

Unlock and Expand: Custom Built Biology for Patients

Molecular Partners AG, Switzerland (SIX: MOLN)



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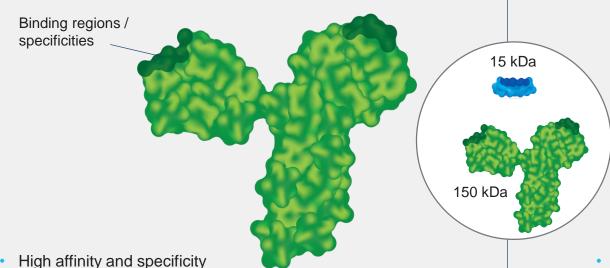
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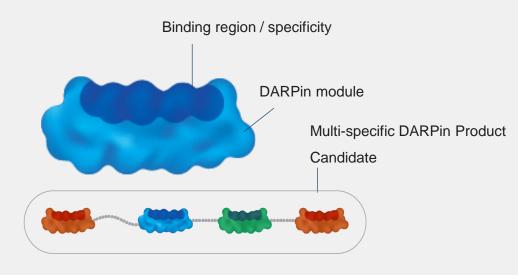


What are DARPin® Proteins

MONOCLONAL ANTIBODIES



MONO-DARPIN PROTEINS



- 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

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



Pioneering DARPin® Solutions: Right Team, Right Time

Proven Team

- Track-record to deliver a Phase 3 ready candidate in 12 months from idea generation
- Strong mix of founders and key new hires
- Increased cash on balance sheet by \$160m in 2020 (Funded into 2023)

Turn-key
Multispecifics
DARPin® Platform

- Fast & differentiated candidates:
 - First & only multi-specific COVID drug in clinical development (ensovibep)
 - AMG 506/MP0310: smart localized immune agonist
 - AML: solving the problem of bi-specifics in AML

Key Value Drivers
Ahead

- Ensovibep: Registrational studies in outpatient setting & hospitalized setting (ACTIV-3)
- Additional AMG 506/MP0310 data, MP0317 FIH in H2 2021
- AML Candidate FIH in 2022
- Abicipar decision

We Are Ready to invest in our exponential growth; to advance a burgeoning pipeline; to continue growing our team; following a clear strategy



EXECUTIVE MANAGEMENT

Executive Management and Senior Leadership Team



Patrick Amstutz, PhD, CEO

- Co-founder, former CBO & COO
- Member of the Board of Directors
- PhD in biochemistry from UZH



Dr. Nicolas Leupin, CMO

- Proven track record in drug development
- Former CMO argenx, senior positions at Celgene



Michael Stumpp, PhD, COO

- Co-founder, previously CSO
- PhD in biochemistry from UZH



Andreas Emmenegger, CFO

- Former CFO Glycart, Finance Roles at Roche
- >20 years experience as CFO of private & listed companies and in fund raising, IPOs



Ana Cerdeira, VP Partnering & Strategy

 Former VP Emerging Markets Portfolio Mgmt. at Takeda



Julien Gander, General Counsel

Director Legal & Group Risk Mgmt and Senior Legal Counsel at Lonza



Senior Leadership Team

Seth Lewis, SVP IR, Comms, Strategy

- Head of IR and Comms at Surface Oncology, Bavarian Nordic A/S, 9 years at Trout Group
- Based in Boston office



Daniel Steiner, SVP Head of Research

- Previously responsible for DARPin® generation, PK extension, enabling work for DARPin selection
- PhD, Univ. of Zurich, Plückthun lab



Alex Zuercher, SVP Development

- Previously VP of Operations & Dir. of CMC at MP
- Cytos Biotechnology and Spirig Pharma



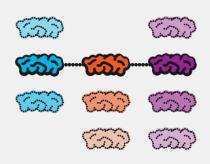
Innate Advantages Combined With Proprietary Approaches

DARPin® Differentiation:

Turn-key multi-specifics

DARPin® Benefit
Solving clinically relevant problems

Candidates
Unlock & Expand



- Small size with single-domain activity
- Up to 6 binders in one candidate
- Open combinatorial space (test 10,000)
- No loss of stability
- Simple, cost-effective manufacturing

Nature's choice for multi-specifics



Localized Activity

 Local and temporal control of activity



Molecular Handcuff

Full shut-down by conformational freeze



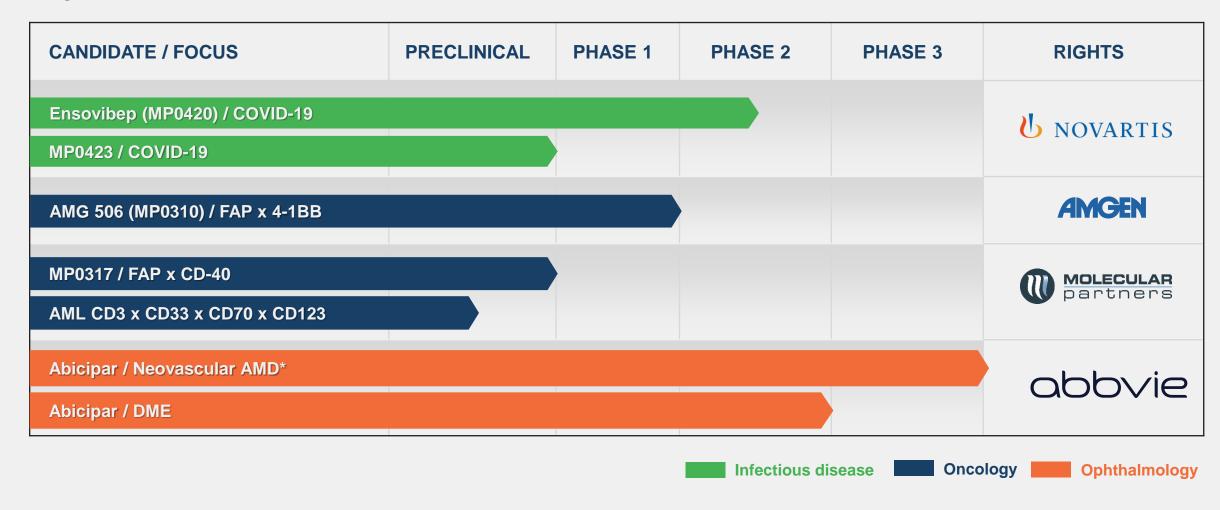
Prevent escape

Prevent escape

- MP0310
- MP0317
- Next-Gen CD3
- MP0274
- MP0423
- MP0250
- Ensovibep
- MP0423



Pipeline





Synergistic Partnerships Built on a Versatile Drug Platform

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



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



Virology

Capability Deal

- Leverage production, global development and distribution of Sandoz Novartis for ensovibep
- Received CHF 60 m to date; CHF 150m milestone payment upon option exercise to license
- 22% royalty on sales in commercial countries



Over ~\$1B in potential milestone across several programs

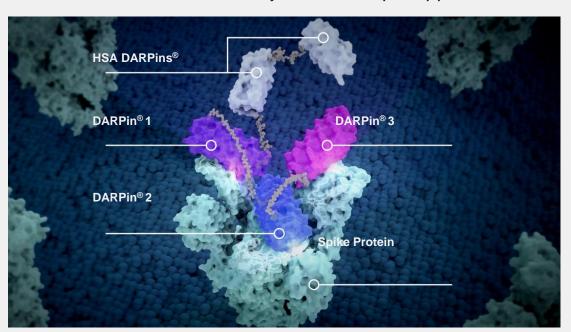




Our COVID-19 Program: Two Outstanding Candidates

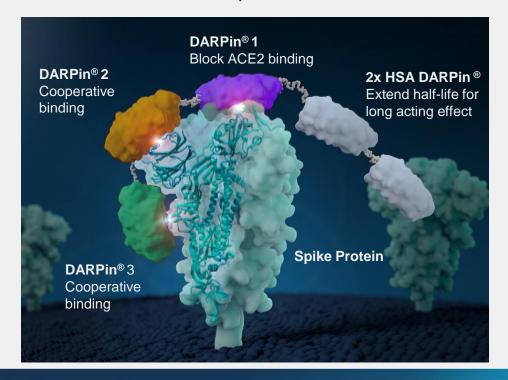
Ensovibep (MP0420)- best-in-class

- 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



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 ensovibep





Cooperative Target Engagement Leads To Super Affinity

DARPin #1; 1 hour off-rate

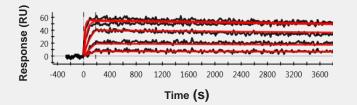


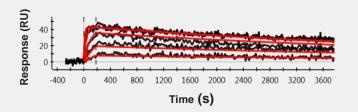
DARPin #2; 1 hour off-rate

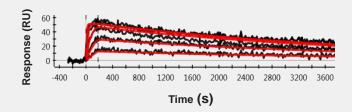


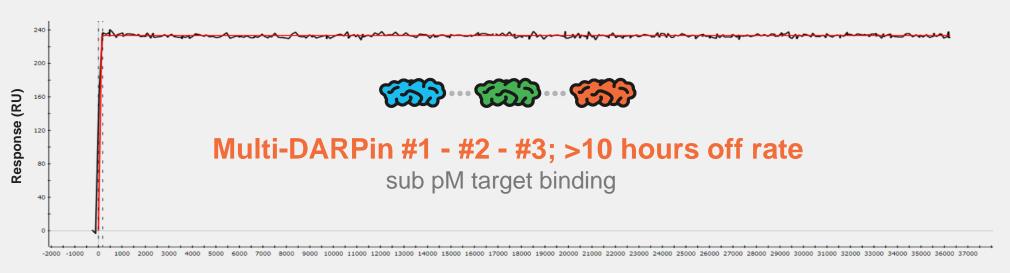
DARPin #3; 1 hour off-rate









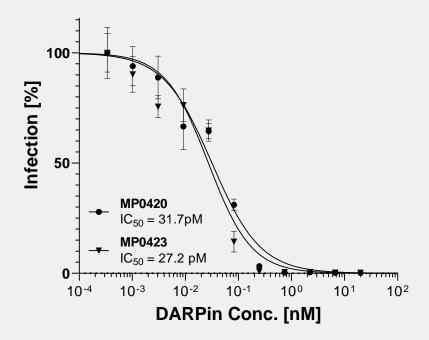


Time (s)



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

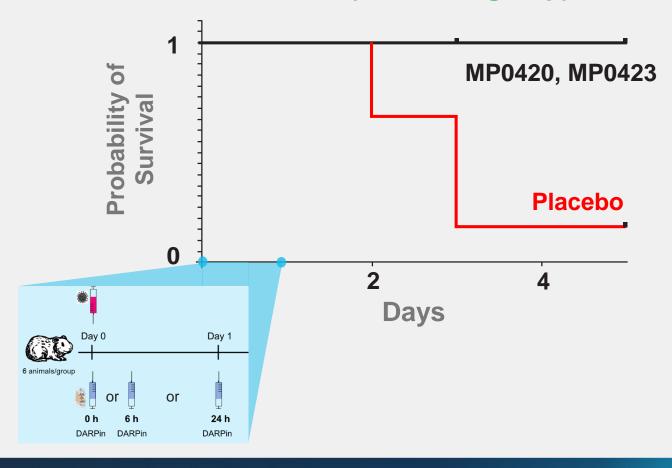
In vitro activity: Pseudotype Neutralization Assay



Highest potency

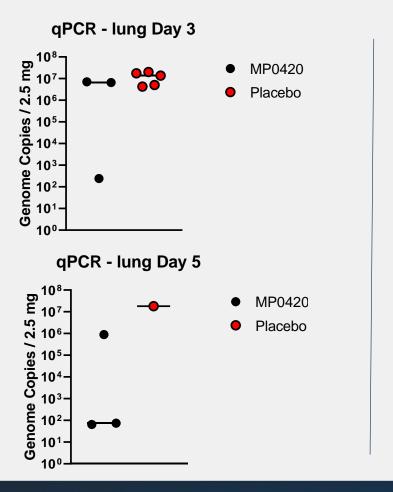
Tri-binding leads potency in the low pM range; likely at the assay limit

In vivo activity: Kaplan Meier Plot - Hamster Model (6 animals/group)

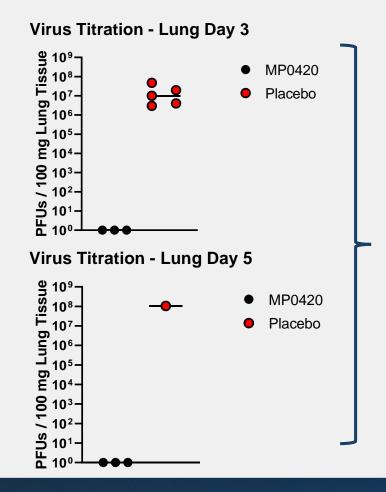


Ensovibep Blocks the Virus and Prevents Infection in the Lung

Viral titer in the lung



Viral infectivity in the lung



Ensovibep blocks viral infectivity completely

New SARS-CoV-2 Variant Analysis – Ensovibep May 2021

Variants	Combined mutations	Neutralization Potency IC50 [ng/mL]
wild type	(Wuhan)	1.0
B.1.1.7 / United Kingdom	69-70 del, del145, E484K, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H	3.2
	69-70 del, del145, S494P, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H	0.8
B.1351 / South Africa	L18F, D80A, D215G, Del242-244, R246I, K417N, E484K, N501Y, D614G, A701V	5.0
P.1 / Brazil	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I, V1176F	1.2
B.1.429 / California (US)	S13I, P26S, W152C, L452R, D614G	0.5
B.1.526 / New York (US)	L5F, T95I, D253G, E484K, D614G, A701V	3.0
	Emerging Variants:	
R.1	W152L, E484K, D624G, G769V	2.4
A.23.1	F157L, V367F, Q613H, D614G, P681R	0.3
	Individual Key Mutations of Variants:	
B.1.617 / India	E484Q	2.3
	L452R	0.5
	D614G	2.4
	G142D, P681R, Q1071H	n.a.
B.1.618 / India	del145	2.1
	del146	n.a.
	E484K	2.7
	D614G	2.4

No liabilities detected to date on any of the global variants of concern

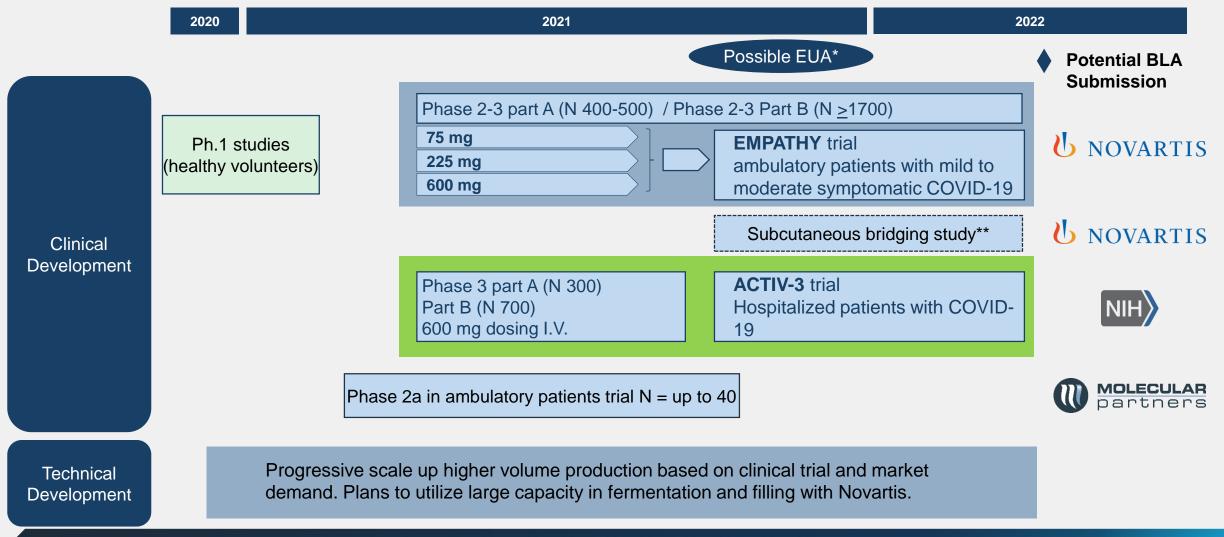
Pseudotype VSV or lentivirus SARS-CoV-2 neutralization assay



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

Draft Development plan for MP0420



MOLECULAR

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

^{**} S.C doses based on active dose in EMPATHY

Ensovibep (MP0420) Phase 1

- Study initiated November 2020, all three cohorts fully enrolled
- Double-blind, placebo controlled trial exploring safety and pharmacokinetics
 - IV administration
 - Up to 24 subjects total, stratified 3:1 (active: placebo)
 - Ages 18-65
- Dose range covers clinical doses in upcoming trials
- Endpoints: safety, tolerability and pharmacokinetics (SAD)
- Status:1st and 2nd cohort completed; 3rd cohort ongoing

Initial findings show ensovibep to be safe and well tolerated with no significant adverse events. Predictable exposure seen post administration, confirming the expected half-life of 2-3 weeks

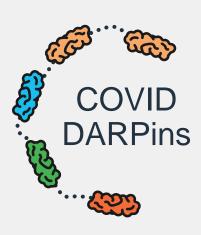


Ensovibep Upcoming Milestones

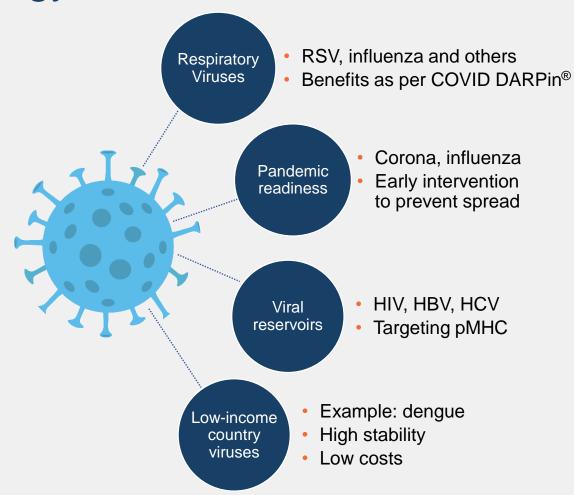
- Final data from phase 1
- Open label 2a initiation
 - 2a results mid 2021
- Additional variant data
- Initiate ACTIV-3 (NIH sponsored)
 - Hospitalized patients (Up to 1,000)
 - Futility analysis following 300 patient data

- Initiate EMPATHY (Novartis / MP)
 - Part A results (N=400-500)
 - Part B initiate (N≥1,700)
 - Potential EUA in 2021
- Potential S.C. bridging trials (Novartis / MP)
 - Initiate once dosing for EMPATHY part B is established

DARPin® Opportunities in Virology

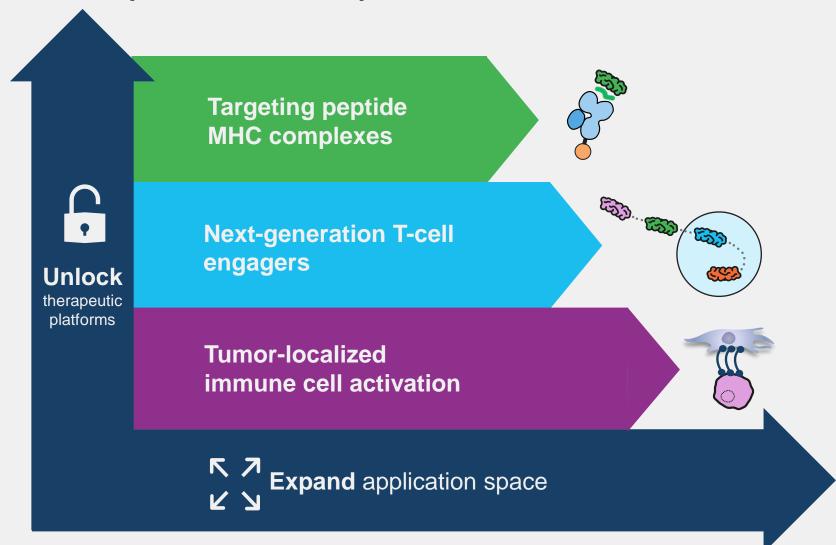


- Multi-valency for superior potency
- Multi-specificity for mutation resistance
- Speed of candidate generation
- High amount & low-cost production
- High stability and solubility for simple administration and distribution





Unlock and Expand: Therapeutic Modalities

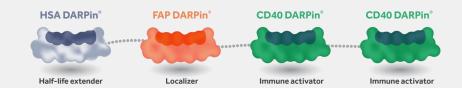




Recent data at AACR Highlight Platform Potential

MP0317 (targeting CD40 and FAP)

 MP0317, a FAPxCD40 targeting multi-specific DARPin® therapeutic, drives immune activation and leads to macrophage repolarization in vitro and ex vivo

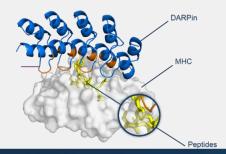


T-cell engager programs

- Novel multi-specific DARPin® T-cell engager with an improved therapeutic window to overcome dose limiting toxicities in AML therapies.
- A solution to T-cell engager toxicity: An anti-CD3 Prodrug DARPin® (CD3-PDD) shows no toxicity, but potent anti-tumor activity in a humanized mouse model

Peptide-MHC program

 Application of the DARPin® technology for specific targeting of tumor-associated MHC class I: peptide complexes



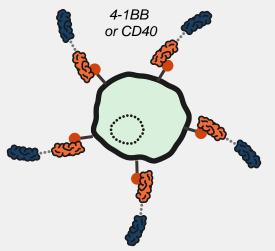




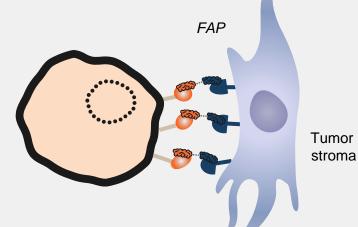
Local Activation of Immune cells: Fibroblast Activation Protein (FAP) as a General Switch

BODY

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



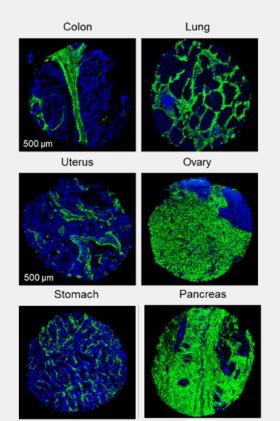




- No activation by mono-binding of FAP or CD40/4-1BB
- Simultaneous binding leads to tumor-local immune activation

TUMOR

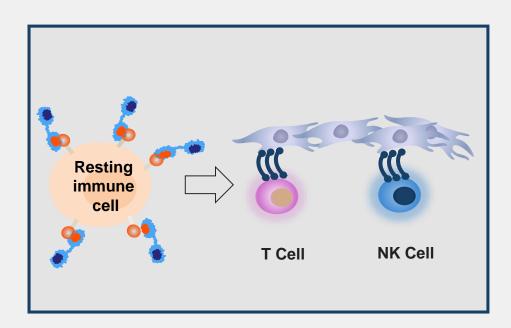
- High FAP concentration near tumor clusters receptors
- Immune cell is activated



Human FAP, DAPI

AMG 506/MP0310: Localized Activation of 4-1BB





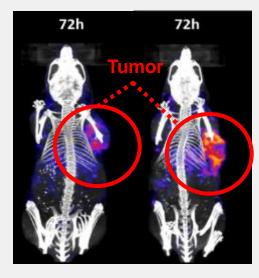
- Good safety profile without major systemic toxicity
 - > No liver toxicity or systemic activation of immune cells
 - > IRRs frequent but manageable
- > MP0310 is observed in tumor tissue
- Tumor biopsies show tumor-localized immune response consistent with the MoA
- Next step: investigate appropriate dosing schedule for sustained activity
- > \$50m upfront, ~\$500m in milestones plus royalties



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

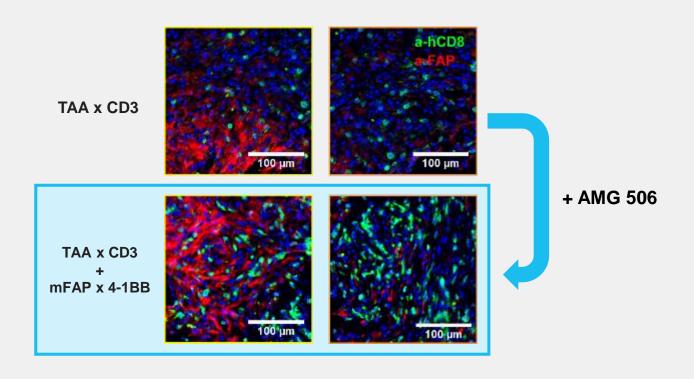
FAP-Mediated Tumor Accumulation of AMG 506

HT-29-T-implanted NSG mice



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

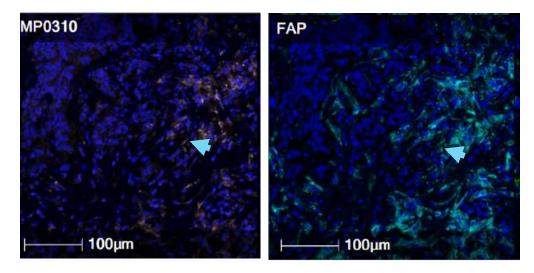
Intratumoral CD8 T cells



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

MP0310 low dose colocalizes with FAP

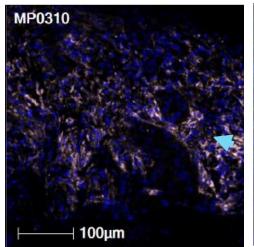
MP0310 < FAP

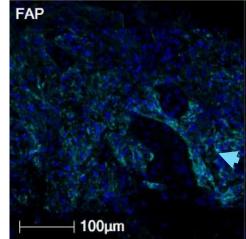


Endometrial carcinoma (Liver metastasis), C1D15

MP0310 high dose saturates FAP

MP0310 > FAP





NSCLC (lung), C1D15

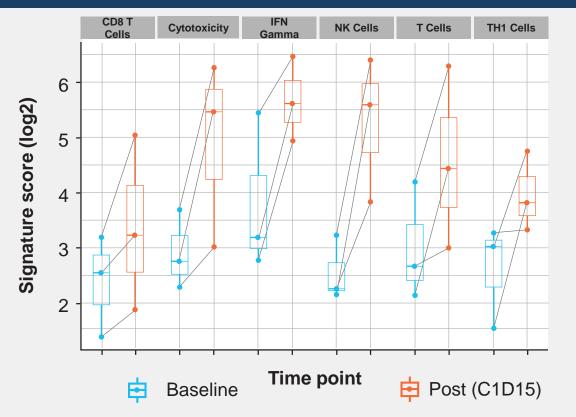
PD Activity in Paired Biopsies Supports AMG 506 / MP0310 MoA on 4-1BB Activation

BLOOD

CD8⁺ T-cells: CD25⁺ 100 80 40 C1D1 C1D8 C2D1 C2D8 Treatment on C1D1 & C2D1 Note: C1D1 & C2D1 predose sample

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

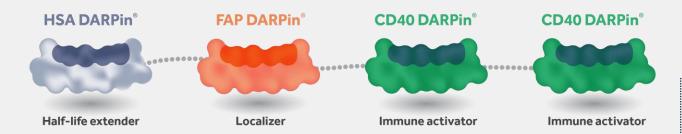
TUMOR

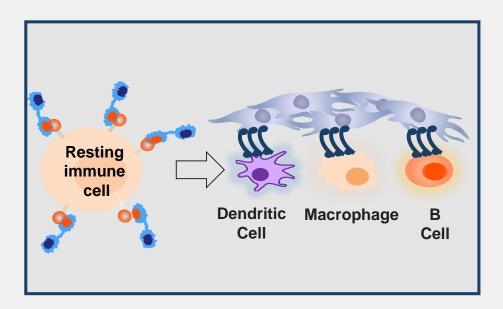


In the tumor, T-cells and NK cells are activated



MP0317: Localized Activation of CD40

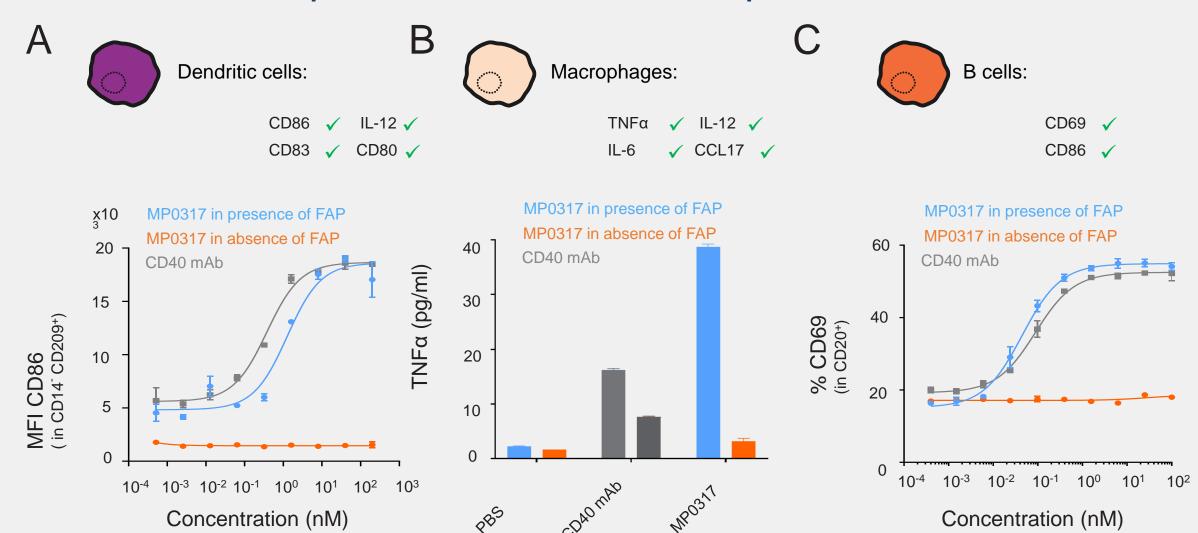




- Highly promising target with potential to significantly impact clinical outcomes for patients
- Complex biology to manage and administer safely and efficaciously
- FAP localization translating well, and will provide insights into dosing strategies
- > First patient in H2 2021
- Clinic design will include early potential for expansion based on activity
- Multiple avenues of combination treatments to explore: Chemo, PD-1, Radiation, etc.

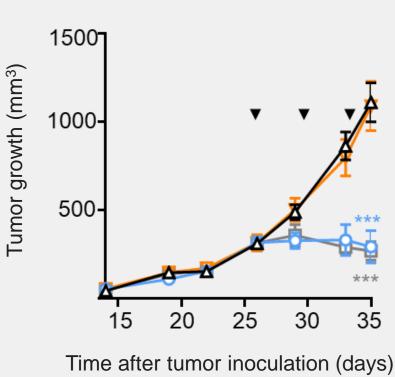


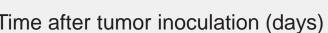
MP0317: FAP-dependent Activation of Specific Immune Cells

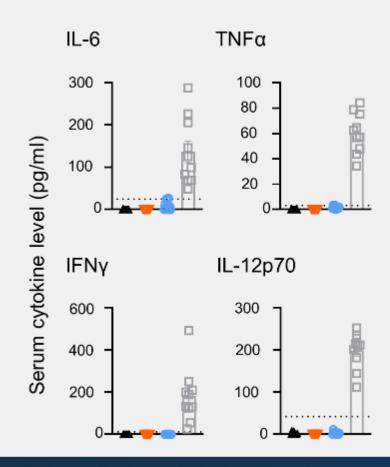


MP0317 Shows Full Activity with No Detectable Side-effects

FAPHIGH TUMOR: MC38-FAP Colorectal cancer







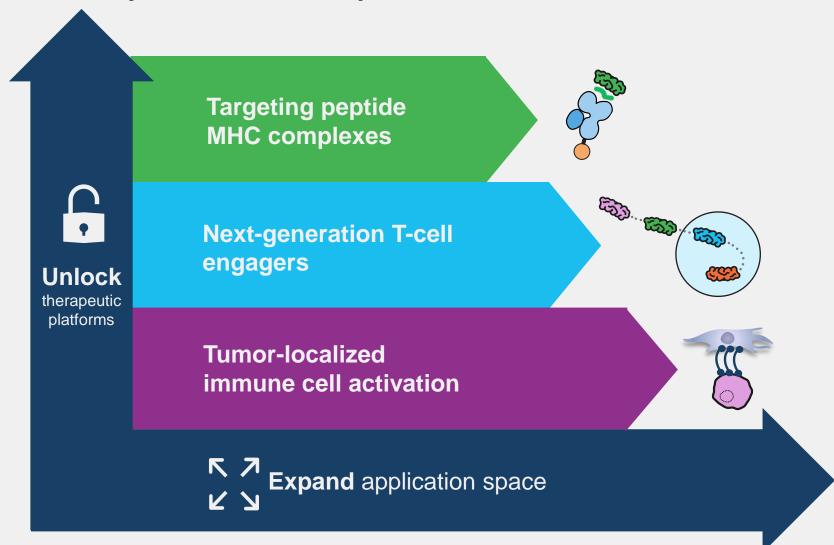
Vehicle

Neg. CTRL* mFAP x mCD40 mCD40 Ab





Unlock and Expand: Therapeutic Modalities





Current Limitations of CD3 Approaches

Safety

Efficacy

Hyperimmune-stimulation

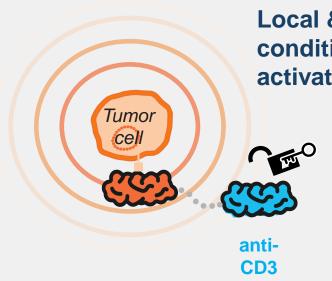
Neurotoxicity

Cytokine release syndrome (CRS)

Tumor escape

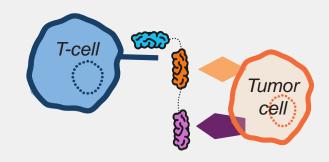
Target engagement

Our Solutions - Next Generation T-cell Engagers

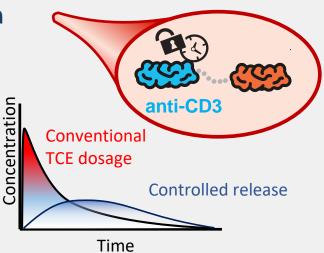


Local & conditional activation

Multi-specific T-cell engagers



Slow activation over time



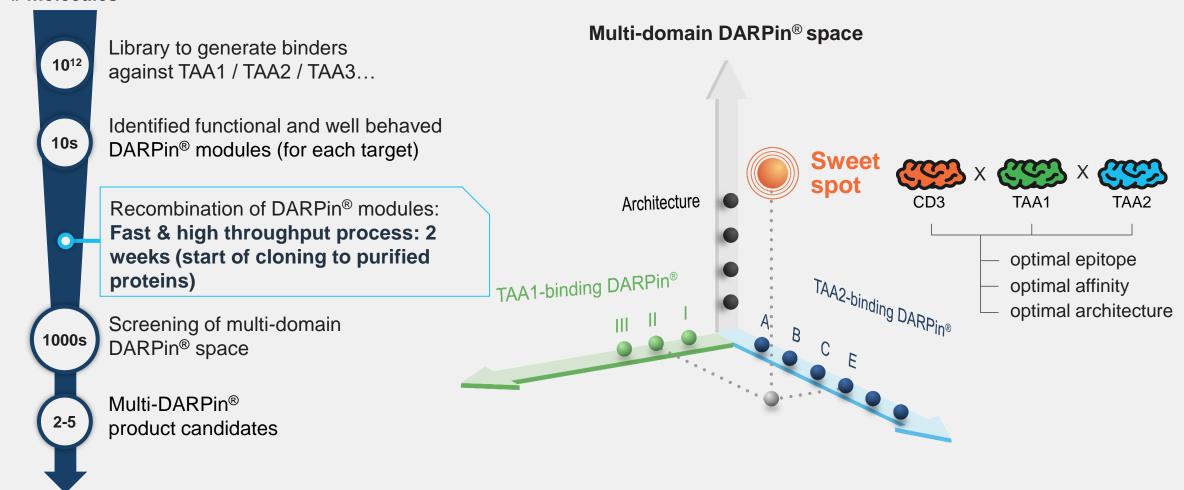
Improve safety to allow optimal dosing and **Deepen Efficacy for longer effect**

Update at AACR 2021

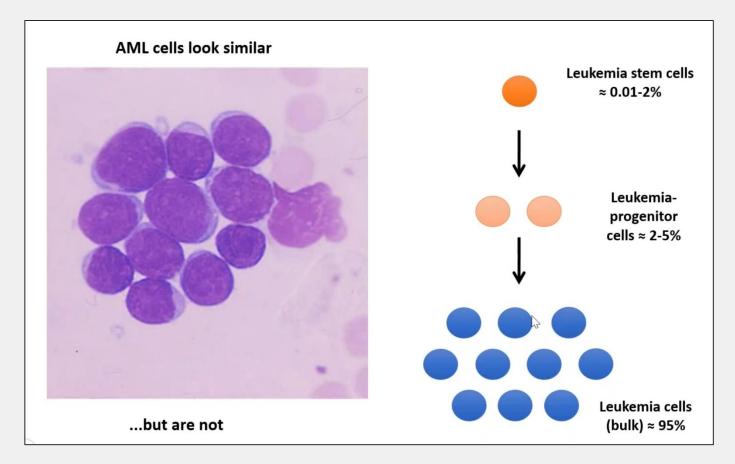


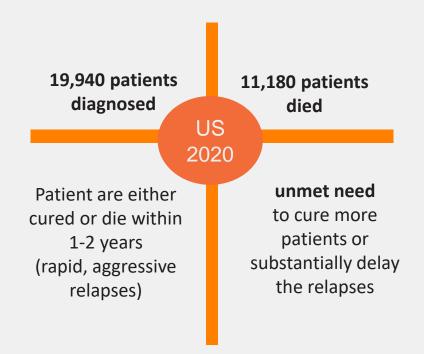
Multi-DARPin® Versatility Allows Screening for Function Sweet Spot

molecules



AML: Deadly Disease for About Half of the Patients





MRD+ is driver of relapse (only partial eradication of leukemic stem cells)

→ for curative intent LSCs need to be fully eradicated, while leaving HSCs untouched

As only in-vitro data available, value proposition derived in-vitro data and scientific concept



The DARPin® Solution: an avidity driven multi-specific DARPin® T-cell engager

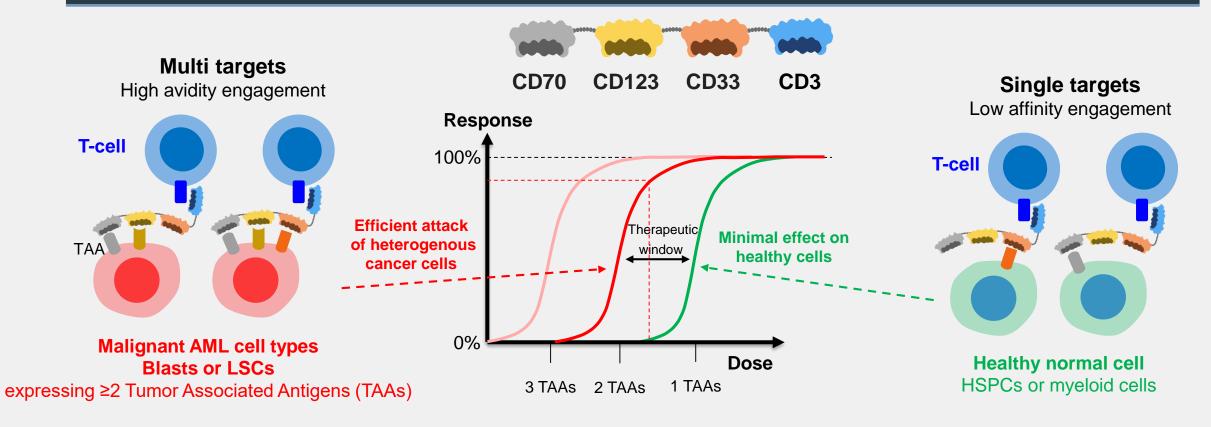


Figure 1. The concept of a multi-specific avidity driven DARPin® T-cell engager in AML

Optimizing the affinity of individual linked TAA binders utilises the avidity effect to deliver high affinity binding in the presence of ≥2 TAA targets on AML cell types e.g. blasts or leukemic stem cells (LSCs), but low affinity binding in the presence of single TAA presenting cell types e.g. hematopoietic stem and progenitor cells (HSPCs). This should reduce effects on off-target healthy cells, increasing the safety window, but still allow elimination of heterogenous malignant cells expressing 2 or 3 TAAs, thereby providing a novel AML treatment

DARPin® solution

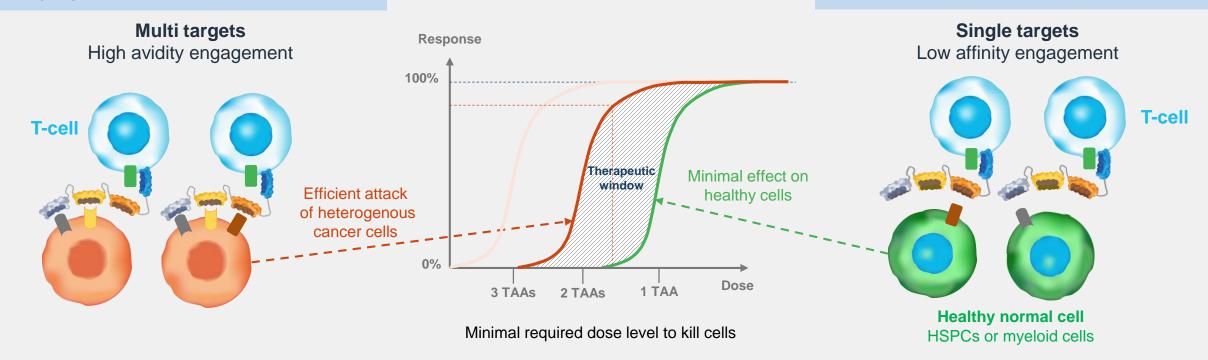
Multi-specific T-cell engager with improved benefit/risk in AML

Efficacy

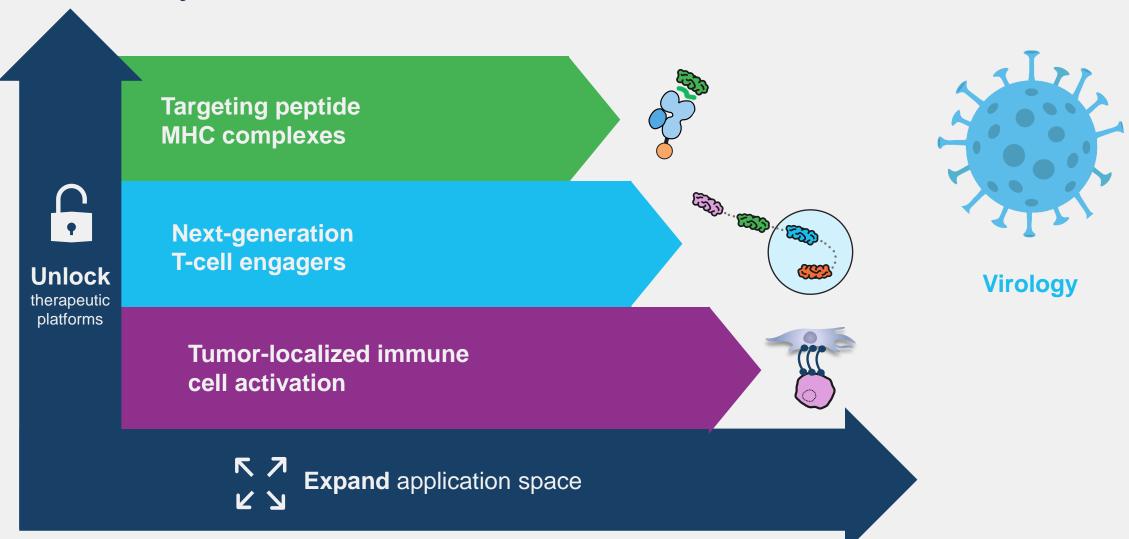
- **Higher dose levels** for efficient killing of cancer cells
- Multiple attack: Specific killing of several malignant cell types
- Prolonged effect: Counteract tumor heterogeneity / targeting leukemic stem cells (LSCs)

Safety

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



Summary and Outlook





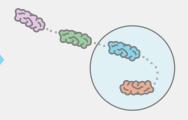
Summary and Outlook

Solid pMHC DARPin® platform established: progressing candidates internally and in partnerships



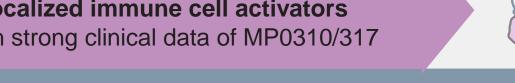


Progressing multi-specific **T-cell Engager** candidates and expanding first product candidates with "controlled activation"



Build on DARPin®
Covid19 success and
expand in virology

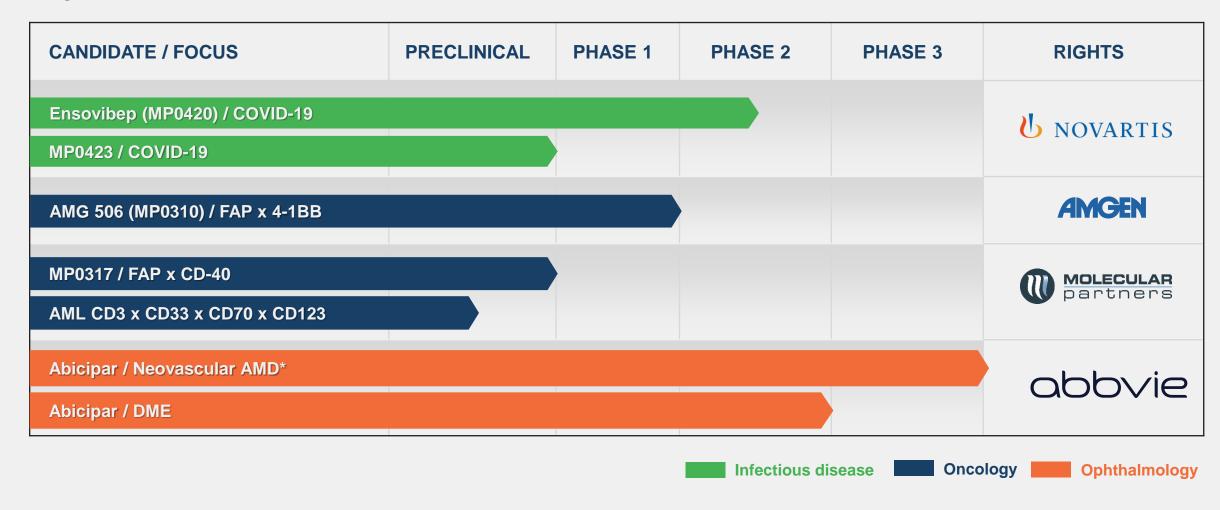
DARPin building blocks ready to expand **tumor-localized immune cell activators** based on strong clinical data of MP0310/317







Pipeline





Upcoming Potential Catalysts Across The Portfolio in 2021

Antiviral portfolio				
Ensovibep (MP0420) MP0423	 POC with potential Emergency Use Authorization in 2021 BLA submission possible in 2022 MP0423 FIH 			
Novel antivirals	 Develop novel DARPins for viral targets with first new target expected to be 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 			
рМНС	 Select Peptides for Candidate Selection – possibly with a partner 			

Funded into 2023

(Not incl. any future proceeds related to partnerships)



Upcoming Catalysts Across The Portfolio

	Antiviral portfolio				
Ensovibep (MP0420) MP0423	 POC with Emergency Use Authorization in 2021 BLA submission possible in 2022 MP0423 FIH 		POC for ensoviber		
Novel antivirals	 Develop novel DARPins for viral targets with first new target anno 	ounced 2021			
Immuno-oncology portfolio					
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T cell engagers	 1st Candidate selected for development Follow-up pipeline established 	AML ca			
рМНС	 Select Peptides for Candidate Selection – possibly with a partne 	r			
Funded into 2023 AbbVie: future of					

(Not incl. any future proceeds related to partnerships)



AbbVie: future of Abicipar



Financial Overview & Milestones:

- Q1 Cash 2021: CHF 145.6 (~\$155m), no debt
 - Successful capital raise of CHF 75m, completed in early July 2020
- Additional funding from Novartis transaction (CHF 60, received in October-November 2020)
 - Funded into 2023, without consideration of potential future milestones and royalties
- ~\$1B in potential payments from R&D partners yet to be realized
 - CHF 150m milestone from Novartis upon option exercise to license 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



