Custom Built Biology for Patients

November 2021

Molecular Partners AG, Switzerland
(SIX: MOLN, NASDAQ: MOLN)

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Pioneering DARPin Therapeutics

COVID19 – Ensovibep (Novartis)

- **EMPATHY** – ambulatory, with Novartis
  - Fully recruited 400 patients in phase 2b
  - Data being collected for full analysis
- Active on **all viral variants of concern,** to date, including **Delta** and all relevant mutated positions on the emerging **Omicron** variant

Local immune agonists

- **AMG 506 / MP0310** – (FAP x 4-1BB, Amgen) weekly dosing; on track to initial read-out in late 2021 / early 2022
- **MP0317** – (FAP x CD40) Phase 1 initiated

AML

- **Triple-TAA-targeting TCE** – lead candidate selected, **MP0533** (CD33 x CD70 x CD123 x CD3)
- Poster presentation accepted – ASH 2021
- First in human 2022

Next Generation Programs

- Outlook on new programs and DARPin platform developments at R&D day Dec. 2021

Abicipar

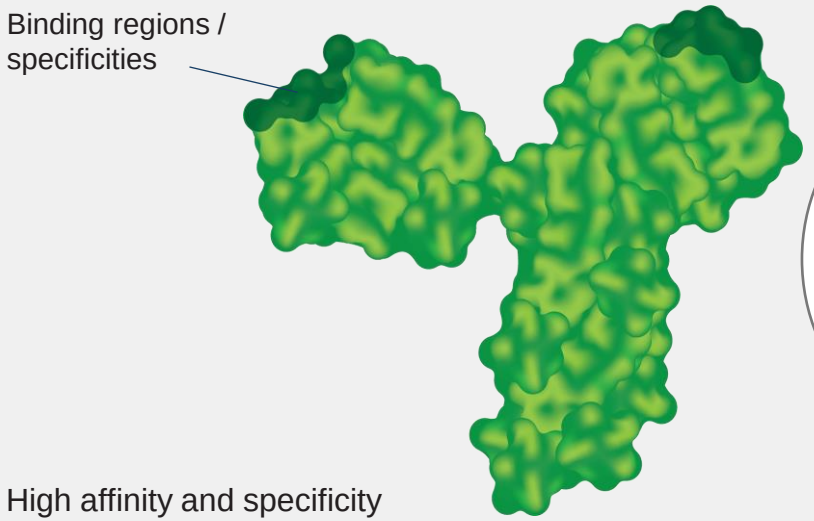
- Molecular Partners regained rights from AbbVie; transition and evaluation of data ongoing

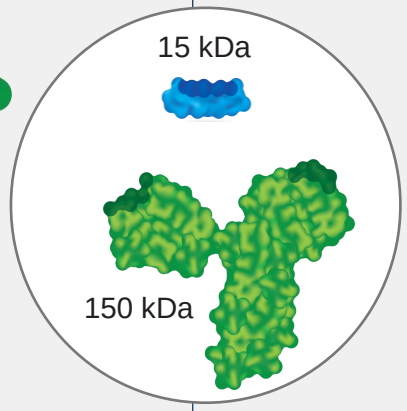
Financials

- Listed on **NASDAQ**
- Raised **CHF 58 million** gross proceeds
- Strong balance sheet, funded into **H2 2023**

What are DARPins

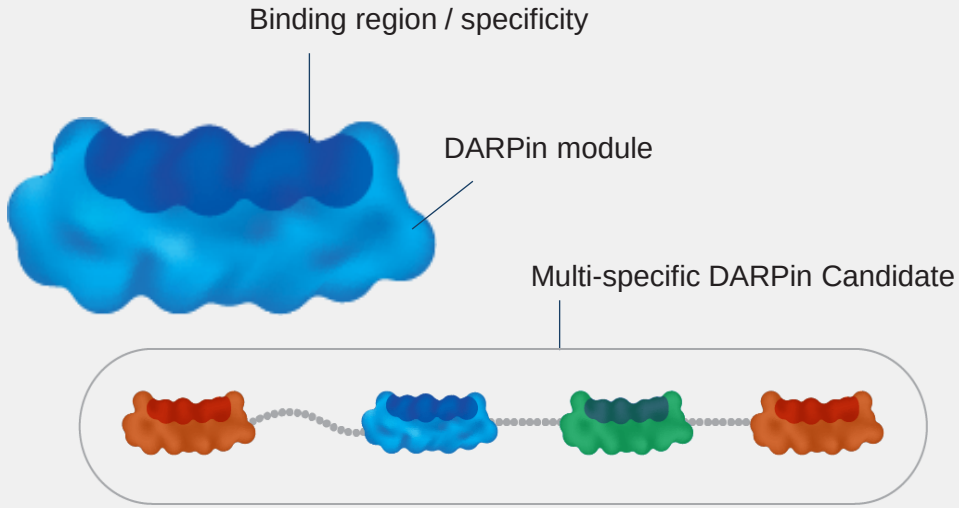
MONOCLONAL ANTIBODIES





- High affinity and specificity
- Large size: 150 kDa
- Complex architecture; 4 proteins with 12 domains
- Long half-life
- Mammalian expression
- Good safety & low immunogenic potential

MONO-DARPin



- High affinity and specificity
- Small size: 15 kDa (1/10 of a monoclonal antibody)
- Simple architecture 1 protein with 1 domain
- Tunable half-life
- High-yield microbial expression; High stability
- Good safety & low immunogenic potential

Multi-DARPin Versatility Allows Screening for Function Sweet Spot

 # molecules

10^{12}

Powerful Libraries with DARPin Binders to any given target

100s

Simple selection of specific DARPin binders (functional, well behaved, highly potent)

Assembly of up to 6 DARPin modules: **Fast & high throughput process: 2 weeks**

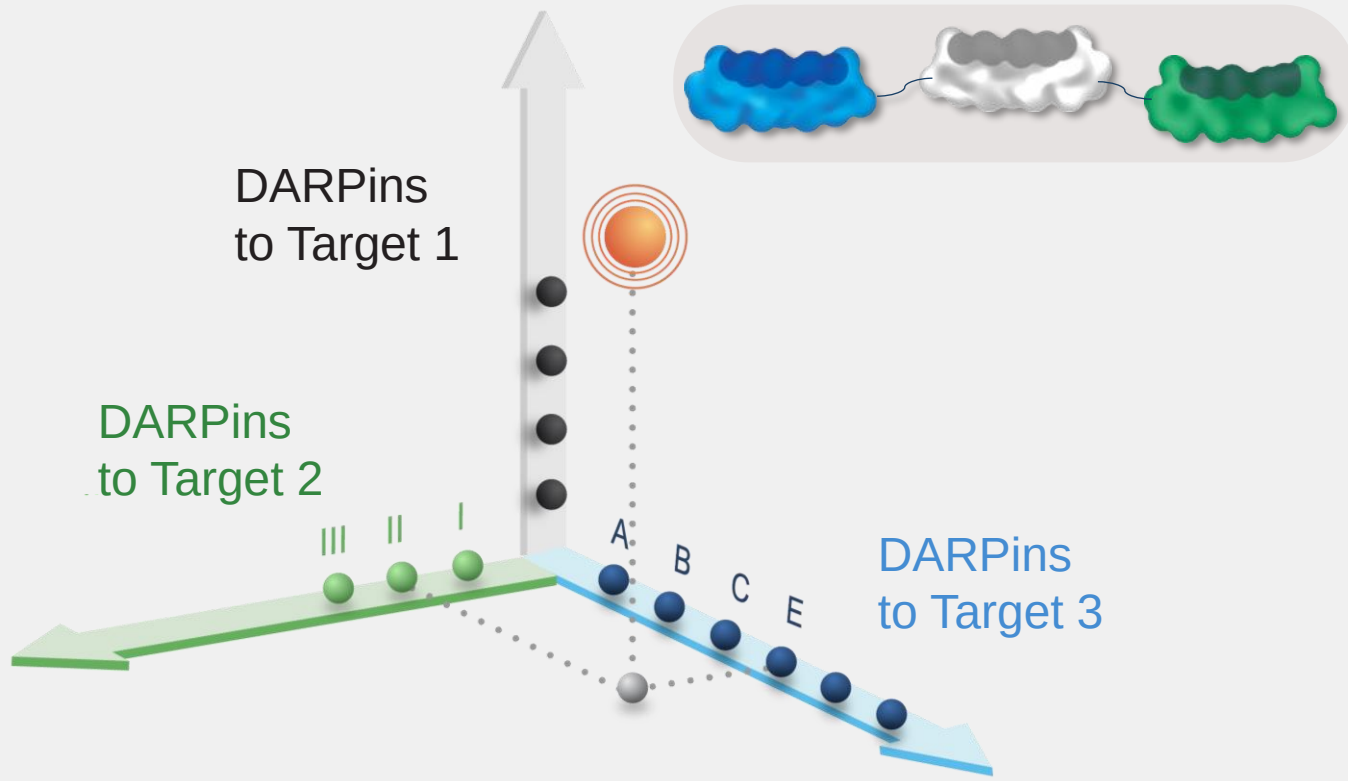
1000s

Screening of multi-domain DARPin space for the SOLUTION

2-5

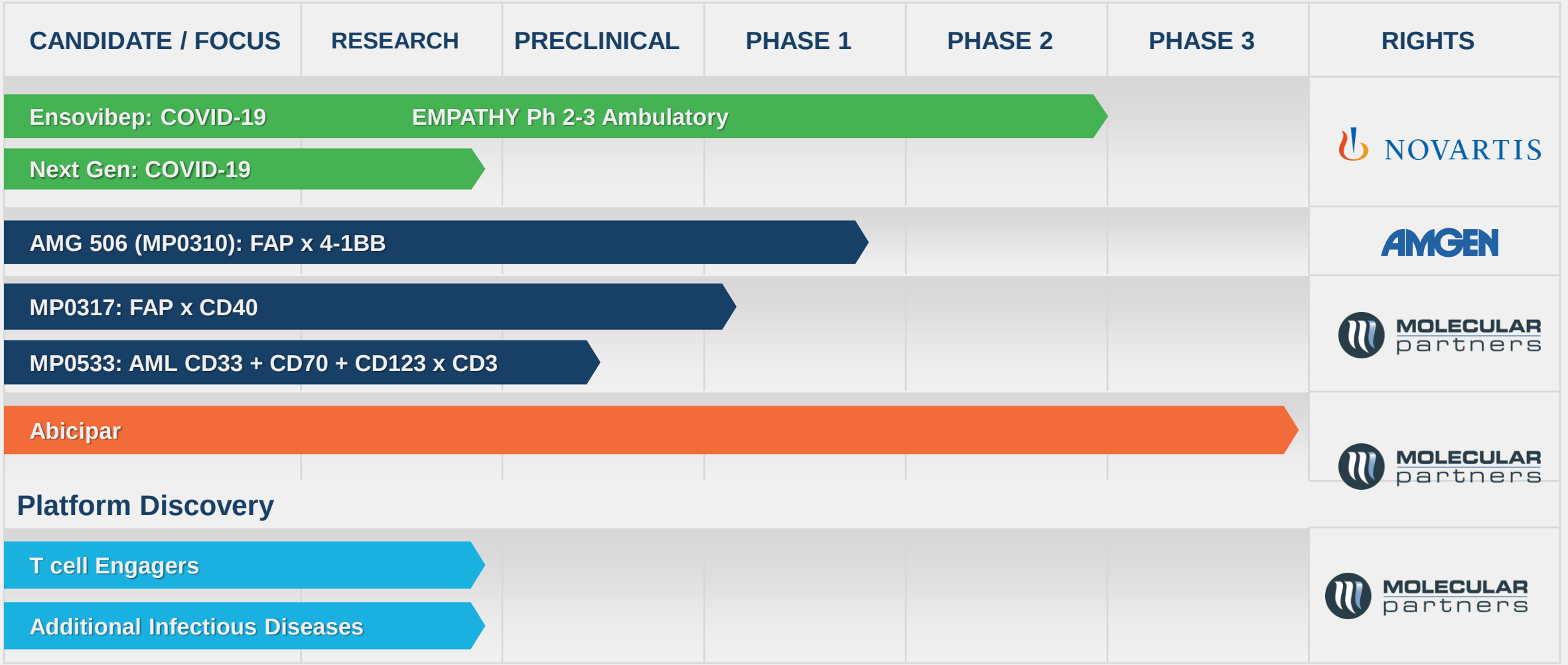
Multispecific DARPin candidates with desired function(s)

Multi-domain DARPin space

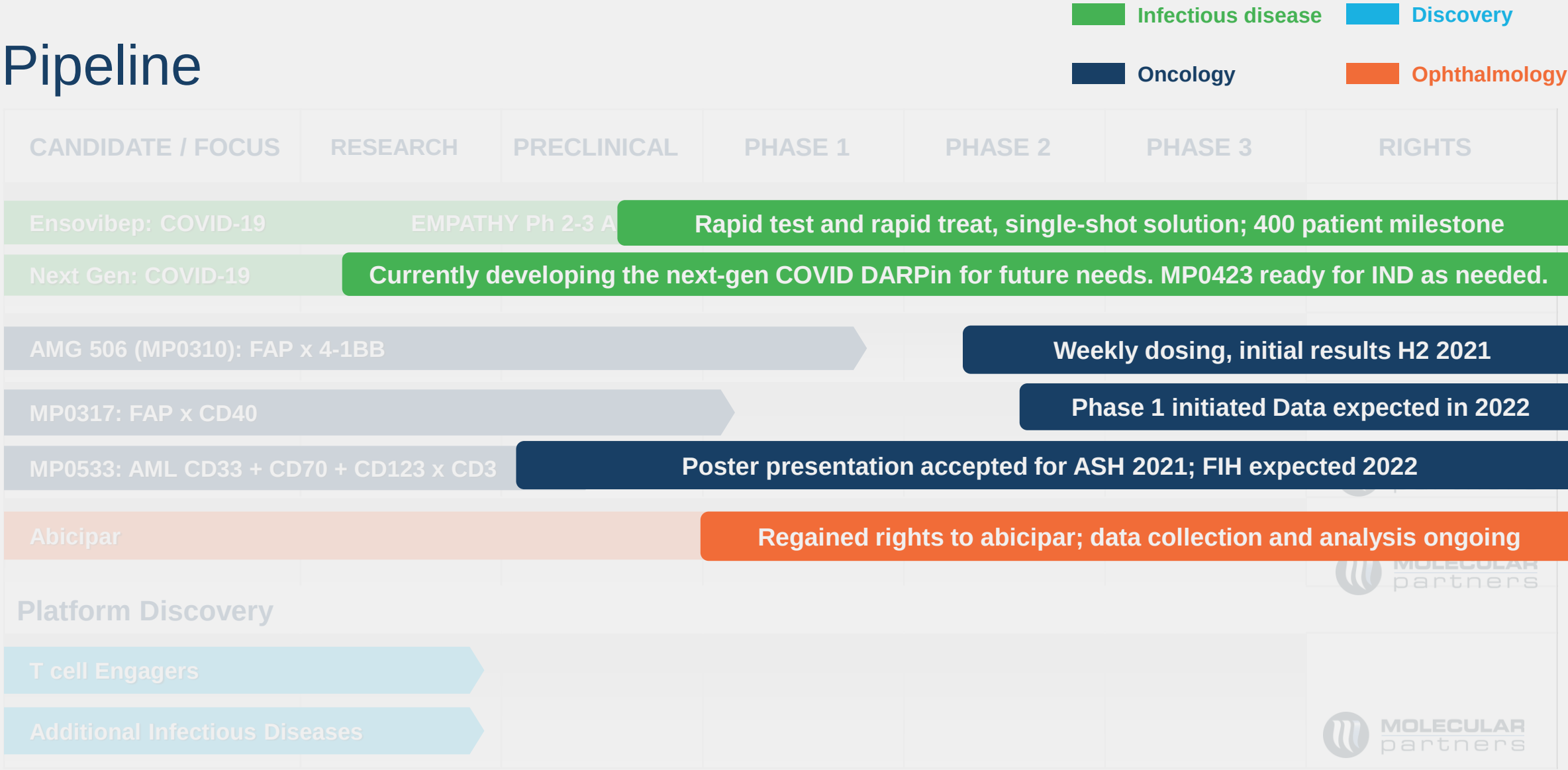


Pipeline

Infectious disease | Discovery | Oncology | Ophthalmology



Pipeline


Infectious disease
Discovery
Oncology
Ophthalmology
CANDIDATE / FOCUS
RESEARCH
PRECLINICAL
PHASE 1
PHASE 2
PHASE 3
RIGHTS
Ensovibep: COVID-19
EMPATHY Ph 2-3 A
Rapid test and rapid treat, single-shot solution; 400 patient milestone
Next Gen: COVID-19
Currently developing the next-gen COVID DARPin for future needs. MP0423 ready for IND as needed.
AMG 506 (MP0310): FAP x 4-1BB
Weekly dosing, initial results H2 2021
MP0317: FAP x CD40
Phase 1 initiated Data expected in 2022
MP0533: AML CD33 + CD70 + CD123 x CD3
Poster presentation accepted for ASH 2021; FIH expected 2022
Abicipar
Regained rights to abicipar; data collection and analysis ongoing
Platform Discovery
T cell Engagers
Additional Infectious Diseases

Ensovibep - Continued Advancement of COVID-19 Clinical Program

Ensovibep: Tri-Specific Antiviral for COVID-19

NOVARTIS

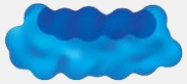
Target **Patient**

- Hundreds of thousands of new cases every day globally, despite vaccines and boosters
- Currently – 6,000 new hospitalizations in the US alone
- Over 5 million reported deaths in the world

Disease **Biology**

- Viral entry dependent on viral spike protein binding to ACE2 receptor
- Spike protein is a trimer with three identical subunits
- Multiple variants evolving mutations in the spike protein and other locations

DARPin **Advantage**

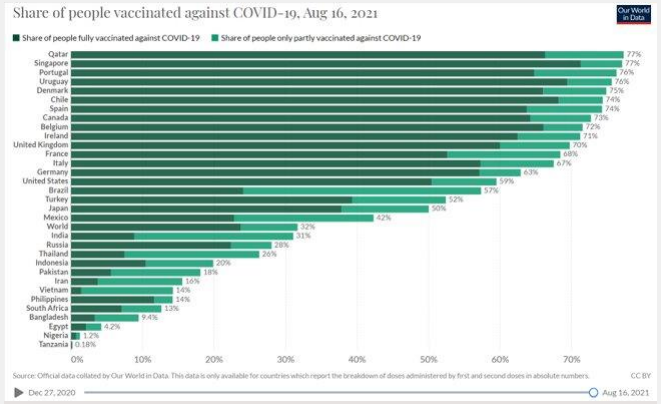


- First and only tri-specific antiviral in development, able to bind all three subunits at once
- Designed for greater viral inhibition through cooperative binding
- Muli-DARPin inhibition retains full potency against all variants of concern, to date

Expected **Milestones**

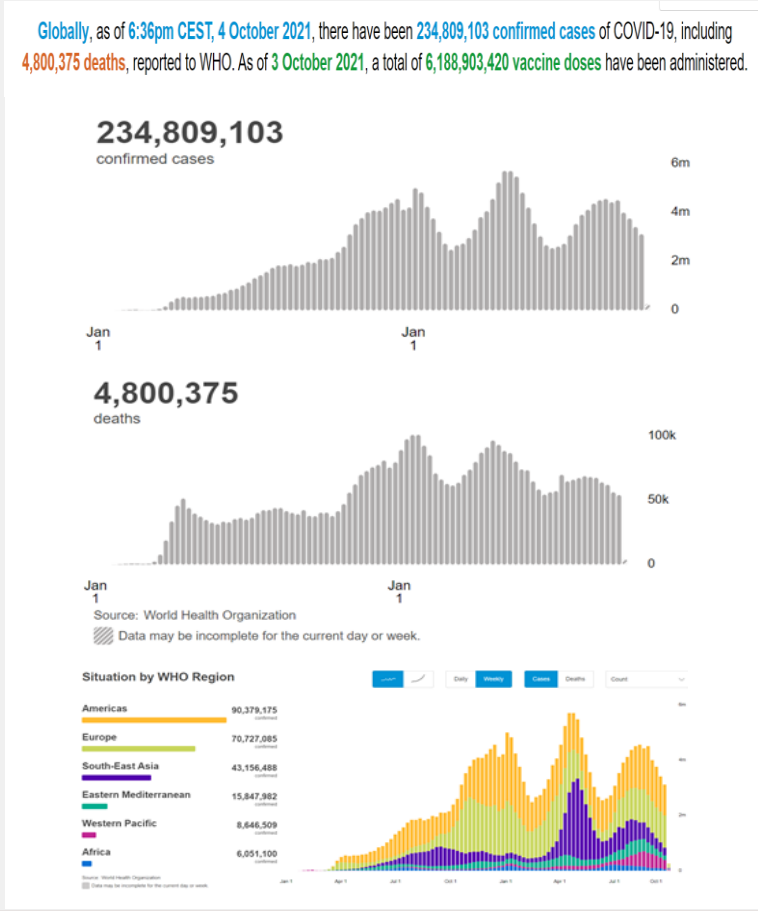
- Phase 2b data from EMPATHY Part A (400pts) in early 2022
- Potential EUA filings based upon data, with full filings thereafter

Therapeutics are Needed Now, More than Ever



Vaccinations **faster and better** than anyone could have hoped

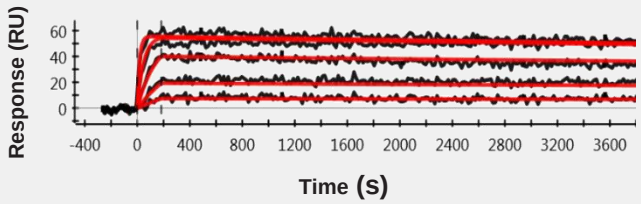
Variants continue to rise globally, challenging the effectivity of vaccines



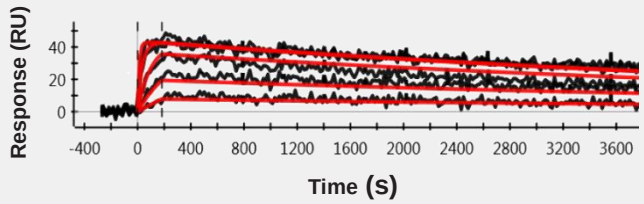
Hospitalizations up again, mostly in unvaccinated group

Cooperative Target Engagement Leads to Super Affinity

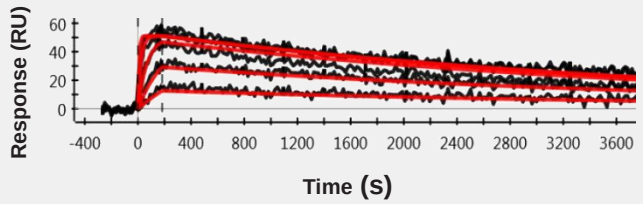
DARPin #1; 1 hour off-rate

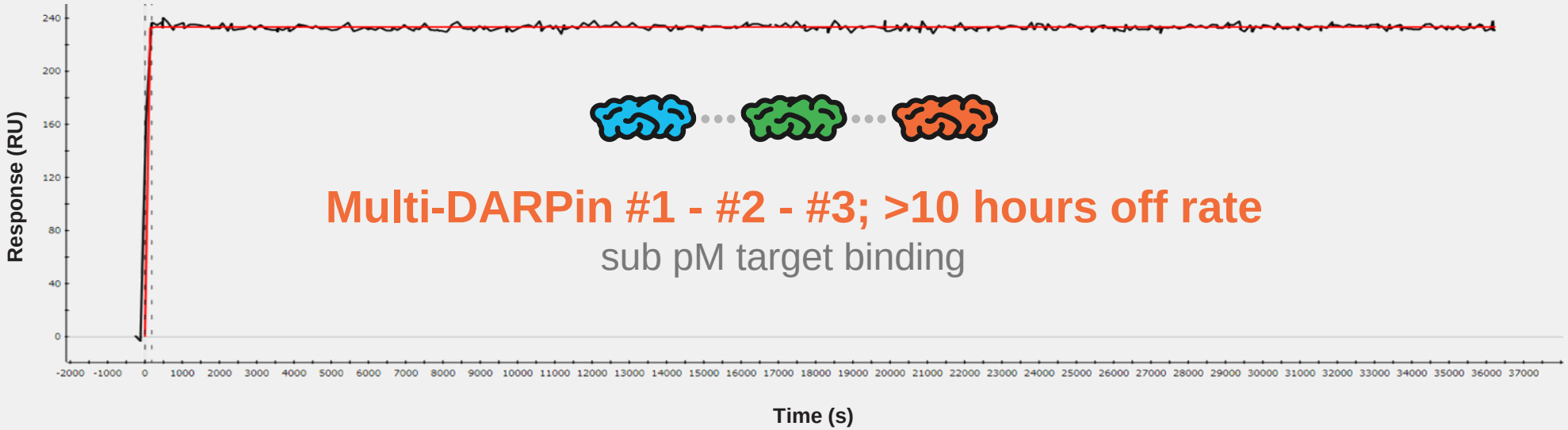


DARPin #2; 1 hour off-rate



DARPin #3; 1 hour off-rate



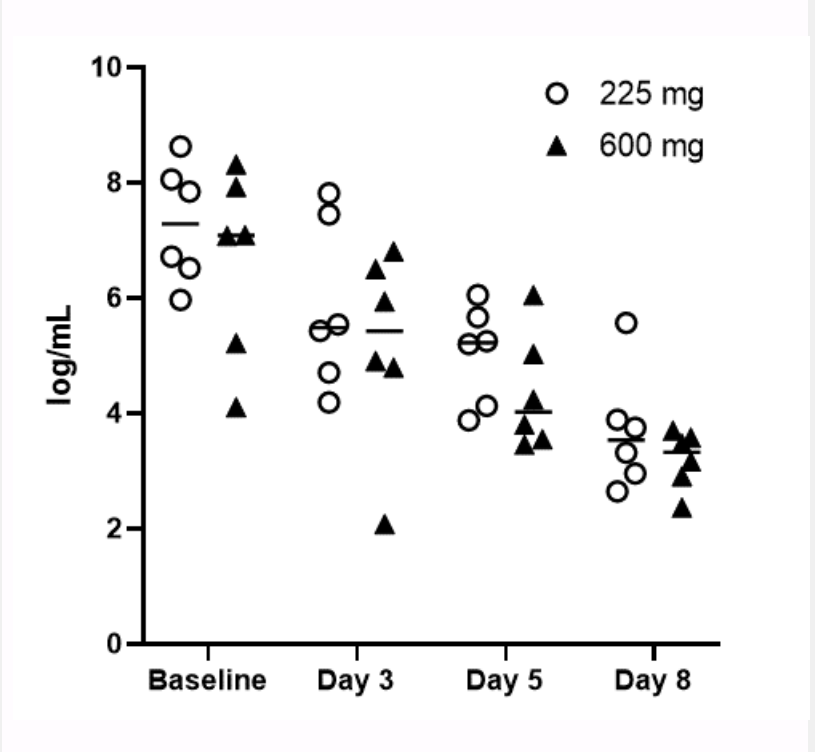


Multi-DARPin #1 - #2 - #3; >10 hours off rate

sub pM target binding

Ensovibep: Current Clinical Status

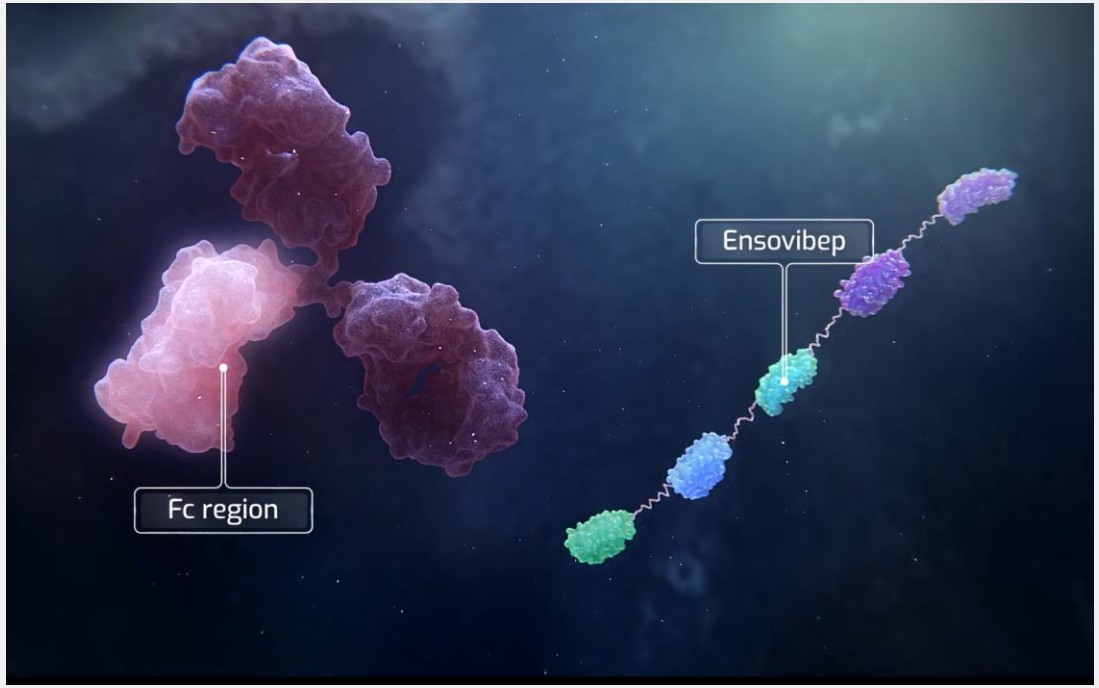
- **Phase 1 results / status:**
  - I.V. administration: safe and well tolerated ✓
  - Bolus administration: completed ✓
  - Subcutaneous (s.c.) administration: ongoing
  - Half-life established: 2-3 weeks ✓
- **Single-arm Phase 2 results:**
  - Safety, half-life and validate viral clearance methods for P2/3 confirmed ✓
- **Empathy study:**
  - Ongoing



Phase 2 Viral Load Analysis - qPCR

(Serology analysis ongoing)

Ensovibep: Opportunity for Ambulatory & Hospitalized Setting



- **Ambulatory setting: Rapid test, rapid treat**
  - Ensovibep: ¼ size of antibody "cocktail"
  - Very high potency
  - Opportunity for small volume s.c. injection
  - Protection against variants

Ensovibep Clinical Development; Registrational Trials

2021	2022

Possible EUA*

Potential BLA submission

EMPATHY

Rapid Test – Rapid Treat

NOVARTIS

PART A: Fully enrolled 400 ambulatory patients with mild to moderate symptomatic COVID-19; Collecting data for analysis

PART B: 1,700+ ambulatory patients on the selected dose level / placebo

Subcutaneous Phase 2/3 studies planned

ACTIV-3

Hospitalized patients with COVID-19-
470 patients randomized; ACTIV-3 will not continue in hospitalized patients

NIH

* Emergency Use Authorization submission, pending interim analysis of data is supportive of EUA

ACTIV-3: Enrollment Stopped Following Futility Analysis

- Ensovibep did not demonstrate benefit over present standard of care in hospitals
  - 470 patients randomized in the ensovibep arm – no safety concerns
  - Futility analysis evaluated patients 5 days post-treatment

- Still a great need for this population – we will review all data, when available, and share any potential learnings to better inform this population
  - 4/5 antivirals that reached futility analysis, were halted
    - Of these, all other molecules have gone on to show efficacy in the ambulatory setting

- Ensovibep ambulatory results – early 2022

Outpatient Efficacy Well Established for Antivirals

ACTIV-3

Candidate	Type	Hospitalized	Outpatient
RegenCov Regeneron	Antibody cocktail	In sub-group seronegative	✓
AZ7442 Astra Zeneca	Antibody; silenced Fc	TBD	✓
Ensovibep Molecular Partners	DARPin	X	TBD
BRII-198 Brii	Antibody	X	✓
Sotrovimab Vir	Antibody	X	✓
Bamlanivimab and etesevimab Eli Lilly	Antibody cocktail	X	✓
Paxlovir Pfizer	Oral protease inhibitor	Enrolling	✓
Molnupiravir Merck	Oral Viral replication inhibitor	X	✓

Novartis Deal Terms

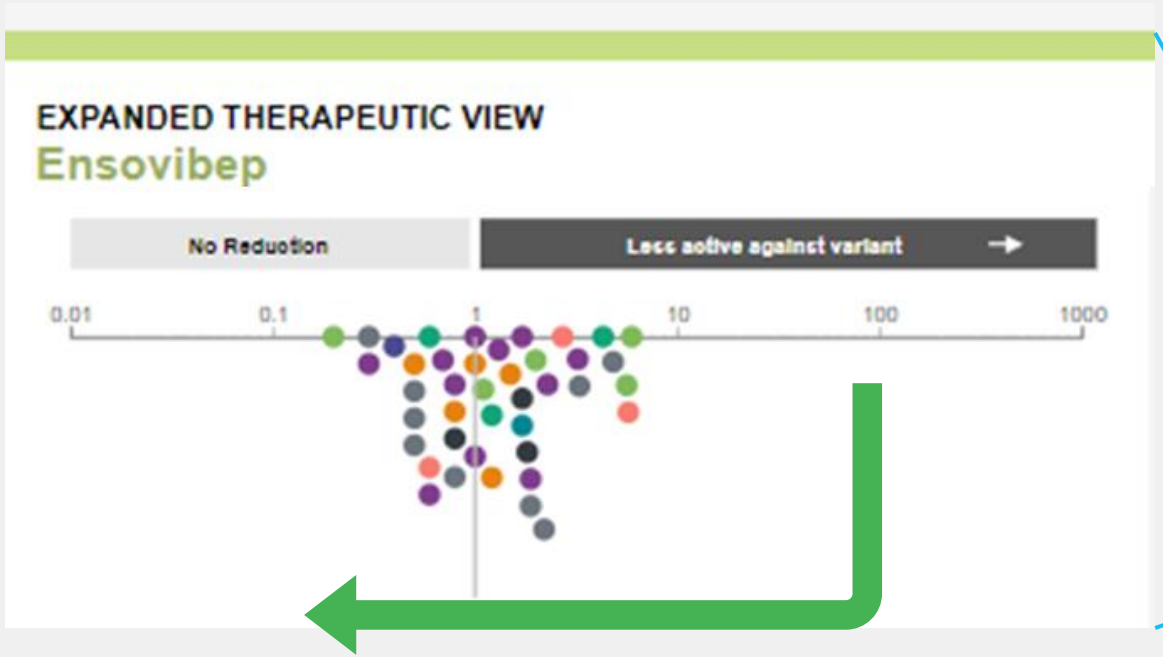
- **CHF 210m in upfront and near-term potential milestones**
  - CHF 60m upfront
    - CHF 20m as a cash payment
    - CHF 40m in MOLN shares
  - CHF 150m milestone payment upon option exercise to license

- **22% royalty on sales in commercial countries**
  - Molecular Partners has agreed to forgo royalties in lower income countries and is aligned with Novartis' plans to ensure affordability based on countries' needs and capabilities.

- **Clinical Development:**
  - Novartis pays for all clinical development of ensovibep and MP0423, beyond phase 1

Cooperative Binding Translates to Prevention of Mutational Escape

Ensovibep maintains activity against all variants of concern



Under 100 ng/ml is considered therapeutically effective

All Variants | Reported *in vitro* Therapeutic Activity

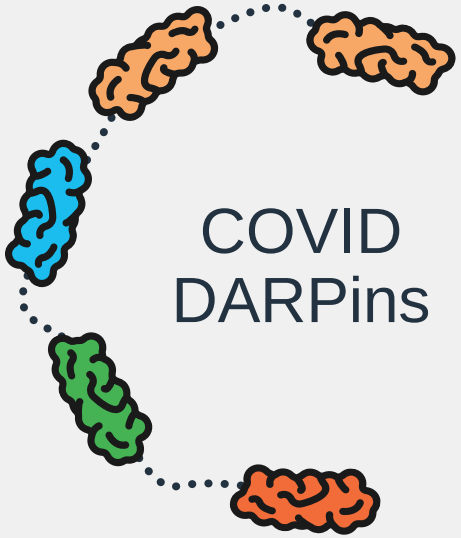
Ensovibep Upcoming Milestones

- Final data from phase 1
- Open label phase 2a results

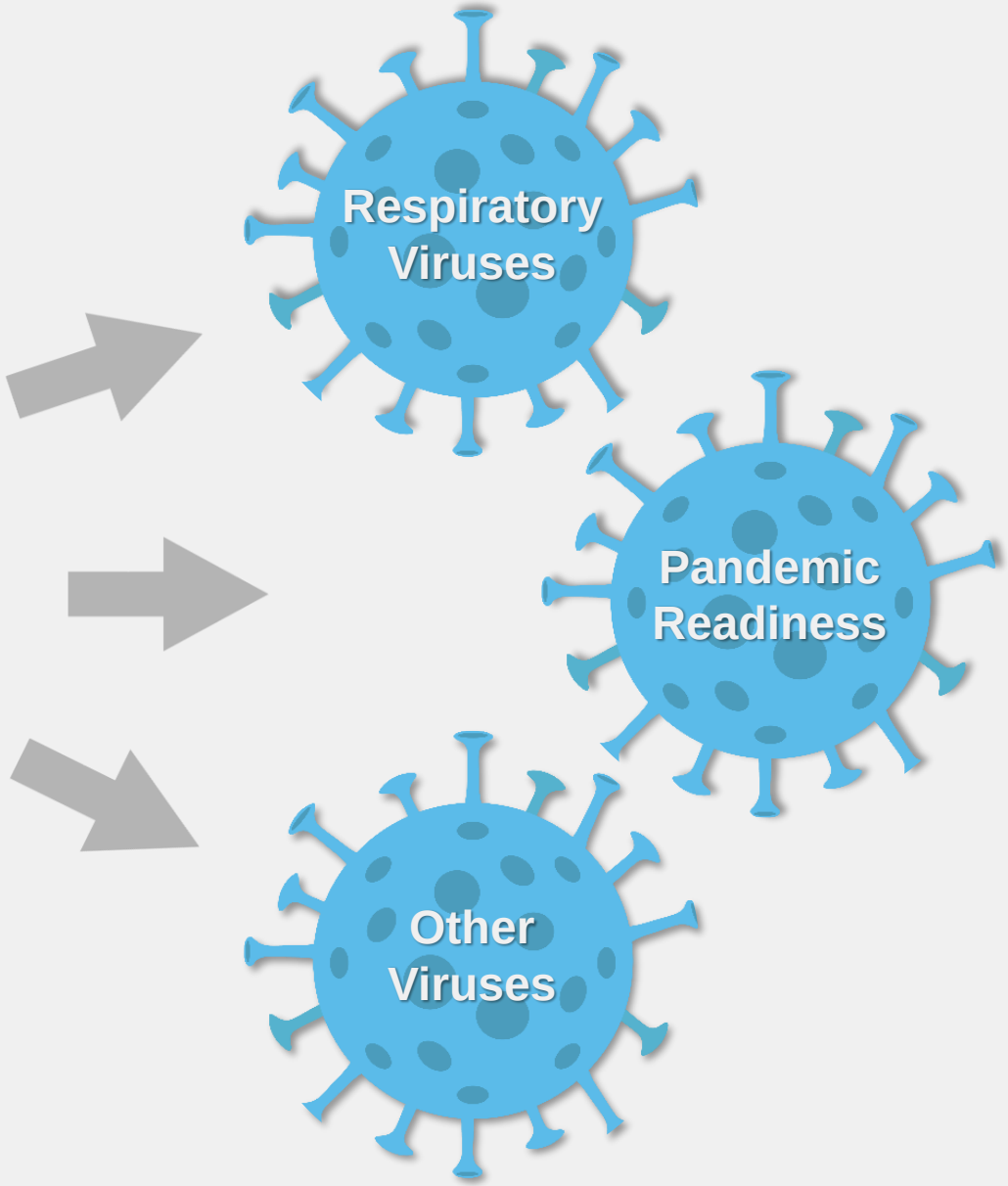
- EMPATHY (Novartis / MP)
  - ✓ 400 patients enrolled
  - Part A results – expected early 2022
  - Part B initiate (N≥1,700)
  - Potential EUA submission early 2022

- S.C. Phase 2/3 study initiation (Novartis / MP)
  - Initiate once dosing for EMPATHY part B is established

DARPin Opportunities in Virology



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



MOLECULAR partners

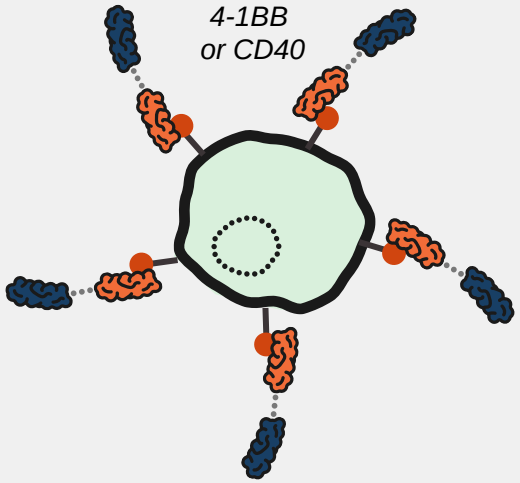
Localized Immune Activators

AMG 506 / MP0310 & MP0317

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

BODY

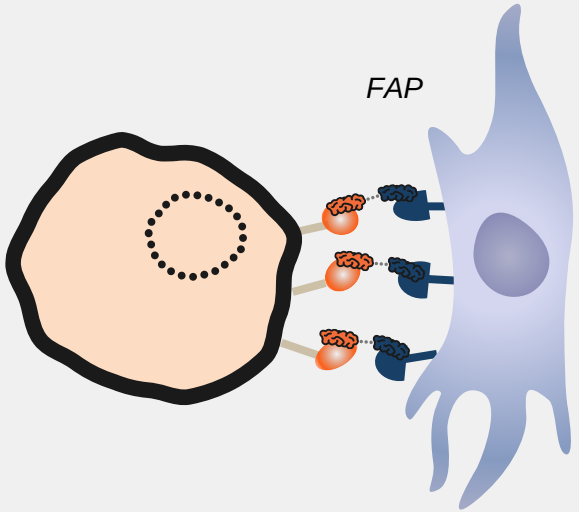
- In normal tissues, receptor is broadly distributed
- Immune cell remains inactive

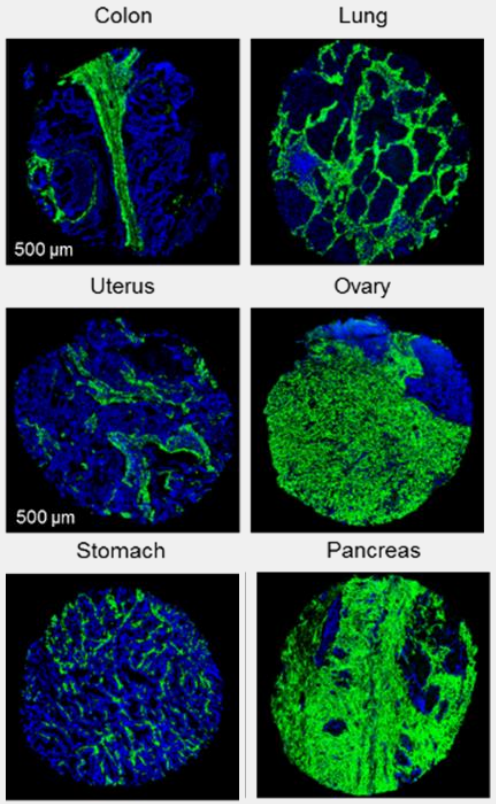


VS

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: Localized Activation of 4-1BB

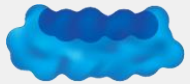
Target **Patient**

- Patients with solid tumors, low T-cell tumor penetration and positive FAP expression
- Patient populations where there are T-cell engagers in development, that can be boosted

Disease **Biology**

- Many solid tumors are surrounded by dense stromal tissue in which FAP expression is high
- 4-1BB activation is a strong recruiter of T cells

DARPin **Advantage**



- Systemic administration of MP0310, with localized activation at site of disease
- MP0310 is observed in tumor tissue, with no liver toxicity or systemic activation of immune cells
- Tumor biopsies show tumor-localized immune response consistent with the MoA

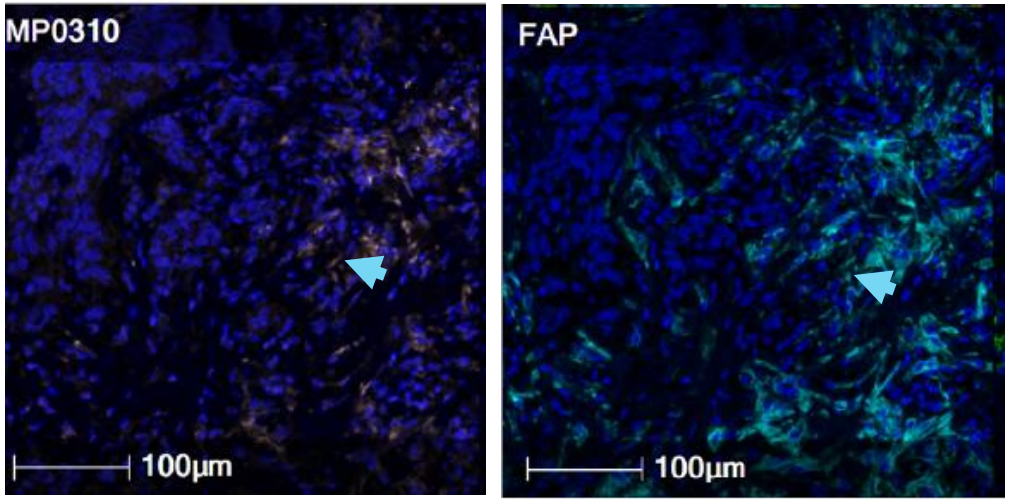
Expected **Milestones**

- Analyze data from ongoing phase 1 study, exploring weekly dosing.
- Determine appropriate next steps with Amgen

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

MP0310 low dose colocalizes with FAP

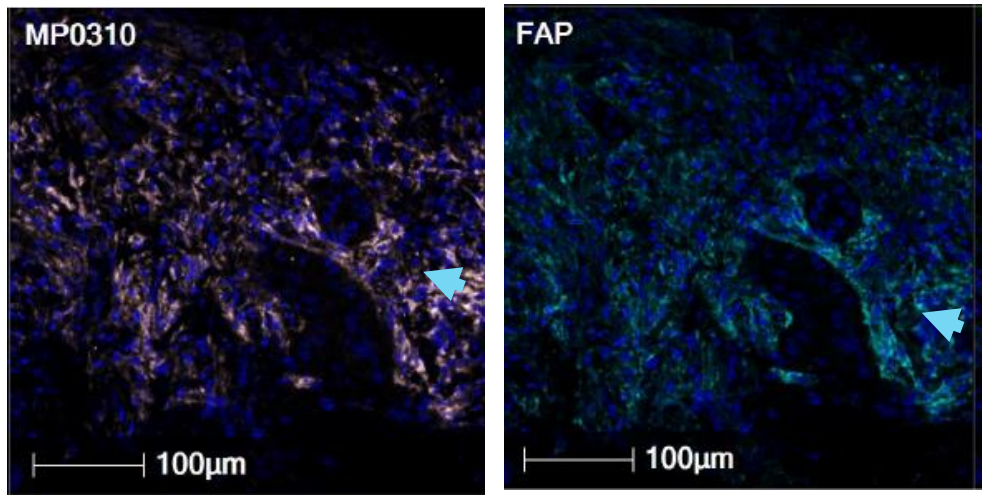
MP0310 < FAP



Endometrial carcinoma (Liver metastasis), C1D15

MP0310 high dose saturates FAP

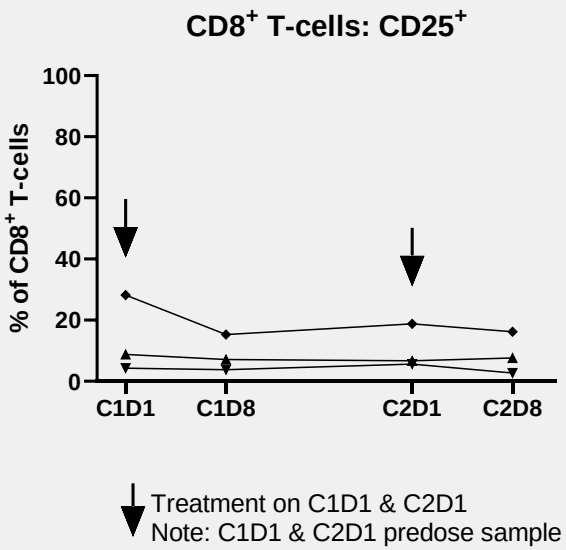
MP0310 > FAP



NSCLC (lung), C1D15

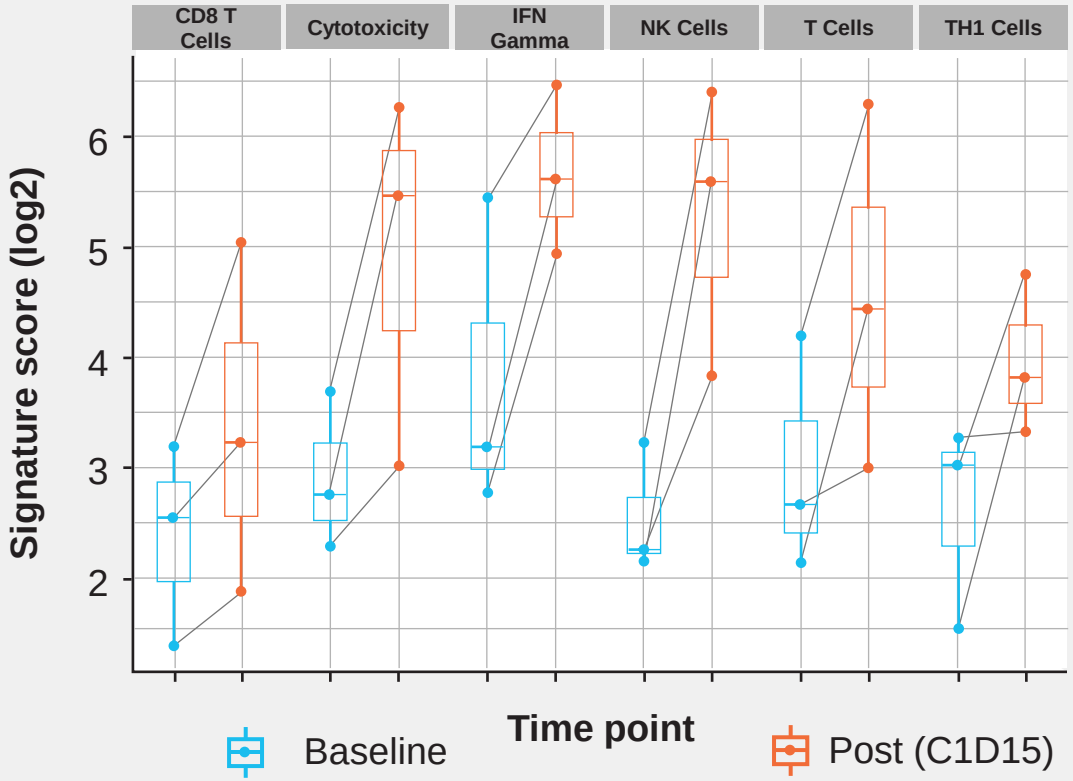
PD Activity in Paired Biopsies Supports AMG 506 / MP0310 MoA on 4-1BB Activation

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

MP0317: Localized Activation of CD40

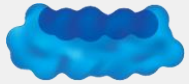
Target **Patient**

- Solid tumor patients with positive FAP expression
- Many patients still fail to benefit from current immunotherapy options, or relapse

Disease **Biology**

- CD40 is a potent activator of dendritic cells, macrophages, and B cells, and has long been considered an attractive immunotherapy target
- Prior attempts at targeting CD40 have shown anti-tumor activity but remain hampered by toxicity issues

DARPin **Advantage**



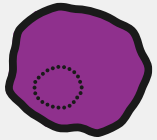
- MP0317 is designed to activate CD40 in a context dependent manner, by anchoring to FAP and activating via clustering
- Preclinical data show local activation of immune cells while limiting off target toxicity

Expected **Milestones**

- FIH studies initiating in Q4 2021
- Initial data in H2 2022
- Rapidly explore expansion arms in phase 1b

MP0317: FAP-dependent Activation of Specific Immune Cells

A

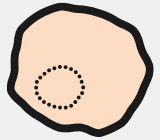


Dendritic cells:

CD86 ✓ IL-12 ✓

CD83 ✓ CD80 ✓

B



Macrophages:

TNFα ✓ IL-12 ✓

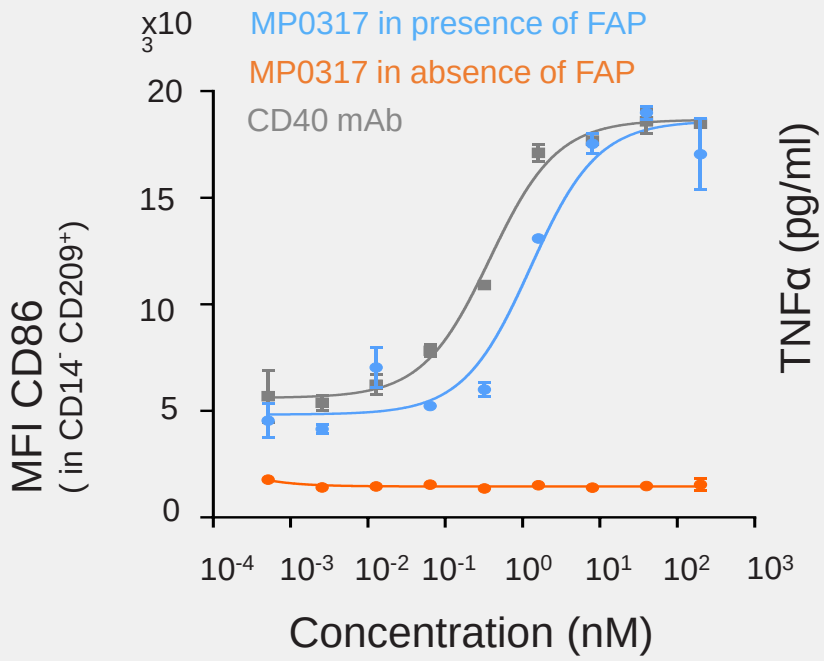
IL-6 ✓ CCL17 ✓

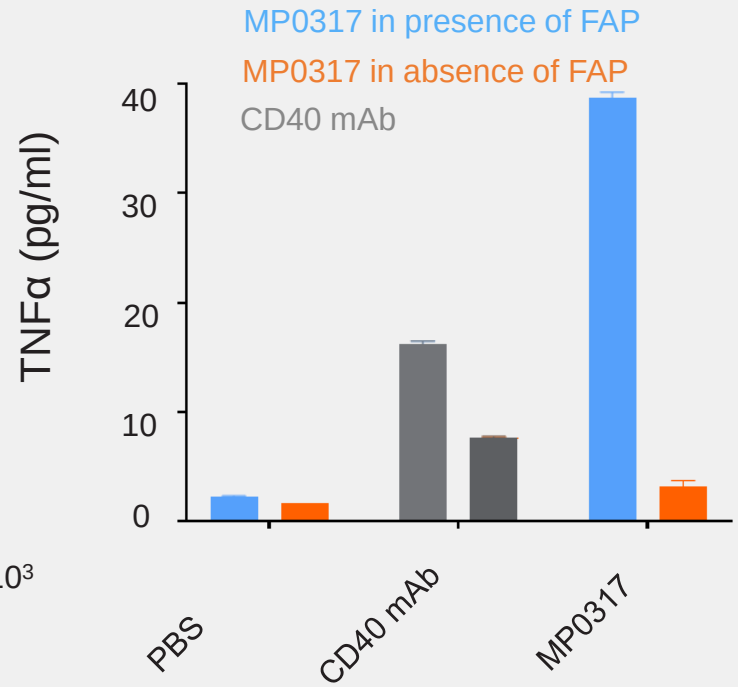
C

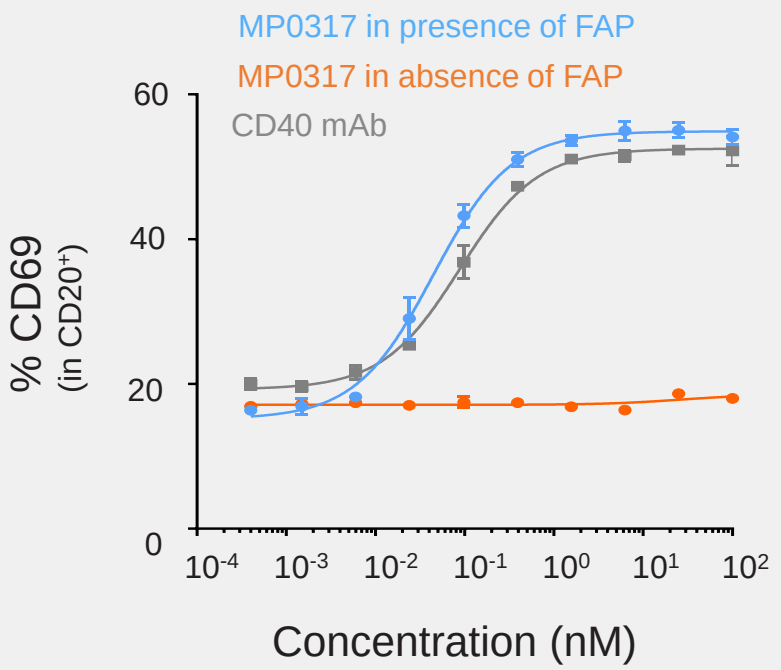
B cells:

CD69 ✓

CD86 ✓

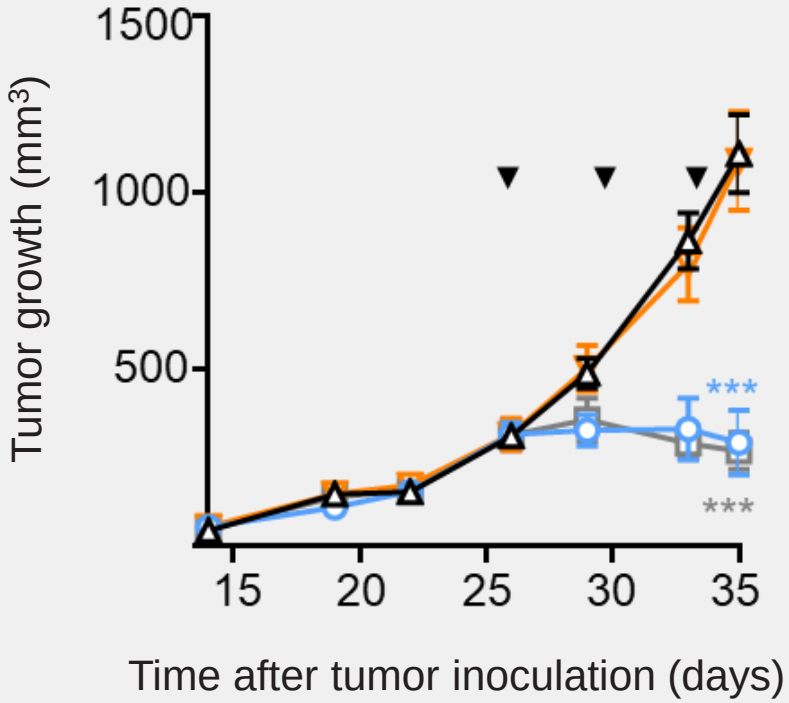


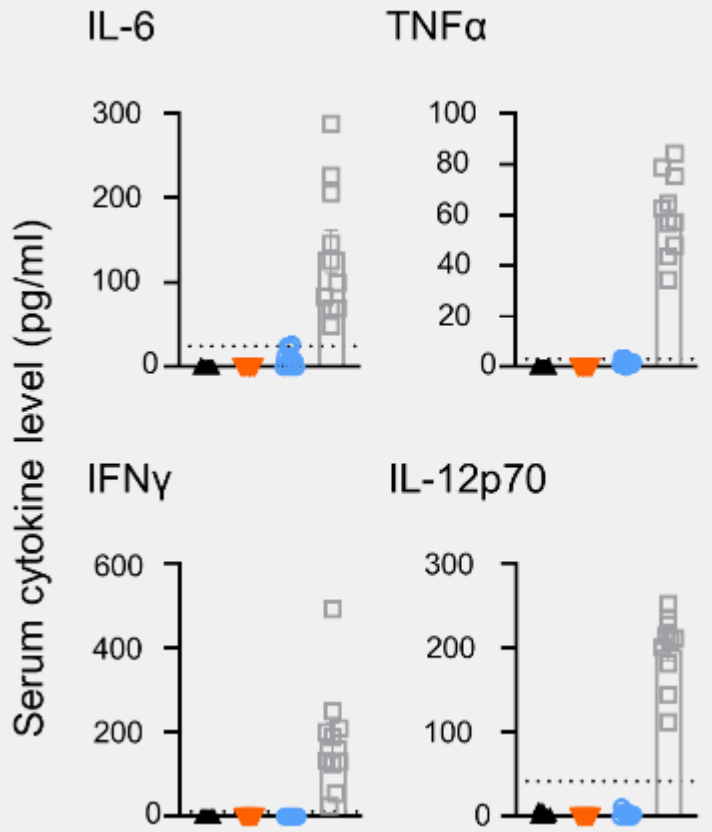




MP0317 Shows Full Activity with No Detectable Side-effects

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





Vehicle

Neg. CTRL*

mFAP x mCD40

mCD40 Ab

New Therapeutic Platforms: Unlocked

MP0533: Tri-specific T-cell Engager for AML

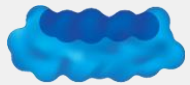
Target **Patient**

- ~20,000 people are diagnosed with AML every year
- Over 50% of patients die in the first year
- High relapse rates

Disease **Biology**

- **Persistence of LSCs is the driver of relapse**
- “MRD+ status” refers to low level disease and can be detected by immunophenotypic or molecular markers
- Current T-cell engager approaches are limited by on-target toxicity (not clean targets)

DARPin **Advantage**



- Avidity driven multispecific DARPin, targeting 3 TAA's, activating CD3
- CD3 T-cell engagement only activated when 2 or more TAA's are bound
- Should allow for broader therapeutic index with reduced safety issues

Expected **Milestones**

- Poster presentation at ASH 2021
- Featured update at MP R&D day, December 15, 2021
- FIH clinical studies in 2022

MP0533 for AML

Multi-specific T-cell engager with improved benefit/risk in AML

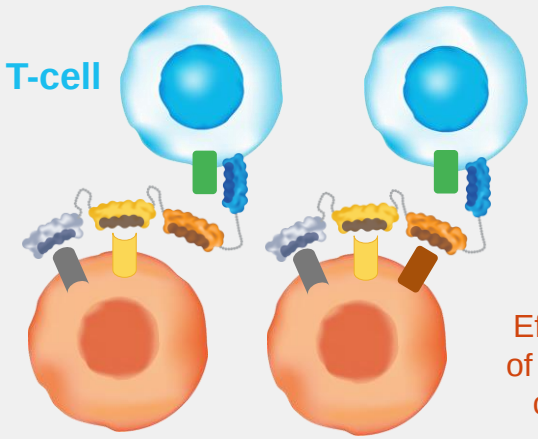
Efficacy

- **Higher dose levels** for efficient killing of cancer cells
- **Multiple attack:** Specific killing of several malignant cell types
- **Prolonged effect**: Counteract tumor heterogeneity / targeting leukemic stem cells (LSCs)

Safety

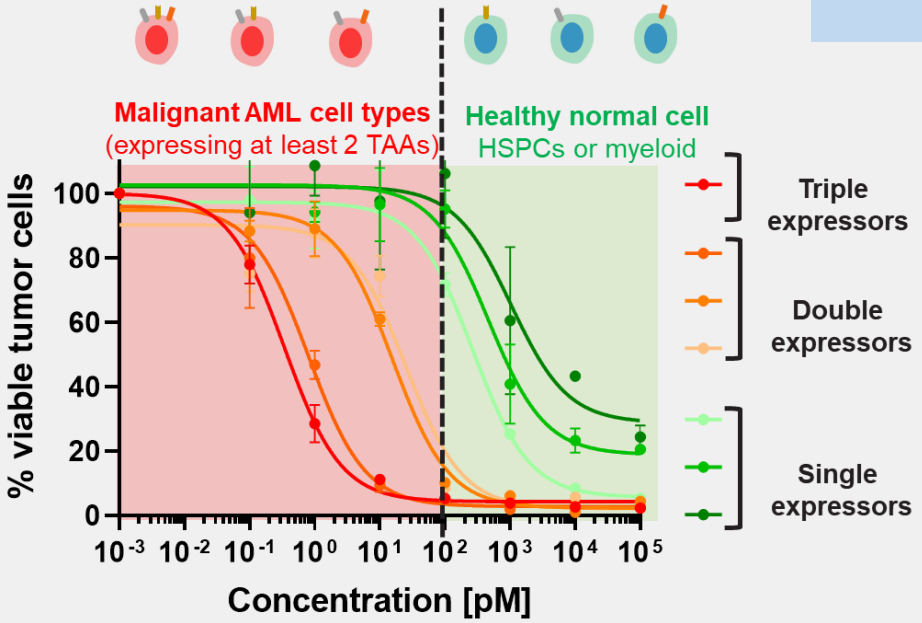
- **Reduce off-tumor effects**
- **Reduce hyper-immune stimulation** (e.g. cytokine release syndrome)

Multi targets
High avidity engagement



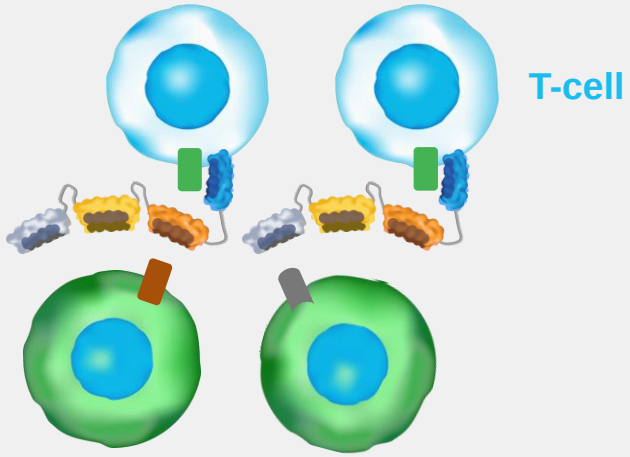
Efficient attack of heterogenous cancer cells

Malignant AML cell types
Blasts or LSCs (≥2 TAAs)



Minimal required dose level to kill cells

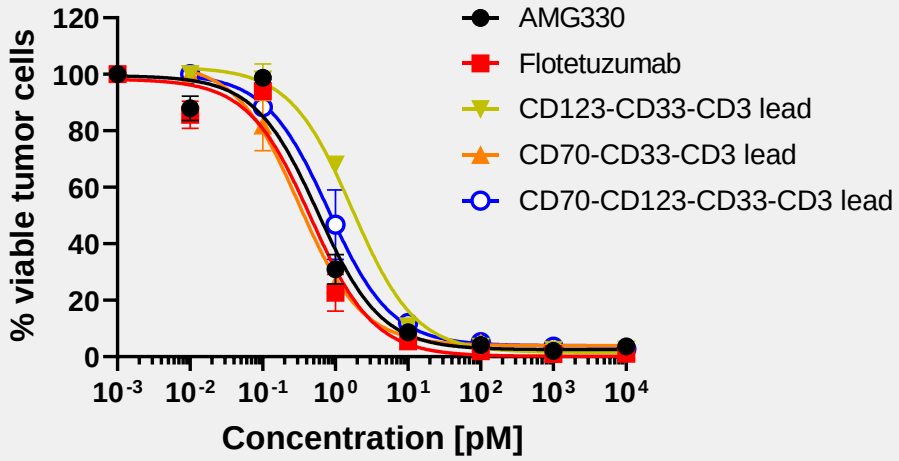
Single targets
Low affinity engagement



Healthy normal cell
HSPCs or myeloid cells

AML Candidates: Retained Potency with Favorable Side Effect Profile *in vitro*

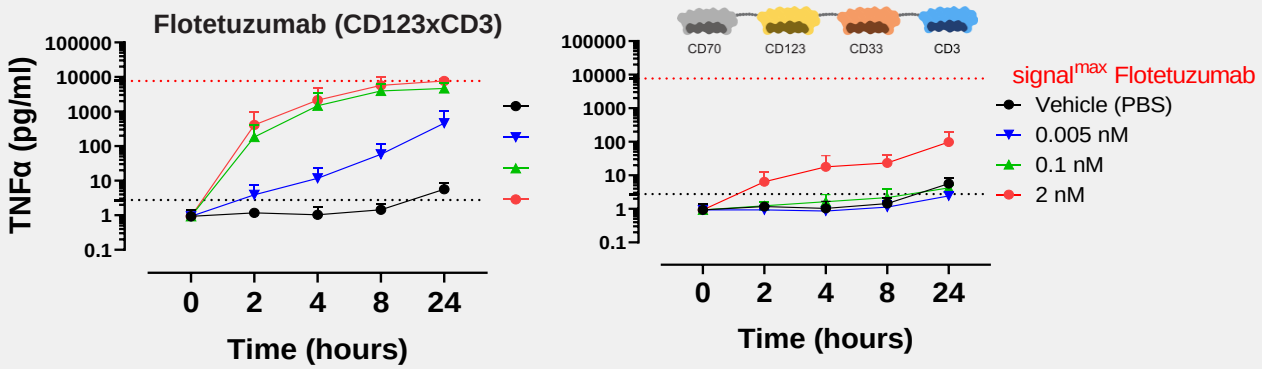
High Potency of Candidates



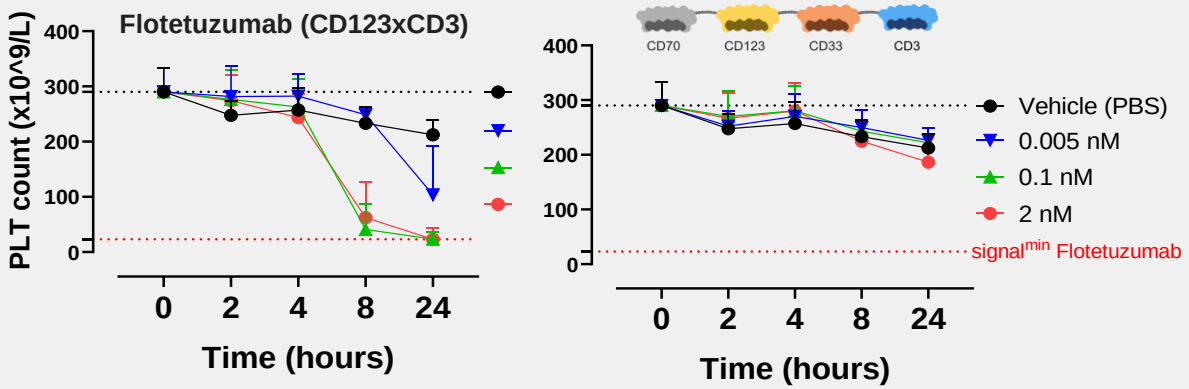
Effect on Healthy Blood Cells

immuneed

TNFα secretion



Platelet Counts

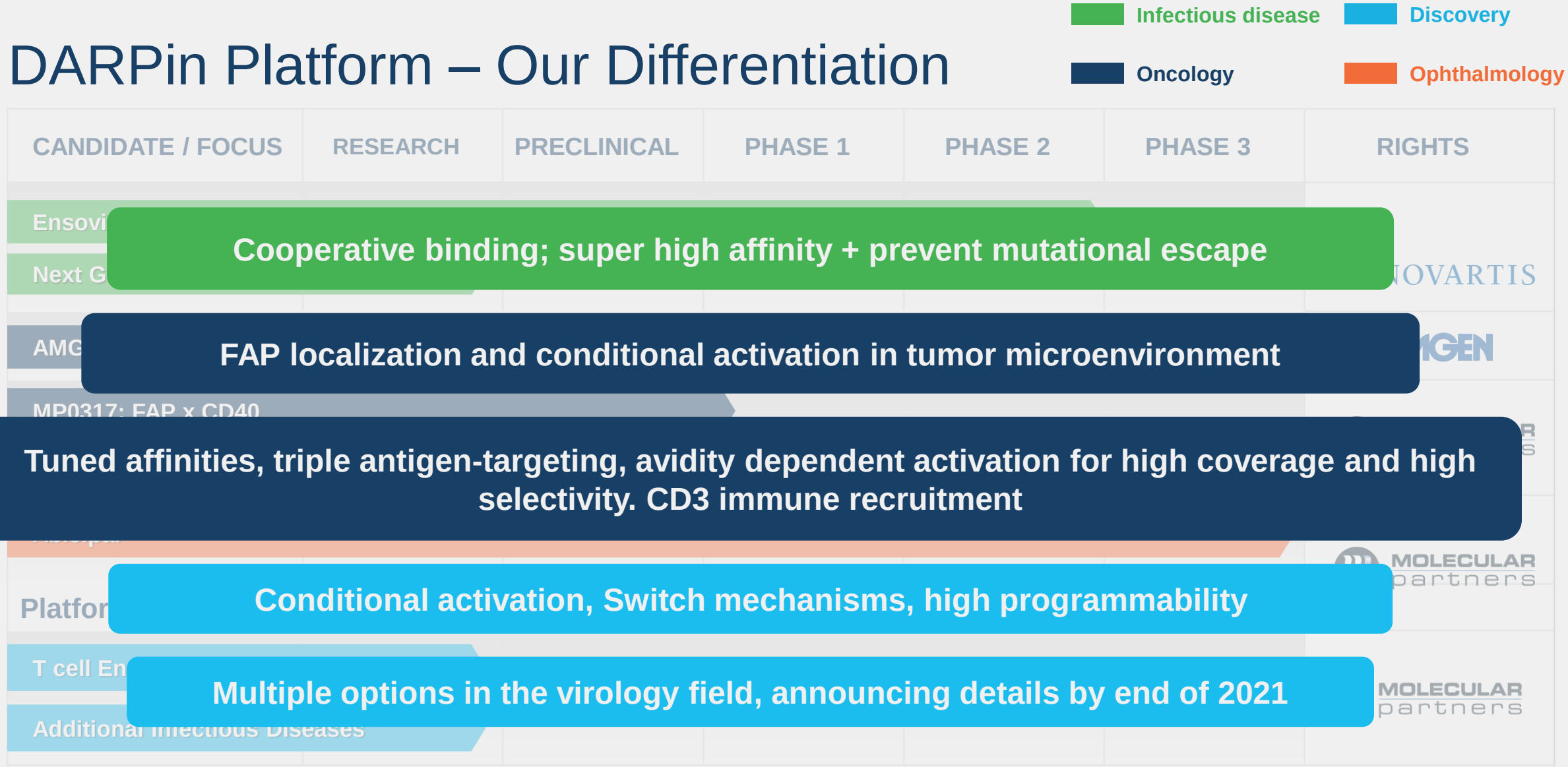


Financials & Outlook

Q3 2021 Financial Highlights

- Ongoing strong financial position with CHF 154.3 million in cash and short-term deposits as of September 30, 2021
- Completed initial public offering of American Depositary Shares (“ADSs”) on the Nasdaq, raising $63.8 million (CHF 58.8 million) in gross proceeds to secure financing of ongoing operations into H2 2023
- Net cash outflow from operating activities of CHF 71.6 million in the first nine months of 2021
  - For the full year 2021, the Company expects total expenses of CHF 70 - 75 million
  - In terms of cash outflow, the Company expects a gross cash utilization of approximately CHF 90 million for the full year 2021, which includes a total of CHF 20 million payable to Novartis for the manufacturing of commercial supply

DARPin Platform – Our Differentiation



Upcoming Potential Catalysts Across the Portfolio

Immuno-oncology portfolio	
AMG 506 (MP0310)	▪ Identify ideal dosing regimen in ongoing Phase 1 (H2/2021) ▪ Amgen potential review in Q4 2021 or early 2022
MP0317	▪ MP0317 Topline data in 2022
MP0533	▪ 1st Candidate selected for development ▪ Update at ASH – FIH in 2022
Antiviral portfolio	
Ensovibep (MP0420)	▪ EMPATHY readout Phase 2b from 400 patients in early 2022; potential for EUA application (US&EU) ▪ BLA submissions possible in 2022
Novel antivirals	▪ Next generation COVID drug, built for the future ▪ Develop novel DARPins for additional viral targets

Funded into H2 2023

(Not incl. any future proceeds related to partnerships)

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