

## Supporting Information

# Severe Acute Respiratory Syndrome-Coronavirus Papain-Like Novel Protease Inhibitors: Design, Synthesis, Protein-Ligand X-ray Structure and Biological Evaluation

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HPLC (Table 1) and HRMS (Table 2) data of inhibitors.

**Table 1.** Purity of inhibitors

<b>Inhibitor</b>	<b>Solvent system*</b>	<b>Retention Time (min)</b>	<b>Purity (%)</b>	<b>Column</b>	<b>Flow rate (mL/min)</b>
<b>7a</b>	A	7.5	95.6	XDB-C18 5 $\mu$ m 4.6 x 150 mm	1.5
<b>7b</b>	A	7.7	95.5	XDB-C18 5 $\mu$ m 4.6 x 150 mm	1.5
<b>15a</b>	B	8.7	96.6	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5
<b>15b</b>	B	8.6	96.0	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5
<b>15c</b>	B	8.6	97.1	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5
<b>15d</b>	B	8.8	98.6	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5
<b>15e</b>	B	8.9	97.2	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5
<b>15f</b>	B	8.5	96.6	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5

<b>15g</b>	B	8.5	98.3	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5
<b>15h</b>	B	8.6	96.9	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5
<b>15i</b>	B	8.3	95.8	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5
<b>15j</b>	B	8.4	98.5	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5
<b>15k</b>	B	8.8	96.1	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5
<b>20</b>	B	8.4	95.5	XDB-C18 5 $\mu$ m 4.6 x 150mm	1.5

\*\*A = Linear gradient from 10% CH<sub>3</sub>CN, 0.05% TFA in 90% H<sub>2</sub>O to 100% CH<sub>3</sub>CN in 18 min.; B= linear gradient from 25% MeOH, 75% 0.05% TFA in water to 90% MeOH, 10% 0.05% TFA in water in 18 min.

**Table 2.** HRMS for inhibitors

<b>15a</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>26</sub> H <sub>31</sub> N <sub>2</sub> O <sub>2</sub> 403.2386, found [M+H] <sup>+</sup> 403.2388
<b>15b</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>26</sub> H <sub>30</sub> N <sub>2</sub> O <sub>2</sub> 402.2307, found [M] <sup>+</sup> 402.2303
<b>15c</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>26</sub> H <sub>30</sub> N <sub>2</sub> O <sub>2</sub> 402.2307, found [M] <sup>+</sup> 402.2299
<b>15d</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>26</sub> H <sub>31</sub> N <sub>2</sub> O <sub>2</sub> 403.2386, found [M+H] <sup>+</sup> 403.2390
<b>15e</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>26</sub> H <sub>31</sub> N <sub>2</sub> O <sub>2</sub> 403.2386, found [M+H] <sup>+</sup> 403.2394
<b>15f</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>26</sub> H <sub>31</sub> N <sub>2</sub> O <sub>2</sub> 403.2386, found [M+H] <sup>+</sup> 403.2392
<b>15g</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>26</sub> H <sub>29</sub> N <sub>2</sub> O <sub>3</sub> 417.2178, found [M+H] <sup>+</sup> 417.2178
<b>15h</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>26</sub> H <sub>29</sub> N <sub>2</sub> O <sub>3</sub> 417.2178, found [M+H] <sup>+</sup> 417.2173
<b>15i</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>25</sub> H <sub>27</sub> N <sub>2</sub> O <sub>3</sub> 403.2022, found [M+H] <sup>+</sup> 403.2025
<b>15j</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>25</sub> H <sub>27</sub> N <sub>2</sub> O <sub>3</sub> 403.2022, found [M+H] <sup>+</sup> 403.2025
<b>15k</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>27</sub> H <sub>31</sub> N <sub>2</sub> O <sub>3</sub> 431.2335, found [M+H] <sup>+</sup> 431.2330
<b>20</b>	HRMS ( <i>m/z</i> ) calcd for C <sub>25</sub> H <sub>30</sub> N <sub>3</sub> O <sub>2</sub> 404.2338, found [M+H] <sup>+</sup> 404.2336