Custom Built Biology for Patients

Octavian Seminar 2021

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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

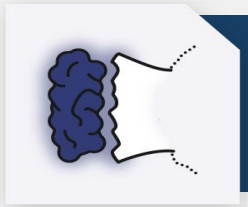
We aim to transform the lives of people with *serious diseases* by delivering truly innovative solutions

our purpose

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

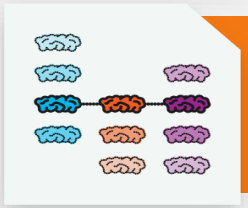
Innate Advantages Combined With Proprietary Approaches

Unique DARPin® Features



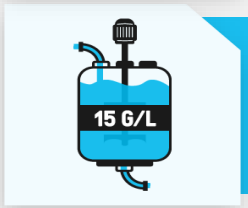
Ideal binding properties

- Perfect fit
- High affinity
- Super specificity



Turn-key multi-specifics

- Small size
- Uni-domain activity
- Up to 7 binders
- Open combinatorial space



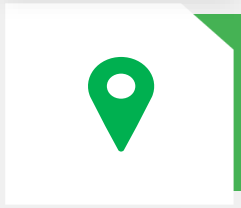
Simple Manufacturing & Storage

- High-yield microbial expression
- High stability

DARPin® Benefit

Tailored Grip

- Match disease requirements



Localized Activity

- Local and temporal control of activity

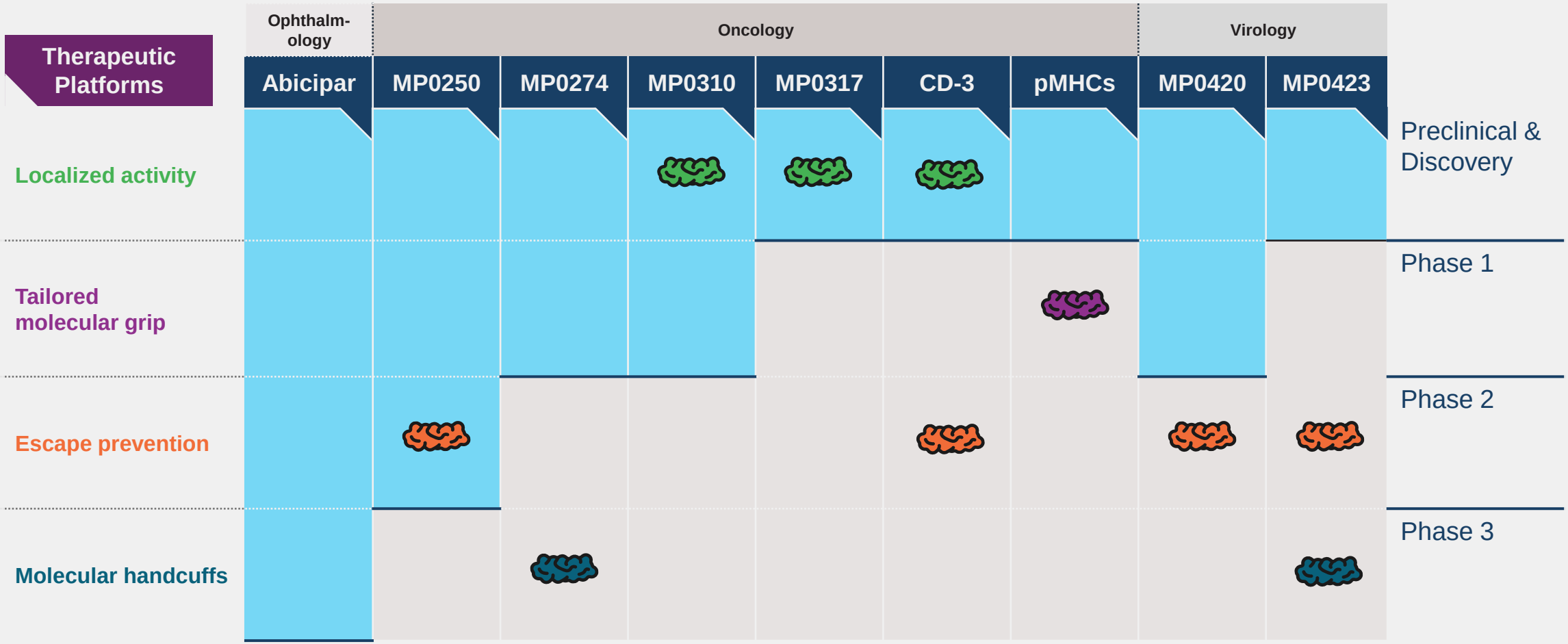
Molecular Handcuff

- Full shut-down by conformational freeze

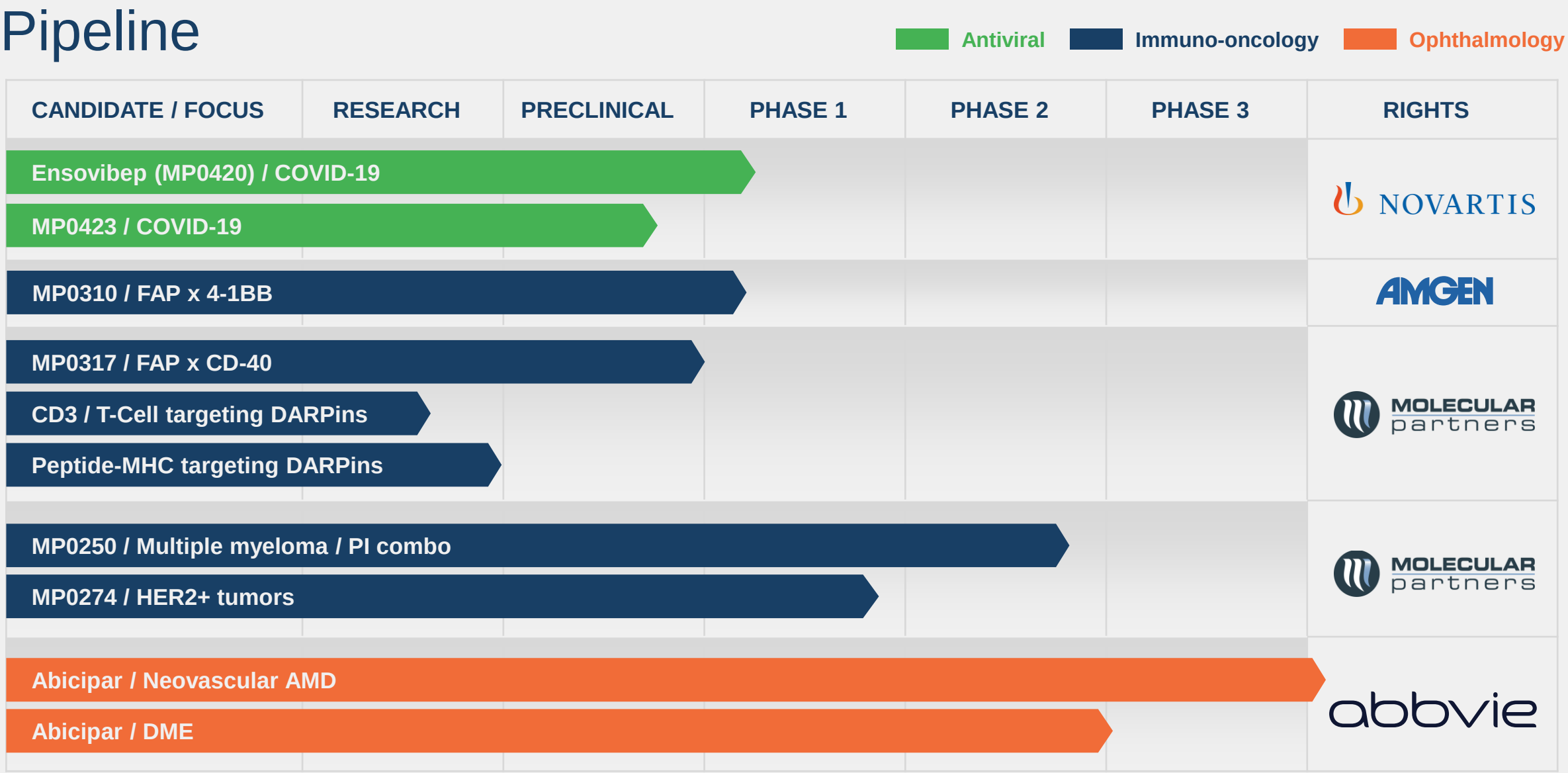
Multi-blocker to prevent escape

- Overcome escape pathways oncology / ID

A Portfolio Strategy Delivering Growth And Innovation



Pipeline


Antiviral
Immuno-oncology
Ophthalmology
CANDIDATE / FOCUS
RESEARCH
PRECLINICAL
PHASE 1
PHASE 2
PHASE 3
RIGHTS
Ensovibep (MP0420) / COVID-19
MP0423 / COVID-19
NOVARTIS
MP0310 / FAP x 4-1BB
AMGEN
MP0317 / FAP x CD-40
CD3 / T-Cell targeting DARPins
Peptide-MHC targeting DARPins
MOLECULAR partners
MP0250 / Multiple myeloma / PI combo
MP0274 / HER2+ tumors
MOLECULAR partners
Abicipar / Neovascular AMD
Abicipar / DME
abbvie

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

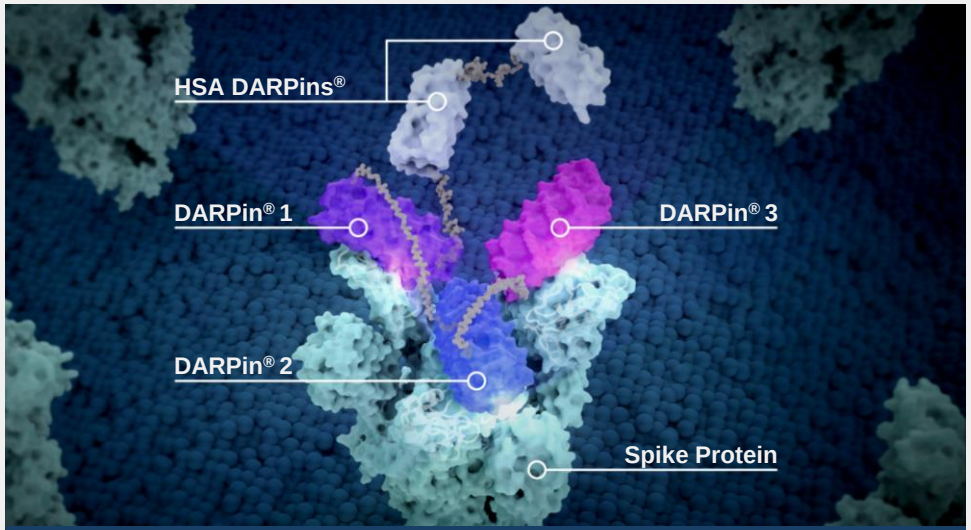
Over ~$1B in potential milestone across multiple programs

Clinical Program: Anti-COVID19

Our COVID-19 Program: Two Outstanding Candidates

MP0420 (ensovibep)– best-in-class

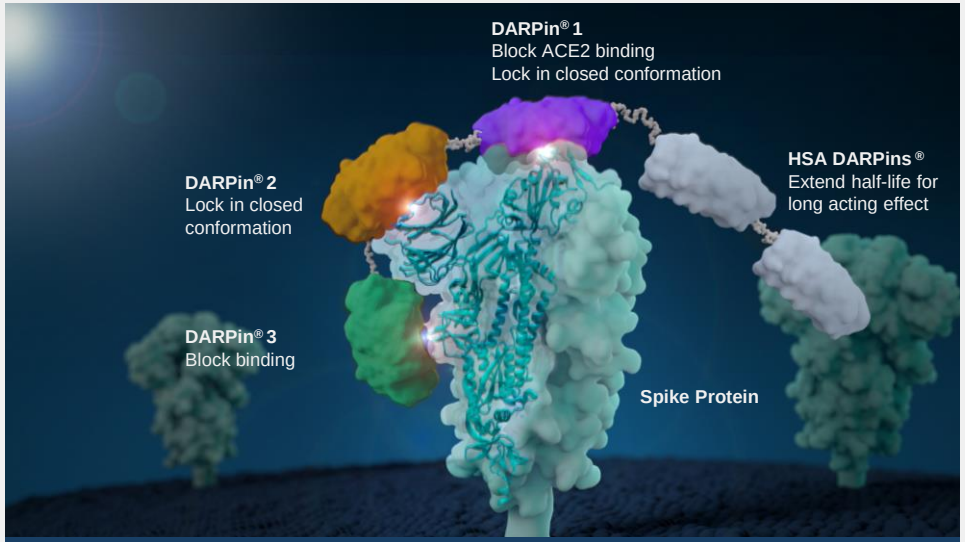
- Tri-specific DARPin® antiviral targeting the RBD for highest potency & to prevent viral escape
- Long half-life (HSA DARPins) – single injection
- Low costs and high numbers of doses available
- Potential for bolus / s.c. injection – simple application



Immediate solution for hospitalized and ambulatory settings

MP0423 – first-in-class

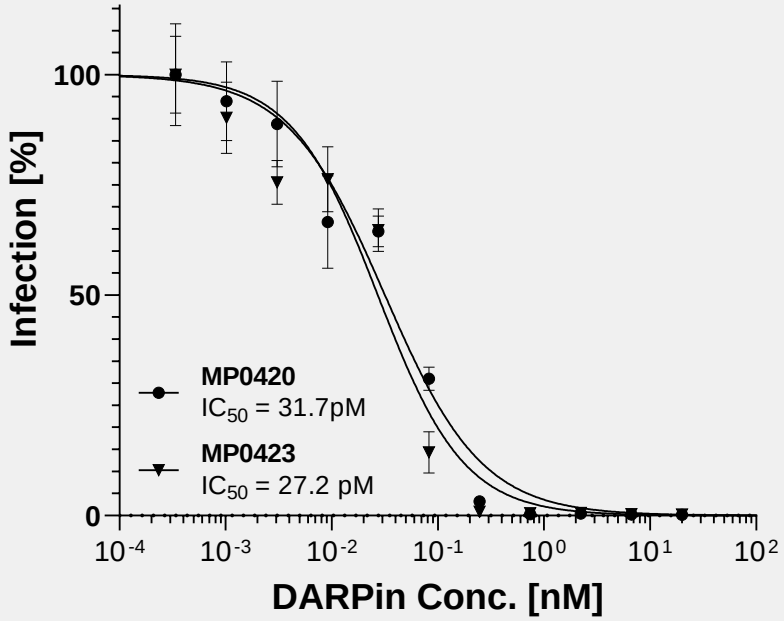
- 3 DARPins blocking different domains of the viral spike
- High activity even if RBD mutates heavily and escapes all vaccines and therapeutic antibodies
- All other benefits of MP0420



Ideal solution for stock-piling and global insurance policy for viral RBD drift

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

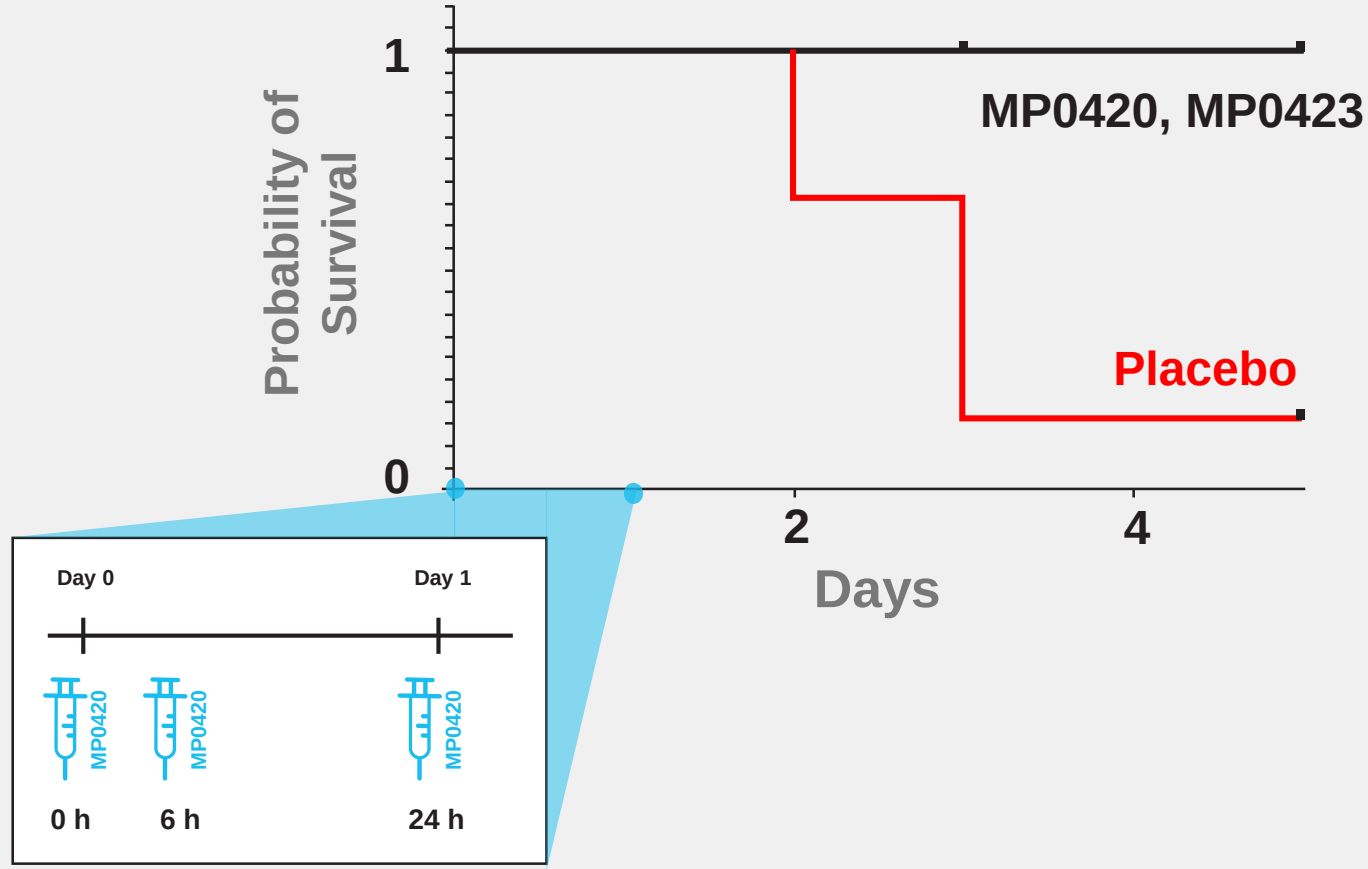
In vitro activity: Pseudotype Neutralization Assay



Highest potency

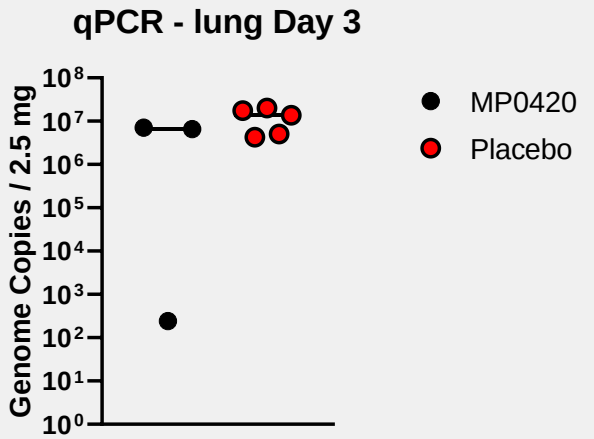
Tri-binding leads to highest affinity and potency in the low pM range; likely at the assay limit

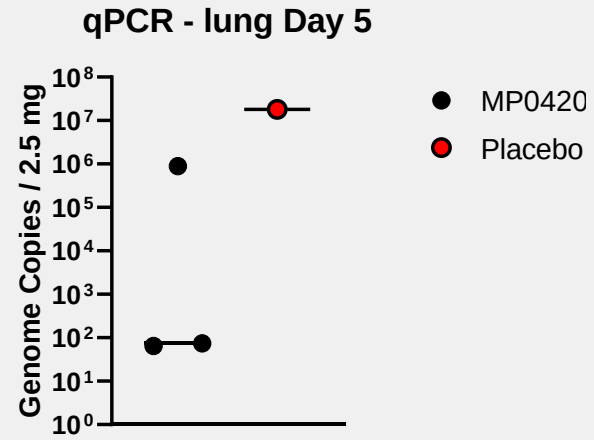
In vivo activity: Kaplan Meier Plot - Hamster Model



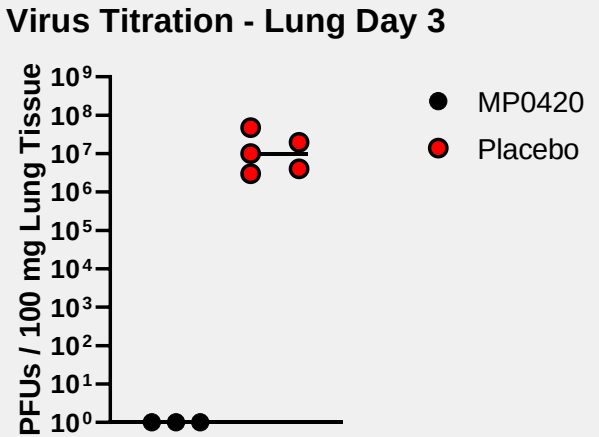
Ensovibep Blocks the Virus and Prevents Infection in the Lung

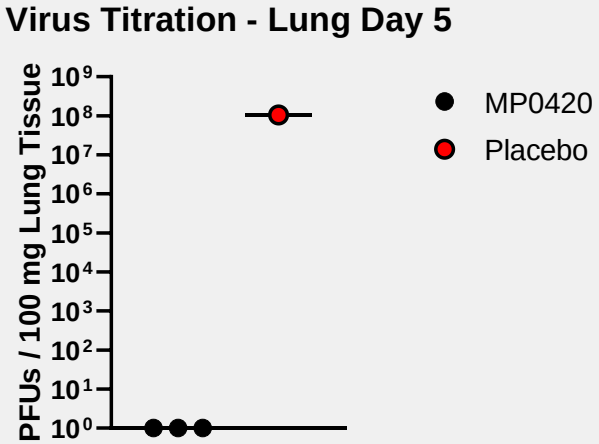
Viral titer in the lung





Viral infectivity in the lung





Ensovibep blocks viral infectivity completely

MP0420 (ensovibep) Phase 1 Ongoing

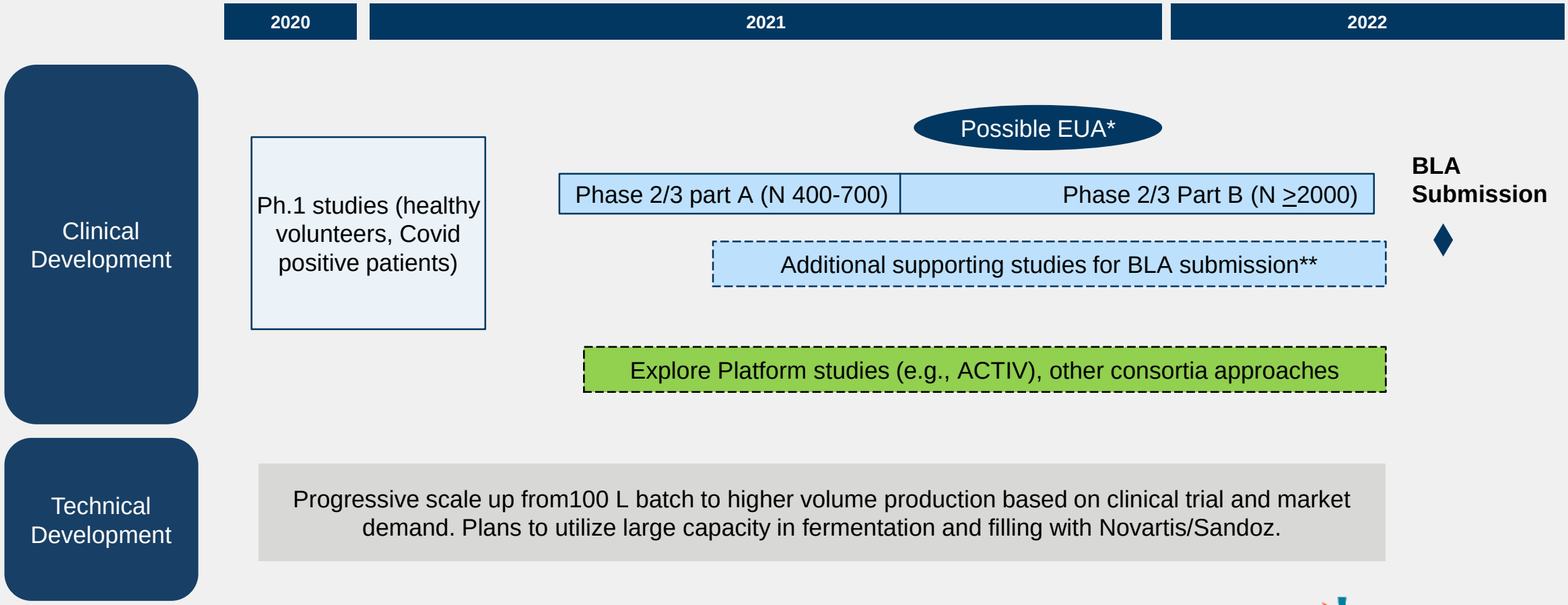
- Study initiated November 2020
- Double-blind, placebo controlled trial exploring safety and PK
  - IV administration
  - Up to 24 subjects total, stratified 3:1 (active: placebo)
  - Ages 18-65
- Dose range include 3 mg/kg (225 mg*), 9 mg/kg (675 mg) and 20 mg/kg (1.5 g)
  - MP0420 is ¼ the molecular weight of an mAb mixture, corresponding to ~ 900 mg, 2.7 g, 6g
- Endpoints: Safety, tolerability and pharmacokinetics (SAD)
- Status: First 2 cohorts fully enrolled, third cohort ongoing

Full data expected by Q1 2021

* Total amount in a person with 75 kg body weight

Novartis: Draft Development plan for MP0420

ALL DATES PRELIMINARY, SUBJECT TO HEALTH AUTHORITY INPUT



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

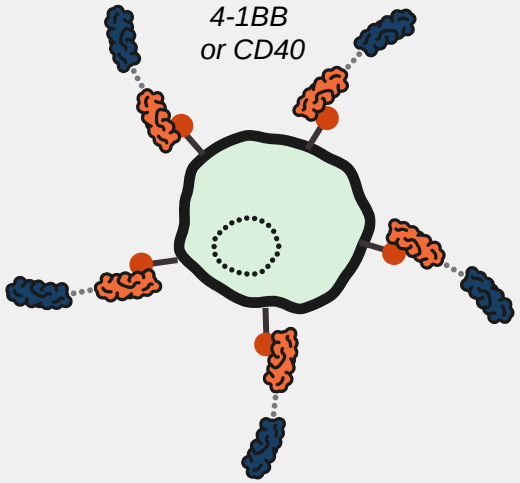
NOVARTIS

Clinical Programs:
Tumor Localized Activators

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

BODY

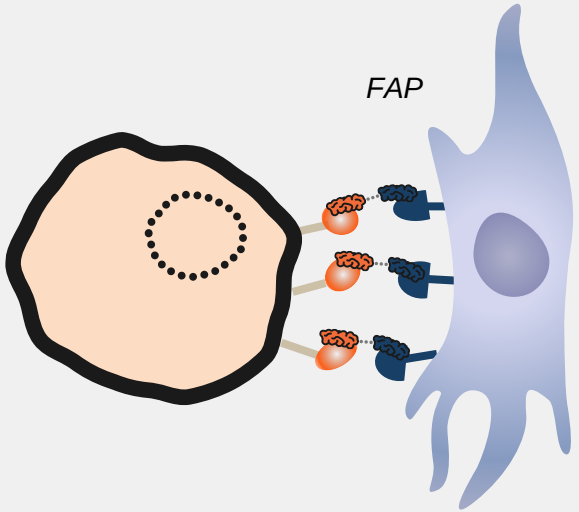
- In normal tissues, receptor is broadly distributed
- Immune cell remains inactive

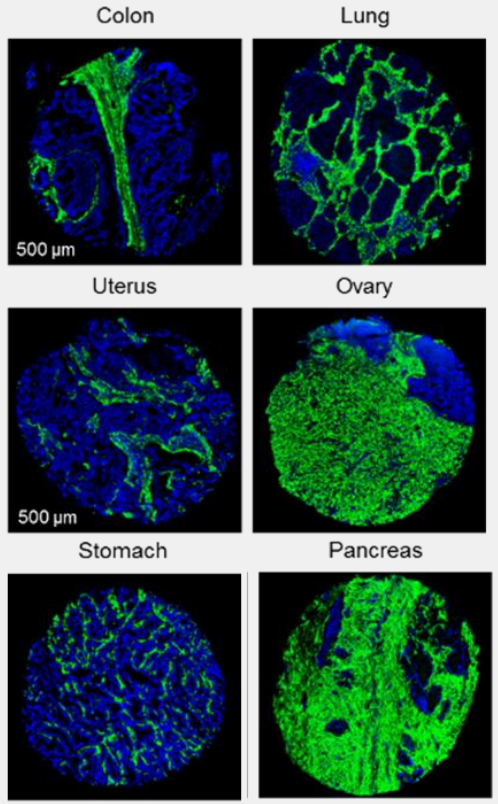


VS

TUMOR

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





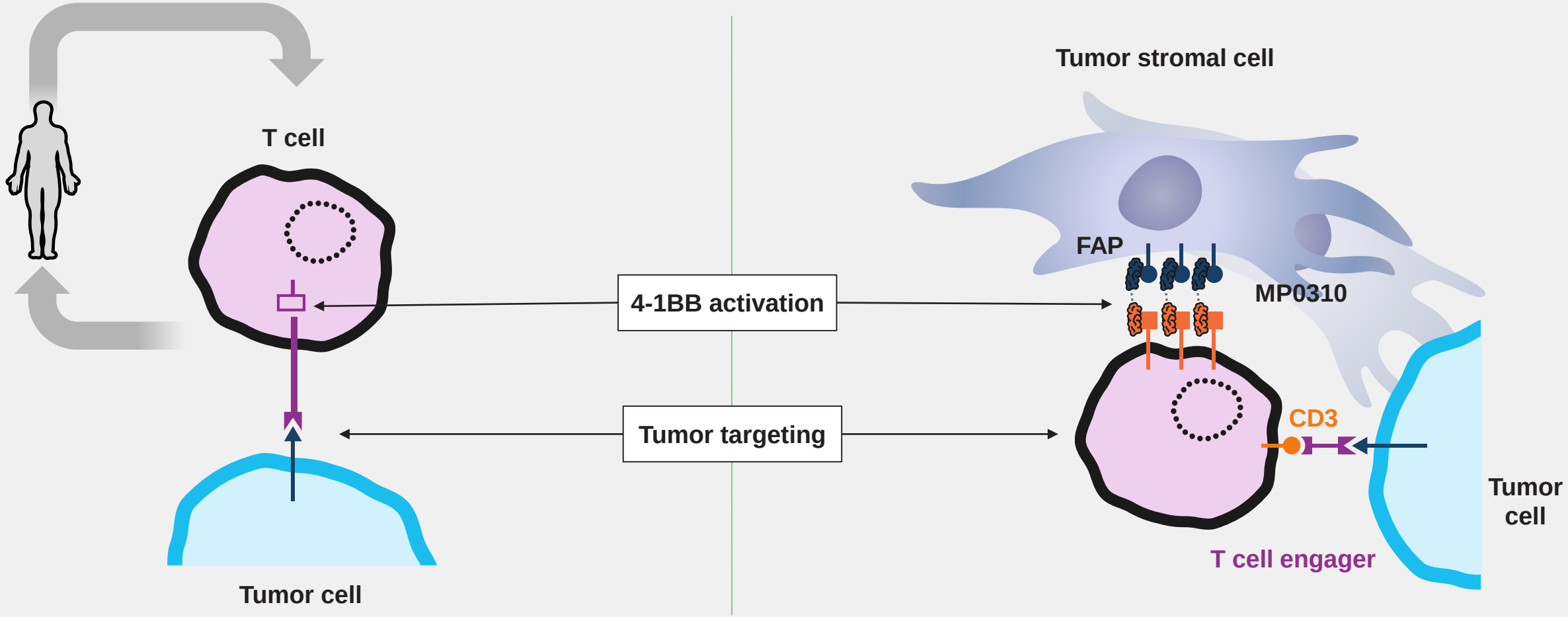
Human FAP, DAPI

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

Application: Local T Cell Targeted Activation

Traditional CAR-T

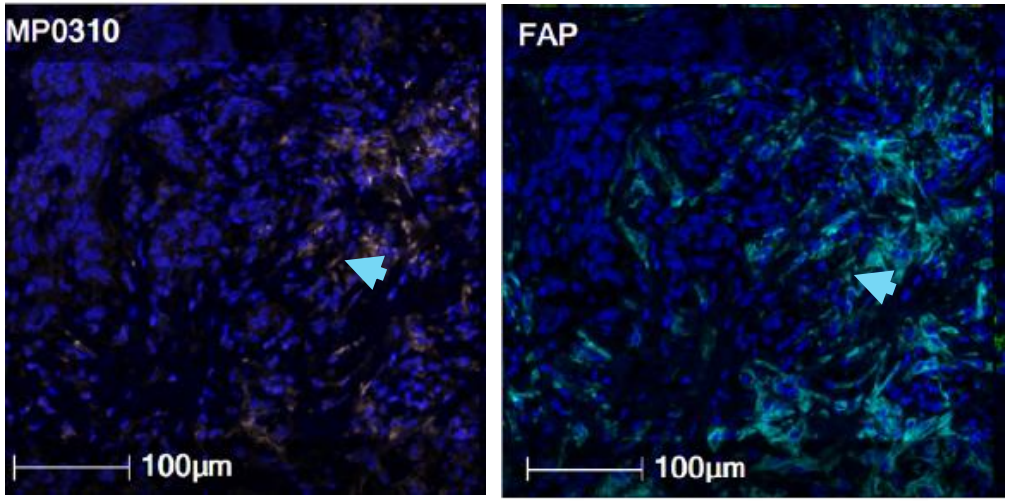
"CAR-T *in situ*"



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

MP0310 (0.5mg/kg) colocalizes with FAP

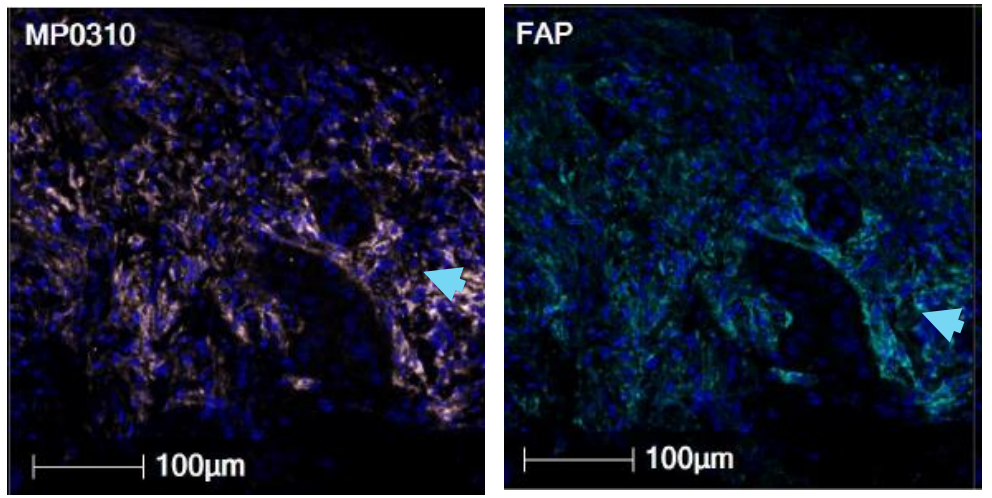
MP0310 < FAP



Endometrial carcinoma (Liver metastasis), C1D15

MP0310 (5mg/kg) saturates FAP

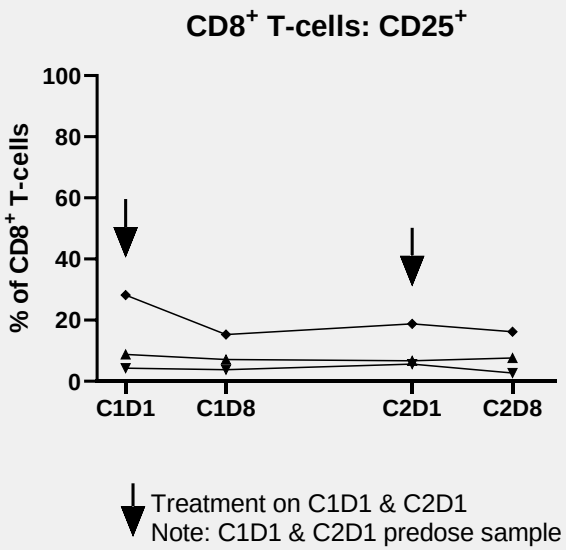
MP0310 > FAP



NSCLC (lung), C1D15

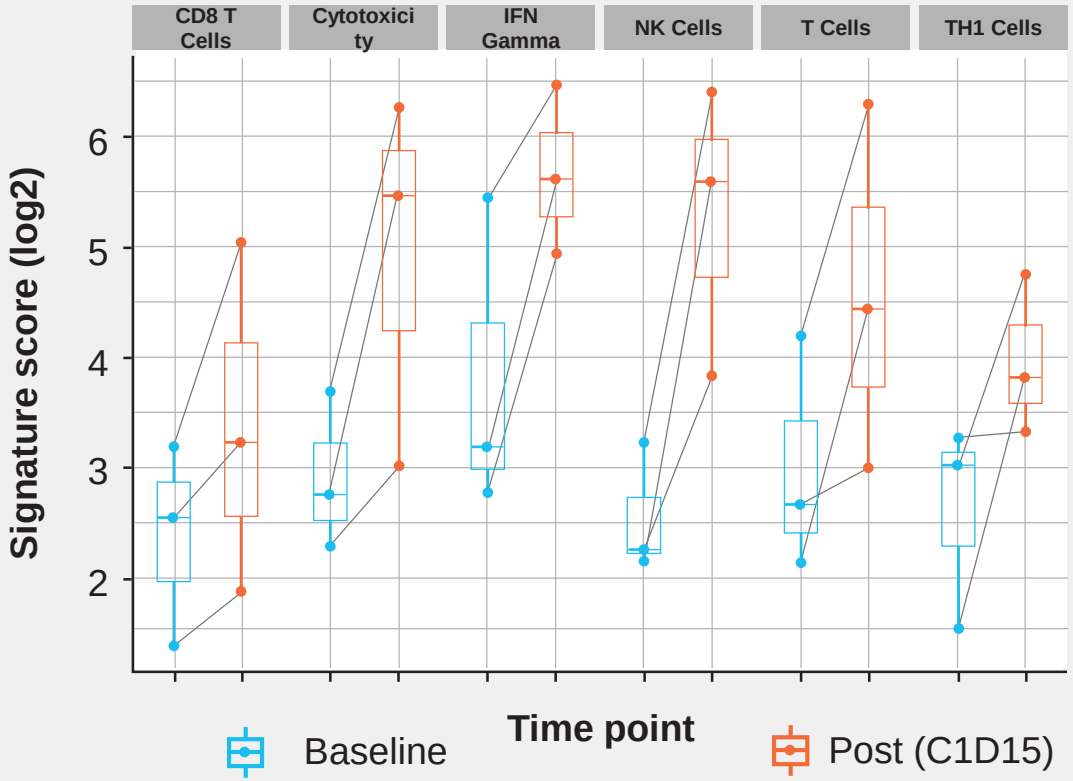
PD Activity in Paired Biopsies Supports AMG 506 / MP0310 MoA on 4-1BB Activation

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

AMG 506 / MP0310 Dose Escalation Completed

Current status

- Executed on schedule through 2020
- 22 patients enrolled, 19 presently evaluable
- 7 dosing cohorts, 8 patients with ≥4 cycles
- 12 patients exhibited infusion related reactions (IRR) G2-3, (22 enrolled)
- No other AEs of special interest
- **No Dose limiting toxicities (DLTs)**

Outlook

- Test weekly dosing
- Show sustained activity after week 4
- Reach evaluation by Amgen

Data as of 30 Nov 2020

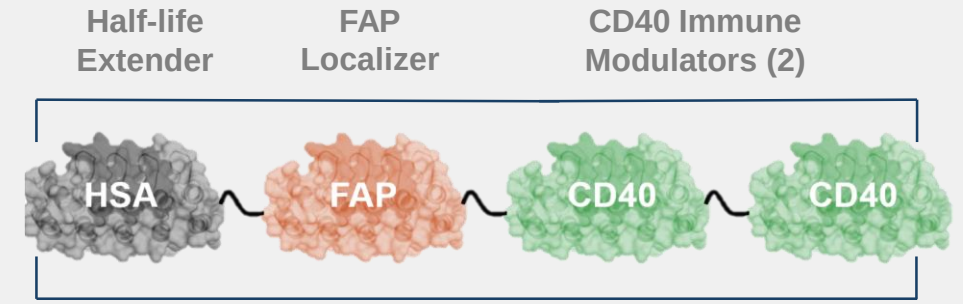
MP0317: Localized Activation of CD40

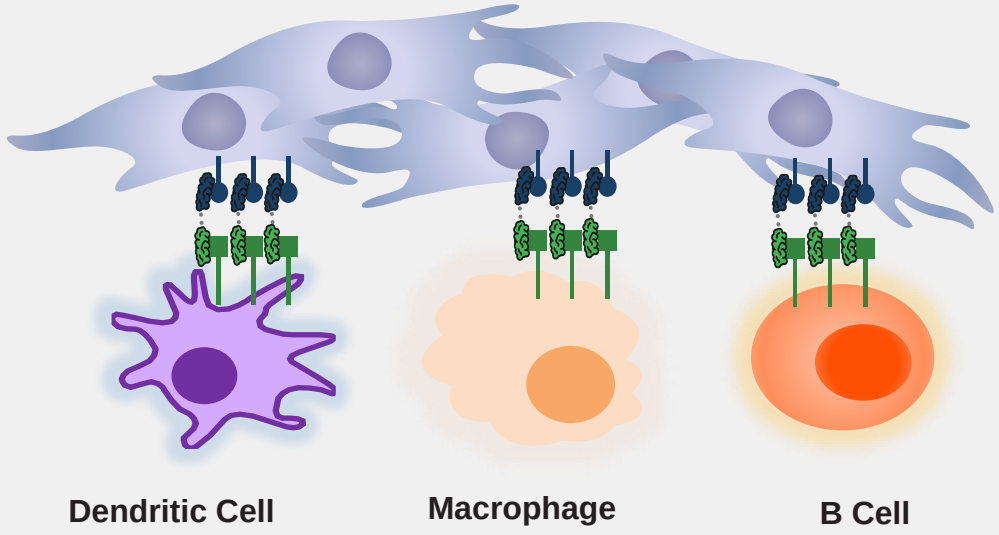
Current limitations and opportunity

- Rather low MTDs for systemic antibody agonists (< 1mg/kg)
- Likely need for combination therapy leading to additional risks for toxicity

Opportunity

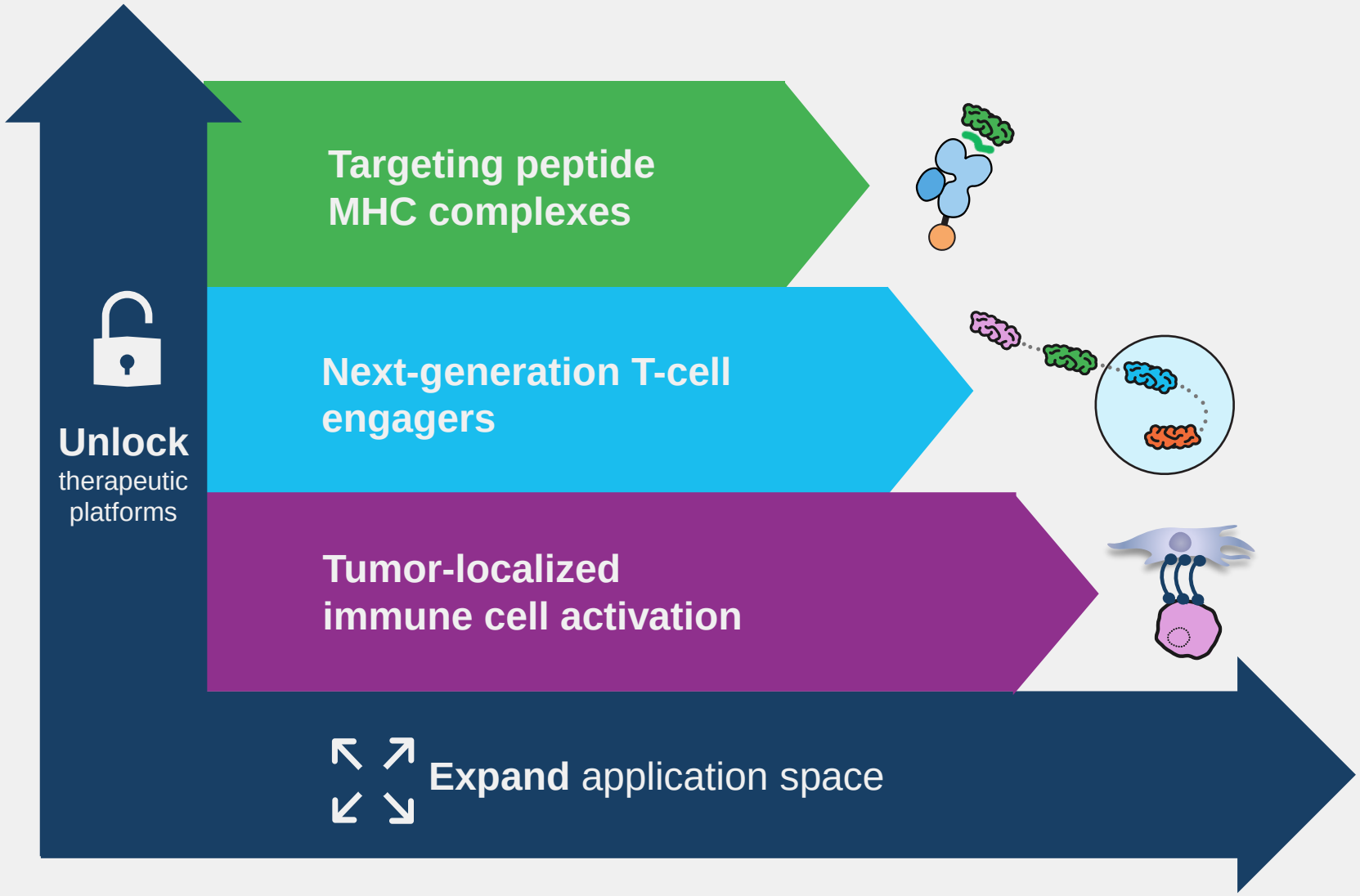
- Localized activation approach to limit systemic side effects and open a therapeutic window for combinations
- FIH H2 2021





New Therapeutic Platforms: Unlocked

Unlock and Expand: Therapeutic Platforms



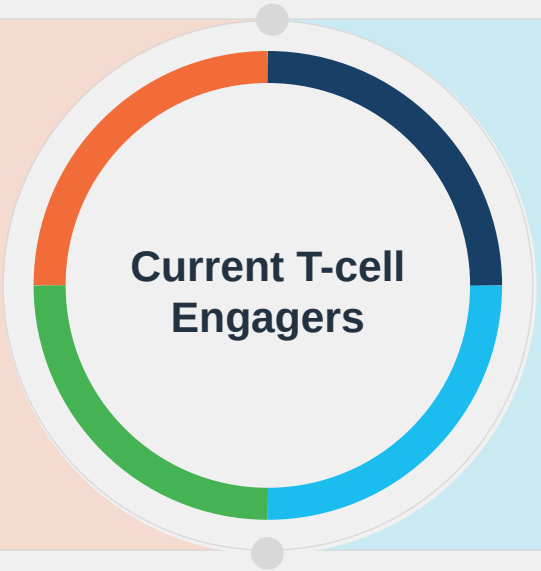
Challenges of T-cell Engagers in the Clinic

Safety

TOXICITY PROFILE LIMITS OPTIMAL DOSING

Attack on healthy tissues
(on-target off-tumor binding)

Hyper-immune stimulation:
CRS and neurotoxicity



Efficacy

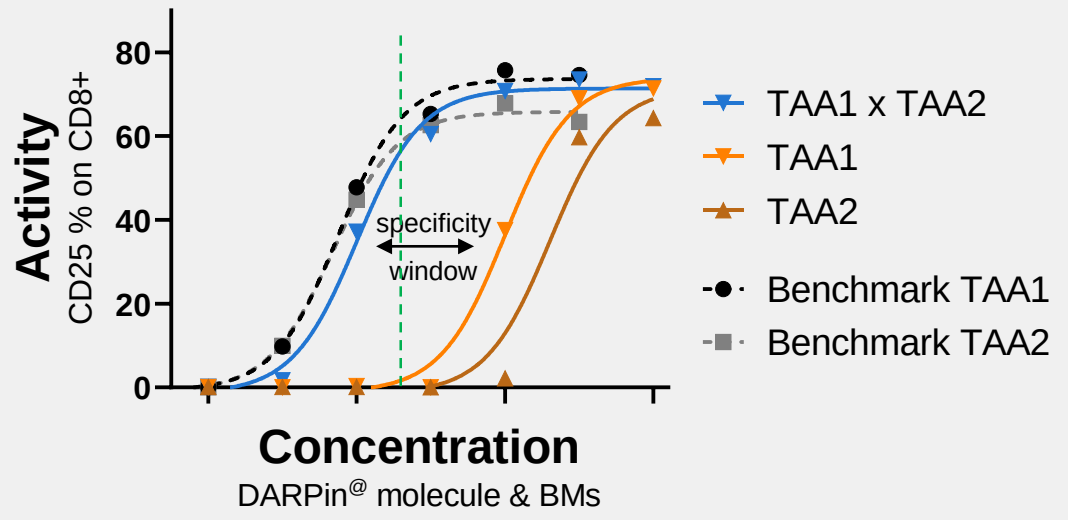
LACKING LONG-LASTING AND DEEP RESPONSES

Tumor escape & relapse
(heterogeneity, target loss,
mutation or downregulation)

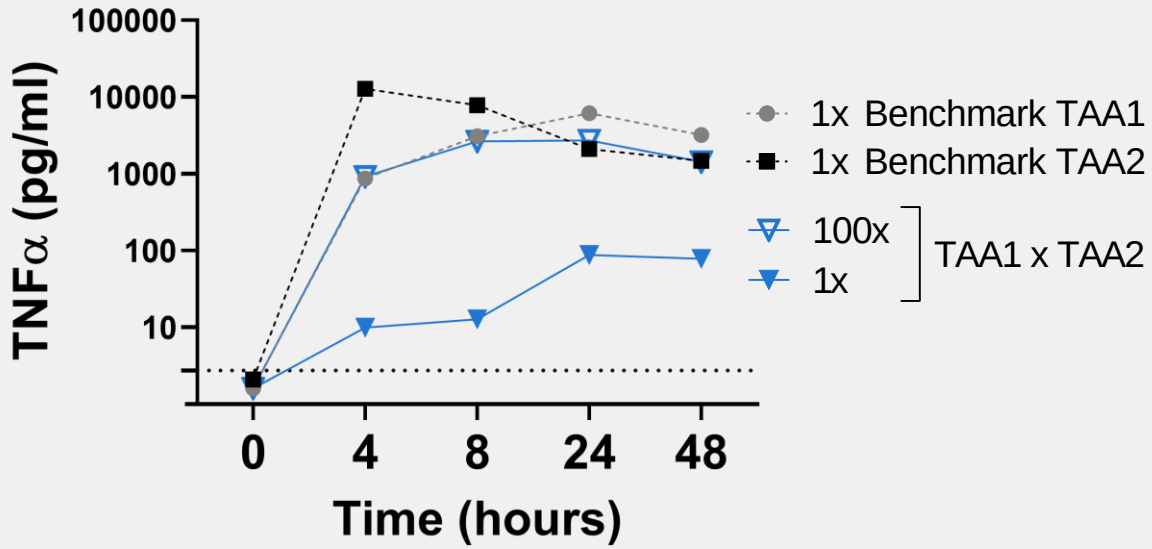
Lack of efficacy in solid tumors
(tissue penetration, suppressive
microenvironment, T-cell exhaustion…)

Multi-DARPins® for AML Show High Potency, Improved Selectivity and Potential for Reduced CRS

In-vitro potency and specificity assessment on AML cells



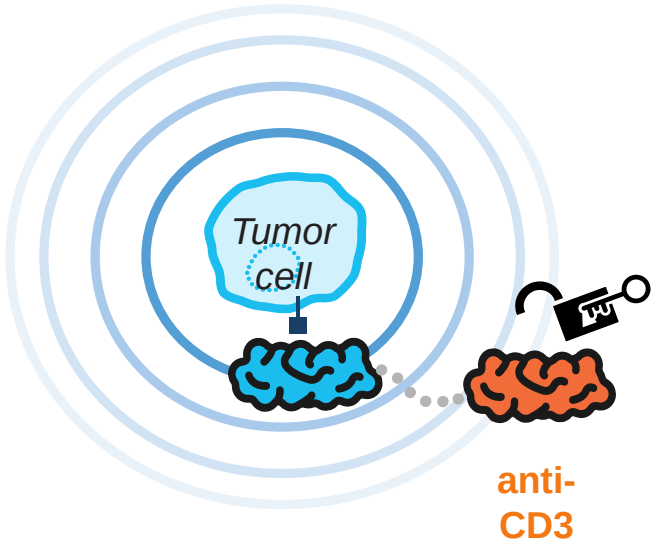
Ex-vivo cytokine release in healthy human whole blood



AACR 2021

Expand with Platform for Controlled Activation of CD3 Effector Function

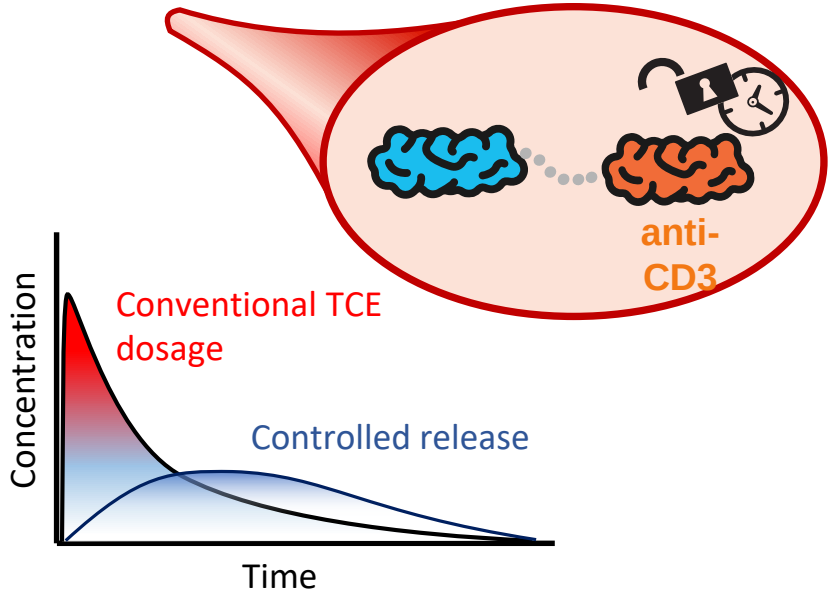
Where
Conditional activation locally in the TME



- Local activation for reduced on-target, off-tumor activity

Inactive at treatment start

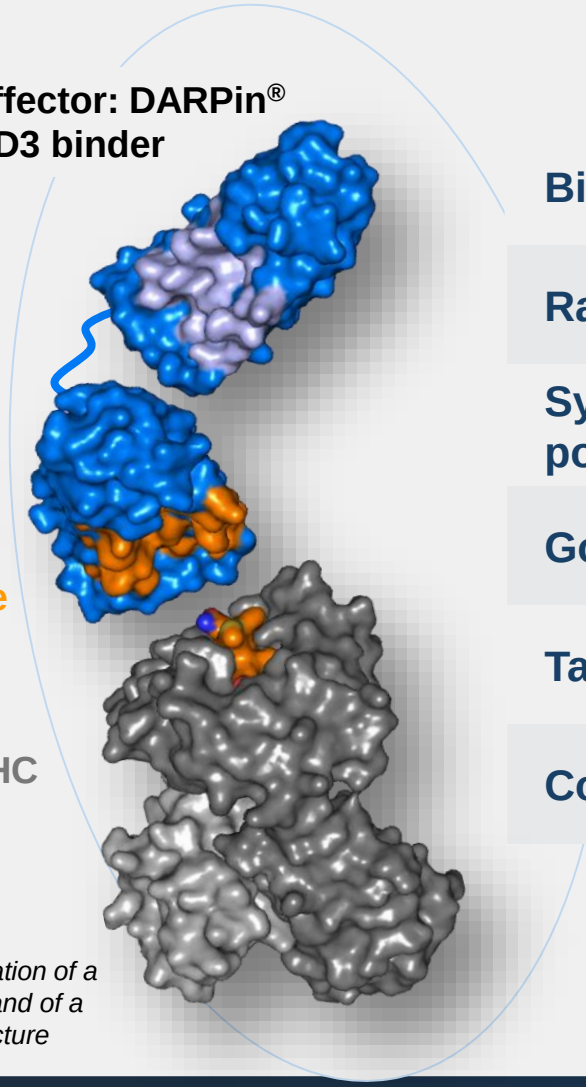
When
Slow activation over time in circulation



- Reduced C_{max} at treatment start, increasing bioactivity over time

AACR 2021

DARPin® Platform Especially well Suited to Address pMHC Targets



Surface representation of a DARPin® domain and of a pMHC crystal structure

Binders with high specificity and high potency	✓
Rapid and reliable generation of pMHC binders	✓
Systemic half-life extension with limited impact on potency	✓
Good developability properties	✓
Target identification and validation	○
Complex clinical development path	○

Summary

Financial Overview & Milestones:

- Cash end November, 2020: ~$200m, no debt
  - Expense guidance for FY2020: CHF 65-75m
  - 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	
MP0420 (ensovibep) 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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