Custom Built Biology for Patients

40th Annual JPM Healthcare Conf.

January 2022

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

Disclaimer

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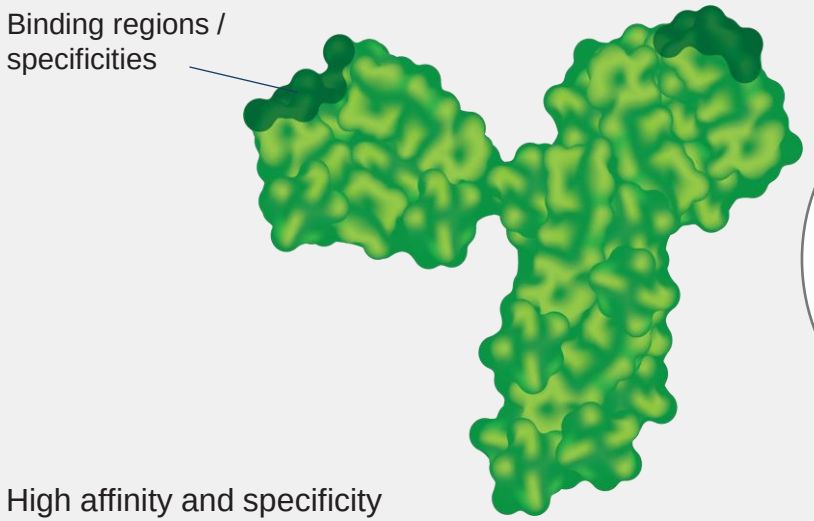
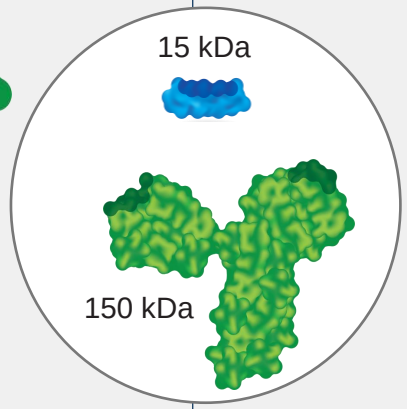
What are DARPins

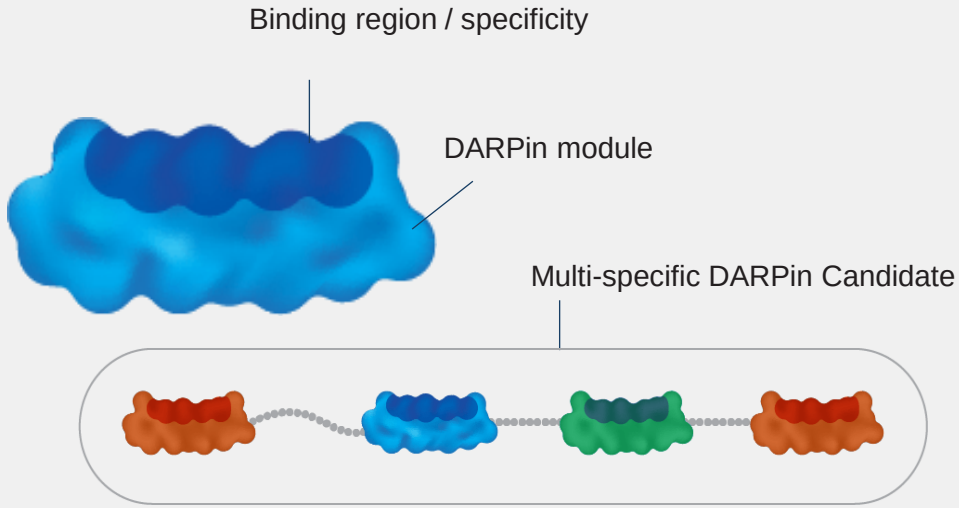
MONOCLONAL ANTIBODIES



- 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

Pipeline

Infectious disease | Discovery Oncology | Oncology | Ophthalmology

Pipeline

CANDIDATE / FOCUS	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	RIGHTS
Ensovibep – Covid	Covid ambulatory – Empathy					NOVARTIS
Next Gen Covid	Future VoC*					MOLECULAR partners
AMG506 / MP0310 FAP x 4-1BB	Solid tumors					AMGEN
MP0317 FAP x CD40	Solid tumors					MOLECULAR partners
MP0533 CD3 x CD33+CD70+CD123	AML					MOLECULAR partners
Abicipar VEGF	wet AMD – Cedar & Sequoia					MOLECULAR partners
Radio Ligand Therapy	Solid tumors					NOVARTIS

Platform Discovery

Radical simplicity & Conditional Activation	MOLECULAR partners
Additional Infectious Diseases	

Pipeline

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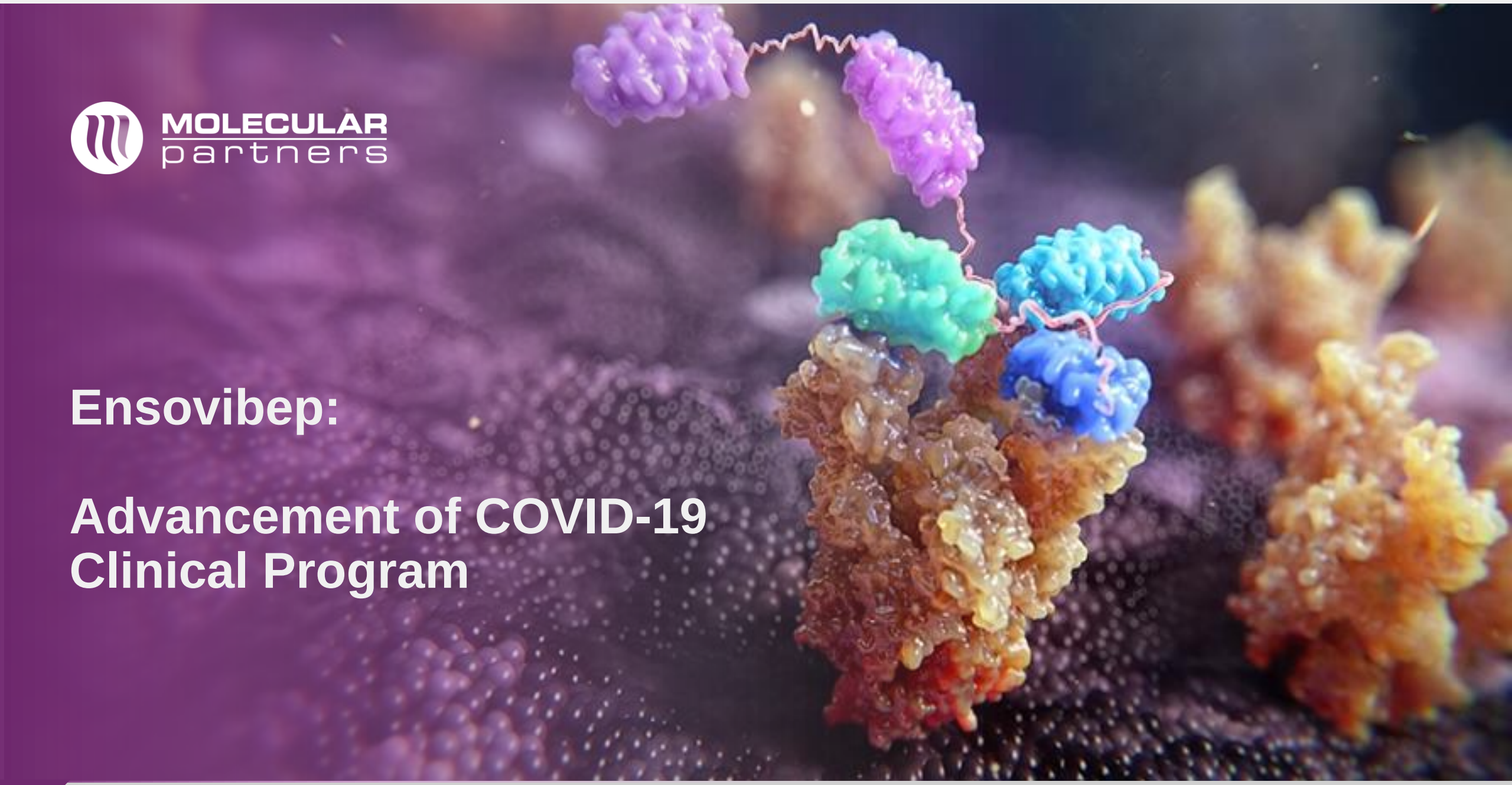
Platform Discovery

- Radical simplicity & Conditional Activation
- Additional Infectious Diseases

MOLECULAR partners

* VoC = Variant of Concern

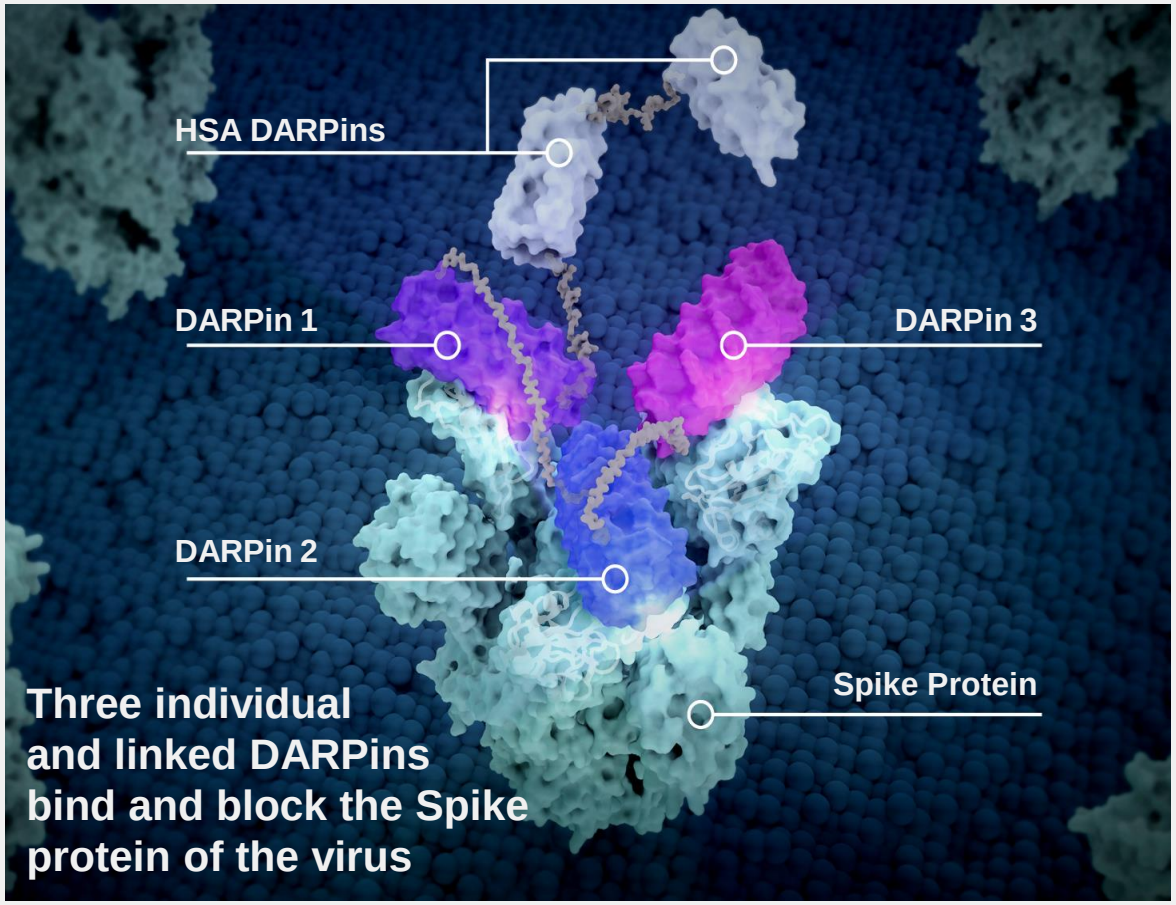


Ensovibep:

Advancement of COVID-19 Clinical Program

Structure and Features of Ensovibep Neutralizing the SARS-CoV-2 Spike Protein

3D model of a DARPin molecule



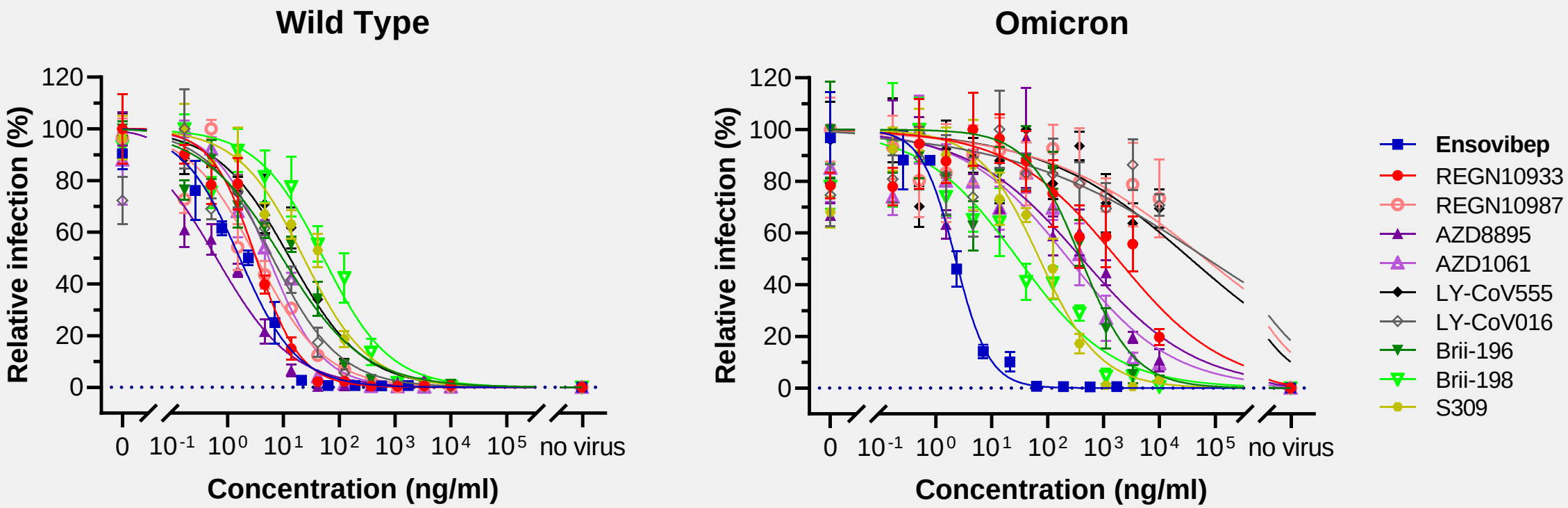
Characteristics

- **High potency**: high binding affinity and avidity leads to one of the highest anti-viral potencies reported to date
- **Pan variant activity**: cooperative binding of different sites allows blocking of all described variants of concern, so far
- **Simple administration**: long-half life, high solubility and low dose activity can allow for single administration via i.v., i.v. bolus, or s.c. injection
- **Supply**: microbial manufacturing in *E.Coli*

DARPin, designed ankyrin repeat proteins; RBD, receptor binding domain; HSA, human serum albumin; SARS-Cov-2, Severe acute respiratory syndrome coronavirus 2.

Walser M. *Biorxiv*. 2021. https://doi.org/10.1101/2020.08.25.256339

Ensovibep Retains Full Activity Against Omicron



Ensovibep Clinical Development; Registrational Trials

2021	2022

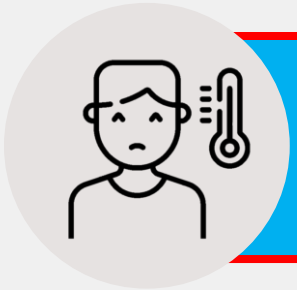
Possible EUA*

Potential BLA submission

EMPATHY

Rapid Test – Rapid Treat

NOVARTIS



PART A: Fully enrolled 400 ambulatory patients with mild to moderate symptomatic COVID-19; Primary endpoint met

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

EMPATHY Part A (Phase 2) Clinical Design and Endpoints

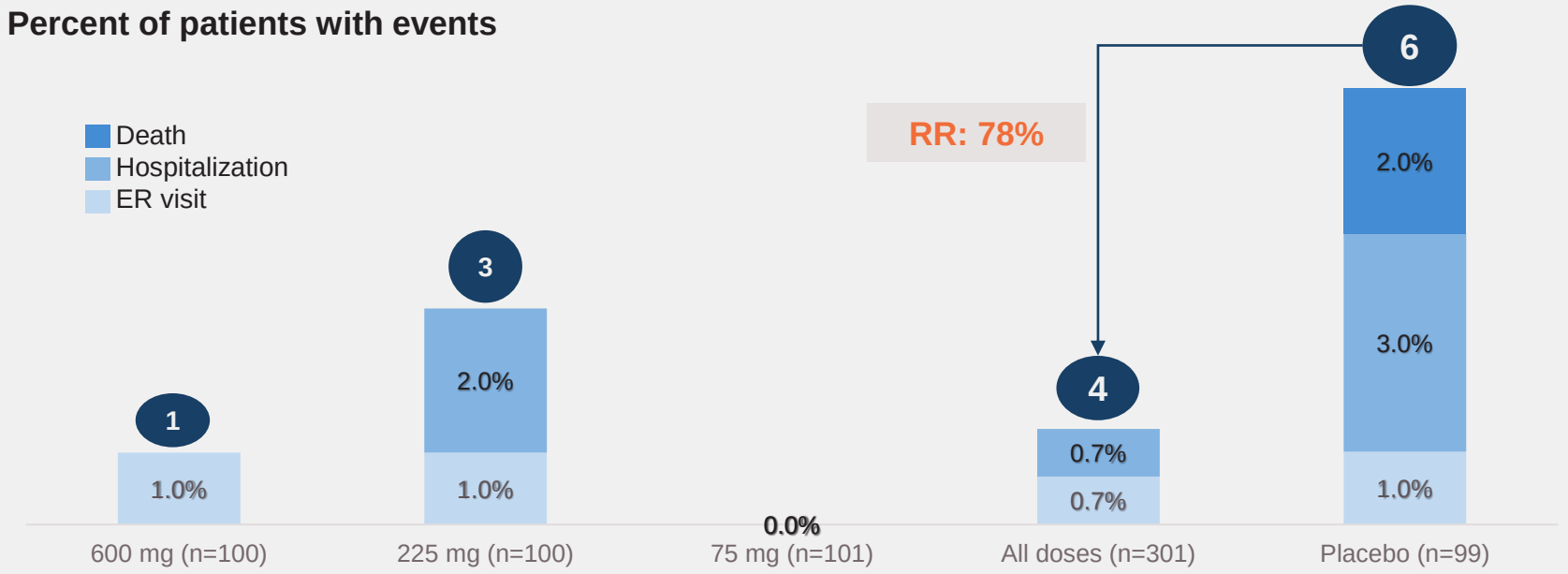
Objective	**Demonstrate superiority of ensovibep, compared to placebo, and select a dose for Phase 3**
Population	• Ambulatory symptomatic patients diagnosed with COVID-19 • Onset of symptoms within 7 days prior to dosing • Positive Rapid Antigen Test on the day of dosing • Vaccinated patients allowed

Primary Endpoint	• **Time-weighted viral load reduction through through Day 8**
Key Secondary Endpoints	• Reduction in ER visits and/or hospitalizations (≥ 24 hours) and/or death up to Day 29 • Time to sustained clinical recovery (resolution or improvement in clinical symptoms) up to Day 29

Cohorts	
ensovibep 600mg i.v.	~ 100 pts
ensovibep 225mg i.v	~ 100 pts
ensovibep 75mg i.v.	~ 100 pts
placebo i.v.	~ 100 pts

EUA Submission Supported by Secondary Endpoint in Reductions in Hospitalization and/or ER Visit, or Death

Patients with hospitalization and/or ER visit related to COVID-19 or death



Numbers indicate absolute number of patients

Note:

In the hierarchy of ER-visit/ hospitalization/ death- patients are counted in the highest category

- ER visits exclude those resulting in hospitalization/ death
- Hospitalizations exclude those that resulted in death

Significant Reductions in Viral Load, Risk of Hospitalization and Death, and Faster Time to Recovery (Top Line Results)

- Statistically significant reduction of viral load from baseline, through Day 8 over placebo for all doses (primary endpoint)
- Fewer hospitalization and/or ER visits related to COVID-19 and no deaths for ensovibep treated patients vs. those on placebo (secondary endpoint)
  - **4/301** patients with hospitalizations and/or ER visits related to COVID-19 or death across all treatment arms
  - **6/99** patients in the Placebo arm
  - Relative risk reduction of **78% for all events; hospitalization, ER visits, and/or death**
    - Relative risk reduction of **87% for hospitalization and/or death***
  - **No deaths** in any treatment groups, whereas **two deaths** occurred in placebo treated patients
- Clinically meaningful benefit for patients treated with ensovibep (secondary endpoint)
  - **Median time to clinical recovery was faster** for ensovibep treated patients vs. placebo
  - **More patients demonstrated clinical recovery** when treated ensovibep vs. placebo (day 29 cutoff)
- No unexpected safety findings were observed in Part A.

*not a pre-specified endpoint

Novartis Deal Terms and Next Steps

Deal Terms

- Novartis option exercise for in-licensing of ensovibep: CHF 150 m
  - CHF 60m previously received at signing of option agreement (20m cash/40m MOLN shares)
- Royalty of 22% 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.

Next Steps

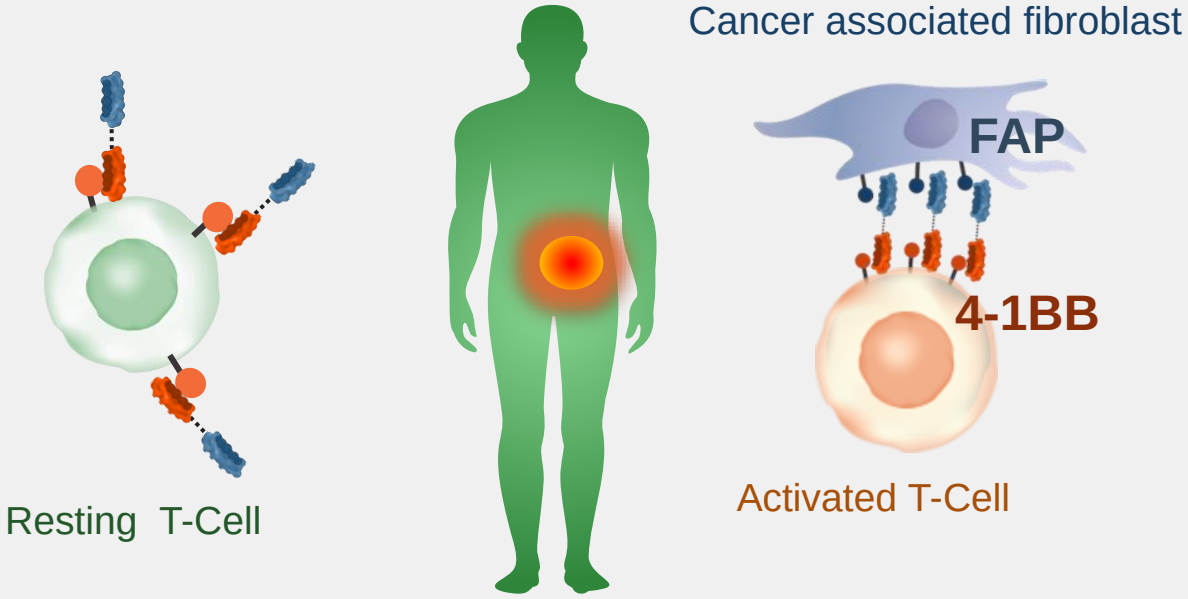
- EUA submission expected early 2022
- Discussion with appropriate federal agencies regarding supply agreements of ensovibep
- Part B initiate (N≥1,700)
- Planned initiation of subcutaneous Phase 2/3 study (led by Novartis)

MP0310 and MP0317

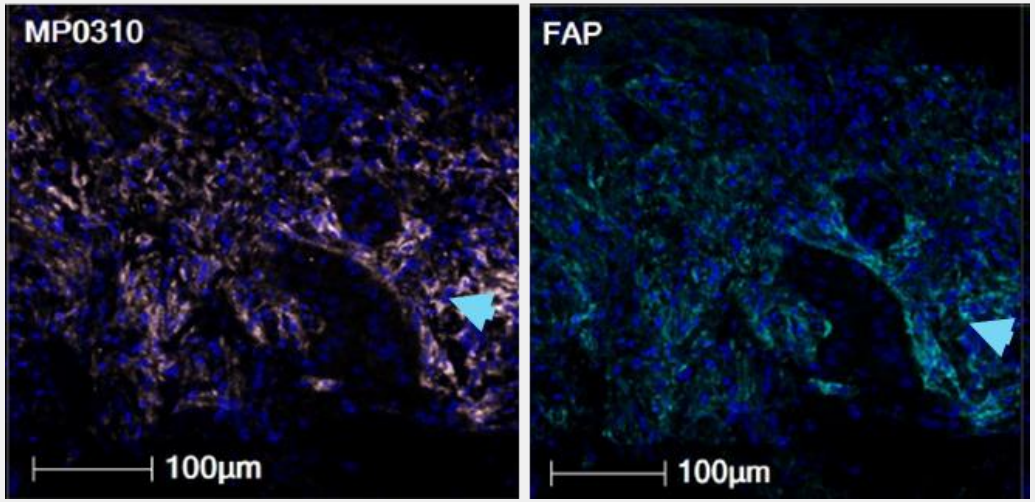
Multispecific Immune Activators

AMG 506 / MP0310: Localized Activation of 4-1BB FAP – an Ideal Target for Tumor-localized Activity

- Immune-cell activation via 4-1BB is associated with liver tox
- MP0310/AMG506 is designed to activate immune cells in the tumor only via FAP clustering



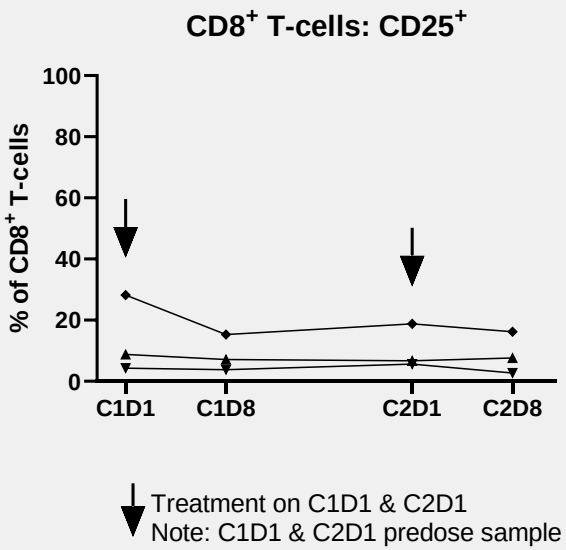
MP0310 & FAP staining in human biopsies from Phase 1 trial



- When dosed systemically, MP0310 bind to and co-localizes with FAP

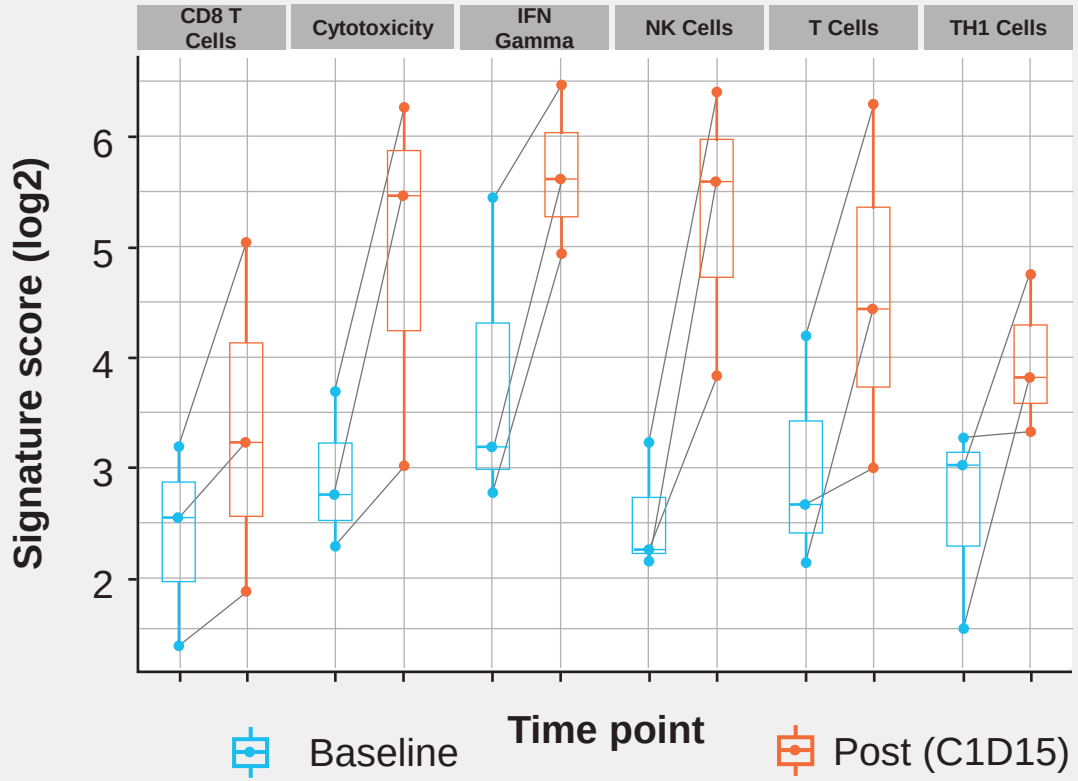
PD Activity in Paired Biopsies Supports AMG 506 / MP0310 MoA on 4-1BB Activation

BLOOD



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

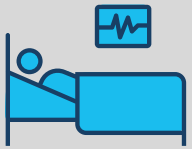
TUMOR



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

MP0317: Localized Activation of CD40

Target Patient

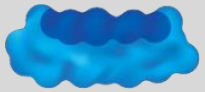


- Solid tumor patients with positive FAP expression
- Many patients still fail to benefit from current immunotherapy options, or relapse

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



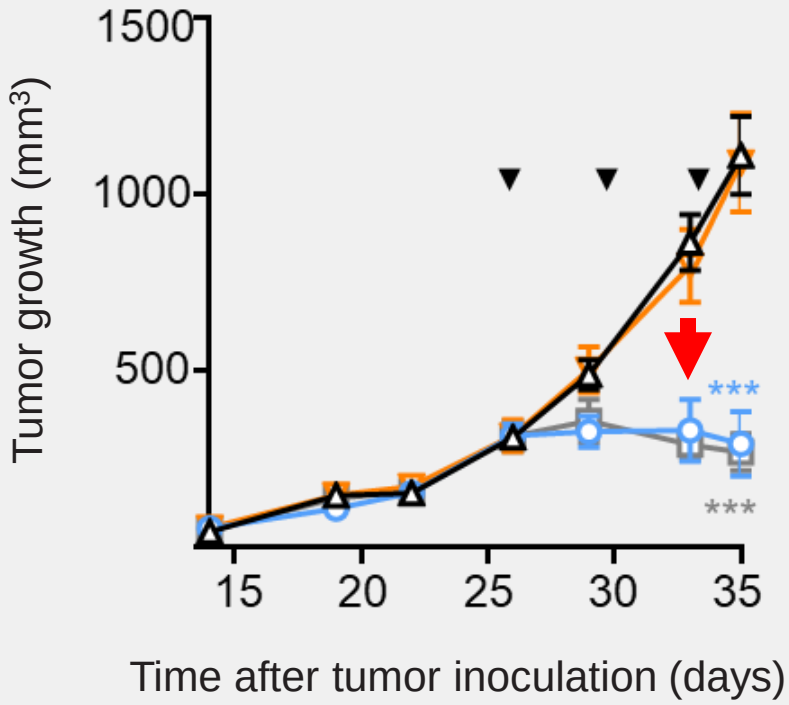
- MP0317 is designed to activate CD40 in a context dependent manner, by anchoring to FAP and activating via clustering
- Preclinical data show local activation of immune cells while limiting off target toxicity

Expected Milestones

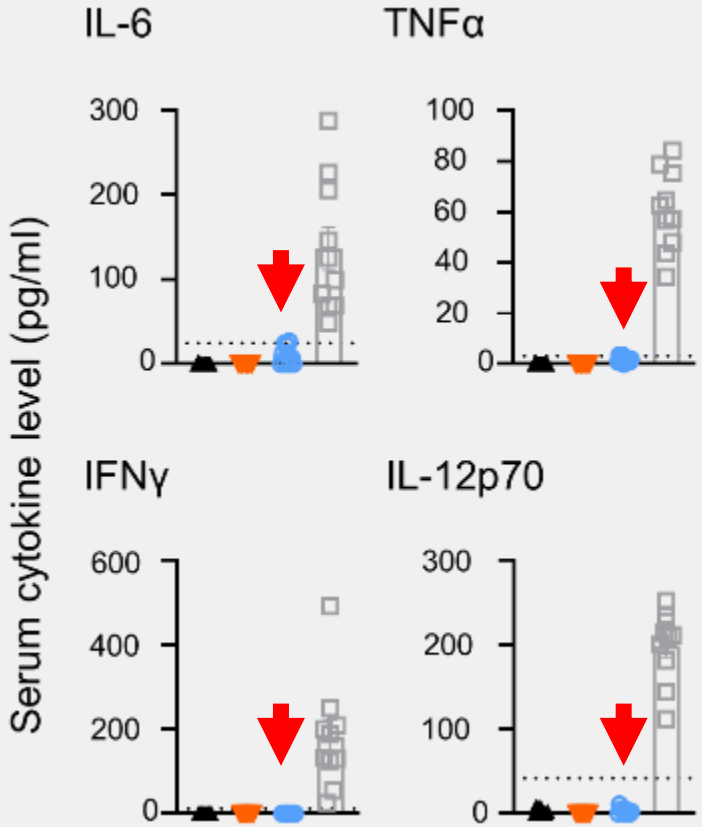
- FIH studies initiated in Q4 2021
- Initial data in H2 2022
- Rapidly explore expansion arms in phase 1b

MP0317 Shows Therapeutic Activity without Cytokine Release

Efficacy



Peripheral cytokine release



Vehicle

Neg. CTRL*

mFAP x mCD40

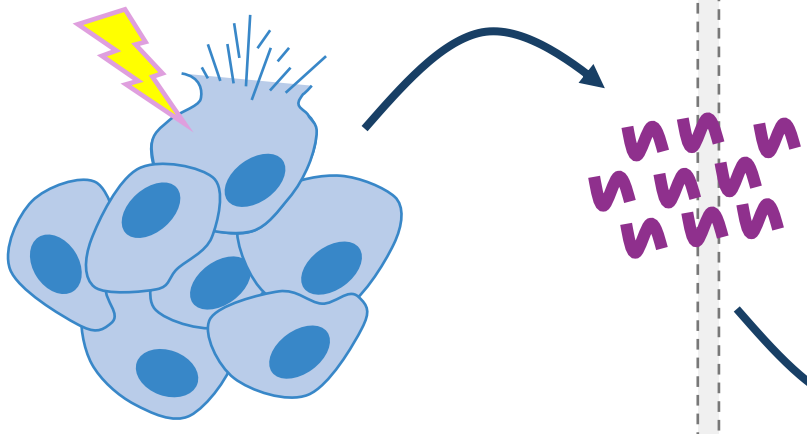
mCD40 Ab

MC38-FAP
Colorectal cancer

CD40 Open for Multiple Combination (IO or Other)

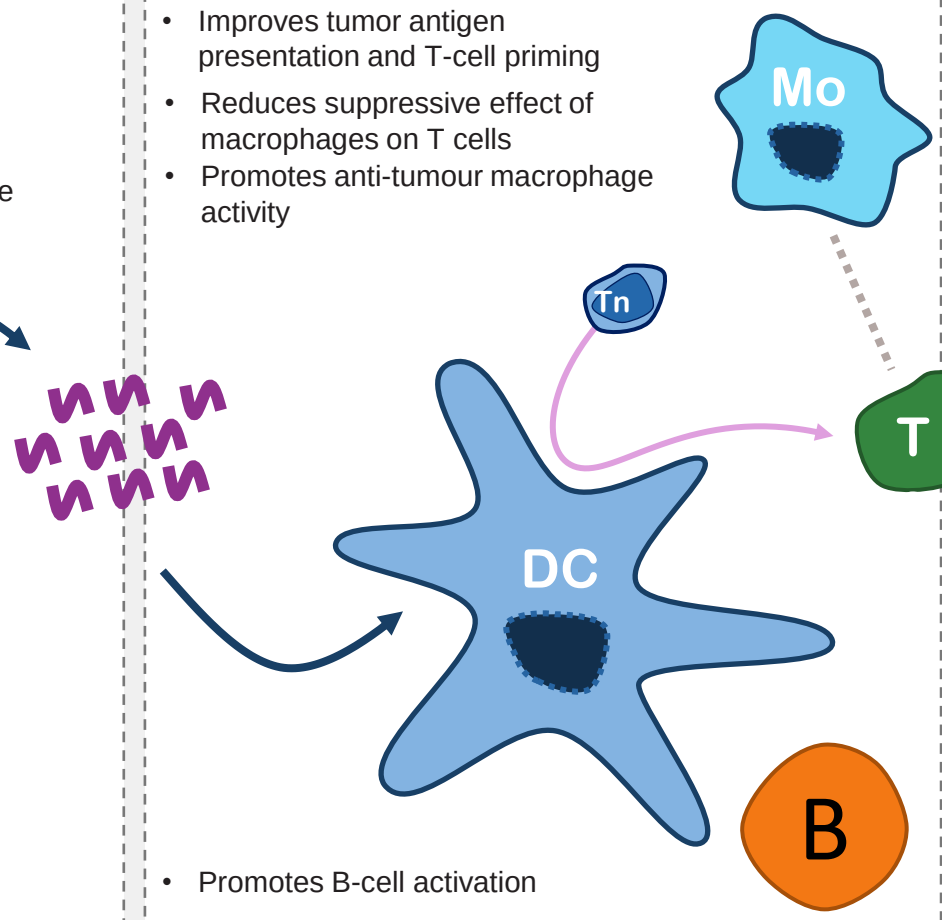
Chemo / Radio Therapy

- Direct tumor killing
- Release of tumor antigens
- Debulking aids immune cell access
- Timing with immunotherapy is important because immune cells can also be damaged



CD40

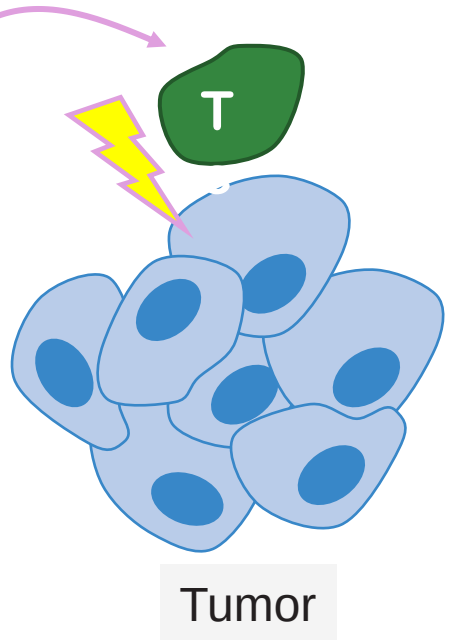
- Improves tumor antigen presentation and T-cell priming
- Reduces suppressive effect of macrophages on T cells
- Promotes anti-tumour macrophage activity

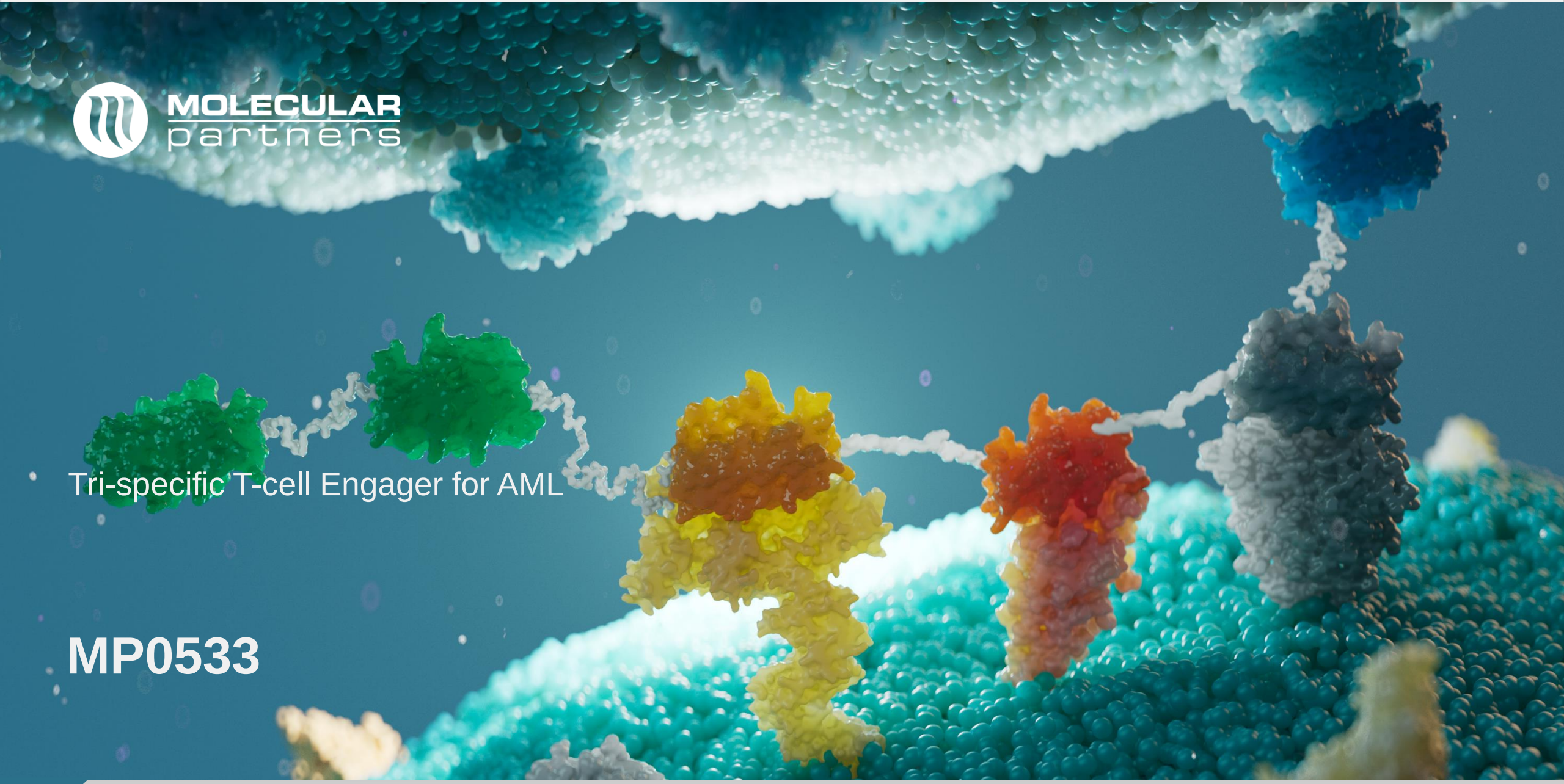


- Promotes B-cell activation

PD-1 or other IO Therapy

- Removes suppression of T-cell responses by PD-L1 in the tumor

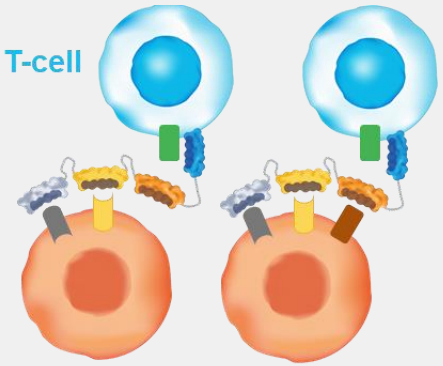



MOLECULAR
partners
Tri-specific T-cell Engager for AML
MP0533

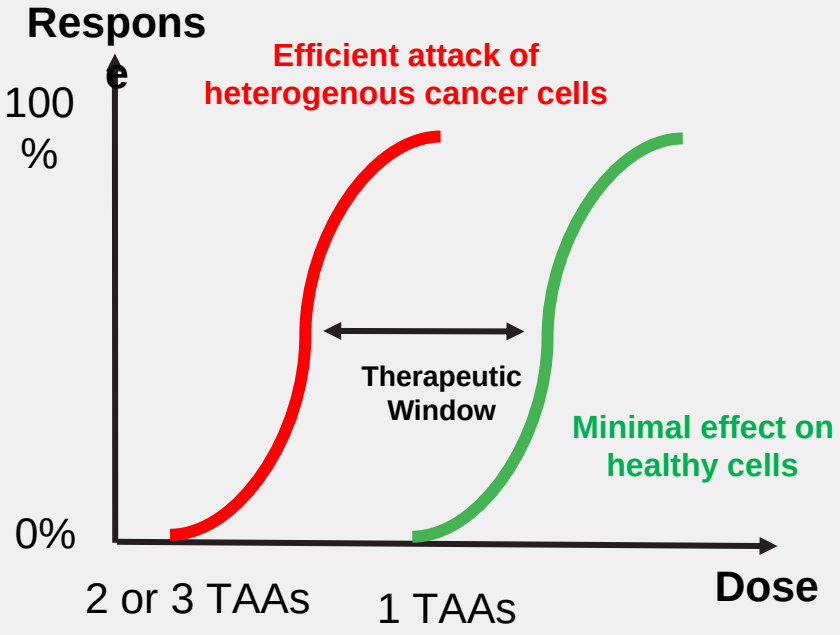
Unlock the value of “not-clean” targets to kill Leukemic Stem Cells and blasts in AML

- Persistence of LSCs is the driver of relapse in AML
- Targets in AML are also on healthy cells, leading to on-target toxicity (not clean targets)
- Goal: avidity-driven killing of LSCs and blast, while less killing of HSPs

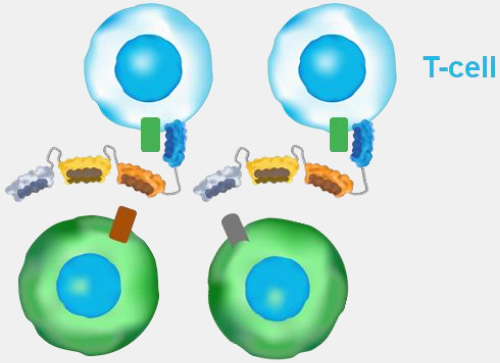
Multi targets
High avidity engagement



Malignant AML cell types - LSCs or blasts
(express 2 or 3 TAAs at high density)

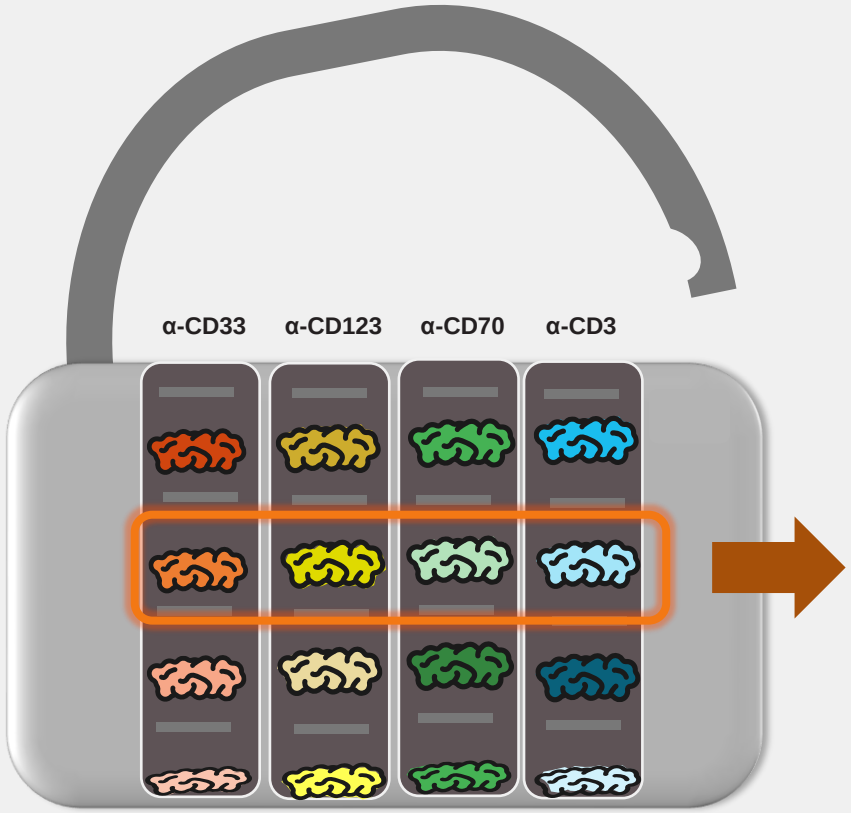


Single targets
Low affinity engagement

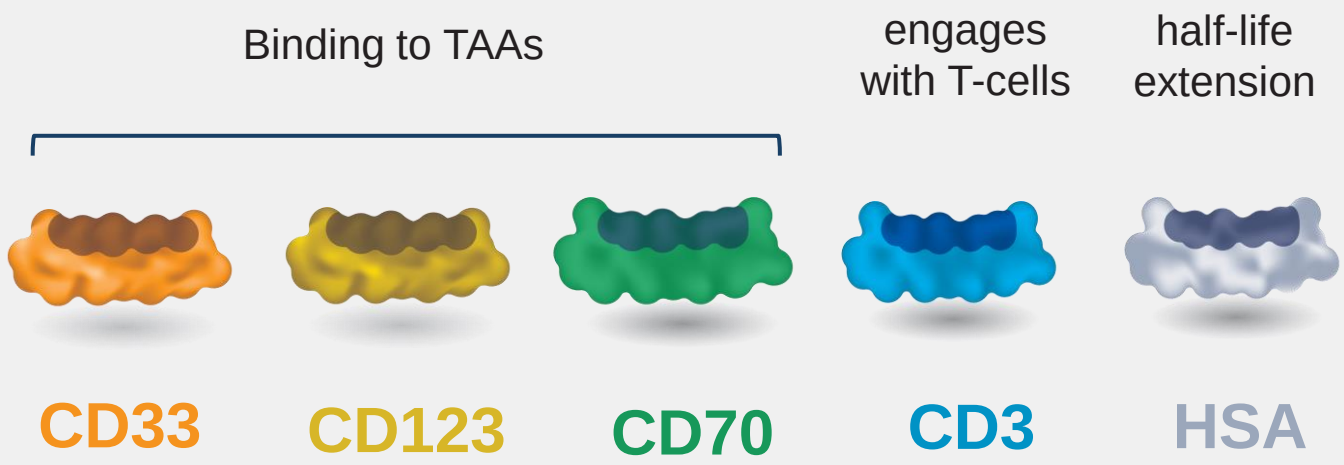


Healthy normal cell
HSPCs or myeloid cells

Exploiting DARPin Platform Versatility for Avidity-driven Killing
Unlocking the value of rare combinations



Each binding domain and each linker was optimized for affinity and steric fit



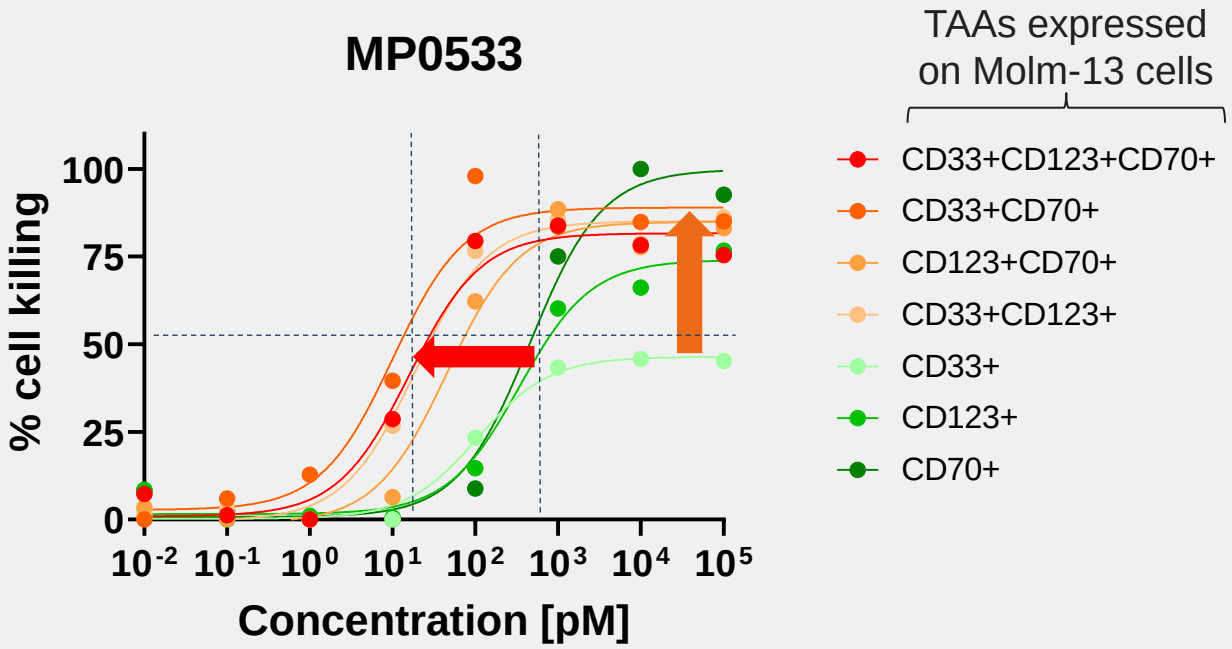
MP0533 Induces Specific Killing of AML Cells Expressing 2 or 3 TAAs

MOLM-13 cells WT
or KO for CD70, CD33 and/or CD123
+ Healthy donor T cells (E:T = 5:1)

MP0533 or controls

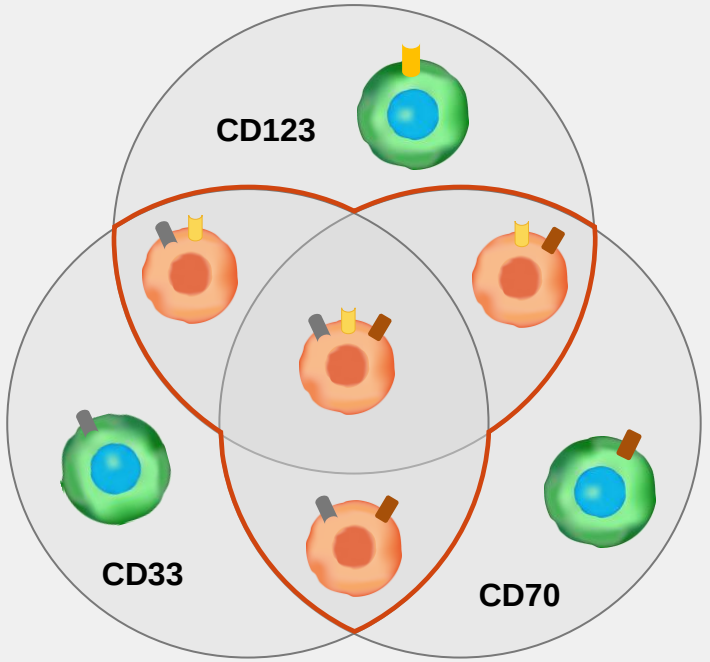
48 hours

Tumor cell killing
T cell activation



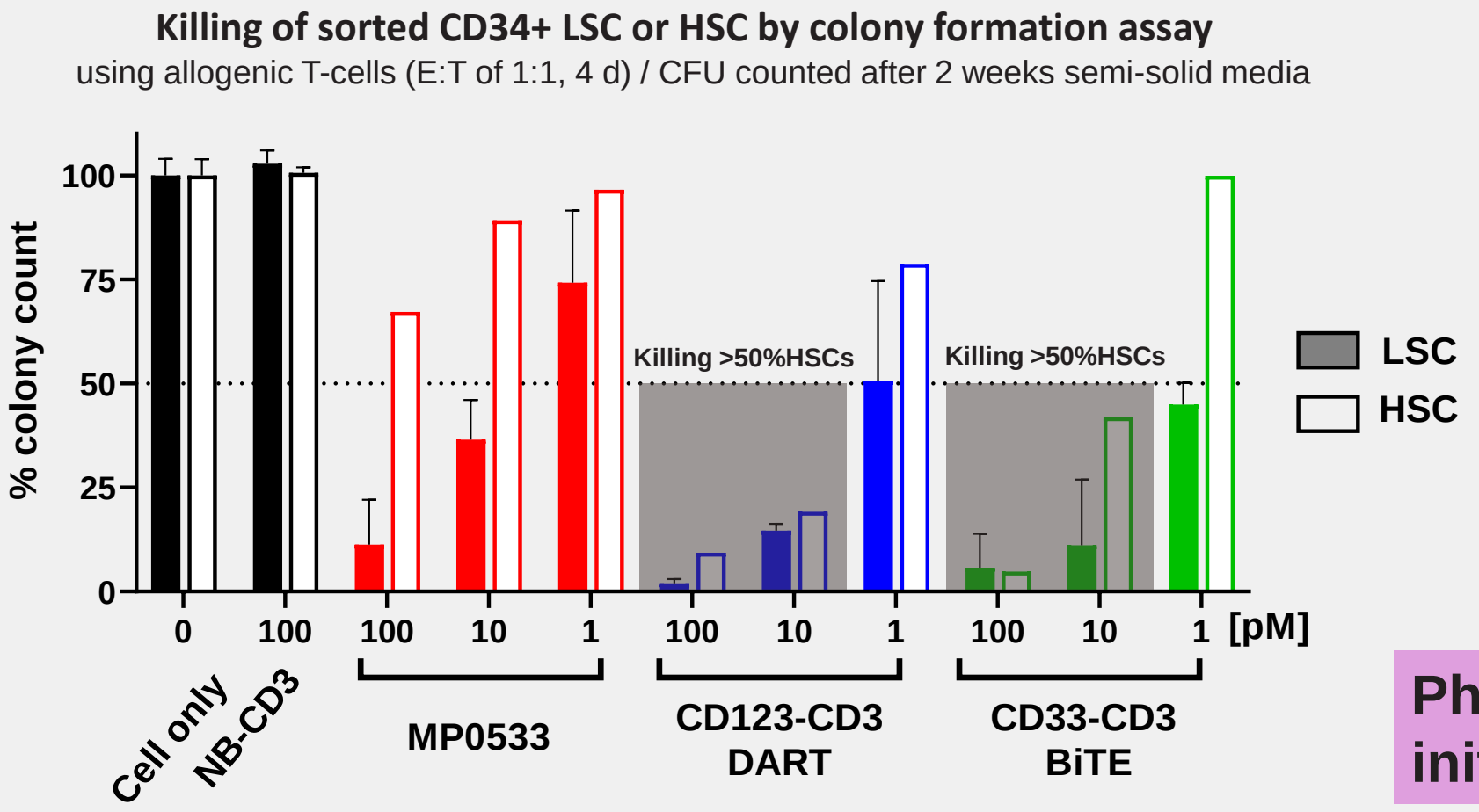
TAAs expressed
on Molm-13 cells

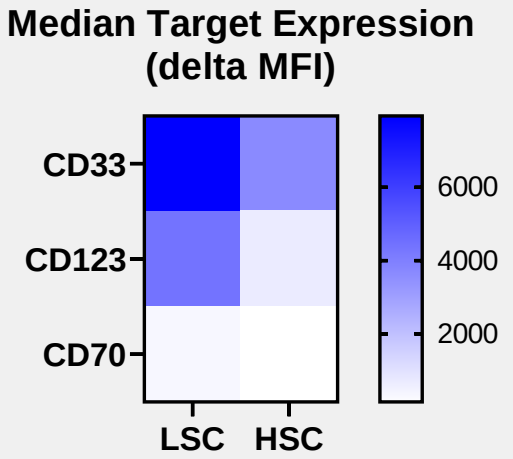
- CD33+CD123+CD70+
- CD33+CD70+
- CD123+CD70+
- CD33+CD123+
- CD33+
- CD123+
- CD70+



MP0533 shows preferential killing of CD34+ LSCs over HSC

Larger therapeutic window as compared to CD123-DART and CD33-bite





Phase 1 clinical trial initiation H2 2022

Summary & Outlook

Ensovibep – Summary and Financial Implications

- **EMPATHY Phase 2 met its primary endpoint**
  - A statistically significant dose-response signal of ensovibep based on change in viral load from baseline, through Day 8
- **Clinically relevant secondary endpoints:**
  - Combined risk reduction (hospitalization, ER visits, and death) of **approximately 80%**
  - No deaths in the ensovibep treated groups
  - Faster recovery and more complete recovery for patients receiving ensovibep vs. placebo
- **75mg identified** as the lowest efficacious and safe dose, to be taken forward in Phase 3 and for **EUA submission**
- **EMPATHY results confirm ensovibep as safe and well-tolerated at all dose levels**

- **Ensovibep show pan-variant-activity, including Omicron**

- **With CHF 150 million option exercise milestone cash runway to extend well into 2025**
  - Excluding any potential royalty income (22%) as well as excluding potential further cash flows to or from R&D partners
  - Molecular Partners expects approximately CHF 133 million cash and cash equivalents as per December 31, 2021*

Pipeline Inflection Points

Infectious disease | Discovery Oncology | Oncology | Ophthalmology

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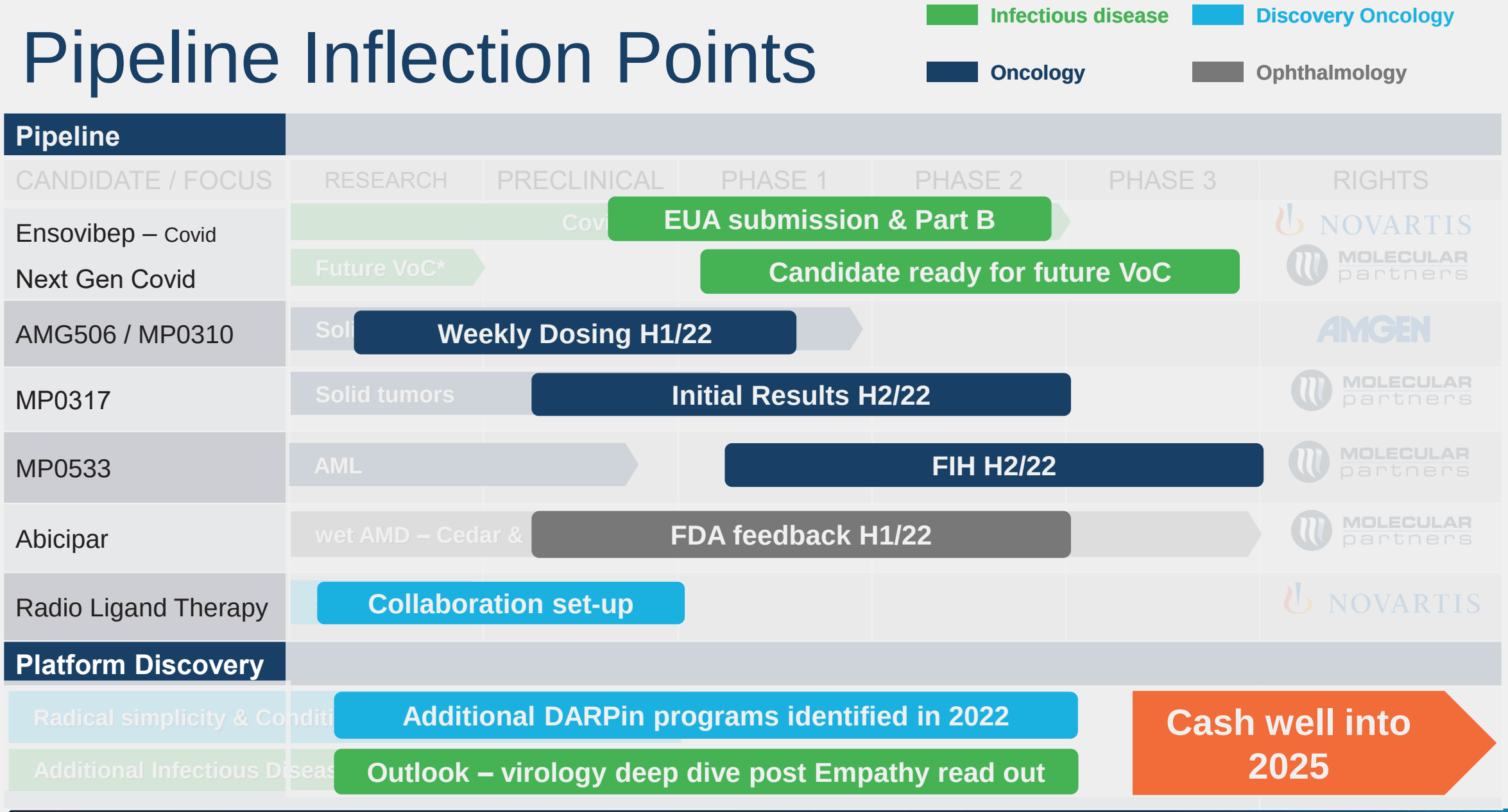
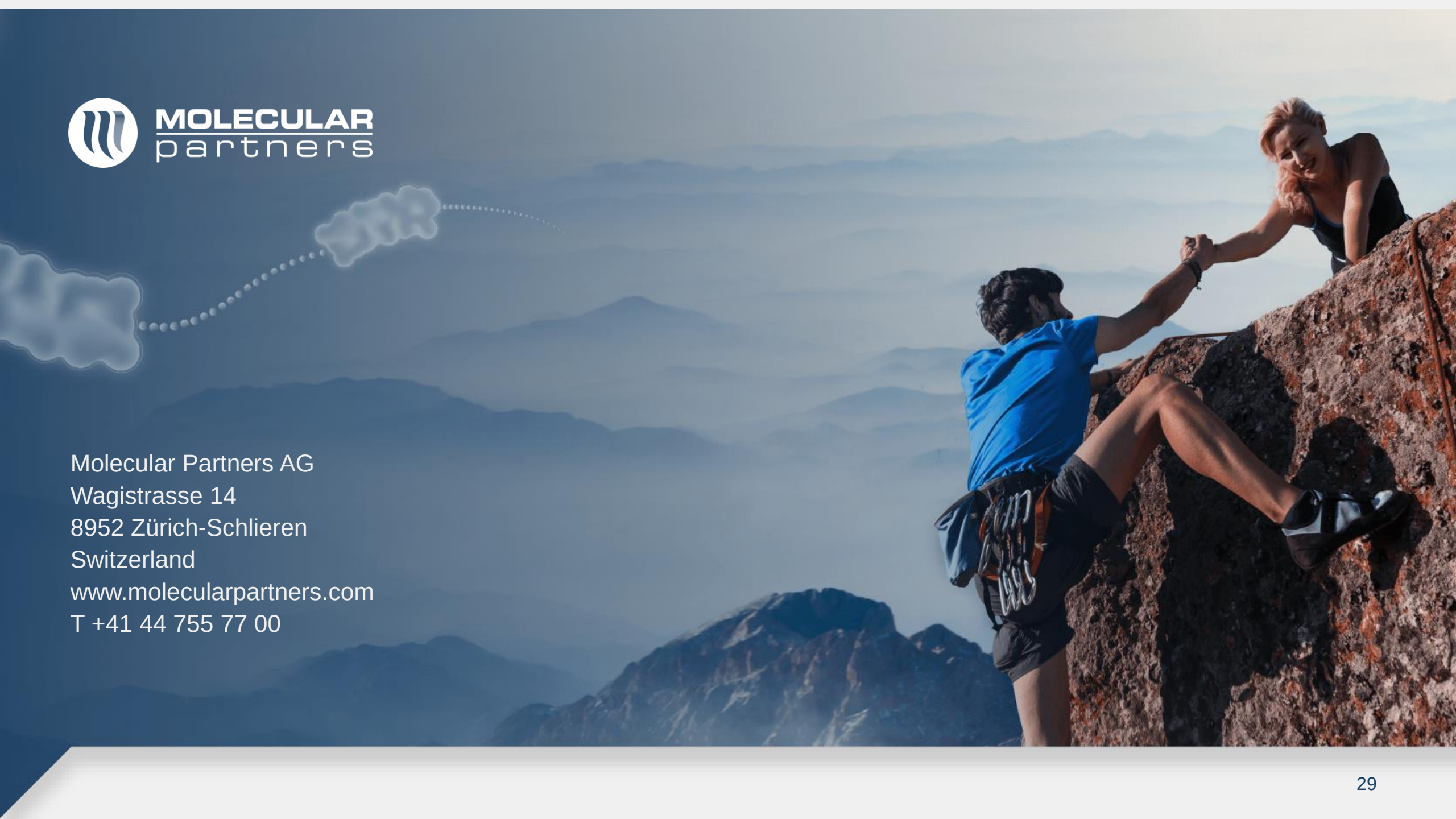
Pipeline Inflection Points





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