Target Product Profiles

Note these are drafts subject to review, these have been prepared as a starting point, if you have useful input, please add it to the COVID Moonshot Forum, or mail to: ed.griffen@medchemica.com.

A Target Product Profile is an outline sketch of what a new drug would have on the label.

There was discussion about an inhaled TPP but the team felt that initially the oral and iv routes were more preferable as the quantity of material needed might make inhaled a tough option.

MedChemica

TPP-1 Hospital IV treatment for critical care

assume age profile mainly >50, gender balanced, high proportion with co-morbidities.

What	Target	Why/questions
protease assay	IC50 <10nM	extrapolation from other anti-viral programs
Viral replication assay	5μM	Realistic target for PK
Plaque reduction assay	5μM	Free drug level
Spectrum	cover > 95% of clinical isolates at IC50 TBC	
Mutant cover	Unknown	Mutation profile unknown: what are common / accessible mutant isoforms?
Other COV viruses	Unknown	Added benefit if shows cross COV species efficacy, potential separate TPP?
Route of administration	iv infusion	Critical care patients, infusion easier than bolus
solubility	>10mg/ml at pH >5	limit for IV infusion
Half life	>=6h (human) estimated from rat & dog	assume PK/PD requires continuous cover over plaque inhibition for 24h max tid dosing
Safety	Reversible and monitorable toxicities No significant DDI - clean in 5 CYP-450 isoforms hERG and NaV1.5 IC50 > 50uM No significant change in QTc Ames negative	DDI is to deal with co-morbitities/ therapies, cardiac safety for COVID risk profile, Ames for manufacturing

TPP-2 Community use for patients and preventative cover for health workers / high risk individuals

assume age profile mainly 18-80, gender balanced, medium proportion with co-morbidities.

What	Target	Why/questions
protease assay	IC50 <10nM	extrapolation from other anti-viral programs
Viral replication assay	5μM	Realistic target for PK
Plaque reduction assay	5μM	
Spectrum	cover > 95% of clinical isolates at IC50 TBC	
Mutant cover	Unknown	Mutation profile unknown: what are common / accessible mutant isoforms?
Other COV viruses	Unknown	Added benefit if shows cross COV species efficacy, potential separate TPP?
Route of administration	oral	Ideally uid but bid acceptance for compliance
solubility	> 5mg/mg	Aim for biopharmaceutical class 1 assuming =<750mg dose
Half life	>=8h (human) estimated from rat & dog	assume PK/PD requires continuous cover over plaque inhibition for 24h max bid dosing
Safety	Reversible and monitorable toxicities No significant DDI - clean in 5 CYP-450 isoforms hERG and NaV1.5 IC50 > 50uM No significant change in QTc Ames negative No mutagenicity or teratogenicity risk	DDI is to deal with co-morbitities/ therapies, cardiac safety for COVID risk profile, Ames for manufacturing Mutagenicity / teratogenicity: patient group will include significant proportion of women of child bearing age.

TPP-3 Strategic Pan Corona Virus early protection - community use for patients and preventative cover for health workers

assume age profile mainly 18-80, gender balanced, medium proportion with co-morbidities.

What	Target	Why/questions
protease assay	IC50 <10nM	extrapolation from other anti-viral programs
Viral replication assay	5μM	Realistic target for PK
Plaque reduction assay	5μM	
Spectrum	cover > 95% of clinical isolates at IC50 TBC	
Mutant cover	Unknown	Mutation profile unknown: what are common / accessible mutant isoforms?
Other COV viruses	Unknown	cross COV species efficacy, requires sequencing and structures of maximum number of corona virus cysteine proteases in SARS-Cov like viruses see https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2176051/pdf/0023-07.pdf
Route of administration	oral	Bid / tid – compromise PK for specturm
solubility	> 5mg/mg	Aim for biopharmaceutical class 1 assuming =<750mg dose
Half life	>=8h (human) estimated from rat & dog	assume PK/PD requires continuous cover over plaque inhibition for 24h max bid dosing
Safety	Reversible and monitorable toxicities No significant DDI - clean in 5 CYP-450 isoforms hERG and NaV1.5 IC50 > 50uM No significant change in QTc Ames negative No mutagenicity or teratogenicity risk	DDI is to deal with co-morbitities/ therapies, cardiac safety for COVID risk profile, Ames for manufacturing Mutagenicity / teratogenicity: patient group will include significant proportion of women of child bearing age.