SUPPLEMENTARY MATERIAL for

Towards a Novel Class of Multitarget Directed Ligands: Dual P2X7 – NMDA Receptors Antagonists

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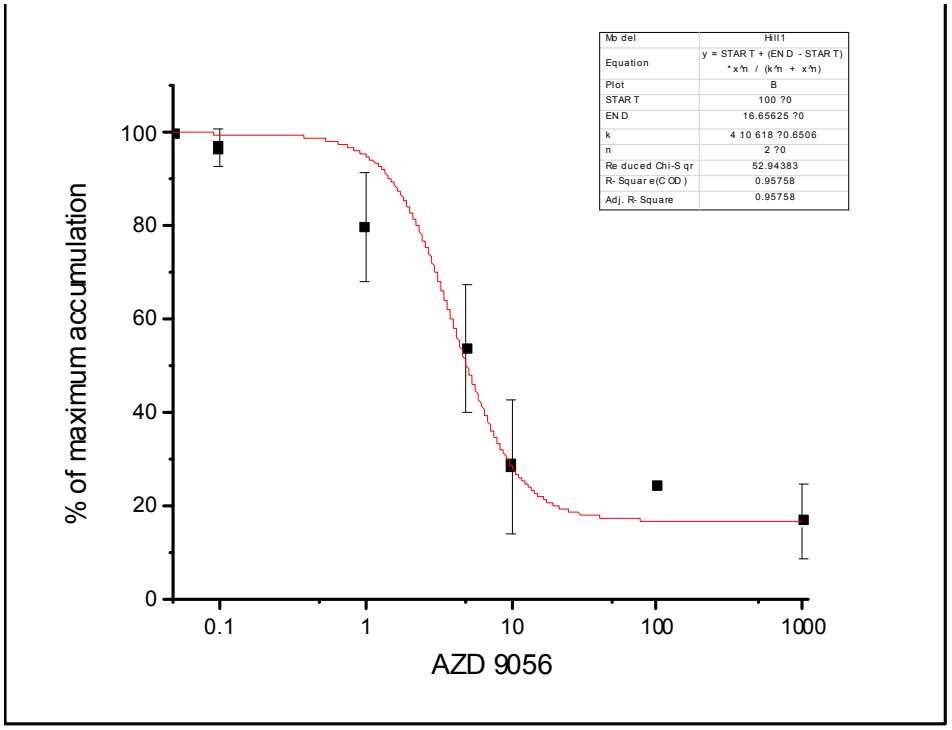
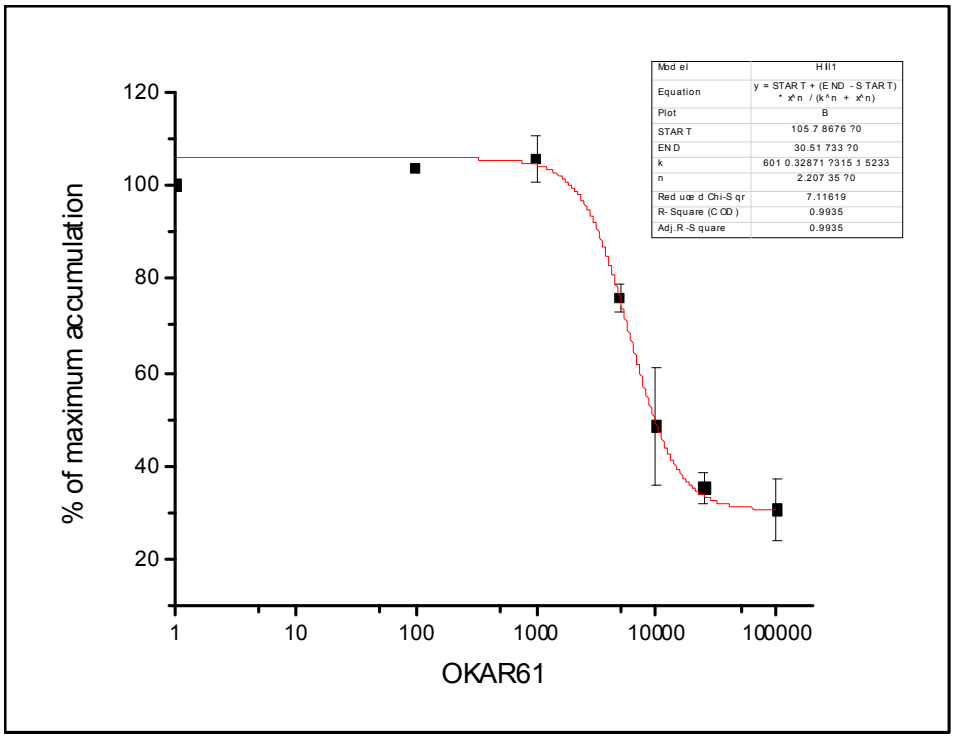
Figures S1-S4. Dose-response curves for antagonist compounds AZD 9056, **9g** and **15a-b** in hP2X7-expressing HEK293 cells.

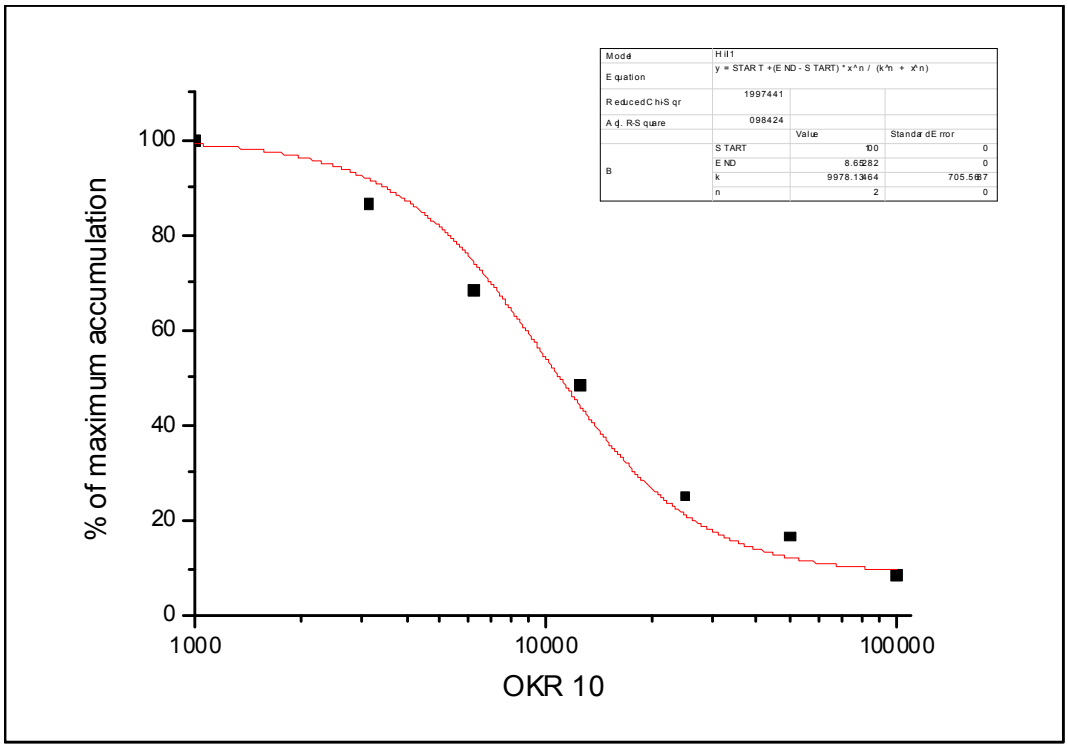
AZD 9056 IC_{50} = 4.1 nM



Compound **9g** IC_{50} = 6 µM



Compound **15a** IC_{50} = 9.9 µM



Compound **15b** IC_{50} = 16.1 µM

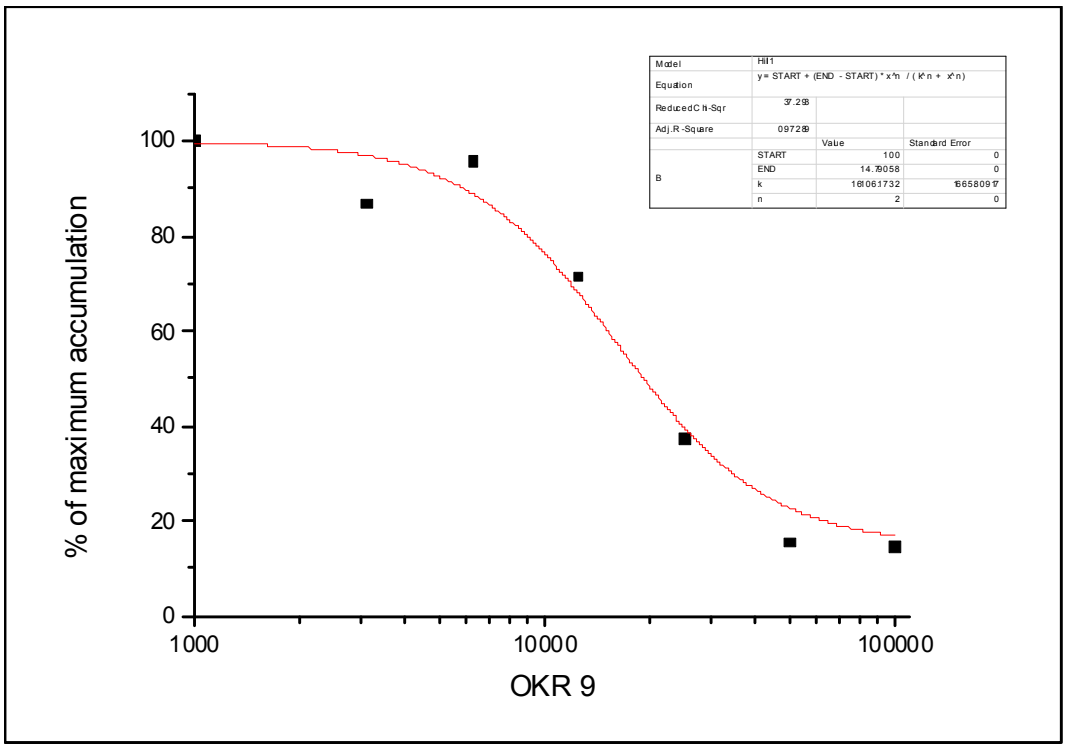
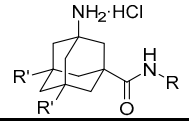
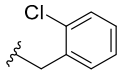
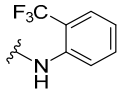
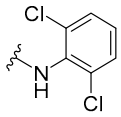
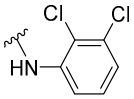
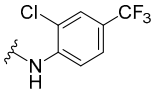
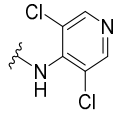
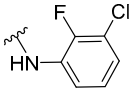
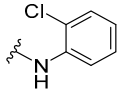
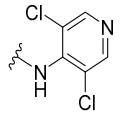
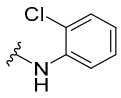


Table S1. NMDA antagonist activity in rat cerebellar granule cells.

Compound			% inhibition[a] or IC_{50}[b]
	R	R'	
2		H	18% / 30%
9a		H	5% / 14%
9b		H	17% / 38%
9c		H	23% / 30%
9d		H	20% / Not assayed
9e		H	6% / 16%
9f		H	11% / 18%
9g		H	468 ± 23
15a		CH_3	20% / 31%
15b		CH_3	7% / 8%

[a]Percentage inhibition values at 100 μM (left) and 300 μM (right) were expressed as percentages, relative to maximum intracellular calcium concentration stimulated by 100 μM NMDA in the presence of 10 μM of glycine. All experiments were repeated at least three times. [b]IC_{50} value was obtained from concentration response curves.