Unlock and Expand: Custom Built Biology for Patients

R&D Day 2020

Molecular Partners AG, Switzerland
(SIX: MOLN)

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R&D Day Speakers

Patrick Amstutz, PhD
Chief Executive Officer, Molecular Partners

Nicolas Leupin, MD
Chief Medical Officer, Molecular Partners

Daniel Steiner, PhD
SVP Research, Molecular Partners

Lutz Hegemann, MD, PhD
Chief Operating Officer, Global Health, Novartis

Mario Sznol, MD
Professor of Medicine (Medical Oncology) / Co-Leader, Cancer Immunology, Yale Cancer Center / Co-Director, Yale SPORE in Skin Cancer

Pioneering DARPin® Therapies to Transform Lives

Overview: Patrick Amstutz

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

Highlights 2020

Opportunity

- First & only multi-specific COVID drug in clinical development (ensovibep)
- Idea to candidate in 12 weeks
- Bench to clinic ~8 months
- Partnered with Novartis to add large scale manufacturing & global reach

Execution

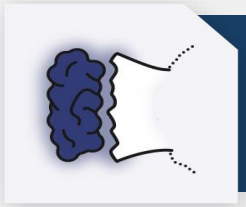
- Expanded development and research pipelines despite lock-down
- Advanced first IO local agonist to highest dose – biological activity observed– dose scheduling ongoing (AMG 506 / MP0310)
- Research driving innovation with next-generation T-cell engagers and pMHC binders

Recognition

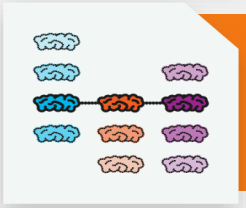
- Increased cash on balance sheet by over $155m in 2020
- Raised $90m
- COVID deal with Novartis adding $65m of cash
- Continued strengthening of the MP team

Innate Advantages Combined With Proprietary Approaches

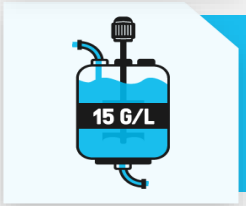
Unique DARPin® Features



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



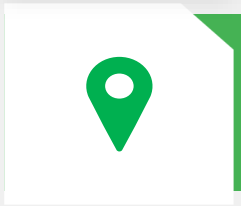
Turn-key multi-specifics
- Small size
- Uni-domain activity
- Up to 7 binders
- Open combinatorial space



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

DARPin® Benefit

Tailored Grip
- Match disease requirements

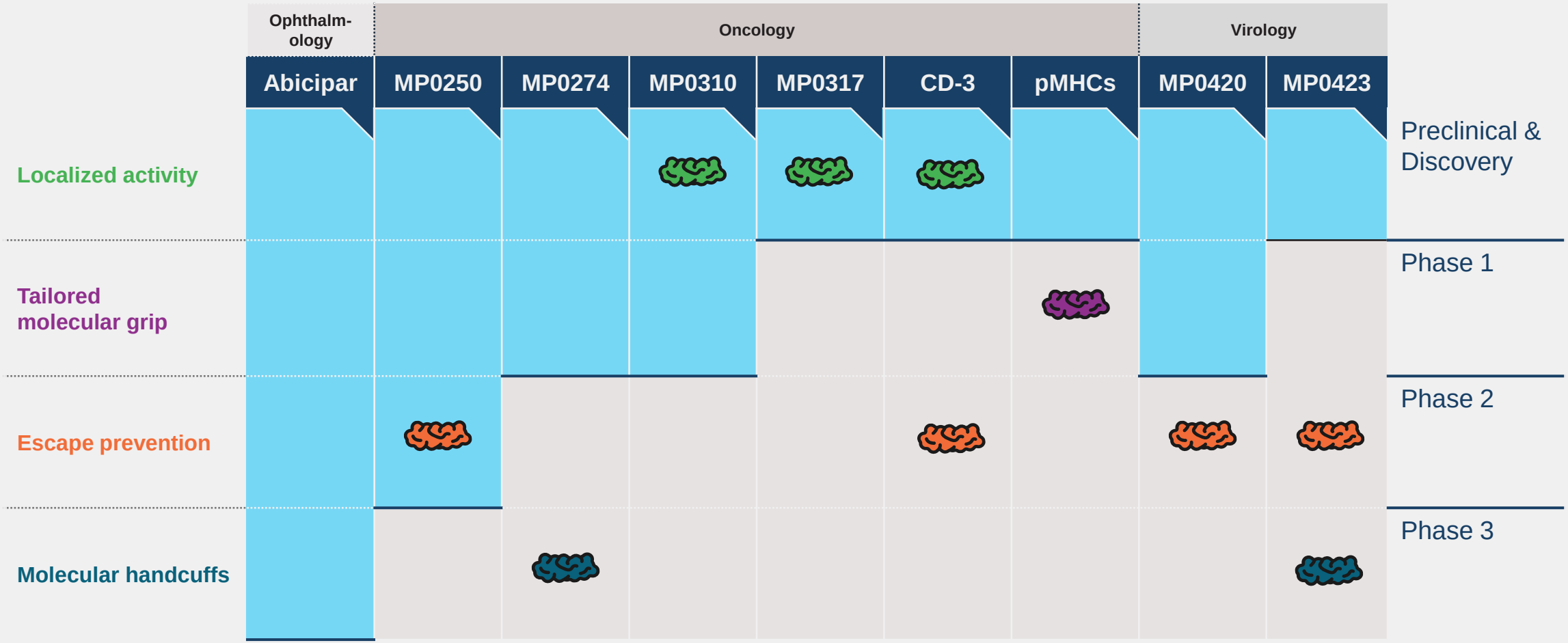


Localized Activity
- Local and temporal control of activity

Molecular Handcuff
- Full shut-down by conformational freeze

Multi-blocker to prevent escape
- Prevent escape

A Portfolio Strategy Delivering Growth And Innovation



Establishing the Platforms with First-Generation Programs

Abicipar

- Two positive clinical trials (CEDAR & SEQUOIA)
- June 2020: CRL received from FDA
- Abbvie next steps decision expected in Q1/2021

MP0250

- Biological activity in combination with Velcade in multiple myeloma
- Principle of blocking escape established
- DARPin® platform systemic POC
  - ✓ Safety and low immunogenicity
  - ✓ ½ life extension: HSA platform

MP0274

- Biological activity in a patient
- Principle of molecular handcuffs established
- DARPin® platform further validated

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

COVID-19 Program Success Opens Path for Antiviral Portfolio

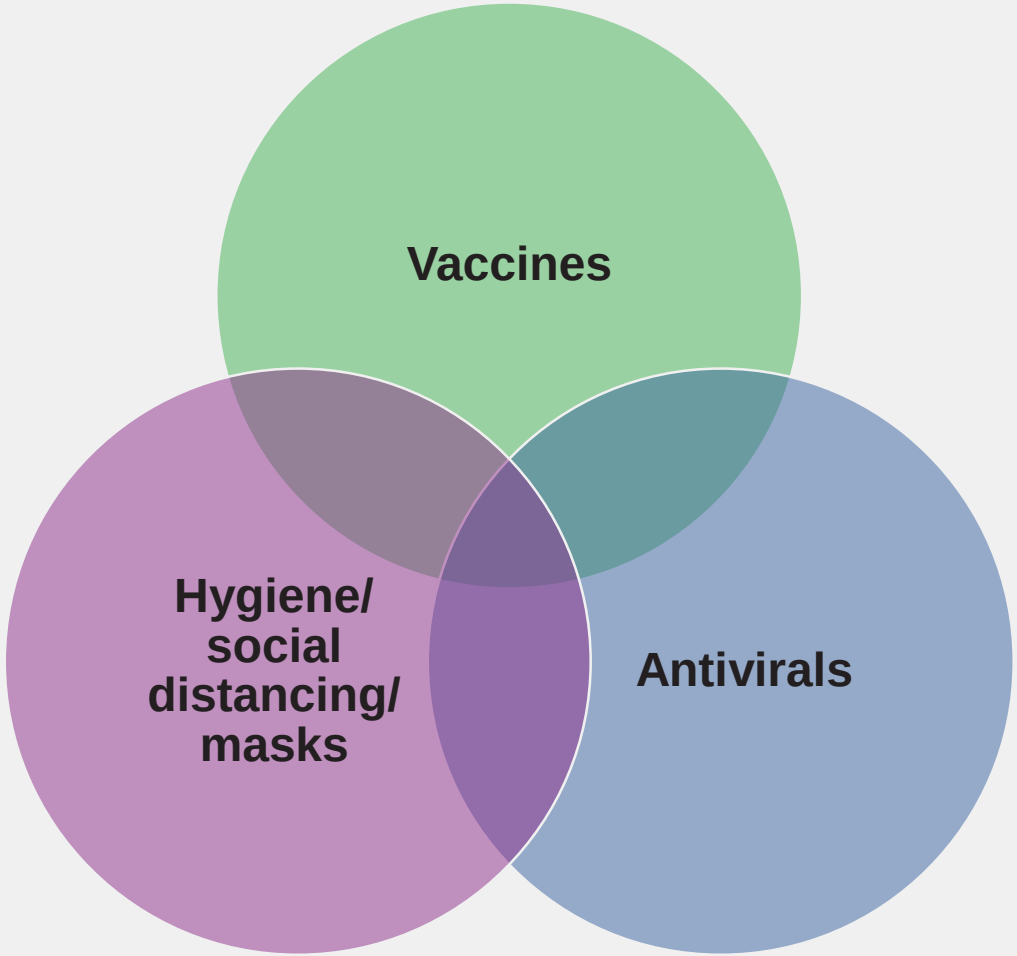
Overview: Patrick Amstutz

Global context: Lutz Hegemann, MD, Ph.D.

Global Pandemics Underscore Major Therapeutic Needs

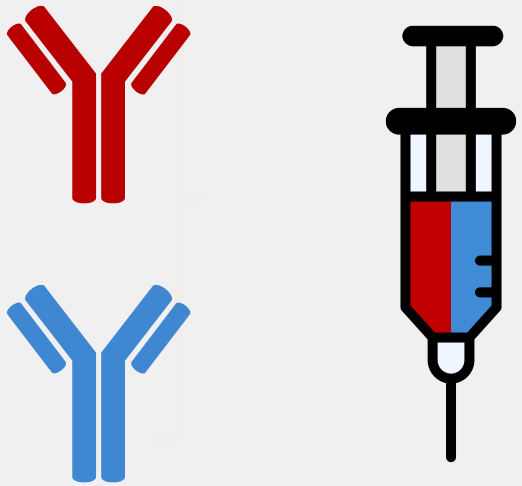
The requirements to reopen the world is a cooperative action between:

- Efficacious vaccines with swift uptake
- Responsible global citizens
- Effective and available antiviral therapies to prevent outbreaks, and to protect those who are at greater risk and will still be infected



Antibody Mixtures Are Sub-optimal Antivirals

Antibody mixture



✓ Effective

however

Monoclonal antibody drawbacks

nature

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NEWS · 11 AUGUST 2020 · CORRECTION 12 AUGUST 2020

Antibody therapies could be a bridge to a coronavirus vaccine – but will the world benefit?

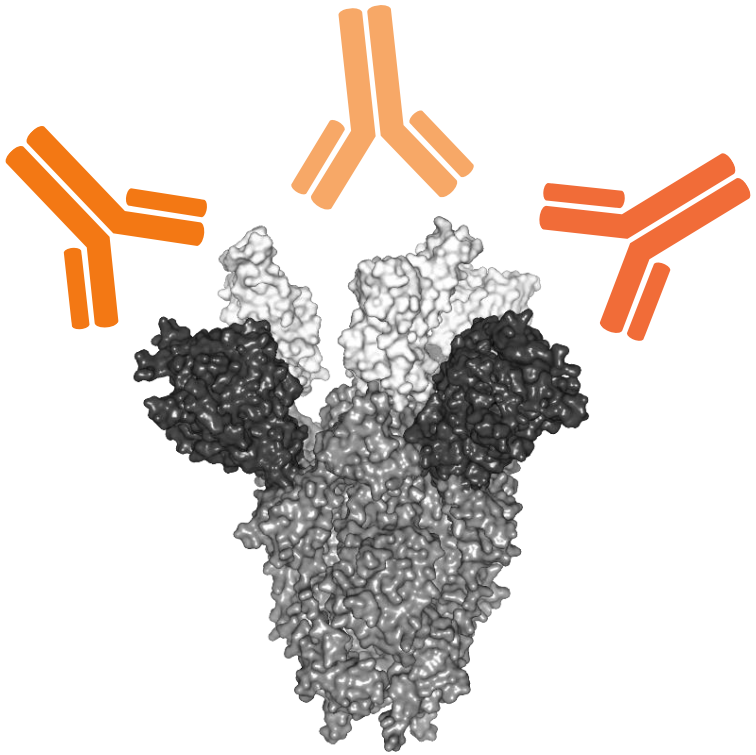
Monoclonal antibodies are complex and expensive to produce, meaning poor countries might be priced out.

X High cost

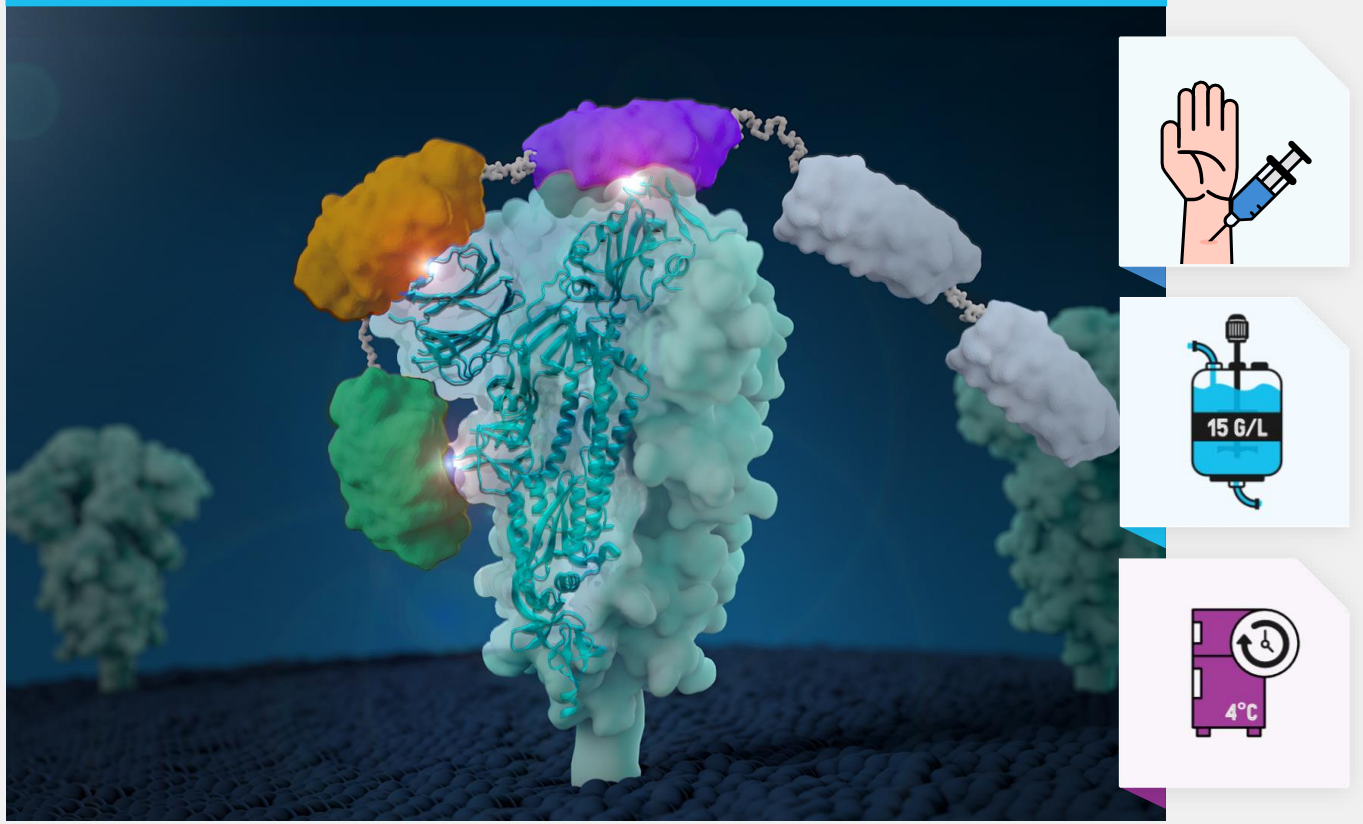
X Limited amounts

One molecule to do the work of several

Antibody Cocktail



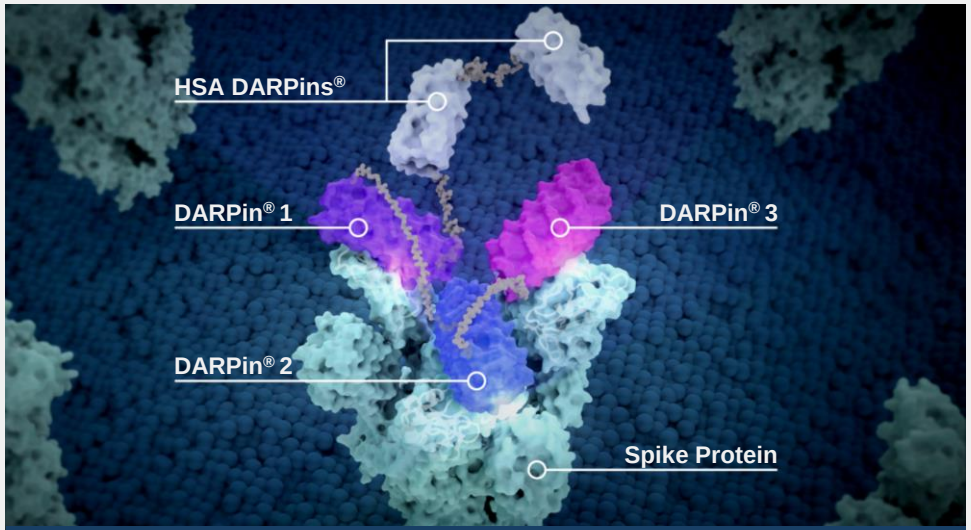
A single DARPin® with multi-specific binding



Our COVID-19 Program: Two Outstanding Candidates

MP0420 (ensovibep)– best-in-class

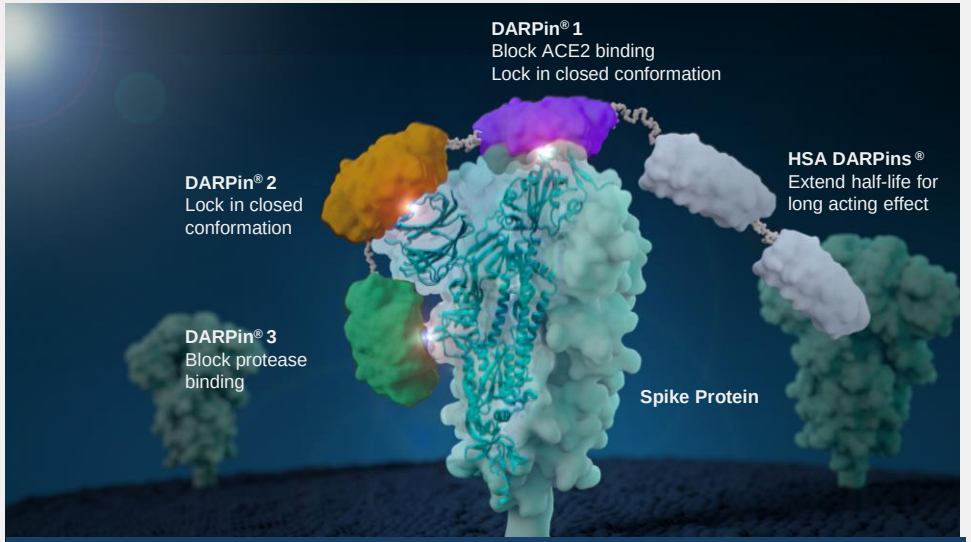
- Tri-specific DARPin® antiviral targeting the RBD for highest potency & to prevent viral escape
- Long half-life (HSA DARPins) – single injection
- Low costs and high numbers of doses available
- Potential for bolus / s.c. injection – simple application



Immediate solution for hospitalized and ambulatory settings

MP0423 – first-in-class

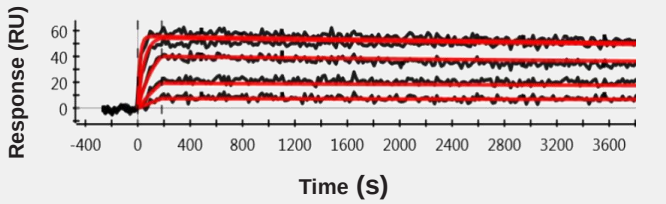
- 3 DARPins blocking different domains of the viral spike
- High activity even if RBD mutates heavily and escapes all vaccines and therapeutic antibodies
- All other benefits of MP0420



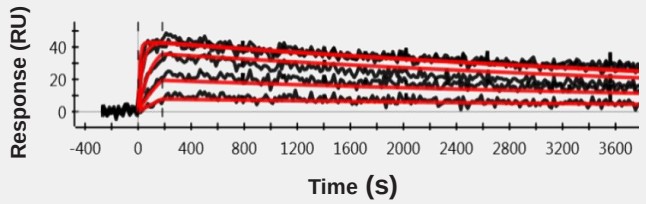
Ideal solution for stock-piling and global insurance policy for viral RBD drift

Cooperative Target Engagement Leads To Super Affinity

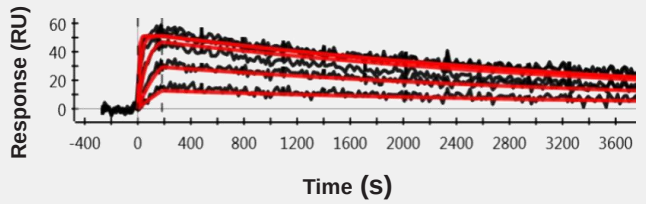
DARPin #1; 1 hour off-rate

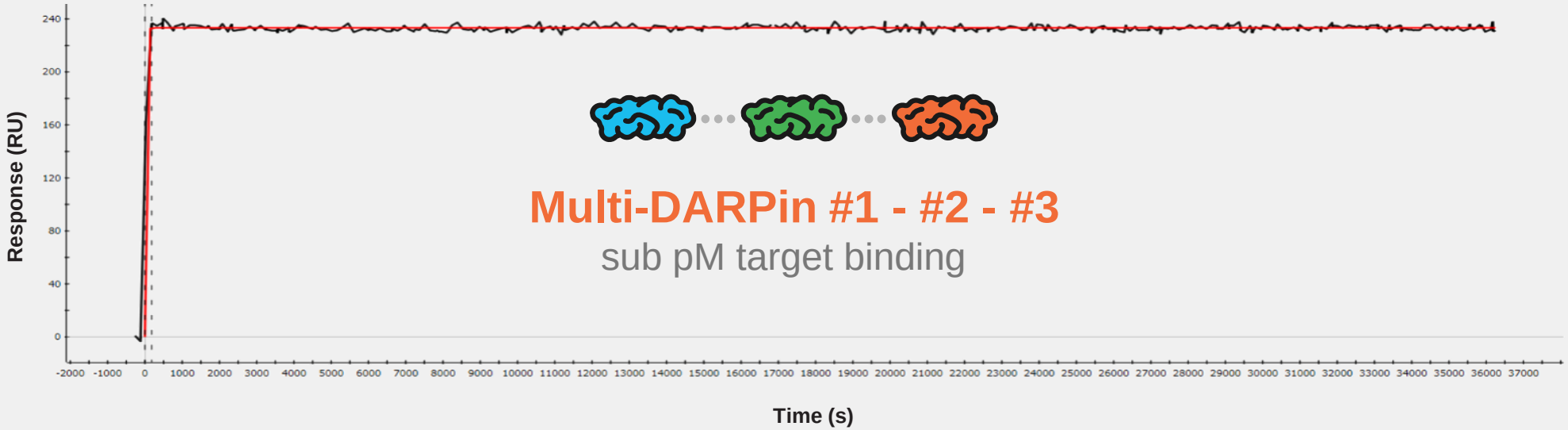


DARPin #2; 1 hour off-rate



DARPin #3; 1 hour off-rate



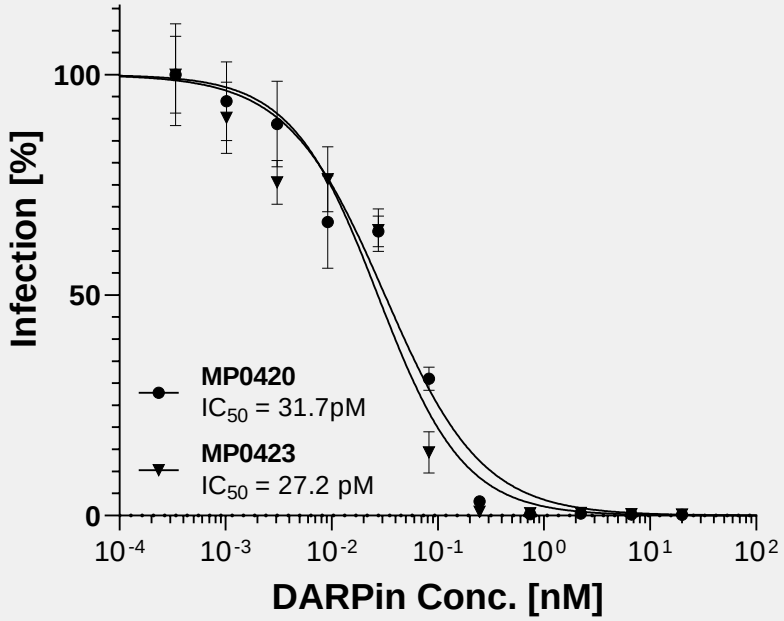


Multi-DARPin #1 - #2 - #3

sub pM target binding

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

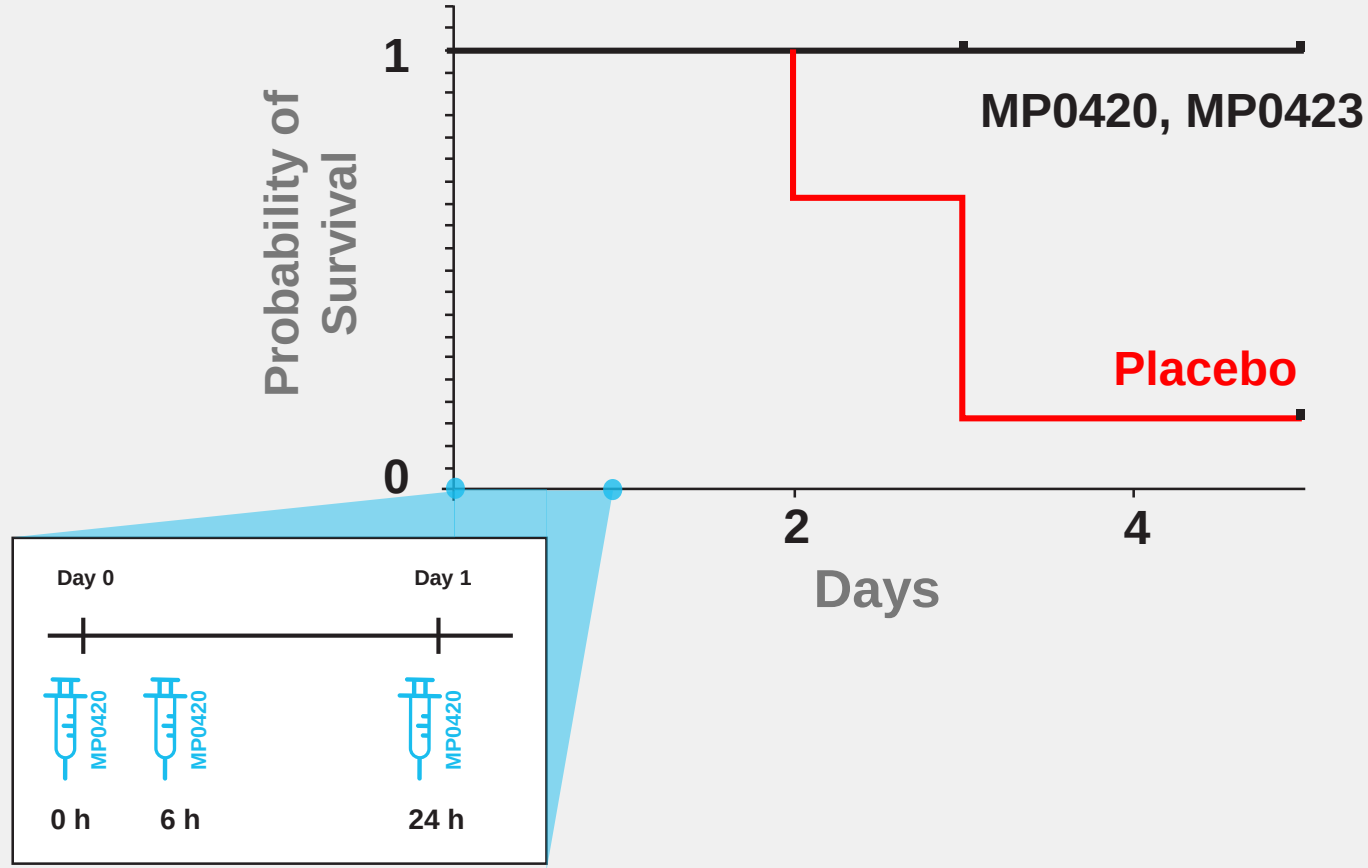
In vitro activity: Pseudotype Neutralization Assay



Highest potency

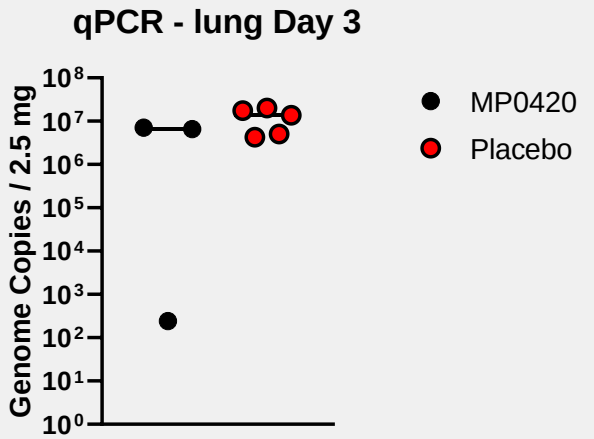
Tri-binding leads to highest affinity and potency in the low pM range; likely at the assay limit

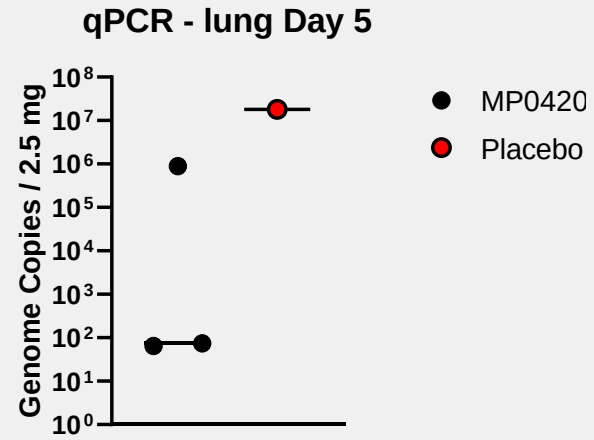
In vivo activity: Kaplan Meier Plot - Hamster Model



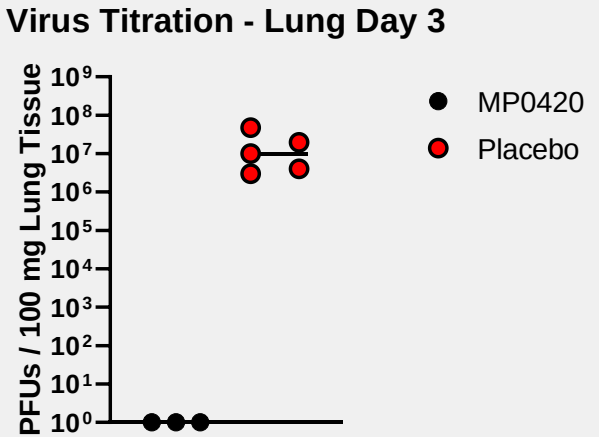
Ensovibep Blocks the Virus and Prevents Infection in the Lung

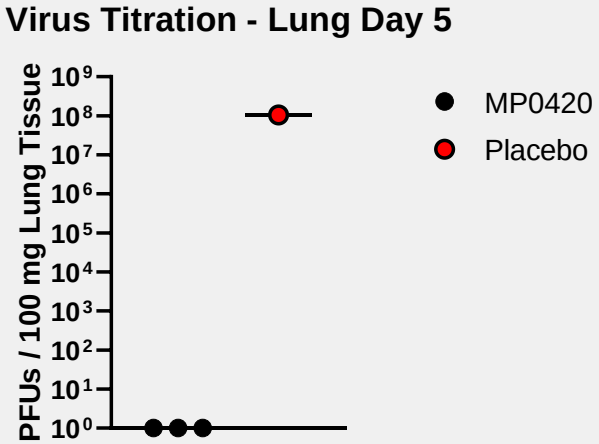
Viral titer in the lung





Viral infectivity in the lung





Ensovibep blocks viral infectivity completely

MP0420 (ensovibep) Phase 1 Ongoing

- Study initiated November 2020, first cohort fully enrolled
- 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 hAB mixture, corresponding to: 900 mg, 2.7 g, 6g
- Endpoints: Safety, tolerability and pharmacokinetics (SAD)
- Status:1st cohort completed; 2nd cohort ongoing

Full data expected by Q1 2021

* Total amount in a person with 75 kg body weight

Novartis Collaboration Highlights Strengths of Each Company

Novartis:
manufacturing, supply and logistics for global reach

Both parties commit to global access, aiming to make candidates available to all countries in need

Molecular Partners:
two multi-specific anti-COVID candidates

Novartis has the clinical expertise and capabilities fast development

Novartis Global Health

Novartis COVID-19 response

Molecular Partners R&D Day
17 December 2020

Dr Lutz Hegemann
COO, Global Health, Novartis

NOVARTIS | Reimagining Medicine

Our response to COVID-19 pandemic

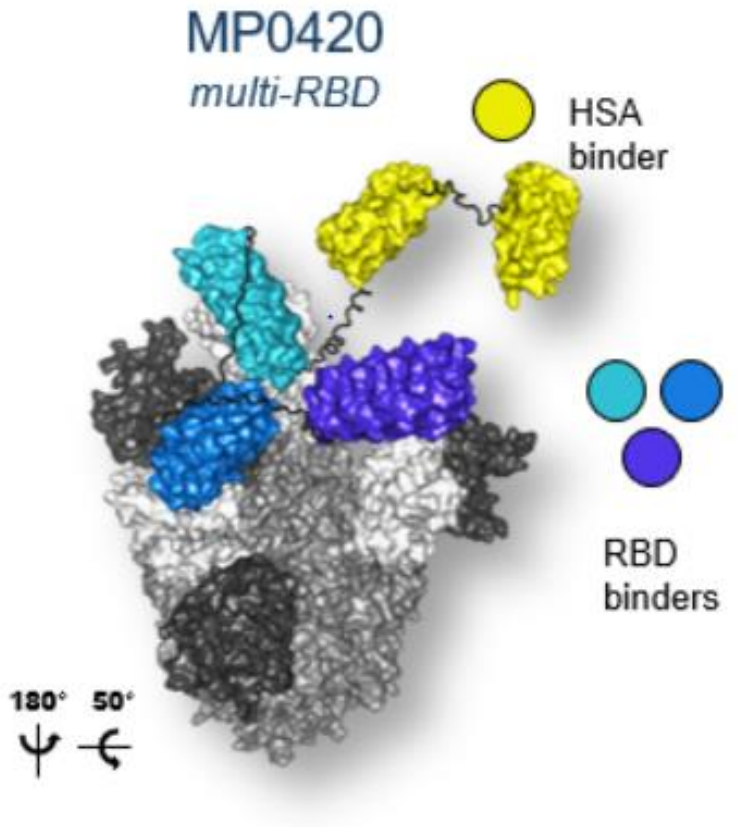
Safety	Ensuring safety and wellbeing of our associates
Resilience	Demonstrating resilience in our core operations (e.g. *supply chain, clinical trials, HCP interactions, etc.)*
Response	Supporting global pandemic response *Financial aid and donations, repurposing of existing medicines, discovery of new medicines through own efforts and partnerships*

An integrated approach will be required

Vaccines	**M**andatory to reach an epidemiological end to the pandemic. However are not a “silver bullet’ and will require continued therapeutic reinforcements
Diagnostics	**F**undamental in outbreak and case management, allowing rapid identification to respond to patient needs
Therapeutics	**C**ritical to reduce hospitalizations and death, reaching and treating patients around the world, at all stages of the disease

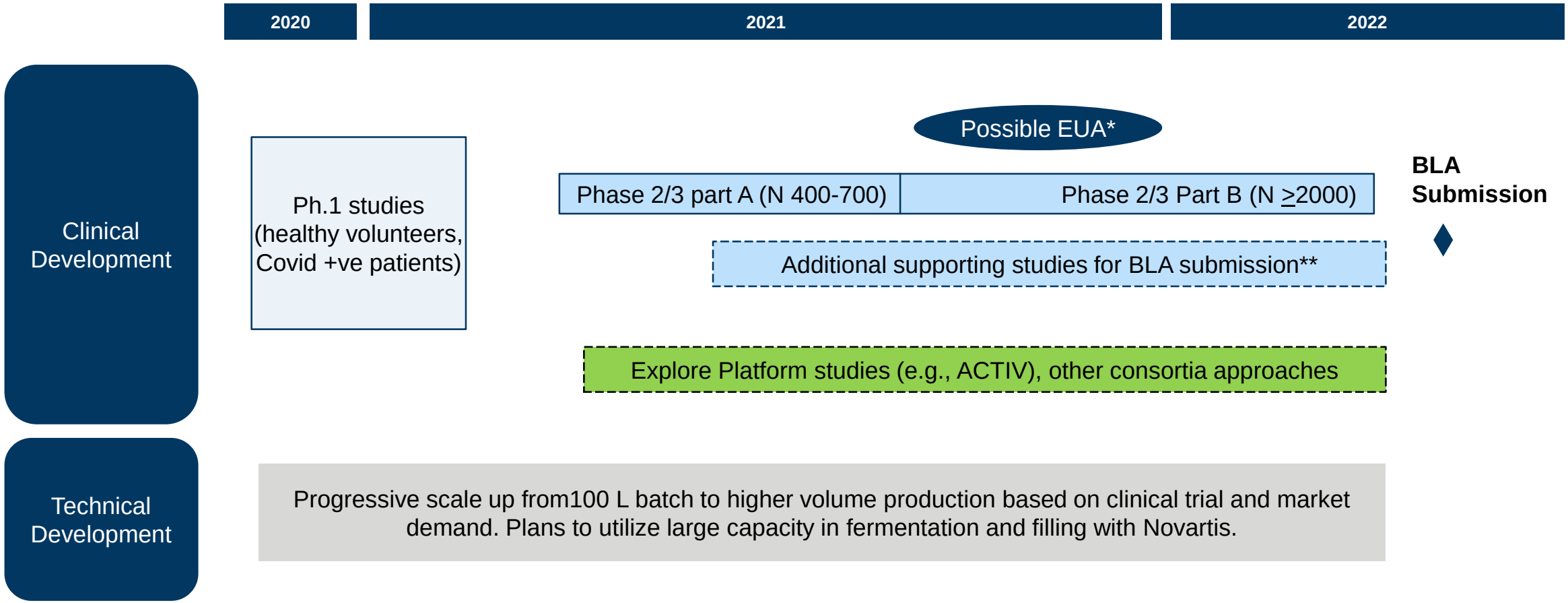
Desired characteristics of a COVID-19 therapeutic

- Can be used at different stages of the disease and in early, pre-symptomatic, high risk groups
- High potency for anti-viral effect in therapeutic setting
- Ease of administration
- Multi-epitope targeting to prevent escape mutations
- Ability to scale up production rapidly
- Good stability and suitable for storage/ transportation to LIC/LMICs



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

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Thank you

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Our Antiviral Portfolio Vision:
Broaden the use and recognition of DARPin® Antivirals

Continue toward POC in COVID in 2021 - Unlock

Clear need and capability of developing multi-specific DARPin antivirals - Expand

Pipeline analysis underway to evaluate viral opportunities of greatest unmet therapeutic need

Clinical Programs: Expanded

Nicolas Leupin, MD, MBA

One Year in Review, the Take Home Messages

1. DARPins continue to deliver on clinical design

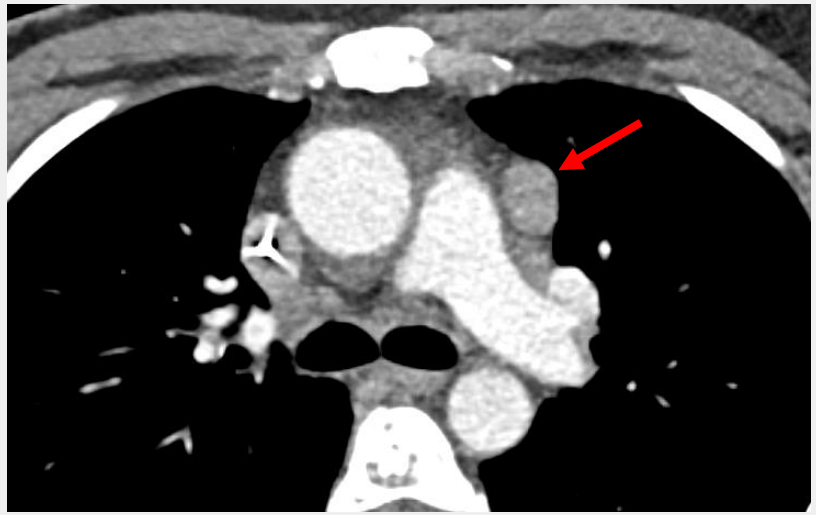
2. We are becoming very efficient at translating an idea and implementing it into the clinic

3. The path to big discoveries and breakthroughs is never easy
   - whether it's success or failure

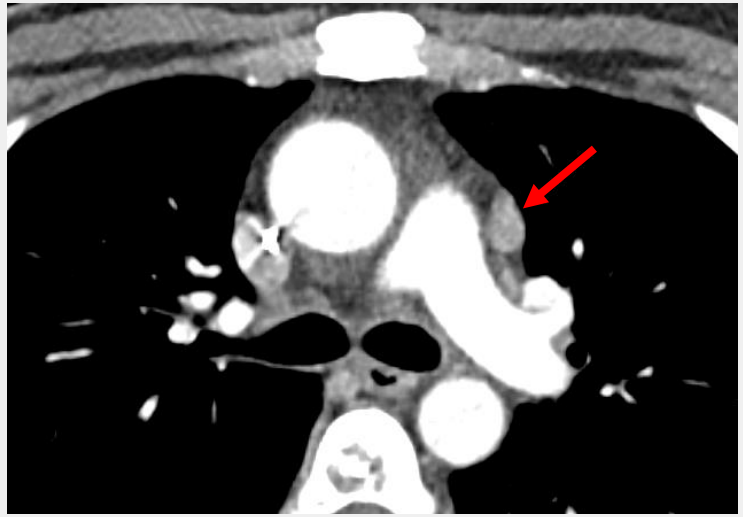
DARPins Continue to Deliver on Clinical Design

45 year old woman, 9 doses of MP0274, achieving partial response (Dec 2020)

2012 initial diagnosis	Breast cancer, stage IV
2012 to 2020	Several lines of anti cancer treatment containing Trastuzumab
Jun 2020	First dose MP0274 (12mg/kg), still ongoing



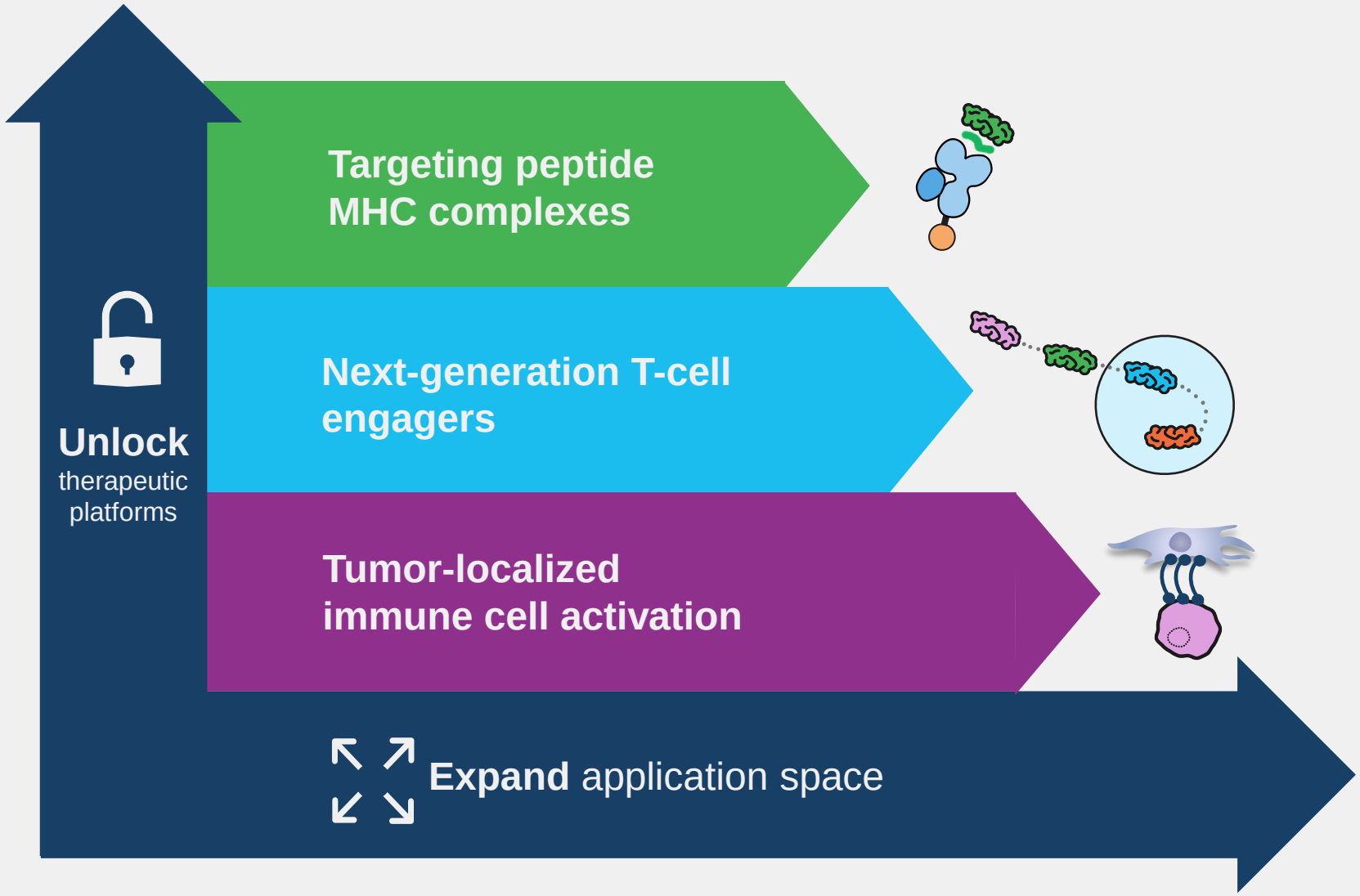
Baseline: May 2020



After 4 MP0274 doses: Aug 2020

Database snapshot on 10Dec2020; clinical data not considered clean; subject to potential change.

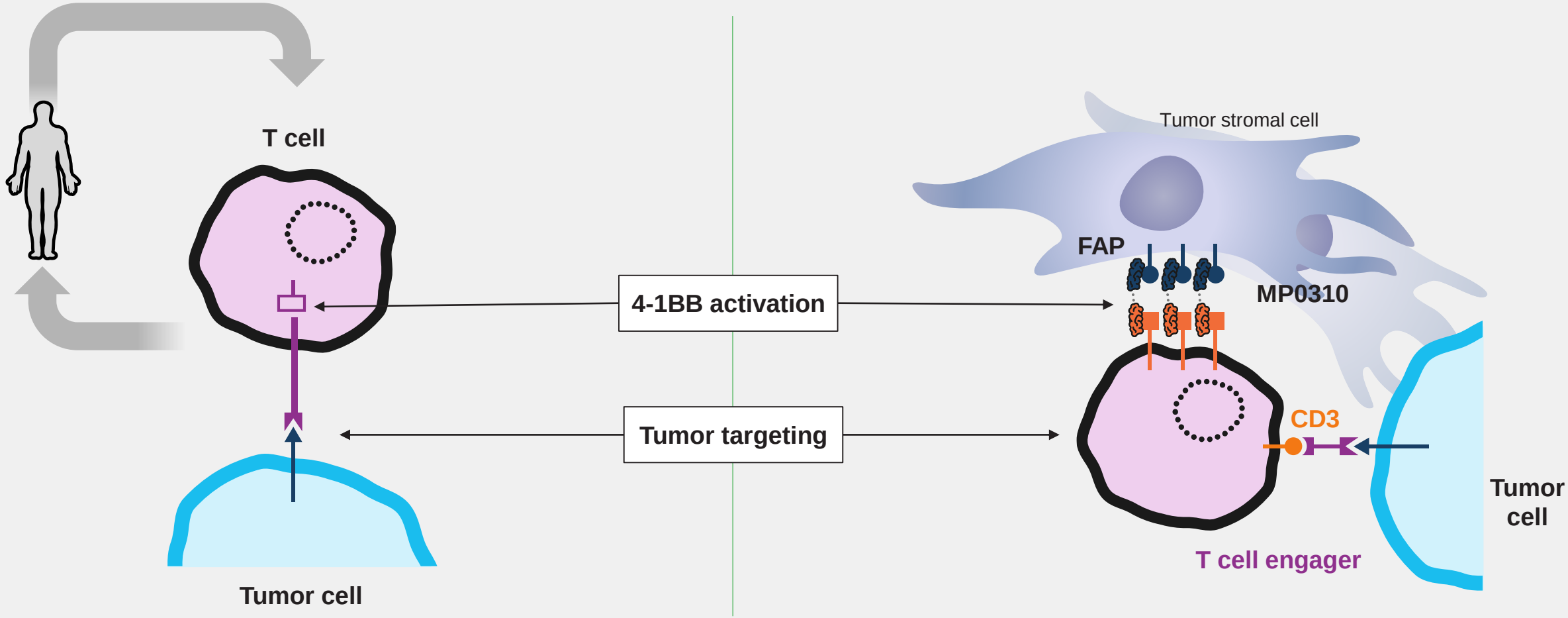
Unlock and Expand: Therapeutic Platforms



Application: Local T Cell Targeted Activation

Traditional CAR-T

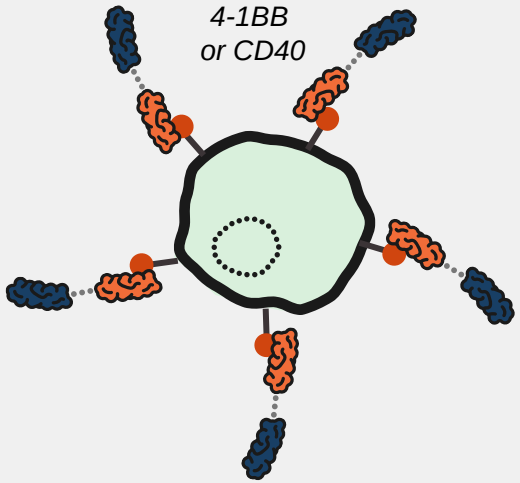
“CAR-T *in situ*”



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

BODY

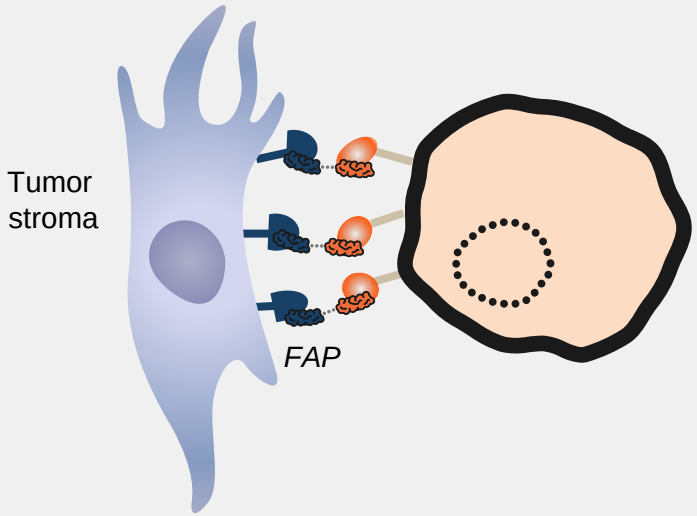
- In normal tissues, receptor is broadly distributed
- Immune cell remains inactive



VS

TUMOR

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



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

AMG 506 / MP0310 and 4-1BB Biology

4-1BB – A Potent Co-stimulatory Molecule of TNFR Family

DC
+Antigen presentation,
B7-1/B7-2, IDO, IL-12, IL-27

Macrophage
+IDO, IL-8

NK Cell
+ADCC, +IFNy

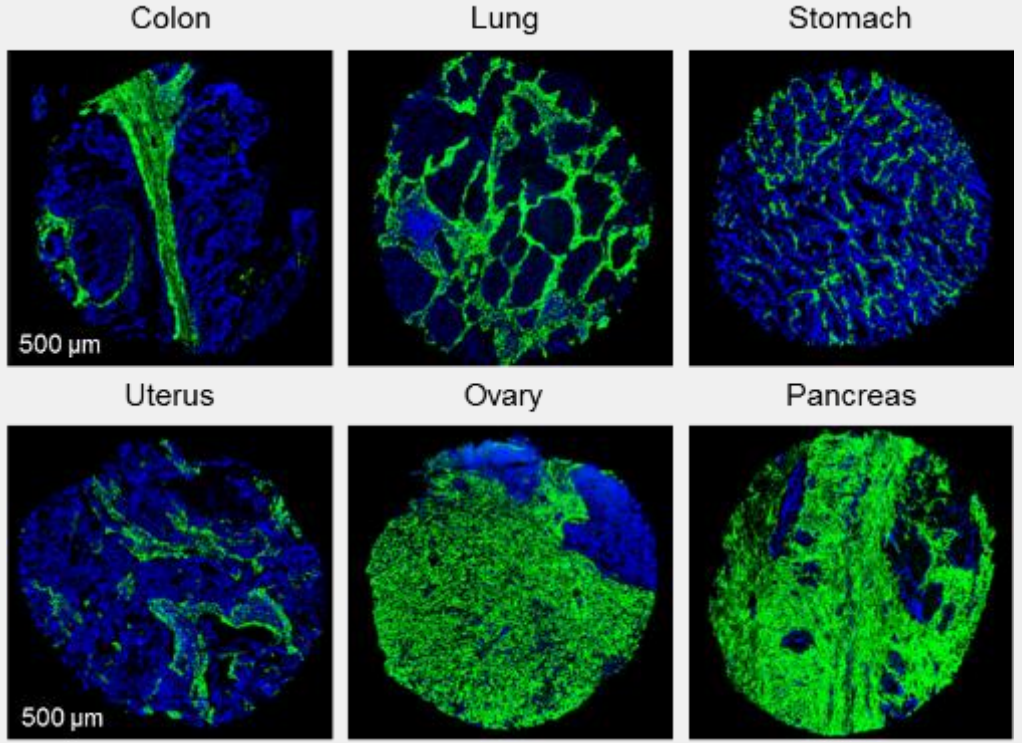
Treg Cells
Suppression, Expansion,
Polarization

CD8+ T Cells
+Cytotoxicity, +IFNy/TNFα,
+Proliferation

CD4+ T Cells
+IFNy, +Proliferation

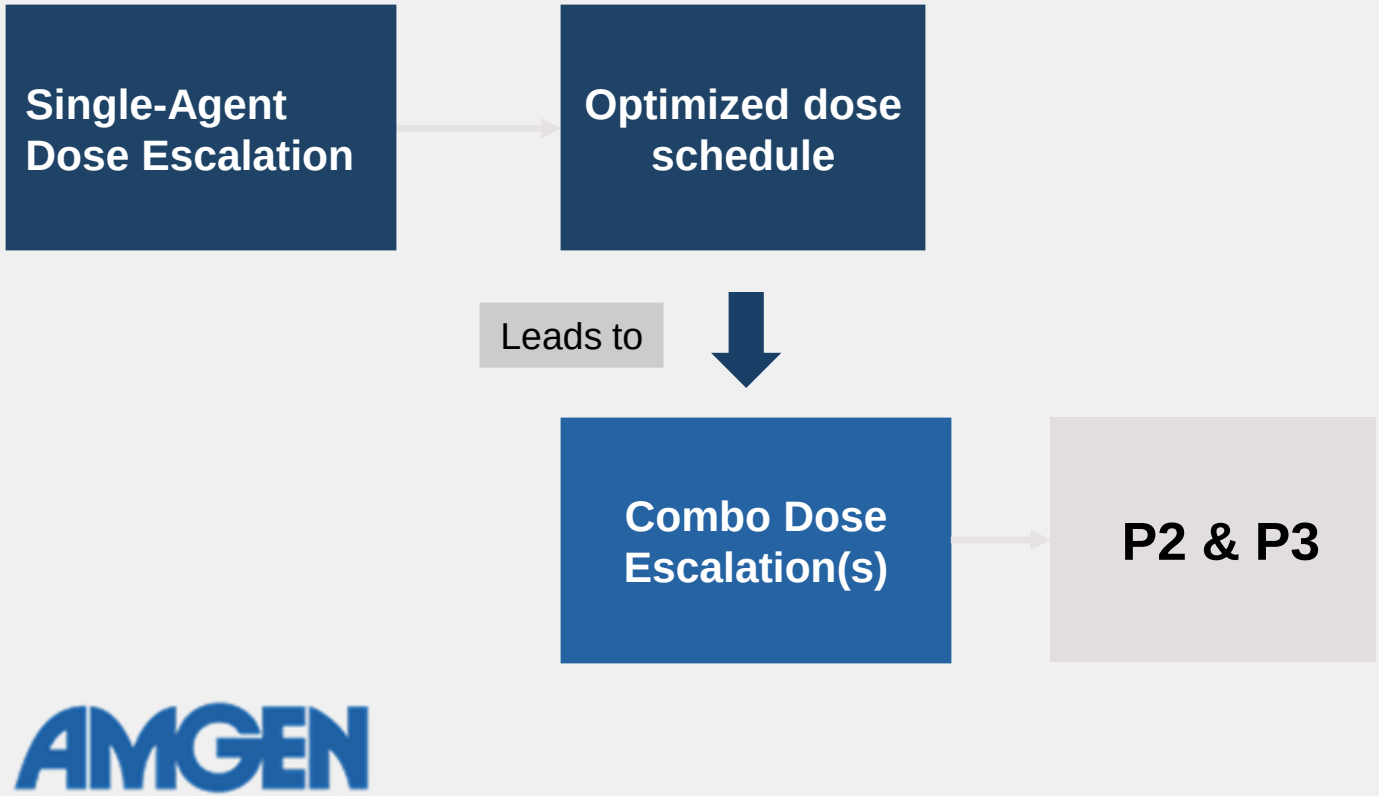
α4-1BB

FAP expression adequate for immune activation in multiple solid tumors



Human FAP, DAPI

Clinical Plan for AMG 506 / MP0310



AMG 506 / MP0310 Dose Escalation Completed

- Executed on schedule through 2020
- 22 patients enrolled, 19 presently evaluable
- 7 dosing cohorts
  - Dosing: 0.015 mg/kg to 12 mg/kg
  - 8 patients with ≥4 cycles
- **No Dose limiting toxicities (DLTs)**
- 12 patients exhibited infusion related reactions (IRR) G2-3, out of 22 enrolled.
- No other AEs of special interest

AESI	N affected pts. / N events	Max. grade
Infusion related reactions > G 1*	12 / 19	3
Cytokine release syndrome – any	0	-
Hepatitis – any	0	-
Pneumonitis – any	0	-
Respiratory distress – any	0	-
Colitis – any	0	-
Endocrinopathies > G 2	0	-
Skin Rash > G 2	0	-
Tumor lysis syndrome – any	0	-
Nephritis > G 1	0	-
Auto-immune disease > G 1	0	-

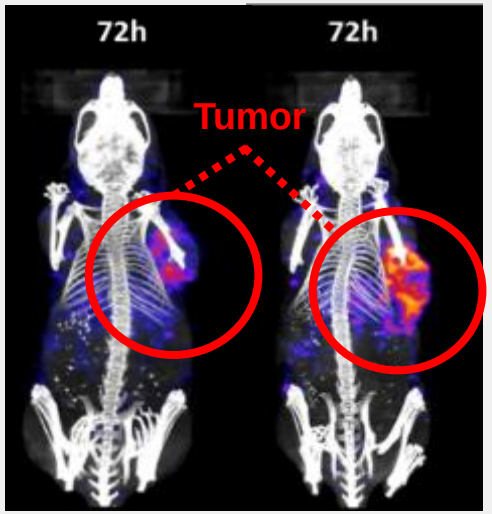
* Not included here: 1 IRR event G1;

Data as of 30 Nov 2020

Combination of AMG 506 / MP0310 and TAA x CD3 Bi-Specific Results in Significant Increase of Intratumoral CD8+ T Cells

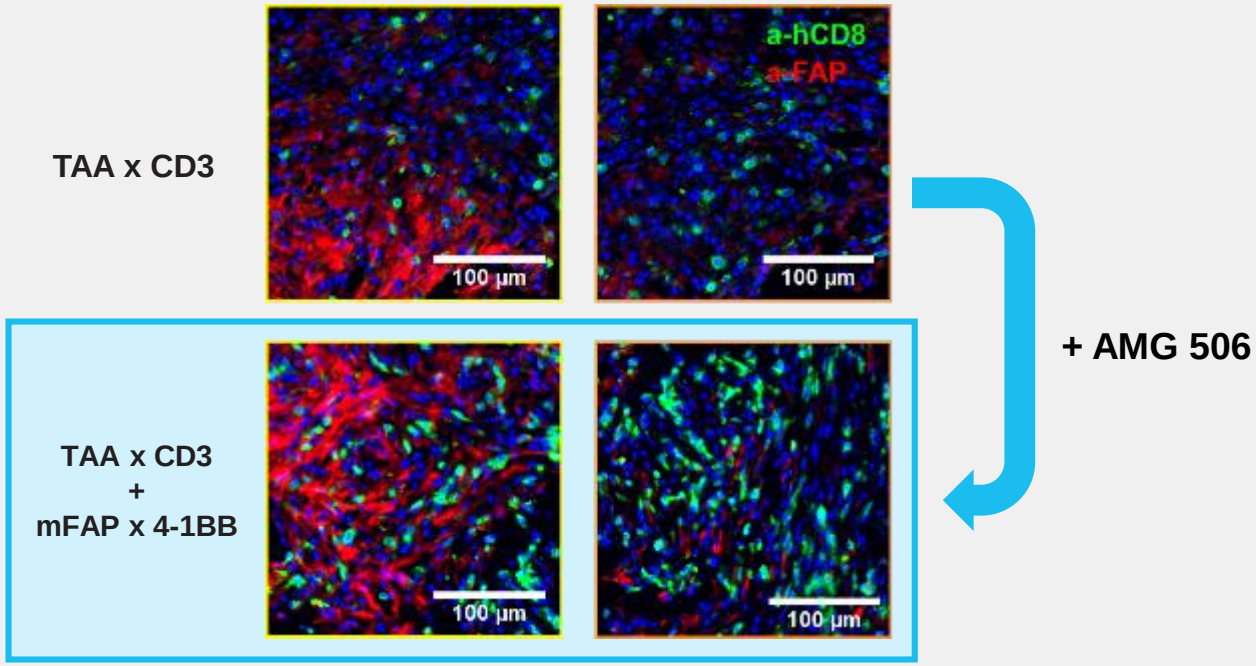
FAP-Mediated Tumor Accumulation of AMG 506

HT-29-T-implanted NSG mice



no-FAP x 4-1BB mFAP x 4-1BB

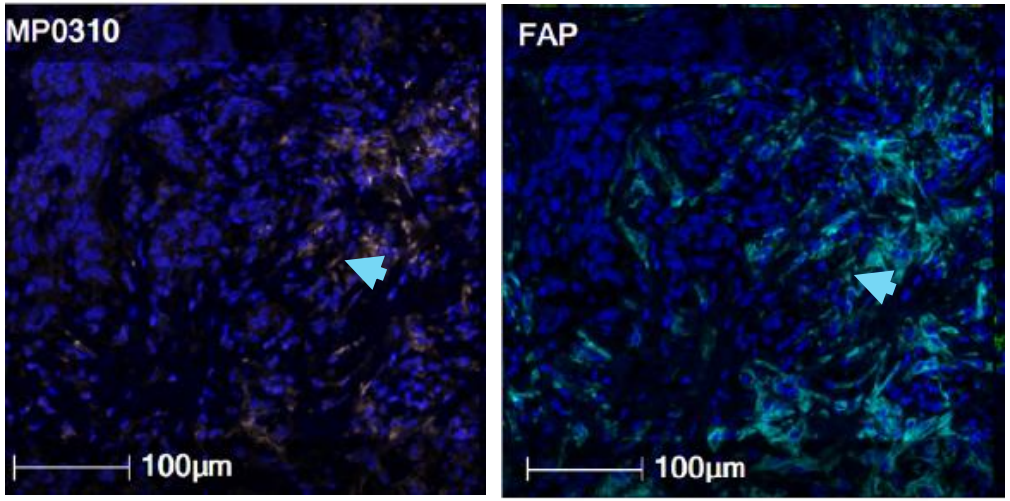
Intratumoral CD8 T cells



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

MP0310 (0.5mg/kg) colocalizes with FAP

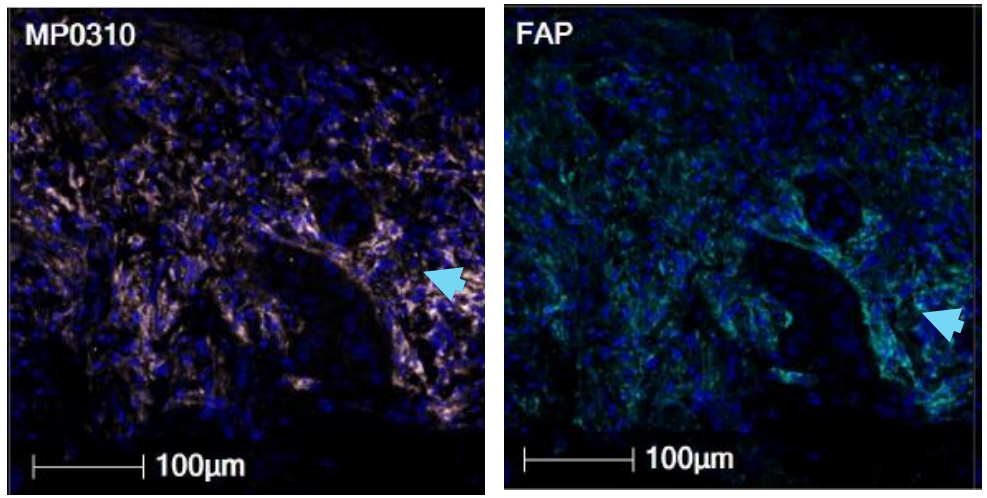
MP0310 < FAP



Endometrial carcinoma (Liver metastasis), C1D15

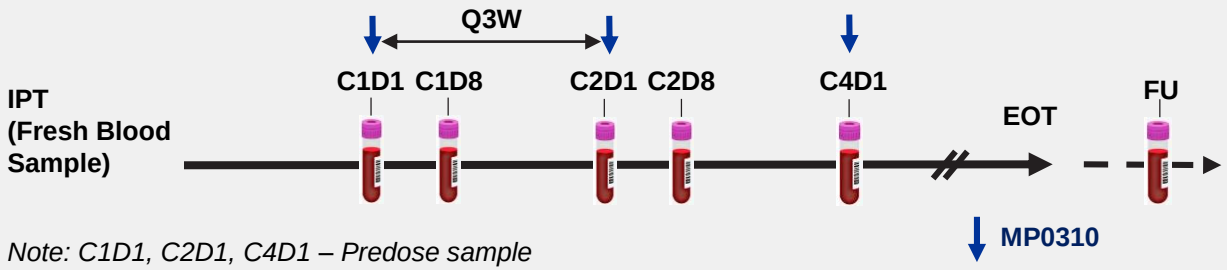
MP0310 (5mg/kg) saturates FAP

MP0310 > FAP



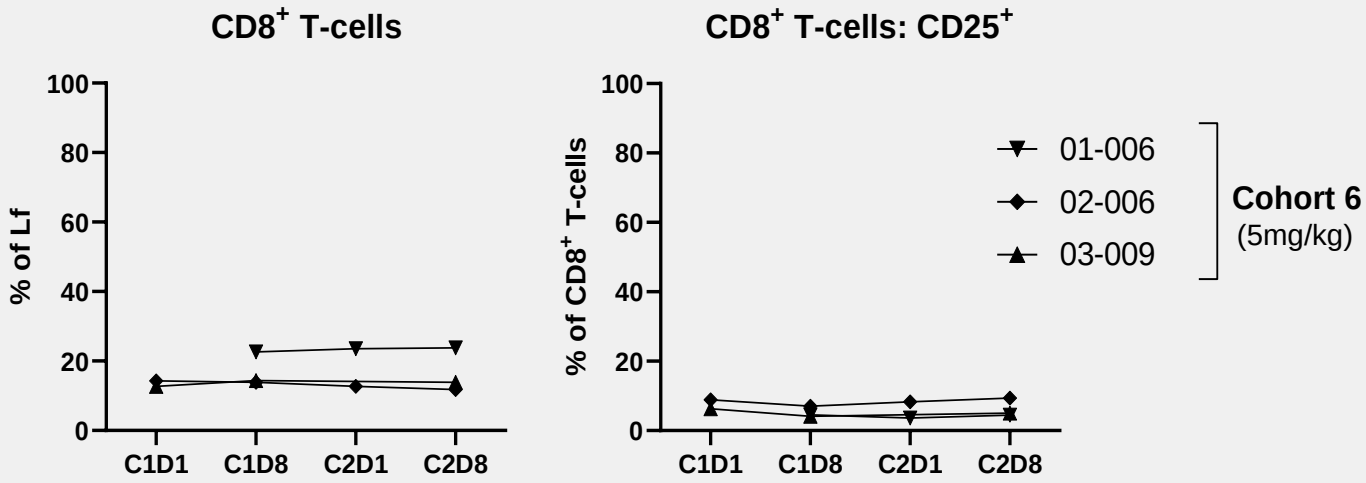
NSCLC (lung), C1D15

AMG 506 / MP0310 Does not Activate T and NK Cells Off-Target



Note: C1D1, C2D1, C4D1 – Predose sample
EOT: end of treatment, FU: follow up sample

No significant changes over time in immune cell subsets in periphery



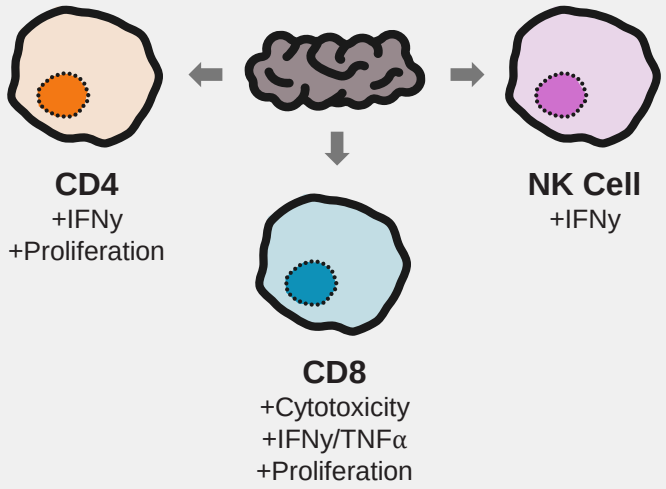
Immune cell subset	Marker
T-cells	CD3
$CD4^+$ T-cells	CD4
$CD8^+$ T-cells	CD8
NK cells	CD3-, CD56
NKT cells	CD3+, CD56
Treg	CD25, CD127dim
B-cells	CD19
Activation	CD25
Activation	PD1

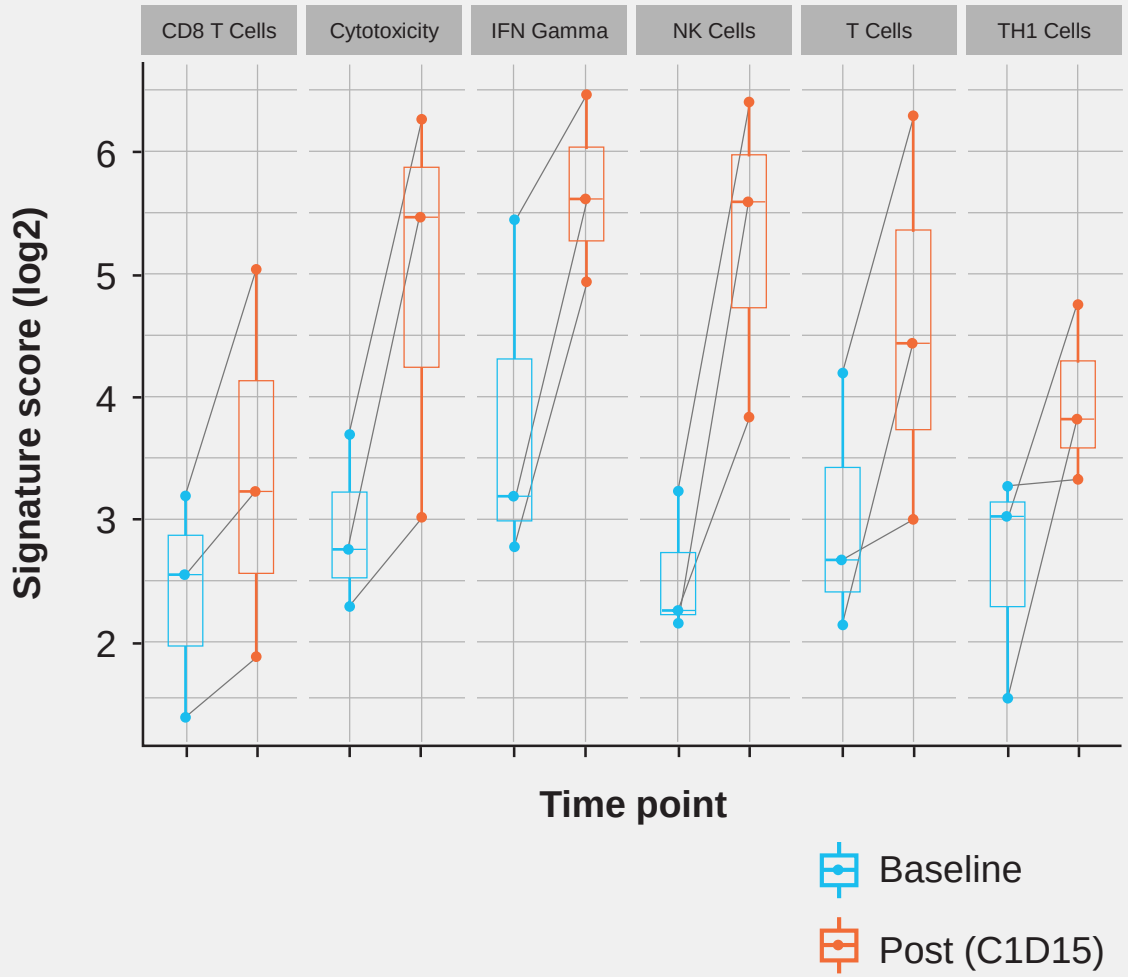
AMG 506 / MP0310 Dose Escalation Completed

- 22 patients enrolled
- 19 presently evaluable
- Typical Phase I population
  - heavily pretreated
  - with different cancer indications
- 8 patients with ≥4 cycles
- 9 patients with PD
- 9 patients with SD
- Cohort 7 not evaluable yet

Cohort	Patient ID	Cancer type	Cycles	Best Response
1	03-001	Mesothelioma	4	SD
0.015mg/kg	03-002	Cutaneous squamous cell	5	SD
	03-003	Mesothelioma	4	SD
2	02-001	Ovarian adenocc	4	PD
0.05mg/kg	01-001	Pancreatic adenocc	3	SD
	03-004	Pancreatic adenocc	2	PD
3	03-005	Endometrial adenocc	2	PD
0.15mg/kg	01-002	Pancreatic adenocc	2	PD
	02-003	Pancreatic adenocc	2	PD
4	03-006	Mesothelioma	5	SD
0.5mg/kg	02-004	Pancreatic adenocc	3	uPD
	01-003	Endometrial adenocc	2	PD
	02-005	Melanoma	5	SD
5	01-004	Adenocc colon	2	PD
1.5mg/kg	03-007	Mesothelioma	6	SD
	03-008	Mesothelioma	4	SD
6	03-009	NSCLC	2	SD
5mg/kg	01-006	Melanoma	2	PD
	02-006	H&N scq.cell cc	2	PD
7	01-007	Adenocc colon	2	Pending
12mg/kg	03-010	Mesothelioma	2	Pending
	02-007	Cervical	1	Pending

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





↑ T and NK population
↑ IFNγ activation and cytotoxicity observed in Cohort 3

AMG 506 / MP0310 – Key messages, Biomarkers

Target occupancy

- **Tumor (mIF)**
  - MP0310 in tumor tissue observed **first time** in cohort 4 (0.5mg/kg) and **colocalizes with FAP**
  - MP0310 accumulates in the tumor in **dose dependent** way; at 0.5 mg/kg MP0310, 50% FAP is occupied; at higher dose (5 mg/kg), MP0310 saturates FAP
- **Blood receptor occupancy (RO):**
  - 41BB RO in fresh blood shows good correlation with PK data

PD activity

- **Tumor (Gene expression):**
  - Significant **immune activation** across multiple immune cells **as expected** by MoA for MP0310
  - **Reduction of myeloid related inhibitory signals** observed
- **Blood (IPT):**
  - For all dose levels tested so far, **no activation of immune cell in the periphery**

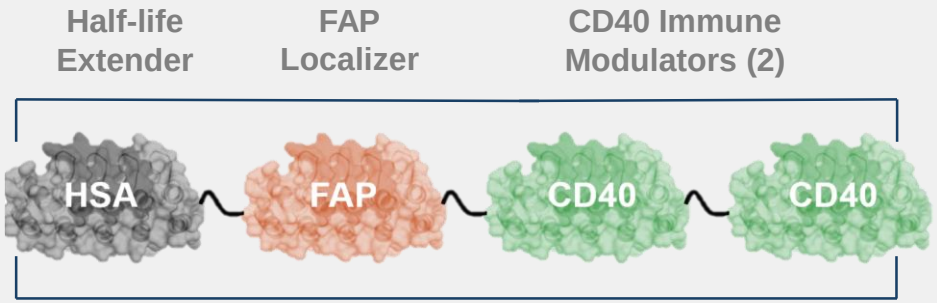
AMG 506 / MP0310 – Key Messages

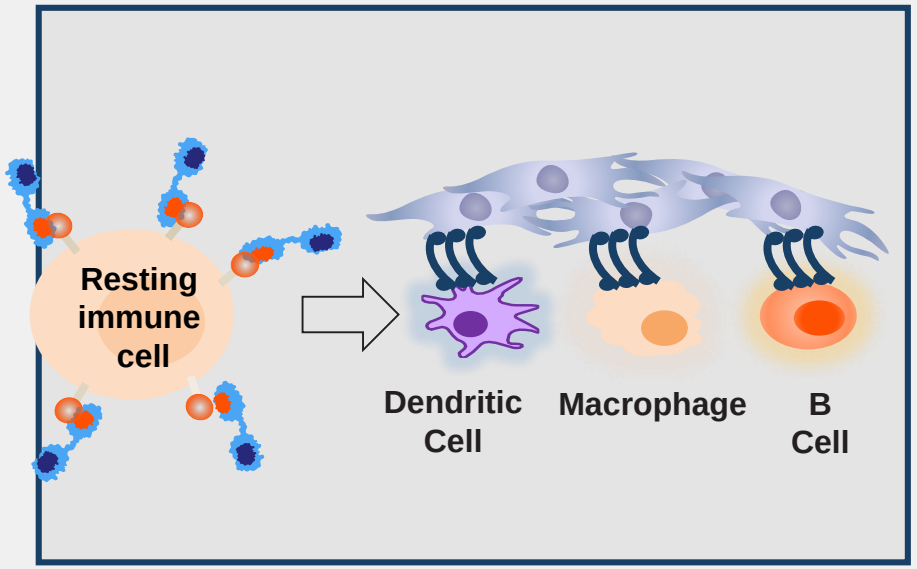
1. **Good safety profile without major systemic toxicity**
    a. No liver toxicity, no systemic activation of immune cells
    b. IRRs frequent but manageable
2. **MP0310 is observed in tumor tissue**
3. **Tumor biopsies show tumor-localized immune response consistent with the MoA** of MP0310
4. **PK profile is dose-dependent** but needs further optimization

Conclusion: MPAG is delivering on this complicated and exciting target

MP0317 and CD40 Biology

MP0317: Localized Activation of CD40



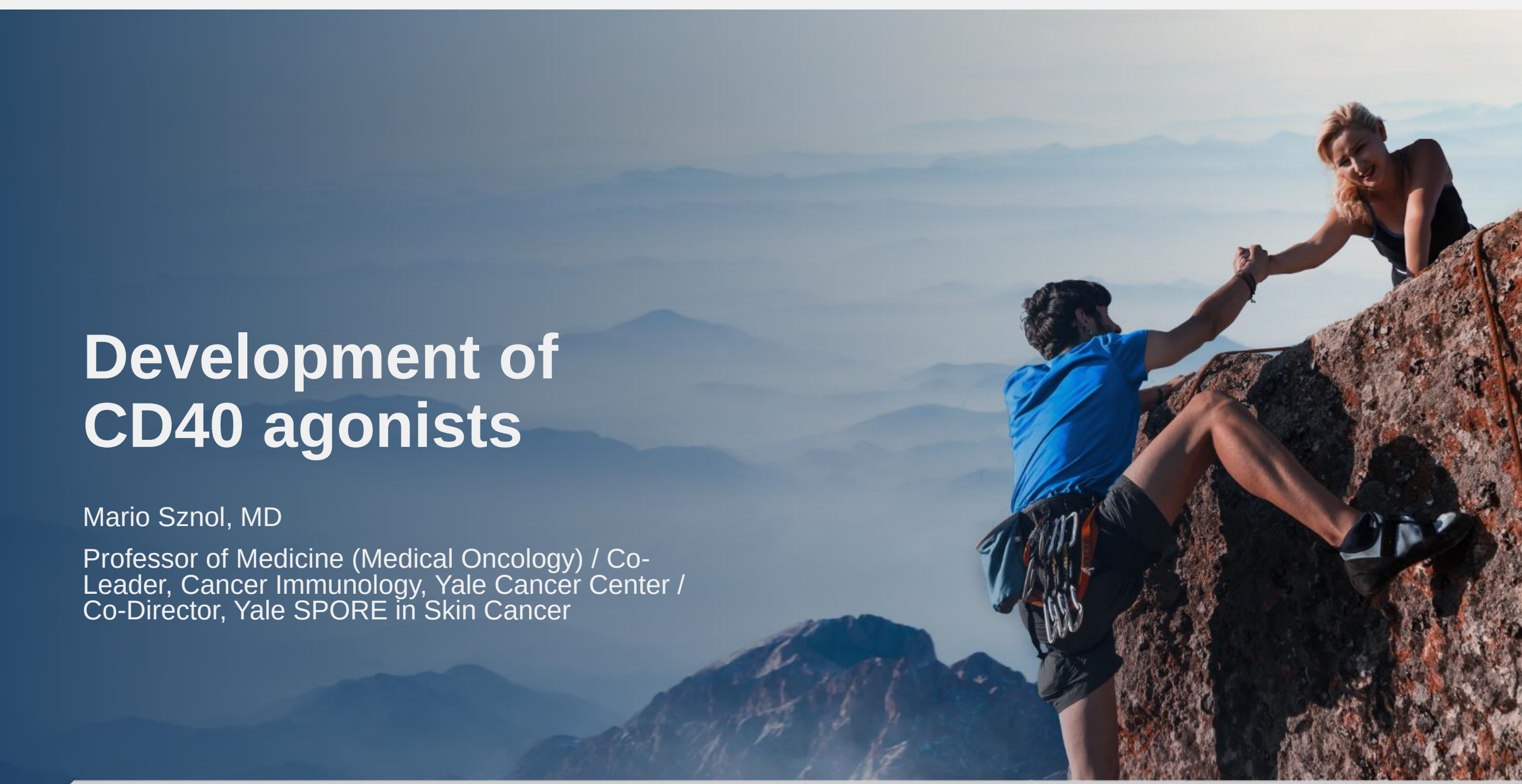


- CD40 serves pivotal role in the immune response via interactions between T cells and antigen-presenting cells
- Novel mode of action: Localized activation of CD40 in a FAP dependent manner, potentially avoiding systemic toxicity, and optimized dosing.
- Additional recruitment of dendritic cells, macrophages, and B cells should allow for robust immune response in the tumor
- Novel trial designs may allow for rapid POC

Development of CD40 agonists

Mario Sznol, MD

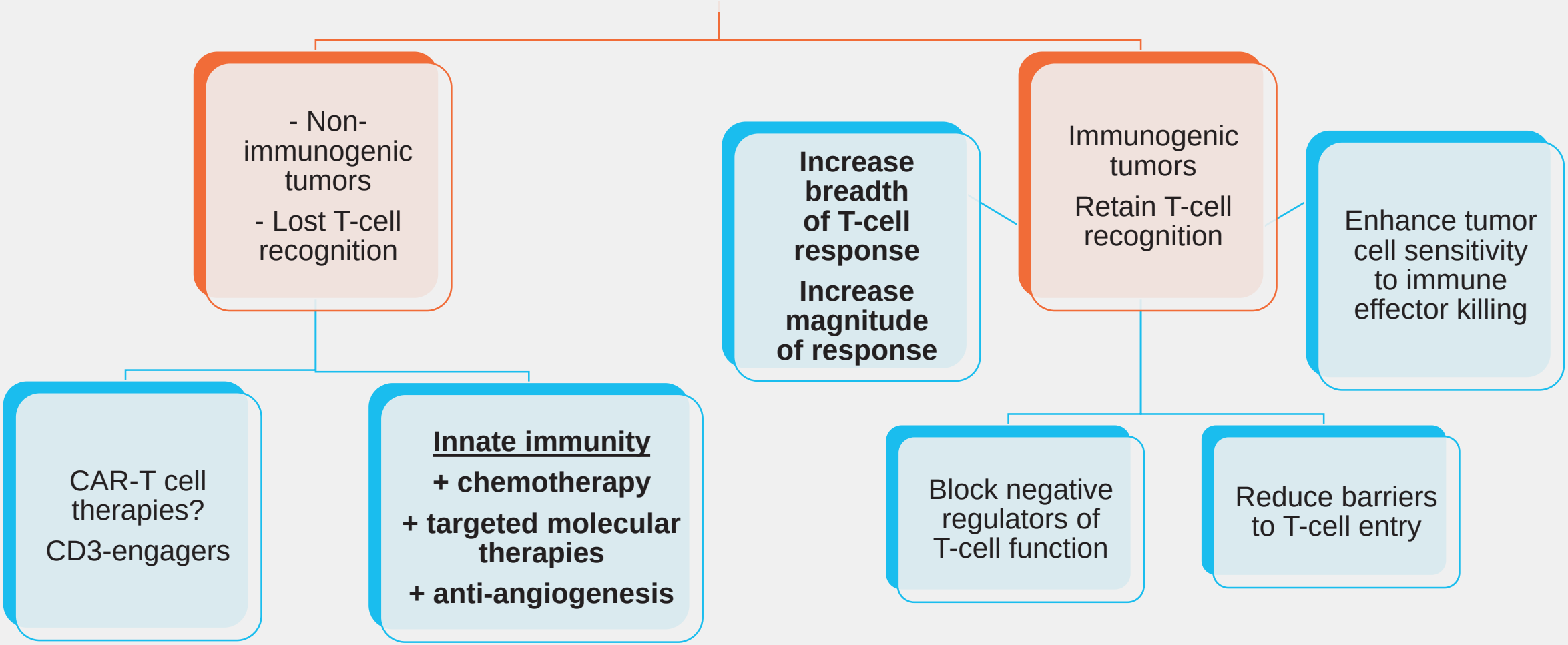
Professor of Medicine (Medical Oncology) / Co-Leader, Cancer Immunology, Yale Cancer Center / Co-Director, Yale SPORE in Skin Cancer



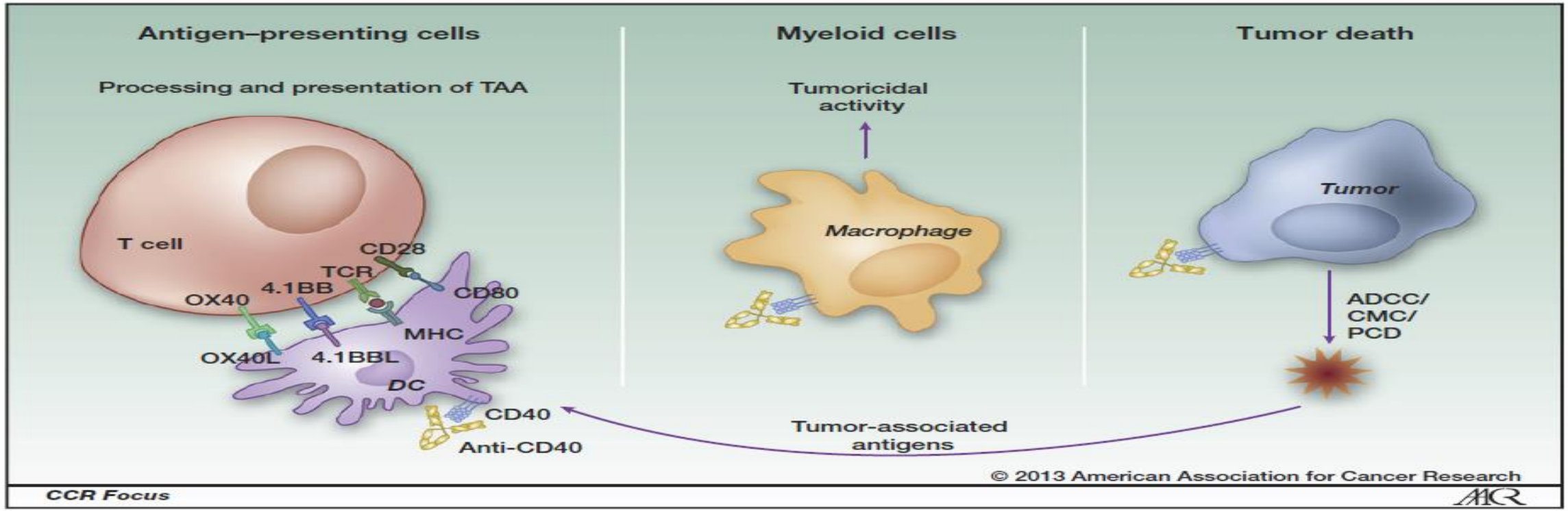
Disclaimer and Experience with CD40 pathway

- Consultant for Molecular Partners
- Consultant for other companies developing CD40 agonists
- Personal clinical experience with APX005M

Improving Anti-tumor Immunity



Agonistic CD40 Antibodies and Cancer Therapy



CD40 present on subset of APC, myeloid cells, B cells, some tumor cells, platelets, fibroblasts, and endothelial cells.

Clin Cancer Res; 19(5); 1035–43. 2013 AACR.

Agonist CD40 may address major mechanisms of resistance

CD40 agonist on macrophages

Increase phagocytosis
Alter tumor promoting properties

Innate immunity
+ chemotherapy
+ targeted molecular therapies
+ anti-angiogenesis

CD40 agonist on dendritic cells/antigen-presenting cells

Increase MHC expression
Increase co-stim (CD80/CD86)
Increase IL-12

- **Increase breadth of T-cell response**
- **Increase magnitude of response**

Antibody Agonist CD40 Agents in Development

- CP-870,893/RO7009789
- APX005M
- ADC-1013
- Chi Lob 7/4
- SEA-CD40
- CDX-1140

Exclusive of bispecifics

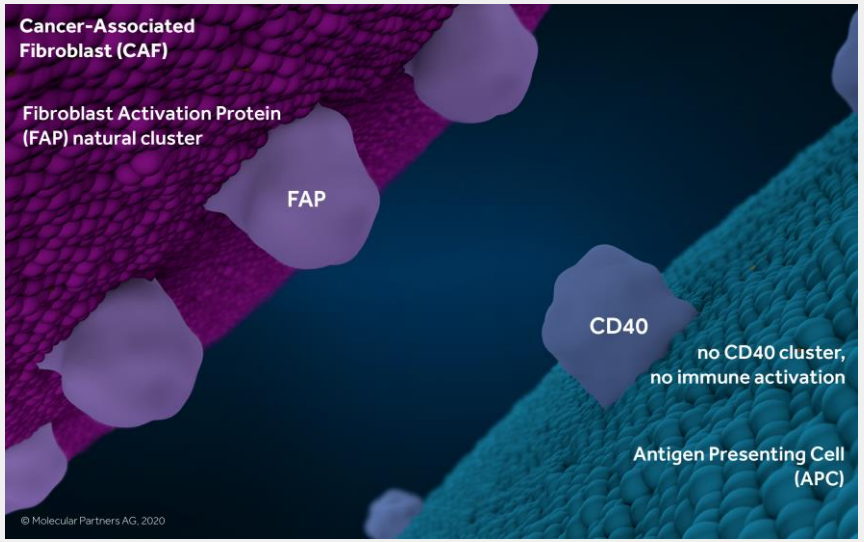
Summary of Clinical Data

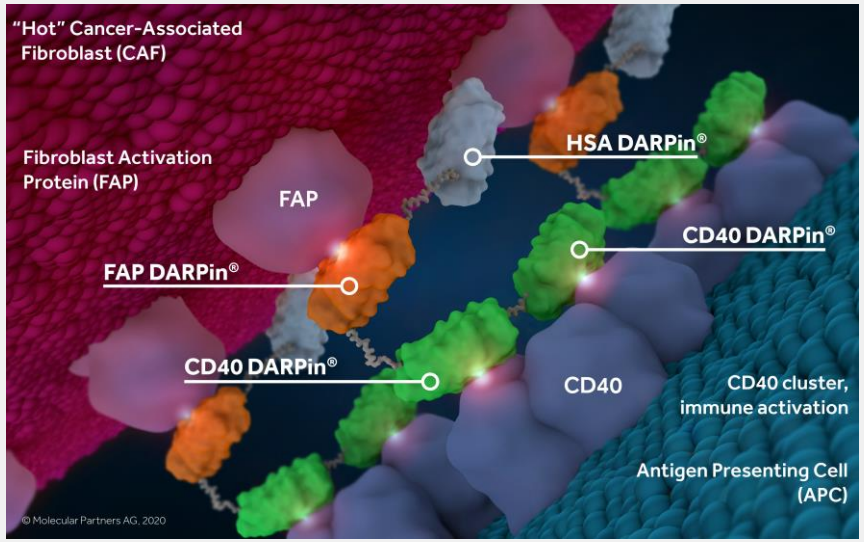
- Low MTD
- Relatively short half-life
- Tolerable adverse events including limited CRS, mild thrombocytopenia, and LFT elevations
- Single agent activity in melanoma
- Activity (+ anti-PD-1) in anti-PD-1 resistant melanoma
- Promising combination activity with gemcitabine and chemotherapy + anti-PD-1 in pancreatic cancer
- Overall limited clinical development as single agent or in combination

CD40 Target - Opportunities and Challenges

- Large in vivo sink + low MTD
  - potential to increase activation within tumor with novel tumor targeted approaches
- Critical/non-redundant target for a subset of patients
  - but may still require combinations for optimal anti-tumor activity
- Promising combinations in preclinical models (not yet tested in clinic)
  - With TLR agonists +/- vaccine
  - + interleukin-2
- Possible enhancement of adoptive cell therapy activity
- For many strategies targeting monocyte/macrophages/myeloid cell/APC/DC, addition of CD40 likely to enhance biological effect
  - Non-T-cell + T-cell dependent activity in chemotherapy/targeted therapy combinations are promising areas of clinical investigation
  - Combination with radiation is another potential area for synergy

CD40 requires clustering for activation

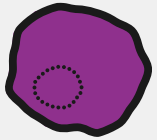




- Efficient signaling through CD40 requires high level of cross-linking
- **Our solution:** a FAP x CD40 bispecific molecule binding a densely expressed tumor associated antigen for clustering

MP0317: FAP-dependent Activation of Specific Immune Cells

A

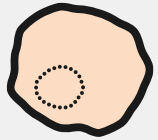


Dendritic cells:

CD86 ✓ IL-12 ✓

CD83 ✓ CD80 ✓

B



Macrophages:

TNFα ✓ IL-12 ✓

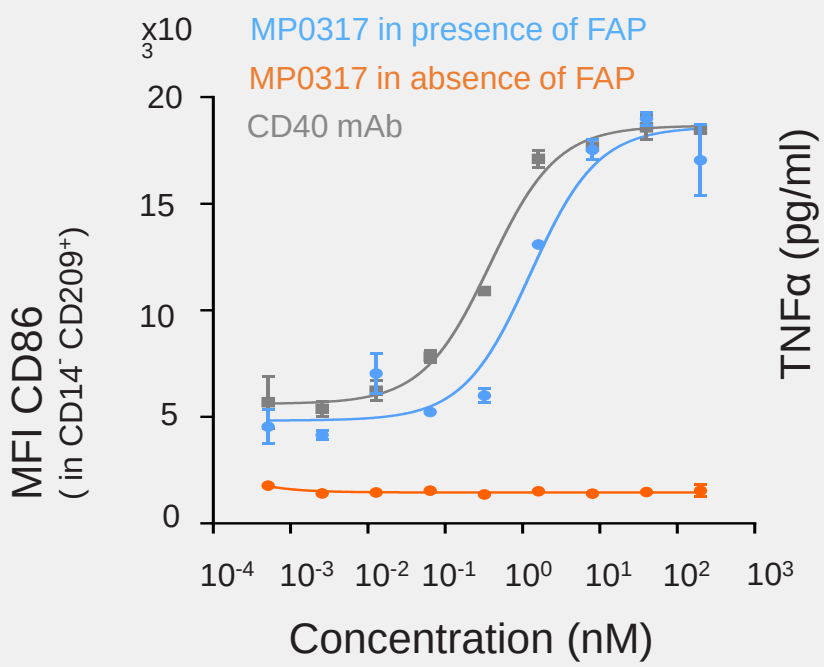
IL-6 ✓ CCL17 ✓

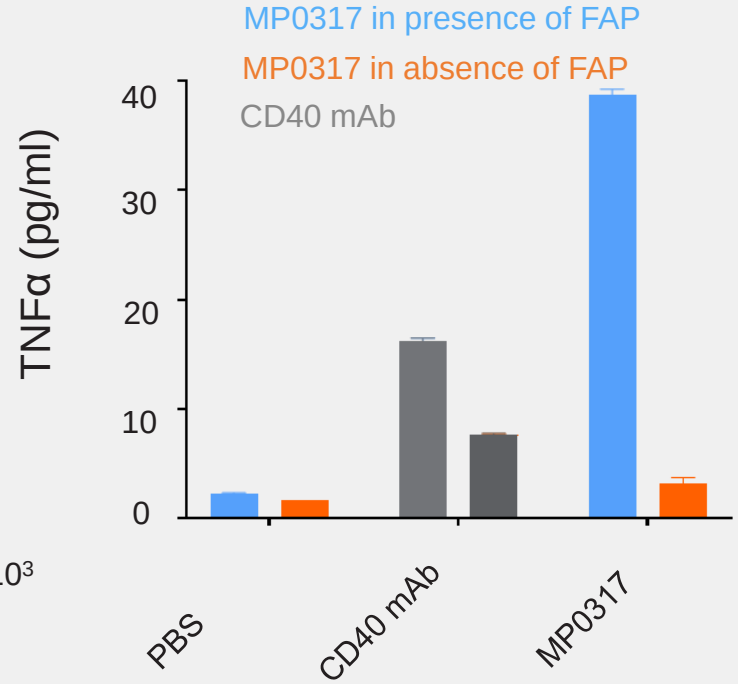
C

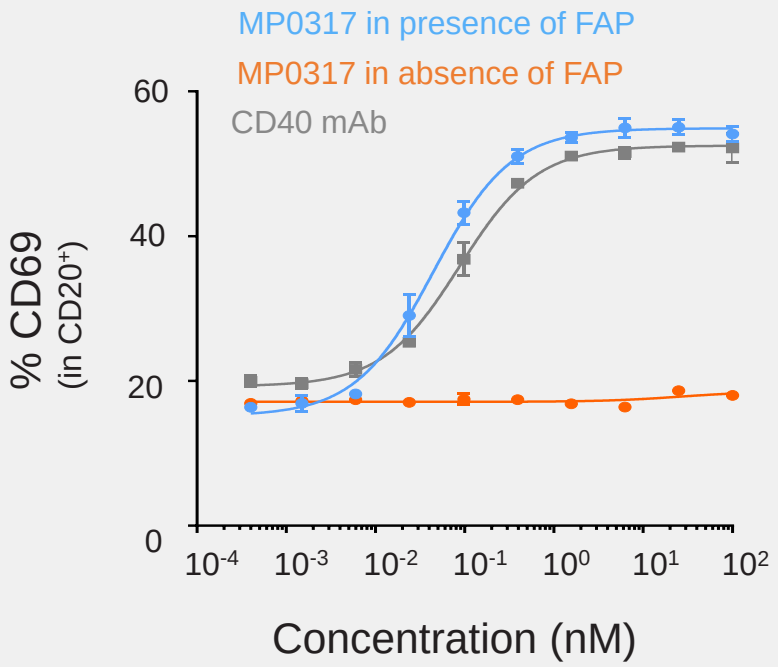
B cells:

CD69 ✓

CD86 ✓

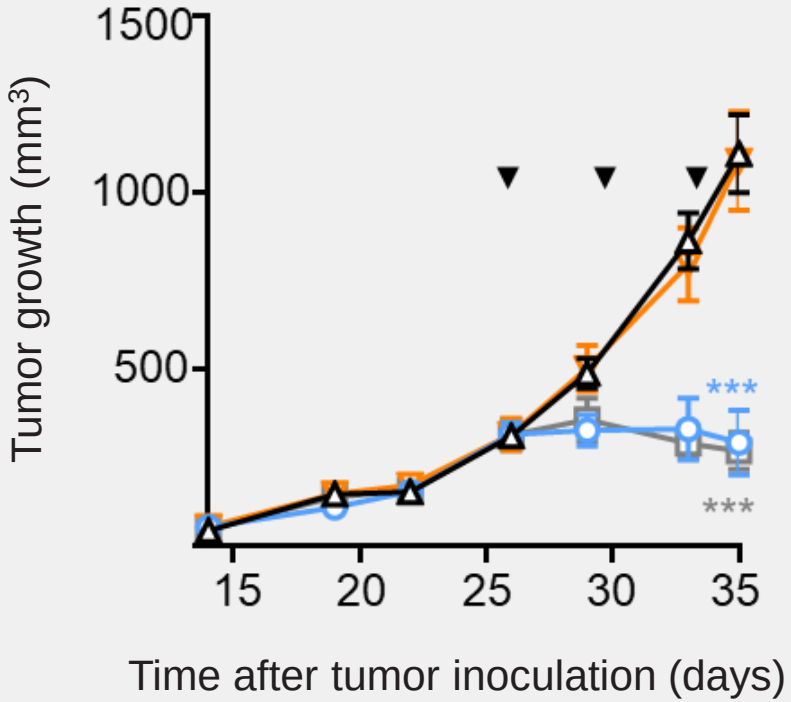


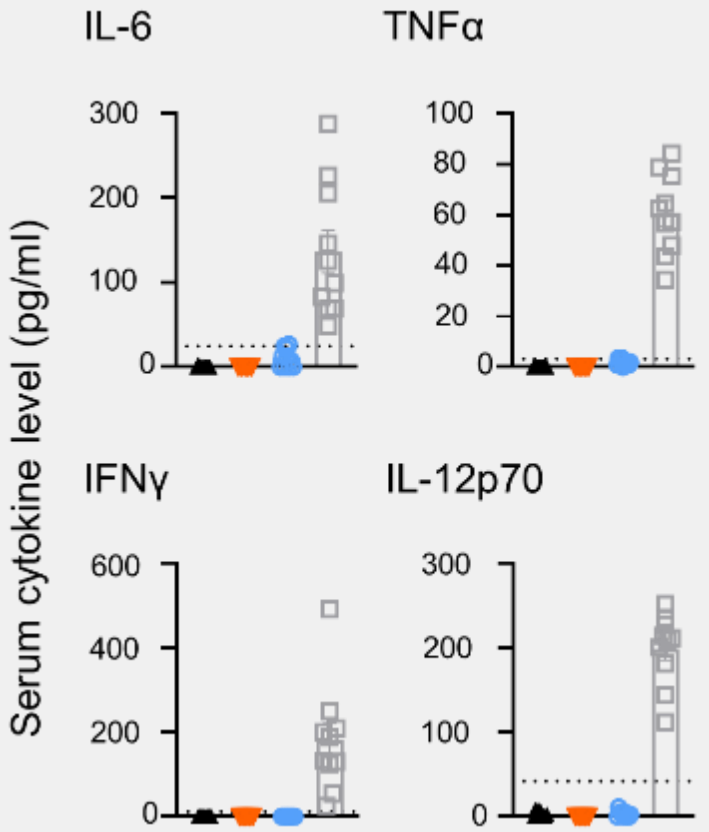




MP0317 Shows Full Activity with No Detectable Side-effects

FAP^{HIGH} TUMOR: MC38-FAP Colorectal cancer





Vehicle

Neg. CTRL*

mFAP x mCD40

mCD40 Ab

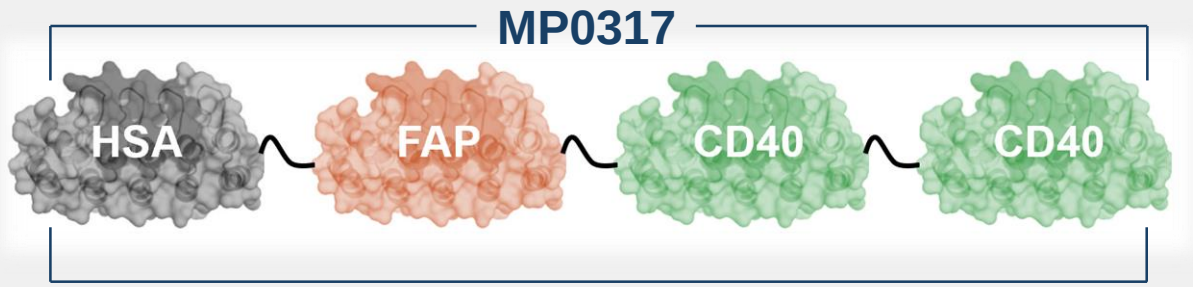
MP0317 – Key messages

CD40 Biology

- Highly promising target with potential to significantly impact clinical outcomes for patients
- Difficult biology to manage, and administer safely and efficaciously

MP0317 Clinical Plans

- FAP localization translating well, and will provide insights into dosing strategies
- First patient now anticipated H2 2021, new clinical material manufactured in H1
- Clinic design will include early potential for expansion based on activity
  - Multiple avenues of combination treatments to explore:
    - Chemo, PD-1, Radiation, etc.



MOLECULAR partners

New Therapeutic Platforms: Unlocked

Daniel Steiner, PhD

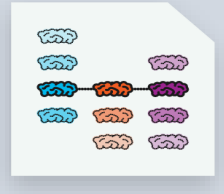
From DARPin® Features to Benefits

DARPin® Facts

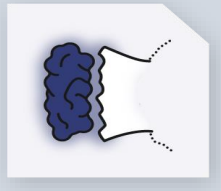
- Small (15 kDa) and simple
- High affinity and specificity
- High stability and solubility
- Well expressed in bacteria
- “Nature’s choice” for multi-specificity
- Tunable systemic half-life
- Safe & efficacious in clinic

Unique DARPin® Features

- **Turn-key Multispecifics:** multi-DARPin® formatting with up to 7 functionalities in one molecule



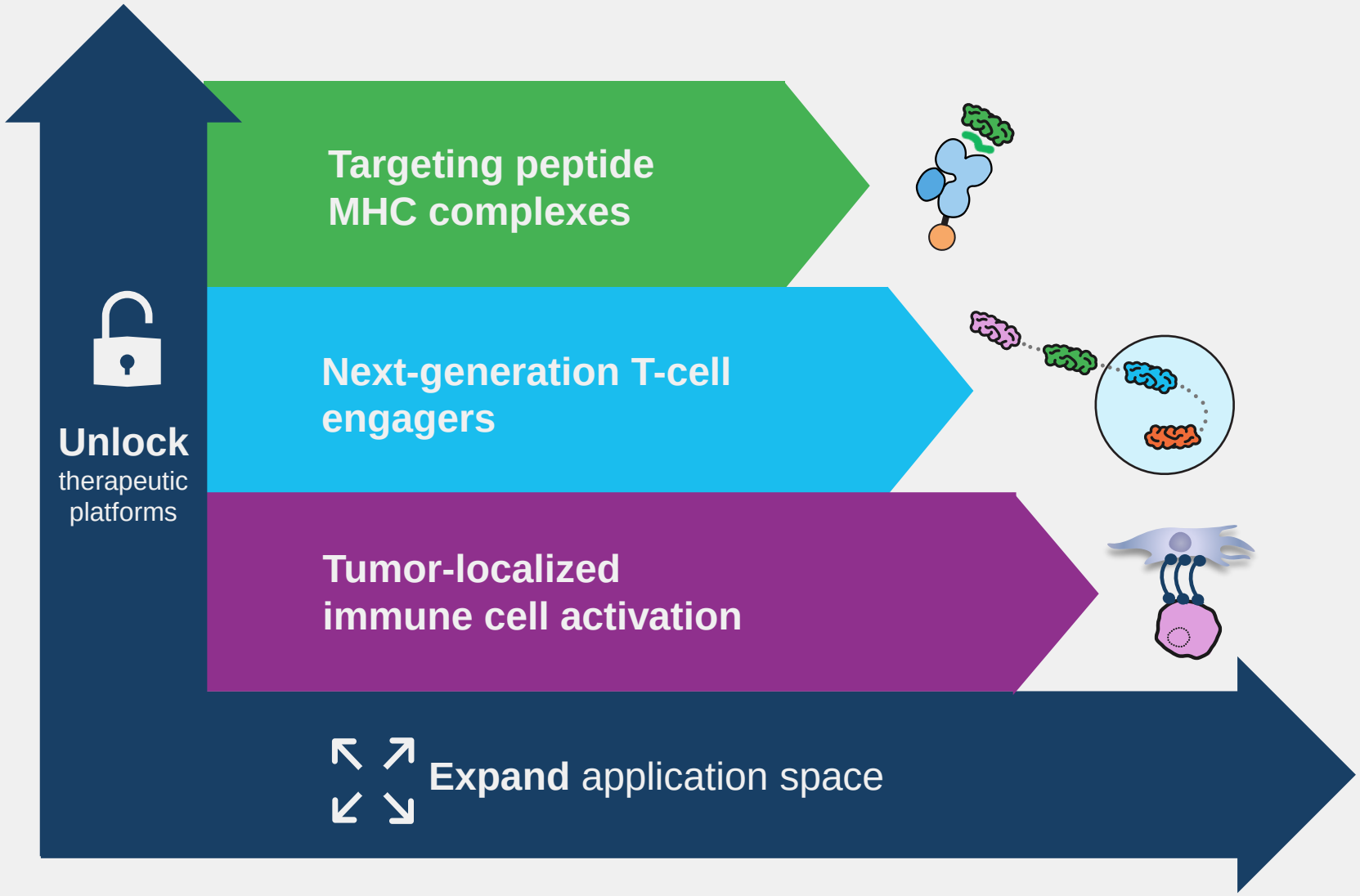
- **Super Specificity:** Based on structure of binding surface



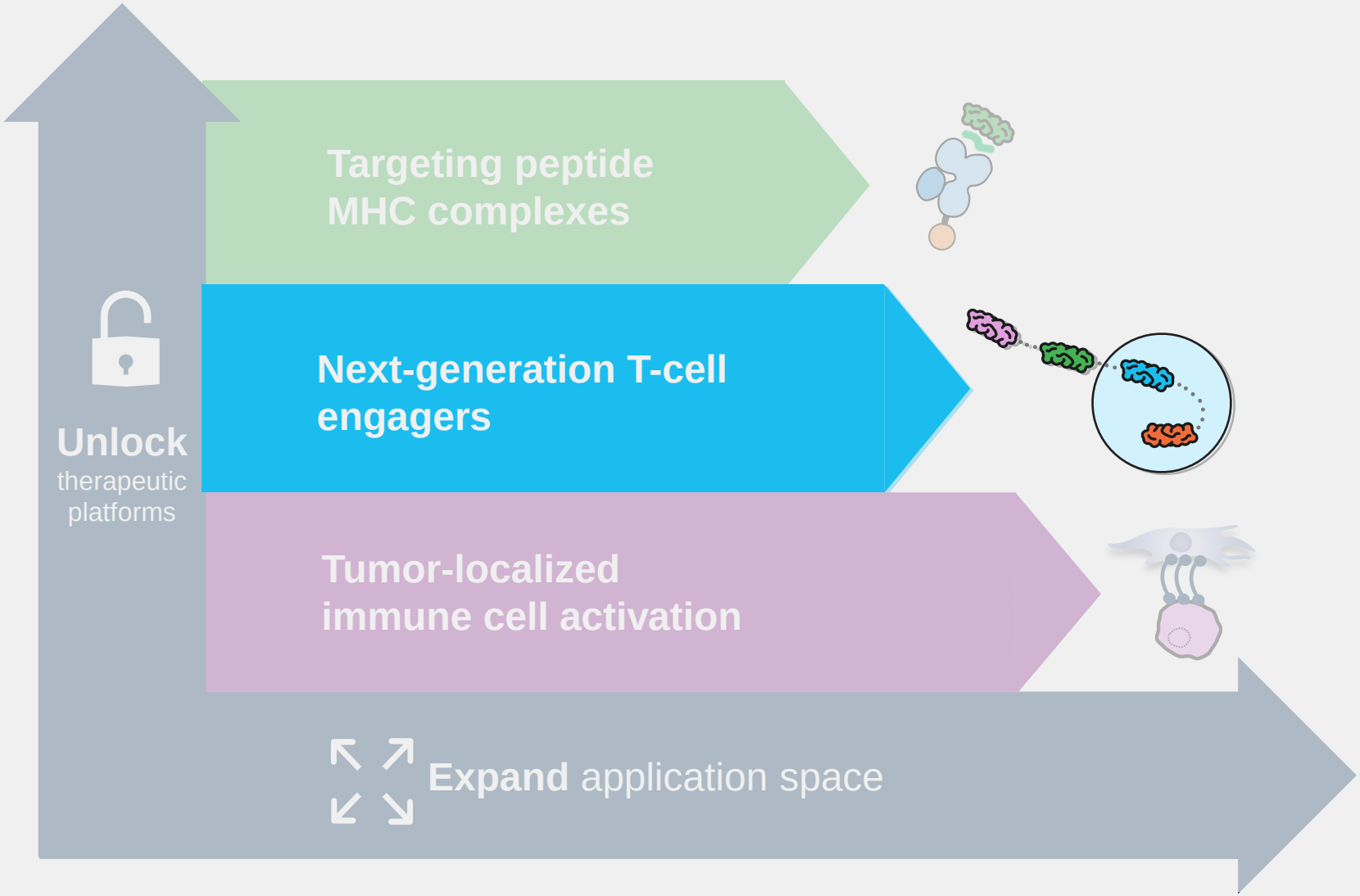
DARPin® Benefit

- **Disease-localized activity** to open the therapeutic window
- **Multi-blocker** to prevent escape and resistance
- **Molecular handcuff** for complete inhibition
- **Tailored “grip”** on hard to bind targets (e.g. pMHC)
- **Broad potential** waiting to be unlocked

Unlock and Expand: Therapeutic Platforms



Unlock and Expand: Therapeutic Platforms



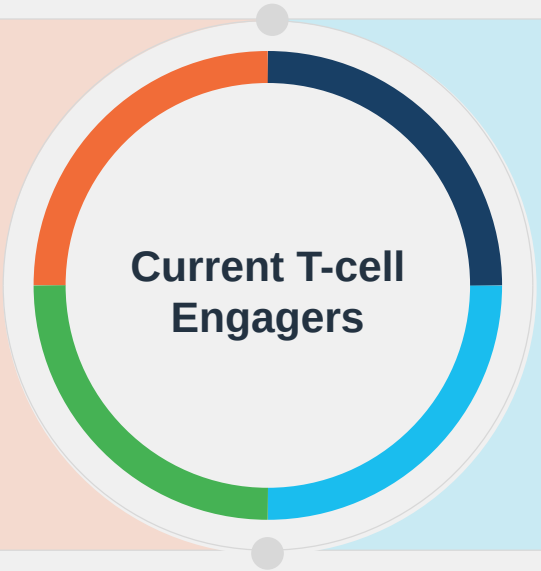
Challenges of T-cell Engagers in the Clinic

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…)

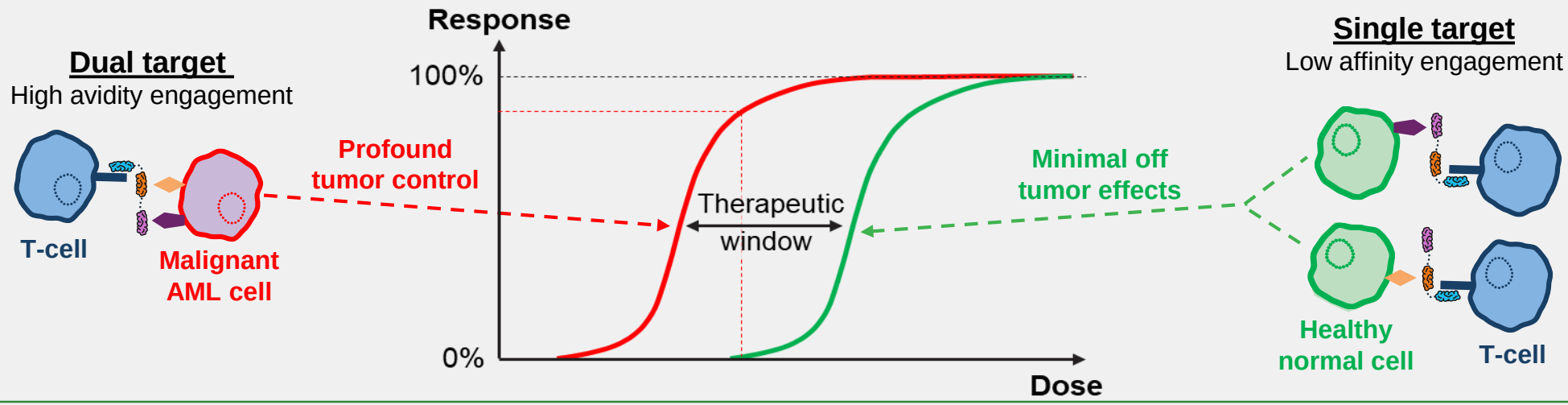
Multi-specific DARPin® T-cell Engager with Improved Benefit/Risk in AML

Medical problem

- **High medical need** and **high relapse rate** in AML with current therapies
- Single-target T-cell engagers show promising efficacy, but optimal biological dose level not reached due to **dose-limiting toxicities**

DARPin® solution

- **Multi-DARPin with enhanced tumor selectivity** to
  (i) reduce off tumor effects, (ii) achieve higher dose levels and ultimately, (iii) better efficacy



Multi-DARPin® Versatility Allows Screening for Function Sweet Spot

 # molecules

10^{12}
Library to generate binders against TAA1 / TAA2 / TAA3…

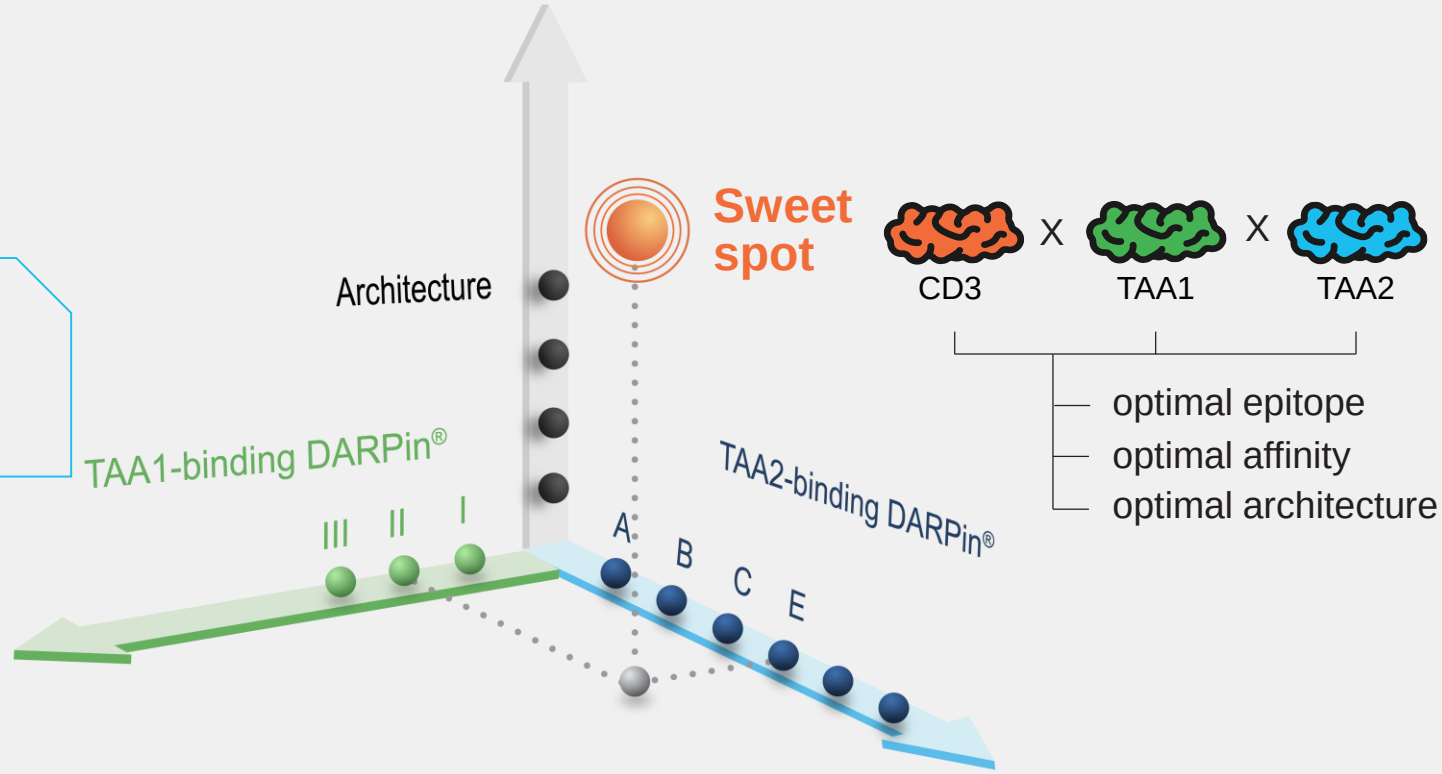
10s
Identified functional and well behaved DARPin® modules (for each target)

Recombination of DARPin® modules: **Fast & high throughput process: 2 weeks (start of cloning to purified proteins)**

1000s
Screening of multi-domain DARPin® space

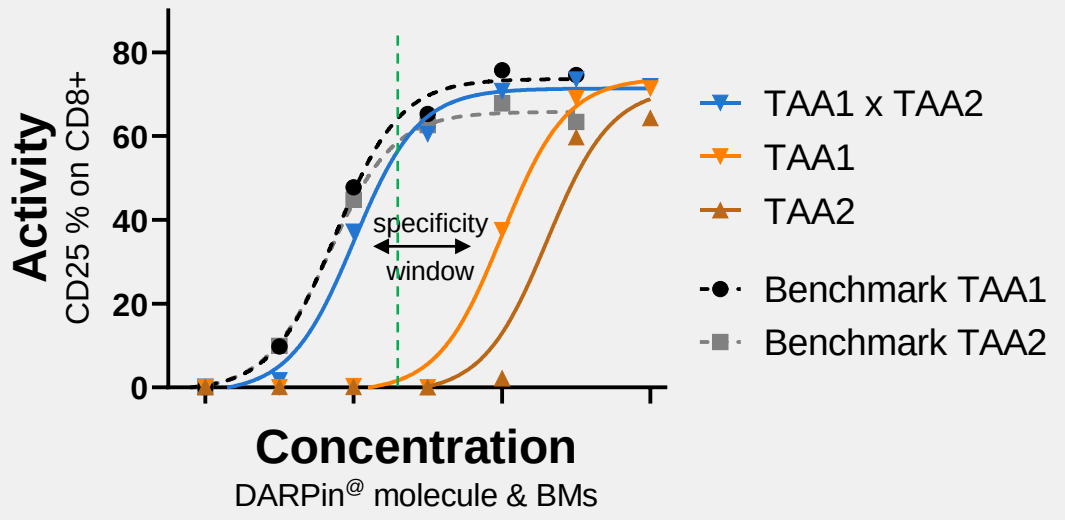
2-5
Multi-DARPin® product candidates

Multi-domain DARPin® space

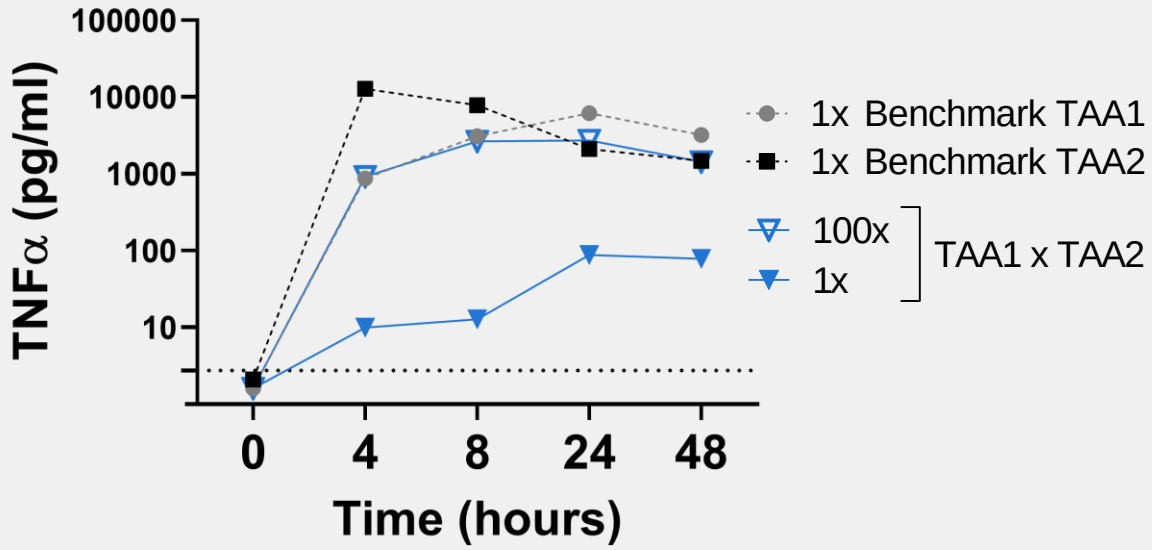


Multi-DARPins® for AML Show High Potency, Improved Selectivity and Potential for Reduced CRS

In-vitro potency and specificity assessment on AML cells



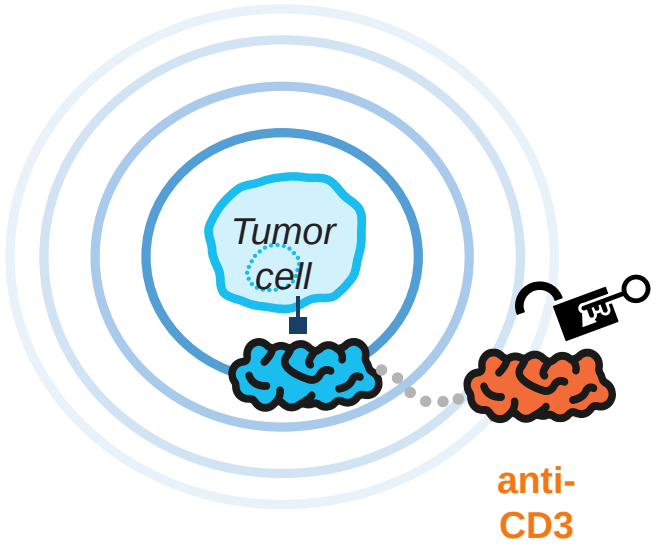
Ex-vivo cytokine release in healthy human whole blood



AACR 2021

Expand with Platform for Controlled Activation of CD3 Effector Function

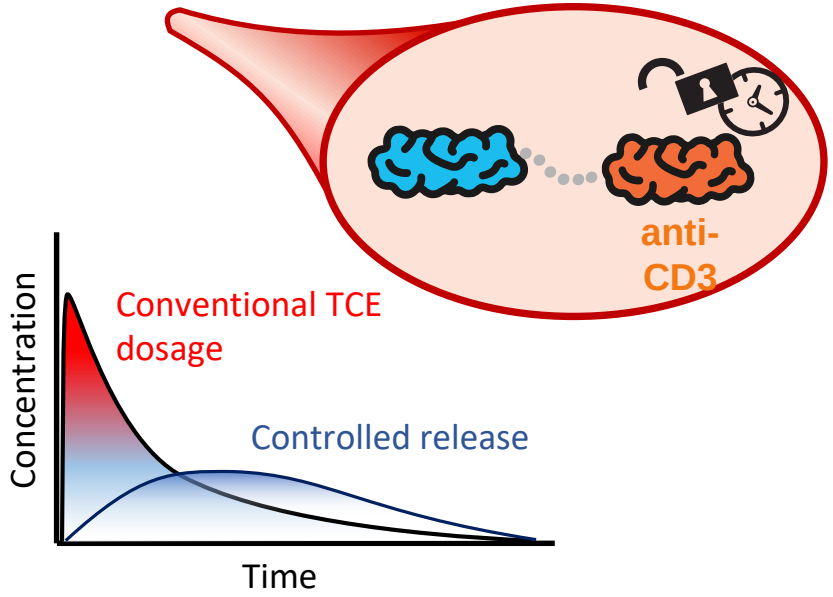
Where
Conditional activation locally in the TME



- 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

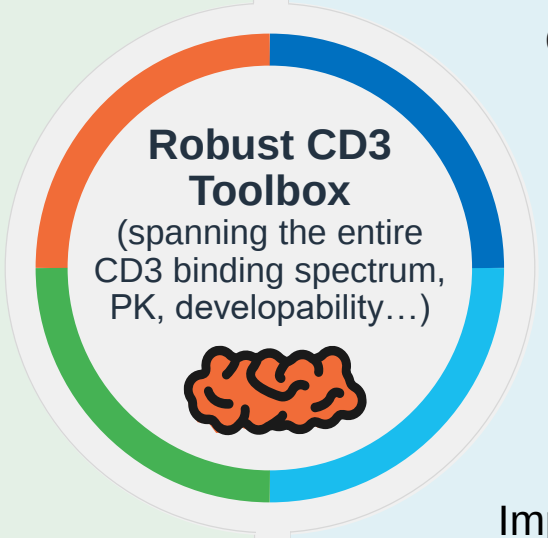
DARPin® solutions for improved benefit-risk profile of T-Cell Engagers

Safety

DECREASED TOXICITY FOR OPTIMAL DOSING

Decreased attack on healthy tissues

Reduced hyper-immune stimulation: CRS and neurotoxicity



Efficacy

LONG-LASTING AND DEEP RESPONSES

Circumvent tumor escape & relapse

Improved efficacy in solid tumors

DARPin® solutions for improved benefit-risk profile of T-Cell Engagers

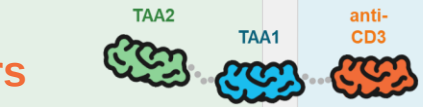
Safety

DECREASED TOXICITY FOR OPTIMAL DOSING

Multi-specific T-cell Engagers with increased selectivity

Decreased attack on healthy tissues

Reduced hyper-immune stimulation: CRS and neurotoxicity



Robust CD3 Toolbox
(spanning the entire CD3 binding spectrum, PK, developability…)

Efficacy

LONG-LASTING AND DEEP RESPONSES

Multi-specific T-cell Engagers to cover heterogeneous tumors

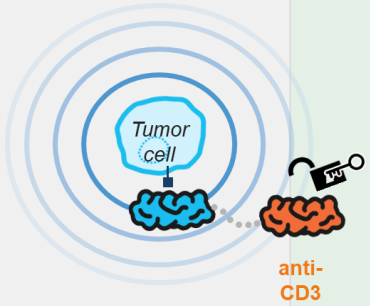
Circumvent tumor escape & relapse

Improved efficacy in solid tumors

DARPin® solutions for improved benefit-risk profile of T-Cell Engagers

Safety

DECREASED TOXICITY FOR OPTIMAL DOSING



Multi-specific T-cell Engagers with increased selectivity

Decreased attack on healthy tissues

Controlled "conditional CD3 activation"

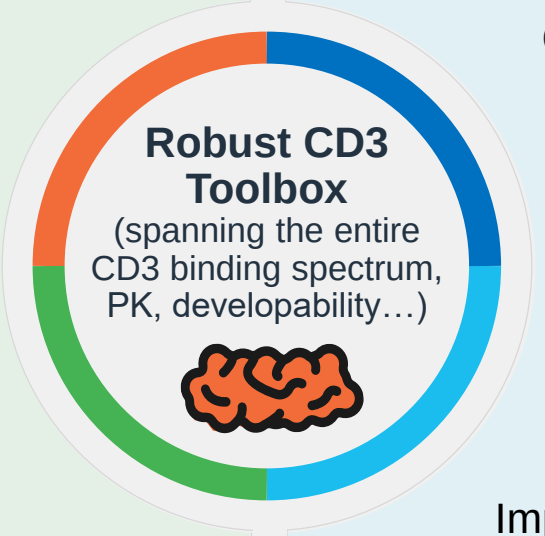
Reduced hyper-immune stimulation: CRS and neurotoxicity

Efficacy

LONG-LASTING AND DEEP RESPONSES

Multi-specific T-cell Engagers to cover heterogeneous tumors

Circumvent tumor escape & relapse



Improved efficacy in solid tumors

DARPin® solutions for improved benefit-risk profile of T-Cell Engagers

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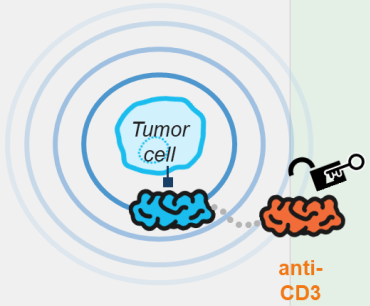

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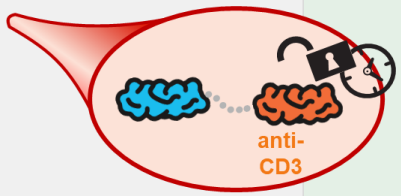

Controlled "slow CD3 activation"

Reduced hyper-immune stimulation: CRS and neurotoxicity

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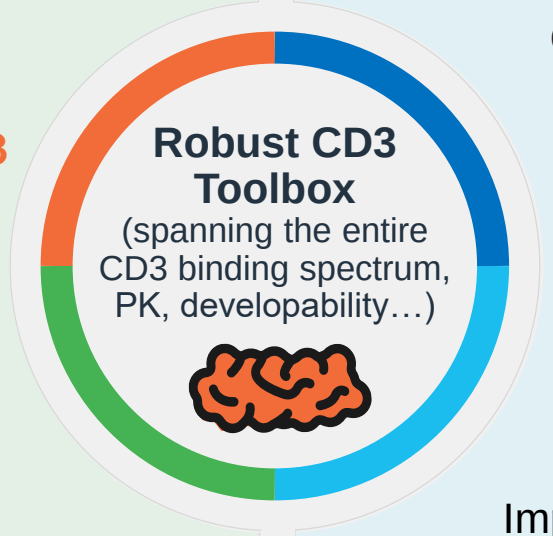

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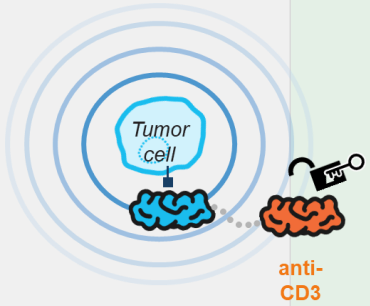

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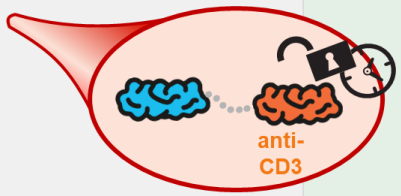

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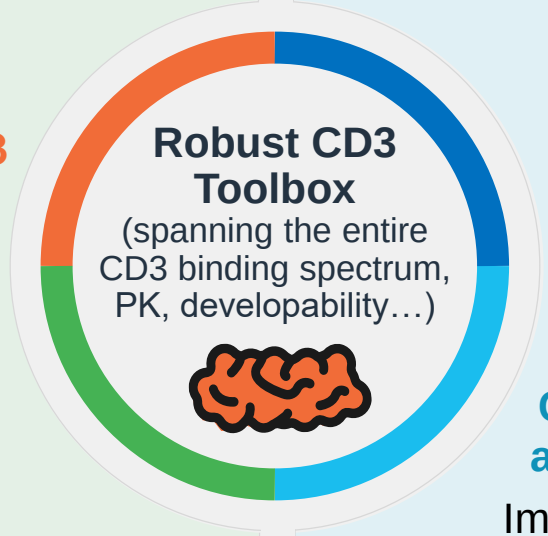
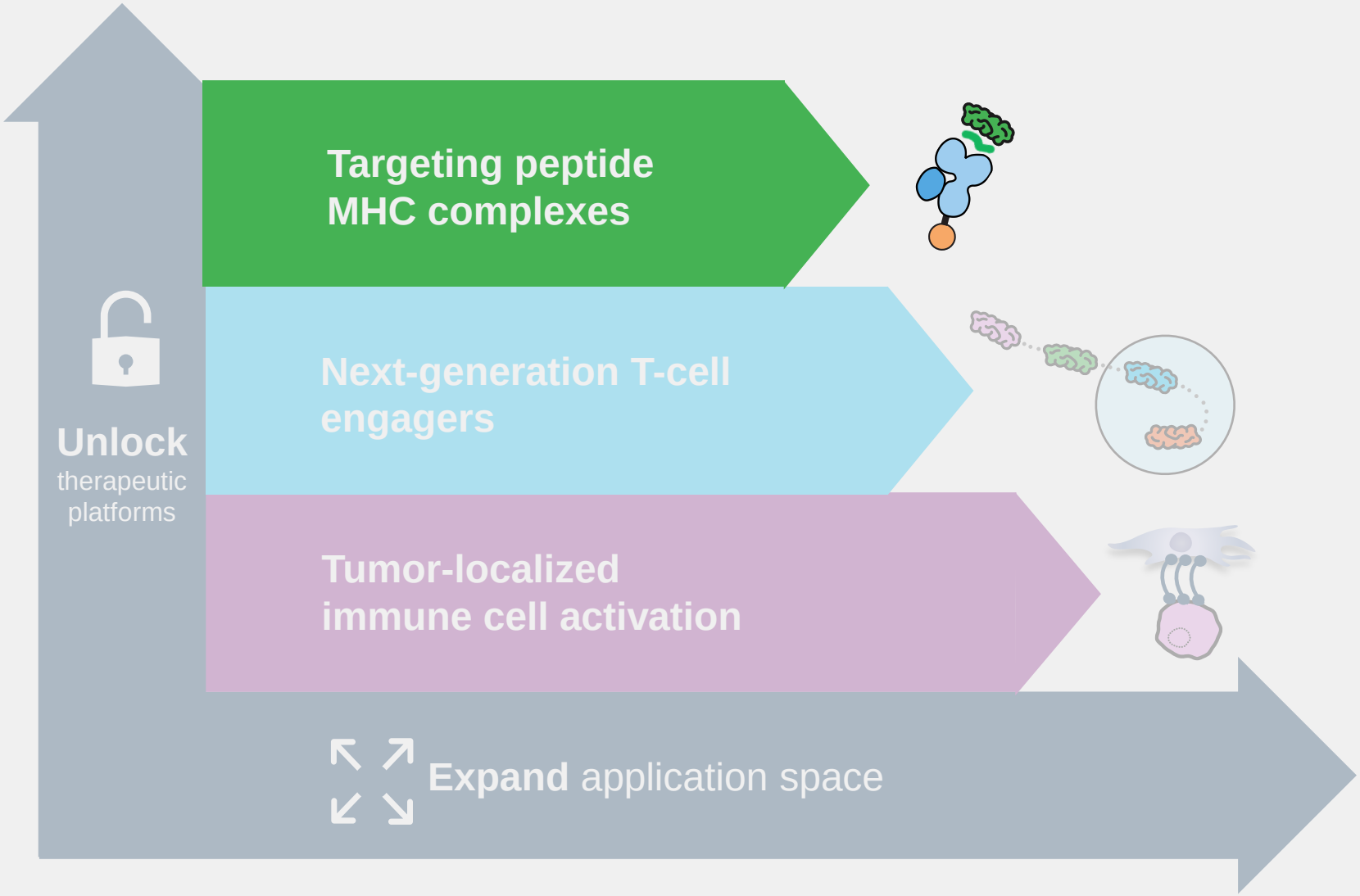


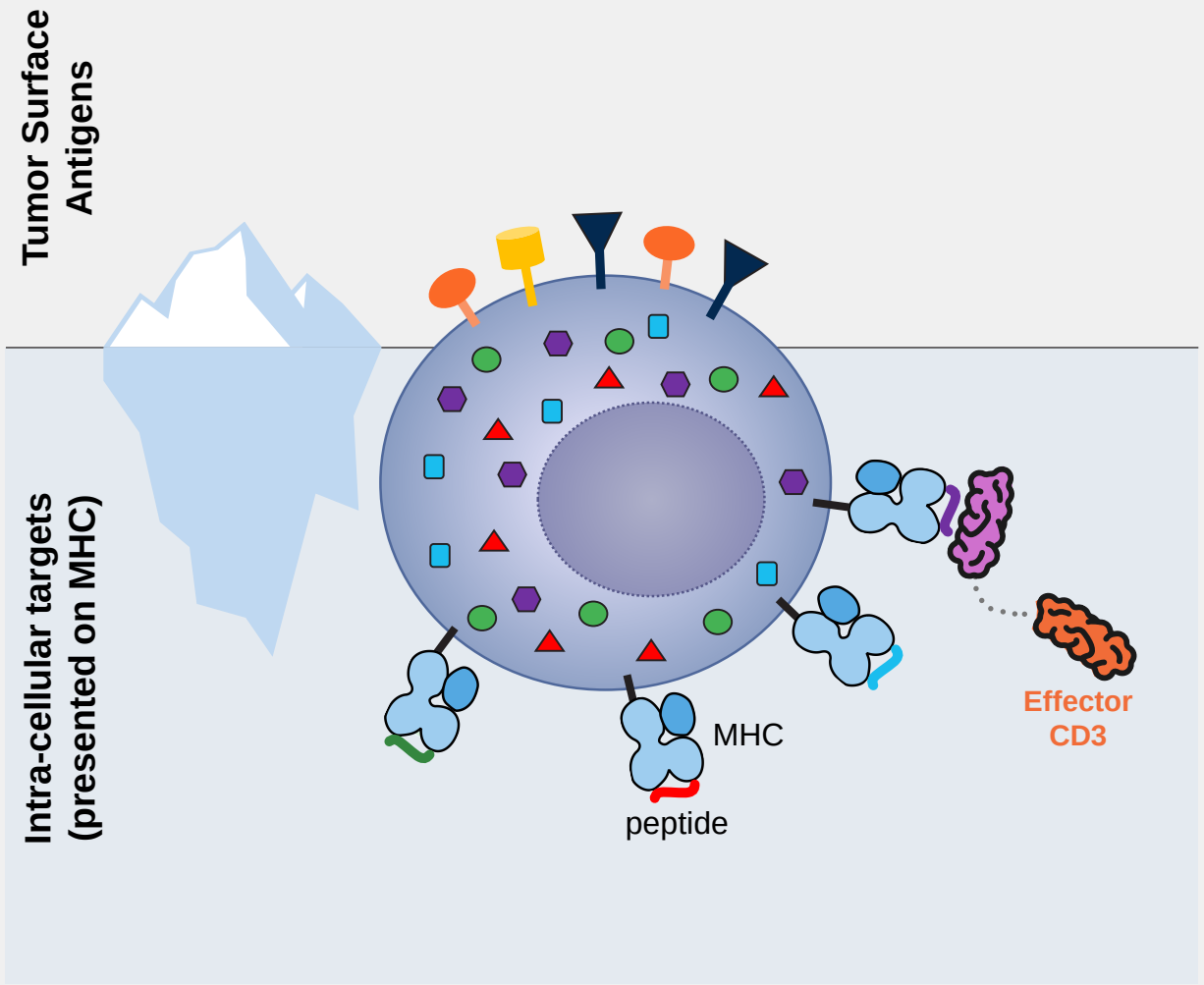
Combination with localized agonist to deepen response

Improved efficacy in solid tumors

Unlock and Expand: Therapeutic Platforms



Peptide MHC Complexes: “Inaccessible” Intracellular Targets

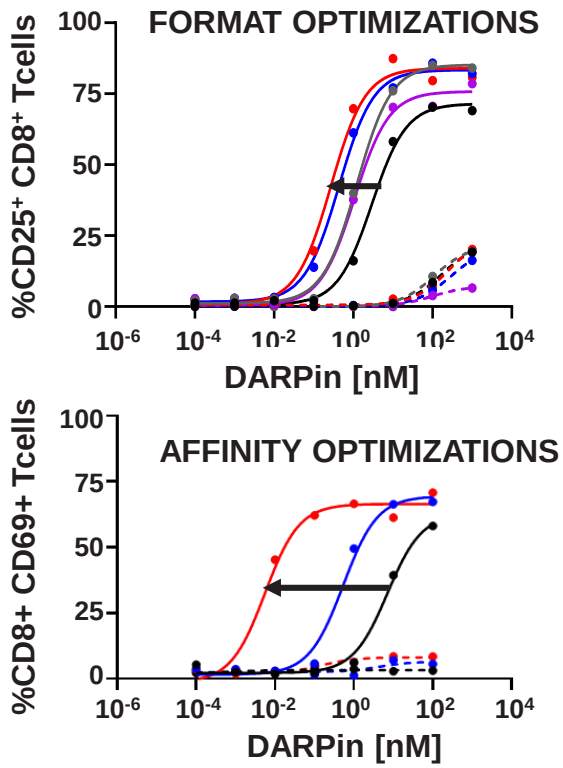


Challenges of the pMHC redirected T-Cell engager field:

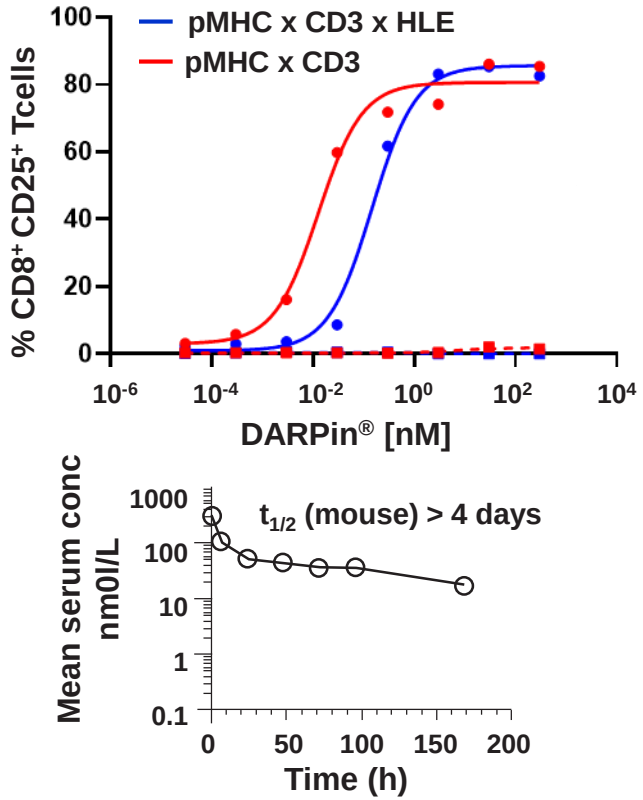
- Generation of binders with high selectivity and high potency
- High investment to generate binders
- Systemic half-life extension often leads to loss of potency
- Developability properties not ideal
- Target identification and validation
- Complex clinical development path

Multiple Technical pMHC Challenges: Solved

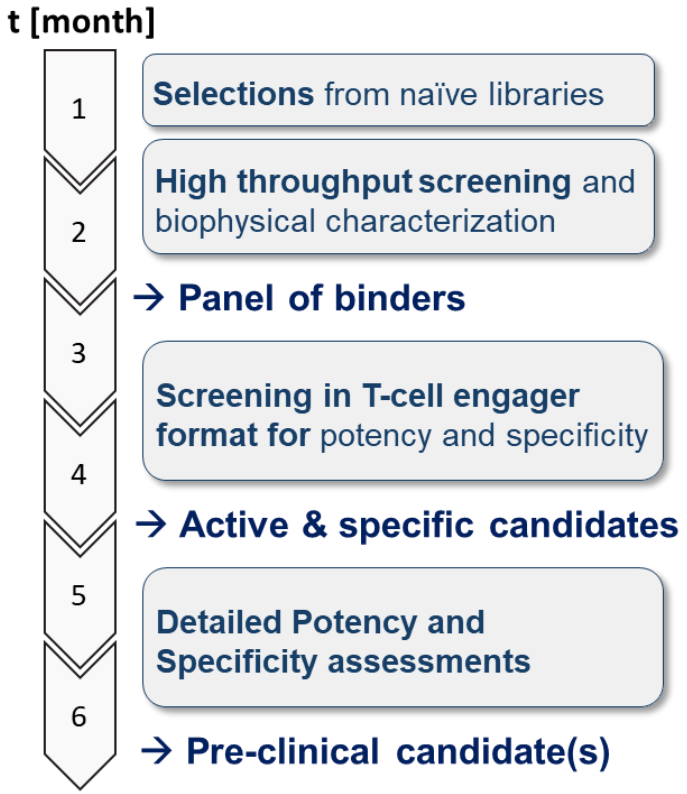
Gained several logs of potency while maintaining selectivity



Achieved good systemic exposure with limited impact on potency

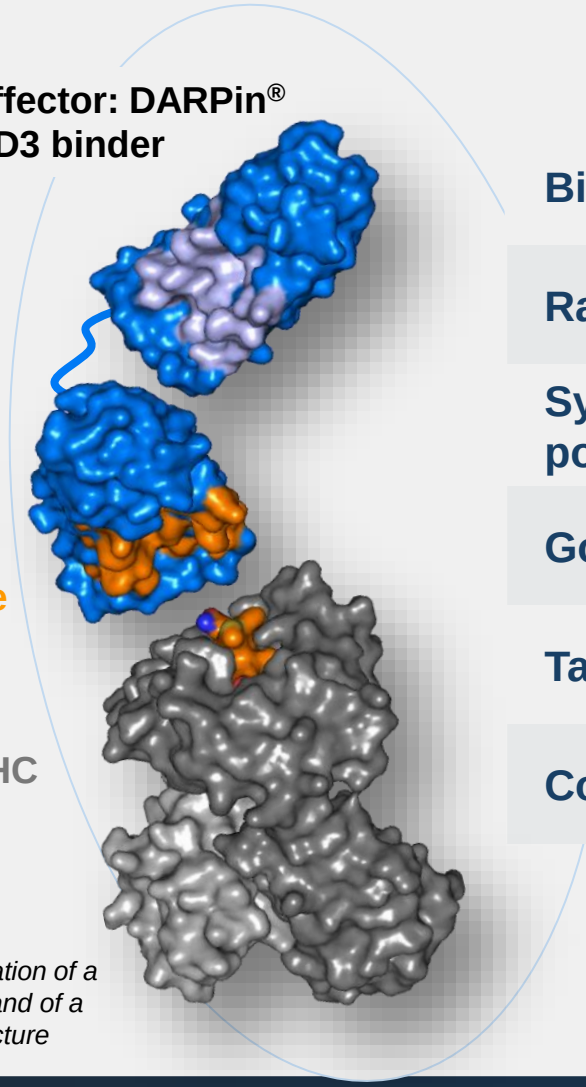


Candidate production for several pMHCs in parallel in less than six months



AACR 2021

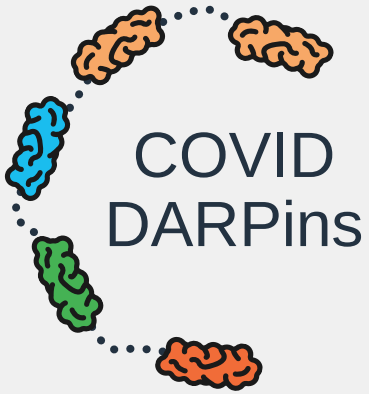
DARPin® Platform Especially well Suited to Address pMHC Targets



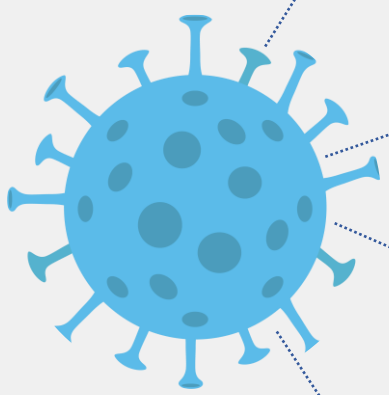
Surface representation of a DARPin® domain and of a pMHC crystal structure

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	○

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

Summary and Outlook Into 2021

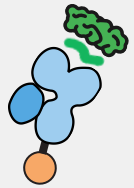
Unlock therapeutic platforms

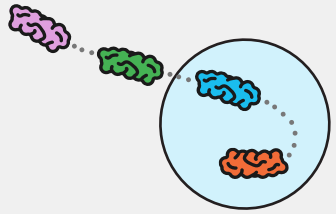
Targeting peptide MHC complexes

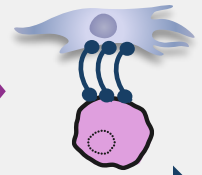
Next-generation T-cell engagers

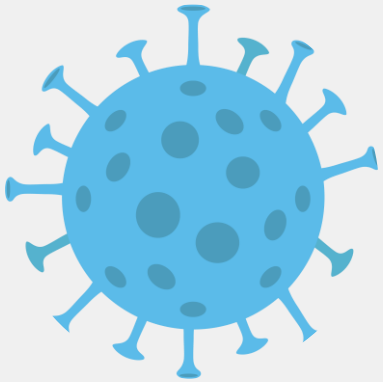
Tumor-localized immune cell activation

Expand application space









Virology

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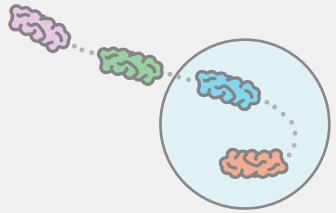
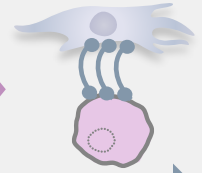


DARPin building blocks ready to expand **tumor-localized immune cell activators** based on strong clinical data of MP0310/317



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Virology

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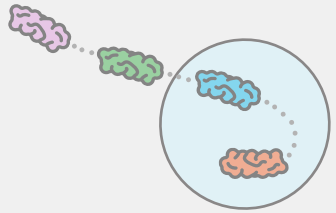
Progressing multi-specific **T-cell Engager** candidates and expanding first product candidates with "controlled activation"



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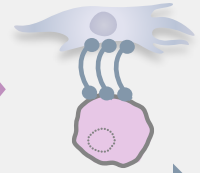

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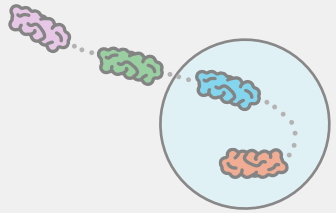

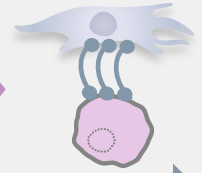

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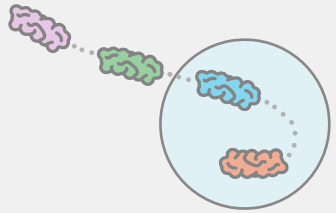

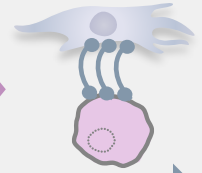

Build on DARPin Covid19 success and **expand in virology**

Conclusions

Patrick Amstutz

Summary

- DARPins show clinical activity
- New team well in place
- MP0310 – strong evidence of activity
- MP0317 – FIH 2021

- CD40 biology is relevant and needs solutions
- Mechanism allows for multiple combination opportunities
- Dosing and administration are key to activity

- Therapeutic Platforms established
- Next gen DARPin®-T-cell engagers on track to deliver 1st candidate.
- Multiple platform expansions to explore
- pMHC platform unlocked

- Novartis Global Heath is highly committed
- Therapeutic are a key piece of the puzzle
- MP0420 on track to POC in 2021

Financial Overview & Milestones:

- Cash 30 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

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(Not incl. any future proceeds related to partnerships)

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POC for MP0420

Establish Dosing for MP0310

FIH of MP0317

Select 1st Candidate

Funded into 2023

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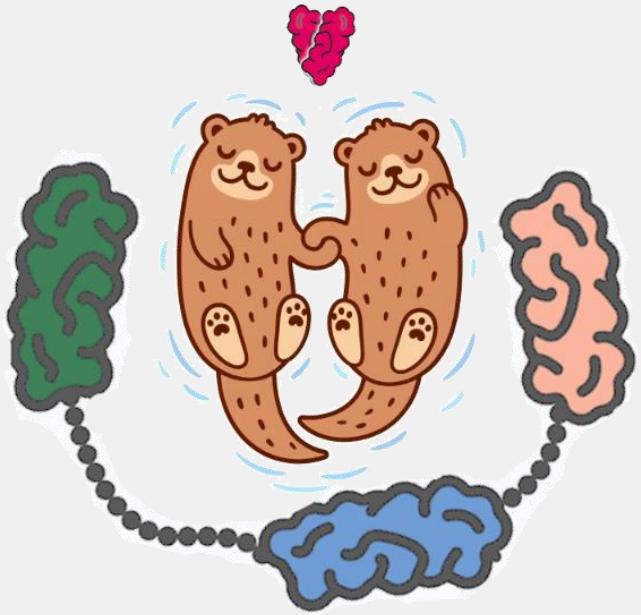
Live, Love, Laugh



MOLECULAR
...otters


Safe and happy holidays
to everyone
MOLECULAR
partners

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