <p>NAME cacc_25 Score -19.67</p>	 <p>NAME mich_86_a2a Score -18.66</p>
 <p>NAME mich_101 Score -17.3</p>	 <p>NAME mich_34 Score -16.96</p>	 <p>NAME cacc_27 Score -16.35</p>	 <p>NAME mich_92_a2a Score -15.47</p>
 <p>NAME cacc_30_a2a Score -13.5</p>	 <p>NAME mich_93 Score -13.44</p>	 <p>NAME mich_4_a2a Score -12.97</p>	 <p>NAME mich_14 Score -12.69</p>
 <p>NAME mich_94_a2a Score -12.56</p>	 <p>NAME mich_95 Score -11.62</p>	 <p>NAME cacc_23_a2a Score -9.373</p>	 <p>NAME cacc_16_a2a_a3 Score -9.087</p>
 <p>NAME mich_109_a2a Score -4.608</p>	 <p>NAME cacc_24 Score -3.101</p>	 <p>NAME mich_10_a2a Score 3.71</p>	 <p>NAME mich_11_a2a Score 20.81</p>