Ensovibep Clinical Results Call

EMPATHY Part A

January 2022

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

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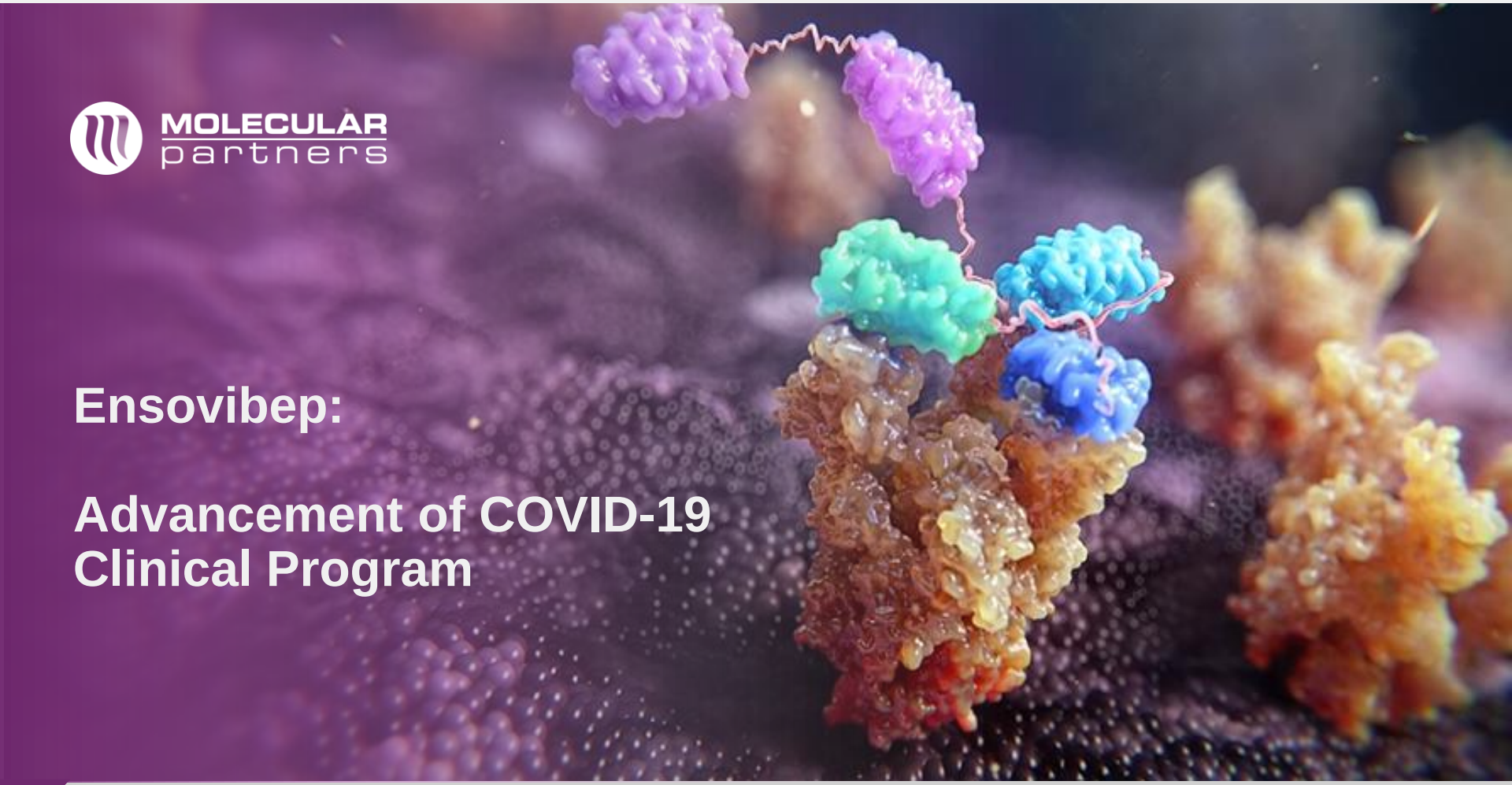
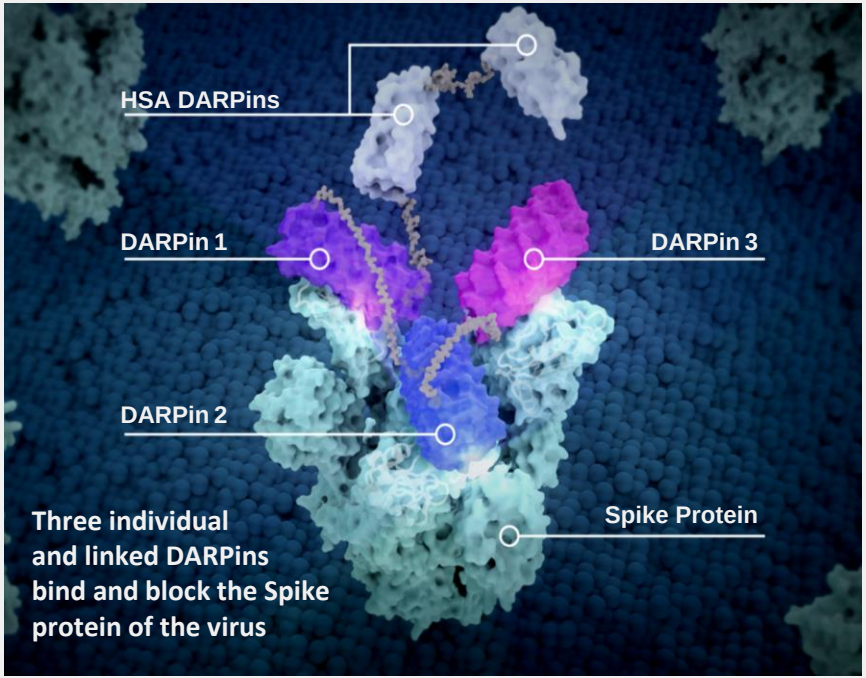


Ensovibep:

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 efficacy 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: Clinical Development Overview

- **Empathy study (top-line analysis):**
  - **Randomized 407 pts in Part A**
    - Mild or moderate symptoms
    - Rapid antigen test positive
    - Un-vaccinated and vaccinated patients
  - **Met primary endpoint:**
    - Significant reduction in viral load ✓
  - Clinically relevant secondary endpoints include:
    - Reduction in risk of hospitalization and/or ER visits due to COVID-19, or deaths ✓
    - Reduction in time to sustained clinical recovery ✓
    - Safe and well-tolerated ✓
  - **Novartis option exercise underway**

- **Phase 1 results / status (48 healthy subjects):**
  - Healthy volunteer safety trial
  - Half-life established: 2-3 weeks
  - i.v. infusion, i.v. bolus, s.c. injection
- **Phase 2 single-arm results (12 pts):**
  - Patients, confirmed COVID positive, with symptoms
  - Validation of methods and approach
- **ACTIV-3 Phase 3 interim results**
  - Hospitalized patients with confirmed COVID
  - High dose of 600 mg tested in ~250 patients, stopped at futility analysis for lack of efficacy
  - ***Safe and well-tolerated (included in ensovibep safety database)***

EMPATHY Phase Part A (Phase 2) Clinical Design and Endpoints

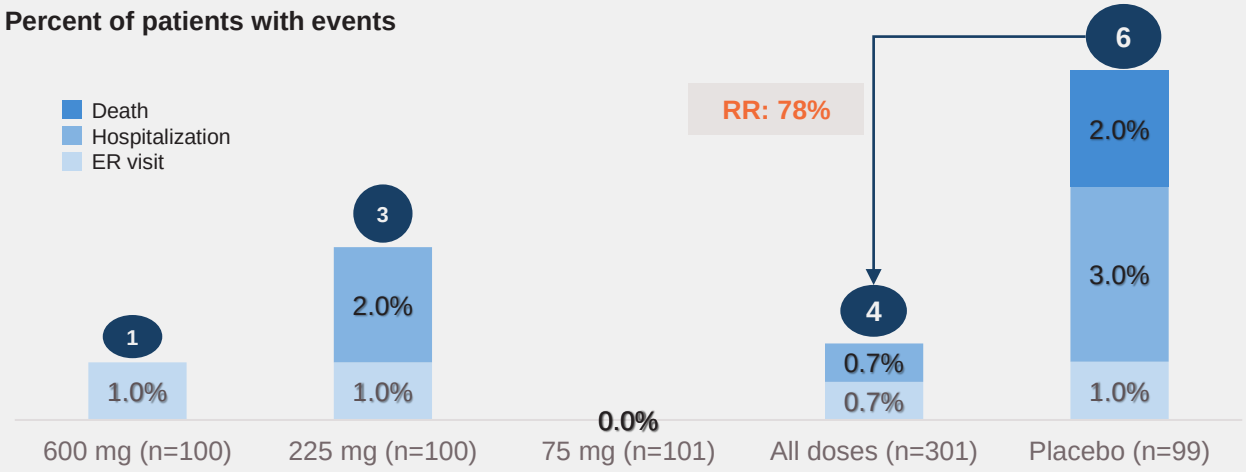
Objective	**Demonstrate superiority of ensovibep, compared to placebo, in reducing SARS-CoV-2 viral load through Day 8 and select a dose for Phase 3 (PoC & DRF)**
Population	• Ambulatory symptomatic adult patients diagnosed with COVID-19 with onset of symptoms within 7 days prior to dosing and with a 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 • 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 End Point in Reductions in Hospitalization and or ER Visit or Death

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



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

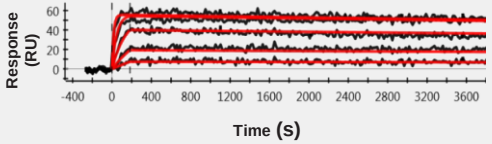
Topline Results Show Significant Reductions in Viral Load, Risk of Hospitalization and Death, and Faster Time to Recovery

- 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

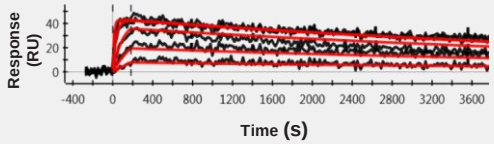
* was not a pre-defined endpoint

Cooperative Target Engagement Leads to Super Affinity

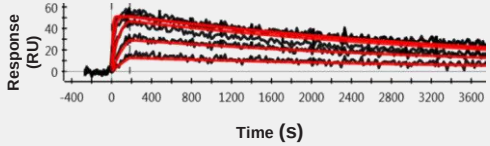
DARPin #1; 1 hour off-rate

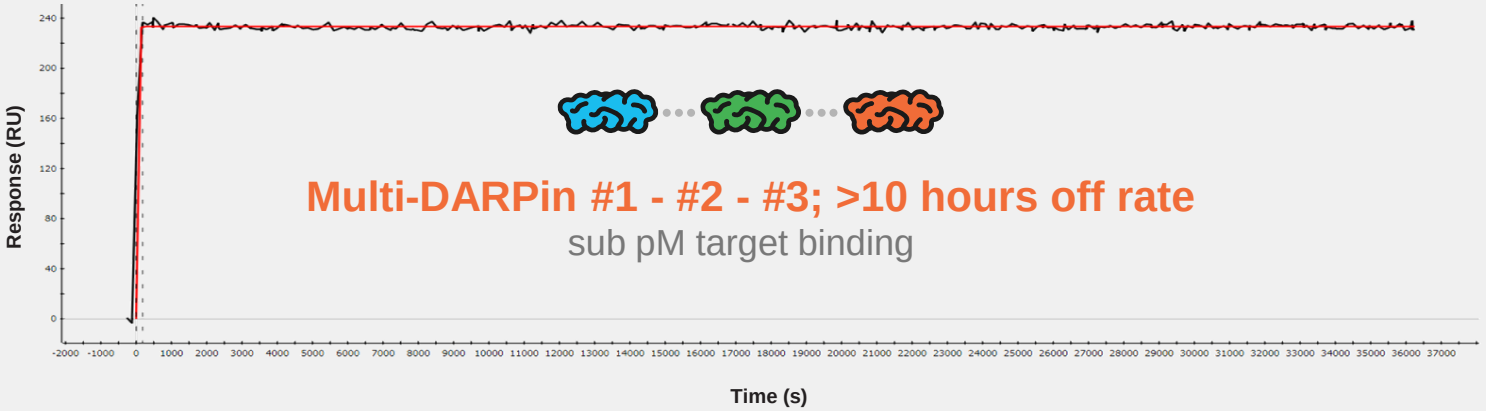


DARPin #2; 1 hour off-rate



DARPin #3; 1 hour off-rate

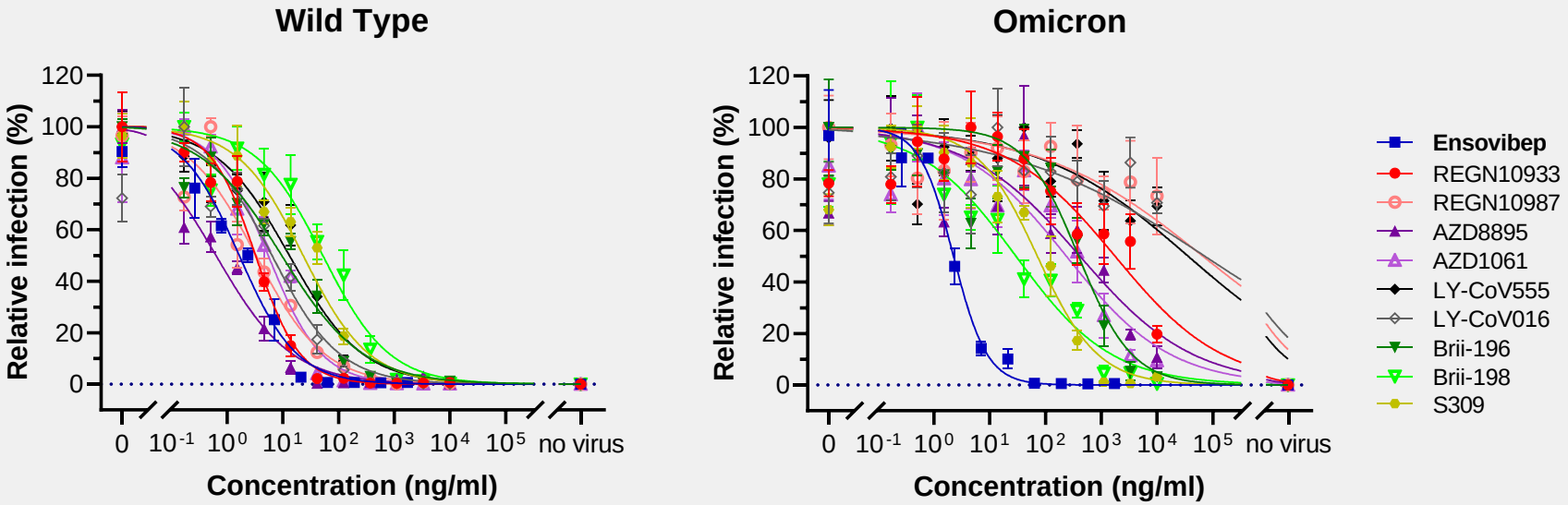




Multi-DARPin #1 - #2 - #3; >10 hours off rate

sub pM target binding

Ensovibep Retains Full Activity Against Omicron



Ensovibep Retains Full Activity Against Omicron – Table

	Wild Type	Omicron (Q493R)	
Compound	IC_{50} (ng/mL)	IC_{50} (ng/mL)	fold change to wt
Ensovibep	1.6	2.2	1.4
REGN10933	3.2	>1000	>100
REGN10987	3.3	>1000	>100
LY-CoV555	13	>1000	>100
LY-CoV016	6.4	>1000	>100
S309	23	72	3.1
AZD8895	0.6	415	>100
AZD1061	5.5	237	43
Brii-196	9.5	392	41
Brii-198	52	30	0.6

*Publicly available sequences of variable domains from monoclonal antibodies were used to generate a panel of antibodies used in this assay

Ensovibep: Tri-Specific Antiviral for COVID-19

NOVARTIS

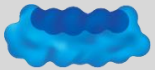
Target Patient

- Presently millions of new cases every day globally, despite vaccines and boosters
- Currently – COVID related hospitalizations remain near all-time highs
- 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
- Retains full potency against all variants of concern, to date, including delta and omicron

Ensovibep Upcoming Milestones

- **EMPATHY (Novartis / MP)**
  - 407 patients enrolled, Part A results - **positive**
  - EUA submission expected early 2022
  - Discussion with appropriate federal agencies regarding supplies of ensovibep
  - Part B initiate (N≥1,700)

  - **Large-scale commercial manufacturing established at Novartis**
  - Microbial production in e. coli

- Planned initiation of subcutaneous Phase 2/3 study (led by Novartis)

Acknowledgments

Covid Project Team (Novartis & Molecular Partners)

Spiez Laboratory – Federal Office of Civil Protection (FOCP)
Group of Olivier Engler

CHUV Lausanne-
Sylvia Rothenberger's group, for performing PsV and authentic virus assays.

University Utrecht
Group of Berend-Jan Bosch for cryo-EM analysis.

National Institute of Health (NIH)
ACTIV team for conducting PsV neutralization assays in collaboration with the Carol Weiss group.

Bundesamt für Gesundheit – BAG

Ensovibep – Summary of EMPATHY Results

- **EMPATHY Phase 2b 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%**
  - 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 has shown pan-variant-activity, including Omicron**

Licensing Agreement with Novartis and Financial Guidance Update

Summary and Terms

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

Summary:

- **Positive EMPATHY results represent a potential immediate and impactful solution in a constantly evolving pandemic**
  - Statistically significant reduction in viral load, reduction in risk of hospitalization and death, and time to recovery.
  - Continued evidence of 'pan-variant' activity across all variants of concern
  - Acceleration of EUA filing, initiate discussions with authorities about stockpiling of ensovibep
- **Novartis' execution of license agreement**
  - CHF 150m option
  - Flat 22% royalty rate in commercial markets
- **Validation of DARPin Platform and Molecular Partners capabilities**
  - 1st multi-DARPin moving to potential approval, paves the way for other multi-specific solutions to any number of biological problems including oncology, infectious diseases or other applications

Pipeline

Infectious disease | Discovery Oncology | Oncology | Ophthalmology

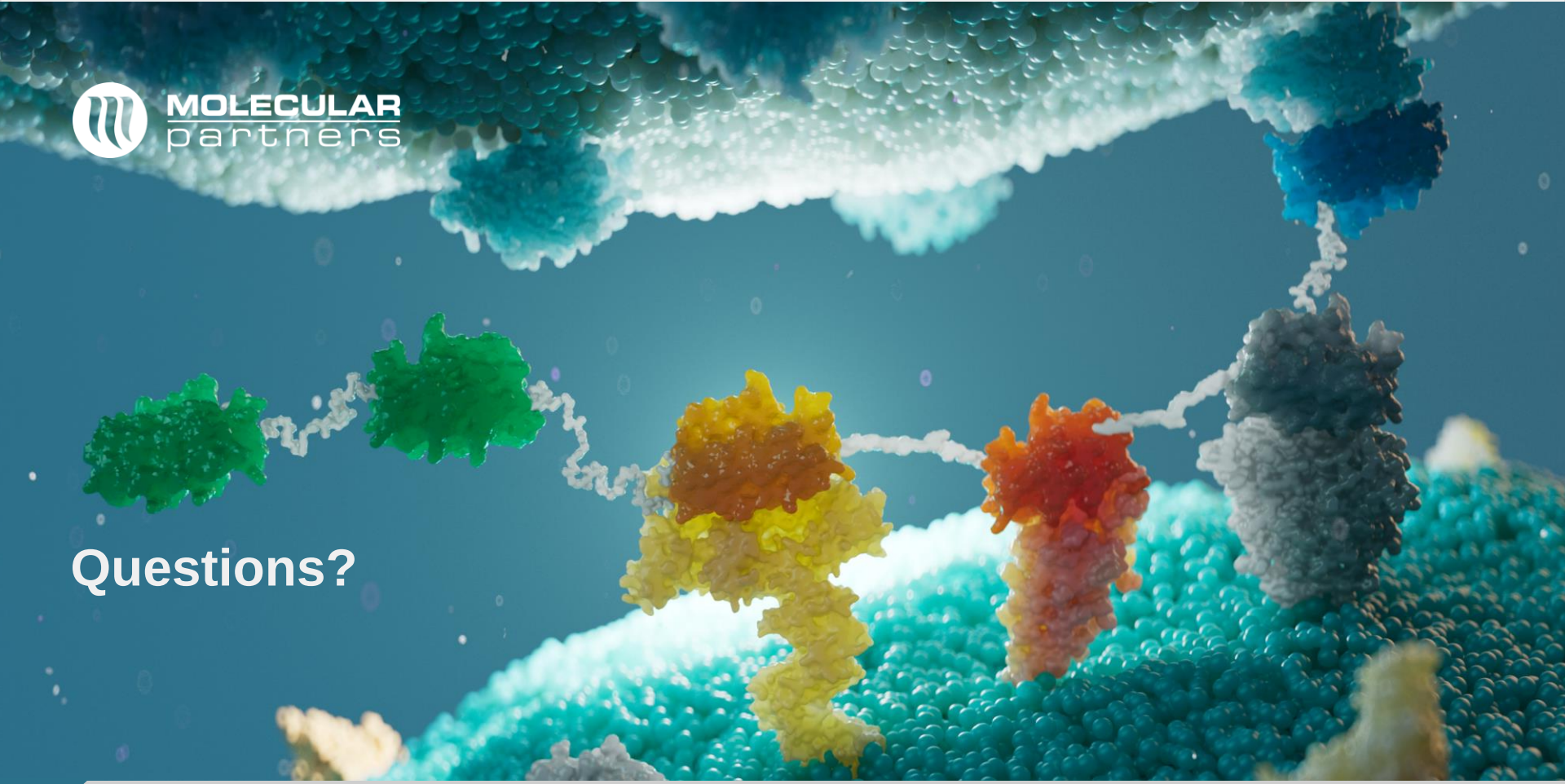
Pipeline

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	

* VoC = Variant of Concern


MOLECULAR
partners
Questions?