Table S1. Inhibitory activity against wild-type (WT) GT1a HCV NS3/4A and D168A proteases in enzymatic assays, with fold change relative to WT indicated in parentheses. The error reported is from the global fit of at least three replicates.

Inhibitor	K_i (nM) (Fold Change)	
	GT1a WT	D168A
Grazoprevir (GZR)	0.21 ± 0.03 †	49.1 ± 1.6 † (234)
5172-mcP1P3	3.29 ± 0.52 †	82.4 ± 4.4
Parent Compound (PC)	3.60 ± 0.44 †	52.0 ± 2.4 § (14)
P_4-1	4.44 ± 0.30	27.9 ± 4.1 § (6)
P_4-2	1.40 ± 0.13	46.4 ± 3.4 § (33)
P_4-3	1.13 ± 0.22 §	36.0 ± 1.8 (32)
P_4-4	1.78 ± 0.30 §	16.0 ± 1.2 § (9)
P_4-5	1.29 ± 0.05	21.7 ± 2.3 § (17)
P_4-6	0.94 ± 0.25	12.7 ± 1.2 § (14)
P_4-7	0.54 ± 0.20	2.3 ± 0.7 § (4)
P_4P_5-1A	11.1 ± 0.5	141 ± 18 (13)
P_4P_5-1B	13.0 ± 0.8	102.0 ± 6.8 (8)
P_4P_5-2A	23.9 ± 1.7 §	215 ± 16 § (9)
P_4P_5-2B	29.5 ± 1.9 §	201 ± 15 (8)
P_4P_5-3A	2.23 ± 0.07	87.3 ± 4.4 (39)
P_4P_5-3B	3.54 ± 0.13	31.6 ± 2.1 (9)
P_4P_5-4	7.10 ± 0.24	81 ± 11 § (11)
P_4P_5-5	31.0 ± 2.74	931 ± 70 § (30)
P_4P_5-6	0.91 ± 0.38	9.68 ± 0.64 § (11)

§Co-crystal structures determined in this work. †Co-crystal structures previously determined by our laboratory (Soumana D.I. et al, *ACS Chem Biol*, 11(4):900, 2016, Romano K.P. et al, *Plos Pathog*, 8(7):e1002832, 2012, and (Matthew N.M. et al, *J. Med. Chem*. 60(13):5699, 2017).