THE COVID MOONSHOT: SARS-COV-2 ORAL ANTIVIRAL THERAPEUTICS FROM AN OPEN SCIENCE GLOBAL COLLABORATION

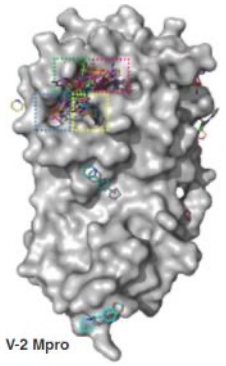
Dr Ed Griffen
MedChemica Ltd.

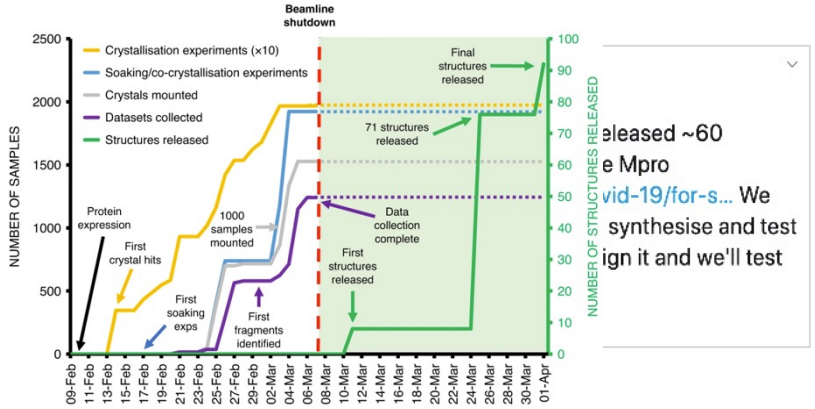
representing
COVID Moonshot Team

DNDi Drugs for Neglected Diseases COVID Moonshot

COVID Moonshot – *spontaneous international collaboration*

Mpro: Validated, Essential, Conserved



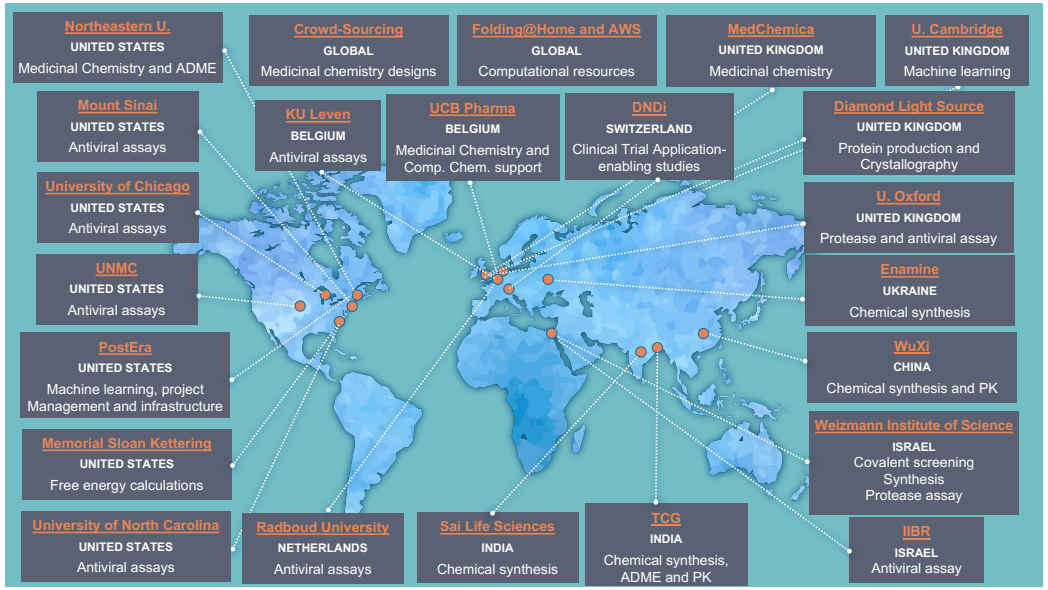


diamond

WEIZMANN INSTITUTE OF SCIENCE

NATURE COMMUNICATIONS | (2020)11:5047 | https://doi.org/10.1038/s41467-020-18709-w
NATURE | (2021) 594, 330-332 | https://doi.org/10.1038/d41586-021-01571-1

>30 groups
Expertise pro bono - Experiments at cost - Philanthropic funding



Unique constitution has led to speed

Open science
Global, highly flexible team
Cumulative 100s of years of big pharma experience
Leading BSL3 antiviral and *in vivo* access

Strategic decisions and funding :

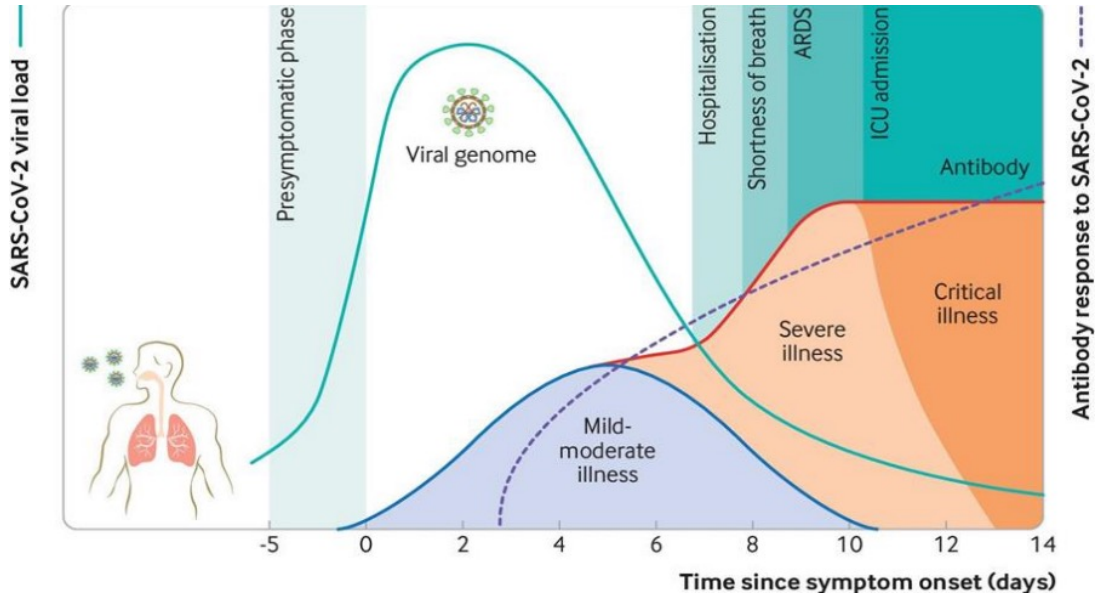
- Alpha Lee – *Postera & U of Cambridge*
- John Chodera – *Memorial Sloane-Kettering*
- Nir London – *Weizmann Institute*
- Frank von Delft – *Diamond & U of Oxford*
- Annette von Delft – *U of Oxford*
- Ben Perry – *DNDi*
- Tatiana Matviuk - *Enamine*
- Ed Griffen – *MedChemica*

DNDi Drugs for Neglected Diseases COVID Moonshot

Clinical ambition: craft the right antiviral

Oral antiviral
Window of opportunity

Virus no longer drives disease
Antivirals less effective
Existing are difficult (IV, $$$), so only trialled here



Muge Cevik et al.
BMJ 2020;371:bmj.m3862

Our goal is an oral antiviral that is <u>very:</u> potent; safe; cheap; and widely useable.

This would:

- Prevent disease: virus *can* be cleared, but must be before immune over-reaction (day 7)
- Prevent spread: post-exposure prophylaxis (before day 0)
- Reach non-vaccinated population *(at risk; non-responsive; vaccine hesitant)*

→ reduce both hospitalisation and mortality

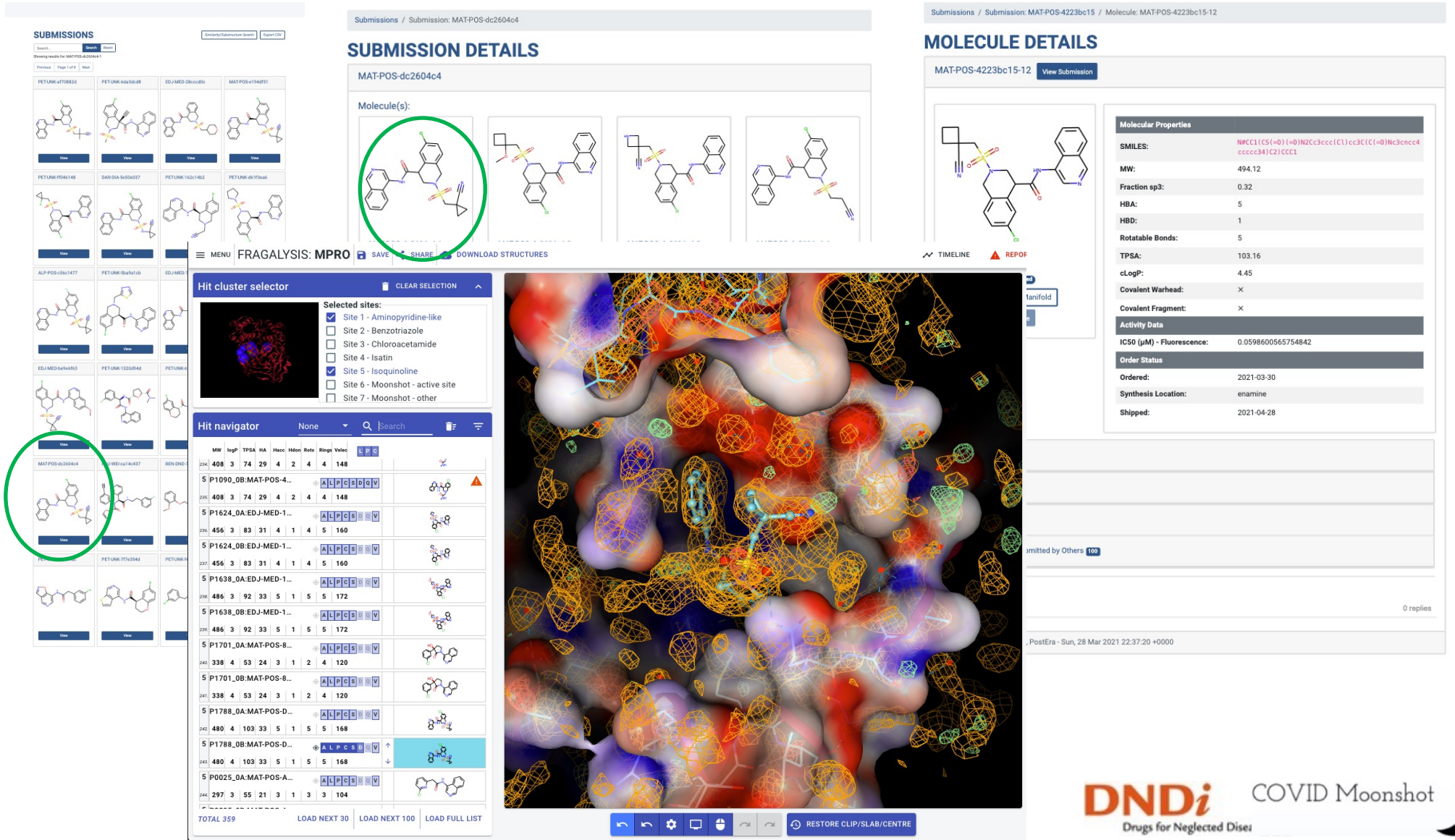
DNDi Drugs for Neglected Diseases COVID Moonshot

Open Science - what is accessible?

Plans and results are available live: https://covid.postera.ai/covid/submissions

x-ray structures: https://fragalysis.diamond.ac.uk/viewer/react/preview/target/Mpro

More via CDD



DNDi Drugs for Neglected Diseases

COVID Moonshot

Open Science - what does it mean?

Aiming for equitable, global access: - Our ambition is a “Direct-to-Generics” strategy

Plans, synthesis completion and assay results are all reported and date stamped

- Open public access includes > 350 protein-ligand crystal structures
- Further detail is available on CDD

Active strategy to maximise public good

- Consequences:
  - Open access to contribute to design
  - Fast collaborations – no CDA, no MTA = access to BSL-3 facilities and animal models
  - Compounds are available in Enamine’s catalogue immediately
  - Of course we post warnings:

All of the substances displayed on this site are designed to be biologically active. The prediction of toxic effects remains an extremely difficult problem. Therefore all materials described here should be treated as having high biological activity with a risk of severe toxicity which may include, but is not limited to: cardiac impairment up to and including the risk of causing cardiac arrest, irreversible liver or renal damage, carcinogenicity, mutagenicity, teratogenicity (risk to the unborn child) and, or generation of a severe allergic response. Unless otherwise stated, no material has been profiled for toxicological effects and therefore no materials should under any circumstances be synthesised and taken for any therapeutic or recreational effect by any person or for any other purpose.

Medicinal Chemistry Target Product Profile

Orally bioavailable inhibitor for therapeutic and prophylactic use

Property	Target range
protease assay	IC_{50} < 50 nM (compromise if clean and anti viral activity sufficient)
viral replication (Vero-E6)	EC_{50} < 0.2µM
plaque reduction (Vero-E6, Calu-3)	EC_{50} < 0.2µM
PK-PD	Cmin > EC90 (plaque reduction) for 24h
Coronavirus spectrum	SARS-CoV2 B1.1.7 , 501.V2, B.1.1.248 variants essential SARS-CoV-1 & MERS desirable
Route of administration	oral
solubility	> 5 mg/mL, >100µM tolerable
half-life	Ideally>= 8 h (human) est from rat and dog
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 Critical transporter check (*e.g.* OATP) hERG and NaV1.5 IC_{50} > 50 µM No significant change in QTc No mutagenicity or teratogenicity risk

DNDi Drugs for Neglected Diseases COVID Moonshot

Assay Challenges

What animal model?

- Ferret default respiratory model – very mild disease, little public PK data to understand metabolic processes, terrible lead times (17 weeks)
- Hamster – severe disease and very strong metabolisers
- ACE-2 Humanised mouse or murine virus – both a compromise

    - Or the pragmatic option: predicted human Cmin cover over EC90 in a relevant cell line?

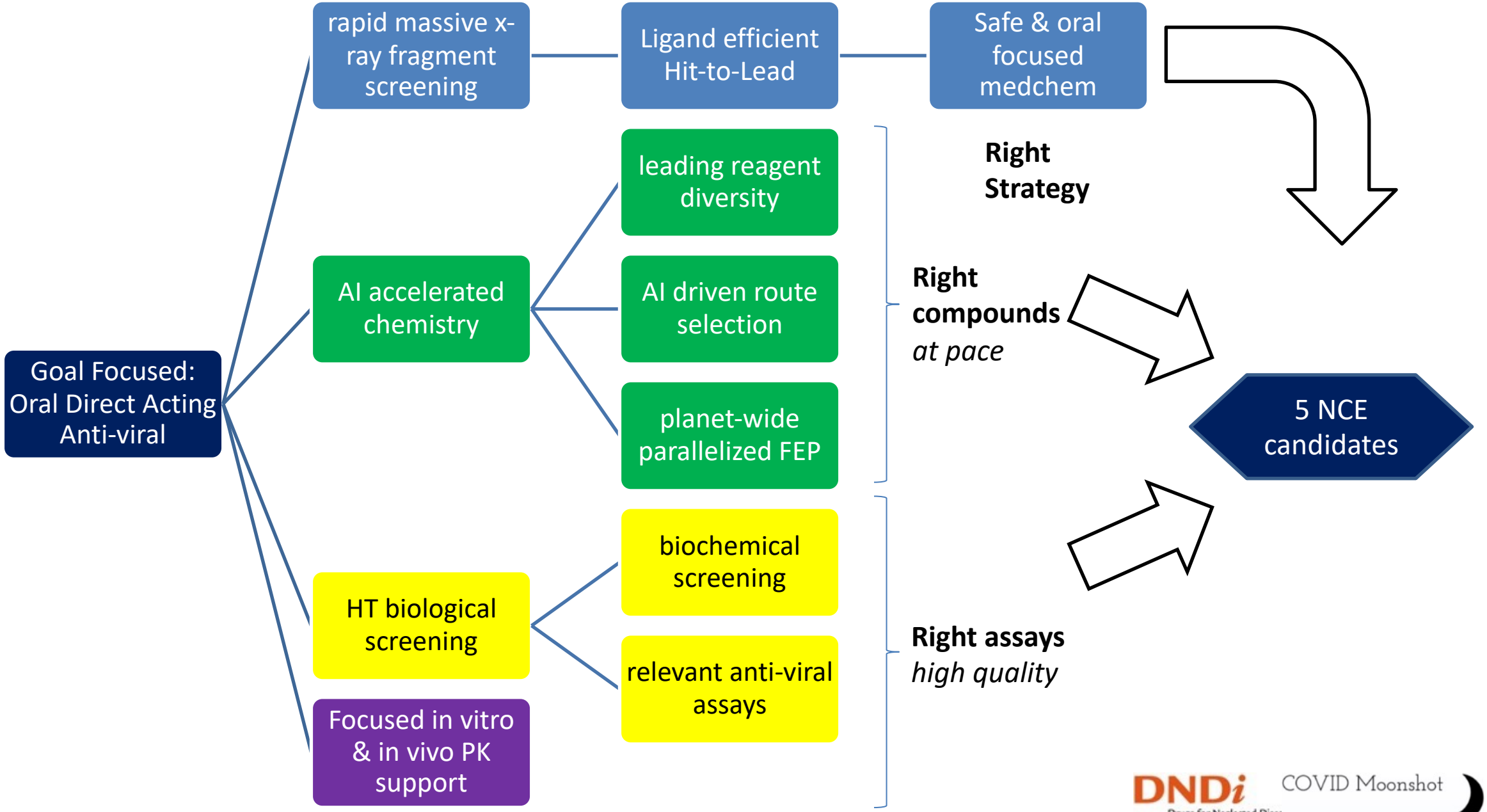
What cell assay is relevant?

- VeroE6 - available but immortalized monkey kidney cell line, interferon deficient , PGP over expressing
- Calu-3, A549 immortal human lung lines
- Replicon assay – only recently available(not March 2020)
- Pneumocytes – the gold standard - not accessible for screening

    - More serious problem is access to BSL-3 facility….
        - Multiple collaborators – IIBR, Oxford, Leuven

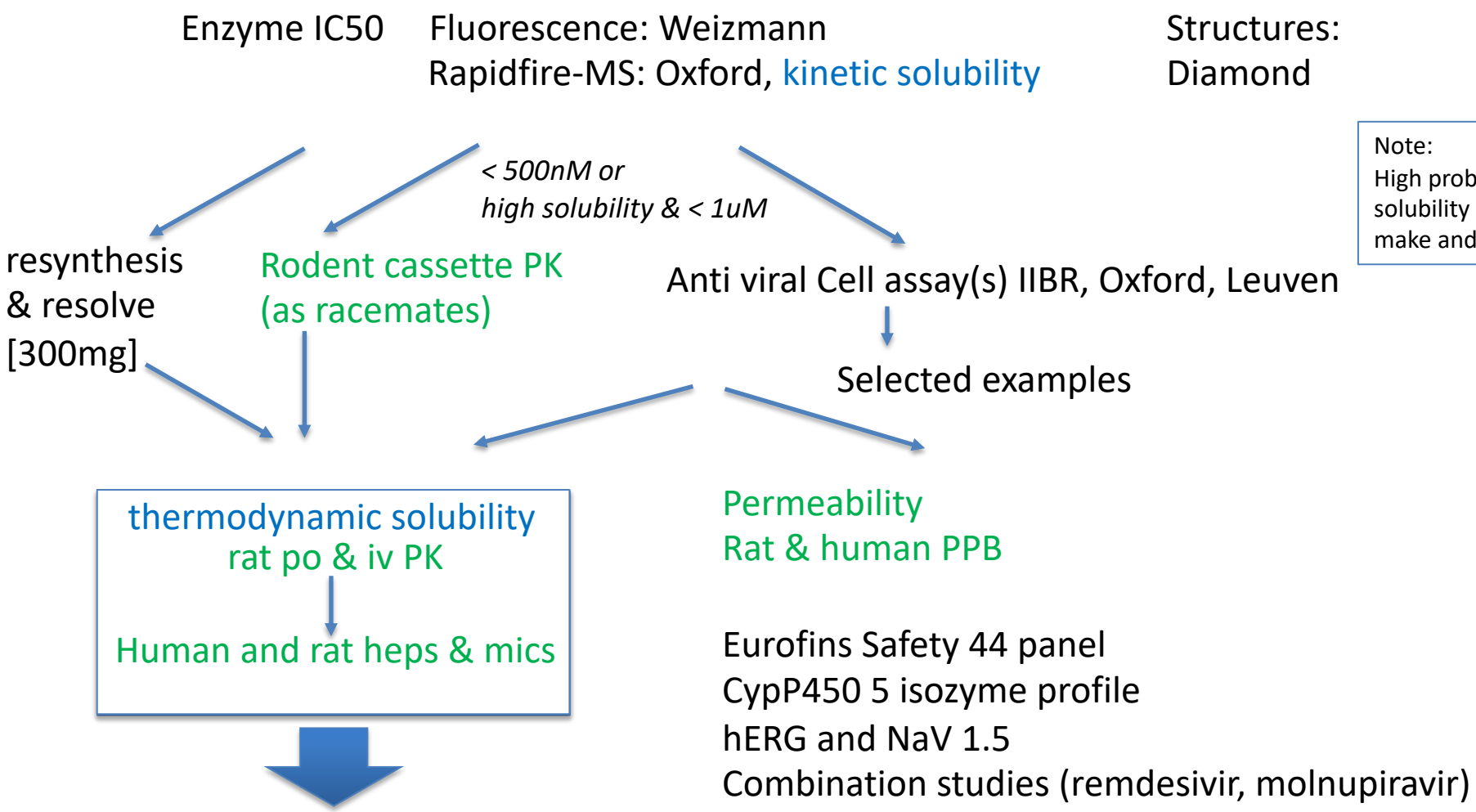
- **Enzyme assays**
    - Mpro not trivial to handle, autocatalytic in own destruction, forms dimer with one active site
        - FRET assay, Weizmann Institute
        - Rapidfire-MS Oxford

Key elements of the COVID Moonshot



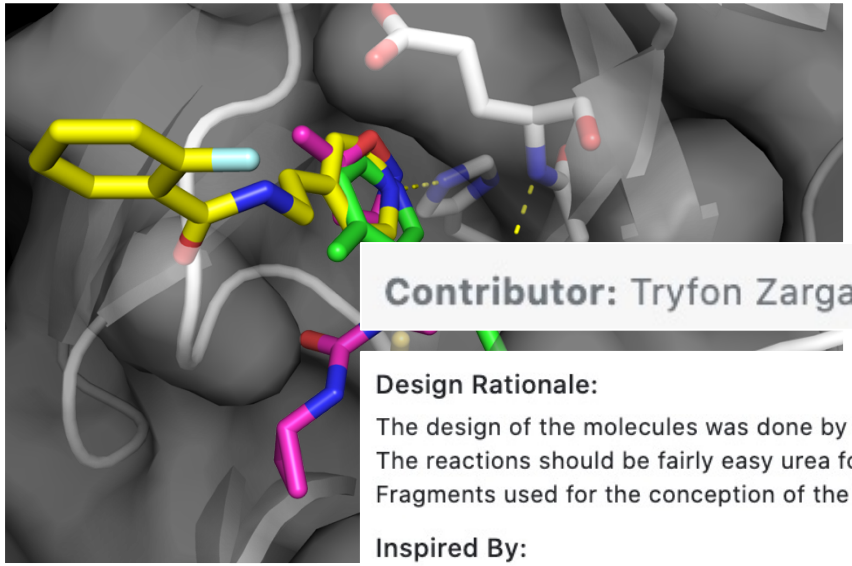
DNDi Drugs for Neglected Diseases COVID Moonshot

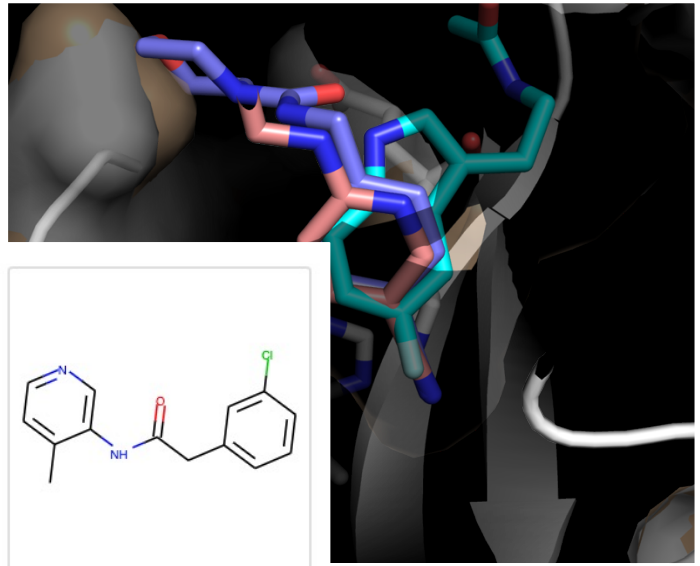
Assay cascade configured to solve problems



Note:
High probability of enzyme IC50 < 1μM : solubility in parallel with enzyme testing, make and resolve before testing.

Aminopyridines by fragment joining



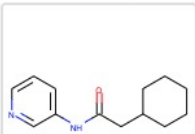


Contributor: Tryfon Zarganis - Tzitzikas, University of Oxford, TDI MedChem

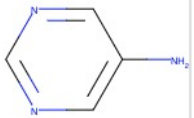
Design Rationale:

The design of the molecules was done by superimposing the different fragments from the crystal structures (by eye). The reactions should be fairly easy urea formation or amide coupling all from readily available starting materials. Fragments used for the conception of the ideas are the following x0107, x0434, x0678, x0748, x0995, x1382

Inspired By:



ALE-HEI-f28a35b5-9



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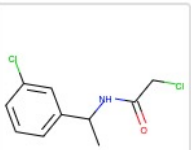

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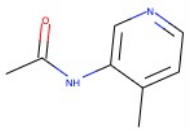

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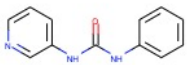


AAR-POS-d2a4d1df-11

TRY-UNI-714a760b-6

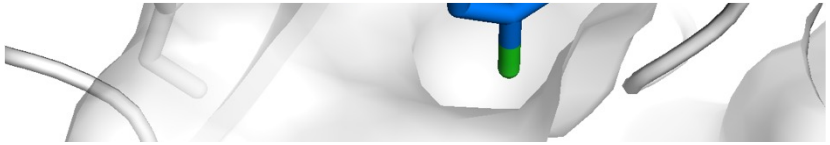
Cc1ccncc1NC(=O)Cc1cccc(Cl)c1

3-aminopyridine-like

Enamine Mcule

MolPort Assayed

View



24μM

COVID Moonshot

Drugs for Neglected Dise

COVID Moonshot – design principles:

Aim for small, efficient molecules

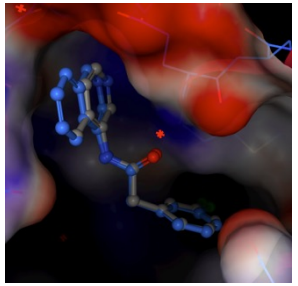
- Less opportunity for off target effects
- Reduce permeability and metabolic risks
- Keep within the substrate envelope to minimize resistance risks
- Simplicity of compounds – reduce cost of development and cost of goods = speed of development and equitable access

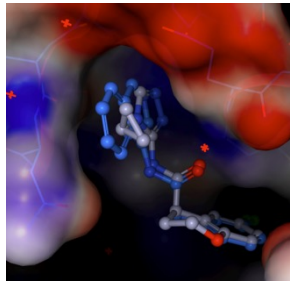
- Avoid peptidomimetics
  - Present a different development and toxicity risk profile

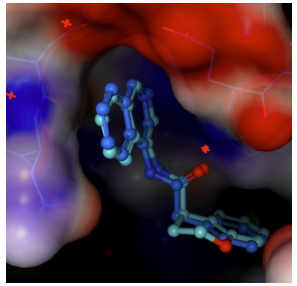
- Covalency
  - Make the compounds potent and selective first add covalent warhead if needed
    - Efficient selective ligand rather than “hot” warhead

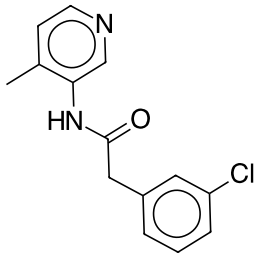
- What effect on broader spectrum “pan coronavirus”? – not a primary goal of this program

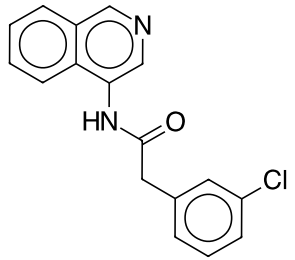
Aminopyridine early optimization

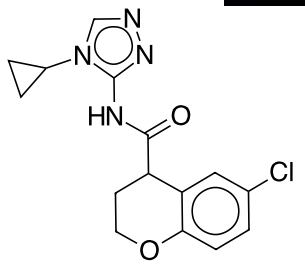


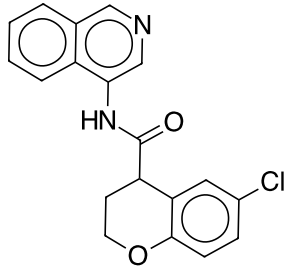








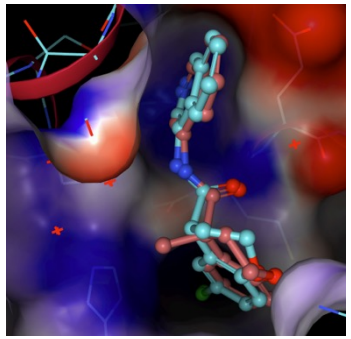


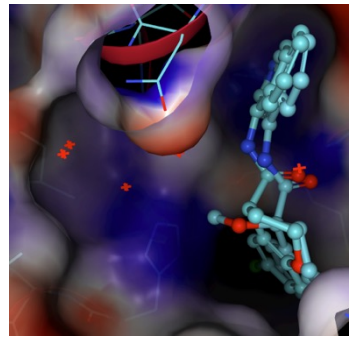


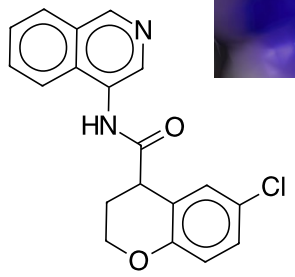
	TRY-UNI-714a760b-6	ADA-UCB-6c2cb422-1	JAG-UCB-a3ef7265-20	VLA-UCB-1dbca3b4-15
Fl IC50	24μM	728nM	598nM(racemate)	360nM(190nM single enantiomer)
RF IC50	14μM	776nM	Inactive	424nM(racemate)
clogP	2.95	3.4	1.9	3.3
LLE(Fl)	1.7	2.7	4.37	3.1
		UCB MedChem team "Part of Enamine REAL" Only 2 made from design	UCB MedChem team "Pharmacophore search of Enamine REAL"	Vladas Oleinikovas, UCB "Expansion round ADA-UCB-6c2cb422-1"

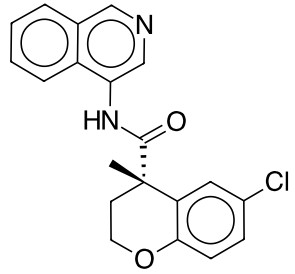
Data quoted is Mpro inhibition IC50, Fl = fluorescence assay, Weizmann Institute, RF = RapidFire , Oxford University

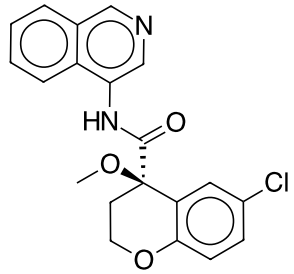
Isoquinolines – building potency









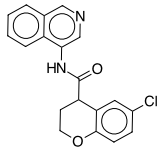
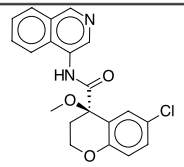


	VLA-UCB-1dbca3b4-15	EDJ-MED-e4b030d8-13	PET-UNK-29afea89-2
Fl IC50	190nM (single enantiomer)	284nM (single enantiomer)	84nM(single enantiomer)
clogP	3.3	3.9	3.2
LLE(Fl)	3.4	2.7	3.9

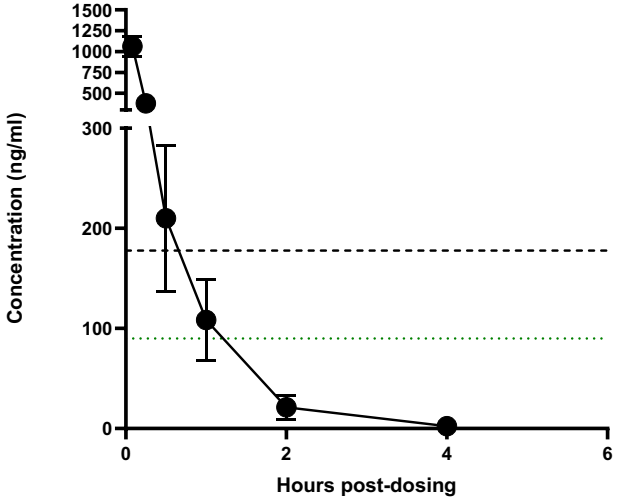
Ed Griffen, MedChemica
"Using MPro-x10942 as structural guidance. Key goal is to bias amide into axial position conformation and add small substituents to increase potency"

Peter Kenny,
"two linker prototypes that might be used to provide access the S1' subsite from the C4 (chiral center) of the dihydrobenzopyran"

Isoquinolines – profiling leads

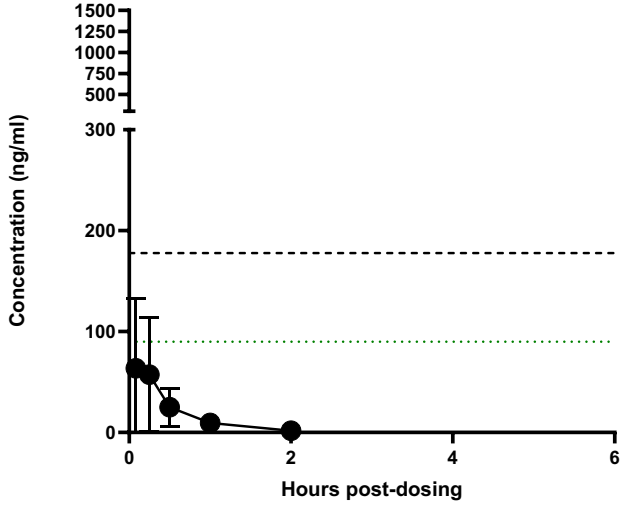
			Activity			ADME						Off-target		*in vitro* stability				*in vivo* PK					
Postera ID	Structure	log P	Antiviral IC50 (μM) *Vero6 CPE (IIBR)*	Antiviral IC50 (μM) *Calu3 FFU (Oxford)*	Protease IC50 (μM) *Fluorescence (Weizmann)*	Solubility (uM)	HLM $t_{1/2}$ (/min) *Human liver microsms*	HLM CLint (μg/min/ mg prot) *Human liver microsms*	RLM $t_{1/2}$ (/min) *Rat liver microsms*	RLM CLint (μg/min/ mg prot) *Rat liver microsms*	permeability Mean Papp (10^{-6}/cms) *MDCK-MDR1 A2B*	CYP inhibition (IC50) *5 Cyp profile*	Protease most potent hit *Nanosyn panel 40 proteases*	Human Heps $t_{1/2}$ (/min) *Human hepatocytes*	Human Heps Clint *Human hepatocytes*	Rat Heps $t_{1/2}$ (/min) *Rat hepatocytes*	Rat Heps Clint *Rat hepatocytes*	Species in vivo	Oral $t_{1/2}$ (/min)	IV $t_{1/2}$ (/min)	Bio-avail.	Free drug hu/rat (%)	Calc.dose 70kg hum (mg)
VLA-UCB-1dbca3b4-15		3.33	2.51	1.06	0.19	33	14	98.3			41	8uM 2C9 3uM 3A4	clean			17.8	78.1	Rat	60	formulation issues	-	**12 (rat)**	
PET-UNK-29afea89-2		3.16	0.5 (n=2)	0.3	0.08 (n=2)	130	97	17	16	109	20			34	19	54	26	Rat	160	104	17	**4 / 10**	

IV 2mg/kg



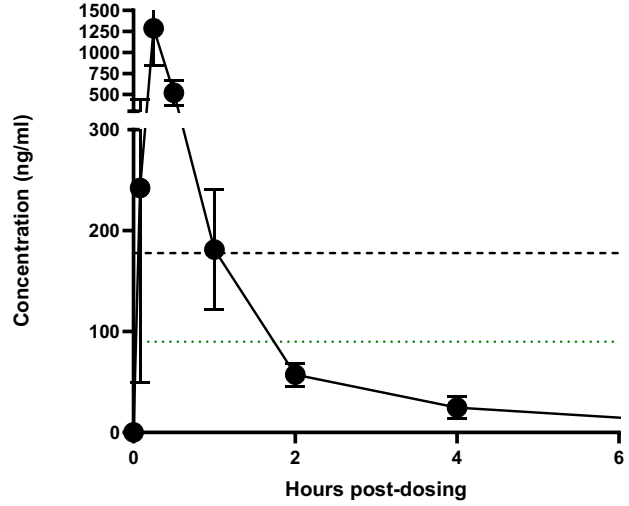
Balb/c mouse

PO 10mg/kg



Balb/c mouse

PO 100mg/kg



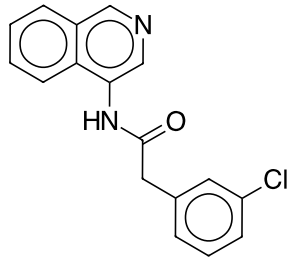
Balb/c mouse

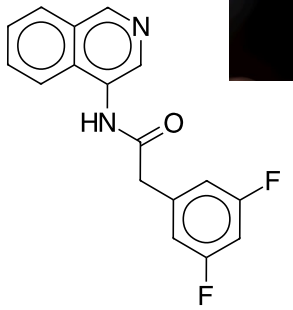
VeroE6 (CPE)

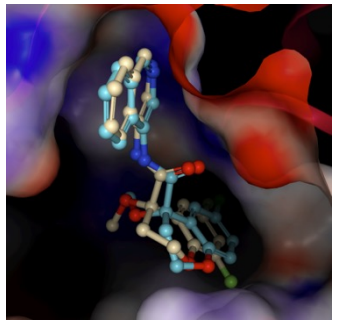
Calu-3 (PFU)

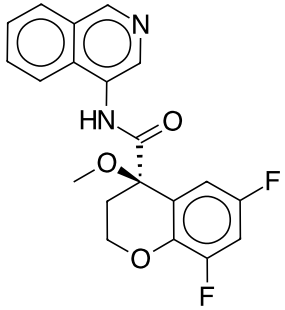
DNDi Drugs for Neglected Diseases COVID Moonshot

Good medicinal chemistry *can* be rewarded







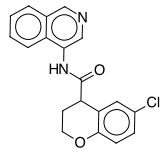
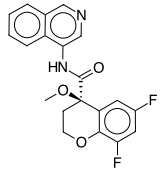
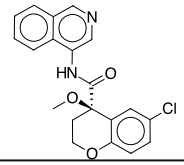


	ADA-UCB-6c2cb422-1	RAL-THA-2d450e86-16	EDJ-MED-37aac4bd-4 MAT-POS-932d1078-3(single enantiomer)
Fl IC50	728nM	569nM	191nM(single enantiomer)
clogP	3.4	3.1	3.3
LLE(Fl)	2.7	3.1	3.1

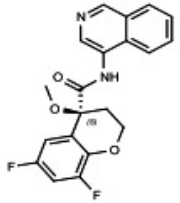
Ralph Robinson, Thames Partners
"Systematic exploration of SAR around MAT-POS-23a8a11a-1 and ADA-UCB-6c2cb422-1 per Design Team discussion"
28 compounds made & assayed

Ed Griffen , MedChemica
"Combination of best S2 SAR - further additions constraining on logP"

Isoquinolines – Pushing the lead compounds

			Activity			ADME						Off-target		*in vitro* stability				*in vivo* PK					
Postera ID	Structure	log P	Antiviral IC50 (µM) *Vero6 CPE (IIBR)*	Antiviral IC50 (µM) *Calu3 FFU (Oxford)*	Protease IC50 (µM) *Fluorescence (Weizmann)*	Solubility (uM)	HLM $t_{1/2}$ (/min) *Human liver microsms*	HLM CLint (µg/min/ mg prot) *Human liver microsms*	RLM $t_{1/2}$ (/min) *Rat liver microsms*	RLM CLint (µg/min/ mg prot) *Rat liver microsms*	permeability Mean Papp (10^{-6}/cms) *MDCK-MDR1 A2B*	CYP inhibition (IC50) *5 Cyp profile*	Protease most potent hit *Nanosyn panel 40 proteases*	Human Heps $t_{1/2}$ (/min) *Human hepatocytes*	Human Heps Clint *Human hepatocytes*	Rat Heps $t_{1/2}$ (/min) *Rat hepatocytes*	Rat Heps Clint *Rat hepatocytes*	Species in vivo	Oral $t_{1/2}$ (/min)	IV $t_{1/2}$ (/min)	Bio-avail.	Free drug hu/rat (%)	Calc.dose 70kg hum (mg)
VLA-UCB-1dbca3b4-15		3.33	2.51	1.06	0.19	33	14	98.3			41	8uM 2C9 3uM 3A4	clean			17.8	78.1	Rat	60	formulation issues	-	**12 (rat)**	
MAT-POS-932d1078-3		2.84	0.3(n=2)	0.126	0.191	375 (kinetic)	68	25	24	70				60	12	56	25	Rat	171	70	31	**10 / 20**	
PET-UNK-29afea89-2		3.16	0.5 (n=2)	0.3	0.08 (n=2)	130	97	17	16	109	20			34	19	54	26	Rat	160	104	17	**4 / 10**	

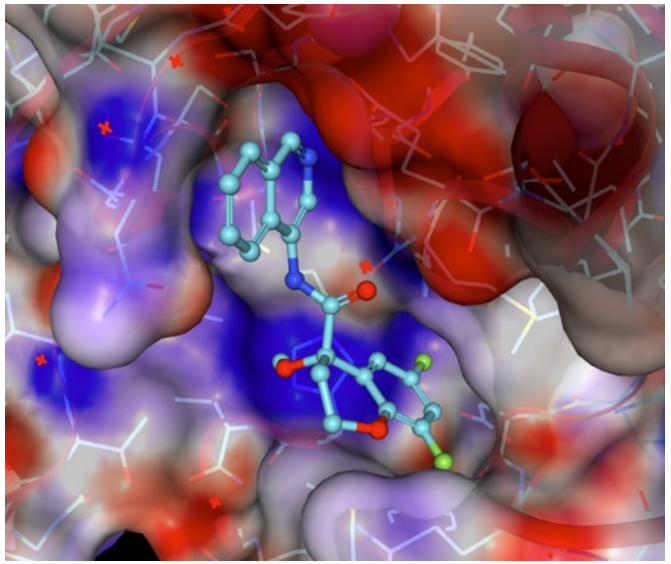
Human Dose Prediction – MAT-POS-932d1078-3

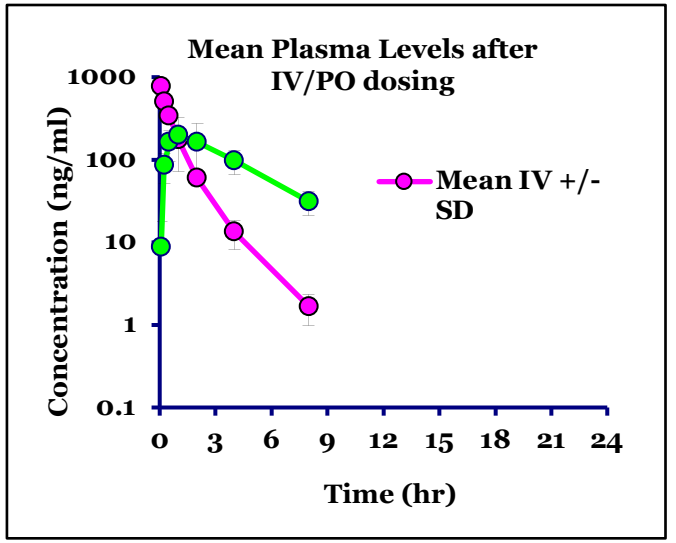
External ID	Structure	MPro Avg IC50 (uM)	Vero6_CoV2_WT_CPE_IIBR: Avg IC50 (µM)	Calu3_FFU Oxford_Zitzmann : IC50 (µM)	PPB_human: PPB (%)	PPB_rat: PPB (%)	PPB_2%_FCS : PPB (%)	Solubility Aqueous Kinetic: Solubility (µM)
MAT-POS-932d1078-3		0.191	0.332	0.126	89.6	79.3	12	375

microsome_human: CLint mean (µl/min/mg)	microsome_rat: CLint mean (µl/min/mg)	microsome_dog: Clint mean (µl/min/mg)	hepatocytes_human: CLint mean (µg/min/10^6 cells)	hepatocytes_rat: CLint mean (µg/min/10^6 cells)
25.3	70.1	44.8	11.6	24.6

Pharmacokinetics_IV:				
Dose (mg/kg)	Vd (avg) (L/kg)	CL (avg) (ml/min/kg)	T1/2 (avg) (h)	AUC last (avg) (ng.h/ml)
2	3.48	56.9	1.17	594

Pharmacokinetics_PO					
Dose (mg/kg)	Cmax (avg) (ng/ml)	Tmax (avg) (h)	T1/2 (avg) (h)	AUC last (avg) (ng.h/ml)	%BA
10	205	0.833	2.86	792	31

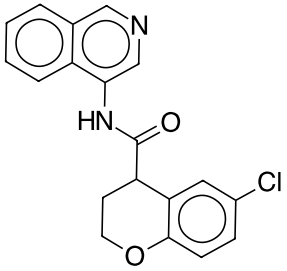




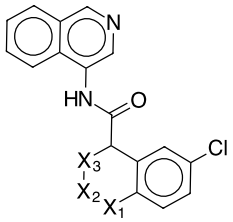
- In vitro and in vivo ADMET measurements with cell potency and PPB
  - Hu dose prediction
    - Average predicted Hu Cl_{plasma} = 7.2 ml/min/kg
    - Predicted human Vss (based on rat) = 1.76 L/kg
    - Predicted human Bioavailability = 63%
    - Predicted human t1/2 = 2.8 h
    - Targeted Cmin,ss = 3.2 µM (EC50 = 333 nM free (378 nM total, Fu assay 0.88), corrected for human fu,p=0.104)
    - 985mg TID (300 – 3000mg) – requires 2nd species to generate precision on estimate

DNDi Drugs for Neglected Diseases COVID Moonshot

Is the benzopyran the problem? Matched Molecular Pair Analysis



VLA-UCB-1dbca3b4-15



X1	X2	X3	IC50/nM
O	CH_2	CH_2	360
CH_2	O	CH_2	7943
CH_2	CH_2	CH_2	316
S	CH_2	CH_2	200
SO_2	CH_2	CH_2	316
NH	CH_2	CH_2	251
NH	C=O	CH_2	398
NMe	CH_2	CH_2	398
NAc	CH_2	CH_2	1000
C=O	NH	CH_2	200
CH_2	NMe	CH_2	1995
CH_2	NAc	CH_2	398
CH_2	NH	CH_2	1995
CH_2	CH_2	NH	1259
CH_2	CH_2	NMe	3162

Polarity tolerated at X_1 and X_2

Non basic tetrahydroisoquinoline looks promising…

Also see poster:

P20: Exploiting automated R group core and table generation from matched molecular pair data to accelerate SARS-CoV2 therapeutic discovery

Lauren Reid, MedChemica

Evaluating Designs: Over Design / Under Design

Over Design:

- Over-estimating ability to predict potency/solubility/clearance
- Molecules are too complex

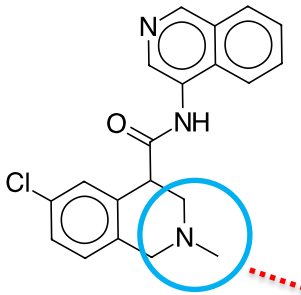
- Hard = slow to make
- Too few molecules made to understand SAR

Under Design:

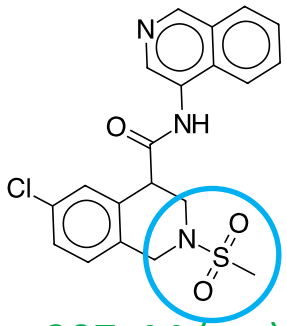
- Failure to take into account established SAR
- Making molecules with poor physical properties
- Making insufficiently diverse compounds

- Inactivity
- Insolubility
- Lack of cell permeability

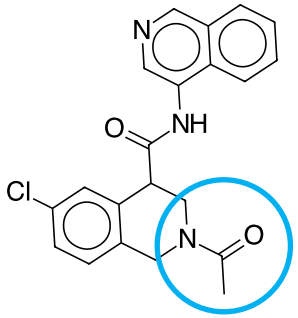
“Goldilock’s” Design MAT-POS-4223bc15



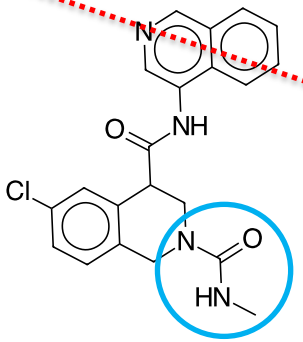
2010nM (rac)[3.14]



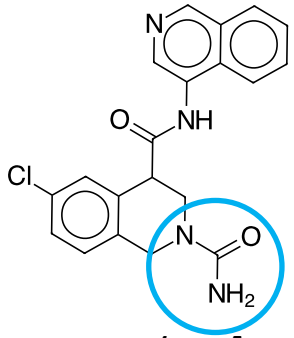
207nM (rac)[1.87]



383nM (rac)[2.37]



272nM (rac)[2.26]



250nM (rac[2.04])

[logP]

Design Rationale:
“Very simple library probing new position of N in the ring”

Requested: 28th February 2021
Shipped: 17th March 2021

Matt Robinson PostEra

- Scan of Gln-189 interaction opportunities

16 sulphonamides
clogP range 2.2 – 3.6

4 sulphonylureas
clogP range 2.5 – 3.7

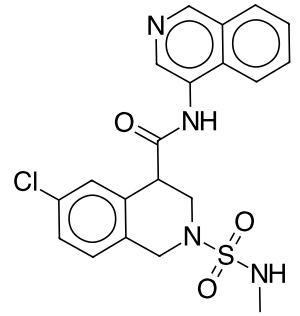
8 amides
clogP range 2.5 – 3.7

1 urea (NMe_2)

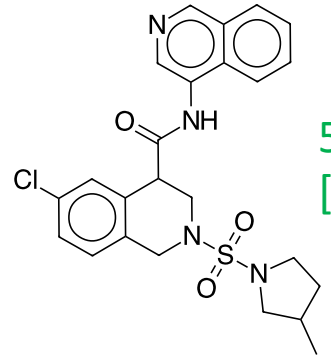
2 carbamates (OMe, OEt)

13 CH_2R: Reductive amination
clogP 1.4 – 4.1 (all mild bases)

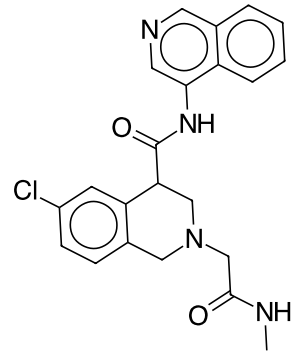
2 2-substituted imidazoles



150nM
[1.6]



52nM
[2.6]

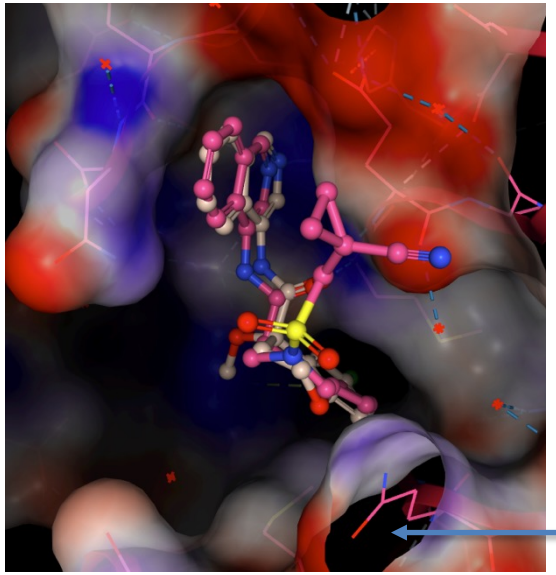


69nM
[2.0]

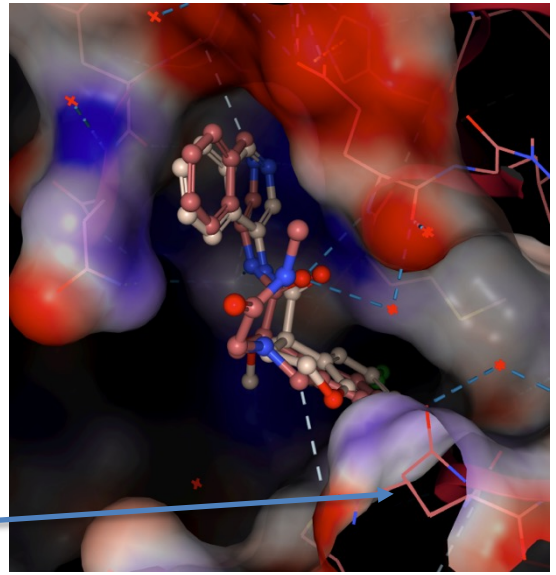
Requested: 30th March 2021
39 Shipped: 28th April 2021

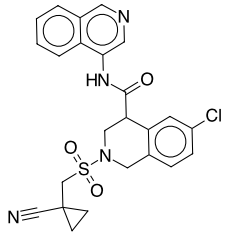
DNDi Drugs for Neglected Diseases COVID Moonshot

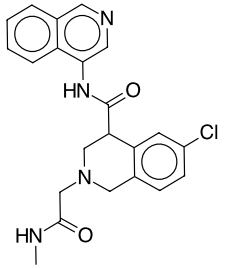
Tetrahydroisoquinolines: profiling in progress



Gln-189

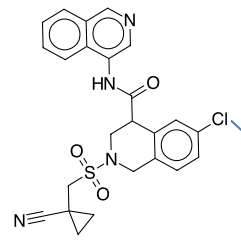




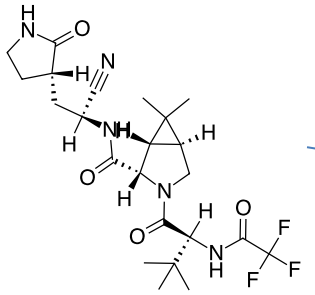


	MAT-POS-dc2604c4-1	MAT-POS-4223bc15-23
Fl IC50	<64nM	69nM
clogP	2.4	2.0
Rat iv Cl(ml/min/kg)	20	
Rat iv Vdss(L/kg)	1.1	
Rat iv t1/2 (h)	1.6	

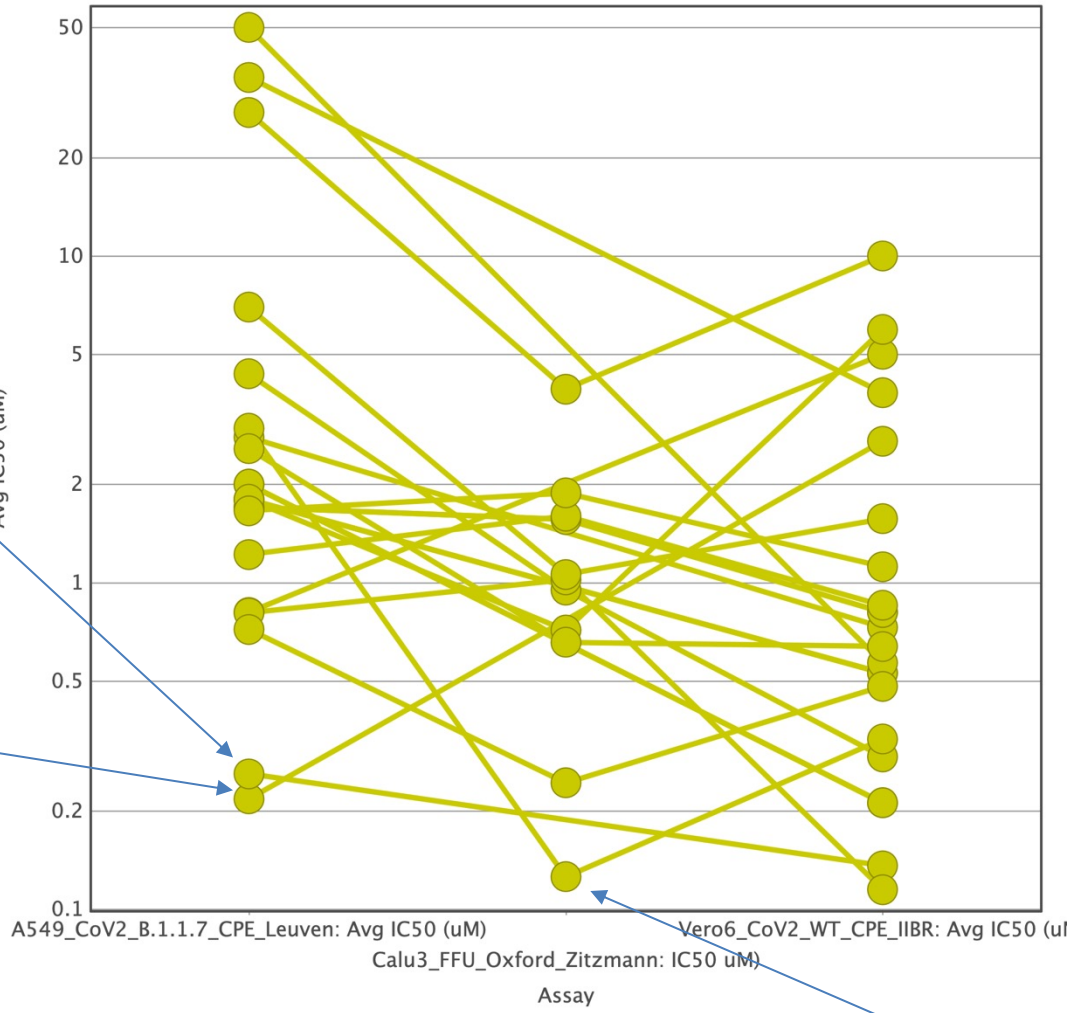
Anti Viral Cell data: context across cell lines



MAT-POS-dc2604c4-1

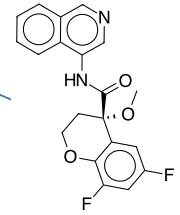


PF-7321332



Lines connect the same compound tested in different cell lines.
Cellular sensitivity:

Calu-3 >= VeroE6 > A549



MAT-POS-932d1078-3

DNDi Drugs for Neglected Diseases COVID Moonshot

Medicinal Chemistry Target Product Profile - Status

Orally bioavailable inhibitor for therapeutic and prophylactic use

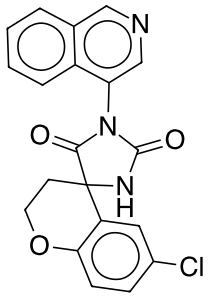
Property	Target range	Cold start – March 2020→ August 2021
protease assay	IC_{50} < 50 nM (compromise if clean and anti viral activity sufficient)	25nM
viral replication (Vero-E6)	EC_{50} < 0.2µM	<0.2 µM VeroE6 CPE
plaque reduction (Vero-E6, Calu-3)	EC_{50} < 0.2µM	~0.25 µM Calu3
PK-PD	Cmin > EC90 (plaque reduction) for 24h	Studies planned once exposure adequate
Coronavirus spectrum	SARS-CoV2 B1.1.7 , 501.V2, B.1.1.248 variants essential SARS-CoV-1 & MERS desirable	Active against B1.1.7 , 501.V2 in cellular assays Compounds tested across coronavirus MPro panel
Route of administration	oral	F > 30% rat
solubility	> 5 mg/mL, >100µM tolerable	>100µM
half-life	Ideally>= 8 h (human) est from rat and dog	Rat 2h, Human predicted PK not yet sufficient
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 Critical transporter check (*e.g.* OATP) hERG and NaV1.5 IC_{50} > 50 µM No significant change in QTc No mutagenicity or teratogenicity risk	Protease panel clean Eurofins / CEREP 44 target panel clean Cyp450: 1.8µM 2C9, 10µM 3A4, mitigation SAR determined Cardiotoxicity in vitro initial compounds clean Live phase planned Ames in progress

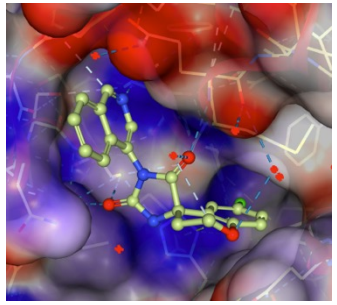
DNDi Drugs for Neglected Diseases COVID Moonshot

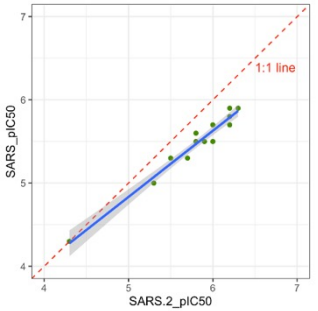
What I couldn’t tell you about in 20 minutes…

- Isoquinoline potency and metabolism SAR – data still incoming, but 6 & 7 substitution looks promising to increase metabolic stability while maintaining potency
- Search for isoquinoline replacements – application of FEP predictions
- Extension into P1’ – synthetic constraints & FEP predictions on a vast scale
- AI supported compound and route design
- Spiro linkers and pan-corona activity

VLA-UCB-29506327-1





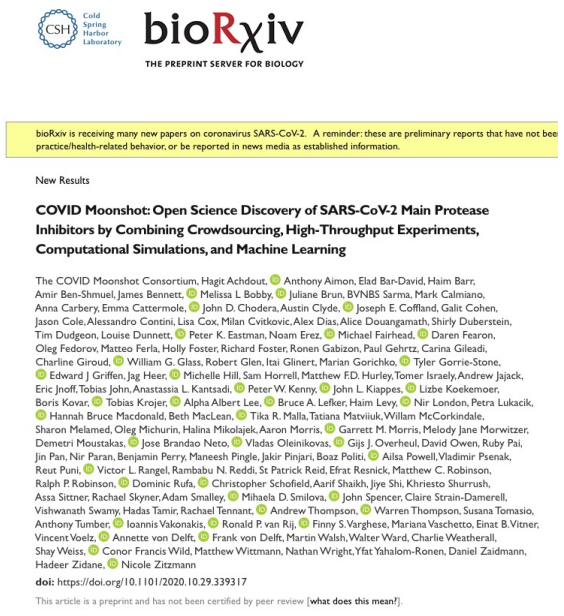


MPro enzyme IC50 (uM)							Human	antiviral EC50(CPE/uM)	
SARS-2	**229E**	**OC43**	**MERS**	**SARS**	**HKU1**	**NL63**	**CatB**	**229E**	**OC43**
4.6	3.2	1.9	32	9.3	1.1	16	>50	2.7	3.3

DNDi Drugs for Neglected Diseases COVID Moonshot

The COVID Moonshot Team

131 co-authors and growing…



bioRxiv is receiving many new papers on coronavirus SARS-CoV-2. A reminder: these are preliminary reports that have not bee practice/health-related behavior, or be reported in news media as established information.

New Results

COVID Moonshot: Open Science Discovery of SARS-CoV-2 Main Protease Inhibitors by Combining Crowdsourcing, High-Throughput Experiments, Computational Simulations, and Machine Learning

The COVID Moonshot Consortium, Hagit Achdout, Anthony Aimon, Elad Bar-David, Haim Barr, Amir Ben-Shmuel, James Bennett, Melissa L. Bobby, Juliane Brun, BVNBS Sarma, Mark Calmiano, Anna Carbery, Emma Cattermole, John D. Chodera, Austin Clyde, Joseph E. Coffland, Galit Cohen, Jason Cole, Alessandro Contini, Lisa Cox, Milan Cvitkovic, Alex Dias, Alice Douangamath, Shirly Duberstein, Tim Dudgeon, Louise Dunnett, Peter K. Eastman, Noam Erez, Michael Fairhead, Daren Fearon, Oleg Fedorov, Matteo Ferla, Holly Foster, Richard Foster, Ronen Gabizon, Paul Gehrtz, Carina Gileadi, Charline Giroud, William G. Glass, Robert Glen, Itai Glinert, Marian Gorichko, Tyler Gorrie-Stone, Edward J Griffen, Jag Heer, Michelle Hill, Sam Horrell, Matthew F.D. Hurley, Tomer Israely, Andrew Jajack, Eric Jnoff, Tobias John, Anastassia L. Kantsadi, Peter W. Kenny, John L. Kiappes, Lizbe Koekemoer, Boris Kovar, Tobias Krojer, Alpha Albert Lee, Bruce A. Lefker, Haim Levy, Nir London, Petra Lukacik, Hannah Bruce Macdonald, Beth MacLean, Tika R. Malla, Tatiana Matviiuk, Willam McCorkindale, Sharon Melamed, Oleg Michurin, Halina Mikolajek, Aaron Morris, Garrett M. Morris, Melody Jane Morwitzer, Demetri Moustakas, Jose Brandao Neto, Vladas Oleinikovas, Gijs J. Overheul, David Owen, Ruby Pai, Jin Pan, Nir Paran, Benjamin Perry, Maneesh Pingle, Jakir Pinjari, Boaz Politi, Ailsa Powell, Vladimir Psenak, Reut Puni, Victor L. Rangel, Rambabu N. Reddi, St Patrick Reid, Efrat Resnick, Matthew C. Robinson, Ralph P. Robinson, Dominic Rufa, Christopher Schofield, Aarif Shaikh, Jiye Shi, Khriesto Shurrush, Assa Sittner, Rachael Skyner, Adam Smalley, Mihaela D. Smilova, John Spencer, Claire Strain-Damerell, Vishwanath Swamy, Hadas Tamir, Rachael Tennant, Andrew Thompson, Warren Thompson, Susana Tomasio, Anthony Tumber, Ioannis Vakonakis, Ronald P. van Rij, Finny S. Varghese, Mariana Vaschetto, Einat B. Vitner, Vincent Voelz, Annette von Delft, Frank von Delft, Martin Walsh, Walter Ward, Charlie Weatherall, Shay Weiss, Conor Francis Wild, Matthew Wittmann, Nathan Wright, Yfat Yahalom-Ronen, Daniel Zaidmann, Hadeer Zidane, Nicole Zitzmann

doi: https://doi.org/10.1101/2020.10.29.339317

This article is a preprint and has not been certified by peer review [what does this mean?].

https://doi.org/10.1101/2020.10.29.339317

Highlighting the design team & chemists

Jag Heer Mark Calmiano Eric Jnoff Vladas Oleinkovas	UCB
Alpha Lee Matt Robinson	Postera AI
Ralph Robinson Bruce Lefker Gwen Fate (PK)	Thames Partners
Ben Perry Peter Sjö	DNDi
Bobby Glen	University of Cambridge
Tatiana Matviuk & all the chemists	Enamine
Haim Barr (Mpro assays)	Weizmann Institute
Darren Fearon (crystallography)	Diamond Light Source

Inspired by patients. Driven by science.

CDD

NOVARTIS

Takeda

DNDi Drugs for Neglected Diseases

COVID Moonshot