

Molecular Partners: Novel Therapeutic Designs Applied

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JP Morgan Healthcare Conference

Molecular Partners AG, Switzerland (SIX: MOLN)

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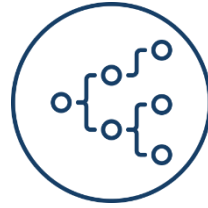
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Molecular Partners in Brief



Strengthened Team, Solid Funding

- ✓ **Nicolas Leupin** as joined as **CMO** from Argenx
- ✓ **Daniel Steiner** assumed leadership of research department
- ✓ **Seth Lewis** joined Boston office to head up global IR, Comms & Strategy
- ✓ **Ana Cerdeira** heading up Portfolio Management and Global Strategy
- ✓ Well financed through mid-2021, **on-track towards recurring income** with expected abicipar launch in 2020 by Allergan



Burgeoning Oncology Pipeline

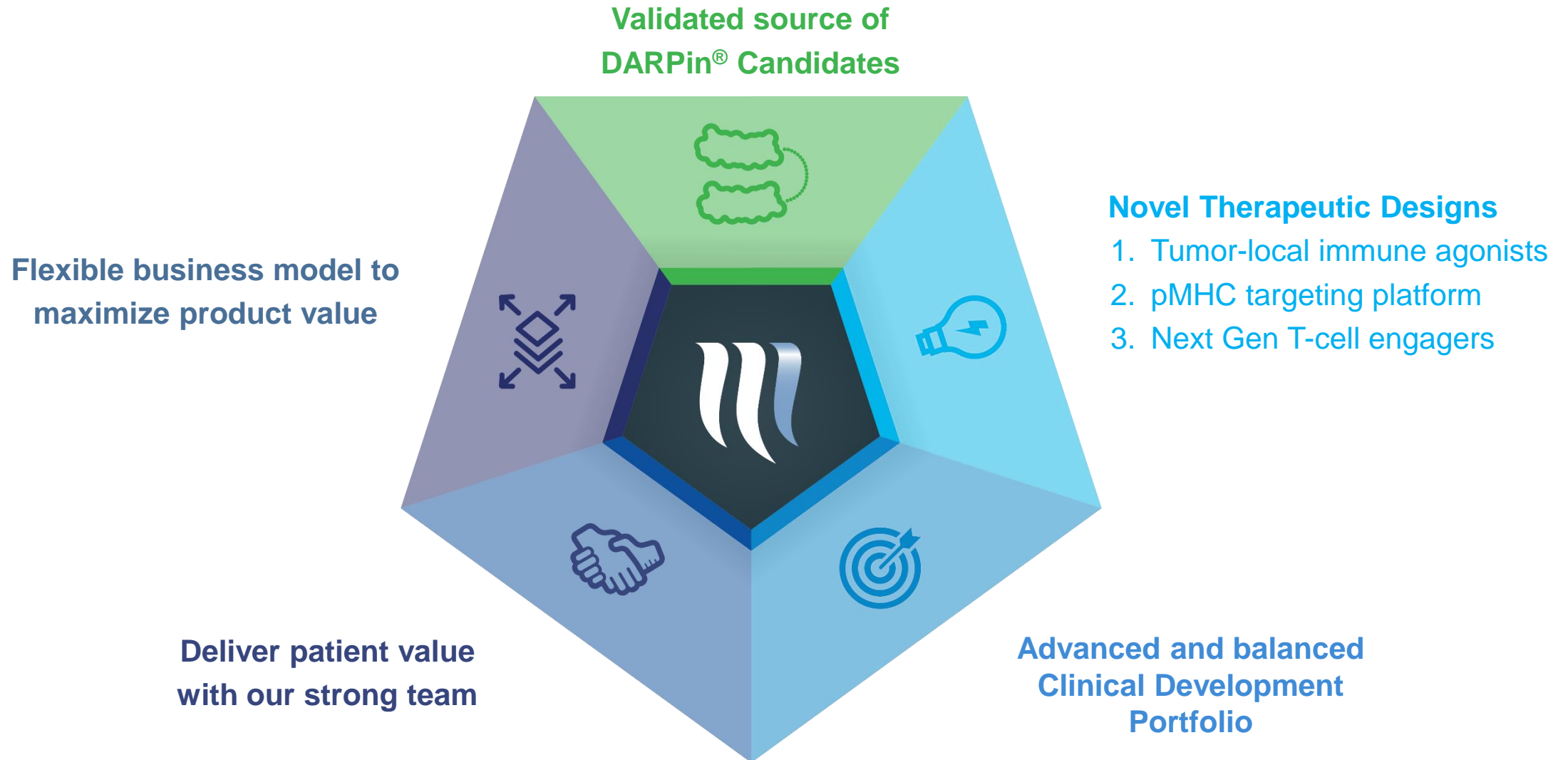
- ✓ **MP0250** focused on MM with unique activity in patients that did not benefit from other treatments
- ✓ **MP0310 (AMG 506)**: Collaboration with Amgen to co-develop MP0310 & first patient cohort dosed in Phase 1 trial
- ✓ New development candidate, **MP0317 (FAPxCD40)**, added to pipeline
- ✓ First DARPin® candidates binding **peptide-MHC** passed specificity threshold



Progress Towards Approval

- ✓ **BLA of abicipar accepted** by FDA, MAA of abicipar validated by EMA
- ✓ **>90% of patients** show vision gains which were maintained in the 2nd year with **q12 dosing** of abicipar
- ✓ MAPLE data supports optimized manufacturing process for **improved tolerability**

Key Advantages of Molecular Partners

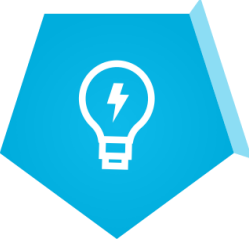


DARPin[®] Platform: A Validated Source for Drug Candidates



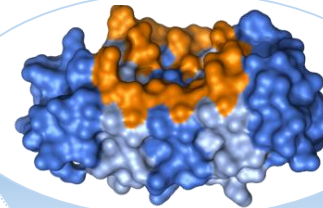
- **Abicipar: Ophthalmic validation**
 - Demonstrated safety and activity in >1,500 patients
 - Manufacturing at commercial scale established
 - Regulatory applications accepted by FDA and EMA
- **MP0250: Systemic validation**
 - Long half-life (HSA DARPin binder, 12 day half-life)
 - Low immunogenicity
 - Proof of multi-DARPin[®] potential to engage with multiple targets simultaneously
- **Novel Therapeutic Designs (NTD) applied**
 - Phase 1 enrolling for MP0310 (AMG 506)

Differentiated Products by Therapeutic Design



DARPin® Features

Rigid-body target binding



DARPin® domain

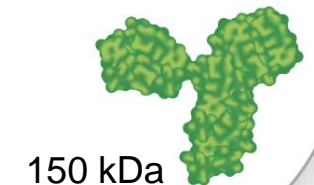


Multi-DARPin® formatting

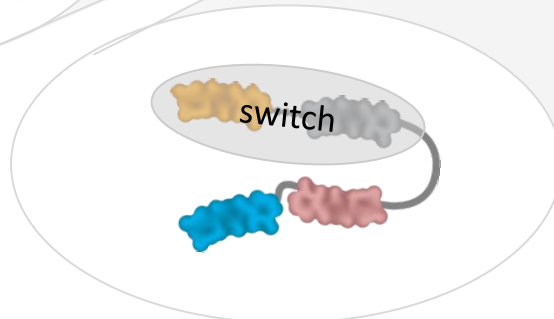
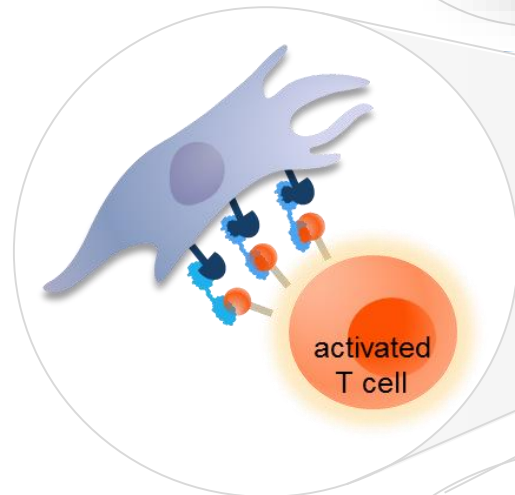
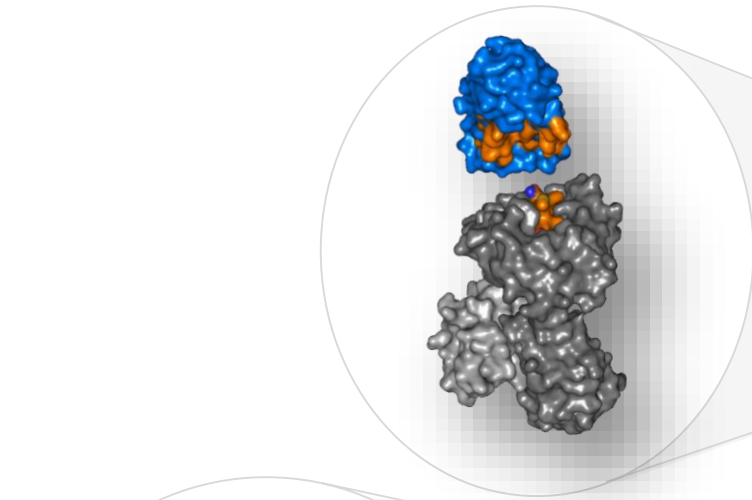
- Small size: 15 kDa
- Simple repetitive architecture: 1 polypeptide
- High affinity and specificity
- Tunable half-life

SCALE

15 kDa 



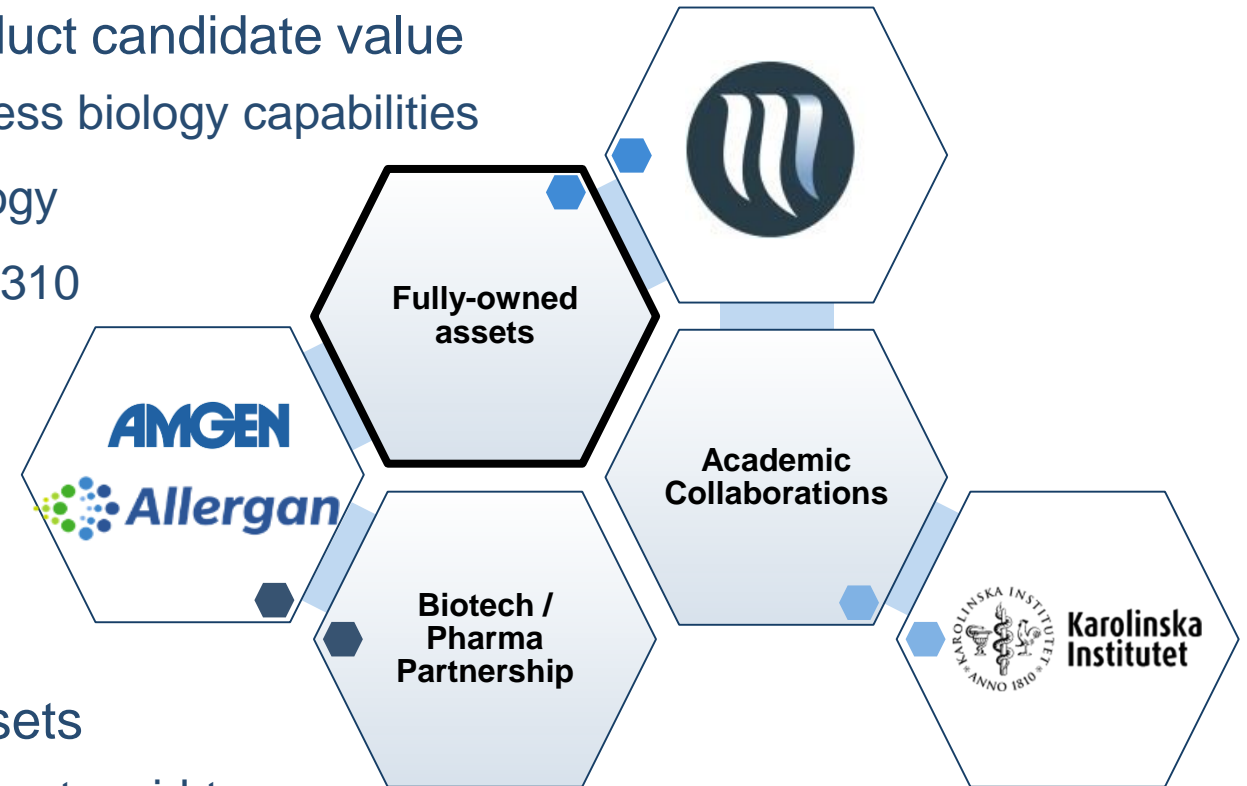
150 kDa



Flexible Business Model to Maximize Product Value

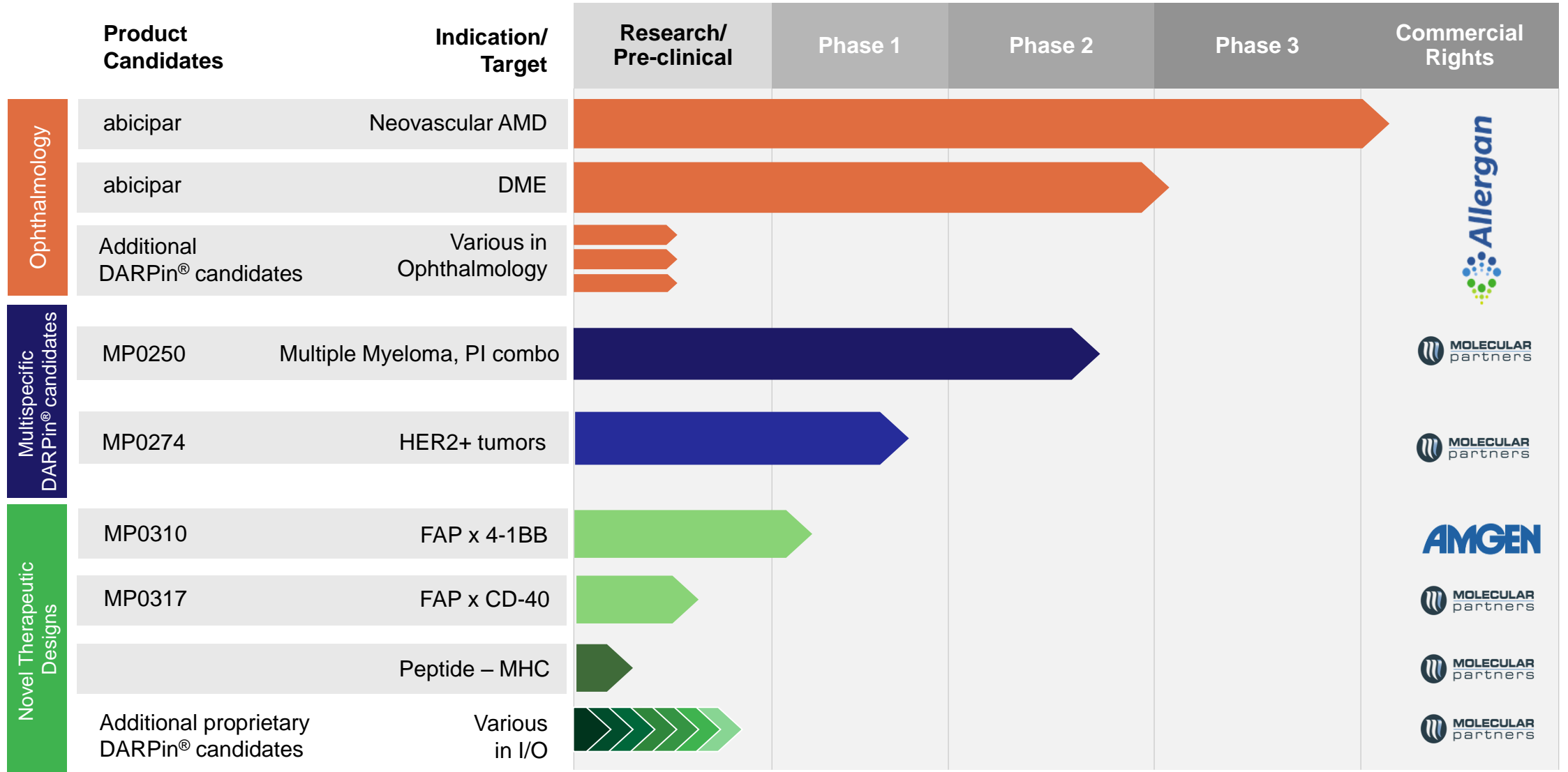


- Investment in **proprietary pipeline** to bring DARPin[®] candidates forward
- Engage in **collaborations** to maximize product candidate value
 - **Academic & industry collaborations** to access biology capabilities
 - **Allergan** is advancing abicipar in ophthalmology
 - Collaboration with **Amgen** to co-develop MP0310

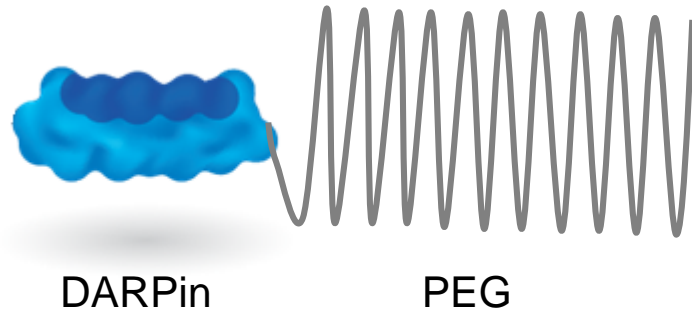


- **Cross-funding** of pipeline via partnered assets
 - AGN: USD 360m in potential MS & DD royalties to mid-teens
 - AMG: USD 50m upfront payment, USD 497m in potential MS & DD royalties to high-teens

A Balanced and Robust Portfolio



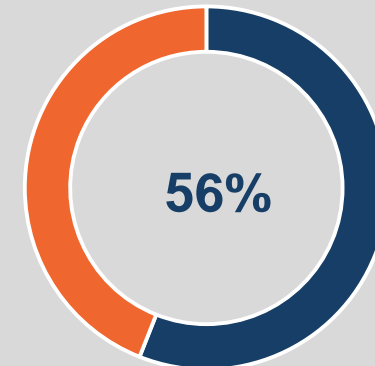
Abicipar has the Potential to be the First Fixed 12 Week anti-VEGF



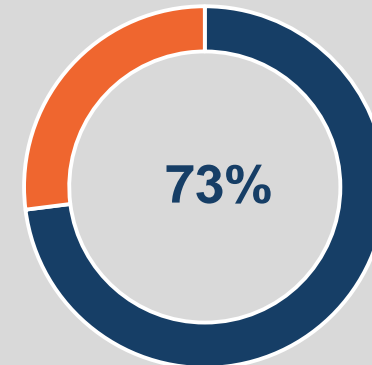
- Long-acting anti-VEGF
- Fix 12-week dosing
- Filed with FDA and EMA
- PDUFA date: summer 2020

When treating nAMD patients, Retina Specialists are looking for:

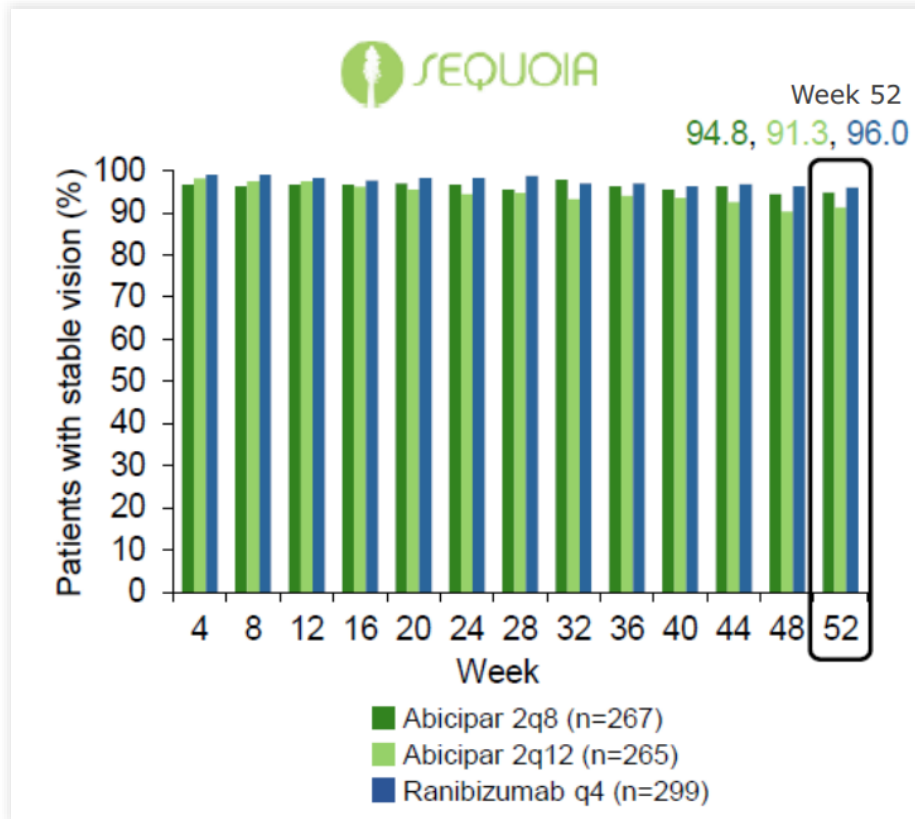
Long-acting / sustained delivery



Reduced Treatment Burden

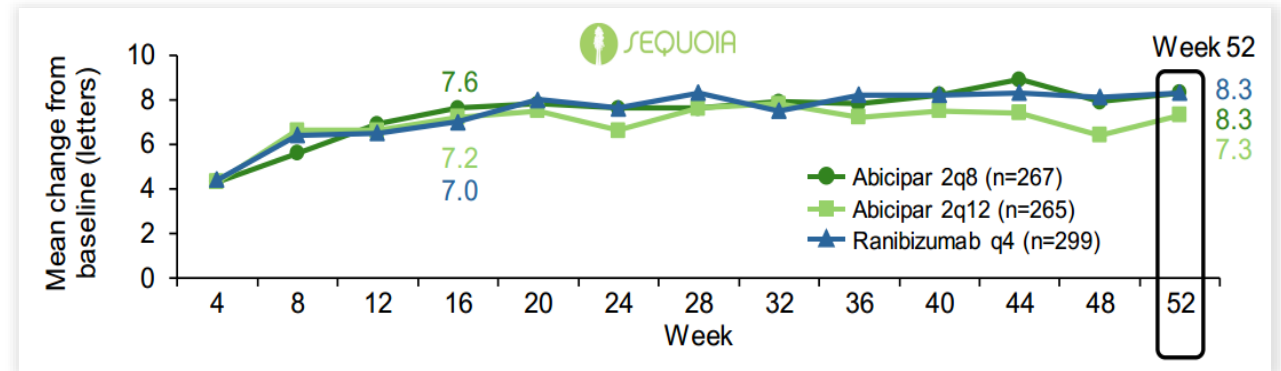


Phase 3 Efficacy Results (SEQUOIA study, 1yr data)

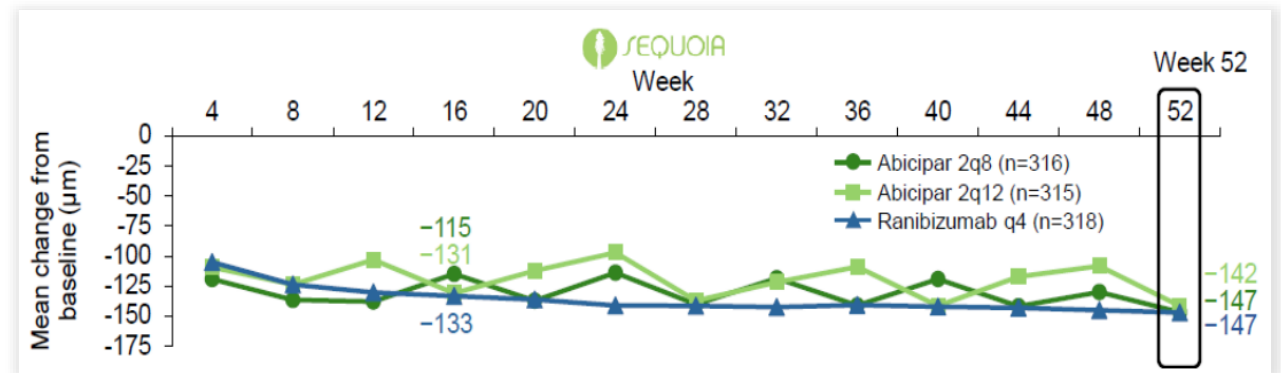


Primary Endpoint: STABLE VISION Abicipar Q8 and Q12 Non-Inferior to Ranibizumab Q4

Source: Allergan July, 2018 and October 2018

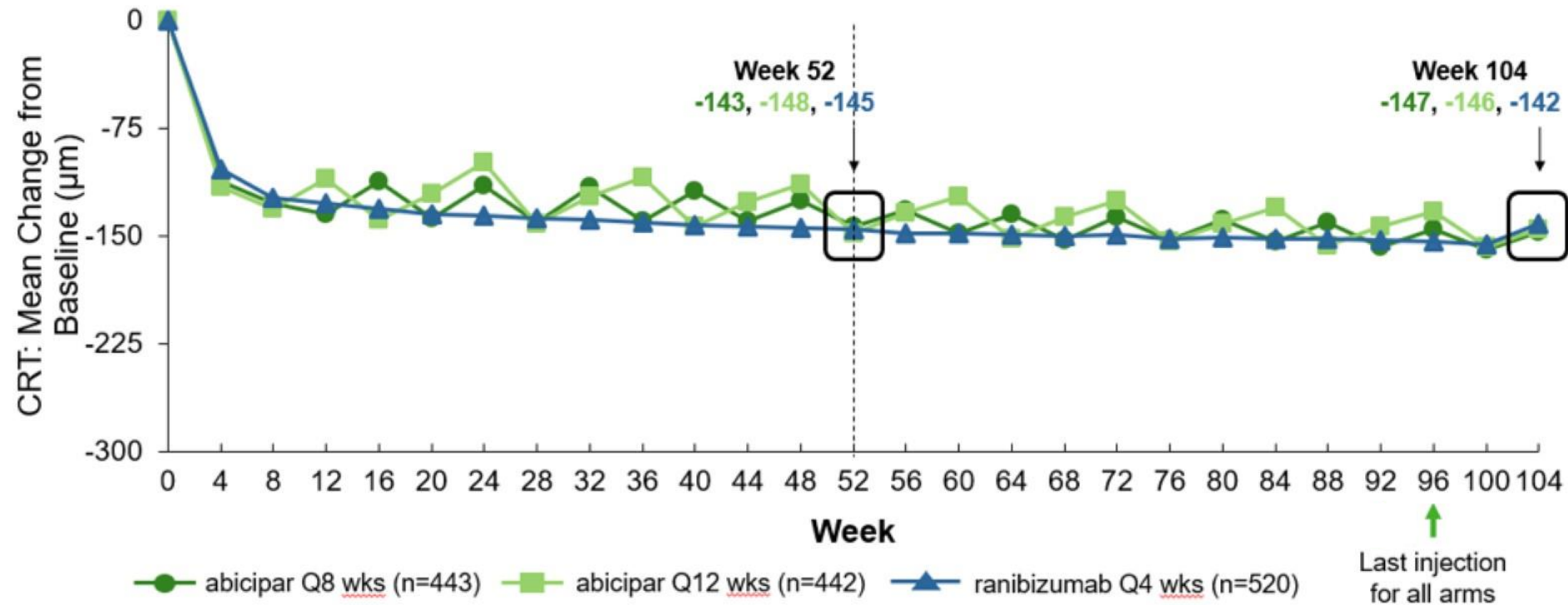


Secondary Endpoint: Change in BCVA From Baseline Abicipar Q8 and Q12 in SEQUOIA Non-Inferior to Ranibizumab



Secondary Endpoint: Change in CRT similar across in all groups

Secondary Endpoint: Mean Change in CRT From Baseline at Weeks 52 and 104

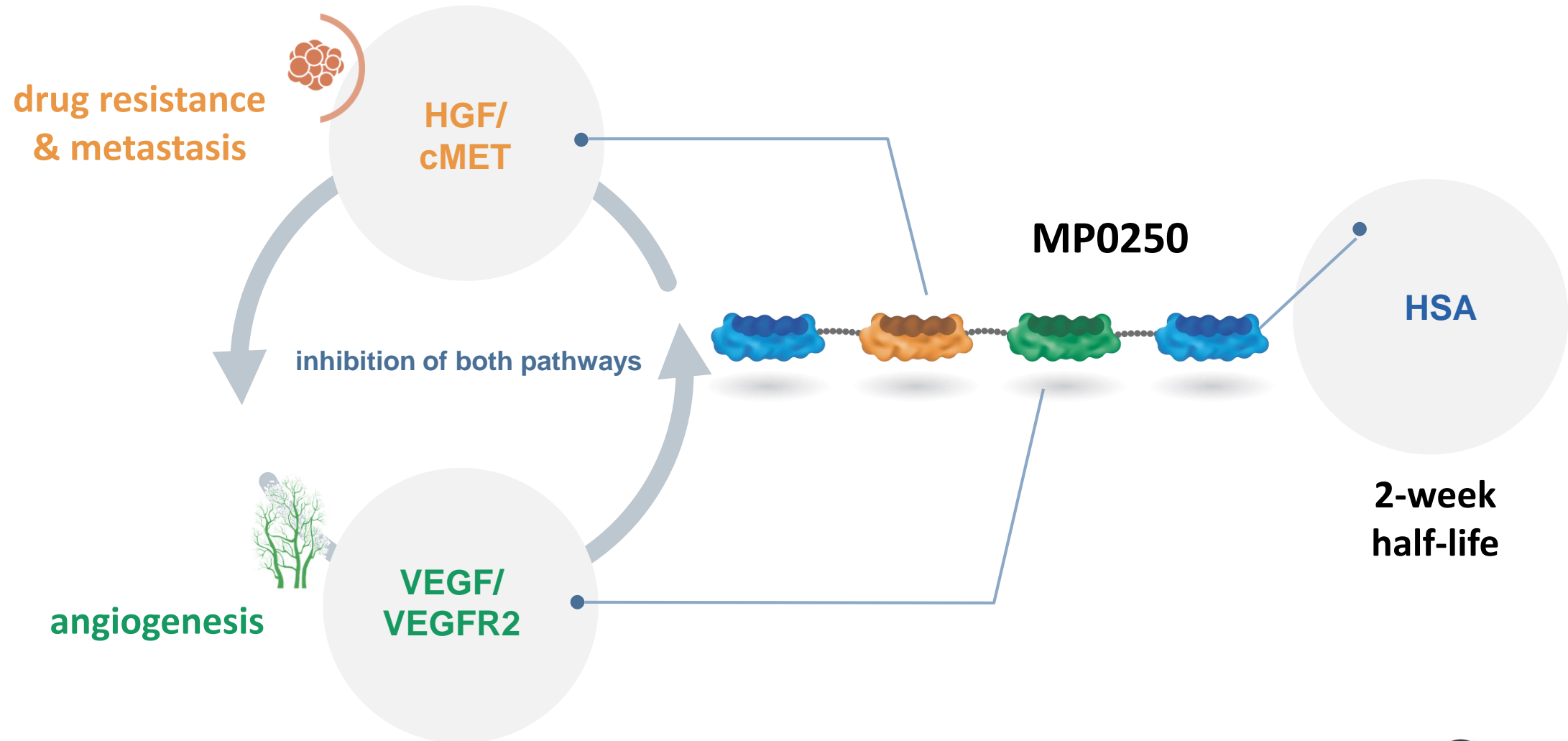


**CRT improvement after initial doses were maintained to Week 104
with quarterly abicipar injections (10) vs. monthly ranibizumab injections (25)**

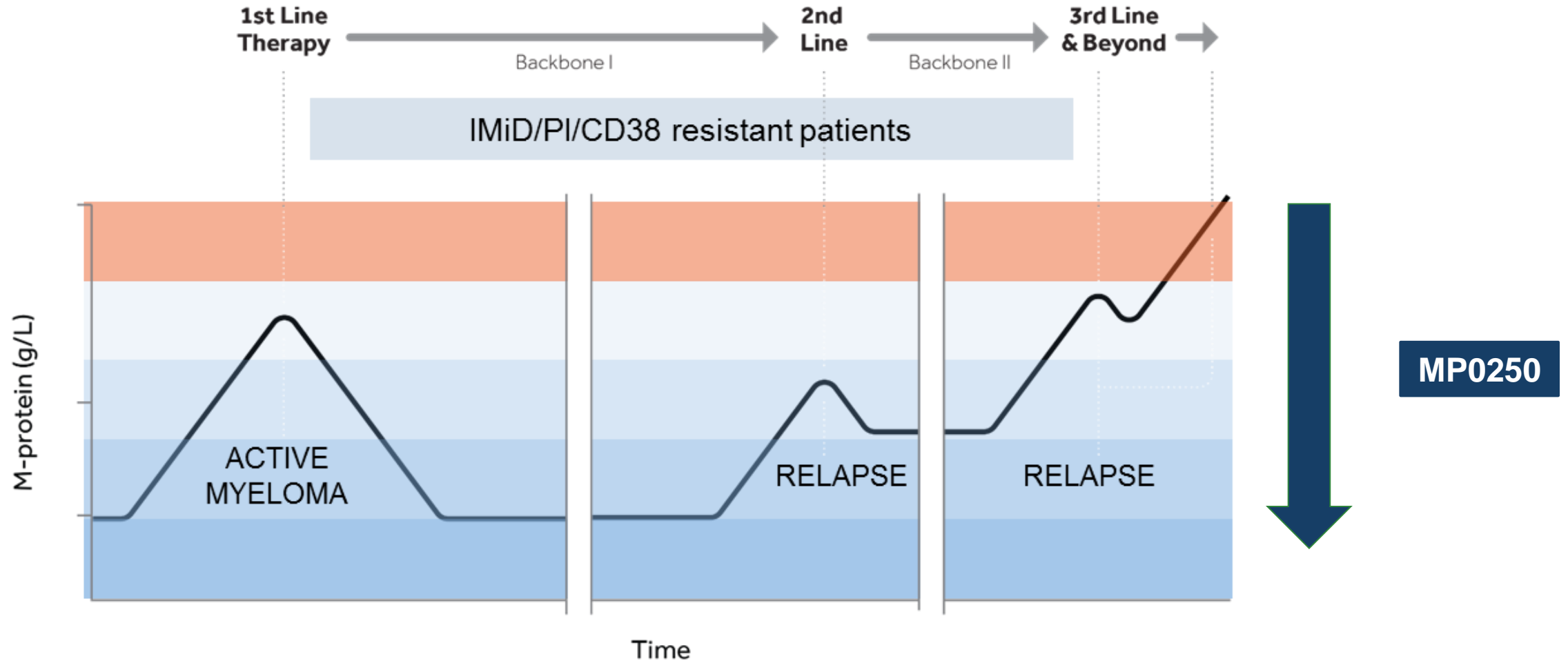
CRT = central retinal thickness

Abicipar is under investigation and the safety and efficacy of this product have not been established.

MP0250: Our First Multi-DARPin[®] Product Candidate

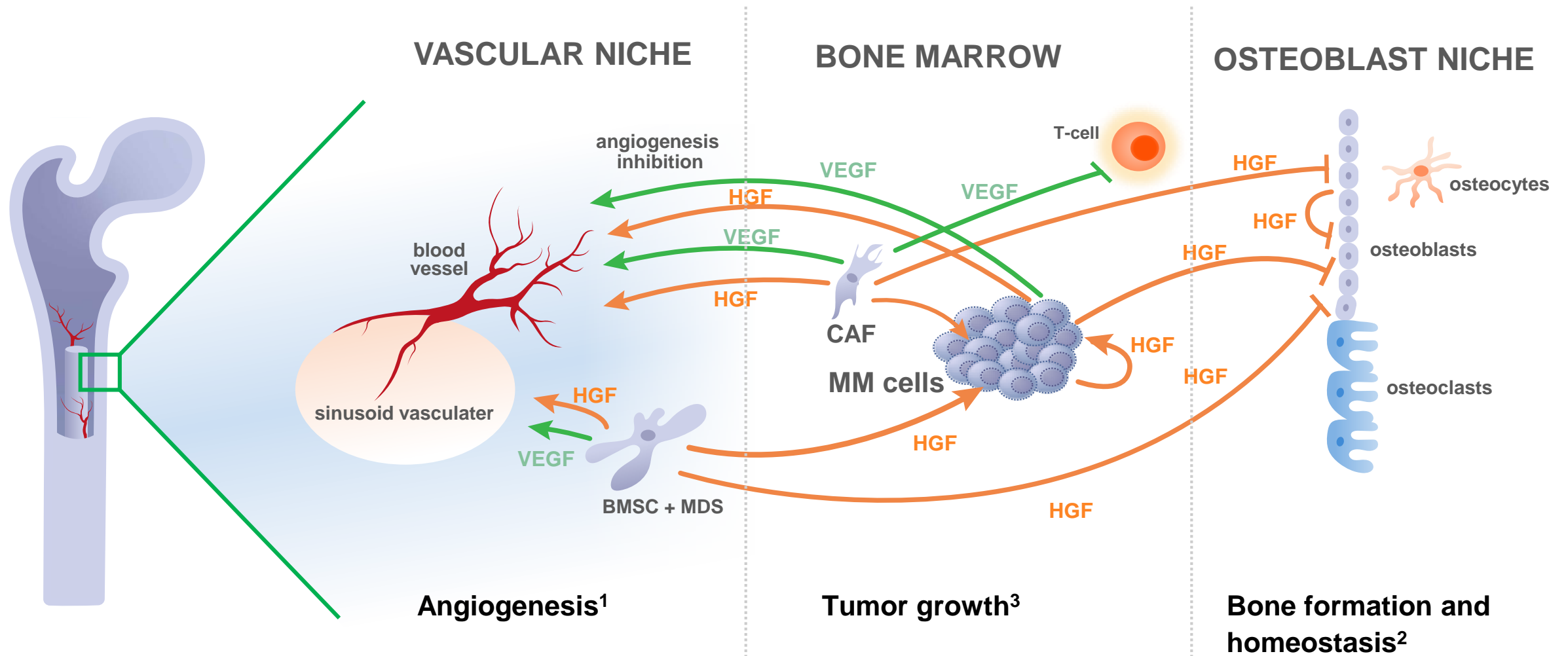


Illustrative course of disease of a MM patient*



* adapted from: Hajek, R. Strategies for the Treatment of Multiple Myeloma in 2013: Moving Toward the Cure. In "Multiple Myeloma: A Quick Reflection on the Fast Progress" (2013).

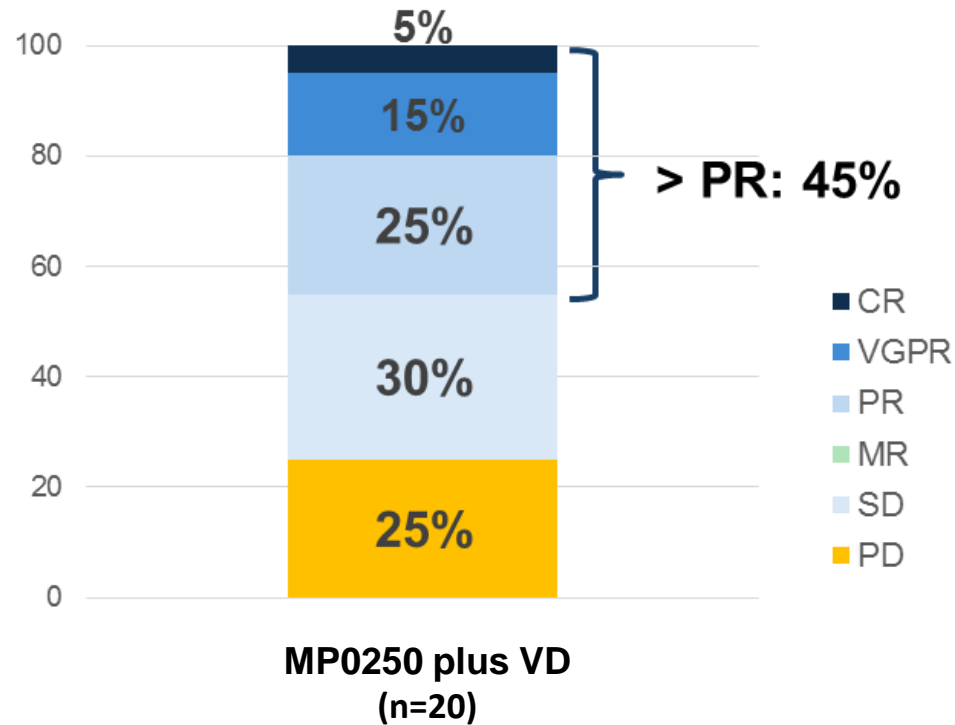
Paradigm Shift from “Chasing Clones” to Tackling Underlying Disease



1. Ria et al., 2011; Ferrucci et al., 2014
 2. Xu et al., 2018; Toscani et al. 2015; Ghorial et al., 2018; Wang et al., 2019
 3. Nass & Efferth, 2018; Palumbo et al., 2011; Rampa et al., 2014; Gotwals et al. 2017

MP0250: Durable & Deep Responses in Diverse MM Phenotypes

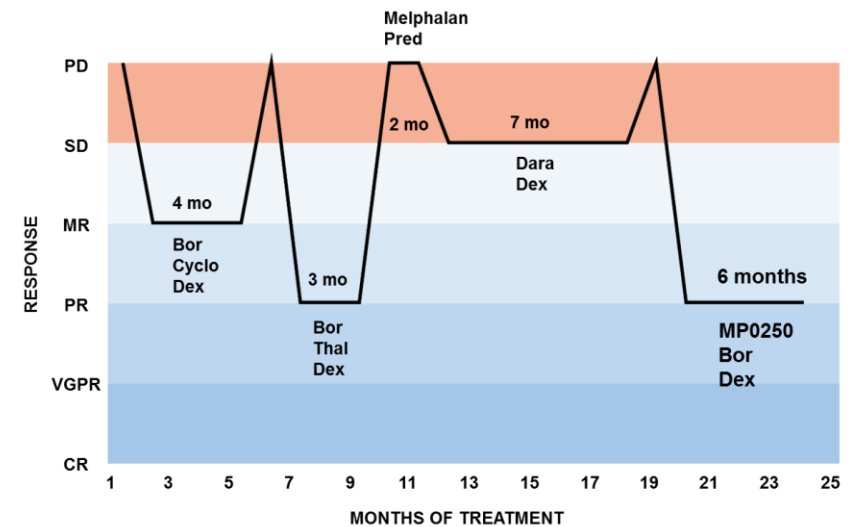
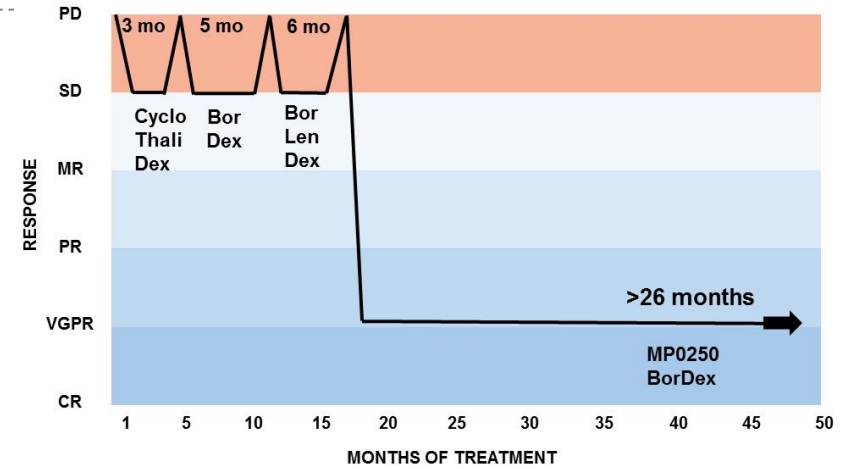
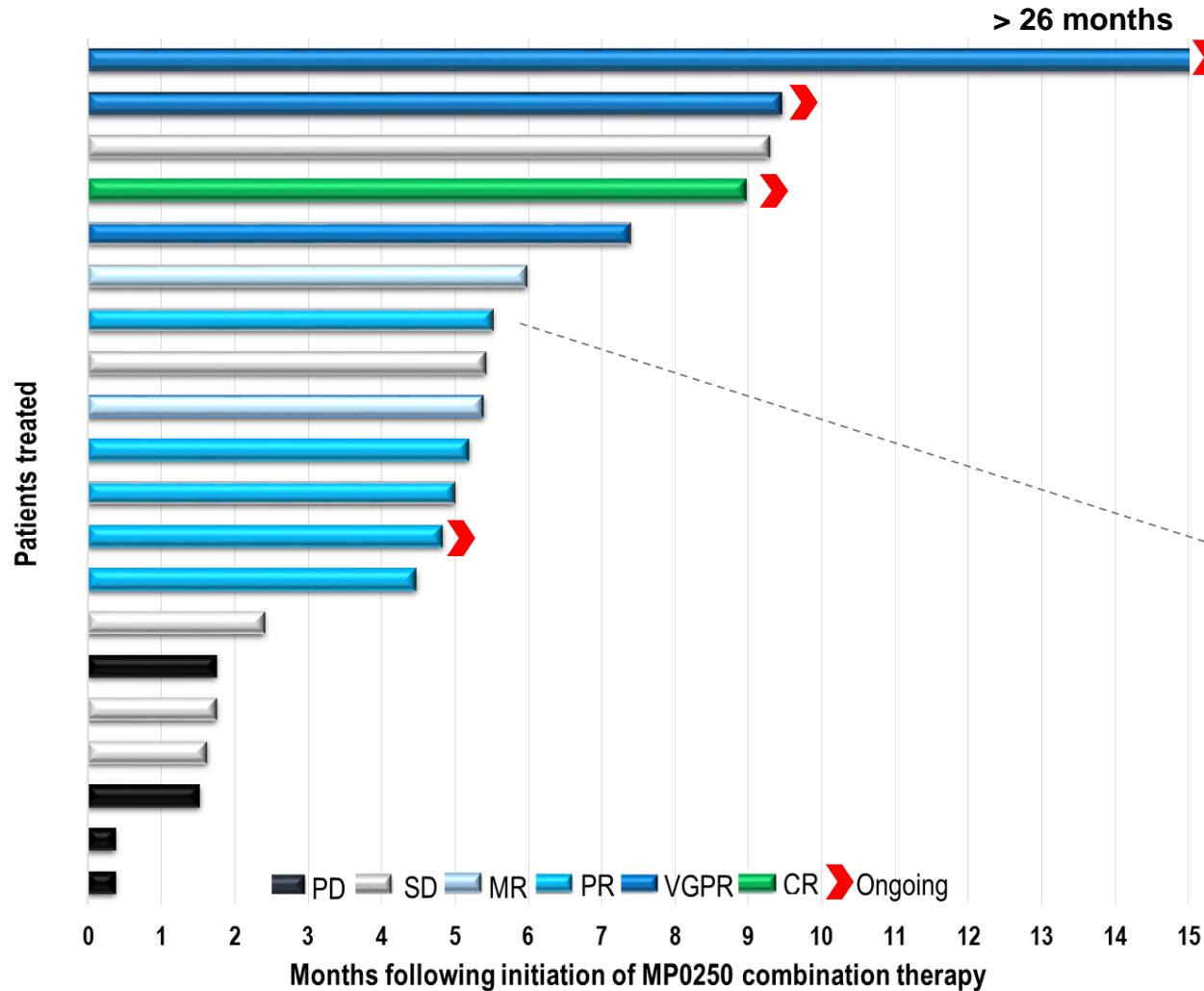
CP-201 trial: MP0250 in combination with bor/dex in R/RMM patients



- **Responses** in patients who had **never responded**
- **Heavily pretreated patients**, representative of typical RRMM population; median of 4 prior lines (n=20)
- 4/6 patients coming **directly from Dara** had clinical benefit (incl. 4/5 Dara-refractory patients)
- 2 Patients with **17p deletion** progressed quickly

MP assessment based on IMWG criteria data cut-off Sep 2019 – as presented at ASH 2019

MP0250: Deep and Durable Responses



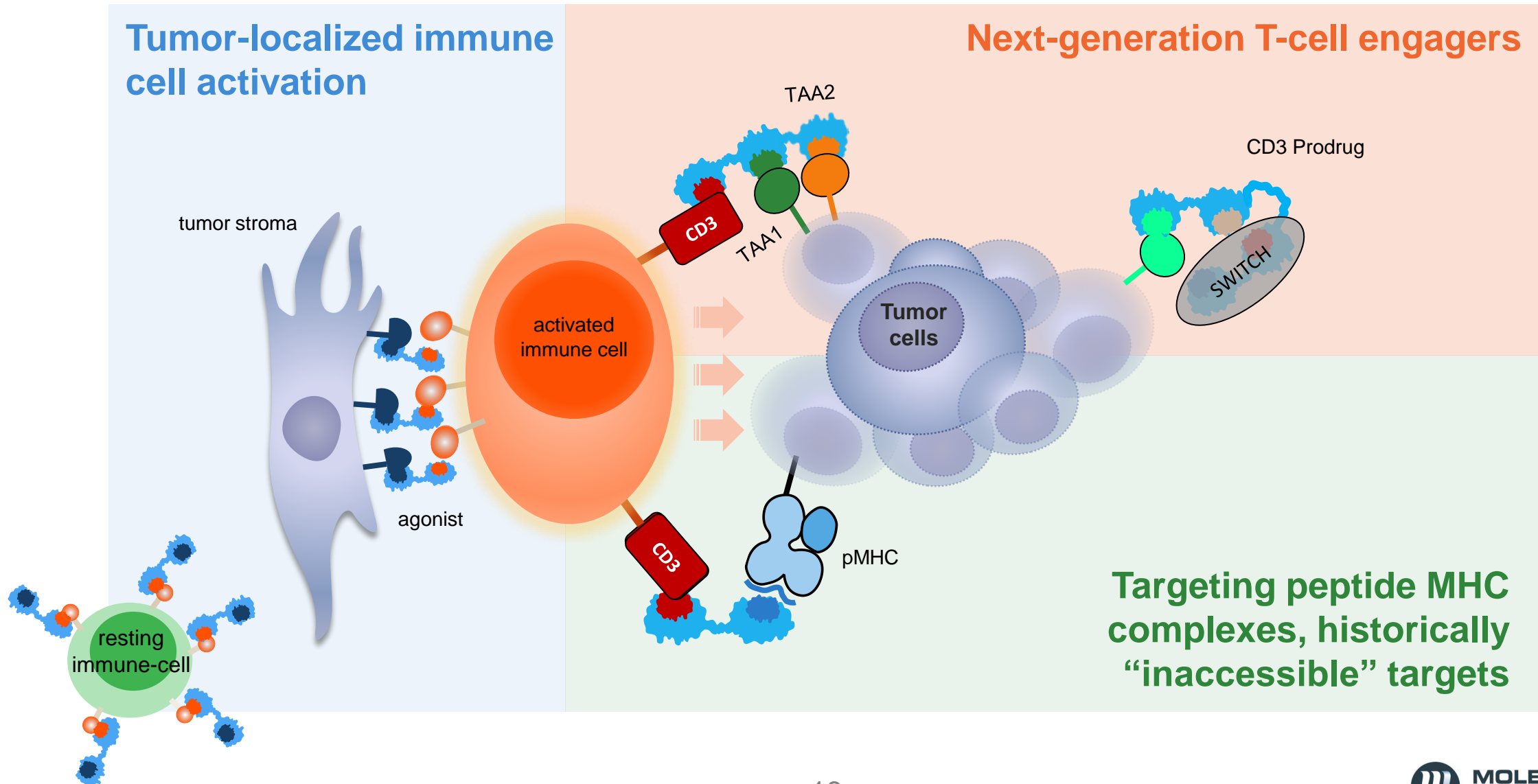
as presented at ASH 2019



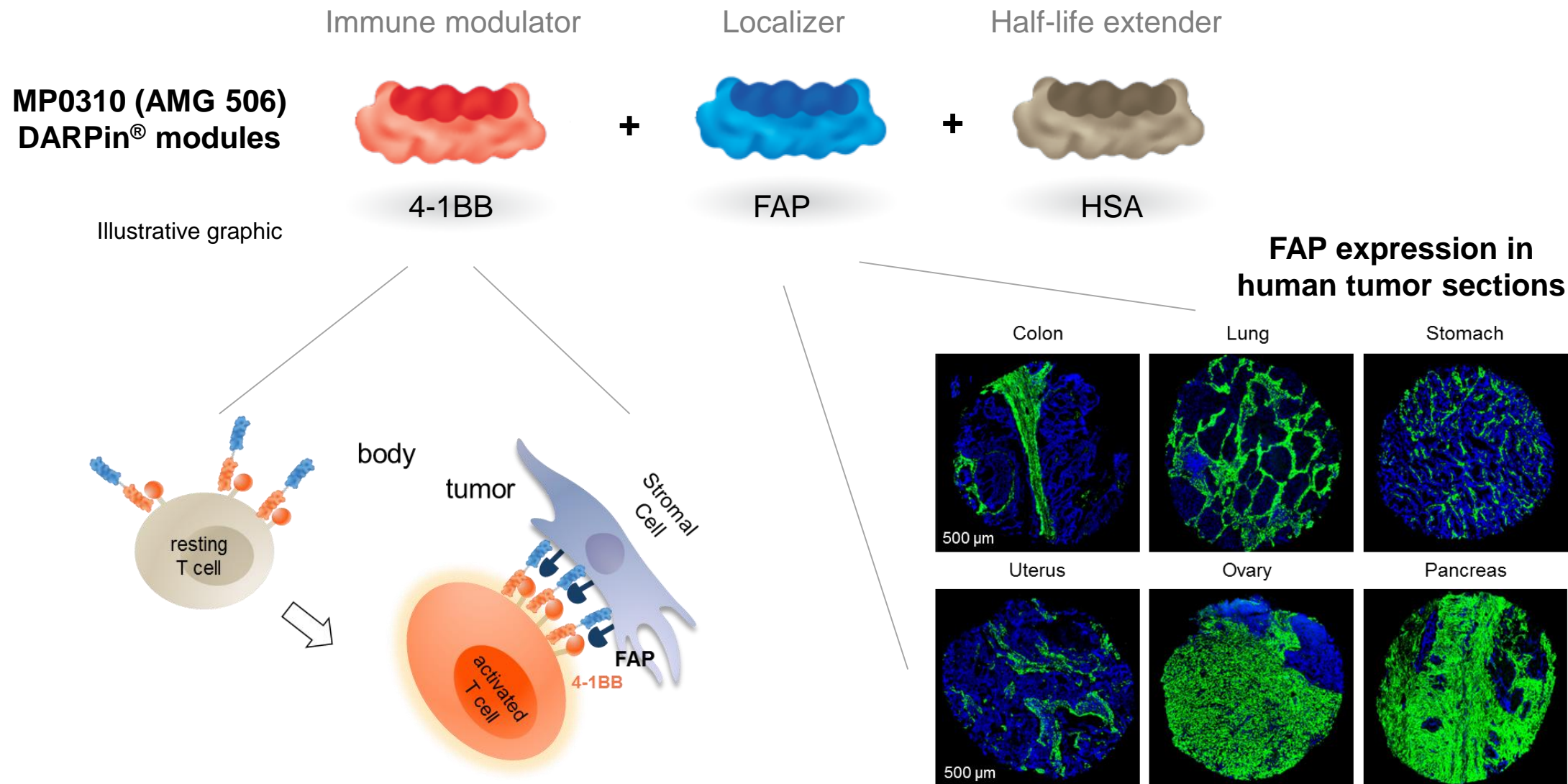
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Novel Therapeutic Designs in Immuno - Oncology

Applying our Therapeutic DARPin® Designs



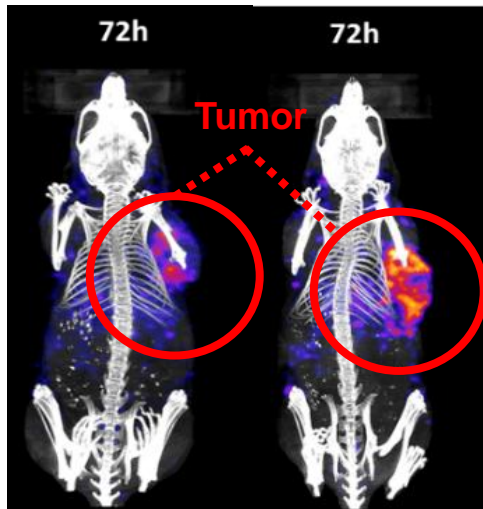
MP0310 (AMG 506; FAP x 4-1BB): Activating T cells in the Tumor



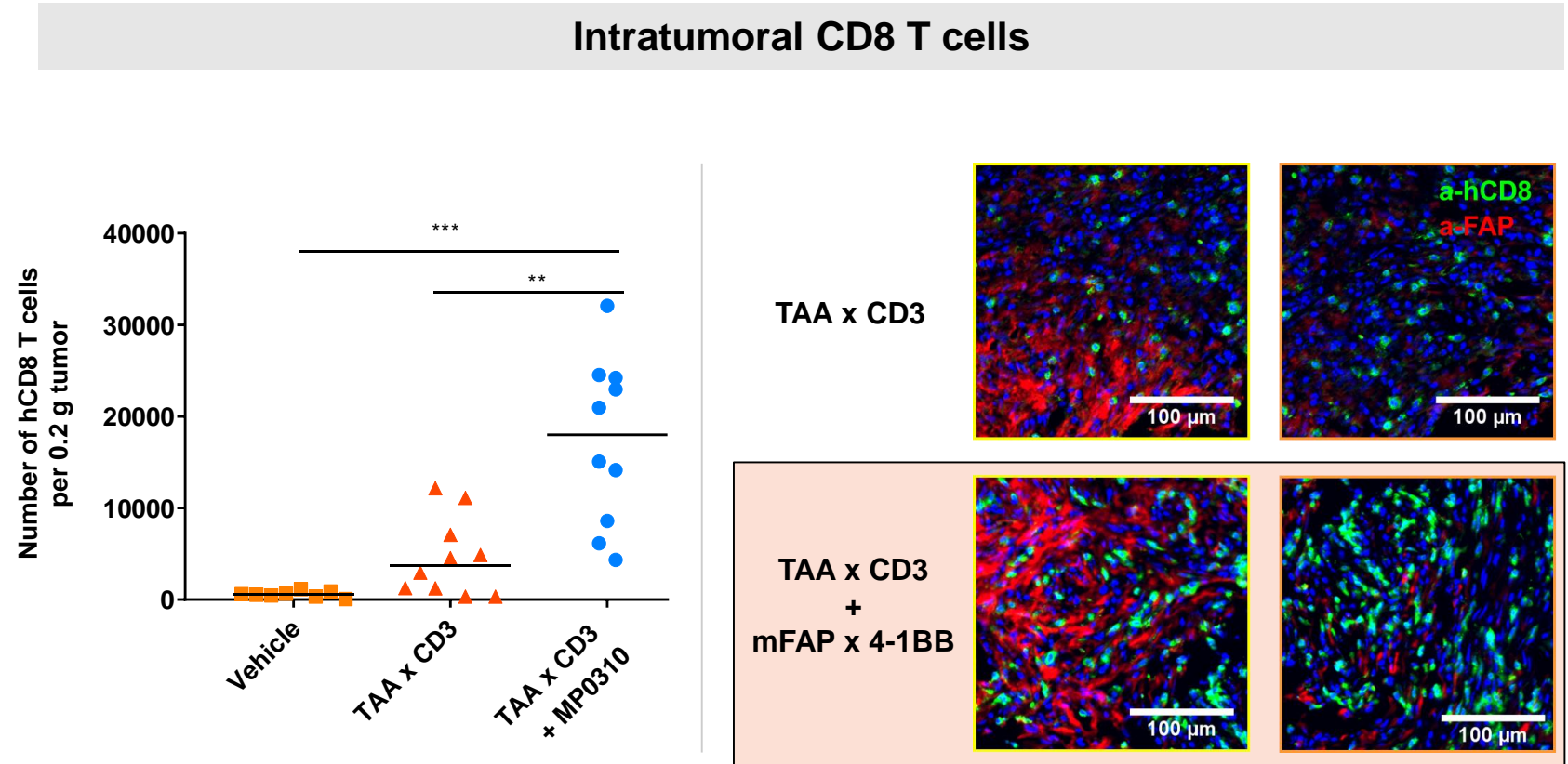
HSA, human serum albumin.

Combined Therapy with MP0310 and TAA x CD3 Bi-Specific Results in Significant Increase of Intratumoral CD8+ T Cells

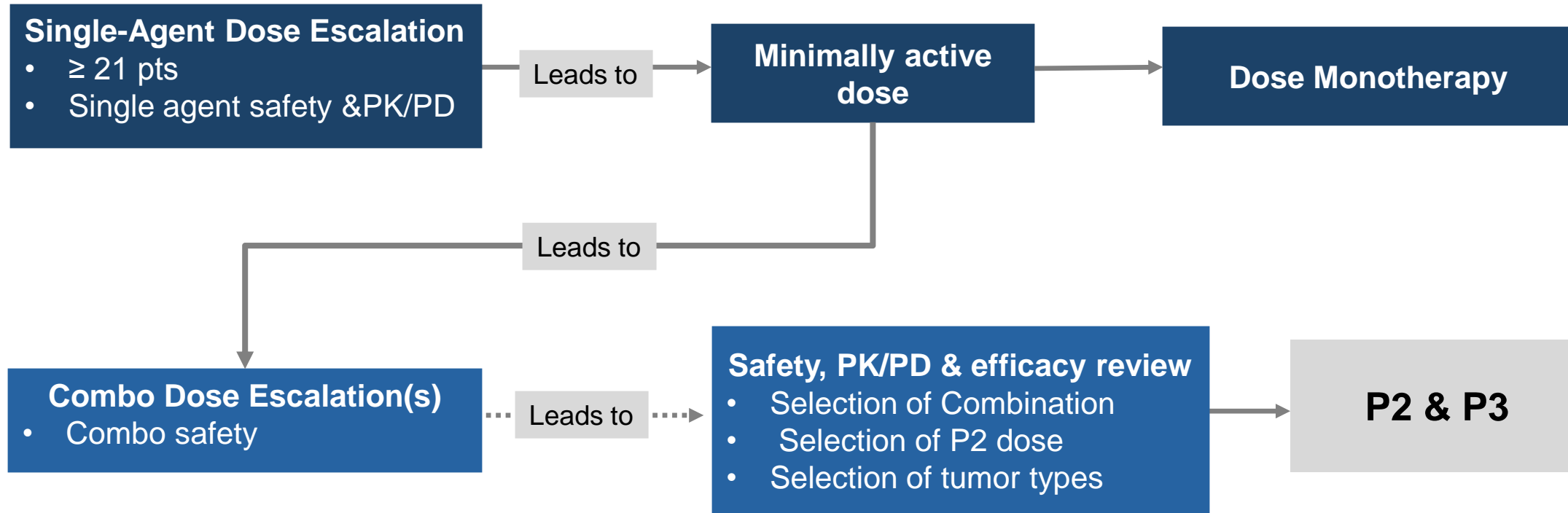
FAP-Mediated Tumor Accumulation of MP0310
HT-29-T-implanted NSG mice



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

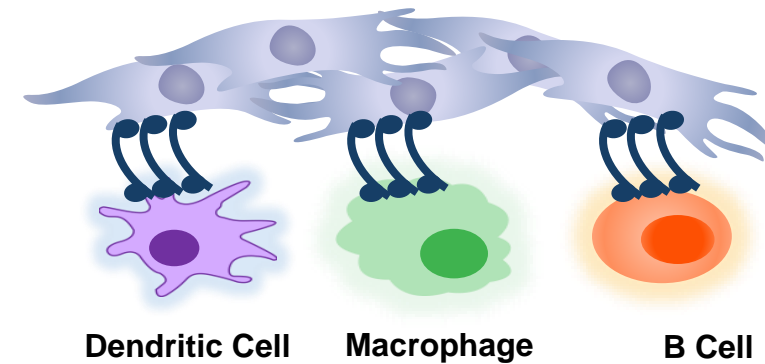
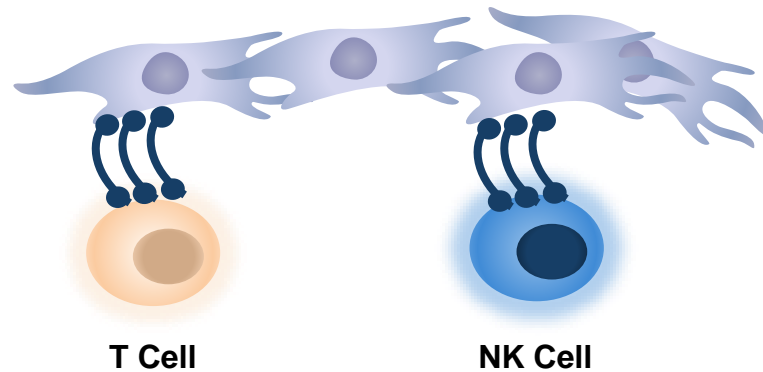
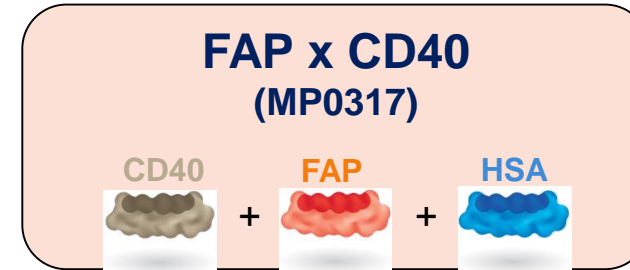
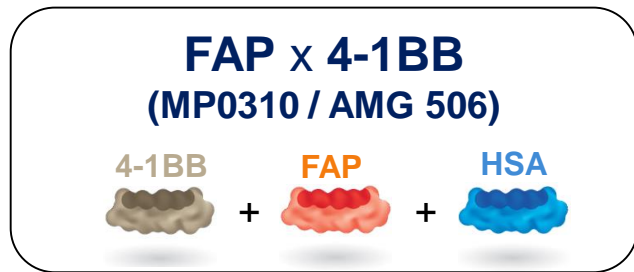


MP0310 (AMG 506) Clinical Study Design

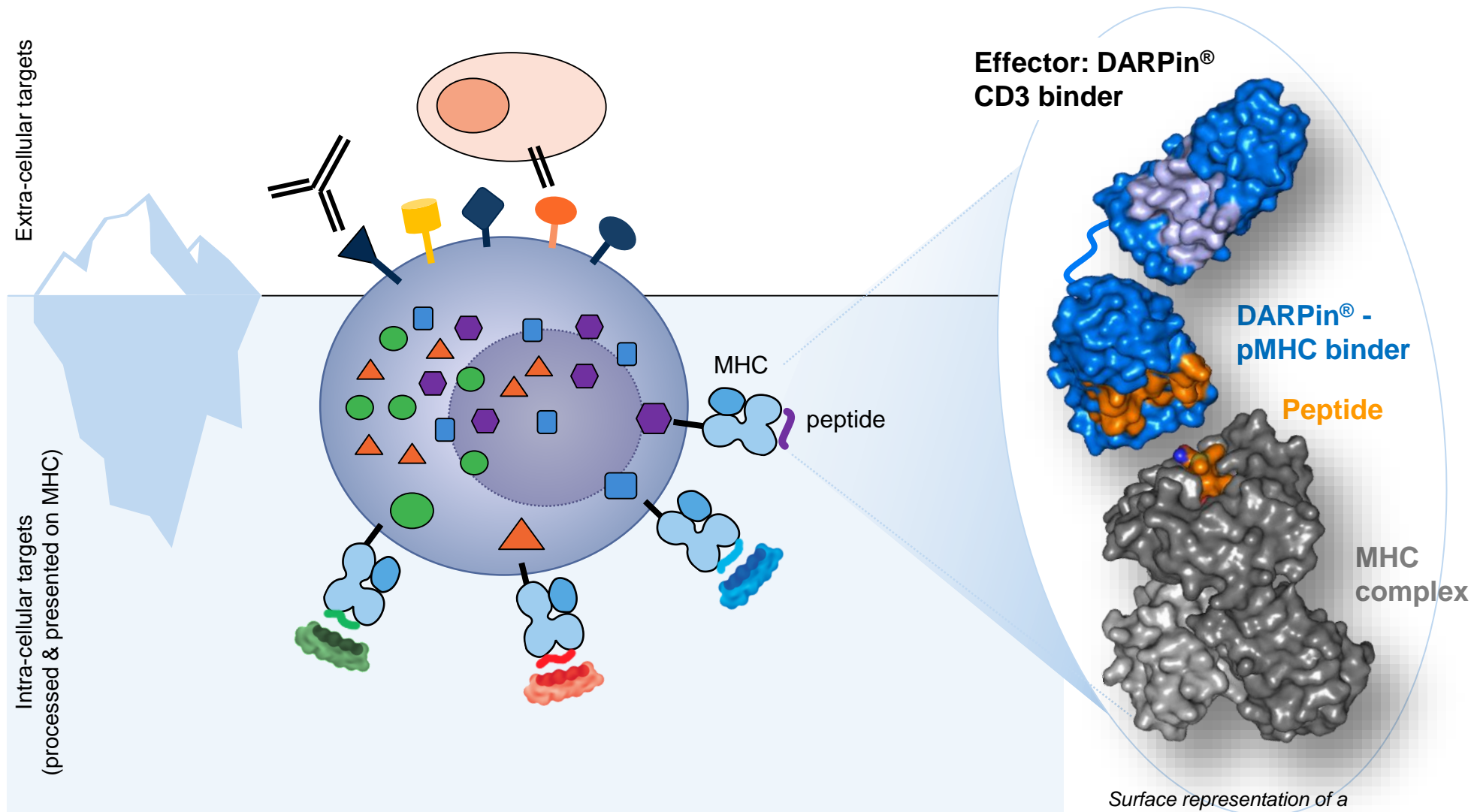


- Dose escalation ongoing
- Expected to start MP0310 (AMG 506) combination trials in 2020

Expanding from Adaptive to Innate Principles: CD40 agonists



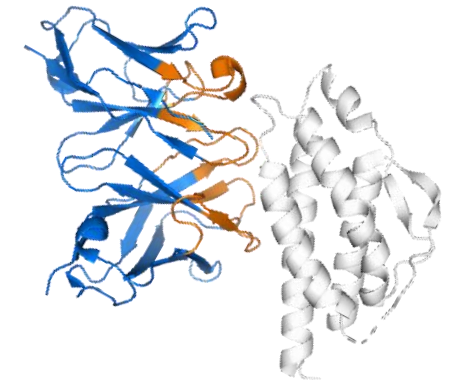
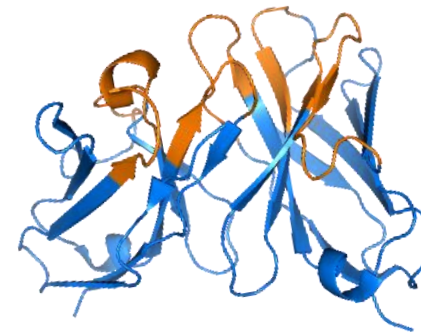
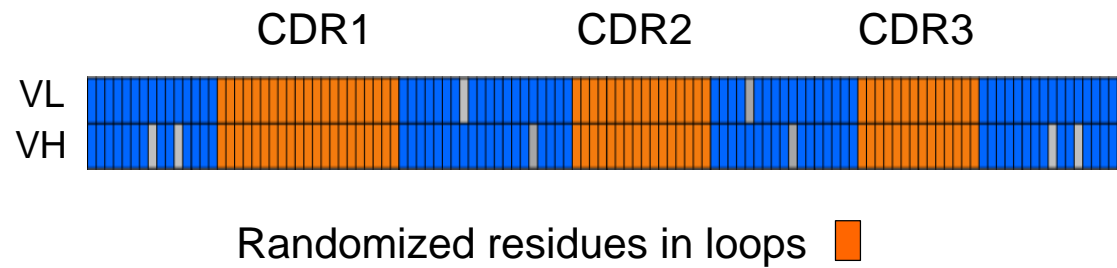
pMHC: Approach for “Inaccessible” Highly Selective Targets



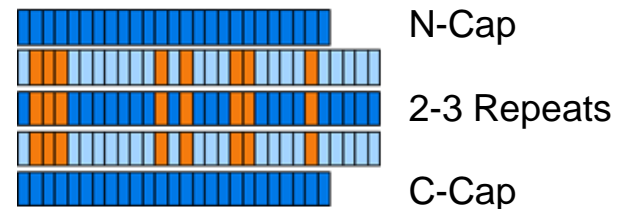
Surface representation of a DARPin® domain and of a MHC-peptide crystal structure

Leveraging DARPin[®] Features for pMHC

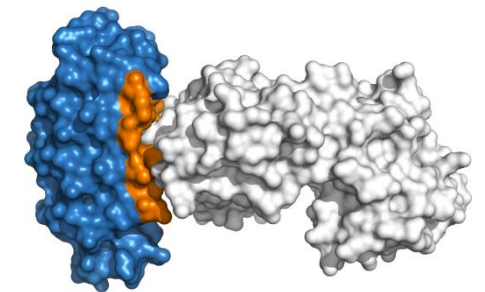
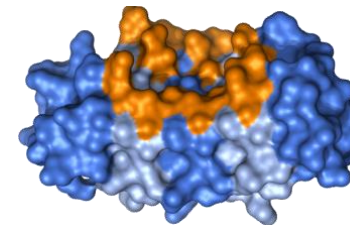
Antibody (Ig-) Domain: binding via flexible loops



DARPin[®] Domain: binding via rigid surface

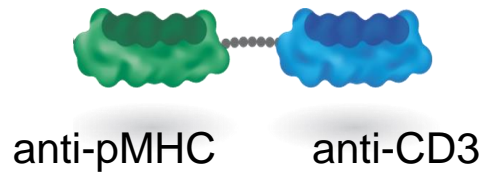


Randomized residues on rigid surface 



pMHC: Rapid and Straightforward Selection of DARPins[®] pMHC Binders with High Selectivity

DARPin[®] candidate



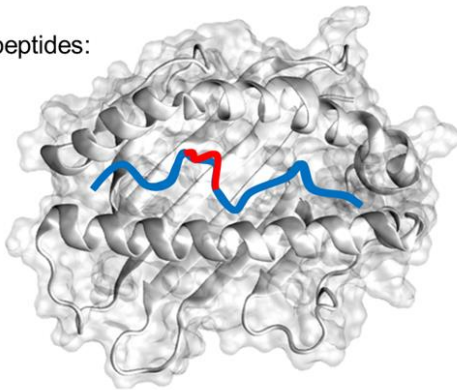
The Alanine Scanning Approach

Wild-type peptide embedded in MHC complex:

RIMYFIENA

Alanine mutated peptides:

AIMYFIENA
 RIMYFIENA
 RIAYFIENA
 RIMAFIENA
 RIMYAIENA
 RIMYFAENA
 RIMYFIANA
 RIMYFIEAA
 RIMYFIENA

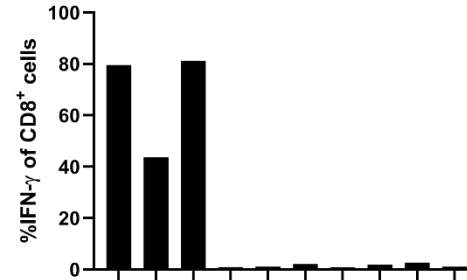


adapted from Knapp B et al. 2014, PLOS Computational Biology

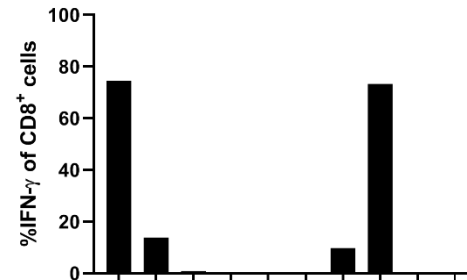
Selectivity

(binding pattern by Alanine scanning)

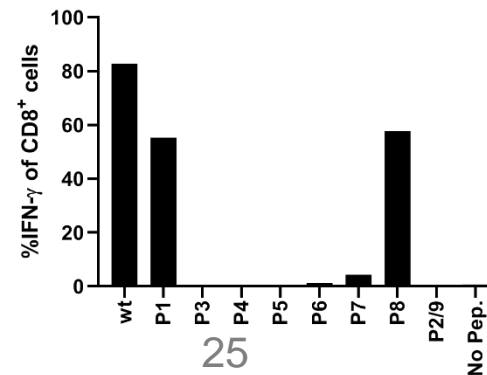
pMHC-A x CD3



pMHC-B x CD3

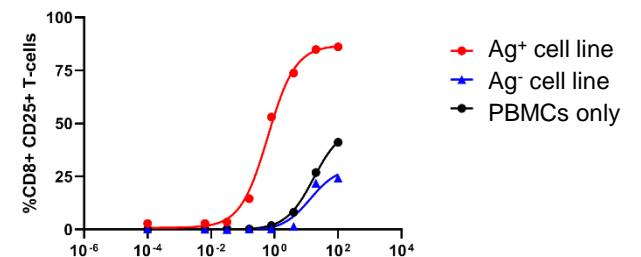
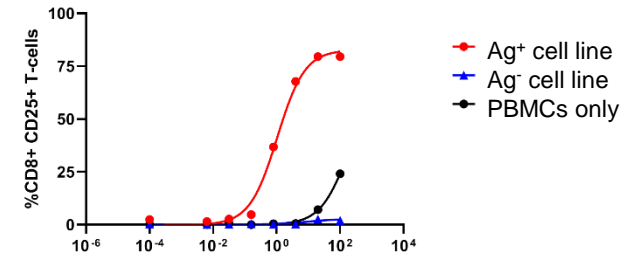
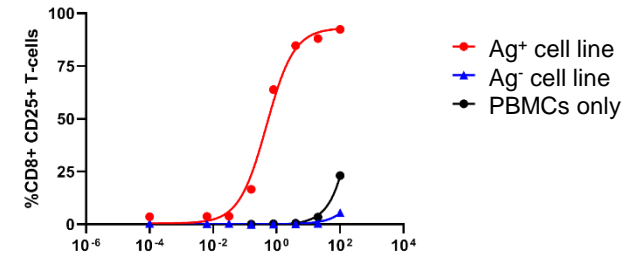


pMHC-C x CD3



Activity & Selectivity

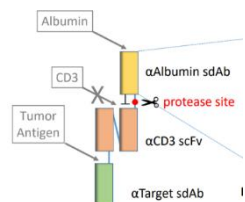
(T cell activation assay)



DARPin[®] T-cell engager [nM]

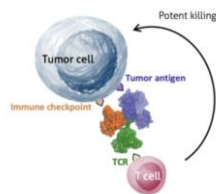
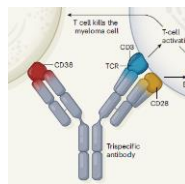
Building Next Generation of DARPin® T-Cell Engagers

T-cell engager field is progressing to the next level to address key limitations



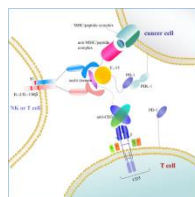
Tumor Activate T-Cell Engager
(e.g. Prodrug by Harpoon)

Co-stimulate T Cell Receptor
(e.g. CD28 by Sanofi)

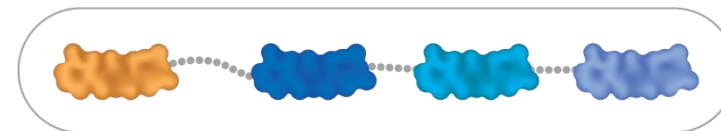


Block Checkpoint in Synapse
(e.g. LocATE by CDR-life)

Integrate Stimulating Features
(e.g. TriTE by TIMMUNE: IL-15 fusion)



Multi-DARPin® T-Cell Engagers for better safety and increased efficacy



Improving Safety

Boosting Activity

Removing Brake

Sustained Activity

Key Advantages of Molecular Partners

Validated source of
DARPin® Candidates

Flexible business model to
maximize product value



Novel Therapeutic Designs

1. Tumor-local immune agonists
2. pMHC targeting platform
3. Next Gen T-cell engagers

**Advanced and balanced
Clinical Development
Portfolio**

**Deliver patient value
with our strong team**

Expected 2020 Catalysts

	2020
Abicipar	<ul style="list-style-type: none"> ▪ Approval and launch in nAMD (US and EU) ▪ Initiation of Abicipar Phase 3 in DME patients
MP0250	<ul style="list-style-type: none"> ▪ Additional P2 data from PI-combo trial ▪ Continued development of MP0250 in partnership
MP0274	<ul style="list-style-type: none"> ▪ Establish dose and define path forward
MP0310	<ul style="list-style-type: none"> ▪ Identify MP0310 dose in ongoing phase 1 ▪ Initiation MP0310 combination trials
Research	<ul style="list-style-type: none"> ▪ Prepare for MP0317 IND submission ▪ Selection of 1st pMHC candidate for development ▪ Multiple updates at AACR & other international conferences

Funding into H2 2021

(excl. any future proceeds related to Abicipar and partnerships;
Cash Q3 19: CHF112mn)

Thank You!



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IR Agenda

February 6, 2020

April 29, 2020

Publication of Full-year Results 2019 (unaudited)

Annual General Meeting