# Custom Built Biology for Patients

January 2022

HC Wainwright Healthcare Conference

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

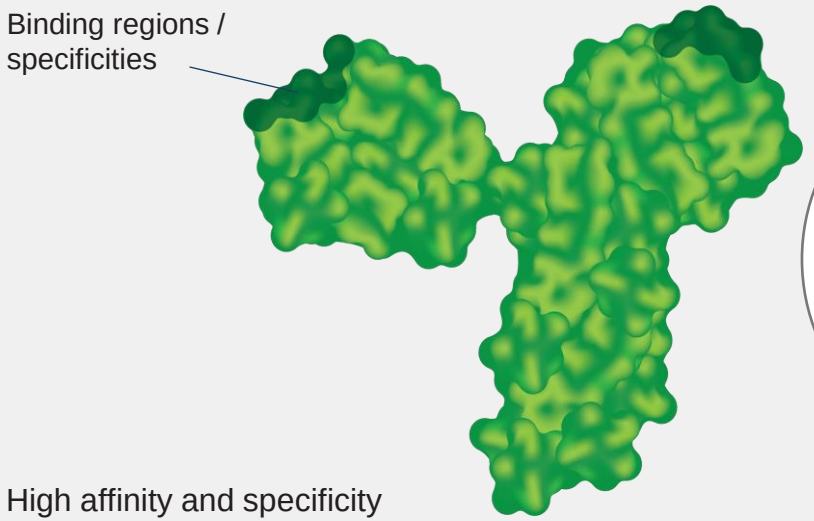
# Disclaimer

This presentation contains forward looking statements. Any statements contained in this presentation that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements regarding the clinical development of Molecular Partners' current or future product candidates, including timing for the potential submission of emergency use authorization for ensovibep, expectations regarding timing for reporting data from ongoing clinical trials or the initiation of future clinical trials, the potential therapeutic and clinical benefits of Molecular Partners' product candidates, the selection and development of future antiviral or other programs, and Molecular Partners' expected expenses and cash utilization for 2021 and that its current cash resources will be sufficient to fund its operations and capital expenditure requirements into H2 2023. These statements may be identified by words such as "anticipate", "believe", "could", "expect", "intend", "may", "plan", "potential", "will", "would" and similar expressions, although not all forward-looking statements may contain these identifying words, and are based on Molecular Partners AG's current beliefs and expectations. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Some of the key factors that could cause actual results to differ from our expectations include our plans to develop and potentially commercialize our product candidates; our reliance on third party partners and collaborators over which we may not always have full control; our ongoing and planned clinical trials and preclinical studies for our product candidates, including the timing of such trials and studies; the risk that the results of preclinical studies and clinical trials may not be predictive of future results in connection with future clinical trials; the timing of and our ability to obtain and maintain regulatory approvals for our product candidates; the extent of clinical trials potentially required for our product candidates; the clinical utility and ability to achieve market acceptance of our product candidates; the potential impact of the COVID19 pandemic on our operations or clinical trials; our plans and development of any new indications for our product candidates; our commercialization, marketing and manufacturing capabilities and strategy; our intellectual property position; our ability to identify and in-license additional product candidates; the adequacy of our cash resources and our anticipated cash utilization; and other risks and uncertainties that are described in the Risk Factors section of Molecular Partners' Registration Statement on Form F-1 filed with Securities and Exchange Commission (SEC) on June 14, 2021 and other filings Molecular Partners makes with the SEC. These documents are available on the Investors page of Molecular Partners' website at http://www.molecularpartners.com.

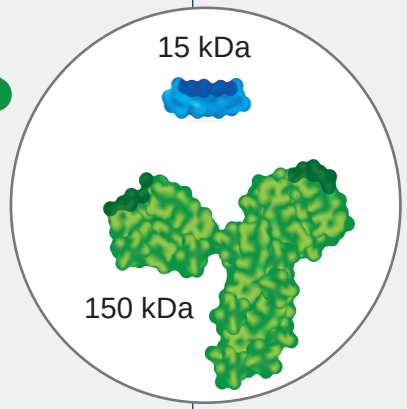
Any forward-looking statements speak only as of the date of this press release and are based on information available to Molecular Partners as of the date of this release, and Molecular Partners assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.

# What are DARPins

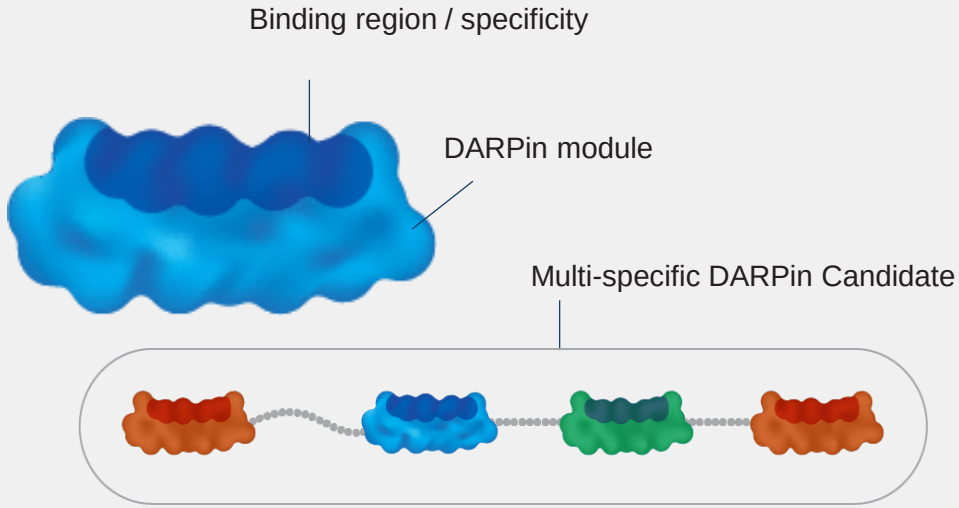
## MONOCLONAL ANTIBODIES




- 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<br>FAP x 4-1BB | Solid tumors | | | | | AMGEN |
| MP0317<br>FAP x CD40 | Solid tumors | | | | | MOLECULAR partners |
| MP0533<br>CD3 x CD33+CD70+CD123 | AML | | | | | MOLECULAR partners |
| Abicipar<br>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

Infectious disease | Discovery Oncology | Oncology | Ophthalmology

## Pipeline

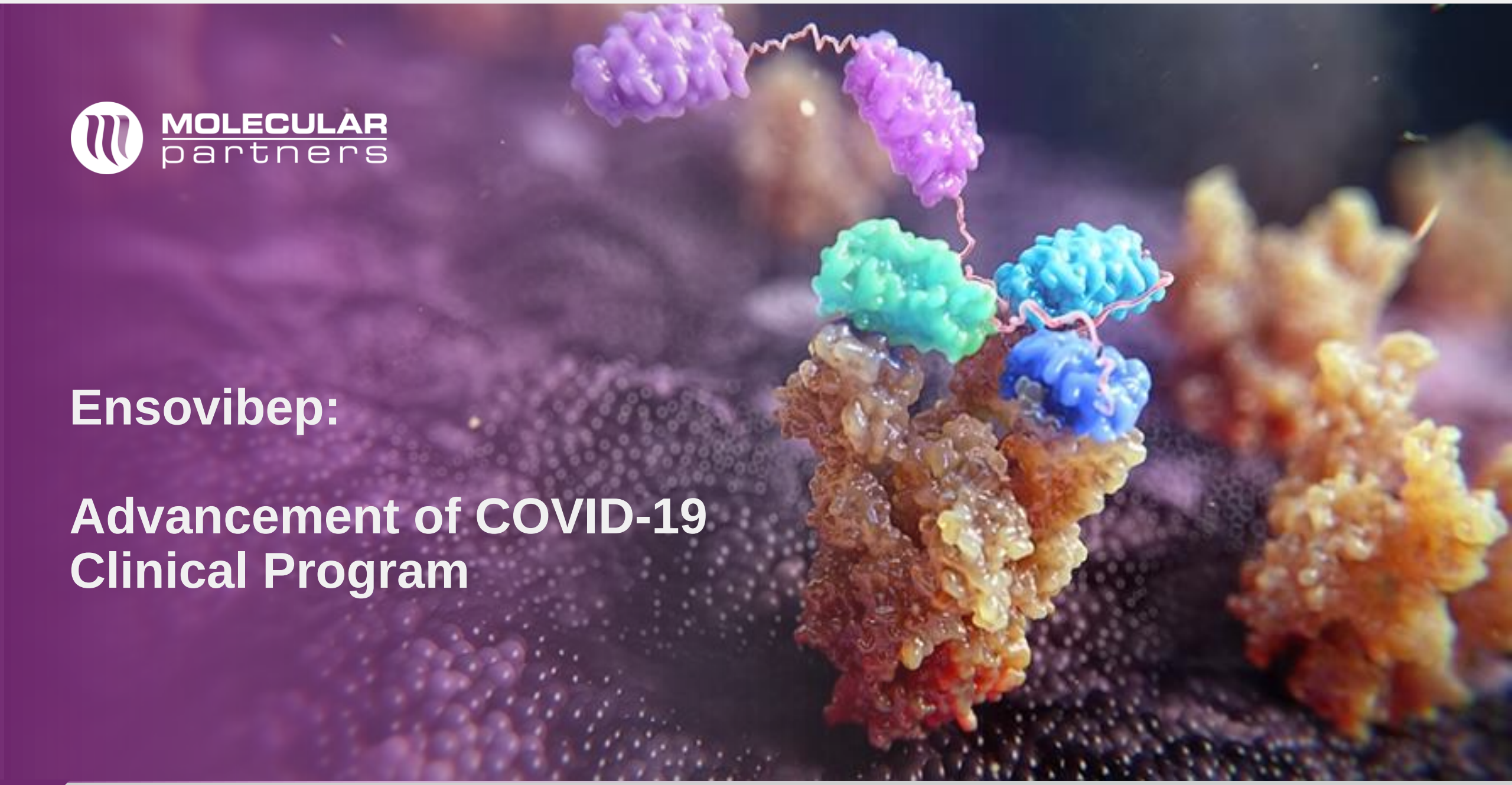
| CANDIDATE / FOCUS | RESEARCH | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | RIGHTS |
|---|---|---|---|---|---|---|
| Ensovibep – Covid | Covid ambulatory – Empathy | | | | | NOVARTIS |
| Next Gen Covid | Future VoC* | | | | | MOLECULAR partners |
| AMG506 / MP0310<br>FAP x 4-1BB | Solid tumors | | |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

## Platform Discovery

- Radical simplicity & Conditional Activation
- Additional Infectious Diseases

MOLECULAR partners

* VoC = Variant of Concern

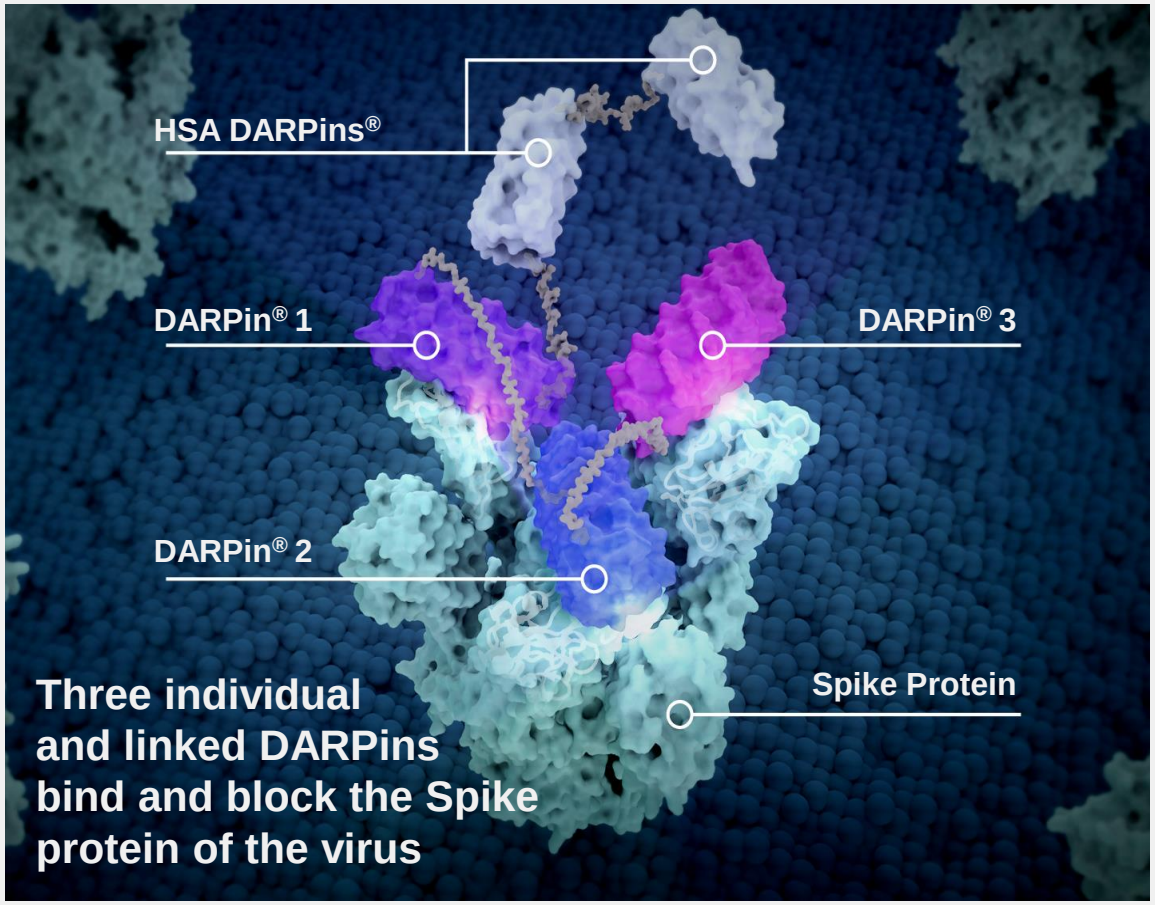


# Ensovibep:

# Advancement of COVID-19 Clinical Program

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

## 3D model of a DARPin® molecule



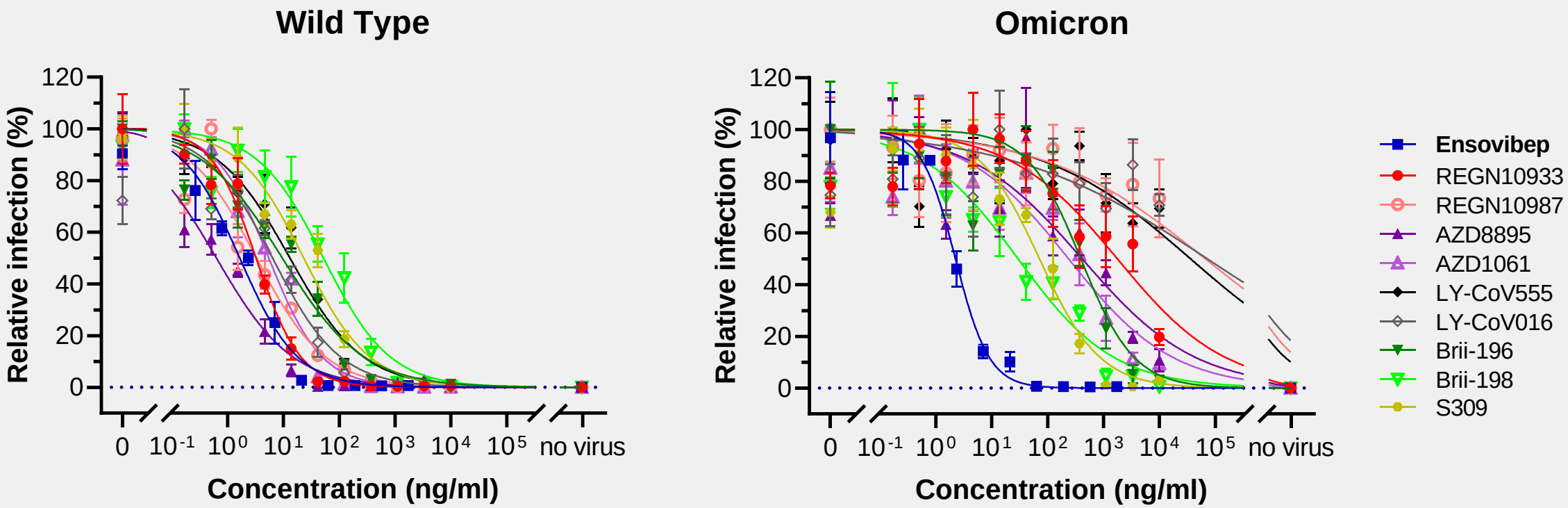

## Characteristics

- 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 |
|---|---|

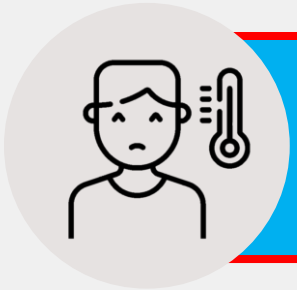
Possible EUA*

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, in reducing SARS-CoV-2 viral load through Day 8 and select a dose for Phase 3 (PoC & DRF)** |
| **Population** | • Ambulatory symptomatic adult patients diagnosed with COVID-19 with onset of symptoms within 7 days prior to dosing and with a positive pre-dose Rapid Antigen Test on the day of dosing |

| | |
|---|---|
| **Primary Endpoint** | • **Time-weighted change from baseline (measured at Day 3, Day 5, and Day 8) in $log_{10}$ SARS-CoV-2 viral load in nasopharyngeal swabs through Day 8** |
| **Key Secondary Endpoints** | • Proportion of patients with hospitalizations (≥ 24 hours of acute care) and/or ER visits related to COVID-19 or death from any cause up to Day 29<br>• Time to sustained clinical recovery based on resolution or improvement in clinical symptoms with no worsening up to Day 29 |

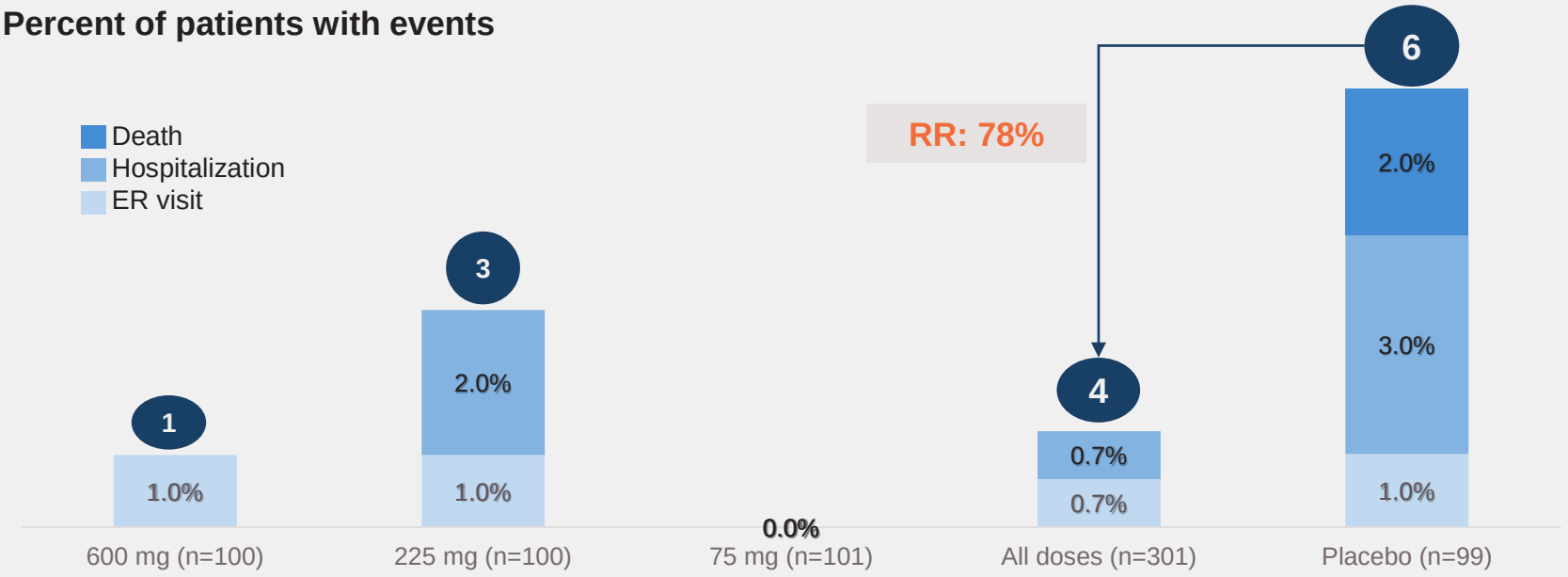
| | |
|---|---|
| ensovibep 600mg i.v. | ~ 100 pts |
| ensovibep 225mg i.v | ~ 100 pts |
| ensovibep 75mg i.v. | ~ 100 pts |
| placebo i.v. | ~ 100 pts |

# 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

**Percent of patients with events**




**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 Updated Financial Guidance

- **Novartis has informed Molecular Partners that it will exercise option for in-licensing of ensovibep**
  - Completion of in-licensing will trigger CHF 150m milestone payment
  - CHF 60m previously received at signing of option agreement (20m cash/40m MOLN shares)
- **22% royalty on sales in commercial countries payable by Novartis following completion of in-licensing**
  - 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.
- **Molecular Partners expects approximately CHF 133 million cash and cash equivalents* as per December 31, 2021**
- **Upon receipt of the CHF 150 million option exercise milestone from Novartis, Molecular Partners now estimates its cash runway to extend well into 2025**
  - Excluding any potential royalty income as well as excluding potential further cash flows to or from R&D partners


# MP0310 and MP0317

Multispecific Immune Activators

# 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**

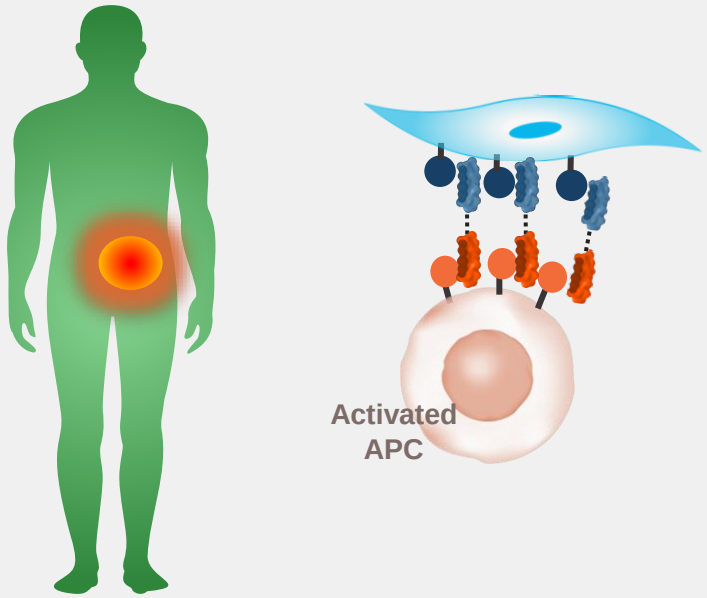
- Systemic administration of MP0310, with localized activation at site of disease
- MP0310 is observed in tumor tissue, with no liver toxicity or systemic activation of immune cells
- Tumor biopsies show tumor-localized immune response consistent with the MoA

**Expected Milestones**

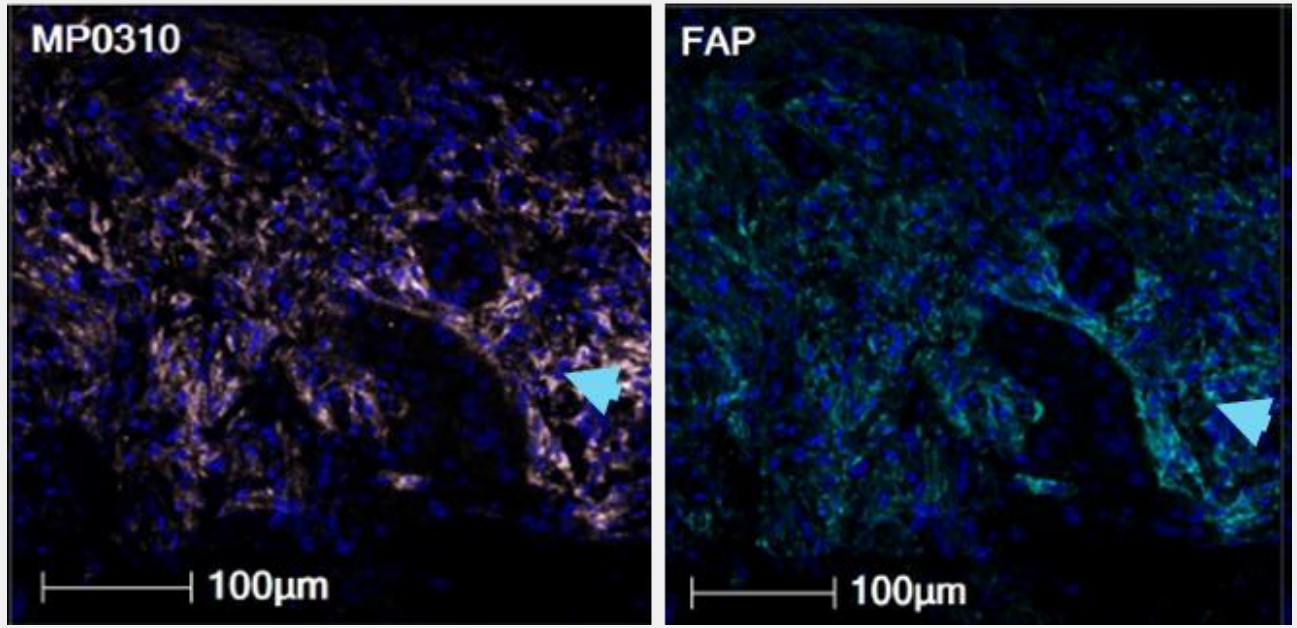
- Analyze data from ongoing phase 1 study, exploring weekly dosing.
- Determine appropriate next steps with Amgen

# FAP – an Ideal Target for Tumor-localized Activity

- FAP is expressed on **activated cancer associated fibroblasts (CAFs)**
- **Overexpression** in the stroma of **many solid tumors**
- Limited expression in normal adult tissues



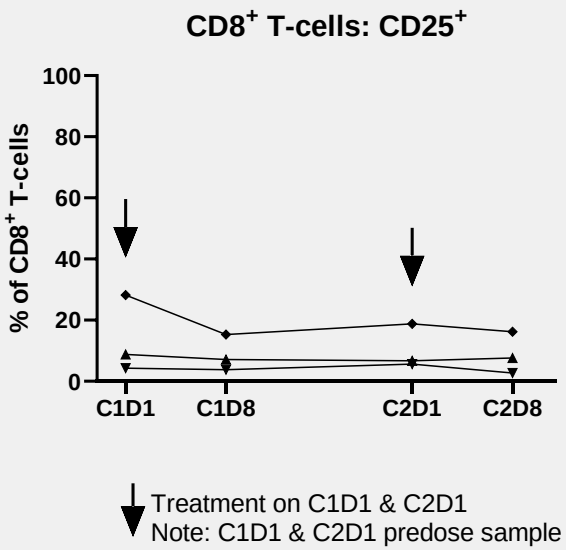

## MP0310 (FAP-4-1BB) Phase 1 human biopsy samples




FAP is a clinically validated target for tumor-localization

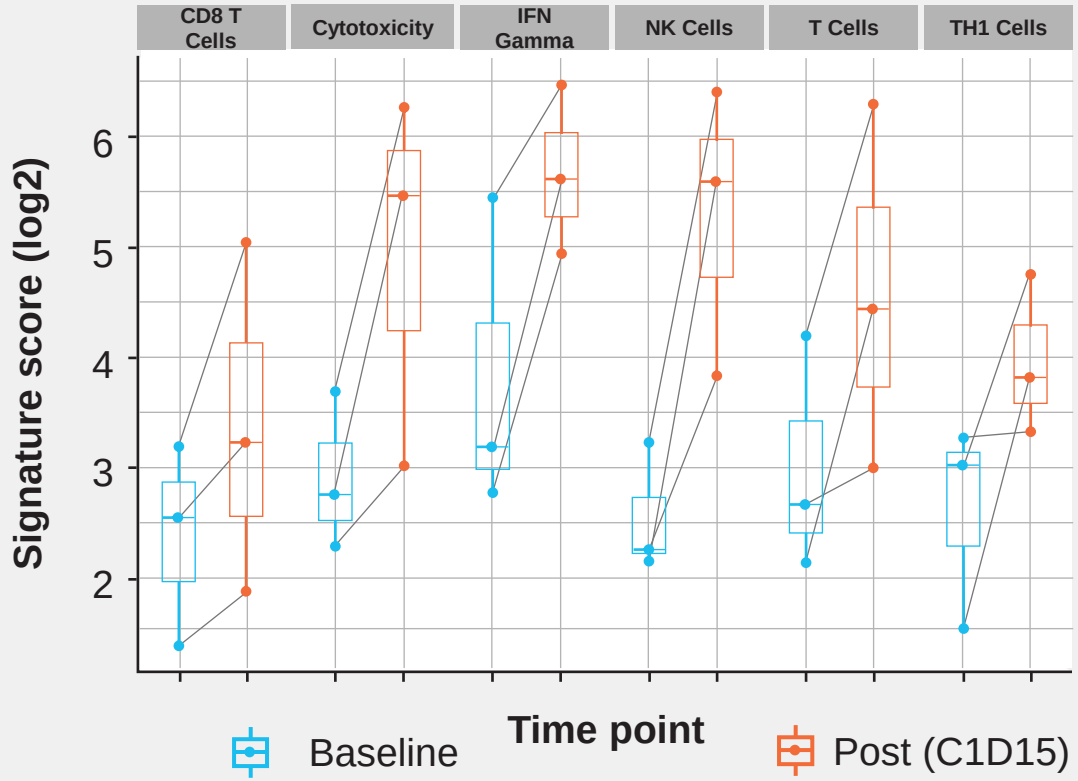
# PD Activity in Paired Biopsies Supports AMG 506 / MP0310 MoA on 4-1BB Activation

## BLOOD




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

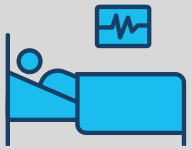
## TUMOR




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

# MP0317: Localized Activation of CD40


**Target Patient**

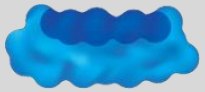


- Solid tumor patients with positive FAP expression
- Many patients still fail to benefit from current immunotherapy options, or relapse

**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

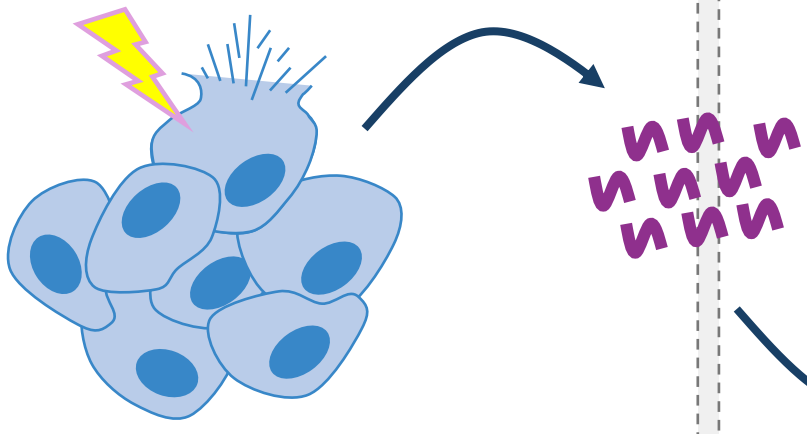
**Expected Milestones**

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

# CD40 Open for Multiple Combination (IO or Other)

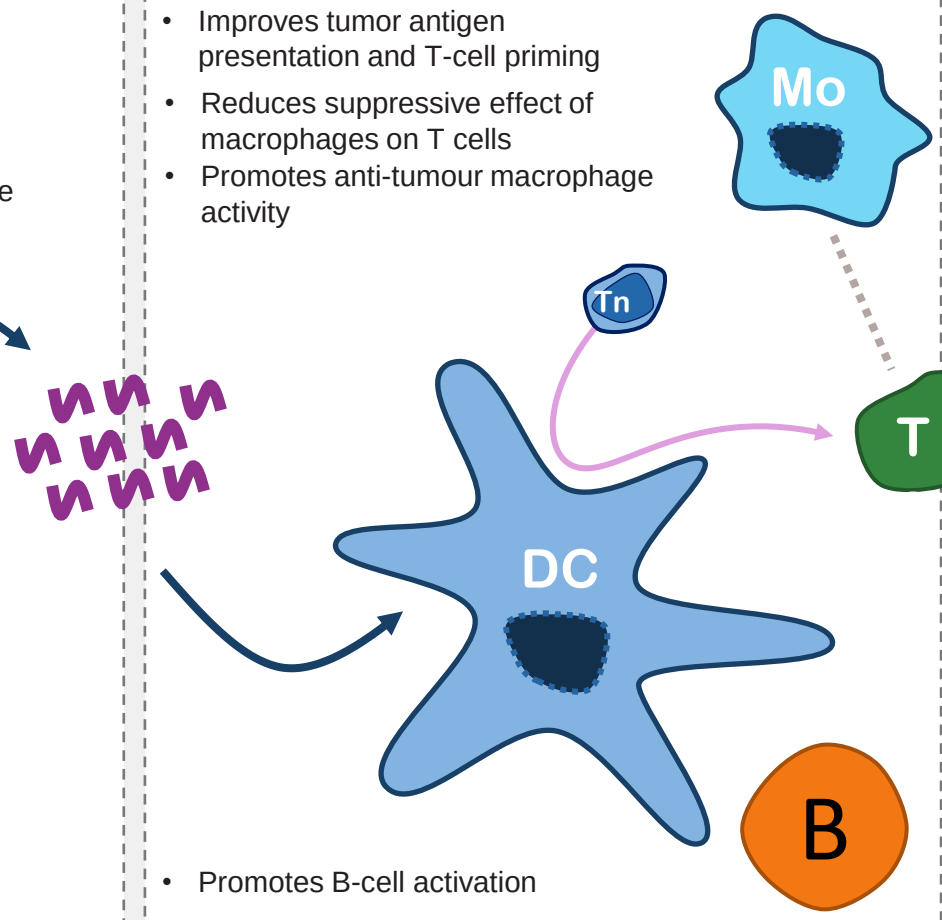
## Chemo / Radio Therapy

- 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

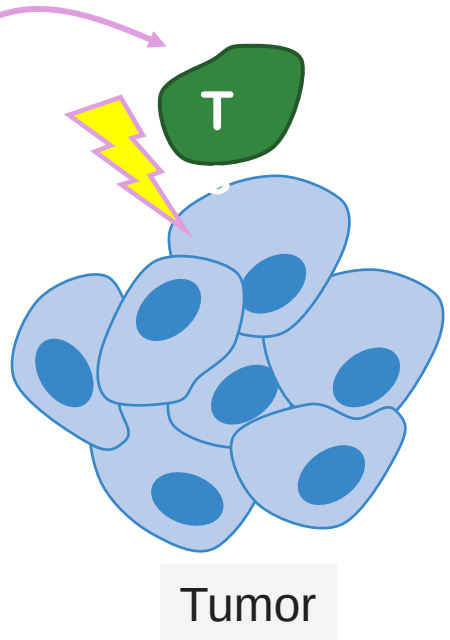
- Improves tumor antigen presentation and T-cell priming
- Reduces suppressive effect of macrophages on T cells
- Promotes anti-tumour macrophage activity

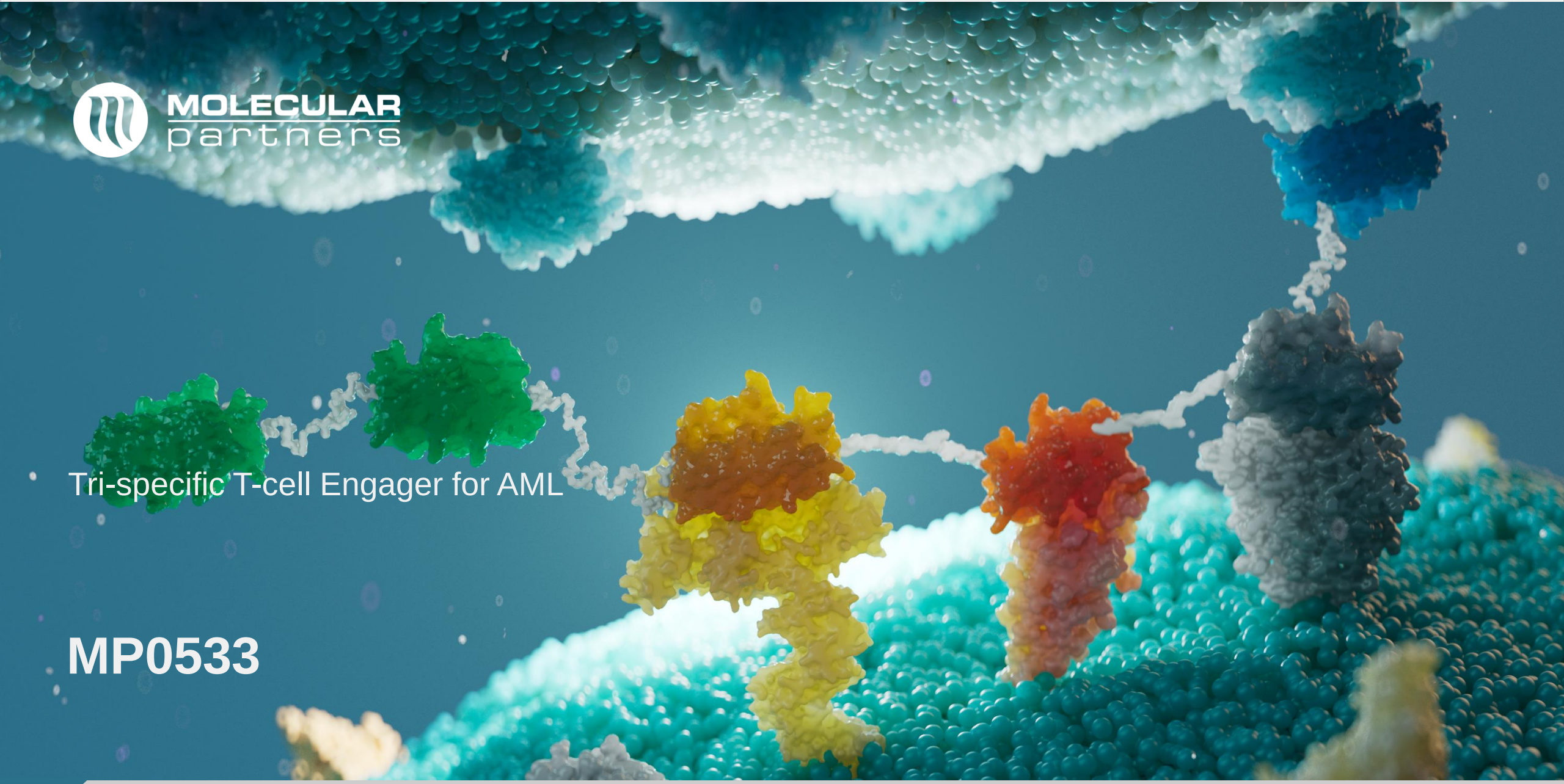



- Promotes B-cell activation

## PD-1 or other IO Therapy

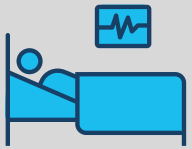
- Removes suppression of T-cell responses by PD-L1 in the tumor




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

# MP0533: Tri-specific T-cell Engager for AML


**Target Patient**

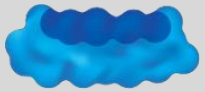


- ~20,000 people are diagnosed with AML every year
- Over 50% of patients die in the first year
- High relapse rates

**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**



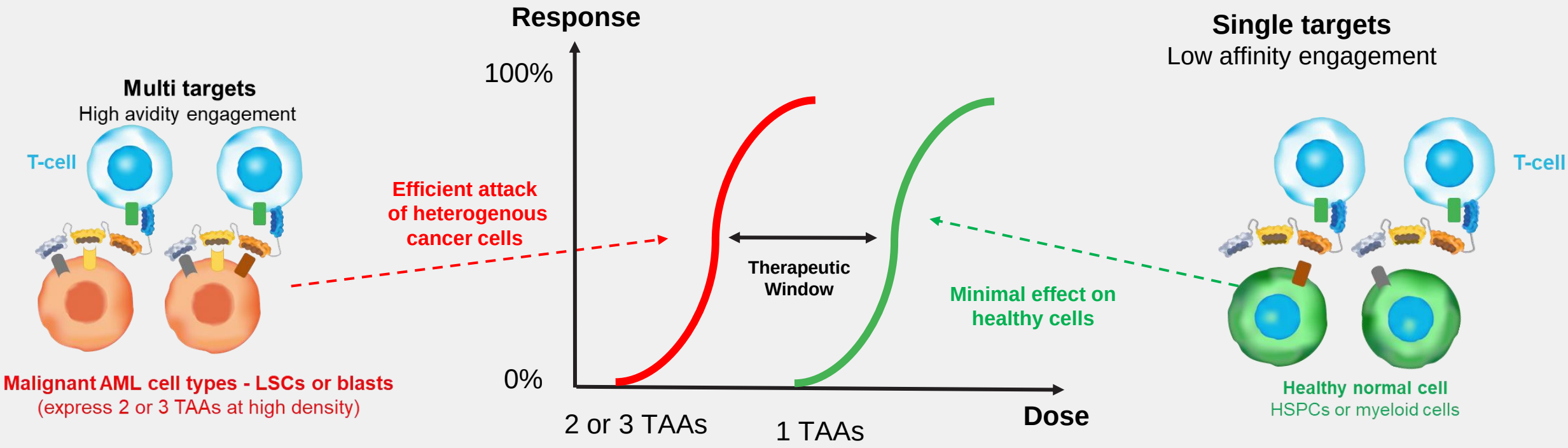
- Avidity driven multispecific DARPin, targeting 3 TAA's, engaging CD3
- T cell are activated only when 2 or more TAA's are bound
- Should allow for broader therapeutic index with reduced safety issues

**Expected Milestones**

- FIH clinical studies in 2022

# The DARPin Solution: a Trispecific CD3 Engager DARPin

*For Specific killing of all LSCs and blasts via avidity-driven T cell engagement*




**CD3 engager**: demonstrated potency in hematological malignancies
**Targeting 3 TAA** in order to:

- Ensure tumor-specificity via avidity-driven T cell activation
- Control tumor heterogeneity

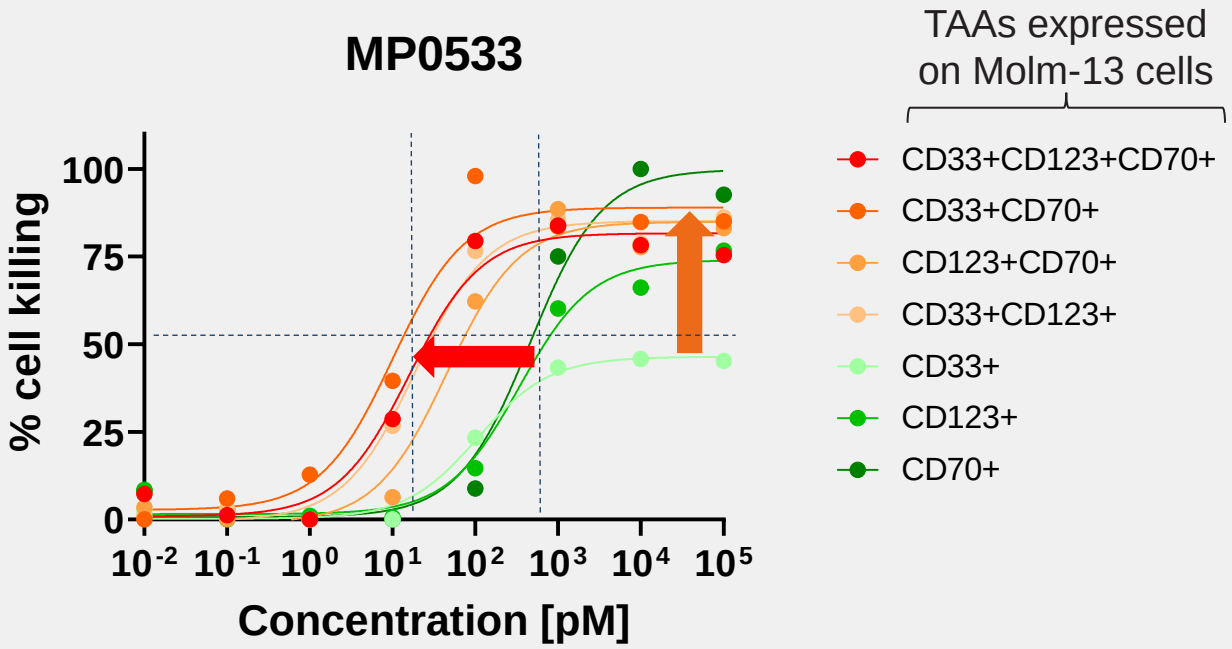
# MP0533 Induces Specific Killing of AML Cells Expressing 2 or 3 TAAs

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

*MP0533 or controls*

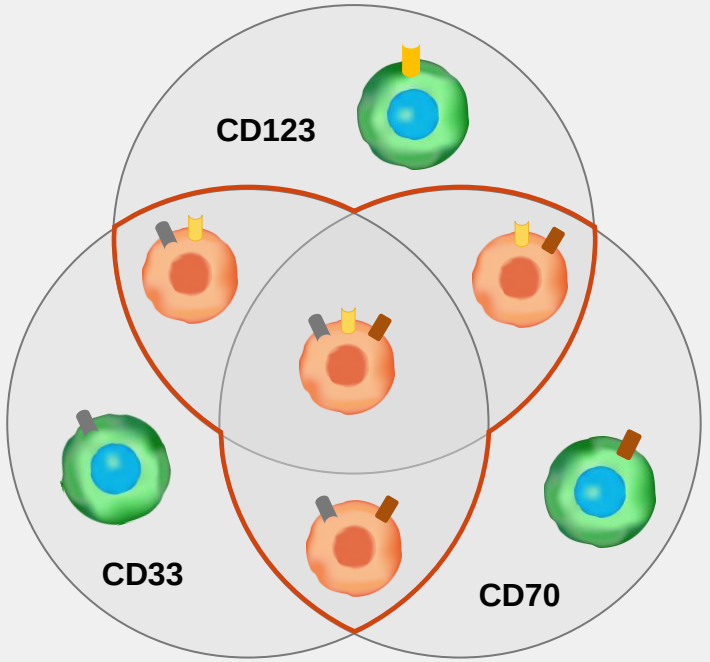
48 hours

Tumor cell killing
T cell activation




TAAs expressed
on Molm-13 cells

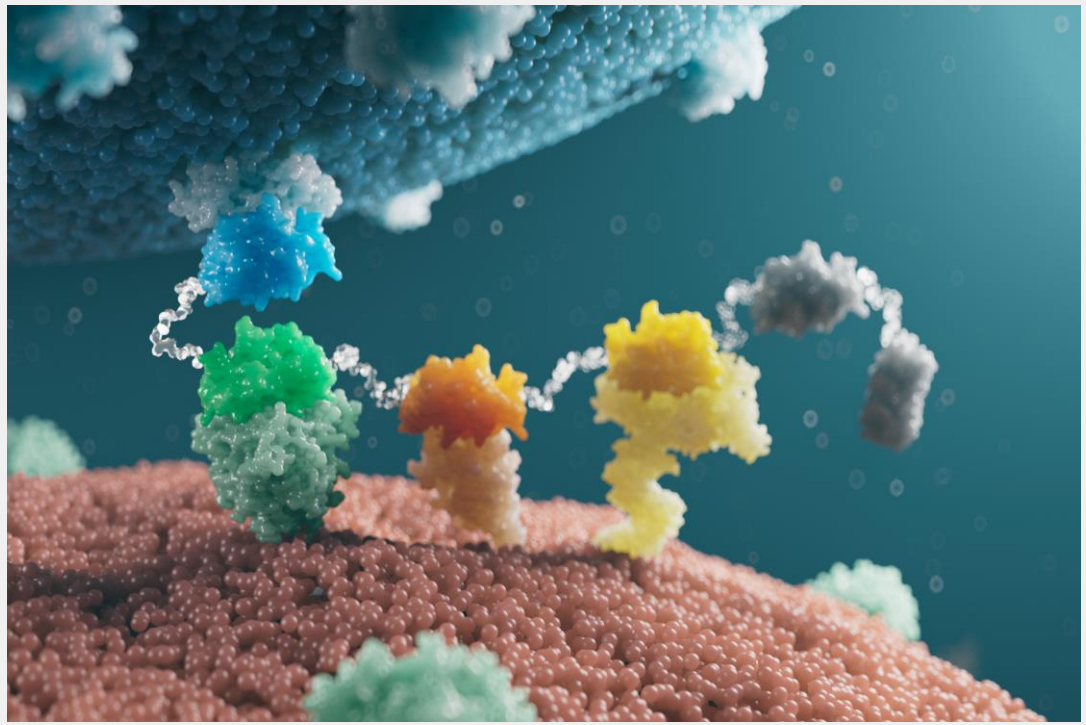
- CD33+CD123+CD70+
- CD33+CD70+
- CD123+CD70+
- CD33+CD123+
- CD33+
- CD123+
- CD70+



# MP0533: a Unique DARPin Solution for AML Patients

- **Properties of an ideal AML drug:**
  - Ensure long term control of the disease by eliminating LSCs ✓
  - Control tumor heterogeneity by targeting multiple Ag ✓
  - Increase the therapeutic window ✓
    - Limited killing of healthy HSCs
    - Reduced CRS

➢ **Phase 1 clinical trial initiation H2 2022**



# Summary & Outlook

# Ensovibep – Summary of EMPATHY Results

- **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-viral-neutralization, including Omicron**

- **With CHF 150 million option exercise milestone cash runway to extend well into 2025**
  - Excluding any potential royalty income 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

## 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<br>FAP x 4-1BB | Solid tumors | | | | | AMGEN |
| MP0317<br>FAP x CD40 | Solid tumors | | | | | MOLECULAR partners |
| MP0533<br>CD3 x CD33+CD70+CD123 | AML | | | | | MOLECULAR partners |
| Abicipar<br>VEGF | wet AMD – Cedar & Sequoia | | | | | MOLECULAR partners |
| Radio Ligand Therapy | Solid tumors | | | | | NOVARTIS |

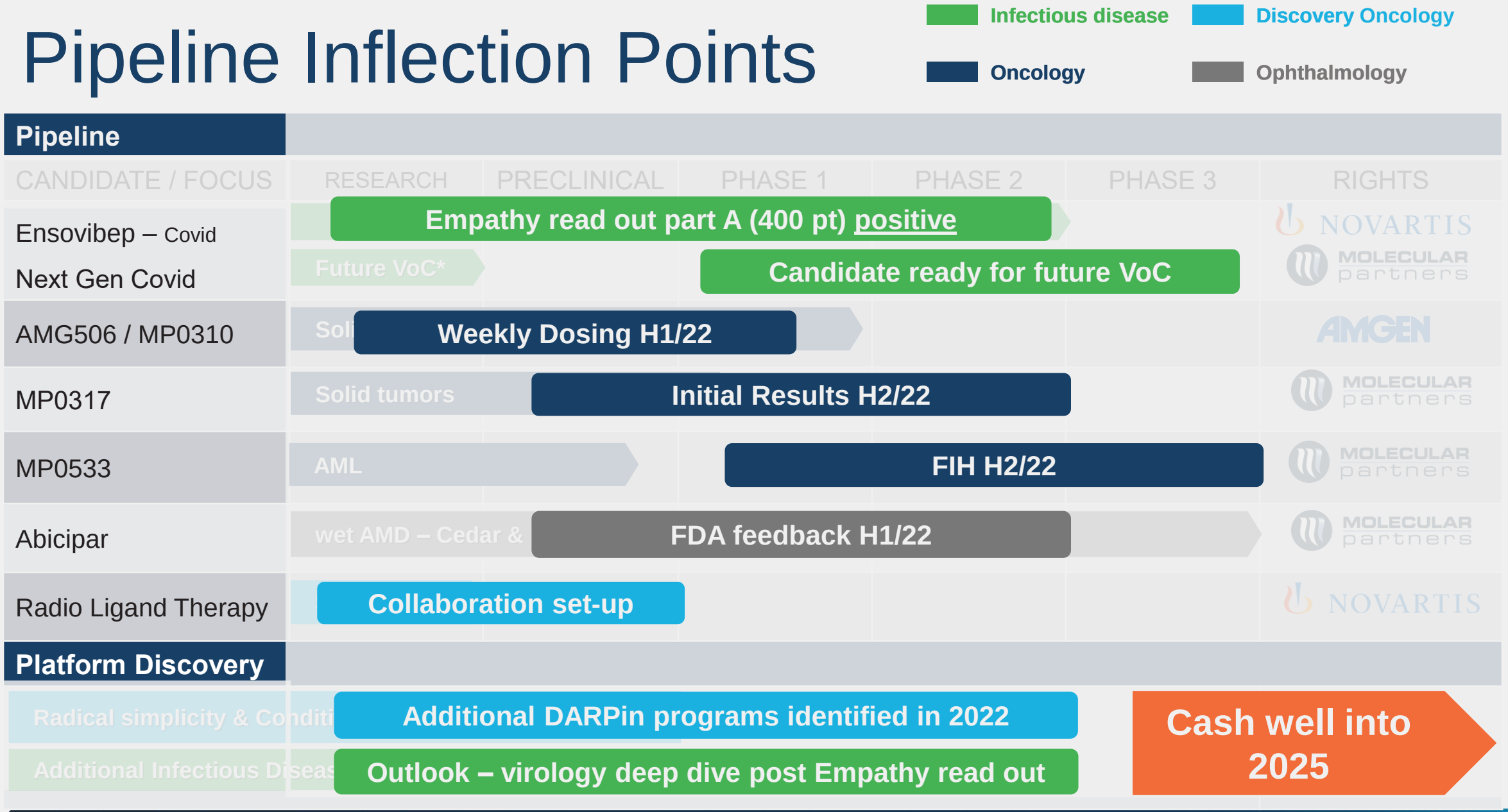
## Platform Discovery

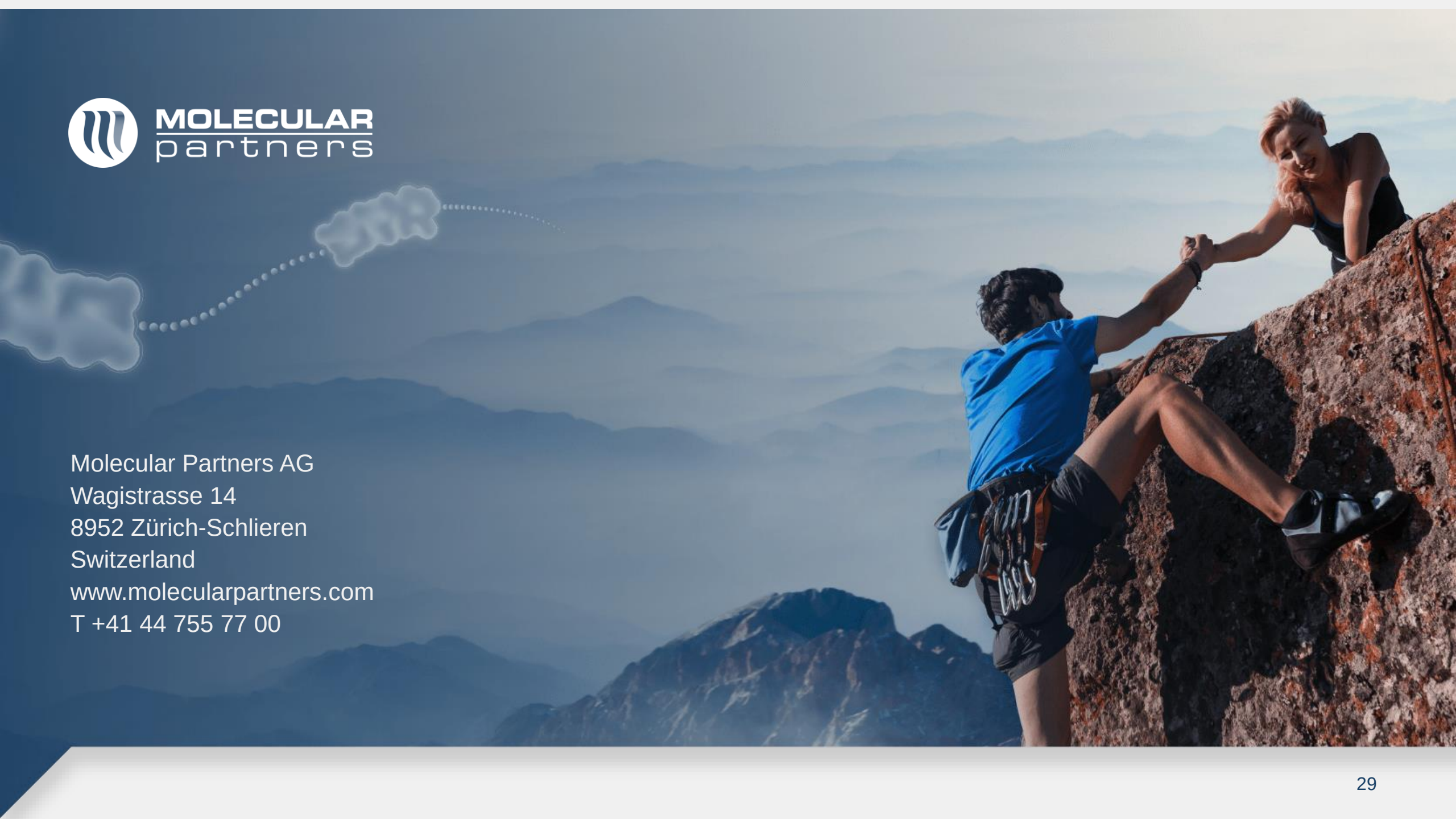
| | |
|---|---|
| Radical simplicity & Conditional Activation | MOLECULAR partners |
| Additional Infectious Diseases | |



* VoC = Variant of Concern

# Pipeline Inflection Points





Molecular Partners AG
Wagistrasse 14
8952 Zürich-Schlieren
Switzerland
www.molecularpartners.com
T +41 44 755 77 00