Custom Built Biology for Patients

March 2021

Molecular Partners AG, Switzerland
(SIX: MOLN)

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Pioneering DARPin® Solutions

We translate the unique properties of the **DARPin® drug class** into patient value

We build a **broad pipeline** of DARPin® therapeutics to address unmet medical need

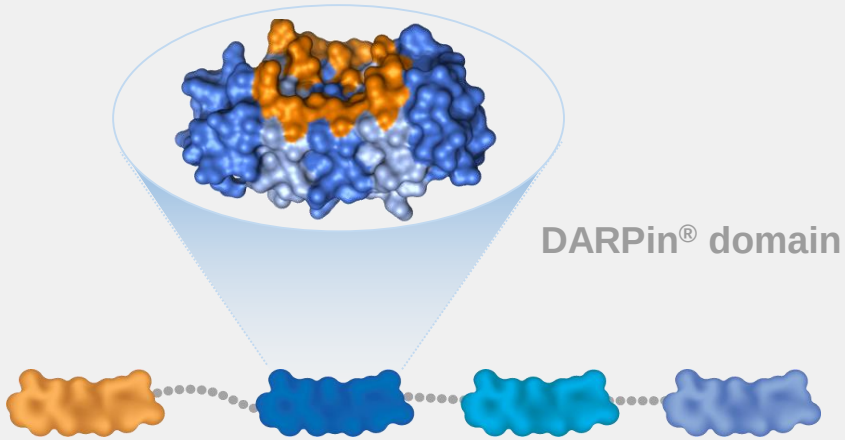
We aim to transform the lives of people with *serious diseases* by delivering truly innovative solutions

our purpose

A global team united around a common purpose of making a positive impact in patients' lives

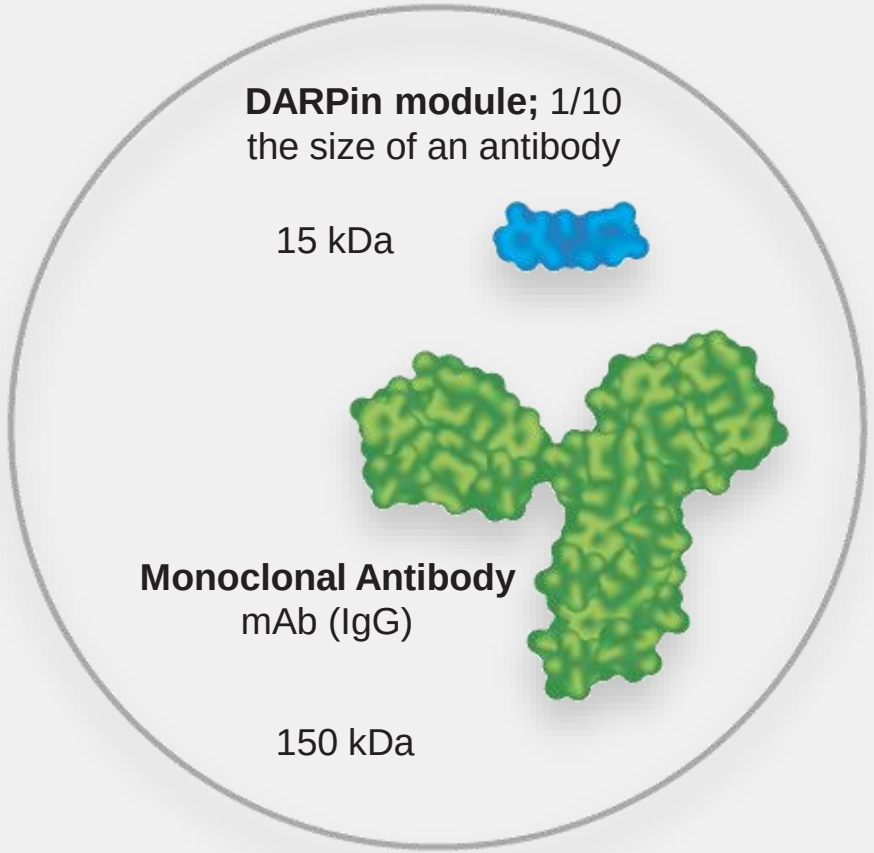
What are DARPin® Proteins

DARPin® Designs



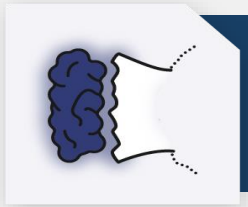
Multi-DARPin® Candidate

- DARPin Module – Small size – 15 kDa
- Multi-DARPins are assembled form mono-DARPins
- Multiple targeting in one Drug Candidate

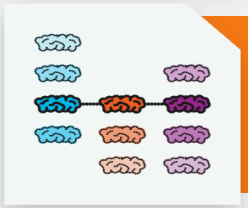


Innate Advantages Combined With Proprietary Approaches

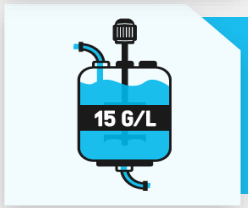
Unique DARPin® Features



Ideal binding properties
- Perfect fit
- High affinity
- Super specificity



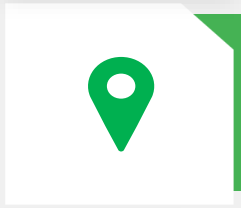
Turn-key multi-specifics
- Small size
- Uni-domain activity
- Up to 7 binders
- Open combinatorial space



Manufacturing & Storage
- High-yield microbial expression
- High stability

DARPin® Benefit

Tailored Grip
- Match disease requirements



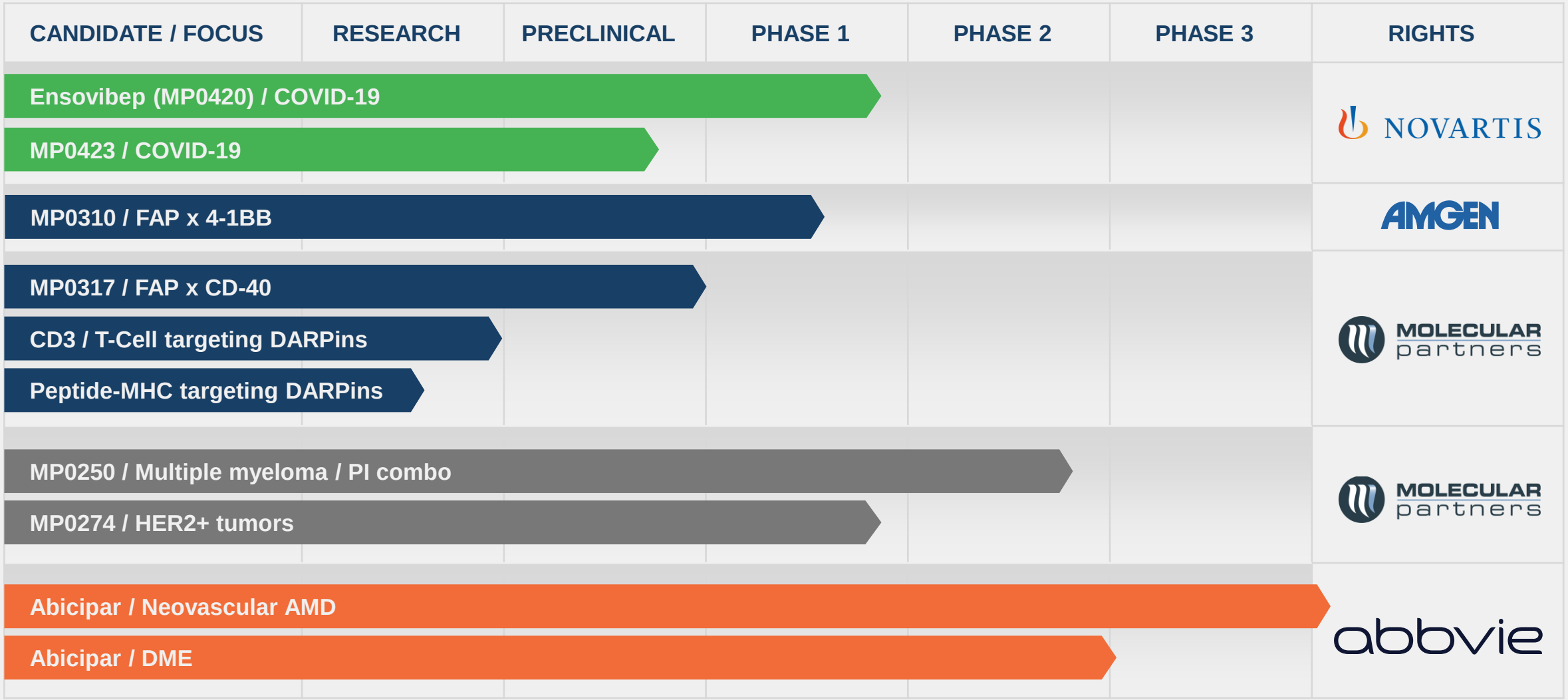
Localized Activity
- Local and temporal control of activity

Molecular Handcuff
- Full shut-down by conformational freeze

Multi-blocker to prevent escape
- Overcome escape pathways oncology / ID

Pipeline

Antiviral | Immuno-oncology | Ophthalmology



Synergistic Partnerships Built on a Versatile Drug Class

Ophthalmology

Therapeutic Area Deal

- Partnership for abicipar, two positive Phase 3 studies.
- Received $150m to date; $360m in potential milestones and teens royalty still possible
- CRL (June 2020): AbbVie evaluating next steps with agency

abbvie

Oncology

Product Combination Deal

- Partnership with Amgen to combine AMG 506 / MP0310 with BiTE® molecules
- Phase 1 conducted by MP and Amgen to develop for combination studies
- ~$500m in milestones and mid teen royalties

AMGEN®

Virology

Capability Deal

- Leverage production, global development and distribution of Sandoz Novartis for MP0420
- ~$165m milestone payment upon commercialization licensure
- 22% royalty on sales

NOVARTIS

Over ~$1B in potential milestone across multiple programs

Clinical Program: Anti-COVID19

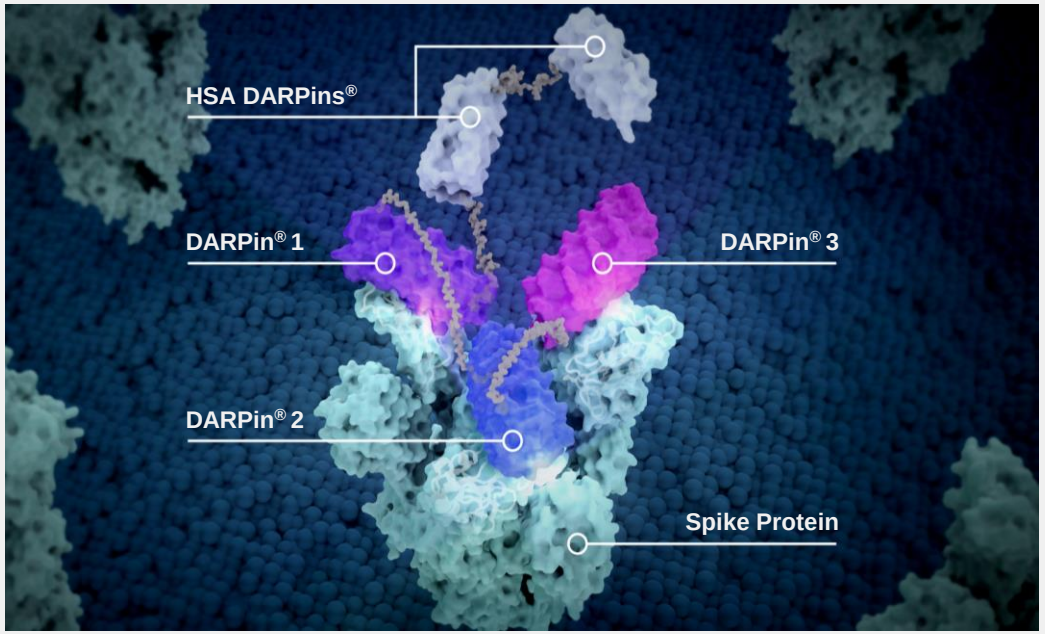
Our COVID-19 Program: Two Outstanding Candidates

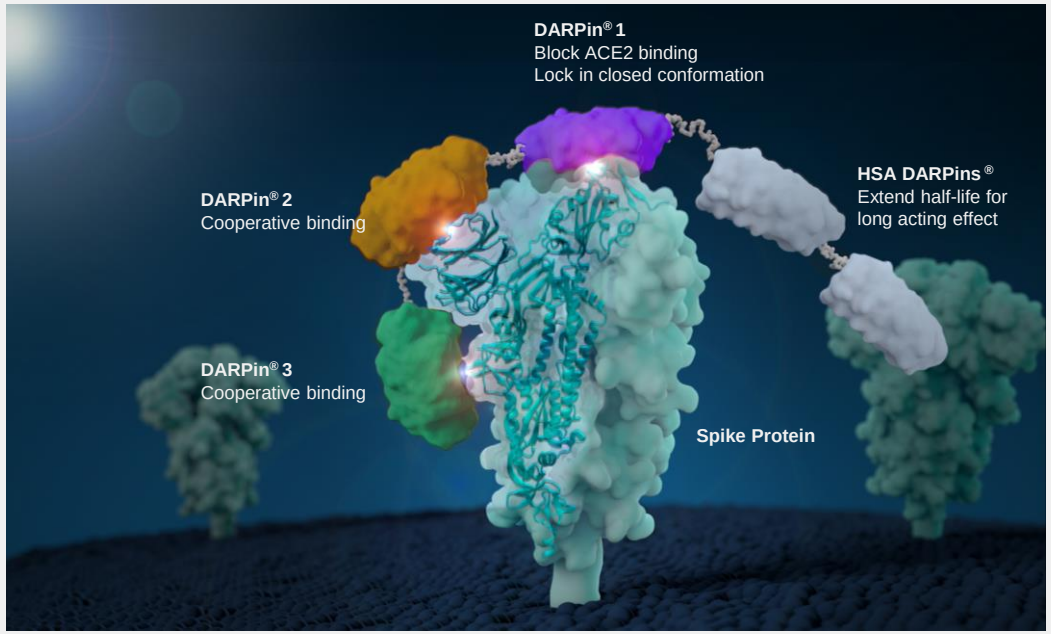
MP0420 (ensovibep)– best-in-class

- Tri-specific DARPin® antiviral targeting the RBD for highest potency & to prevent viral escape
- Long half-life (HSA DARPins) – single injection
- Low costs and high numbers of doses available
- Potential for bolus / s.c. injection – simple application

MP0423 – first-in-class

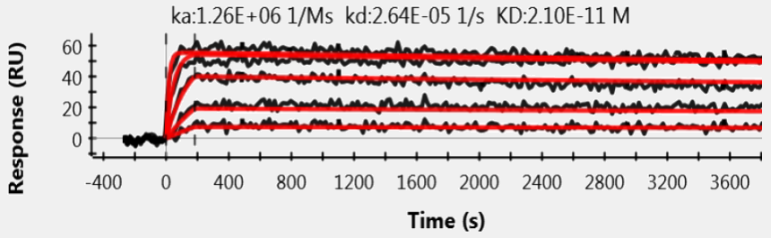
- 3 DARPins blocking different domains of the viral spike
- High activity even if RBD mutates heavily and escapes all vaccines and therapeutic antibodies
- All other benefits of MP0420



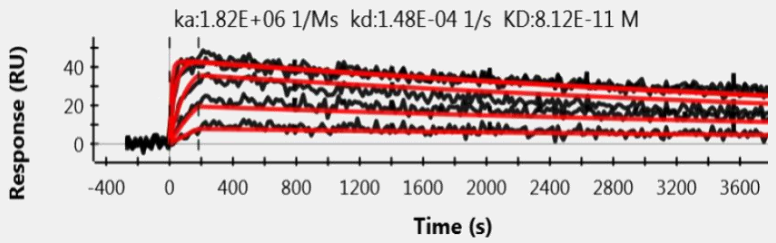


Rational Design for Cooperative Binding: sub-pM binding

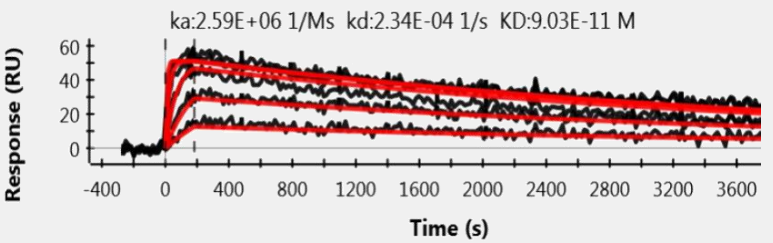
DARPin A – 1 hour off-rate



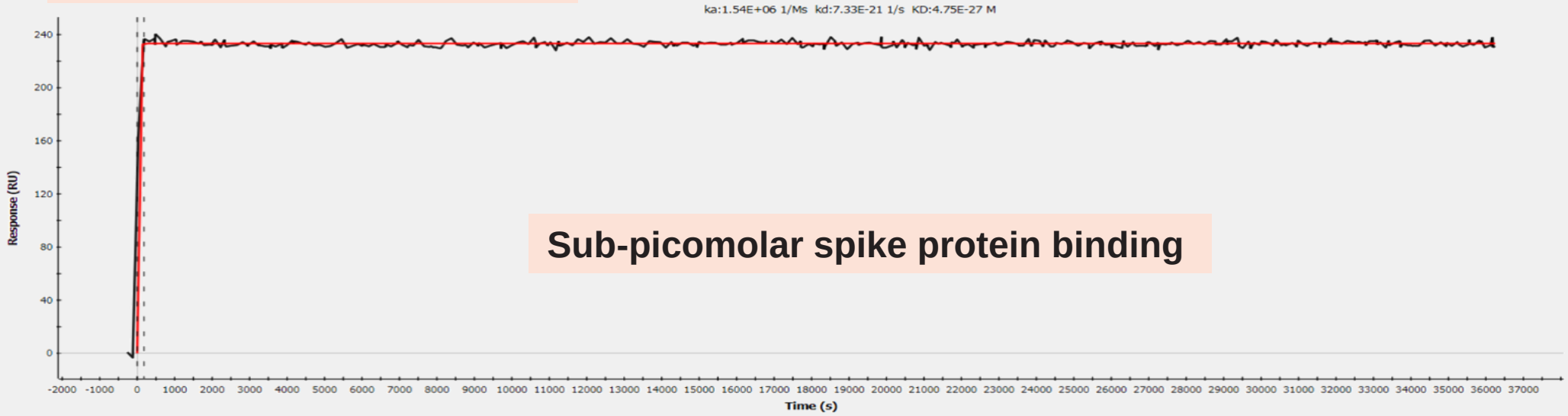
DARPin B – 1 hour off-rate



DARPin C – 1 hour off-rate



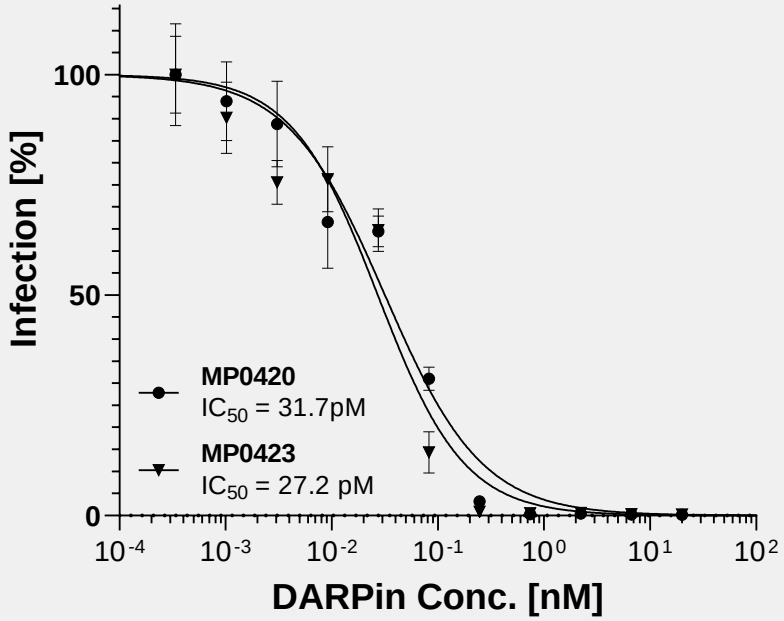
DARPin A-B-C – 10 hour off-rate



Sub-picomolar spike protein binding

High Potency Inhibition Translates To *In Vivo* Prophylactic And Therapeutic Properties

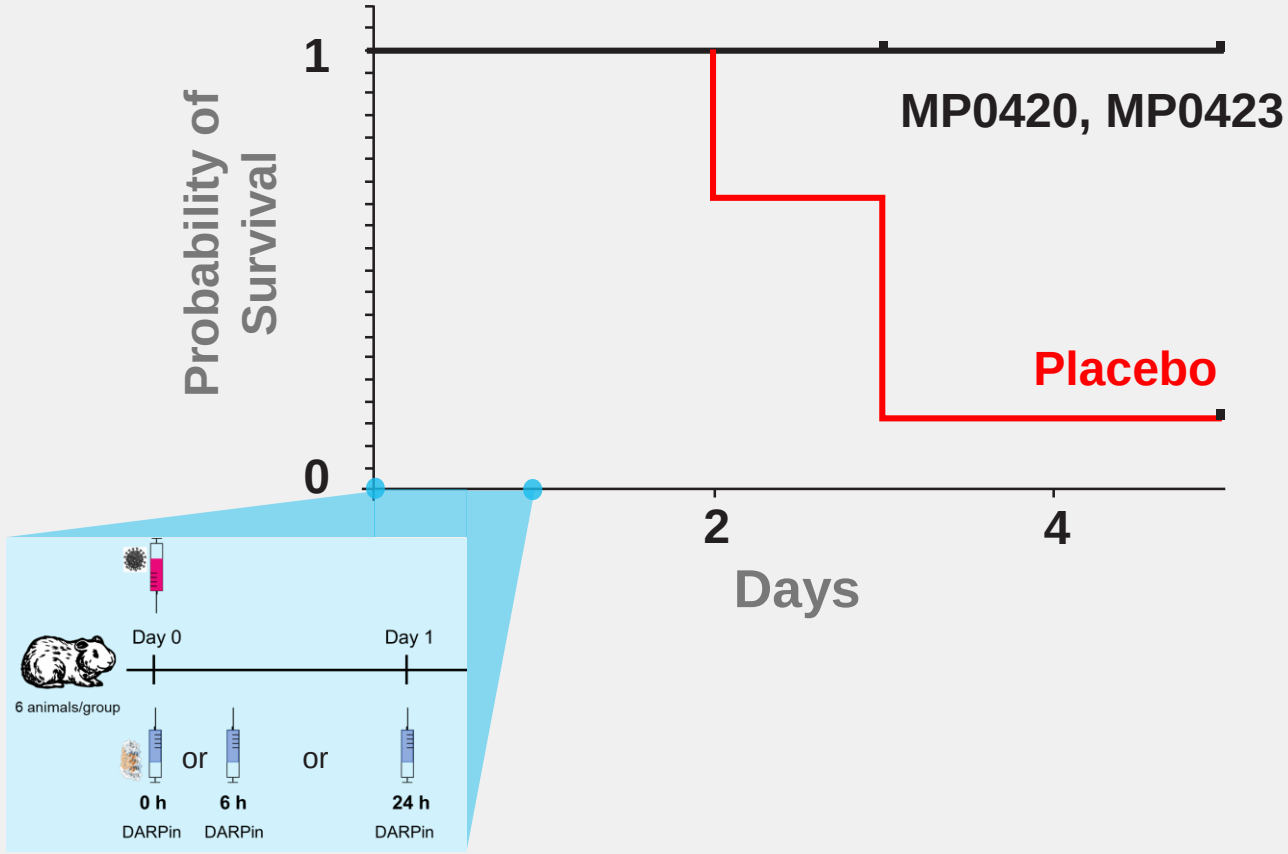
In vitro activity: Pseudotype Neutralization Assay



Highest potency

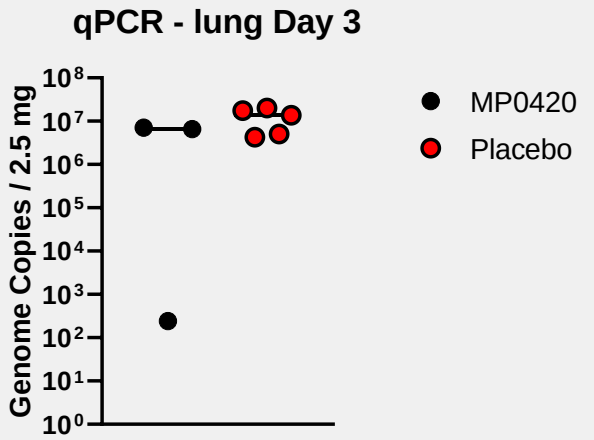
Tri-binding leads potency in the low pM range; likely at the assay limit

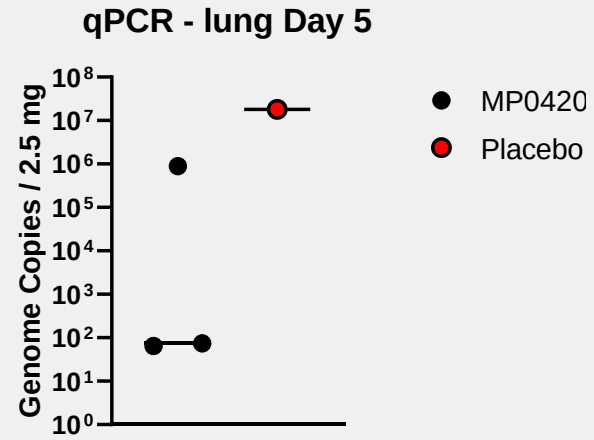
In vivo activity: Kaplan Meier Plot - Hamster Model (6 animals/group)



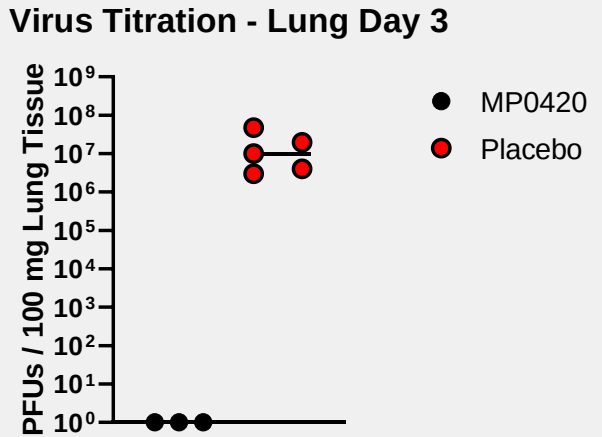
Ensovibep Blocks the Virus and Prevents Infection in the Lung

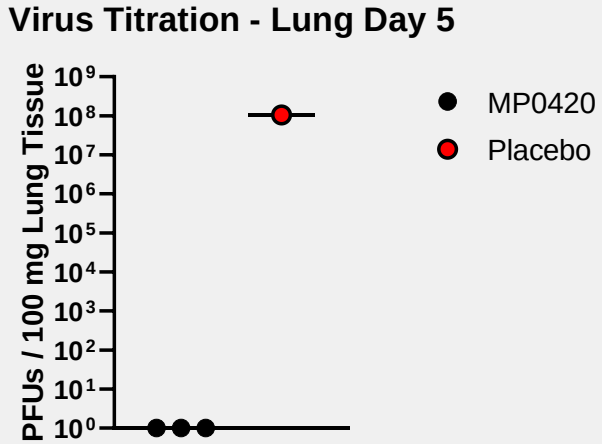
Viral titer in the lung





Viral infectivity in the lung

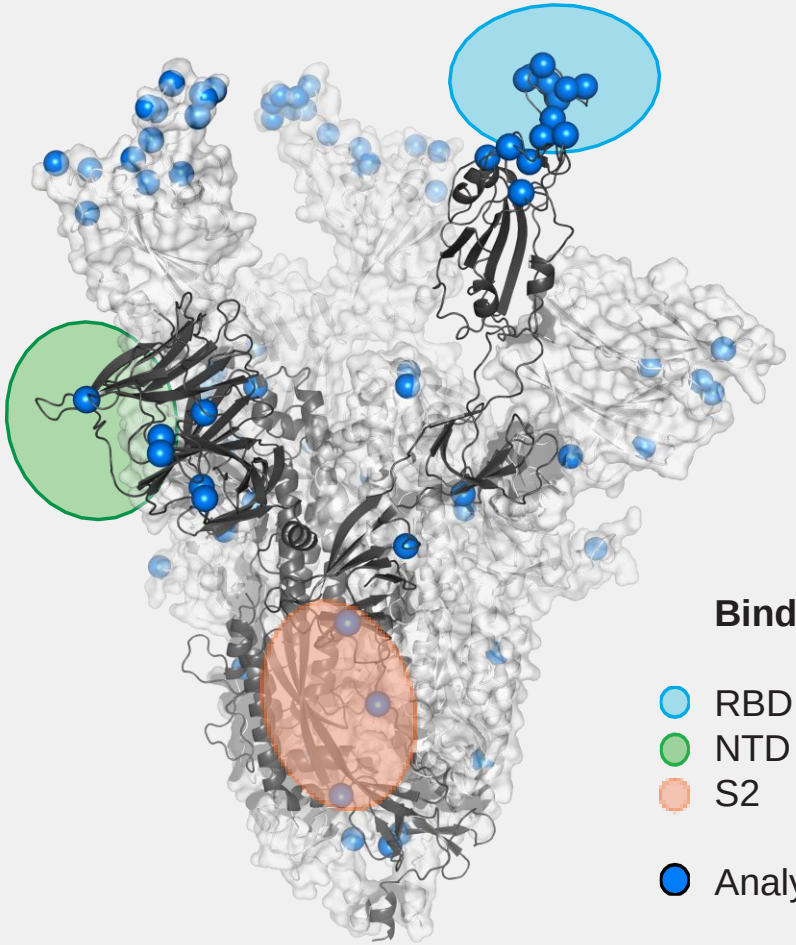




Ensovibep blocks viral infectivity completely

SARS-Cov2 Spike Protein: domains, mutations, variants

Spike Protein, Epitopes, Mutations

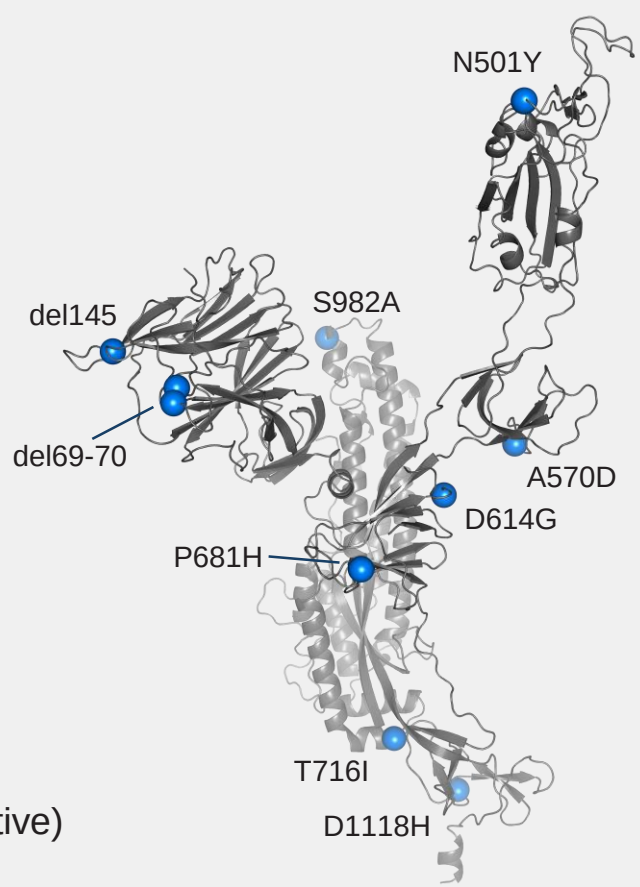


Binding regions:

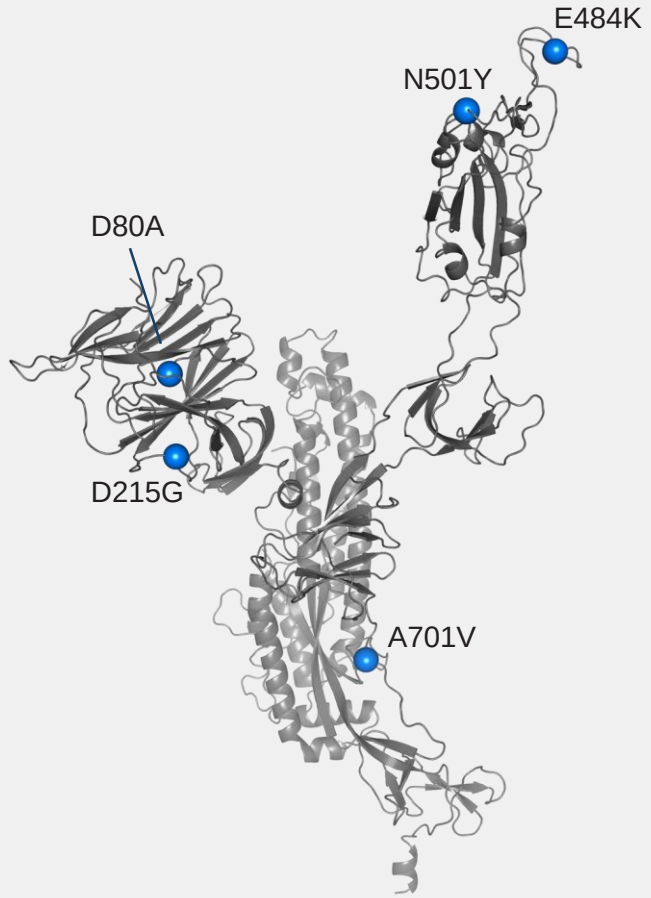
- RBD DARPin
- NTD DARPin
- S2 DARPin (putative)

- Analyzed mutations

UK and SA variant



UK Variant



South African Variant

Potency of our Candidates on viral mutants & variants

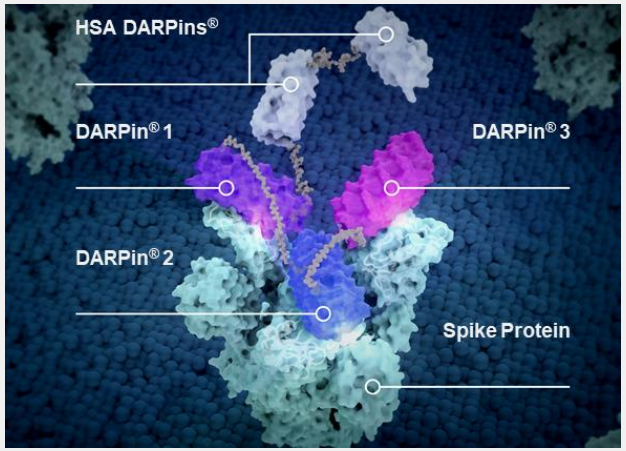
Variants	Rational	VSV Neutralizaiton Assay IC_{50} [ng/mL]			
		MP0420	MP0423	REGN 0933	REGN 10987
wild type	(Wuhan)	**1.0**	**3.1**	**3.9**	**6.1**
B.1.351	(SA, Δ5)*	**3.0**	**2.4**	**19.4**	**6.2**
B.1.1.7	(UK, Δ9)**	**1.7**	**70.1**	**2.4**	**3.5**
Individual Mutations: Residues in variants					
N501Y	in UK, SA, BRA variants; increases RBD/ACE2 interaction[1]	0.5	1.4	4.3	5.8
E484K	in SA, BRA variants; increases RBD/ACE2 interaction[1]	2.7	1.8	17	5.8
K417E	residue mutated to N/T in SA, BRA variants	0.5	1.2	>100	1.5
Y453F	key residue evolved in Danish mink farms variants	3.2	2	>100	11.8
Individual Mutations: Highly frequent mutations					
D614G	Wide global spread	2.4	2.8	n.d.	n.d.
S477N	Wide global spread	1.9	0.8	n.d.	n.d.
N439K	Wide spread in northern amerika, UK; increases RBD/ACE2 interaction[1]	1.3	2.5	2.8	30.1
A222V	Wide European spread	2.2	3.1	7	2.9
Individual Mutations: RBD epitope or reported resistance for other therapeutics					
G446V		1.7	1	1.5	>100
G476S		1.5	3.1	n.d.	n.d.
T478I		2.7	2.8	4	7
P479S		2.1	1.5	3.7	9.8
V483A		2.3	1.9	n.d.	n.d.
F486V	reduces RBD/ACE2 interaction non-fit virus[1]; key residue DARPin RBD binder[2]	>100	7.7	>100	4.4
Q493K		7.9	2.4	>100	10
F490S	Reduces RBD/ACE2 interaction[1]	3.8	1.6	3.1	9.2

Legend for the table

- n.d.: not determined
- Mutations (SA)*: D80A, D215G, E484K, N501Y, A701V
- Mutations (UK)**: del69-70, del145, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
- Redish shade: IC50 values between >100 ng/mL (outside therapeutically active range)
- [1] Influence of residue mutations on spike protein binding to human ACE2 (Yi et al. 2020)
  - Increase: stronger ACE2 binding = fitter virus
  - Decrease: weaker ACE2 binding = unfit virus
- [2] Predicted interaction residue for DARPin RBD binder (Walser et al. 2020)

Cooperative binding – potency of the modules

Variants	Rational	VSV Neutralizaiton Assay IC_{50} [ng/mL]			
		MP0420	Mono-valent RBD Binders in MP0420		
			RBD-1	RBD-2	RBD-3
wild type	(Wuhan)	**1**	7.2	2.1	13.3
B.1.351	(SA, Δ5)*	**3.0**	76	26	>100
B.1.1.7	(UK, Δ9)**	**1.7**	4.6	5.4	11.7
Individual Mutations : Residues in variants					
N501Y	in UK, SA, BRA variants; increases RBD/ACE2 interaction[1]	**0.5**	9.1	4.8	27.8
E484K	in SA, BRA variants; increases RBD/ACE2 interaction[1]	**2.7**	64.2	10.2	>100
K417E	residue mutated to N/T in SA, BRA variants	**0.5**	1.8	1	3.6
Y453F	key residue evolved in Danish mink farms variants	**3.2**	10.9	5.9	3.3
Individual Mutations: Highly frequent mutations					
D614G	Wide global spread	**2.4**	11.9	6.2	23
S477N	Wide global spread	**1.9**	3	2	9
N439K	Wide spread in northern amerika, UK; increases RBD/ACE2 interaction[1]	**1.3**	7.3	5.3	12.9
A222V	Wide European spread	**2.2**	3.3	4.6	19.5
Individual Mutations: Within RBD epitope of DARPins or reported resistance mutation for other therapeutic					
G446V		**1.7**	0.7	1.8	2.3
G476S		**1.5**	2.3	3.7	29
T478I		**2.7**	11.2	3.1	16.7
P479S		**2.1**	7.2	2.3	27.6
V483A		**2.3**	21.8	8.4	21.3
F486V	reduces RBD/ACE2 interaction non-fit virus[1]; key residue DARPin RBD binder[2]	**>100**	>100	>100	>100
Q493K		**7.9**	30	28.2	45.8
F490S	Reduces RBD/ACE2 interaction[1]	**3.8**	2.3	1.7	8.1



Ensovibep Phase 1 Results support progress to Phase 2/3

- Double-blind, placebo controlled trial exploring safety and exposure.
  - IV administration, SAD
  - Up to 24 subjects total, stratified 3:1 (active: placebo)
  - Ages 18-65
- Dose range include 3 mg/kg (225 mg*), 9 mg/kg (675 mg*) and 20 mg/kg (1.5 g*) cohorts
  - MP0420 dose levels correspond to an Ab concentration of ~ 900 mg, 2.7 g, 6g
- Status: Cohort 1 completed with 100 day follow-up; Cohort 2 ongoing follow up; Cohort 3 delayed due to shutdown in the UK
- Results from dose cohorts 1 & 2 allow progress to Phase 2/3
  - ✓ Relevant doses covered
  - ✓ No safety signals reported
  - ✓ Half-life: ~14 days

* Total amount in a person with 75 kg body weight

Novartis: Draft Development plan for MP0420

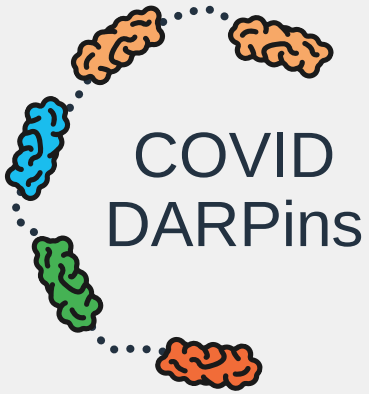
ALL DATES PRELIMINARY, SUBJECT TO HEALTH AUTHORITY INPUT

	2020	2021	2022
Clinical Development	Ph.1 studies (healthy volunteers)	Possible EUA* Phase 2/3 part A (N 400-700) | Phase 2/3 Part B (N ≥2000) Additional supporting studies for BLA submission** Explore Platform studies (e.g., ACTIV), other consortia approaches	**BLA Submission** ♦
Technical Development	Progressive scale up from100 L batch to higher volume production based on clinical trial and market demand. Plans to utilize large capacity in fermentation and filling with Novartis/Sandoz.		

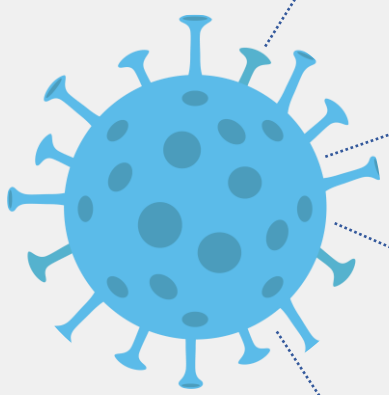
* Emergency Use Authorization submission, pending interim analysis of data is supportive of EUA
** Could involve additional dosing/ administration or treatment subtypes/ settings

NOVARTIS

DARPin® Opportunities in Virology



- **Multi-valency** for superior potency
- **Multi-specificity** for mutation resistance
- **Speed of candidate generation**
- **High amount & low-cost production**
- **High stability and solubility** for simple administration and distribution



Respiratory Viruses
- RSV, influenza and others
- Benefits as per COVID DARPin®

Pandemic readiness
- Corona, influenza
- Early intervention to prevent spread

Viral reservoirs
- HIV, HBV, HCV
- Targeting pMHC

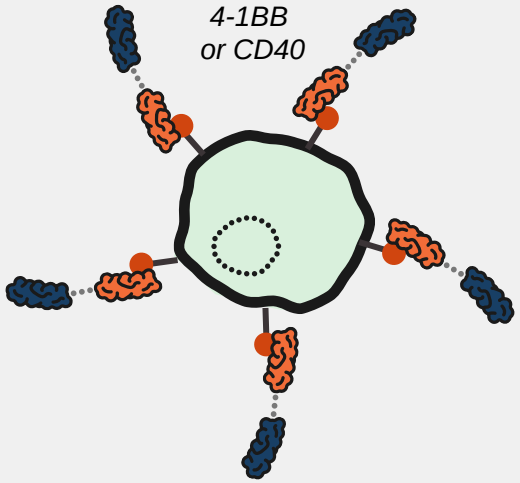
Low-income country viruses
- Example: dengue
- High stability
- Low costs

Clinical Programs:
Tumor Localized Activators

Local Activation of Immune cells: Fibroblast Activation Protein (FAP) as a General Switch

BODY

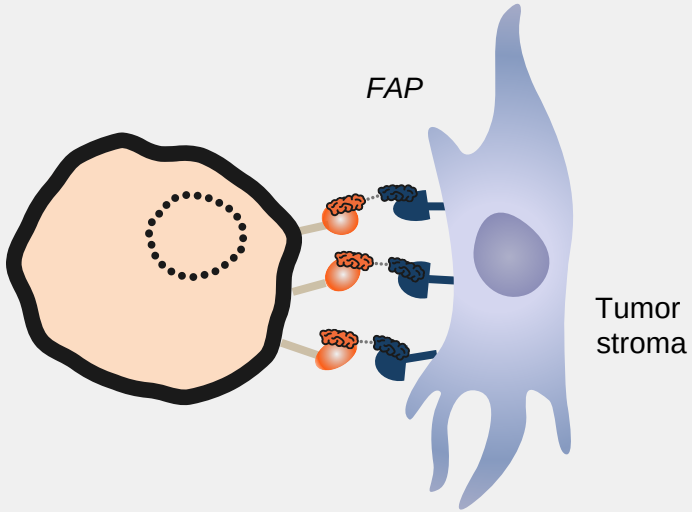
- In normal tissues, receptor is broadly distributed
- Immune cell remains inactive

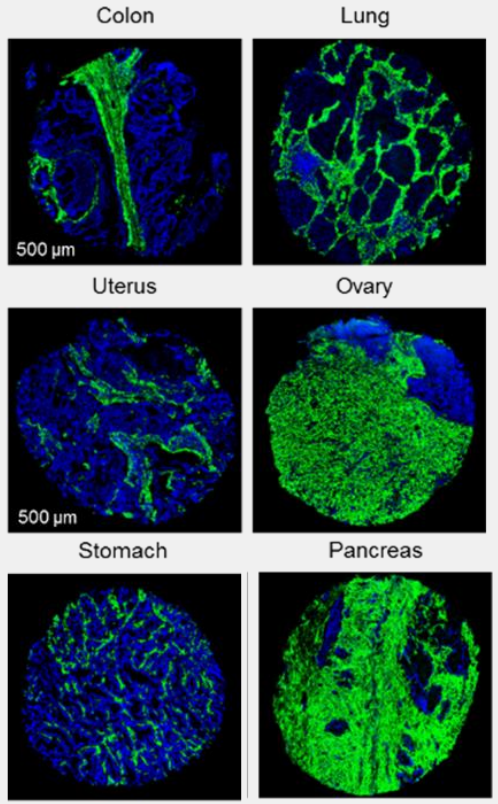


VS

TUMOR

- High FAP concentration near tumor clusters receptors
- Immune cell is activated





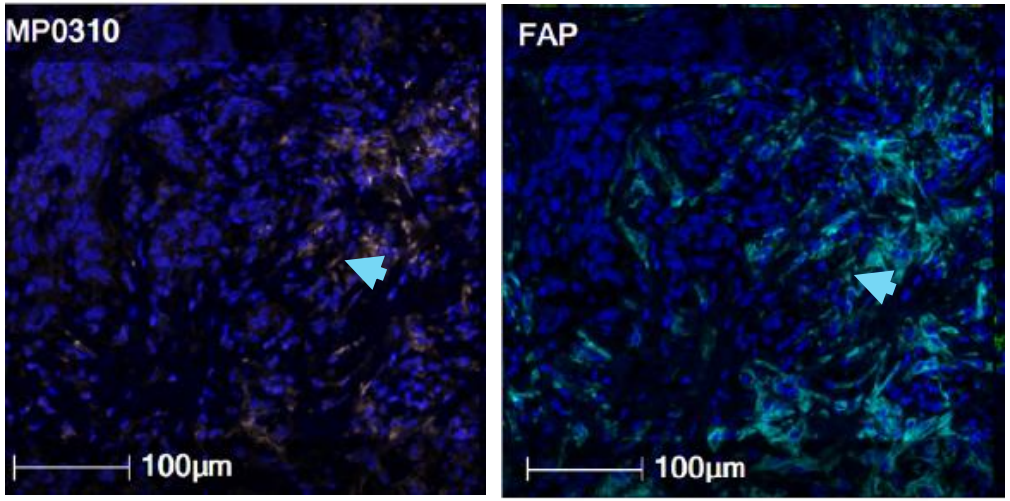
Human FAP, DAPI

- No activation by mono-binding of FAP or CD40/4-1BB
- Simultaneous binding leads to tumor-local immune activation

AMG 506 / MP0310 Accumulates in Tumor Tissue in Dose Dependent Manner

MP0310 low dose colocalizes with FAP

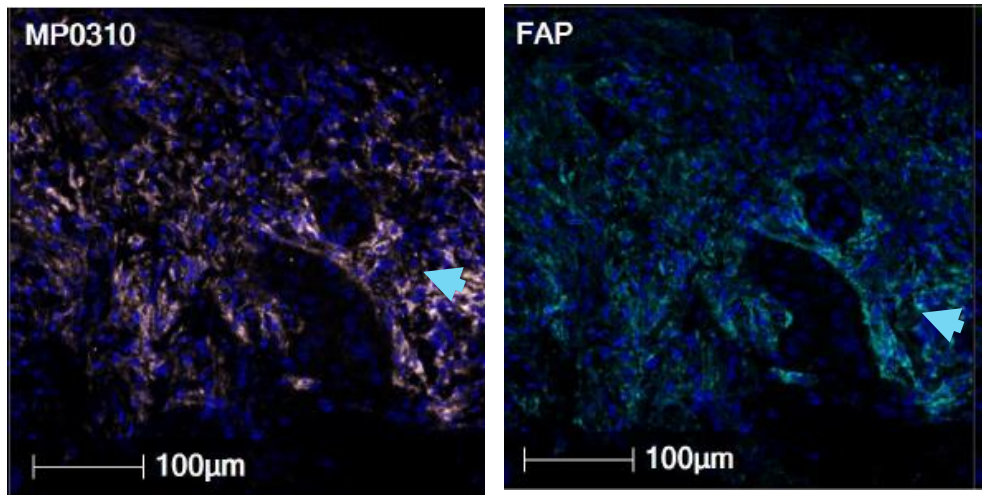
MP0310 < FAP



Endometrial carcinoma (Liver metastasis), C1D15

MP0310 high dose saturates FAP

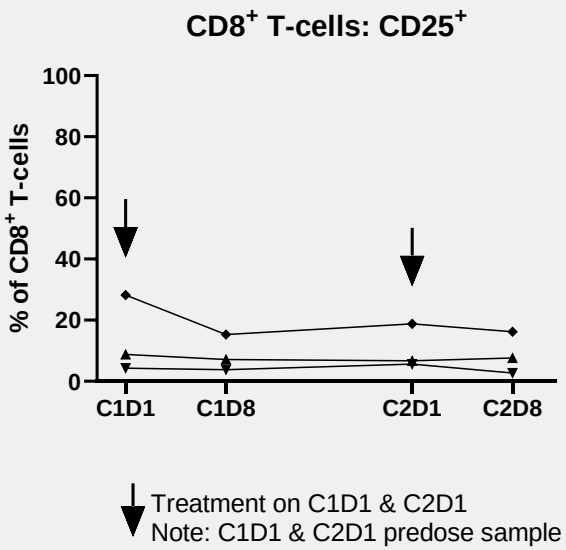
MP0310 > FAP



NSCLC (lung), C1D15

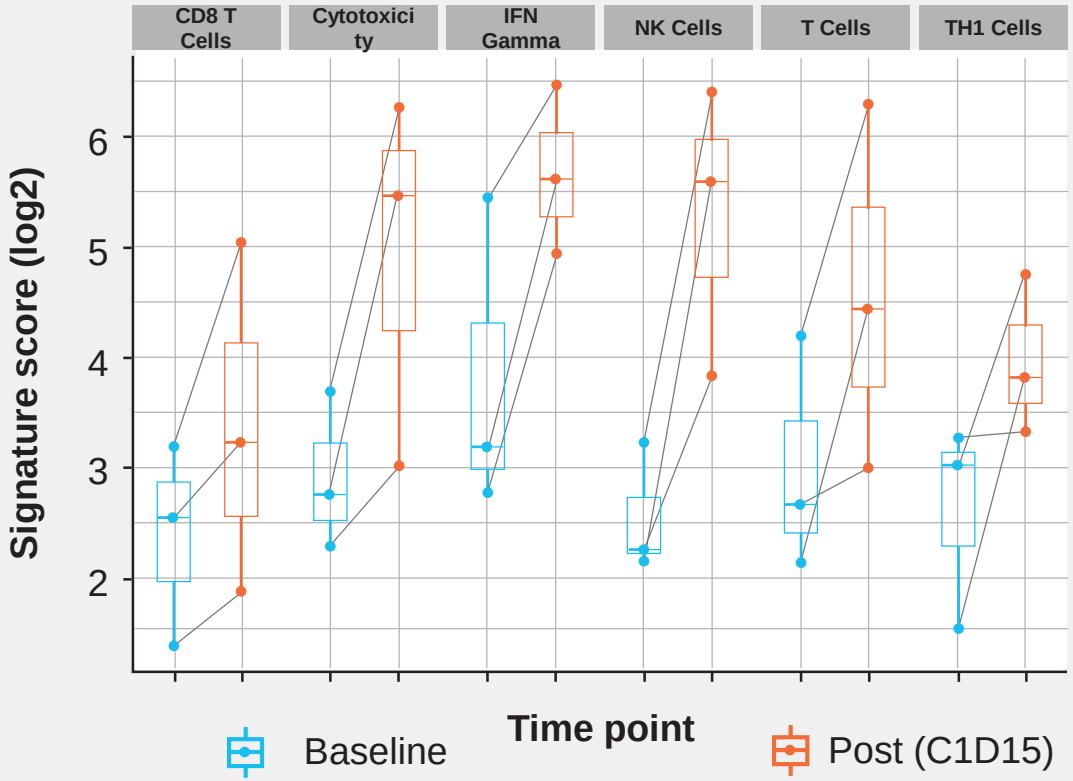
PD Activity in Paired Biopsies Supports AMG 506 / MP0310 MoA on 4-1BB Activation

BLOOD



- In the blood, immune cells remain inactive (CD8+ & CD4+ T-cells, Treg, NKT, B-cells, NK)

TUMOR

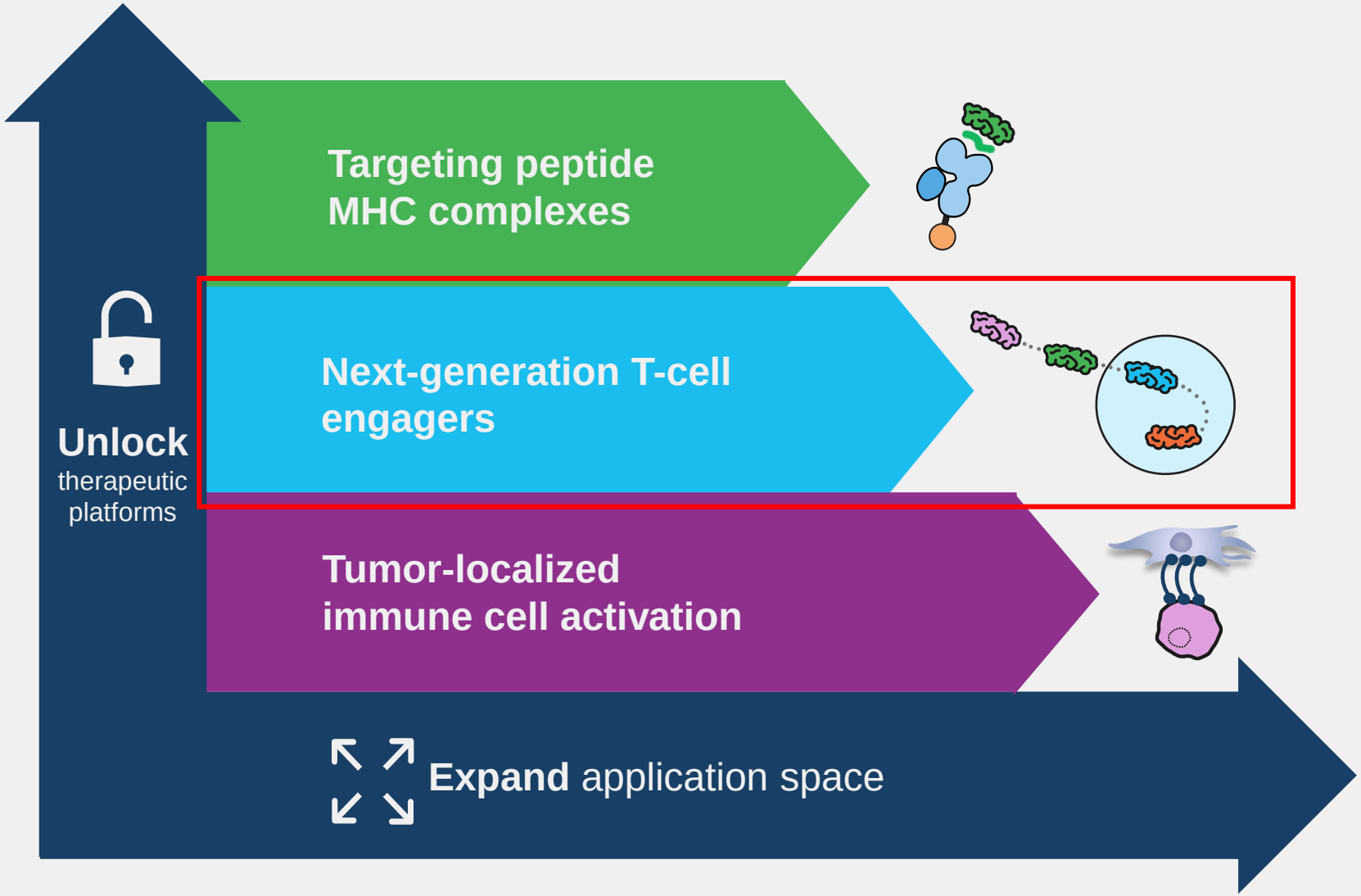


- In the tumor, T-cells and NK cells are activated

MOLECULAR partners

New Therapeutic Platforms: Unlocked

Unlock and Expand: Therapeutic Platforms



Current Limitations of CD3 Approaches

Safety

Hyperimmune-stimulation

Neurotoxicity

Cytokine release syndrome (CRS)

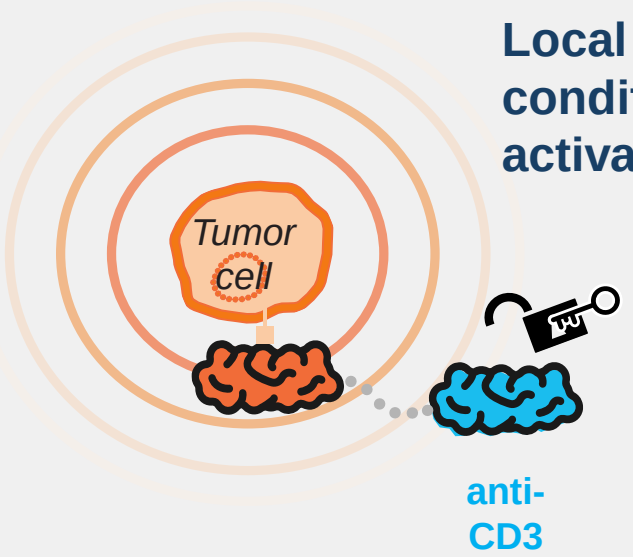
Efficacy

Tumor escape

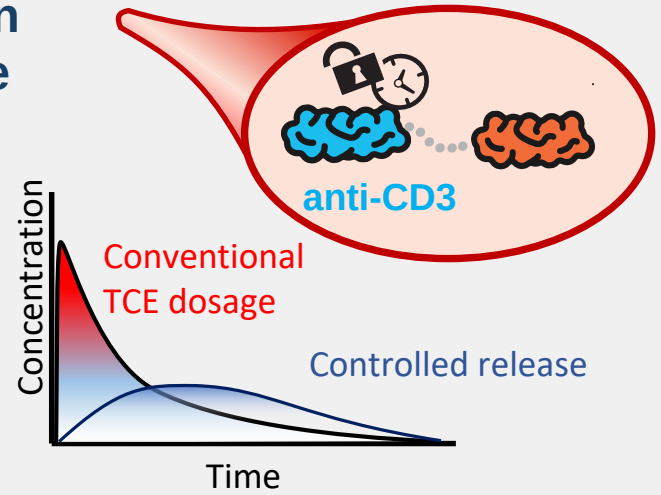
Target engagement

Our Solutions - Next Generation T-cell Engagers

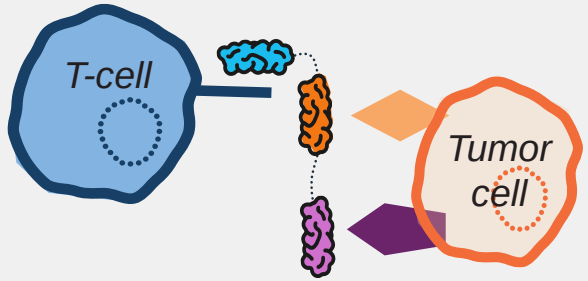
Local & conditional activation



Slow activation over time



Multi-specific T-cell engagers



Improve safety to allow optimal dosing and
Deepen Efficacy for longer effect

Up-date at AACR 2021

Summary

Financial Overview & Milestones:

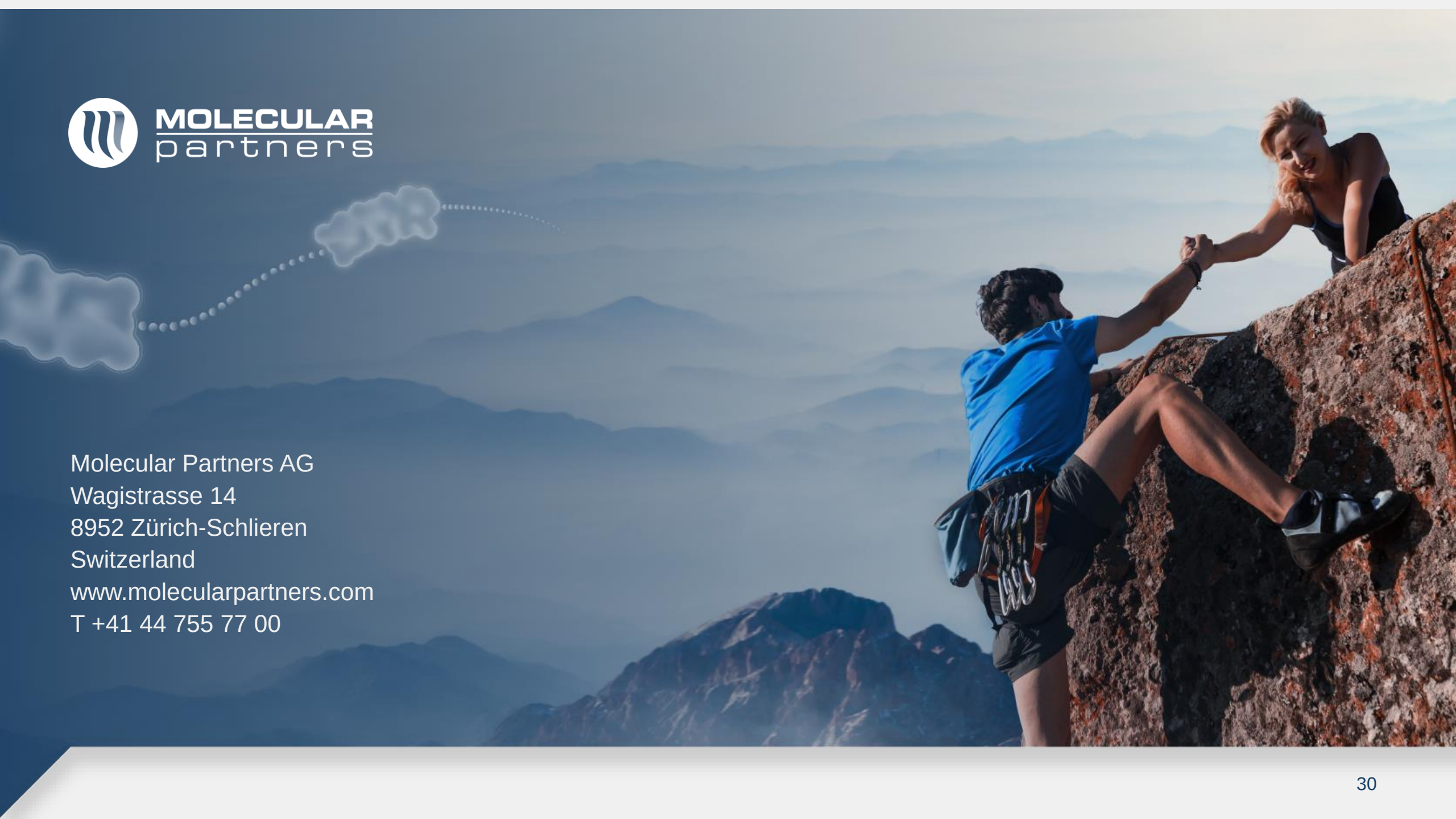
- YE Cash 2020: ~174M CHF, no debt
  - Successful capital raise of CHF 80m, completed in early July 2020
- Additional funding from Novartis transaction (CHF 60m, received per end October 2020)
  - Funded into 2023, without consideration of future milestones
- ~$1B in potential milestones from R&D partners yet to be realized
  - $165m milestone from Novartis upon commercial licensure of COVID-DARPins
  - ~$500m in milestones from Amgen for AMG 506 / MP0310
  - >$360M in approval and commercial milestones associated with Abicipar
- Up to double-digit royalties outstanding with current R&D partners

Upcoming Catalysts Across The Portfolio in 2021

Antiviral portfolio	
Ensovibep (MP0420) MP0423	▪ POC with EUA/BLA and approval in 2021 ▪ Emergency Use Authorization and/or BLA submission possible in 2021 ▪ MP0423 FIH
Novel antivirals	▪ Develop novel DARPins for viral targets with first new target announced 2021
Immuno-oncology portfolio	
AMG 506 (MP0310)	▪ Identify ideal dosing regimen in ongoing Phase 1 (H1/2021) ▪ Amgen potential combination trials (H2/2021)
MP0317	▪ MP0317 FIH in H2 2021
T cell engagers	▪ 1st Candidate selected for development ▪ Follow-up pipeline established
pMHC	▪ Select Peptides for Candidate Selection – possibly with a partner

Funded into 2023

(Not incl. any future proceeds related to partnerships)



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