

Figure S1

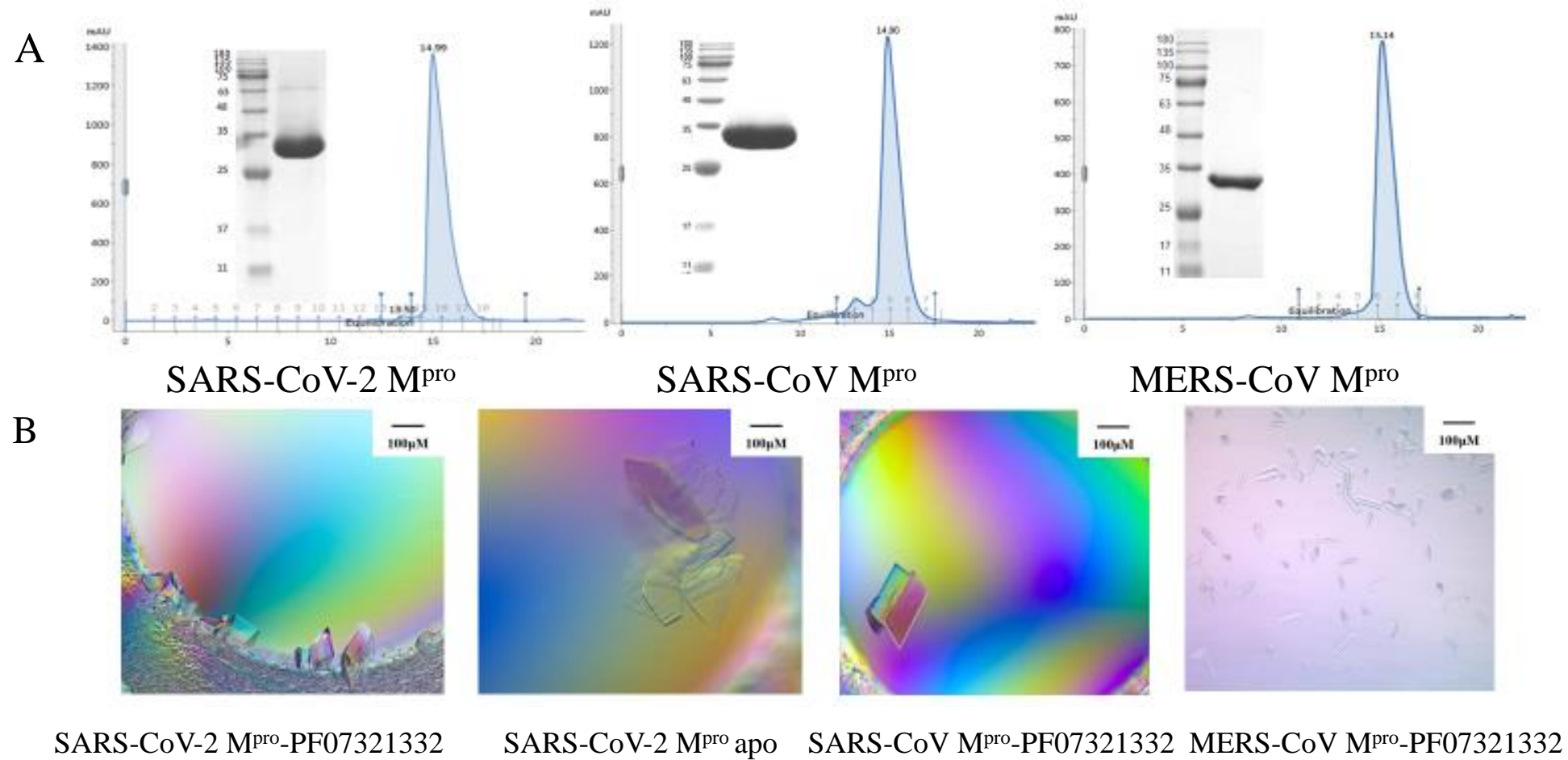


Figure S1 A Purification of human CoVs . B Crystals of SARS-Cov-2 and human CoVs with PF07321332.

Figure S2

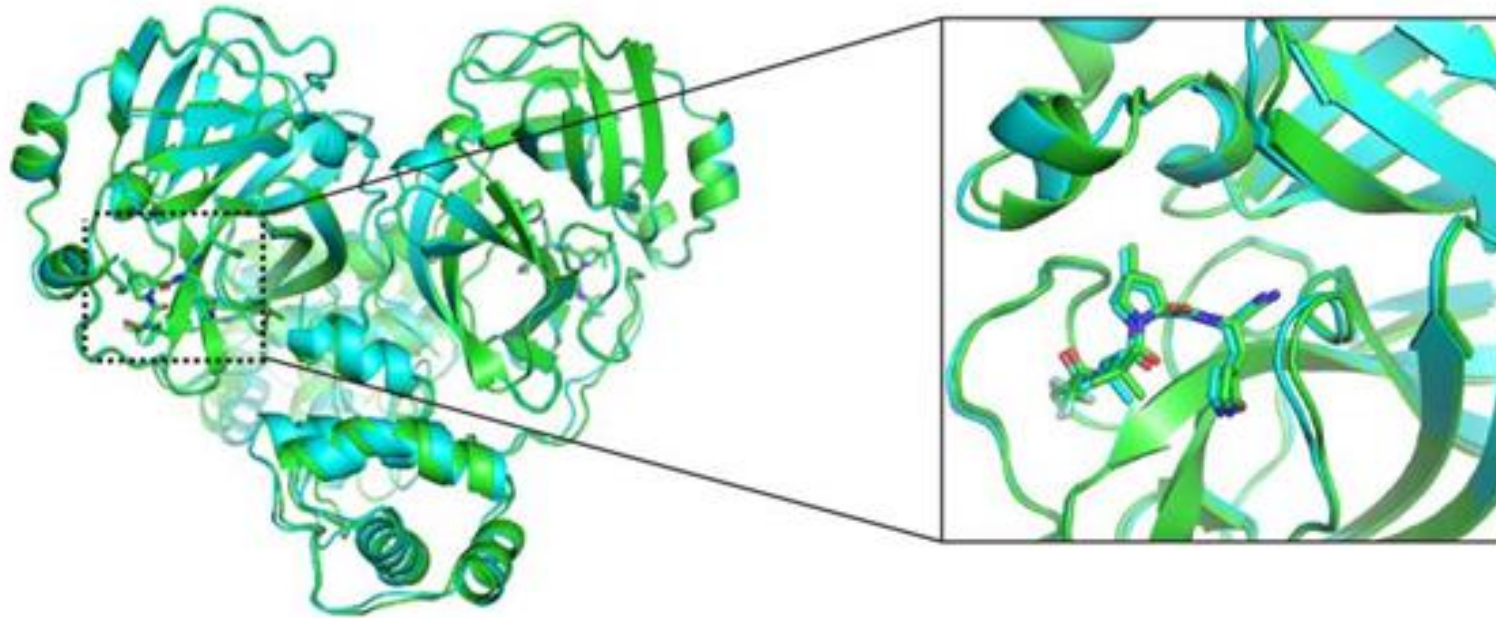


Figure S2 Structural comparison of PF-07321332/SARS-CoV-2 M<sup>pro</sup> complexes obtained by [cocrystallization](#) (green) with soaking (cyan).

Figure S3

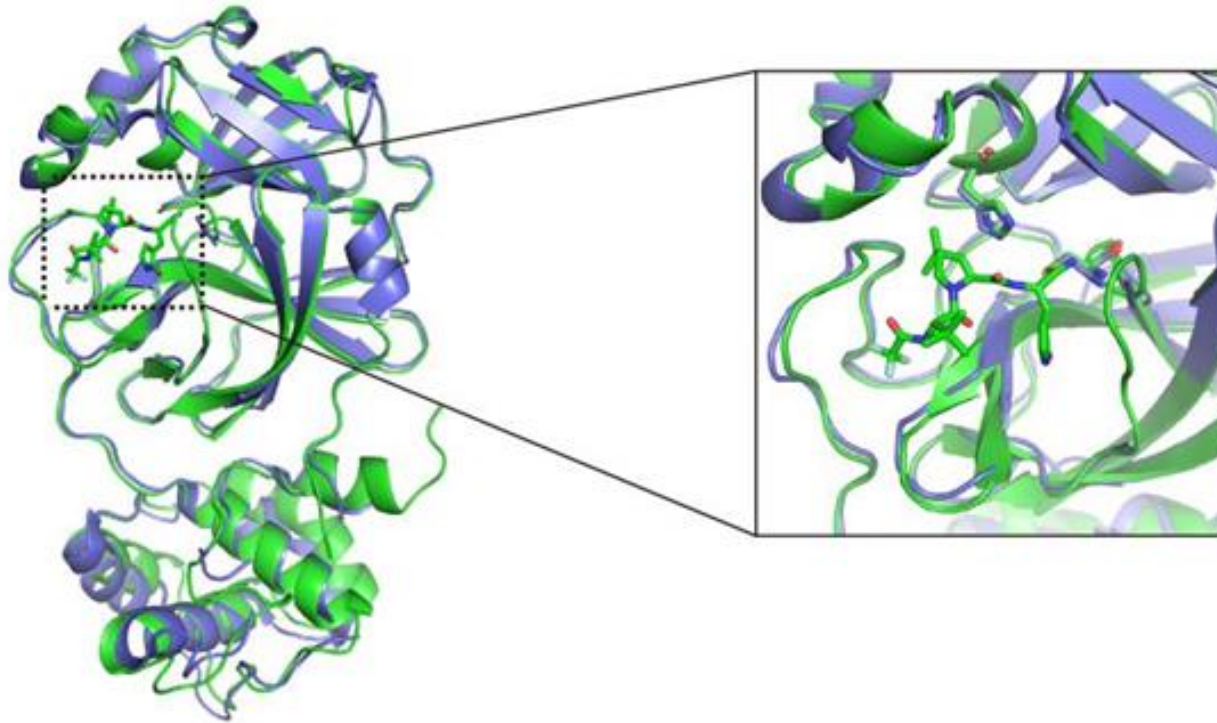


Figure S3 Structural comparison of PF-07321332/SARS-CoV-2 M<sup>pro</sup> complexes obtained by [cocrySTALLIZATION](#) (green) with apo M<sup>pro</sup> (slate).

Table S1

Table S1 Summarize of recently reported covalent inhibitors against SARS-CoV-2 M<sup>pro</sup>.

Inhibitors	Inhibitory activity against SARS-CoV-2 M <sup>pro</sup>	Crystal structure in complex with SARS-CoV-2 M <sup>pro</sup> (PDB ID)	Reference
N3	$k_3/K_i = 11,300 \pm 880 \text{ M}^{-1}$	6LU7	12
13b	$IC_{50} = 0.67 \pm 0.18 \mu\text{M}$	6Y2F	14
11a	$IC_{50} = 0.053 \pm 0.005 \mu\text{M}$	6LZE	6
Boceprevir	$IC_{50} = 8.0 \mu\text{M}$	7BRP	24
Carmofur	$IC_{50} = 1.82 \mu\text{M}$	7BUY	17
GC376	$IC_{50} = 0.15 \mu\text{M}$	7D1M	24
5h	$K_i = 17.6 \pm 3.2 \text{ nM}$	7JKV	25
MPI3	$IC_{50} = 8.5 \pm 1.5 \text{ nM}$	7JQO	27
PF-07321332	$IC_{50} = 0.023 \mu\text{M}$	7VLQ	This