Target Product Profile - Jan 2021

Community use oral SARS-CoV-2 main viral protease inhibitor with potential for future pandemic extension

COVID Moonshot
MedChemica
CREATING A STEP CHANGE IN MEDICINAL CHEMISTRY

Property	Target range	Rationale
Protease assay	IC_{50} < 50 nM (compromise if clean and anti viral activity sufficient)	Extrapolation from other anti-viral programs
Viral replication	EC_{50} < 0.2µM (Vero-E6, and Calu-3)	Suppression of virus at achievable blood levels
Plaque reduction	EC_{50} < 0.2µM (Vero-E6, and Calu-3)	Suppression of virus at achievable blood levels
PK-PD	Cmin > EC90(plaque reduction) for 24h	Assume constant suppression of viral replication
Coronavirus spectrum	SARS-CoV2 B1.1.7 , B.1.1.248 variants essential, SARS-CoV1 & MERS desirable	Treat vaccine resistant variants and future pandemic preparation.
Route of administration	oral	bid/tid(qid)- compromise PK for potency if pharmacodynamic effect achieved
Solubility	> 5 mg/mL	Aim for biopharmaceutical class 1 assuming <= 750 mg dose
Half-life	Ideally>= 8 h (human) estimated from rat and dog PK	Assume PK/PD requires continuous cover over viral replication for 24 h
Safety	No significant protease activity > 50% at 10µM (Nanosyn 61 protease panel) Only reversible and monitorable toxicities (NOAEL > 30x Cmax) No significant DDI - clean in 5 CYP450 isoforms hERG and NaV1.5 IC_{50} > 50 µM No significant change in QTc Ames negative No mutagenicity or teratogenicity risk	No significant toxicological delays to development Avoid DDI to support co-morbidities & combination therapy, Critical cardiac safety for COVID-19 risk profile Low carcinogenicity risk reduces delays in manufacturing Patient group will include significant proportion of women of childbearing age