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Supporting information for article:

3D structures of the *Plasmodium vivax* subtilisin-like drug target SUB1 reveal conformational changes to accommodate a substrate-derived α-ketoamide inhibitor

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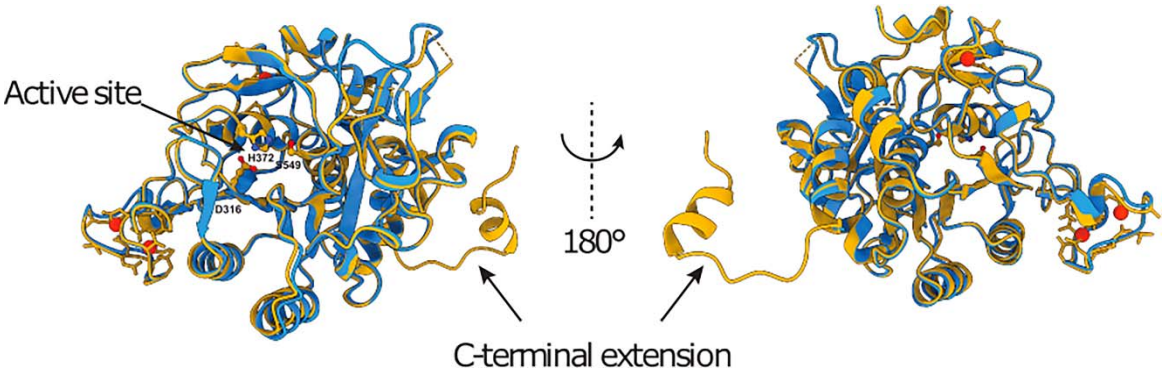

Figure S1 Superposition of the crystal structures of $PvS1_{FL\text{-}bac}$ (blue, PDB 4tr2, residues Tyr_{277}-Lys_{611}) with $PvS1_{Cat}$ (yellow) catalytic domains. The three main residues of PvS1 active site (D_{316}, H_{372} and S_{549}) and calcium ions (in red) are shown.

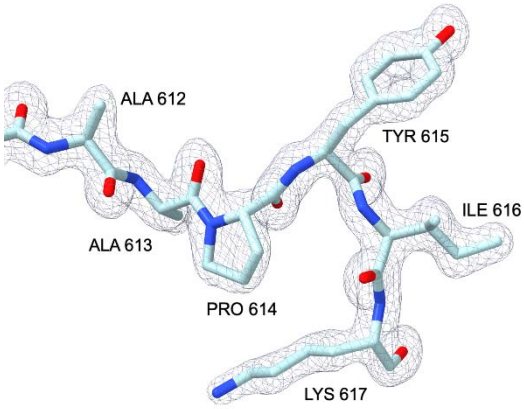

Figure S2 Electron density of $PvS1_{Cat\text{-}Tryps}$ small C-terminal peptide extension 612-617 that is engaged in crystal contacts.

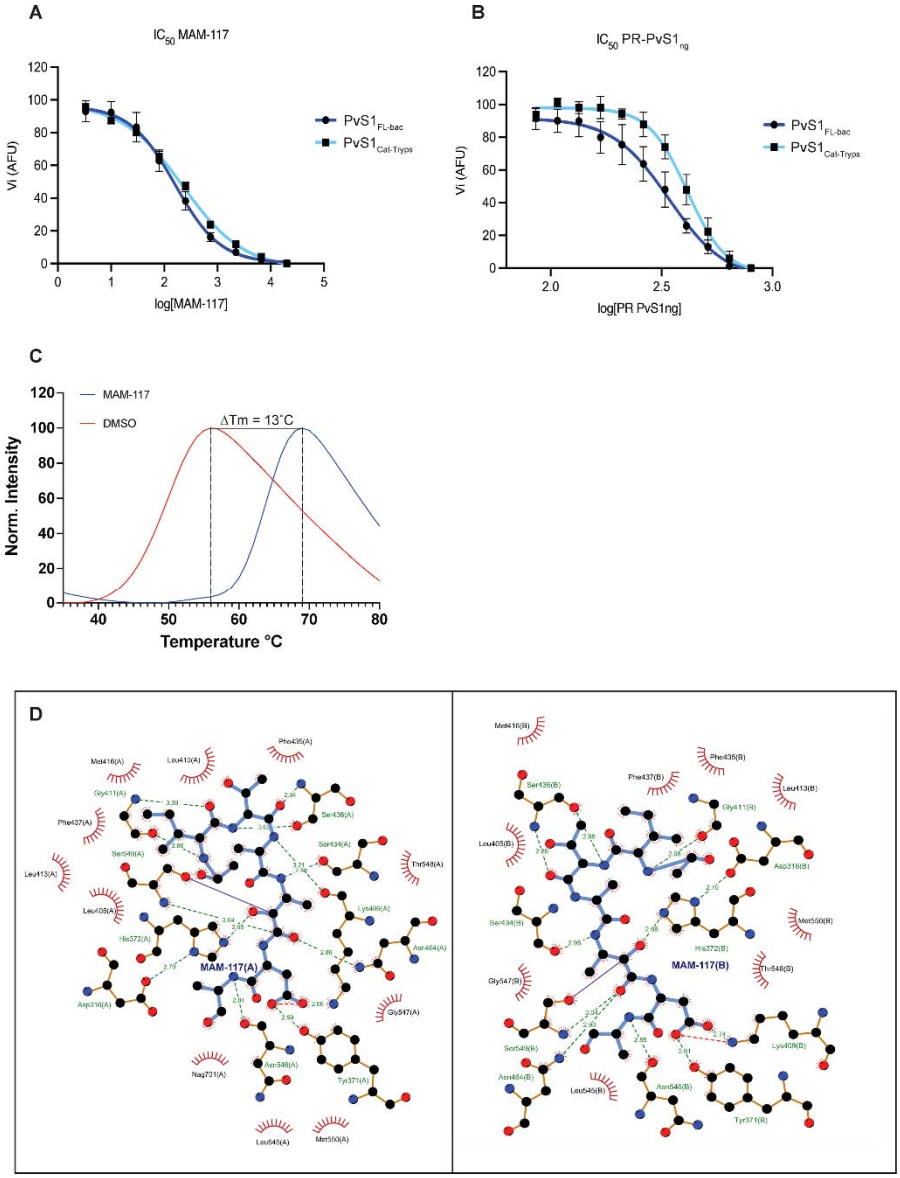

Figure S3 **A:** IC_{50} determination of MAM-117 for recombinant $PvS1_{FL\text{-}bac}$ (164.8 ±27.3 nM) and $PvS1_{Cat\text{-}Tryps}$ (225.5 ±32.8 nM) active enzymes. **B:** IC_{50} determination of PR-$PvS1_{ng}$ pro-region for recombinant $PvS1_{FL\text{-}bac}$ (325.9 ±19.4 nM) and $PvS1_{Cat\text{-}Tryps}$ (430.3 ±40.3 nM) active enzymes. **C:** Melting temperatures (Tm) of $PvS1_{Cat\text{-}Tryps}$ with DMSO or MAM-117 determined with the ThermoFluor assay.

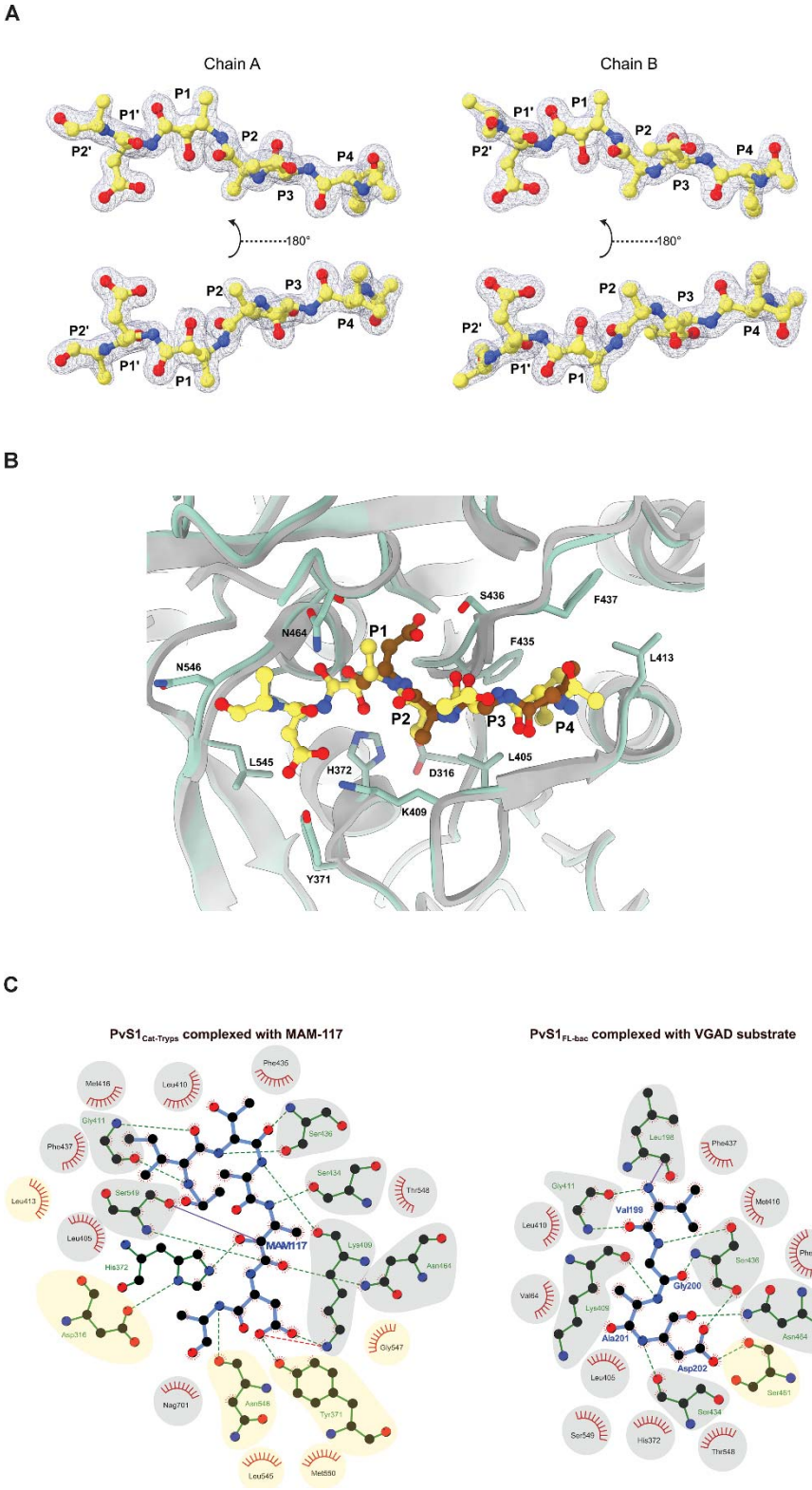

Figure S4 **A**: Electron density of the MAM-117 inhibitor present in chains A and B of the asymmetric unit, viewed at two different angles. **B**: Superposition of $PvS1_{Cat\text{-}Tryps}$ (green) and $PvS1_{FL\text{-}bac}$ (grey) crystal structures complexed with MAM-117 (yellow) or with PvS1 primary auto-maturation site (peptide V_{199}-G_{200}-A_{201}-D_{202}, brown). The P4-P1 positions of MAM-117 and PvS1 auto-

maturation site are indicated. **C:** Ligplot analysis showing the shared (in grey) or unique (in orange) interactions between PvS1 and MAM-117 (left panel) or PvS1 primary auto-maturation site (peptide V_{199}-G_{200}-A_{201}-D_{202}, right panel) from the complex crystal structures shown in (B).