

Custom Built Biology for Patients

Corporate Deck September 2021 Molecular Partners AG, Switzerland (SIX: MOLN, NASDAQ: MOLN)

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Pioneering DARPin® Therapeutics

COVID19 – Ensovibep (Novartis)

- Phase 1 & small trial in patients completed
- 2 pivotal trials ongoing, recruiting well
 - **EMPATHY** ambulatory
 - ACTIV-3 hospitalized
- Activity on all viral variants of concern

Local immune agonists

- AMG 506 / MP0310 (FAP x 4-1BB, Amgen) weekly dosing; on track to initial read-out in H2/2021
- MP0317 (FAP x CD40) on track to FIH in H2/2021

AML (CD33+CD70+CD123 x CD3)

- **Triple-TAA-targeting TCE** on track for candidate selection in H2/2021
- First in human 2022

- Financials
 - Listed on NASDAQ
 - Raised CHF 58 million gross proceeds
 - Strong balance sheet, funded into H2 2023
- Infectious disease
 - Announcing new programs at R&D day Dec.
 2021
- Abicipar
 - Molecular Partners will regain rights from AbbVie; transition and evaluation of data initiated



What are DARPin[®] Proteins





Multi-DARPin® Versatility Allows Screening for Function Sweet Spot

molecules



Super Large Libraries with DARPin Binders to any given target

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

Assembly of up to 6 DARPin[®] modules: Fast & high throughput process: 2 weeks

Screening of multi-domain DARPin[®] space for the SOLUTION

Specific Multi-DARPin® product candidate with desired function

Multi-domain DARPin[®] space



					Infectious disease	Discovery
Pipeline					Oncology	Ophthalmology
CANDIDATE / FOCUS	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	RIGHTS
Ensovibep (MP0420) / COVID-19		ACTIV-3 Ph 3 Hospitalized				
Ensovibep (MP0420) / COVID-19		EMPATHY Ph 2-3 Ambulatory				U NOVARTIS
Next Gen / COVID-19						
AMG 506 (MP0310) / FAP x 4-1BB						AMGEN
MP0317 / FAP x CD40						
AML CD3 x CD33 + CD70	+ CD123					W partners
Abicipar						MOLECULAR partners
Platform Discovery						
T cell Engagers						
Additional Infectious Dise	eases					W partners



				-	Infectious disease	Discovery
Pipeline					Oncology	Ophthalmology
CANDIDATE / FOCUS	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	RIGHTS
			os No active	e immune engage	ment; improving cha	inces of success
		EMPATHY Ph 2-3 Ambulatory Rapid test and rapid treat, single-shot solution				-shot solution
	MP0423 r	eady for IND as ne	eded. Currently o	developing the ne	ext-gen COVID DARP	in for future needs
AMG 506 (MP0310) / FAP	x 4-1BB			Wee	ekly dosing, initial re	sults H2 2021
MP0317 / FAP x CD40					FIH expe	cted H2 2021
			Candidate to b	e announced H2	2021; FIH expected 2	022
Abicipar Mol	lecular Partners	to regain rights to	abicipar; will an best pa	alyze improveme th forward	nts done and data co	llected to consider
Platform Discovery						
						MOLECULAR
						partners





COVID-19 Program Success Opens Path for Antiviral Portfolio

Therapeutics Are Needed Now, More Than Ever



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Vaccinations faster and better than anyone could have hoped Variants continue to rise globally, challenging effectivity of vaccines



Globally, as of 4:06pm CEST 18 August 2021, there have been 208,470,375 confirmed cases of COVID



Hospitalizations are up again, mostly in the unvaccinated



Targeting the Ambulatory and Mild to Moderate Hospitalized





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 Response (RU) Response (RU) Response (RU) 40 40 40 20 20 20 -400 0 400 800 1200 1600 2000 2400 2800 3200 3600 400 400 800 1200 1600 2000 2400 2800 3200 3600 400 400 800 1200 1600 2000 2400 2800 3200 3600 Time (S) Time (S) Time (S) 240 200 **(5**) (**5**) Response (RU) 160 120 Multi-DARPin #1 - #2 - #3; >10 hours off rate sub pM target binding 40



High Potency Inhibition Translates to in vivo Therapeutic Properties

In vivo activity: Rescues test animals from death



Completely blocks infectivity in vivo





Our COVID-19 Program - Ensovibep

- Tri-specific DARPin[®] antiviral targeting the viral spike protein
- Designed to reach highest potency
- Designed to prevent viral escape; Inhibits all known variants of concern to date
- Phase 1:
 - I.V. administration safe and well tolerated
 - Bolus administration completed
 - Subcutaneous ongoing
 - Half life established at 2-3 weeks
- Single-arm Phase 2 results confirm safety, half life and validate viral clearance methods for P2/3





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



Ensovibep Clinical Development; Registrational Trials





Global Clinical Trial Sites of Ensovibep





Cooperative Binding Translates to Prevention of Mutational Escape

Lineage (Origin)	VSV or Lentivirus Pseudotype Neutralization Assay IC ₅₀ [ng/mL]
Reference	1.0
	1.1
Alpha / B.1.1.7 / United Kingdom	1.7
	0.9
Beta / B.1.351 / South Africa	5.0
	1.2
	1.2
Gamma /P.1 / Brazii	0.7
Delta / B.1.617.2 / India	2.4
Ensilon / B 1 429 / California (LIS)	2.2
Epsilon / B. 1.423 / California (03)	0.9
Eta / B 1 525 / Nigoria	6.2
Lta / D.1.323 / Nigeria	6.8
Lambda / C.37 / Peru	0.5
lota/ B.1.526 / New York (US)	3.0
R.1	2.4
A 22 1	1.6
A.23.1	0.3
Kappa / P 1 617 1 / India	3.2
Карра / Б. 1.017.1 / Шиla	2.0
B.1.618 / India	8.1

All Variants | Reported in vitro Therapeutic Activity





Ensovibep Upcoming Milestones

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

- EMPATHY (Novartis / MP)
 - Part A results (N=400)
 - Part B initiate (N≥1,700)
 - Potential EUA submission 2021 / 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





COVID

DARPins

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Localized Immune Activators

AMG 506 / MP0310 & MP0317



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

High FAP concentration near

FAP

tumor clusters receptors

Immune cell is activated

BODY

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

TUMOR

Tumor stroma





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





- 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





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



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

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

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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
- 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



MP0317 Shows Full Activity with No Detectable Side-effects

FAPHIGH TUMOR: MC38-FAP Colorectal cancer







New Therapeutic Platforms: Unlocked

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Next Generation T-cell Engagers



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

Updated at AACR 2021



AML: Deadly Disease for About Half of the Patients





MRD-status in NPM1-mutated AML in PB after 2nd induction chemotherapy was the only significant prognostic factor (Ivy. NEJM 2016)

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)

Our DARPin Approach:

- target LSCs and blasts, while sparing healthy cells, incl. HSPCs, and
- Use multi-targeting avidity to attack cancer cells, mainly
- Greater therapeutic window due to the lack of CRS and other toxicities



DARPin[®] Solution Multi-specific T-cell engager with improved benefit/risk in AML





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

High Potency of Candidates

Effect on Healthy Blood Cells





Molecular partners



Financials & Outlook

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H1 2021 Financial Highlights

- Ongoing strong financial position with CHF 174.3 million in cash and short-term deposits as of June 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 52.5 million in H1 2021
- Unchanged FY 2021 guidance



Financial Guidance for Full-Year 2021

- Total expenses of CHF 65-75 million, of which around CHF 7 million non-cash effective costs
- Gross cash burn of CHF 85-95 million, incl. CHF 20 million payable to Novartis for the manufacturing of commercial supply of Ensovibep
- With CHF 174.3 million cash at hand (incl. short-term time deposits) and no debt, the Company is funded into H2 2023, excluding any potential receipts from R&D partners
- Guidance subject to progress and changes of pipeline





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 (H2/2021) 		
MP0317	 MP0317 FIH in H2 2021 		
MP0-AML	 1st Candidate selected for development Update at ASH – FIH in 2022 		
Antiviral portfolio			
Ensovibep (MP0420)	 EMPATHY readout Phase 2b from 400 patients in H2 2021; potential for EUA applications (US&EU) ACTIV-3 futility analysis from 300 patients in H2 2021 with full data in 2022 BLA submission possible in 2022 		
Novel antivirals	 Next generation COVID drug, built for the future Develop novel DARPins for viral targets with new programs expected to be announced in R&D day 2021 		
	Funded into H2 2023 (Not incl. any future proceeds related to partnerships)		





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