

Table S4: **Reproduction of the crystal water molecules in simulations of the complexed A-site.**

water molecule ↓	G1491U_PAR	G1491A_PAR	U1406C/U1495A_PAR	U1495C_PAR	NON_MUT_PAR
W1	+	–	+	+	+
W4	+	+	+	+	+
(W7)	(–)	(–)	(–)	(–)	(–)
W8 (W54)	+ (–)	– (+)	+ (–)	– (–)	+ (–)
W9 (W2)	+ (+)	– (+)	– (+)	+ (+)	+ (+)
W12	–	–	–	–	–
W13	+	–	–	–	+
W14	+	+	+	+	+
W15	–	–	–	–	–
W19	–	–	–	–	+
W20	–	+	–	+	+
W25	+	+	+	+	+
W27	+	–	–	–	–
W28	+	–	–	+	–
W32	+	+	–	+	+
W44	+	+	–	+	+
(W45)	(–)	(–)	(–)	(–)	(–)
W49	+	+	+ ( <i>near</i> )	+	+
W51	–	+	+	+	–

Selected water molecules of the 1J7T crystal structure and the corresponding water density areas in the MD simulations with paromomycin. “+” denotes water density areas higher than 0.22 water molecules per Å<sup>3</sup> observed in the position of the corresponding crystallographic water molecule; “–” denotes lack of high water density in this position. Brackets denote analogous water molecules located in the symmetric part of the RNA fragment.