

Supplementary Table 1. In vivo anti-SARS-CoV-2 efficacy of compounds targeting the viral life cycle.

| virus life cycle stage | Compound name | Primary indication | Clinical Phase for COVID-19 | in vivo performance | | References |
|--|-------------------|----------------------|-----------------------------|--|------------------------|------------|
| | | | | Compared to vehicle | compared to Remdesivir | |
| attachment and entry | camostat mesilate | pancreatitis | Phase 2 | about 1 log reduction in an ex vivo model (PCLS) | | (1) |
| | umifenovir | influenza | No clinical benefit | no in vivo data | | (2) |
| | baricitinib | rheumatoid arthritis | Phase 3 | no effect on virus replication | | (3, 4) |
| initiation translation of polyproteins | Plitidepsin | multiple myeloma | Phase 2/3 | 1.5-2 log reduction, 4/8 achieved clearance in a mouse model | non-superior | (5) |
| | Ternatin-4 | Preclinical compound | | no in vivo data | | (6, 7) |
| | zotatifin | Phase 1 for cancer | Phase 1 | no in vivo data | | (6, 7) |
| | homoharringtonine | leukemia | | 6/6 mice achieved clearance on 5 dpi | | This study |
| proteolytic processing | MI-09 | SARS-CoV-2 | animal model | about 2 log reduction, clearance not achieved | | (8) |
| | MI-30 | SARS-CoV-2 | animal model | about 2 log reduction, clearance not achieved | | (8) |
| | lopinavir | AIDS | No clinical | no effect on virus | | (9) |

| | | | | | |
|---------------------------------|-------------------|-------------|--------------------------------|---|------|
| | ritonavir | AIDS | benefit No clinical benefit | replication no effect on virus replication | (9) |
| transcription & RNA replication | remdesivir | coronavirus | FDA-approved | 10/36 rhesus macaques achieved clearance on 7 dpi | (10) |
| | EIDD-2801/MK-4482 | coronavirus | Phase 2a | 4/8 mice achieved clearance if treatment started 24 h after exposure in the LoM model | (11) |
| multiple steps | clofazimine | leprosy | Phase 2 | 1-2 log reduction in hamster model, clearance not achieved | (12) |
| | ranitidine | bismuth | anti-ulcer citrate | 1-1.5 log reduction, clearance not achieved | (13) |

Supplementary Table2. Homoharringtonine (HHT) exhibits broad-spectrum inhibition efficacy against coronaviruses.

| coronavirus | Abbreviation | Genus | IC50 (nM) | Reference |
|---|--------------|-------|-----------|--------------------------|
| Middle East respiratory syndrome coronavirus | MERS | Beta | 71.8 | Dyall et al. 2014(14) |
| Mouse hepatitis coronavirus | MHV | Beta | 12 | Cao et al. 2015(15) |
| Bovine coronavirus | BCoV | Beta | <<1uM | Cao et al. 2015(15) |
| Human enteric coronavirus | HECoV | Beta | <<1uM | Cao et al. 2015(15) |
| Porcine epidemic diarrhea virus | PEDV | Alpha | 112 | Dong et al. 2018(16) |
| Severe acute respiratory syndrome coronavirus 2 | SARS-CoV-2 | Beta | ~100 | Wen et al. 2021(17) |
| Severe acute respiratory syndrome coronavirus 2 | SARS-CoV-2 | Beta | 30 | Ianevski et al. 2020(18) |
| Severe acute respiratory syndrome coronavirus 2 | SARS-CoV-2 | Beta | 2.1uM** | Choy et al. 2020(19) |
| Porcine epidemic diarrhea virus | PEDV | Alpha | <<100 | This study |
| Porcine deltacoronavirus | PDCoV | Delta | <<100 | This study |
| Swine acute diarrhea syndrome coronavirus | SADS-CoV | Alpha | <100 | This study |

** [Note - Choy et al.'s study reported a much larger IC50 value for multiple drugs, including HHT and Remdisivir (In Choy et al.'s study, IC50 of Remdisivir against SARS-CoV-2 was 26.9uM, while in many other studies, it was about 1uM(2, 20).]

Supplementary Table 3. Basic information of the first 4 patients enrolled in ChiCTR2100049182.

| | age(years) | sex | Cancer type |
|----|------------|--------|---|
| P1 | 63 | female | Lung cancer |
| P2 | 50 | male | Colorectal cancer with lung metastasis |
| P3 | 74 | male | Colorectal cancer with lung metastasis |
| P4 | 48 | male | Nasopharynx cancer with lung metastasis |

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