

Corporate Presentation

June 14, 2024

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The DARPin Modality and Molecular Partners' Strategy



What we invented

- New class of therapeutics: Designed Ankyrin Repeat Proteins (DARPins)
- DARPins to close the gap between small molecules and antibodies
- 7 clinical-stage compounds, >2500 patients treated

How we apply it

- Unique DARPin solutions for a defined medical problems not addressable by antibody designs
- Demonstrate true patient value with early clinical readouts
- Combine our capabilities with world-class partners to deliver innovative therapeutics



Corporate Highlights

MP0533	 Novel tetra-specific T cell engager for R/R AML and high-risk MDS/AML patients ASH 2023: encouraging initial clinical data with acceptable safety and initial antitumor activity Phase 1/2a study with dose-escalation well on track; dosing patients in DR 7 ongoing
Radio-DARPin Therapy (RDT) & MP0712	 Successful RDT platform optimization to reduce kidney accumulation and increase tumor uptake Announced MP0712 as lead DLL3-targeted ²¹²Pb-labelled RDT to be co-developed with Orano Med Preclinical data on MP0712 presented at SNMMI 2024: positive tumor to kidney ratio, efficacy & safety
Switch-DARPin & MP0621	 Demonstrated conditional, target-specific immune activation for Switch-DARPin platform First program: MP0621, a cKit x CD16a x CD47 Switch-DARPin, as next-gen therapeutic supporting HSCT for AML patients & beyond; MP0621 selected as lead candidate to move into development Initial preclinical data presented at EHA 2024 indicate encouraging efficacy and safety profile
MP0317	 Bi-specific CD40 agonist targeting FAP for tumor-localized immune activation: Favorable safety profile and confirmed tumor-localized CD40 activation leading to remodeling of TME in patients
Operations	 Strong financial position with CHF ~174 M in cash as of March 31, 2024 Capitalized well into 2026



AML, acute myeloid leukemia; ASH, American Society of Hematology; DLL3, Delta-like ligand 3; DR, dose-regimen; EANM, European Association of Nuclear Medicine; FAP, fibroblast activation protein; MDS, myelodysplastic syndrome; RDT, Radio-DARPin Therapy; R/R, relapsed/refractory; SITC, Society for Immunotherapy of Cancer; TME, tumor microenvironment.

Pipeline

MODALITY	CANDIDATE	RESEARCH	PRE-CLINICAL	PHASE 1	PHASE 2	RIGHTS	
Tetra-specific T cell Engager	MP0533	R/R AML and AML CD33 x CD123 x C	/ MDS D70 x CD3			Molecular partners	
Radio-DARPin	MP0712	SCLC & NETs DLL3	Co-development*			Molecular partners	
Therapy	Undisclosed Programs	Solid Tumors	In-house programs			MOLECULAR partners	
	Undisclosed Programs	Solid Tumors	2 partnered programs			ပံ novartis	
Switch-DARPin	MP0621	AML / HSCT cKIT x CD16a x CD47					
	Undisclosed Program	Immune cell engager				partners	
Localized Agonist	MP0317	Advanced Solid Tu FAP x CD40	umors			Molecular partners	



*The co-development agreement with Orano Med includes up to 3 potential oncology targets including DLL3. AML, acute myeloid leukemia; DLL3, Delta-like ligand 3; HSCT, hematopoietic stem cell transplant; MDS, myelodysplastic syndrome; NET, neuroendocrine tumor; R/R, relapsed/refractory; SCLC, small cell lung cancer.



MP0533

Tetra-specific T-cell Engager for AML

Patients with AML Have a High Unmet Medical Need

69 YEARS
OLD31.7%Median age of AML
patients at diagnosis1Overall 5-year
survival rate1

Despite 50 years of progress, elderly and frail patients are often not eligible for high-intensity conditioning and HSCT, and thus have limited treatment options and poor survival outcomes²

- Lack of broad and clean AML surface targets
- Risk of clonal escape even after high-intensity conditioning/HSCT





MP0533: Avidity-Driven Selectivity for Cancer Cells in AML

Problem: AML tumor-associated antigens are expressed on healthy cells



- AML remains a deadly disease and persistence of leukemic stem cells (LSCs) drives relapse
- **AML cell population is heterogeneous**: individual AML blasts and LSCs lack a clean target. AML cells can be differentiated from healthy cells (e.g. HSCs) by their **co-expression of specific targets** (e.g. CD33, CD123, CD70)

HSA

CD33

CD123

Target localizers

CD70

CD3

Immune

activato

Solution: MP0533 – Avidity-driven selectivity and killing by T cells



 MP0533 is designed to induce T cell-mediated killing preferentially when two or three target antigens (CD33, CD123, CD70) are co-expressed

Half-life extender

MP0533 is hypothesized to preserve healthy cells hence opening a therapeutic window

HSA

• MP0533 has the potential to kill all AML cells (blasts and LSCs) despite heterogeneity, ensuring **long term disease control**



MP0533 Phase 1 Dose-escalation Trial in R/R AML patients



Study currently dosing patients in DR 7, plans to update in H2 2024



AML, acute myeloid leukemia; D, treatment cycle day; DLT, dose-limiting toxicity; DR, dose regimen; FIH, first-in-human; MDS, myelodysplastic syndrome; n, number of patients; PD, pharmacodynamic; PK, pharmacokinetics; POC, proof of concept; RP2D-R, recommended phase 2 DR; R/R, relapsed/refractory.

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MP0533 - Patient Characteristics and Safety Profile

PATIENT CHARACTERISTICS DR COHORTS 1–6 (n=28)		MP0533-RELATED TEAEs [‡]				
Sex, n (%) Female / male	14 (50) / 14 (50)	Ventricular extrasystoles Renal failure	1	= C	Grade 1 = Mild Grade 2 = Moderate	
Age Mean / Median (range)	68 / 74 (22–82)	Pneumonia Platelet count decreased Neutropenic colitis	1	Grade 3 = SevereGrade 4 = Life threatening		
ECOG PS, n (%) 0 / 1 / 2	11 (39) / 14 (50) / 3 (11)	Nausea Lymphopenia	3			
Hematologic malignancy, n (%) AML / MDS/AML	19 (68) / 9 (32)	Lymphocyte count decreased Intervertebral discitis	2			
ELN risk category, n (%) Intermediate / adverse	4 (14) / 24 (86)*	Infusion related reaction Hepatic cytolysis		35	19	
No. of prior systemic treatment lines, n (%) 1 / 2 / ≥3	12 (43) / 9 (32) / 7 (25)	Headache Erythema multiforme	2			
*TP53 mutated: 7 (25%)		Erysipelas Dissiminated intravascular coagulation				
Acceptable safety profile for MP0533 reported for DR 1-6 [‡] :		Cytokine release syndrome Cellulitis	18	13		
 IRR and CRS are the most frequent MP0533-related TEAEs (mostly Grade 1-2, occasional Grade 3) No DLTs up to DR 6 		Biood fibrinogen decreased Bacteraemia Angina unstable				

Data cut-off: 12 March 2024 Preliminary data as study is ongoing, subject to final data validation.

MOLECULAR partners [‡]TEAEs of n=1 of grade 1 were removed from the graph for display purposes. AE, adverse event; CRS, cytokine release syndrome; ELN, European LeukemiaNet; IRR, infusion-related reaction; TEAE, treatment-emerging AE.

MP0533 Treatment & Clinical Response

Four responders reported in DR 3-6:

- CR in 1 patient at DR 4
- MLFS in 3 patients, 1 each at DR 3, DR 5 and DR 6

Currently dosing patients in DR 7



MOLECULARData cut-off: 12 March 2024DartnersPreliminary data as study is ongoing, s

Preliminary data as study is ongoing, subject to final data validation.

1. Döhner et al. Blood 2022;140(12)1345-77. CR, complete response; CRi, CR with incomplete hematologic recovery; ELN, European LeukemiaNet; MLFS, morphologic leukemia-free state.

MP0533 – AML blast decrease from baseline in BM aspirates



MOLECULAR
partnersData cut-off: 11 March 2024
Preliminary data as study is ongoing, subject to final data validation.

MP0533 Phase 1 Dose-escalation Trial in R/R AML patients



**optional D12 if DR 6–7 transition from step-up dose to target dose is not tolerated

Study currently dosing patients in DR 7, next update in H2 2024



clonality

STUDY OBJECTIVES

Preliminary activity / PD

- Clinical response as per

Blasts and LSCs counts

- Effector T cell activity and

tumor:effector cell ratio

MP0533 presence in BM

- Target (co-)expression

Evolution of disease

ELN (incl. MRD status)

Safety / tolerability,

• PK / exposure,

AML, acute myeloid leukemia; D, treatment cycle day; DLT, dose-limiting toxicity; DR, dose regimen; MDS, myelodysplastic syndrome; n, number of patients; PD, pharmacodynamic; PK, pharmacokinetics; POC, proof of concept; RP2D-R, recommended phase 2 DR; R/R, relapsed/refractory.

MP0533 Outlook

- 28 AML patients treated (across cohorts 1–6) passed DLT period
- Acceptable safety with IRRs & CRS as most frequent MP0533-related TEAEs
- Clinical response rate (1 responder per cohort, DR 3-6, as per ELN) reflects disease heterogeneity & ongoing dose escalation
- Encouraging reduction in BM blasts observed
- 9 clinical sites (across 4 countries in Europe) actively recruiting patients up to cohort 7



- Protocol amended to allow for higher doses beyond DR7 in r/r AML or MDS/AML
- Further clinical & translational analysis on-going, to support defining optimal development path
- In addition to r/r AML population, evaluating development opportunities in 1st line in fit and unfit patient populations
- Clinical update on the program in H2 2024



AML, acute myeloid leukemia; BM, bone marrow; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; DR, dose regimen, ELN, European leukemia network; IRR, infusion-related reaction; PD, pharmacodynamics; PK, pharmacokinetics; R/R, relapsed / refractory; TEAE, treatment-emerging adverse event



Radio-DARPin Therapy & MP0712 as first program

Platform & Pipeline



Ideal Properties of Radiotherapy Product Candidate





LMW Molecules as Ideal Vectors but Limited Target Space

<u>MOLECULAR</u>



* Source: Guggenheim Securities Report 2023 ** e.g. FAP, CAIX, FOLR1, NTSR1, Eph2A, GPC3, MC2R, GRPR, ITGB6 LMW, low molecular weight; NET, neuroendocrine tumor

Our Engineering Strategy for Radio-DARPin Therapy (RDT)





Evolution of Surface Engineering for RDT Engine





AT PROGRAM START: Iterative rounds of DARPin surface engineering and *in-vivo* testing needed to reach low kidney accumulation



TODAY: A single round of DARPin surface engineering to reach low kidney values for many DARPin binders



* Kidney value of best surface variant per engineering round displayed in graph: 4h timepoint in wt or tumor-bearing mice; DARPins conjugated to different chelators and labelled with different radioisotopes

Systemic Half-life Extension (HLE) Increases Tumor Uptake

Establishing a HLE toolbox with different "strengths & properties" to tailor to specific needs



T: Tumor; B: Blood

partners

Her2 and DLL3 DARPins conjugated to different chelators, labelled with different radioisotopes; and tested in different mouse tumor models; aSA: HLE moieties binging to serum albumin

Radio-DARPin Platform Ready to Deliver Product Candidates





BB: Brush border of proximal tubular cells in the kidney with megalin/cubilin receptor complex * Data presented at various scientific conferences, including AACR 2023 (<u>Bosshart et al.</u>), SNMMI 2023 (<u>Lizak et al.</u>), EANM 2023 (<u>Lizak et al.</u>), and others

MP0712: The first ²¹²Pb-DLL3 Targeted Radiotherapy

Combining distinctive DARPin features with the power of ²¹²Pb for efficacious cancer therapy

SCLC as Indication

- Aggressive cancer with high unmet medical need
 2L: mPFS ~3m; 5y OS ~3%^{1,2}
- DLL3 is expressed in >85% of pts³

DLL3: A promising Target

- Homogeneous tumor expression, but low expression level in pts
- No expression in healthy tissues
- New treatments with room for improvement: Tarlatamab (AMGEN) for 2L+; ORR ~40%

Diverse set of DARPins against DLL3

- Good developability
- Specific binding with high affinity

PRODUCT COMPOSITION



²¹²Pb for Targeted Alpha Therapy

- Strong cytotoxicity (dsDNA breaks)
- Single alpha decay (limited free daughters)
 - \rightarrow Limited irradiation of healthy tissues
- Relatively short half-life (10.6 h)
 - → Fast energy deposition (efficacy)
 - \rightarrow Easier waste management

Co-Development with Orano Med

- The leader for ²¹²Pb & a committed partner
- Reliable & scalable ²¹²Pb production
- Independent production capacities (substantial inventory of purified ²³²Th)

ASCO: Ph2 clinical data 212 Pb-DOTAMTATE (AlphaMedixTM) showed an ORR of 55.6% 4



1) Treatment of refractory and relapsed small cell lung cancer, UpToDate

2) SEER 3) Rojo *et al., Lung Cancer*, 2020

4) Strosberg et al., ASCO 2024 presentation



Favorable Safety & Potent Efficacy of ²¹²Pb-DLL3 RDT Candidate



- All treatments up to 40 µCi were well tolerated
- → Treatment shows a favorable safety profile suggesting its potential for clinical use

Lizak et al, SNMMI 2024 (oral presentation)



CD1 wt mice Dose: 10 to 40 µCi of ²¹²Pb at 0.01 mg/kg of DLL3 DARPin

Efficacy in MC38-hDLL3 Model



- Significant and durable inhibition of tumor growth (comparable to benchmark mAb)
- → Treatment shows profound antitumor activity at clinically relevant dose

Mice xenografted s.c. with hDLL3-MC38 (Biocytogen) Dose: 10 μCi of ²¹²Pb at 0.01 mg/kg of DLL3 DARPin [1] Sharma *et al., Cancer Res*, 2017; [2] Korsen *et al., PNAS*, 2022



MP0712: ²¹²Pb-DLL3 Lead Candidate with Attractive BioD Profile



Time Point	Tumor : Kidney
4 h	1.4 : 1
24 h	2.5 : 1
AUC	2.1 : 1

- MP0712 selected as Lead Candidate for ²¹²Pb-DLL3 Radio-DARPin Therapy
- Encouraging biodistribution profile with T:K Ratio >2 in MC38 model
- Similar profile in NCI-H82 model (patient relevant DLL3 expression) with T:K Ratio >1 (data not shown)



Mice xenografted s.c. with hDLL3-MC38 (Biocytogen) Dose: 10 µCi of ²¹²Pb at 0.01 mg/kg of DLL3 DARPin BioD, biodistribution; AUC, area under the curve.



Co-development of Radio-DARPin Therapeutics with Orano Med







- Co-development collaboration*, 50:50 cost and profit share
- Access to future manufacturing applying ²¹²Pb
- Up to three tumor antigens incl. DLL3
- Molecular Partners commercialization rights for DLL3





Summary – Radio-DARPin Therapy (RDT) & MP0712

- Successful RDT platform optimization for reduced kidney accumulation and increased tumor uptake
- ✓ MP0712 selected as Lead Candidate for ²¹²Pb-DLL3 targeted Radio-DARPin Therapy
- ✓ IND-enabling activities initiated with Orano Med;
 FIH clinical data expected in 2025





Outlook:

- Advance MP0712 and additional pipeline candidates
- Evolve RDT platform
- Progress collaboration projects with Orano Med and Novartis





Switch-DARPin Platform & MP0621 as first program for HSCT in AML

Targeted and conditional activation of immune cells

Next-Generation Conditioning for HSCT in AML and Beyond

HSCT is potentially curative for AML, however:

Conditioning regimens followed by HSCT do not always kill all AML cells^{1,2}

→ Many patients relapse post HSCT, especially AML patients with poor cytogenetic risk profile

High-intensity conditioning regimen bears high toxicity^{1,2}

→ Many patients receive reduced intensity conditioning with higher risk of relapse or do not qualify for HSCT



Opportunity for next-generation conditioning regimen

- Induce deep molecular remission to kill all AML clones, including in patients with poor cytogenetic risk profile
- Limit toxicity to allow access to HSCT for more AML patients, including elderly or frail patients
- Beyond AML: broaden applicability of HSCT for other diseases (e.g., genetic diseases) by improving safety of conditioning regimen



MP0621: cKit x CD16a x CD47 Switch-DARPin Our solution for a safe conditioning regimen and long-term disease control **cKit (CD117)** Essential for HSC maintenance and renewal Switch-DARPin **Challenge:** optimal HSC depletion requires both cKit blocking AND potent immune cell mediated killing Prevents peripheral CD47 blockade cKit-CD16a-CD47 Switch-DARPin proposed to demonstrate full activity Higher safety Expected better biodistribution Allows use of Fc-engaging modalities α-cKit α-cKit **Mask** (to α-CD47) α-HSA **α-CD47** α -CD16a CD47 innate checkpoint blockade Innate immune cell engager Block "do-not-eat-me" signal = enhances phagocytosis CD16a effector function High expression on HSC = target for ADCC and ADCP ADCC and ADCP induction ٠ No impact of inhibitory Fc Reduced CRS (compared to TCE) ٠

ADCC, antibody-dependent cell-mediated cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; CRS, cytokine release syndrome; TCE, T-cell engager

Switch-DARPin POC - CD47 is Blocked Only on cKit Positive Cells





MP0621 shows superior ADCP activity compared to a combo of anti-cKit Ab* + Magrolimab

ADCP assay M0-like Macrophages + Kasumi-1 AML cell line



*Fc-active version of JSP-191, reproduced by MP



MP0621 depletes cKit+ cells in the bone marrow without affecting circulating immune cells in humanized mice





Potential logic-gated Switch-DARPin Concepts Swiss knives for enhanced immune engagers



✓ CD3 TCE CLINICALLY VALIDATED



Switch-DARPin & MP0621 – Summary

Summary

- Dual-binding DARPin (the "Switch") provides a logic-gated "on/off" function to a multi-specific DARPin
- Conditional, target-specific immune activation demonstrated for Switch-DARPin platform in vitro
- MP0621 as first program: a cKit x CD16a x CD47 Switch-DARPin as next-gen therapeutic supporting HSCT for AML patients & beyond
- Positive preclinical data presented at EHA 2024: MP0621 effectively depletes targeted cells *in vivo* with a safe profile



Outlook

- Advance MP0621 into IND-enabling studies with FIH in 2025
- Preclinical proof-of-concept data from NHP study in H2 2024, with strong translational value
- Leverage Switch-DARPin platform for next-generation immune cell engagers





MP0317

Tumor-localized Immunotherapy

MP0317: Unlocking CD40 Activity Through Local Activation

Problem: Toxicity of CD40 Antibodies Has So Far Limited Their Activity



- CD40 agonists can activate B cells, DCs and MΦ to enhance the efficacy of IO drugs, especially in "cold tumors"
- Systemic activation of CD40 via mAbs has been hampered by significant toxicities, therefore limiting their potential of reaching a therapeutically active dose

Solution: MP0317 – FAP-dependent tumor-localized CD40 activation





- **FAP is a validated tumor target** overexpressed in at least 28 different cancer types and its expression is not downregulated during disease progression
- MP0317 is designed to bind tumor-localized FAP and induce CD40-mediated activation of immune cells in the tumor, thereby overcoming systemic toxicity and allowing a wider therapeutic dosing range



MP0317 Phase 1 Study Design and Status



STUDY DESIGN

- FIH, multi-center, dose-escalation study of MP0317 monotherapy (9 dose cohorts; Q1W and Q3W dosing; NCT05098405)
- Eligible patients: adults with advanced solid tumors
- **Primary objectives:** safety/tolerability, recommended dose for expansion & combination
- Secondary objectives: PK, PD, and preliminary antitumor activity
- **Centers:** 4 sites in France and The Netherlands



MP0317 Phase 1 Study Final Data at ASCO 2024

• A total of 46 patients treated in 9 cohorts

- Median age (range): 63 years (35–79)
- ECOG PS 0 / 1, n (%): 22 (48) / 24 (52)
- Medial prior regimen (range): 4 (1–13)
- Favorable safety profile across all tested dose cohorts up to highest planned dose (10 mg/kg)
 - Only 1 patient with a DLT (cohort 6; Grade 3 AST and ALT increase)
 - Most frequent Ars: fatigue and Grade 1–2 IRRs
- Clinical evidence of tumor-localized CD40 pathway and immune cell activation, leading to TME remodeling

MOLECULAR partners



Steeghs et al. ASCO 2024 poster presentation.

ALT, alanine aminotransferase; AR, adverse reaction; AST, aspartate aminotransferase; DLT, dose-limiting toxicity; IRR, infusion-related reaction; PD, pharmacodynamic; TME, tumor microenvironment; Q1W, weekly dosing; Q3W, every-3-weeks dosing.

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MP0317 Serum PK is Suitable for Q3 and Q1 dosing



- PK profile is consistent with half-life extended properties of DARPins
- MP0317 exposure shows dose-proportionality throughout the treatment period analyzed
- Sustained exposure is observed at higher doses with both regimens overcoming TMDD and the impact of ADAs



MP0317 Tumor-localized CD40 Activation and TME Modulation

MP0317 higher doses and

detected in tumor (n=20)

MP0317 <u>low</u> doses or not detected in tumor (n=6)



Evaluable paired tumor biopsies from treated patients were analyzed with mIF. Low doses: ≤0.1mg/kg; higher doses: ≥0.3mg/kg. Upper (75%), median, and lower (25%) percentiles are indicated. P-values are derived from paired ranked sum Wilcoxon test.

- Bulk RNA sequencing in paired tumor biopsies (n=19) shows that MP0317 presence tends to be associated with:
 - Increase in abundance of plasma and T follicular helper cells
 - DC maturation gene signature
 - IFNγ downstream activation gene signature scores
- Increases observed in CXCL10 serum levels corroborate these findings





Outlook

2024 Outlook and Upcoming Milestones

MP0533	 Update from Phase 1/2a trial to be presented at a scientific congress in H2 2024 Expansion of enrollment to higher dose cohorts planned in H2 (protocol amendment submitted) Plans for future clinical development strategy, incl. opportunities in r/r AML and 1L fit and unfit patients
Radio-DARPin Therapy & MP0712	 Advance MP0712 into IND-enabling studies with FIH & clinical data in 2025 Nominate additional RDT targets and pipeline candidates Continue to progress RDT collaborations with Orano Med and Novartis
Switch-DARPin & MP0621	 Advance MP0621 into IND-enabling studies with FIH in 2025 Preclinical proof-of-concept data from NHP study in H2 2024, with strong translational value Leverage Switch-DARPin platform for next-generation immune cell engagers
MP0317	 Final data from the FIH dose-escalation Phase 1 study to be presented in 2024 Partnering for clinical development in combination settings

CHF ~174 million cash* (incl. short-term time deposits) ensures funding well into 2026





Thank You