

# The DARPin<sup>®</sup> Difference

Offering Patients a New Dimension of  
Protein Therapeutics

*Patrick Amstutz, CEO Molecular Partners*

*JP Morgan Healthcare Conference, January 2017*

*Presentation of Molecular Partners AG, Switzerland (Ticker: MOLN)*



# Disclaimer

This presentation is not an offer to sell or a solicitation of offers to purchase or subscribe for shares of Molecular Partners AG, nor shall it or any part of it nor the fact of its distribution form the basis of, or be relied on in connection with, any contract or investment decision. This presentation is not an offering circular within the meaning of Article 652a of the Swiss Code of Obligations, nor is it a listing prospectus as defined in the listing rules of the SIX Swiss Exchange AG or a prospectus under any other applicable laws. Copies of this presentation may not be sent to countries, or distributed in or sent from countries, in which this is barred or prohibited by law. This document is not a prospectus or a prospectus equivalent document and investors should not subscribe for or purchase any securities referred to in this document. This document does not constitute a recommendation regarding the shares.

This presentation contains specific forward-looking statements, beliefs or opinions, including statements with respect to the product pipelines, potential benefits of product candidates and objectives, estimated market sizes and opportunities as well as the milestone potential under existing collaboration agreements, which are based on current beliefs, expectations and projections about future events, e.g. statements including terms like “potential”, “believe”, “assume”, “expect”, “forecast”, “project”, “may”, “could”, “might”, “will” or similar expressions. Such forward-looking statements are subject to known and unknown risks, uncertainties and other factors which may result in a substantial divergence between the actual results, financial situation, development or performance of Molecular Partners AG and investments and those explicitly or implicitly presumed in these statements. There are a number of factors that could cause actual results and developments to differ materially from those expressed or implied by these statements and forecasts. Past performance of Molecular Partners AG cannot be relied on as a guide to future performance. Forward-looking statements speak only as of the date of this presentation and Molecular Partners AG, its directors, officers, employees, agents, counsel and advisers expressly disclaim any obligations or undertaking to release any update of, or revisions to, any forward looking statements in this presentation. No statement in this document or any related materials or given at this presentation is intended as a profit forecast or a profit estimate and no statement in this document or any related materials or given at this presentation should be interpreted to mean that earnings per share for the current or future financial periods would necessarily match or exceed historical published earnings per share. As a result, you are cautioned not to place any undue reliance on such forward-looking statements.

Unless stated otherwise the information provided in this presentation are based on company information. This presentation is intended to provide a general overview of Molecular Partners AG's business and does not purport to deal with all aspects and details regarding Molecular Partners AG. Accordingly, neither Molecular Partners AG nor any of its directors, officers, employees, agents, counsel or advisers nor any other person makes any representation or warranty, express or implied, as to, and accordingly no reliance should be placed on, the accuracy or completeness of the information contained in the presentation or of the views given or implied. Neither Molecular Partners AG nor any of its directors, officers, employees, agents, counsel or advisers nor any other person shall have any liability whatsoever for any errors or omissions or any loss howsoever arising, directly or indirectly, from any use of this information or its contents or otherwise arising in connection therewith.

The material contained in this presentation reflects current legislation and the business and financial affairs of Molecular Partners AG which are subject to change and audit.

# Molecular Partners: Who We Are



## Teamwork

- Swiss biotech
- 100 team members
- Discovery to phase 2 (POC)
- Science & patients first



## DARPin® Therapies

- High patient value
- DARPin® Difference
- Abicipar in phase 3 (ophtha)
- MP0250 in phase 2 (onco)
- Broad preclin. I/O\* portfolio



## Long-term Partnerships

- Alliance with Allergan
- Swiss listing (MOLN)
- Cash CHF186mn\*\*
- Financed well beyond key value inflection points



## DARPin® Platform

- DARPin® Difference: unlock novel modes of action
- Proof of Platform in the eye and systemically
- Fast and cost effective drug discovery engine

\*I/O, immuno-oncology; \*\* as of Q3/16.

# DARPin<sup>®</sup> Difference



## Patient Benefit



## Differentiation

## Status

I/O* DARPin <sup>®</sup> protein – opening new therapeutic window for combinations	Localized activity, ...	Preclin
MP0274: forcing Her2+ cancer cells into apoptosis with a new mode of action (MoA)	Molecular Master switch / Handcuff	Ph1
MP0250: new solution when cancers become resistant to standard therapies	Blocking two escape pathways	Ph2
Abicipar: less frequent ocular injections	Long-acting DARPin <sup>®</sup> protein	Ph3

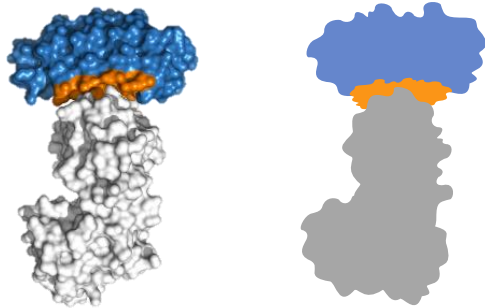
**Our Strategy: Differentiated DARPin products with high patient value**

\*I/O, immuno-oncology.

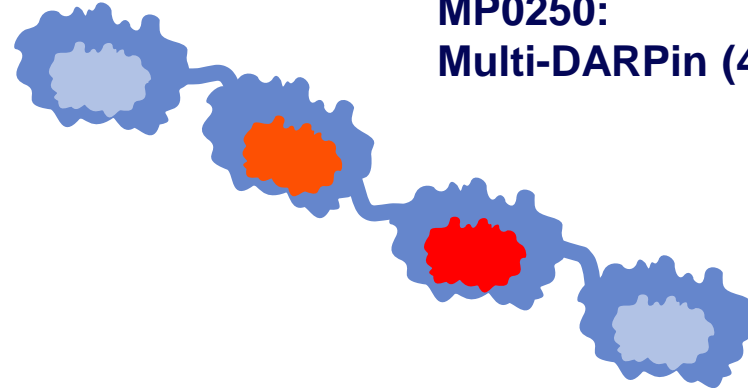
# DARPin<sup>®</sup> Proteins: A Different Class of Therapeutics

DARPin<sup>®</sup> is a registered trademark owned by Molecular Partners AG

**Abicipar:  
Mono-DARPin**



**MP0250:  
Multi-DARPin (4x)**



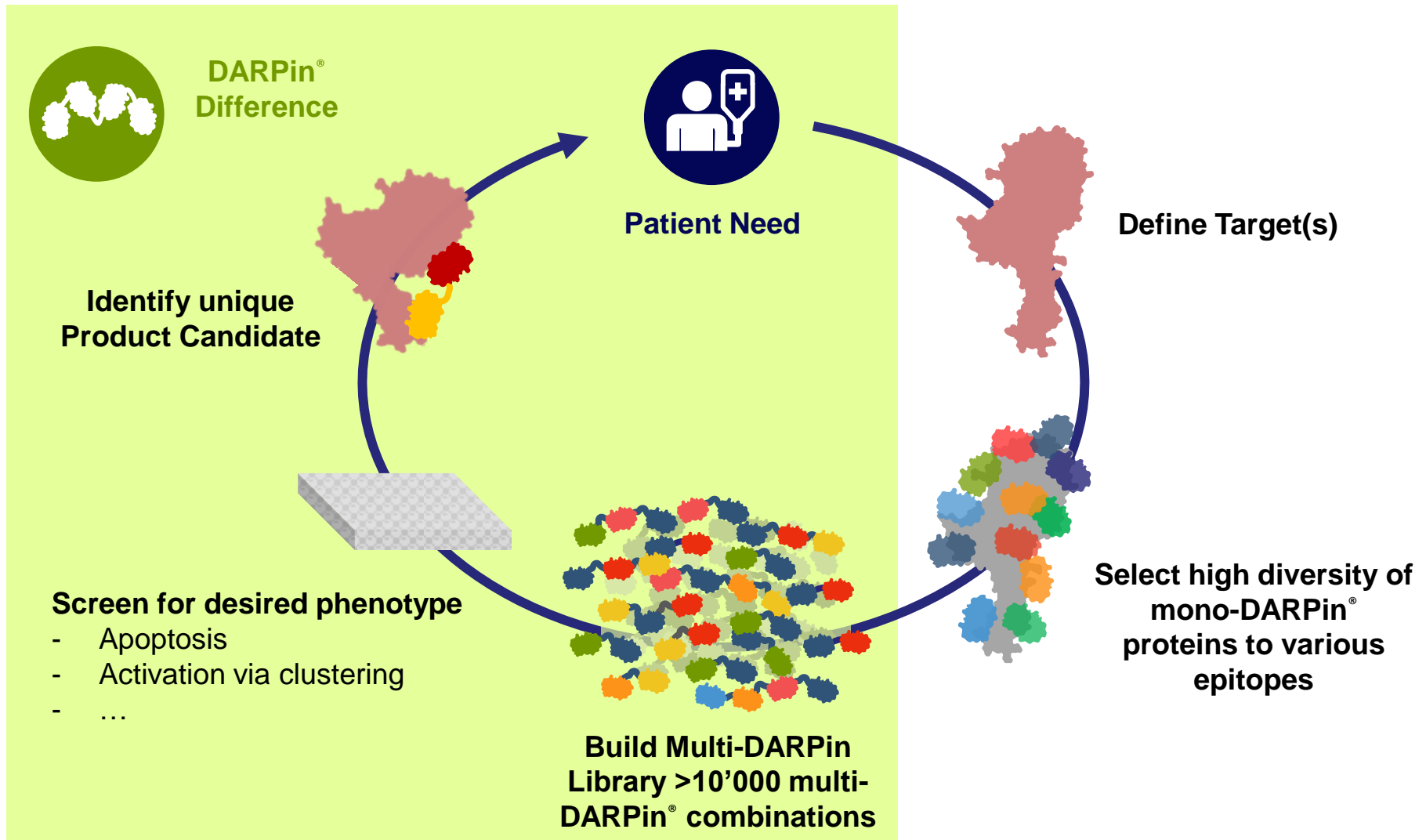
- **Mono-DARPin<sup>®</sup>**: selected to bind a given target with high affinity & specificity (large libraries)
- **Multi-DARPin<sup>®</sup>**: linked mono-DARPins<sup>®</sup> (up to six) & directly used for **functional screening**
- **Ideal properties**: mono- & multi-DARPins<sup>®</sup> are soluble, stable with a high-yield production
- **Natural principle**: repeat proteins were evolved as binders in multifunctional contexts

**Proof of Platform:** Low immunogenicity\* and long half-life in bloodstream and eye\*\*

\*MP0250 phase 1 study results show sustained exposure indicating absence of clearing antibodies;

\*\*Systemic half-life of ~12 d (MP0250 phase 1), 14 d in the eye (Abicipar).

# Pathway to the DARPin<sup>®</sup> Difference



# Long-term Partnerships: Investors & Pharma

## Balance capital markets and pharma partnering as sources of capital

- > CHF 360mn collected so far from investors and partners
- Remain in strong cash position to fund pipeline progress



## Strategic alliance with Allergan in ophthalmology

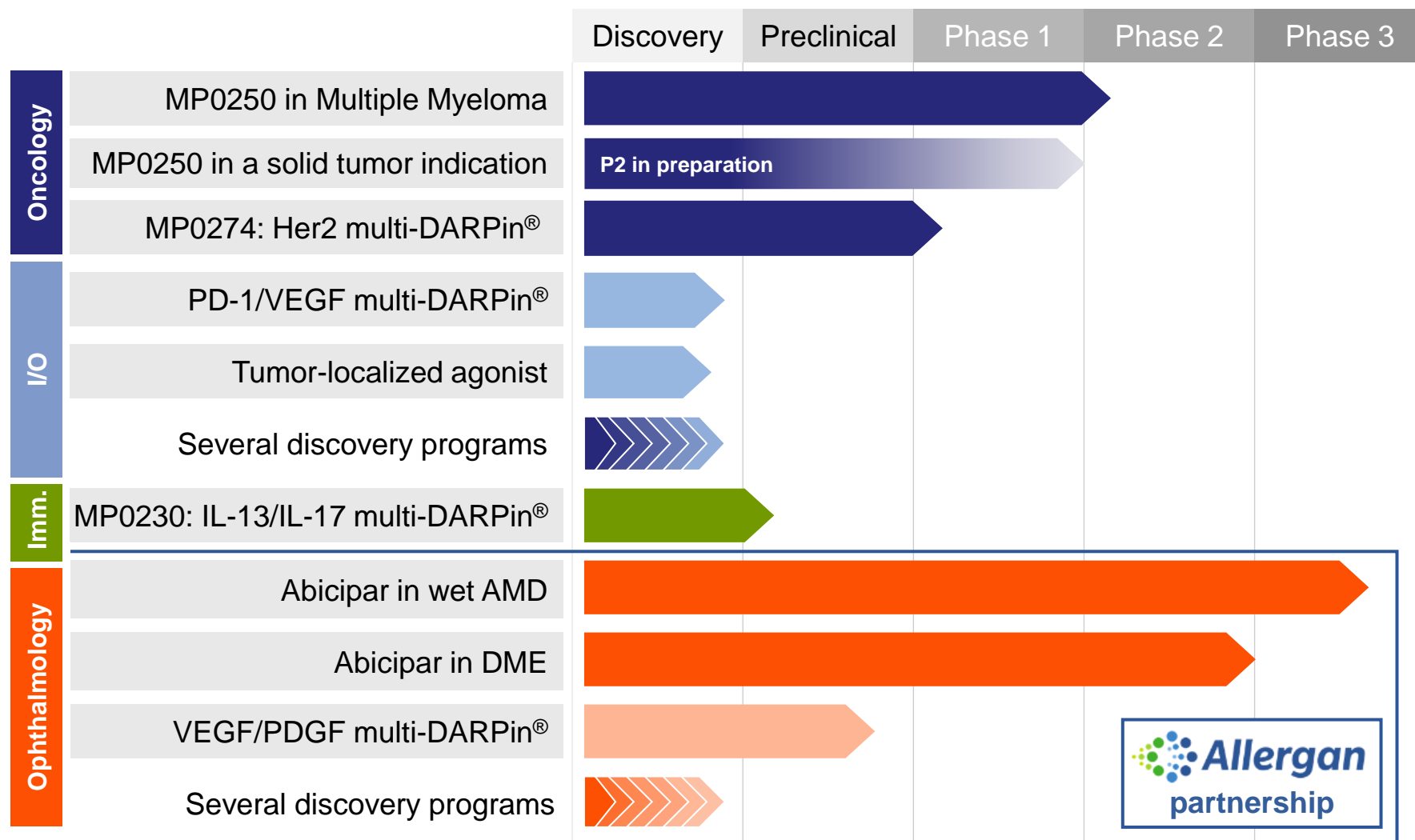
- Initiated with Abicipar in 2011
  - Up to \$360mn open milestone potential & low double-digit to mid-teen tiered royalties
- Expanded into broad discovery alliance in 2012
  - Potential \$1.7bn future milestone & tiered royalties to the mid-teens range



## Partnering strategy: leverage the potential of the DARPin® platform

- Platform and pipeline are deeper than what Molecular Partners can access alone
- Partnering opportunities open on multiple levels

# Balanced Portfolio



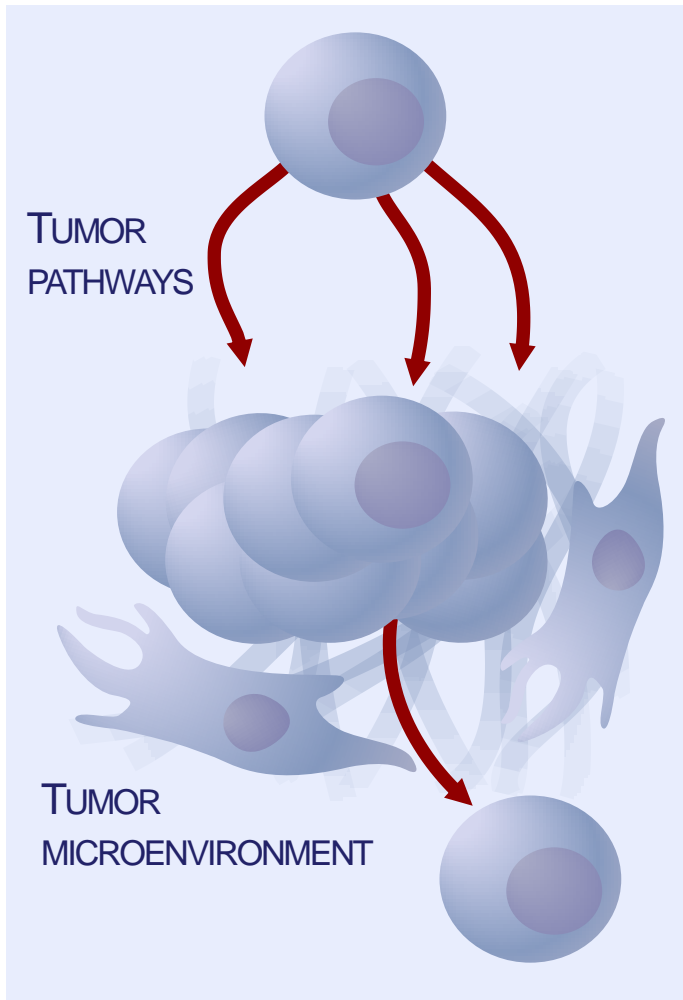


# Oncology



**MOLECULAR**  
partners

# Cancer Is Complex and Difficult to Treat



## Current Challenges

- Unlimited growth
- Sustained angiogenesis
- Tissue invasion & metastasis
- Evades body's immune defense



## Current Strategies

- Attack from several angles (combo treatment)
- Activate immune system (immuno-oncology)



## DARPin<sup>®</sup> Difference

- DARPin<sup>®</sup> candidates targeting multiple pathways
- Tumor-restricted multi-DARPin<sup>®</sup> candidates
- Novel Modes of Actions (MoAs)

# MP0250: An Ideal Combination (anti-VEGF & HGF)

MP0250

## MP0250

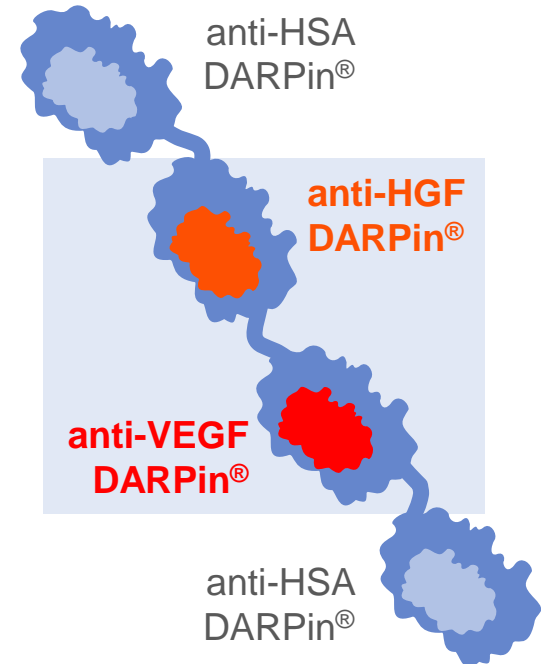
- First bi-specific biologic targeting VEGF and HGF
- Molecular Partners holds all rights

## Development Stage

- Phase 1: solid tumor study
  - Demonstrated good tolerability and exposure, encouraging efficacy
- Phase 2: multiple myeloma study
  - Regulatory submission Q4/2016
  - Initial safety data expected 2017
  - Initial efficacy data expected 2018
- Additional Phase 2 for solid tumor indication planned for 2017

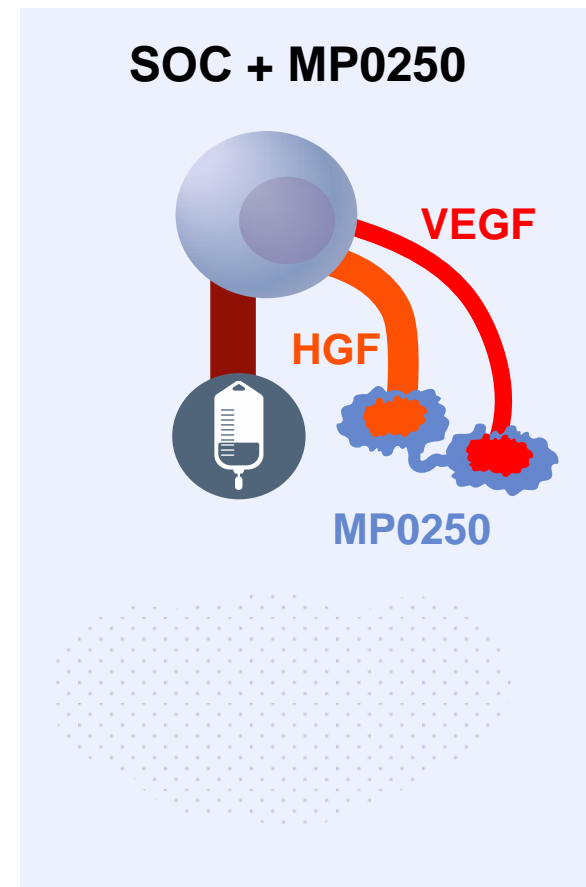
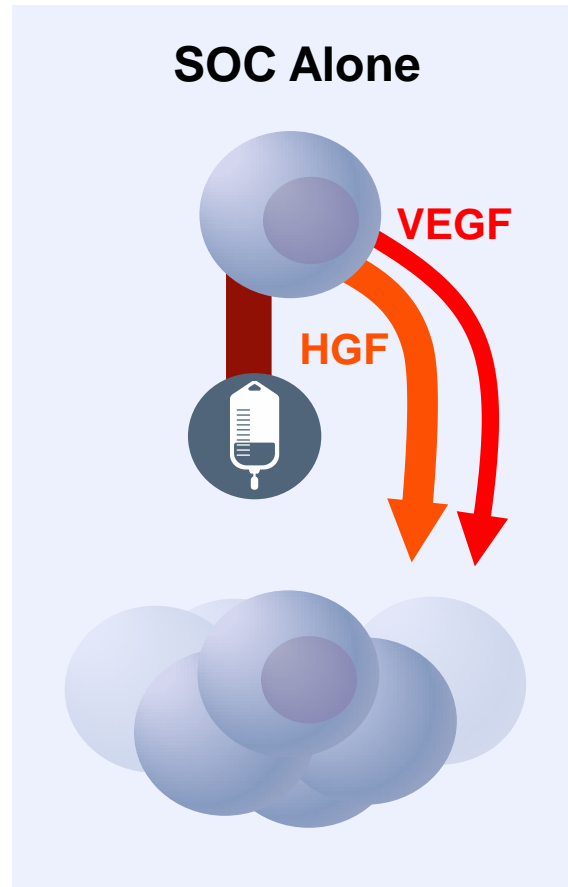
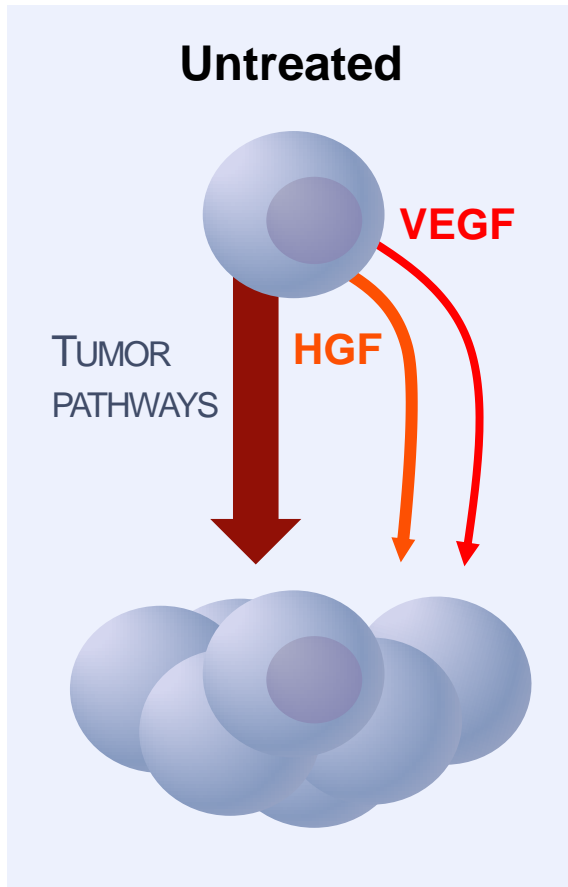
## Differentiation & Potential Benefit

- Ideal for patients with likely VEGF- and/or HGF-mediated escape from previous treatment
- Can be combined with standard therapy



# MP0250 Blocks Tumor Escape

MP0250

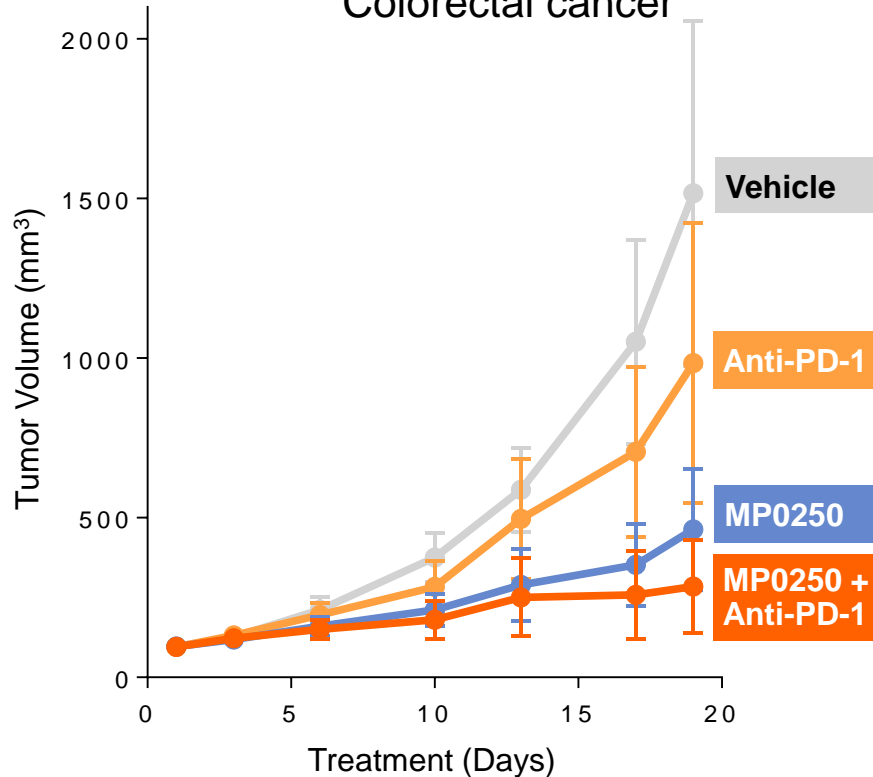


# MP0250: Combination with Chemotherapy and Biologics Across Diverse Cancers

MP0250

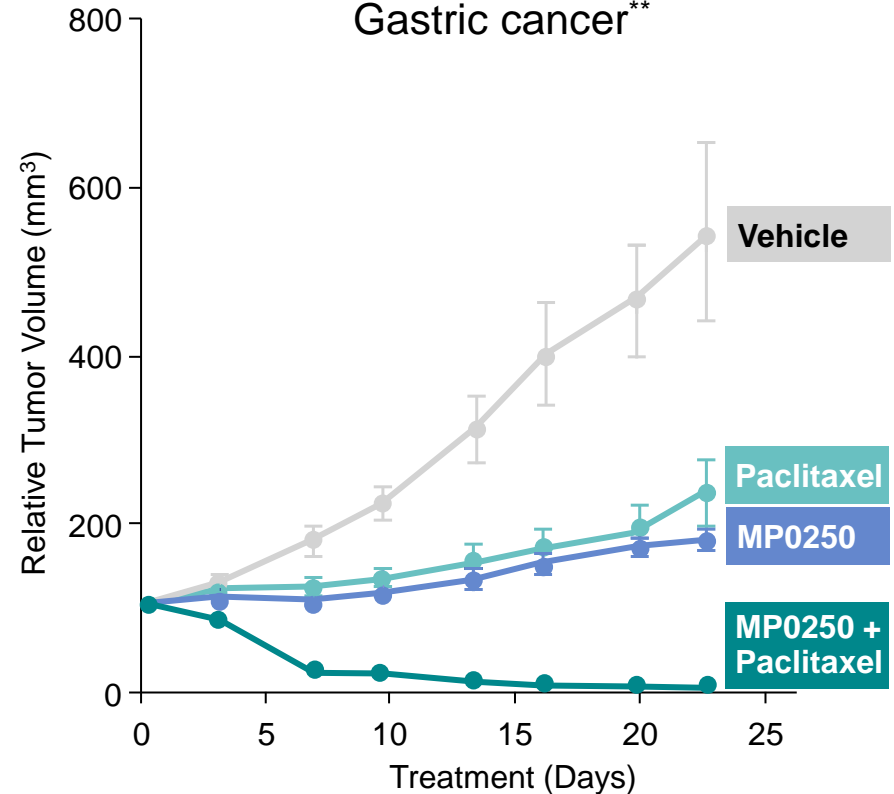
## MP0250 + PD-1 mAb

Colorectal cancer\*



## MP0250 + Paclitaxel

Gastric cancer\*\*



- MP0250 has also been tested in preclinical models of renal, liver and lung cancer

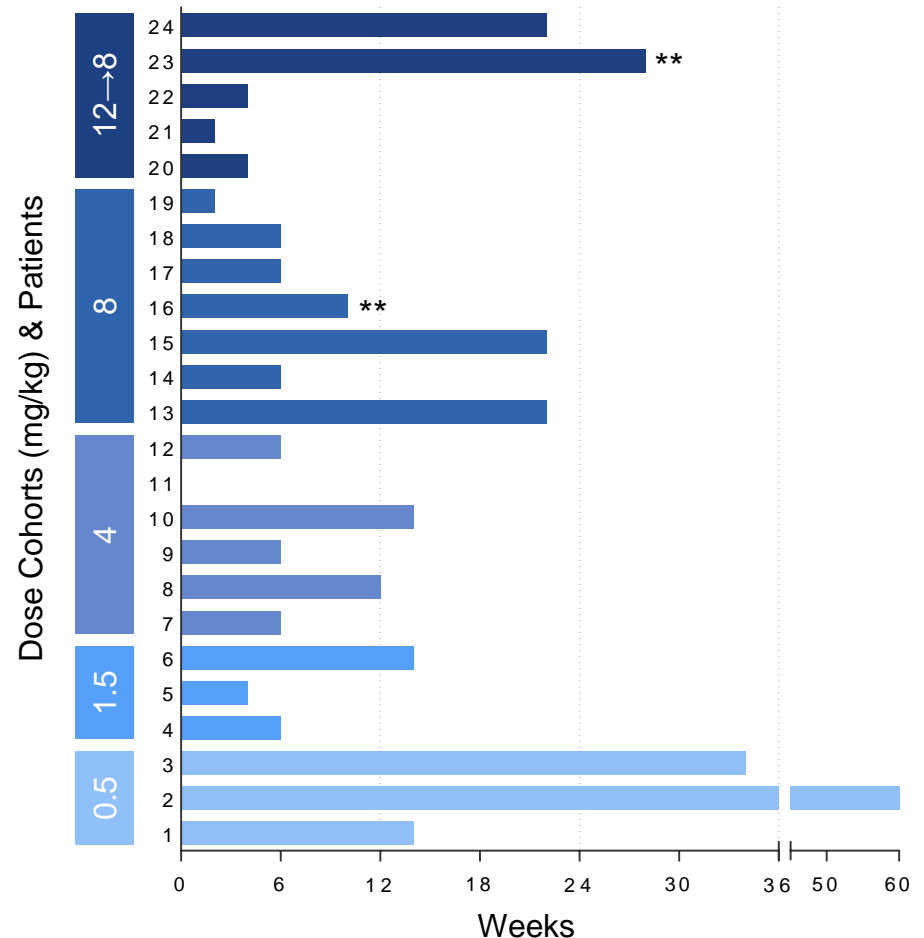
\*MC38 syngeneic mouse model; \*\*Patient-derived xenograft: GXA 3027.

# MP0250: Good Tolerability and Signs of Efficacy in Phase 1 Solid Tumor Study

MP0250

- Tolerability
  - MTD determined (8 mg/kg/q2w)
  - Main AEs consistent with profound VEGF pathway inhibition
    - Hypertension (66%), partially Grade 3
    - Proteinuria (29%), mainly Grade 1 or 2
- Systemic data
  - Half-life: 12 days
  - No clearing or neutralizing ADA
- Efficacy
  - Significant reductions in tumor volume in 2 patients with 1 confirmed PR
  - Stable disease at  $\geq 12$  wk in 10 patients (42%)

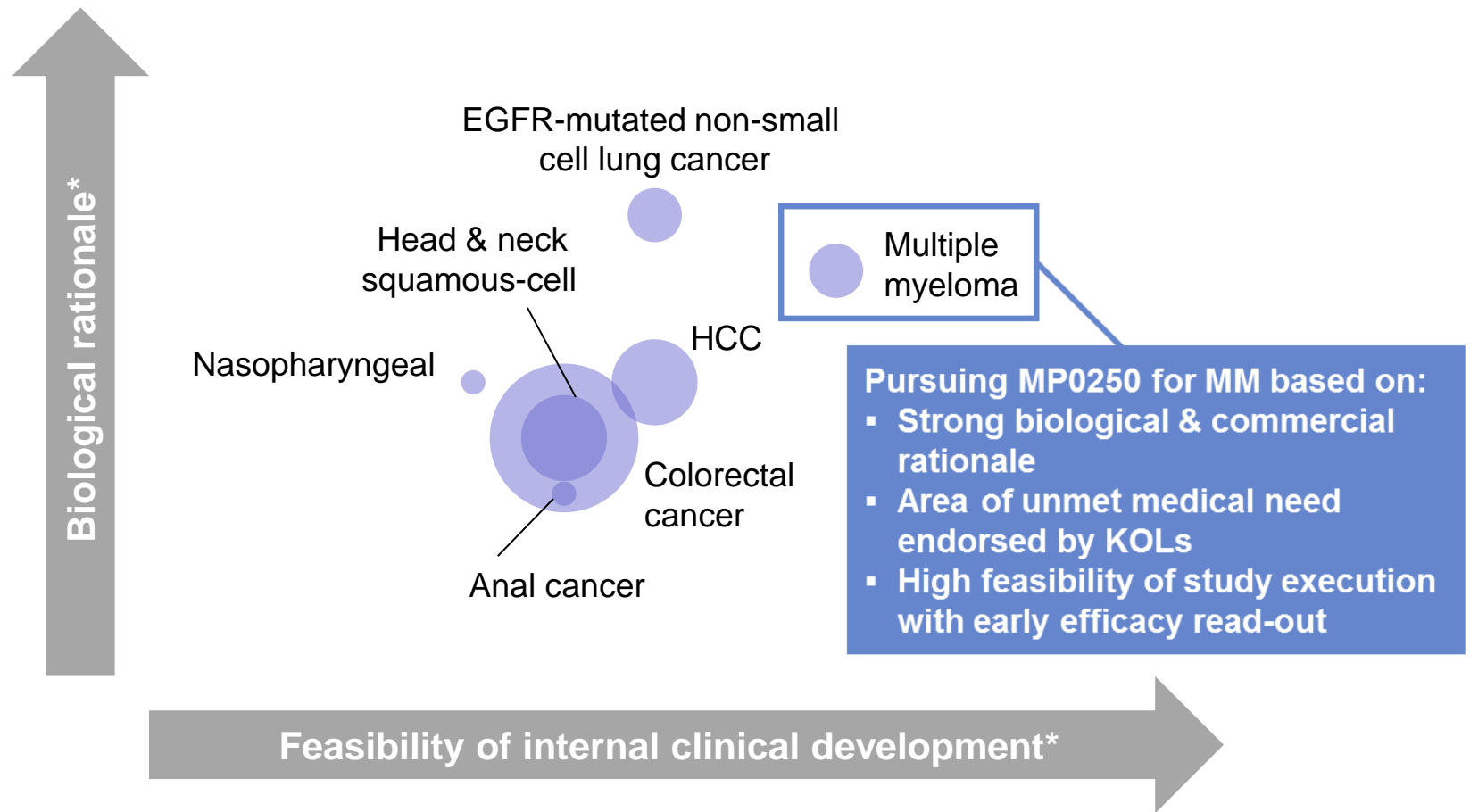
Treatment Duration of Individual Patients (N=24)\*



\*Study ongoing. Data cut-off June 2016 (N=24 patients). \*\*Ongoing.

# Internal Evaluation of MP0250 Potential

MP0250



Bubble size indicates estimated relative market potential (incidences; source: Datamonitor).

\*Based on internal assessment on speed to market and complexity of development program.

Potential of gastric cancer, renal cancer and other cancers under evaluation.

# Preclinical and Clinical Data Support MP0250 + SOC for Multiple Myeloma

MP0250

## Preclinical Rationale

### Tumor Growth H929 Xenograft

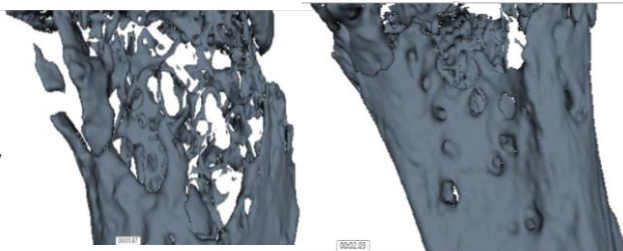
Vehicle

MP0250 +  
Bortezomib

Muscle  
invasion



Bone  
morphology



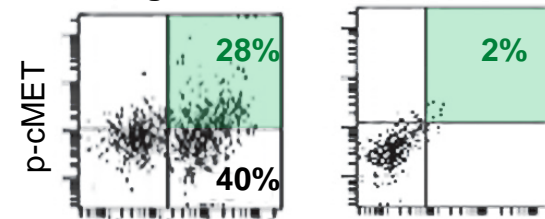
## Clinical Rationale

### HGF Rationale

#### HGF Receptor Activation<sup>1</sup>

Newly  
diagnosed

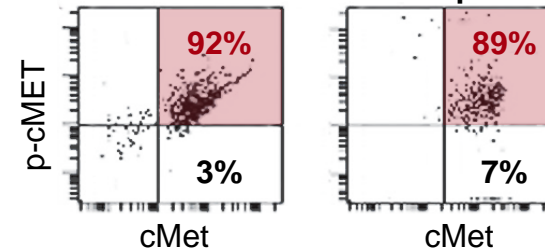
On partial  
remission



**SOC**

Resistant

Relapsed



### VEGF Rationale

A small MM study of bevacizumab (Avastin<sup>®</sup>) + bortezomib (Velcade<sup>®</sup>) demonstrated benefit over bortezomib alone<sup>2</sup>

1. Moschetta M, et al. Clin Cancer Res 2013;19:4371-82; 2. White D, et al. Cancer 2013;119:339-47.



# MP0274: Killing Her2+ Cells with New MoA

MP0274

MP0274

- Multi-DARPin<sup>®</sup> protein binding two distinct HER2 epitopes
- Indications: patients with HER2-addicted tumors
- Molecular Partners holds all rights

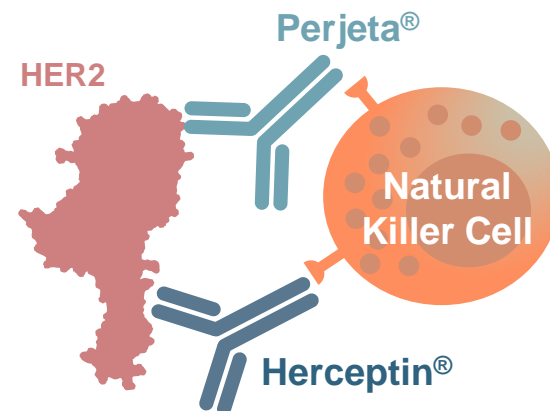
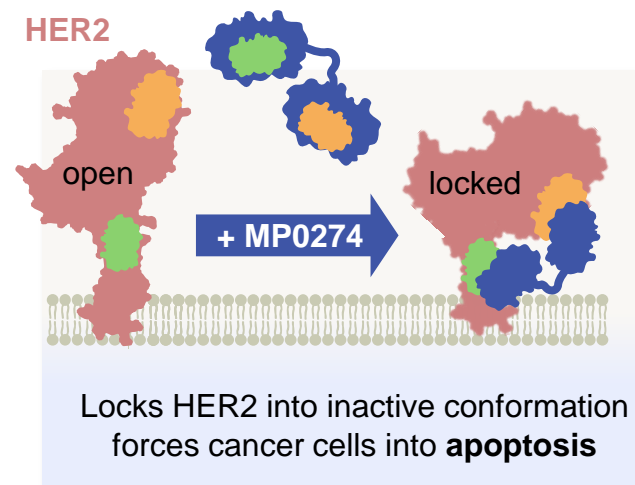
Development Stage

- First regulatory submission completed Q4/2016

Differentiation & Potential Benefit

- Induces apoptosis (cell death) in Her2 positive tumor cells without ADCC\*
- New MoA may help patients not adequately responding to current therapies

## DARPin<sup>®</sup> Handcuff as Master Switch



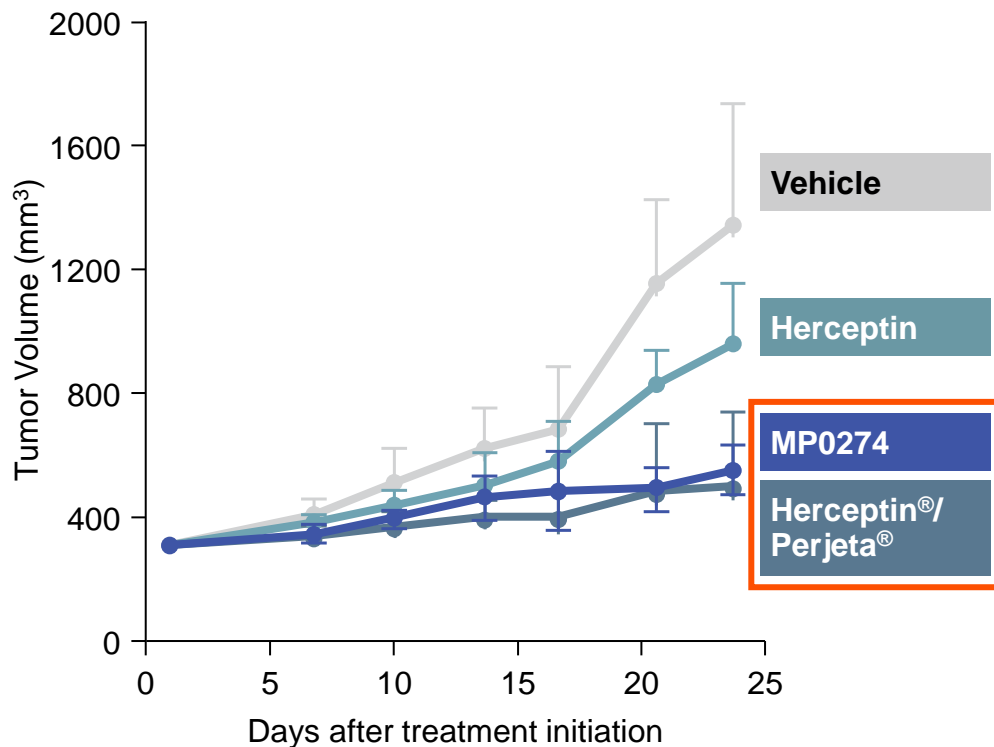
\*ADCC, antibody dependent cell-mediated cytotoxicity.

# MP0274 Kills by Apoptosis, Not ADCC

MP0274

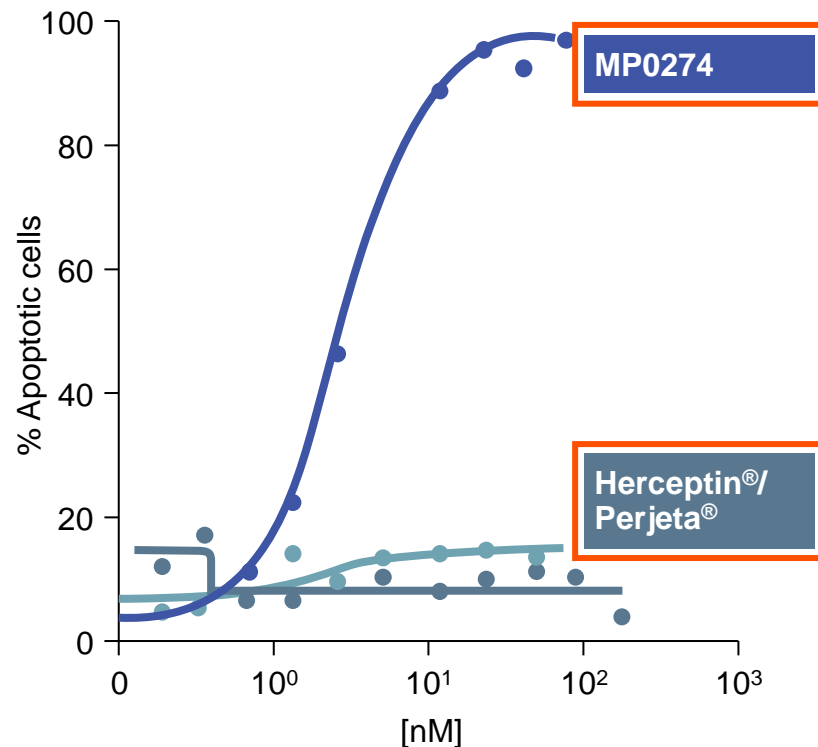
## Tumor Volume

PDX: Breast Cancer HER2+



## Tumor Cell Apoptosis

BT474



- MP0274 is as efficacious as SOC without the help of the immune system
- New MoA may help patients not adequately responding to current therapies

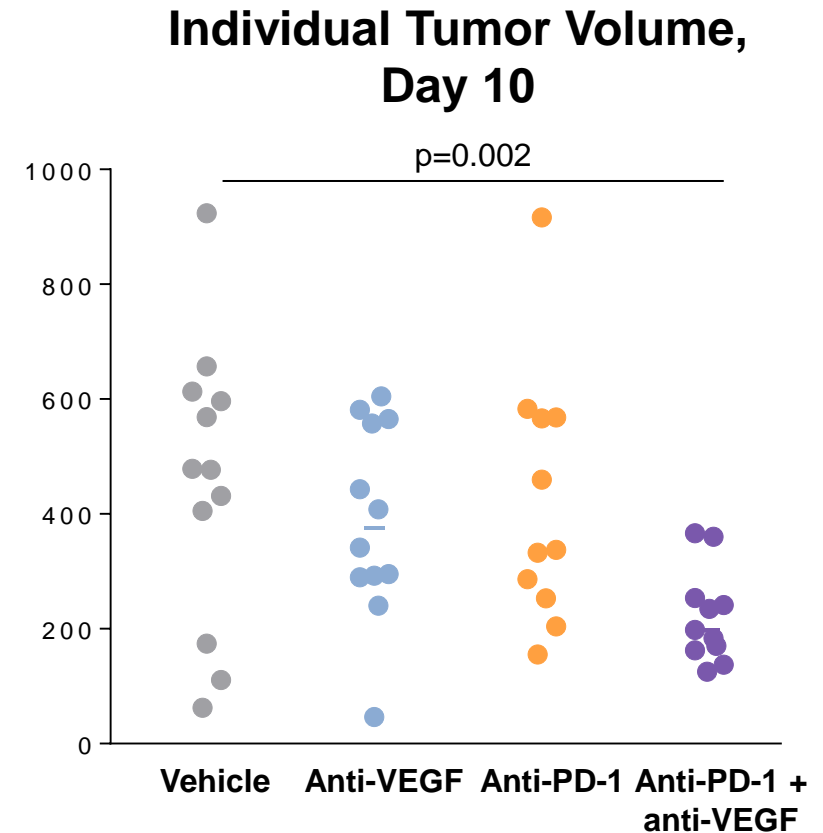
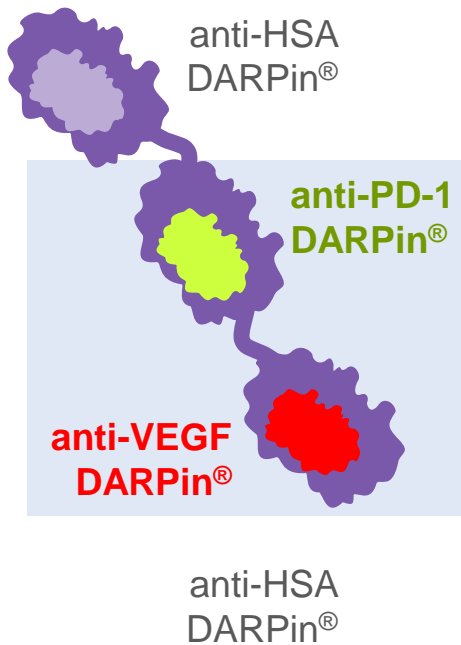
# Immuno-Oncology



**MOLECULAR**  
partners

# Activity of PD-1 and VEGF Multi-DARPin® Protein

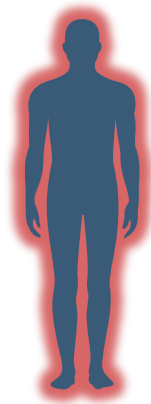
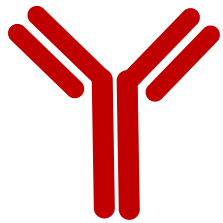
PD-1/VEGF



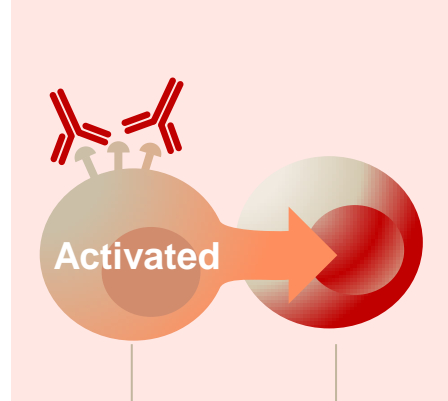
- PD-1 and VEGF show additive and/or synergistic activity

# Unleashing Potential of Agonists in I/O

## Agonistic mAb: Limitations



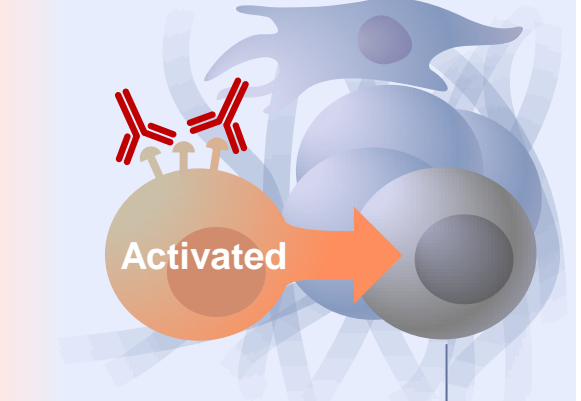
CIRCULATION (SYSTEMIC)



T-cell

Cell

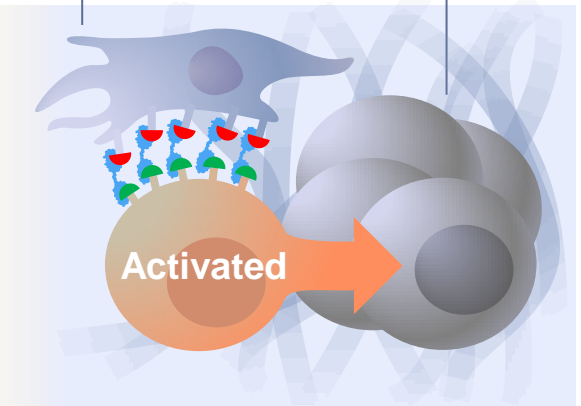
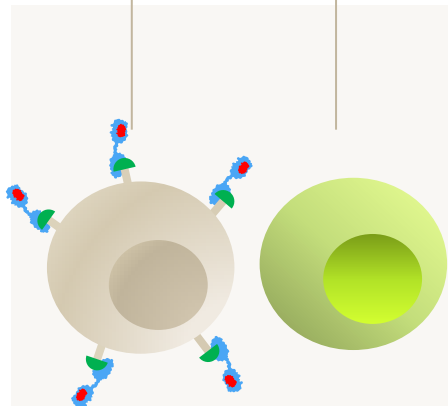
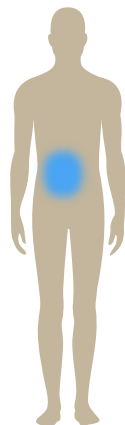
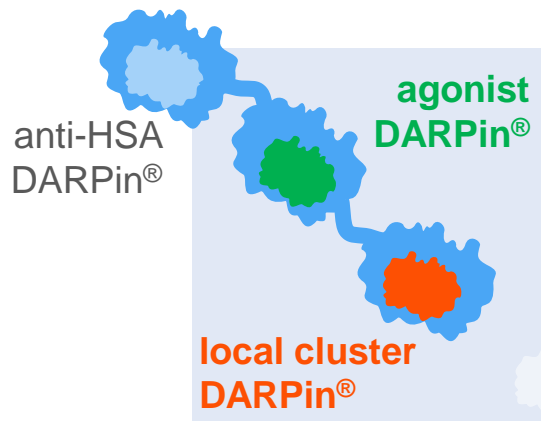
TUMOR MICROENVIRONMENT



Tumor Stroma

Tumor Cell

## Tumor-localized DARPin® Agonists



# Ophthalmology

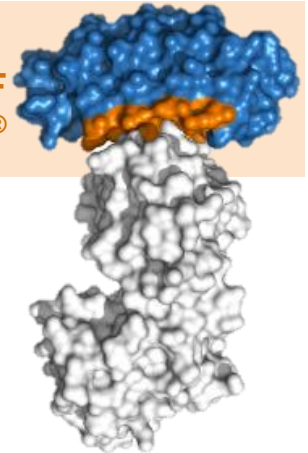
# Abicipar: Most Advanced DARPin<sup>®</sup> Therapy

Abicipar

## Abicipar

- Long-acting pegylated mono-DARPin<sup>®</sup> protein blocking VEGF
- Indications: Wet AMD & DME
- Global license agreement with Allergan
- All development costs with Allergan

anti-VEGF  
DARPin<sup>®</sup>



## Development Stage

- Phase 3
  - 2 registration-enabling studies in wet AMD initiated July 2015
- Phase 2
  - DME data presented at AAO 2016, Start of Phase 3 in 2017

## Market & Potential Differentiation

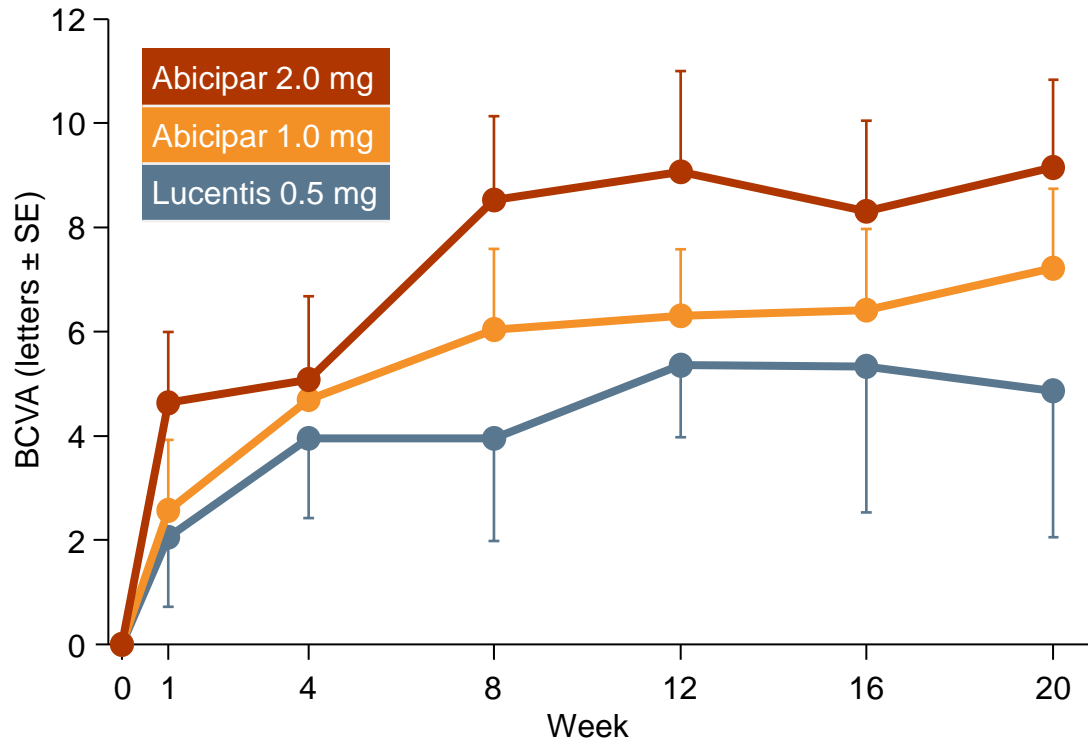
- Current anti-VEGFs (Lucentis & Eylea) market: > 8 bn USD \*
- SOC require intensive monitoring & frequent intravitreal injection
- Significant unmet medical need for less frequent injections and doctors visits

\* Reported by EvaluatePharma®, a service of Evaluate Ltd. (UK), [www.evaluategroup.com](http://www.evaluategroup.com). Accessed 27 Apr 2015.

# Phase 2 Data Suggest Quarterly Dosing for Wet AMD

Abicipar

## Change of Best-Corrected Visual Acuity (BCVA)\*



## Safety Data

Vision gain (letters)		Safety (n/N)
Wk 16	Wk 20	AEs†
8.2	9.0	2/23
6.3	7.1	3/25
5.3	4.7	0/16

The abicipar formulation has been further optimized for safety for use in Ph 3 trials

Dosing



Allergan, 12 August 2014.

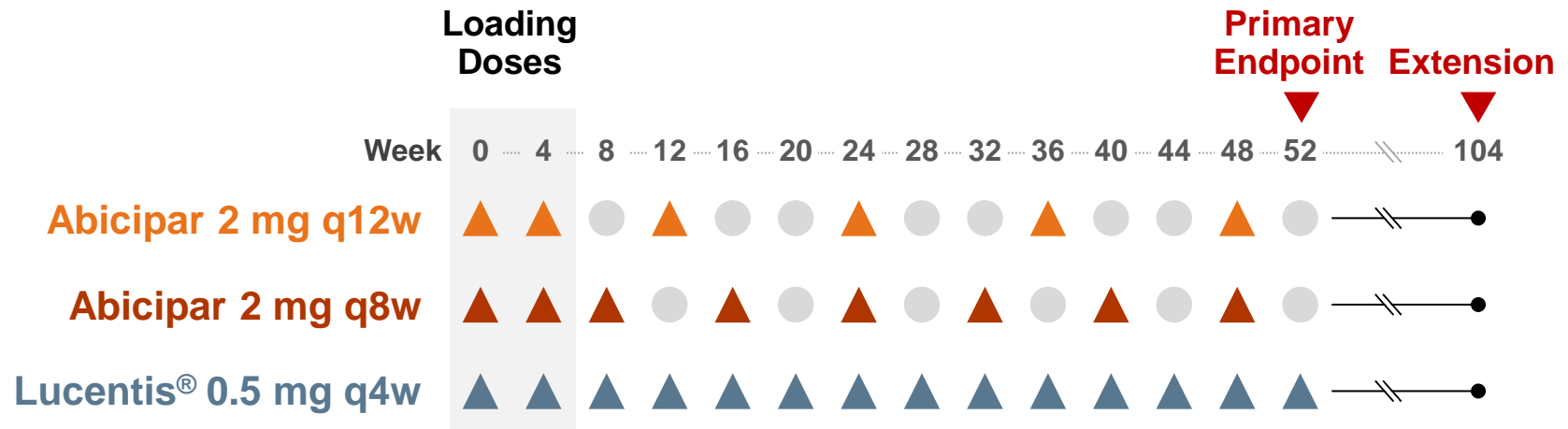
\*Study not powered to reach statistical significance; †Ocular inflammation.

AE, adverse event.



# CEDAR and SEQUOIA: Abicipar Registration Studies in Wet AMD

Abicipar

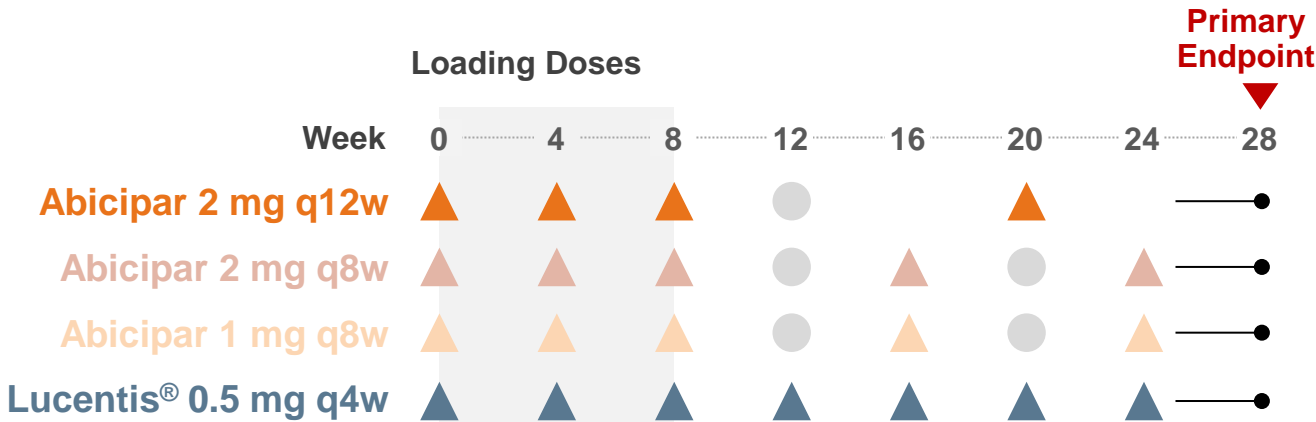


- 2 parallel, randomized, double-blind phase 3 studies
  - Expected global enrollment: 900 patients/study
  - Estimated study completion: Aug 2018 – expected launch in 2020\*
- Drug Safety Monitoring Committee (DSMC): no changes recommended Q4/16
- Next milestone: full enrollment of the study expected Aug 2017

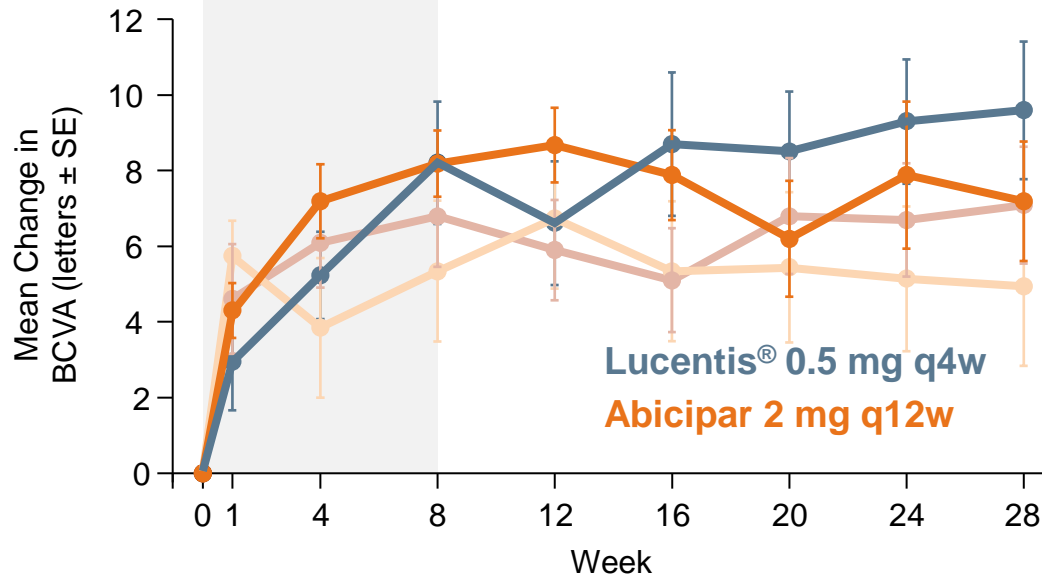
\*Abicipar under development and control of Allergan.

# Phase 2 Data: Long Duration of Action in DME

Abicipar



Vision gain (letters)	Safety
Wk 28	AEs (n/N)
7.2	4/45
7.1	5/41
4.9	7/43
9.6	0/21



The abicipar formulation has been further optimized for safety for use in Ph 3 trials

# AGN View on Abicipar at JPM 2017

**STRONG R&D PIPELINE TO DRIVE FUTURE GROWTH WITH  
"6 STARS" IN PHASE 3 IN 2017**



**ALLERGAN**  
GROWTH PHARMA LEADER

JPMORGAN CONFERENCE  
January 9, 2017

Brent Saunders  
Chairman and CEO



# DARPin® Strategy in Ophthalmology



**Value**

**Status**

**Discovery Alliance: Multi-DARPin® concepts in the eye**

**Next generation products**

**Preclin**

**Abicipar in DME: less frequent ocular injections**

**Start of phase 3 as early de-risking for safety read-out**

**Ph2**

**Abicipar in wet AMD: less frequent ocular injections**

**Low biology risk with meaningful differentiation**

**Ph3**

**Extract from ALLERGAN Presentation; JP Morgan Conference; January 9, 2017 by Brent Saunders; Chairman and CEO**

**ABICIPAR**



AMD  
DME

Recombinant designed ankyrin repeat protein. Potent blocker of all forms of soluble VEGF-A

2020  
2022

**\$1.5B-\$3B**

- Reduction in injection burden is a significant unmet need
- Offers sustained efficacy with fewer injections

# Summary

# Outlook 2017 & Beyond

	2017	2018
MP0250: Multiple Myeloma	Initial safety data Ph2	Initial efficacy data Ph2
MP0250: additional solid tumor ind.	Submission for Ph2	Initial data Ph2
MP0274: Her2 multi-DARPin®	First dosing in Ph1	Initial data Ph1
PD-1/VEGF multi-DARPin®	Preclinical data	
Tumor-restricted agonist		
Several discovery programs		
MP0230: IL-13&IL-17 multi-DARPin®	Decision on development strategy	
Abicipar*: wet AMD	Full enrollment of Ph3	1-year efficacy data Ph3
Abicipar*: DME	Start of Ph3	

**Cash CHF 186mn (Q3/16)**

**Financed well beyond key value inflection points**

\*Abicipar under development and control of Allergan.

# Conclusions



- Balanced & differentiated clinical DARPin® portfolio:
  - Abicipar in phase 3 in wet AMD and phase 2 concluded in DME
  - MP0250 phase 2 submitted in MM and solid tumor phase 2 in prep.
  - MP0274 phase 1 submitted in Her2 positive cancers
- Broad DARPin® portfolio in immuno-oncology



- Financed well beyond key value inflection points
- Full pipeline allows exploration of collaboration opportunities



- Strong and experienced team
- Culture of teamwork and «science and patients first»



- With proof of platform, we now focus on making the “DARPin® Difference” real for patients

Thanks!