SUPPORTING INFORMATION

Plasmodium falciparum Subtilisin-like Protease 1: Discovery of Potent Difluorostatone-based Inhibitors

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**Figure S1.** Docked pose of 3 (light yellow sticks) in the cavity of the PfSUB1 (PDB ID: 4LVN). H-bonds are indicated by black dotted lines. The catalytic triad is represented by salmon sticks while the other residues in the binding site were represented by lines. Molecular graphics were generated by PyMOL (The PyMOL Molecular Graphics System, v1.6-alpha; Schrodinger LLC: New York, 2013). Nonpolar hydrogens were omitted for clarity.

**Figure S2.** Docked pose of 9 (light yellow sticks) in the cavity of the PfSUB1 (PDB ID: 4LVN). H-bonds are indicated by black dotted lines. Catalytic triad is represented by salmon sticks while the other residues in the binding site were represented by lines. Molecular graphics were generated by PyMOL (The PyMOL Molecular Graphics System, v1.6-alpha; Schrodinger LLC: New York, 2013). Nonpolar hydrogens were omitted for clarity.
Figure S3. Docked pose of 17 (light green sticks) in its neutral state, in the cavity of the PfSUB1 (PDB ID: 4LVN). H-bonds are indicated by black dotted lines. Catalytic triad is represented by salmon sticks while the other residues in the binding site were represented by lines. Molecular graphics were generated by PyMOL (The PyMOL Molecular Graphics System, v1.6-alpha; Schrodinger LLC: New York, 2013). Nonpolar hydrogens were omitted for clarity.

Figure S4. Docked pose of 17 (light green sticks) in its protonated state, in the cavity of the PfSUB1 (PDB ID: 4LVN). H-bonds are indicated by black dotted lines. Catalytic triad is represented by salmon sticks while the other residues in the binding site were represented by lines. Molecular graphics were generated by PyMOL (The PyMOL Molecular Graphics System, v1.6-alpha; Schrodinger LLC: New York, 2013). Nonpolar hydrogens were omitted for clarity.
Figure S5. Docked pose of 18 (blue sticks) in the cavity of the PfSUB1 (PDB ID: 4LVN). H-bonds are indicated by black dotted lines. Catalytic triad is represented by salmon sticks while the other residues in the binding site were represented by lines. Accordingly, the Goldscore value is 67.34, while the $\Delta G_{\text{bind}}$ is -71.95 kcal/mol. Molecular graphics were generated by PyMOL (The PyMOL Molecular Graphics System, v1.6-alpha; Schrodinger LLC: New York, 2013). Nonpolar hydrogens were omitted for clarity.
$^{1}$H NMR spectra
26g

26h
2R,4R-26m (precursor)

27a