

The DARPin[®] Difference

Offering Patients a New Dimension of
Protein Therapeutics

Patrick Amstutz, acting CEO

Cowen and Company 37th Annual Health Care Conference - 07 March 2017
Molecular Partners AG, Switzerland (SIX: MOLN)

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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 (optha)
 - MP0250 in phase 2 (onco)
 - MP0274 in phase 1 (onco)
 - Broad preclin. I/O portfolio



Long-term Partnerships

- Alliance with Allergan
- Swiss listing (MOLN)
 - Cash CHF180mn*
 - Financed well beyond key value inflection points

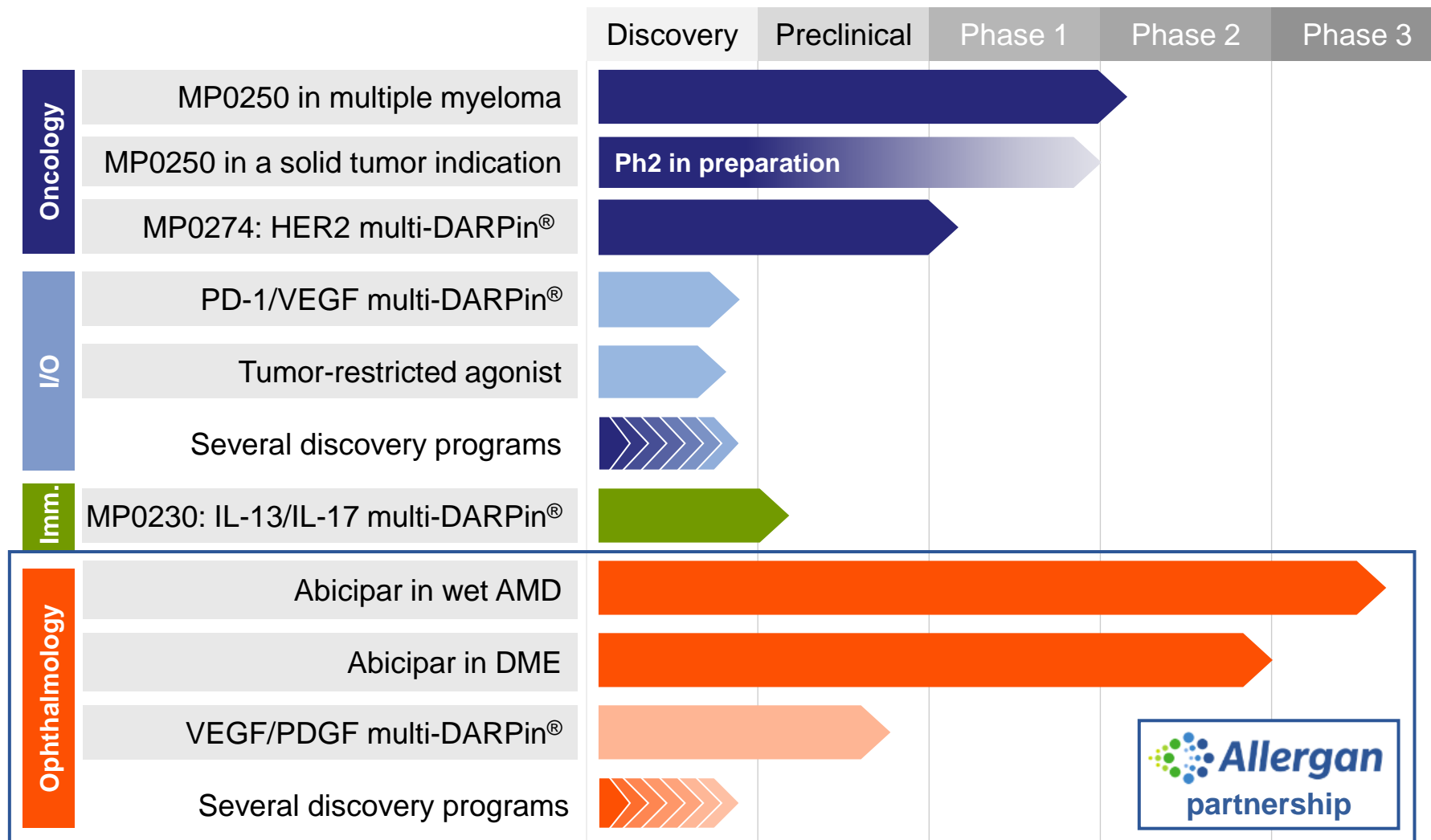


DARPin® Platform

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

*As of Q4/16.
I/O, immuno-oncology.

Balanced Portfolio



AMD, age-related macular degeneration; DME, diabetic macular edema.

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 \$1.4bn future milestone & tiered royalties to the mid-teen range

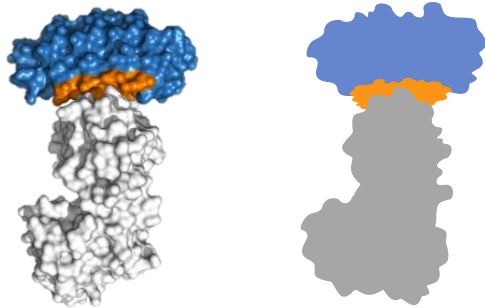
Partnering strategy: leverage the potential of the DARPin® platform

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

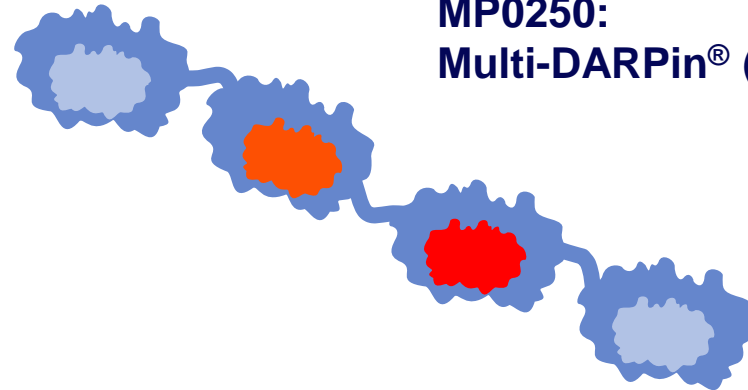
DARPin[®] Proteins: A Different Class of Therapeutics

DARPin[®] is a registered trademark owned by Molecular Partners AG

**Abicipar:
Mono-DARPin[®]**



**MP0250:
Multi-DARPin[®] (4x)**



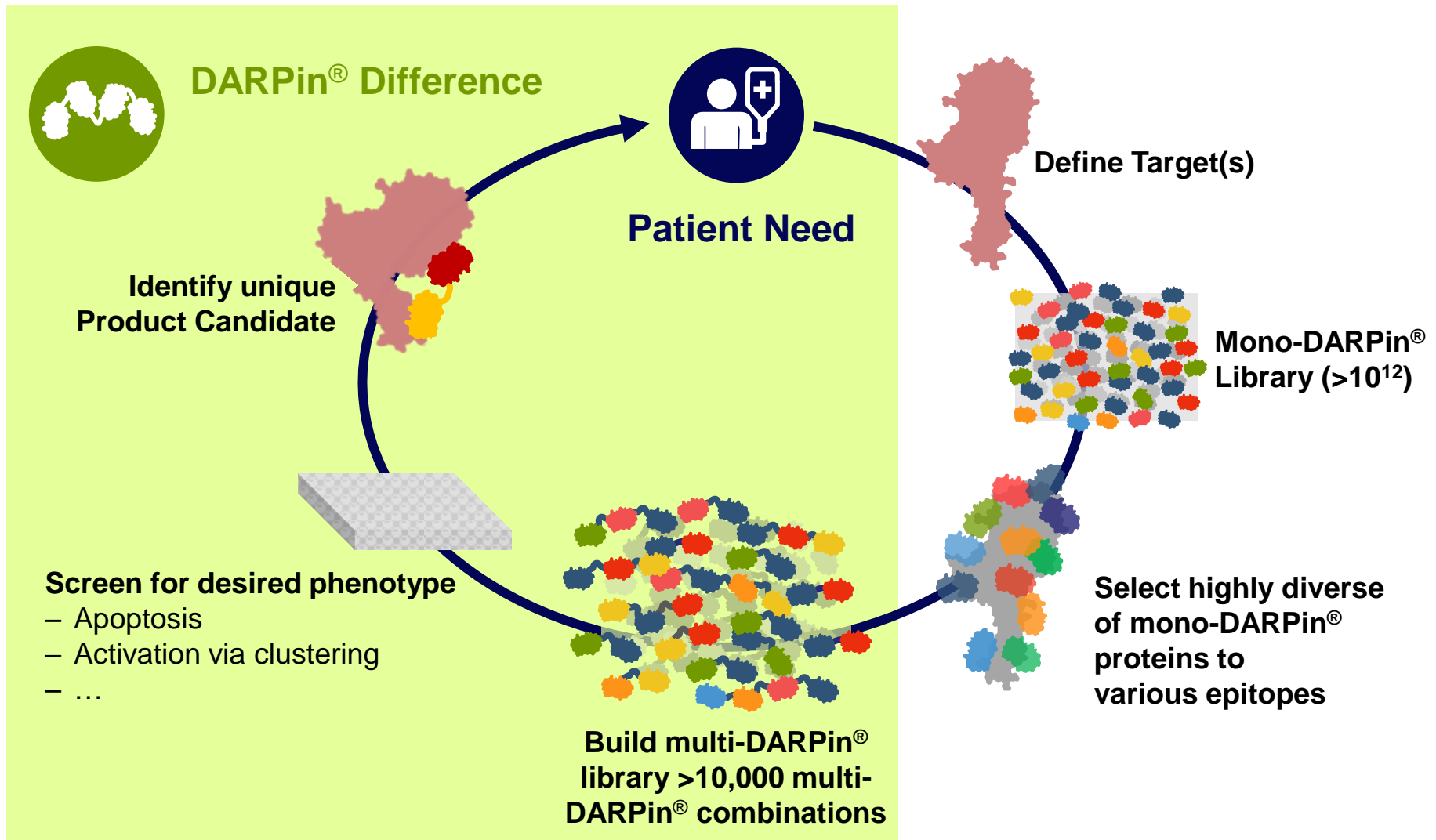
- **Mono-DARPin[®]**: selected to bind a given target with high affinity & specificity (large libraries)
- **Multi-DARPin[®]**: linked mono-DARPin[®] (\geq **six**) & directly used for **functional screening**
- **Ideal properties**: mono- & multi-DARPin[®] are soluble, stable with a high-yield production
- **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[®] Difference



DARPin[®] Difference



DARPin[®] Differentiation



Patient Benefit

Status

<u>I/O DARPin[®] proteins</u> : Tumor-restricted activity, ...	Opening a new therapeutic window for combinations	Preclin
<u>MP0274</u> : Molecular Handcuff forcing HER2+ cancer cells into apoptosis	For patient not profiting from SOC antibodies with ADCC	Ph1
<u>MP0250</u> : Blocking two escape pathways	Restore activity of SOC when cancer becomes resistant	Ph2
<u>Abicipar</u> : Long-acting DARPin [®] protein	Less frequent ocular injections	Ph3

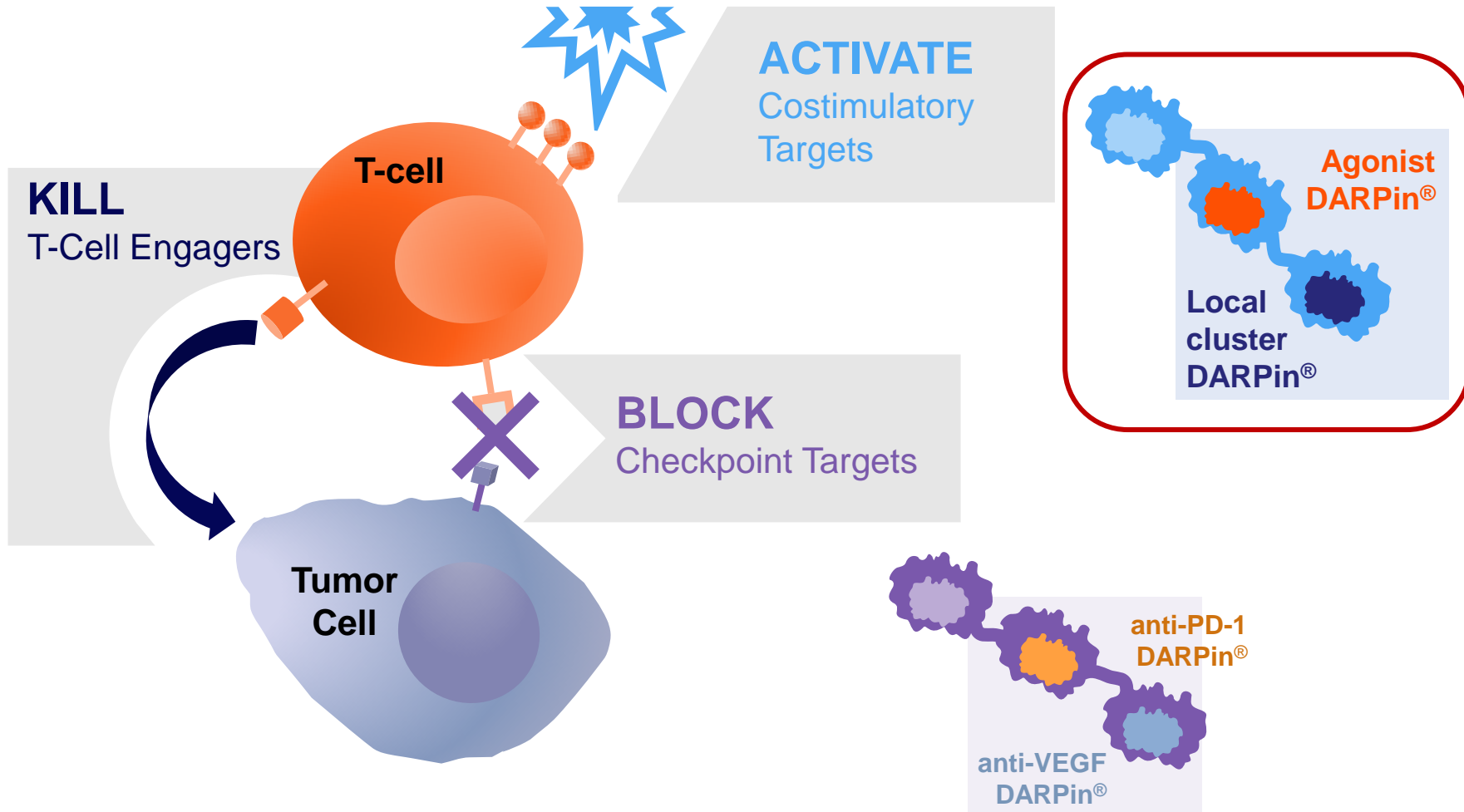
Our strategy: Differentiated DARPin[®] products with high patient value

Oncology & Immuno Oncology



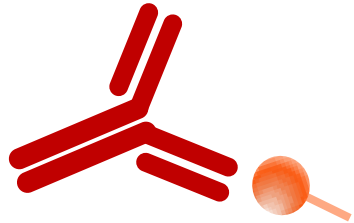
MOLECULAR
partners

Molecular Partners Strategy for T-Cells



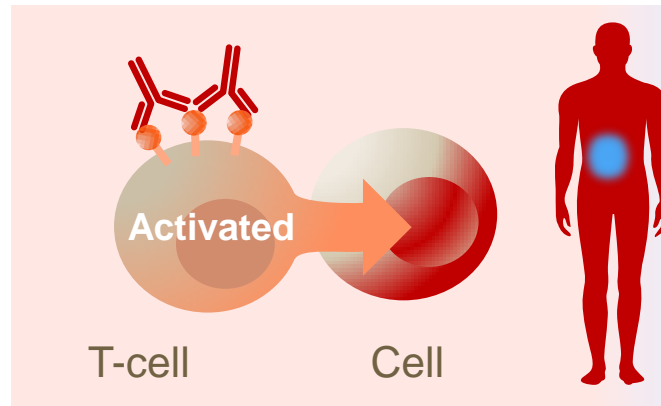
Unleashing Potential of Agonists in I/O

Agonistic mAb:

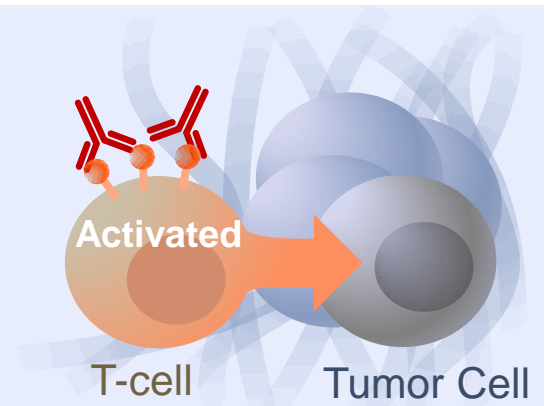


T-cell agonist target

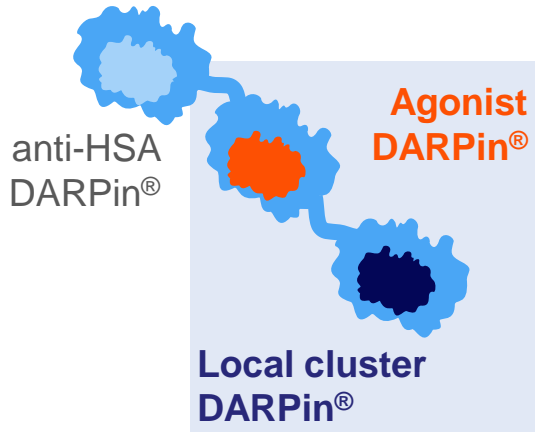
IN CIRCULATION (SYSTEMIC)



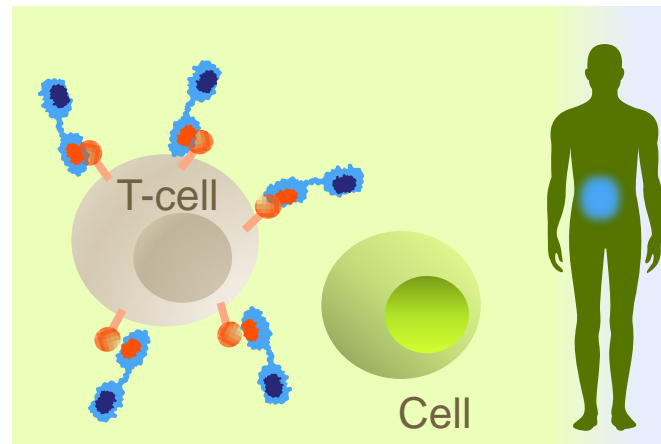
IN THE TUMOR



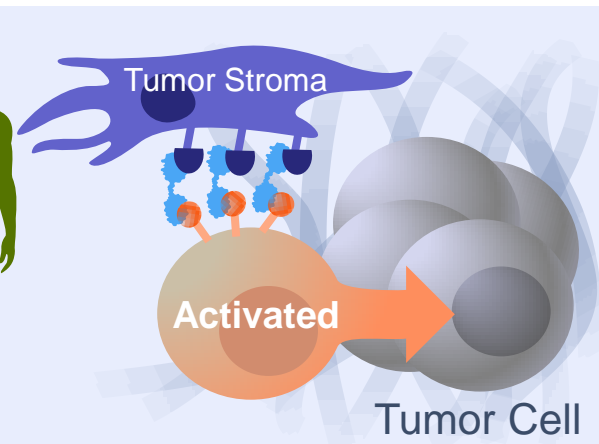
Tumor-restricted DARPin® Agonists



IN CIRCULATION (SYSTEMIC)



IN THE TUMOR



MP0274: Killing Her2+ Cells with New MoA

MP0274

MP0274

- Multi-DARPin[®] protein binding two distinct HER2 epitopes
- Indications: patients with HER2-addicted tumors
- Molecular Partners holds all rights

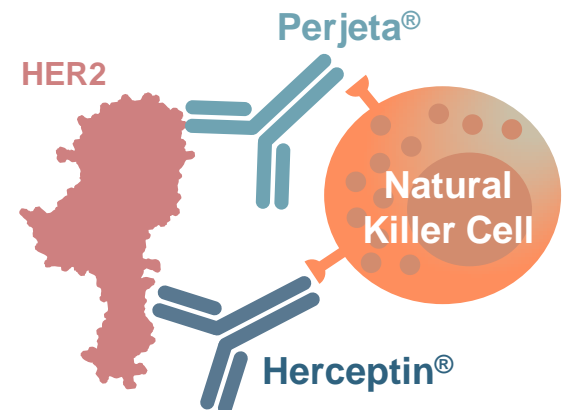
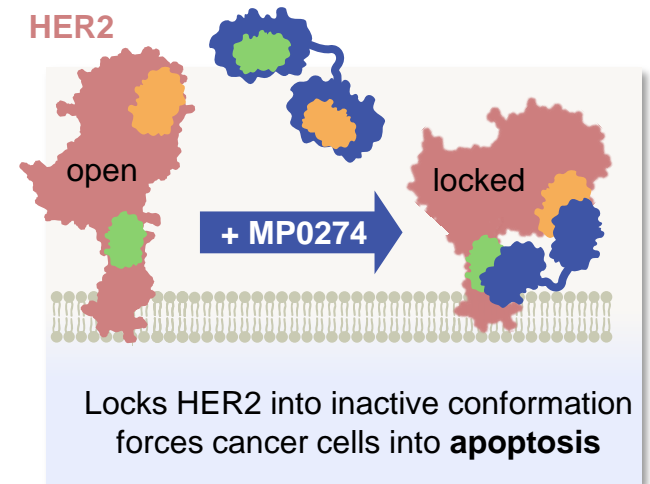
Development Stage

- 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[®] Handcuff as Master Switch



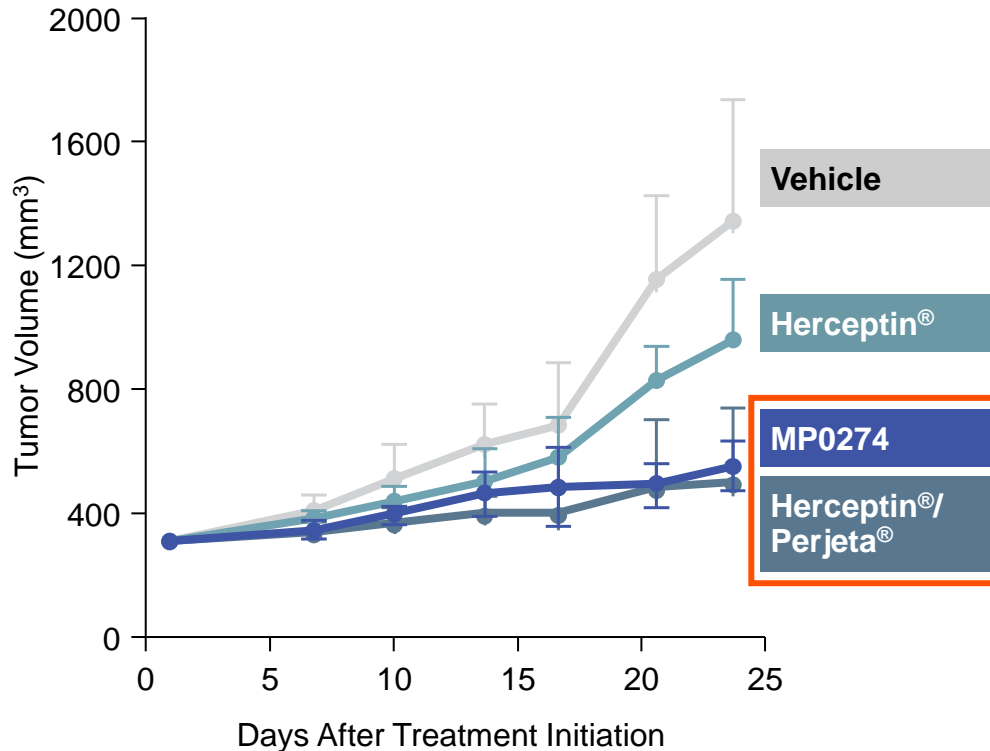
*ADCC, antibody dependent cell-mediated cytotoxicity.

MP0274 Kills by Apoptosis, Not ADCC

MP0274

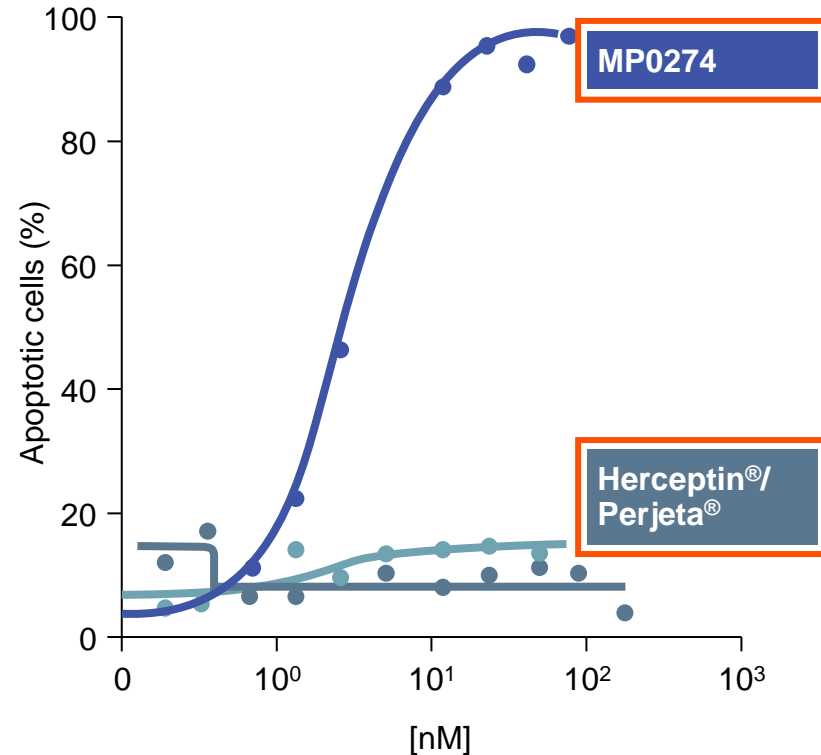
Tumor Volume

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 who do not adequately respond to current therapies

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

MP0250

MP0250

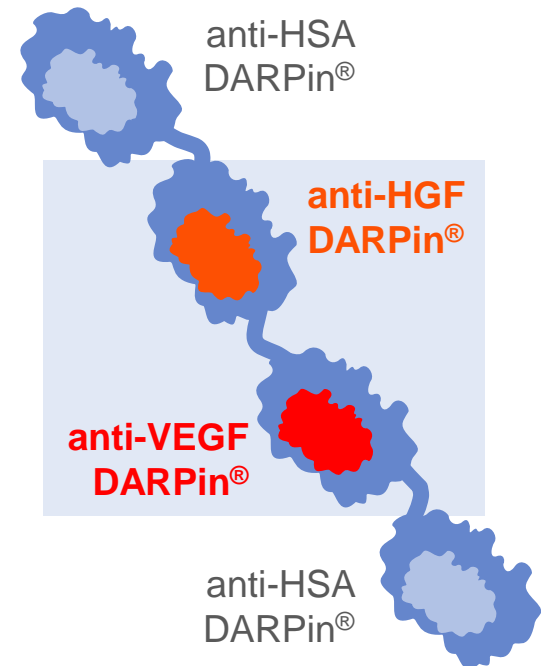
- First bi-specific biologic targeting VEGF and HGF
- Molecular Partners holds all rights

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

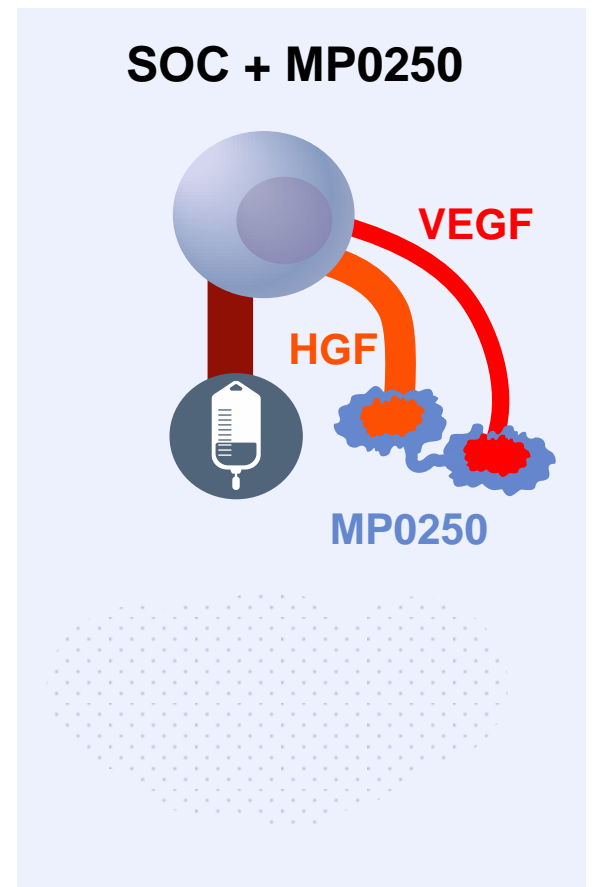
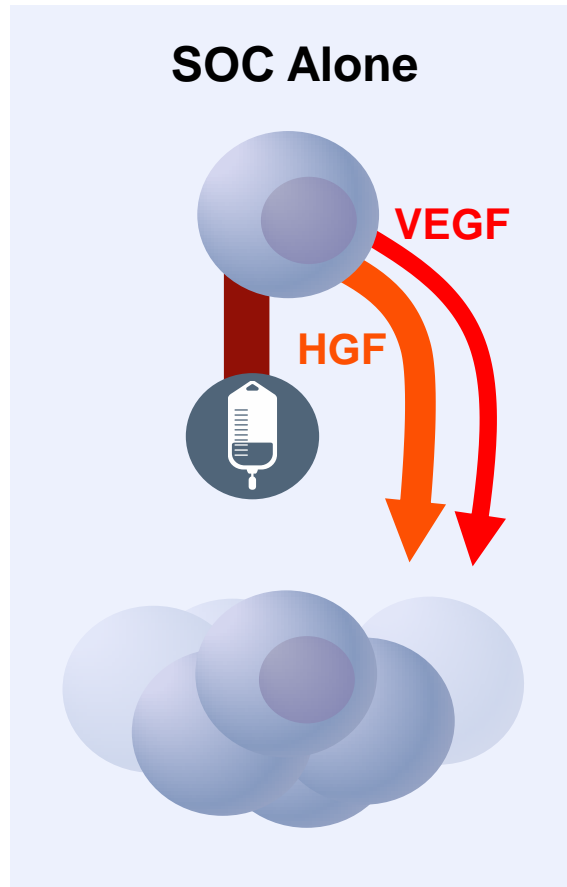
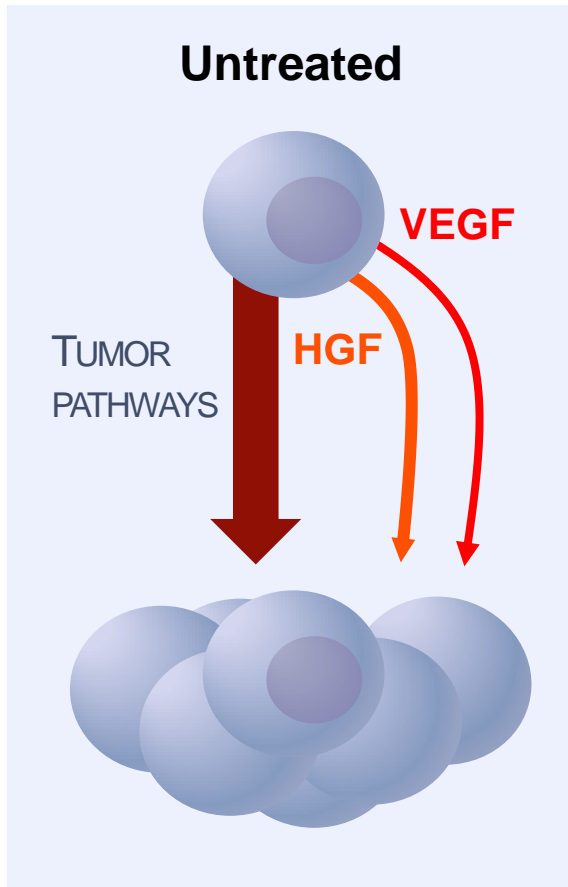
Differentiation & Potential Benefit

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



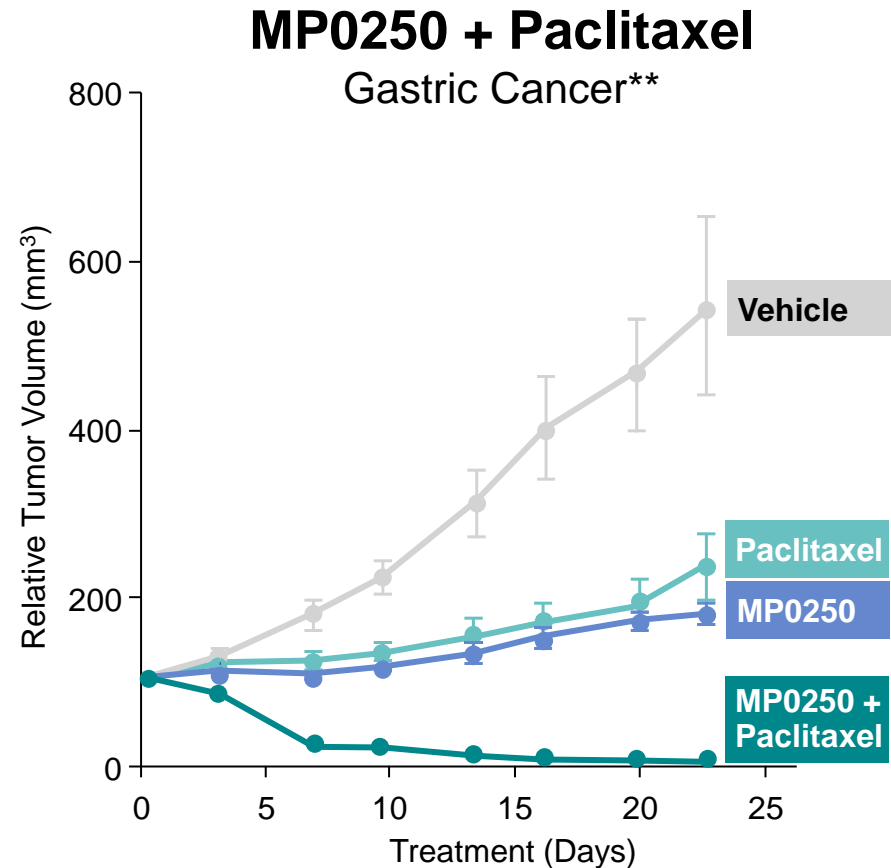
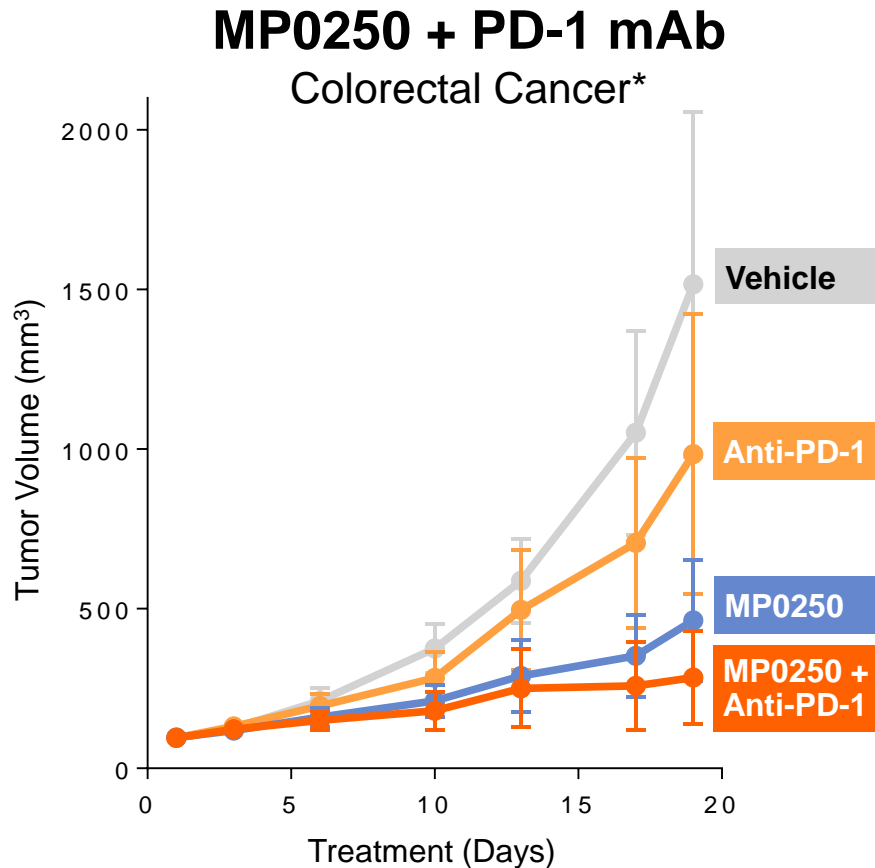
MP0250 Blocks Tumor Escape

MP0250



MP0250: Combination With Chemotherapy and Biologics Across Diverse Cancers

MP0250



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

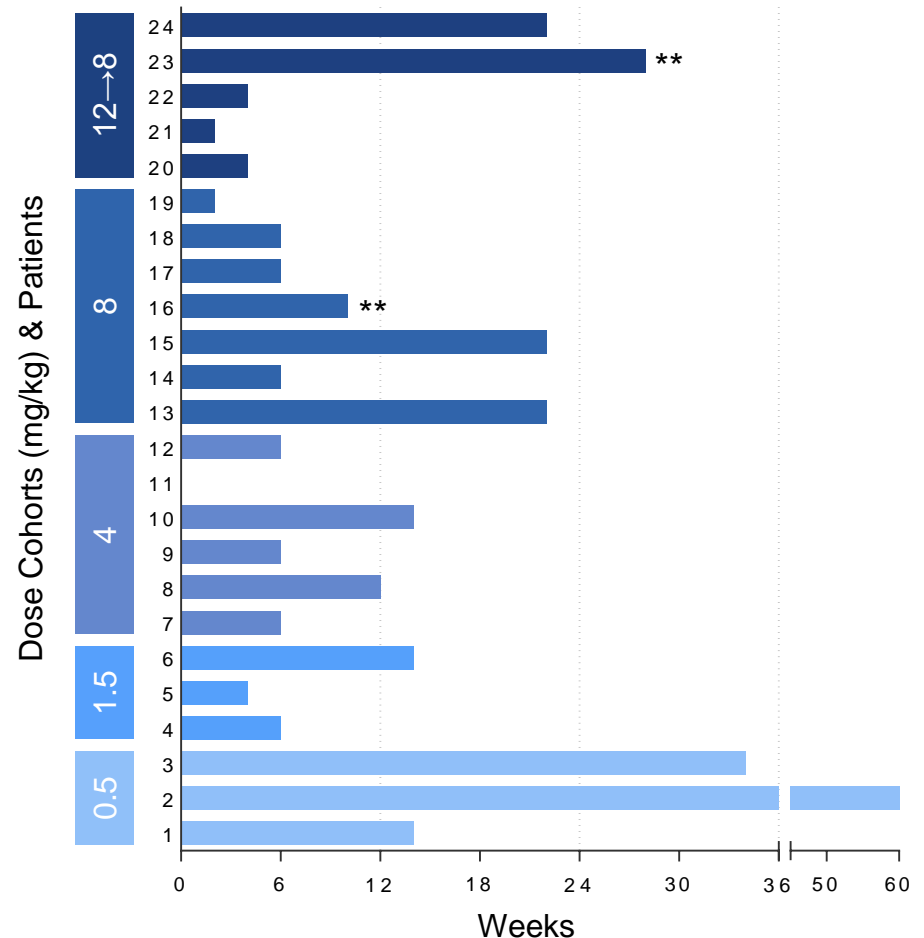
*MC38 syngeneic mouse model; **Patient-derived xenograft: GXA 3027.

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 (0/24 patients)
- Efficacy
 - Significant reductions in tumor volume in 2 patients with 1 confirmed PR
 - Stable disease at ≥ 12 wk in 10 patients (42%)

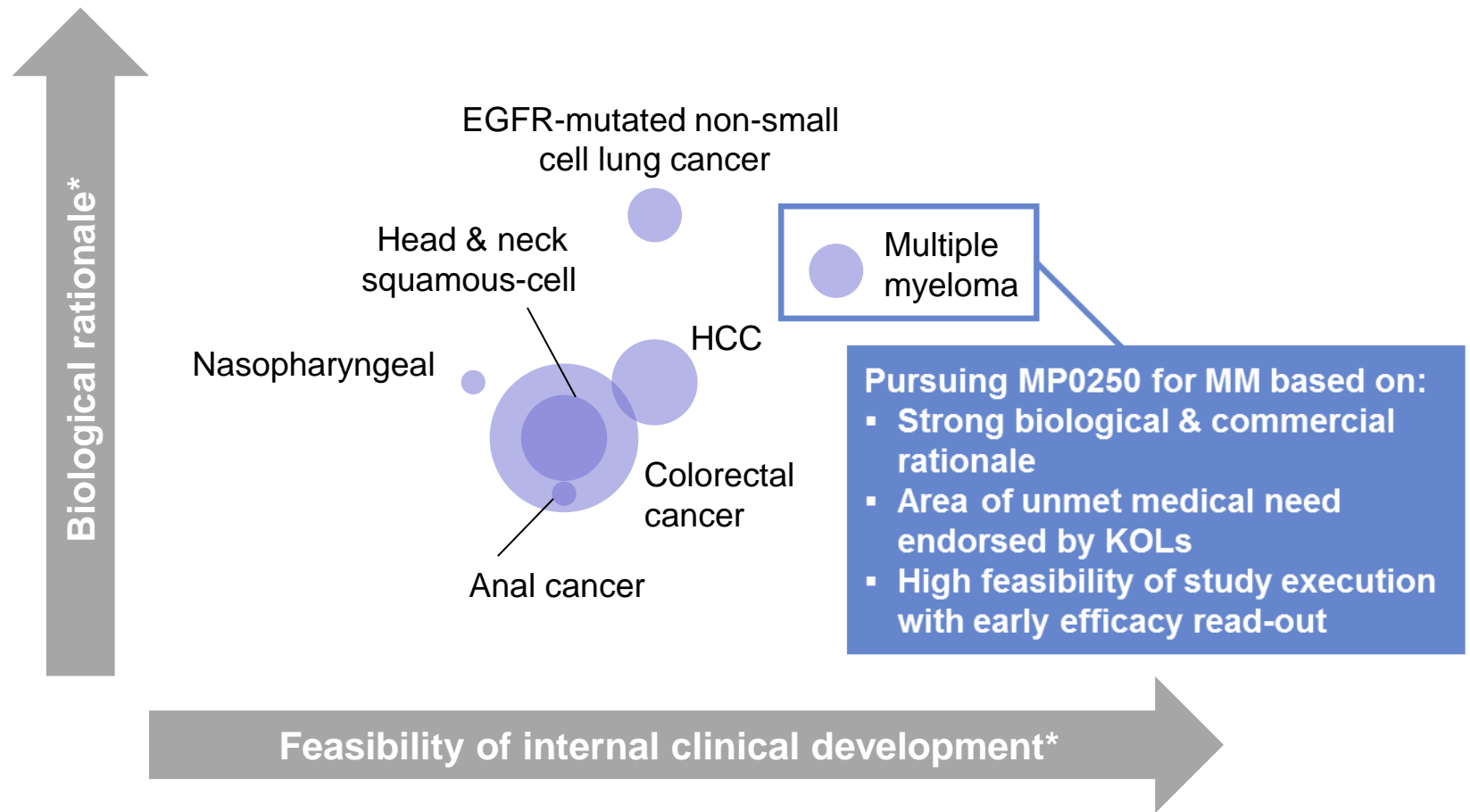
Treatment Duration of Individual Patients (N=24)*



*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

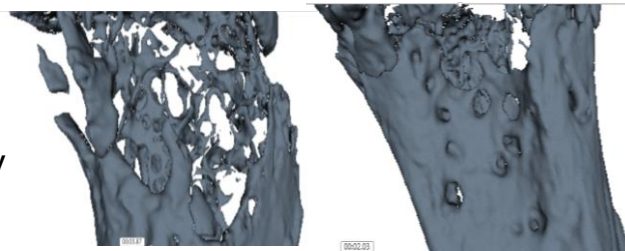
Vehicle

MP0250 +
Bortezomib

Muscle
invasion



Bone
morphology



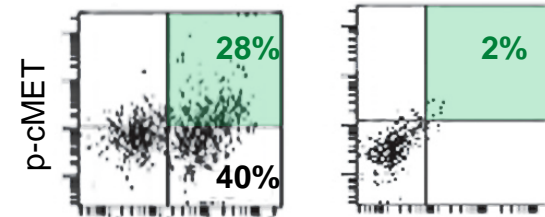
Clinical Rationale

HGF Rationale

HGF Receptor Activation¹

Newly
diagnosed

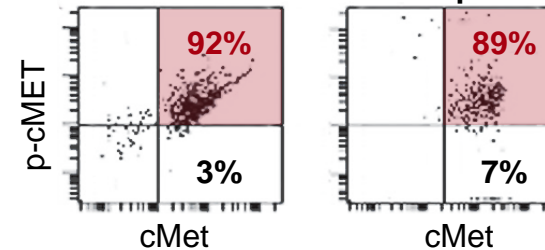
On partial
remission



SOC

Resistant

Relapsed



VEGF Rationale

A small MM study of bevacizumab (Avastin[®]) + bortezomib (Velcade[®]) demonstrated benefit over bortezomib alone²

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

Ophthalmology

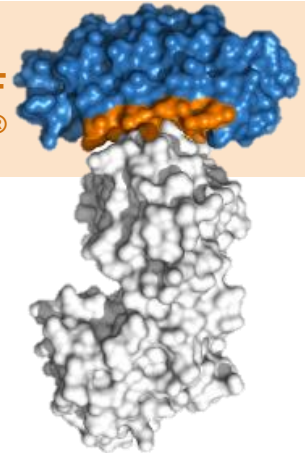
Abicipar: Most Advanced DARPin® Therapy

Abicipar

Abicipar

- Long-acting pegylated mono-DARPin® protein blocking VEGF
- Indications: Wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME)
- Global license agreement with Allergan

anti-VEGF
DARPin®



Development Stage

- Phase 3
 - 2 registration-enabling studies in wet AMD initiated July 2015
 - Clinical trial in DME planned by Allergan for H2 2017
- Phase 2
 - DME data presented at AAO 2016

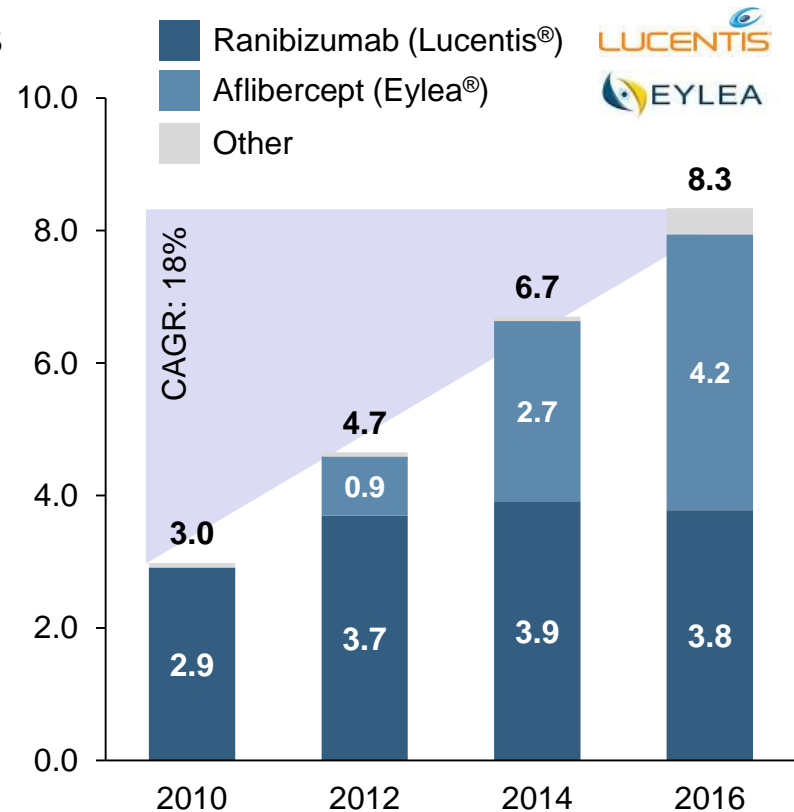
Differentiation & Potential Benefit

- Less frequent ocular injections compared with standard of care
- All development costs borne by Allergan

Retinal Diseases: Unmet Medical Needs Remain

- Wet AMD and DME are leading causes of blindness in western world
- Large and rapidly growing group driven by aging population
- Current standard of care is Lucentis® and Eylea®
- Significant unmet medical need for less frequent injections and doctor office visits

Global Wet AMD and DME Market Size (USDbn)^{1*}



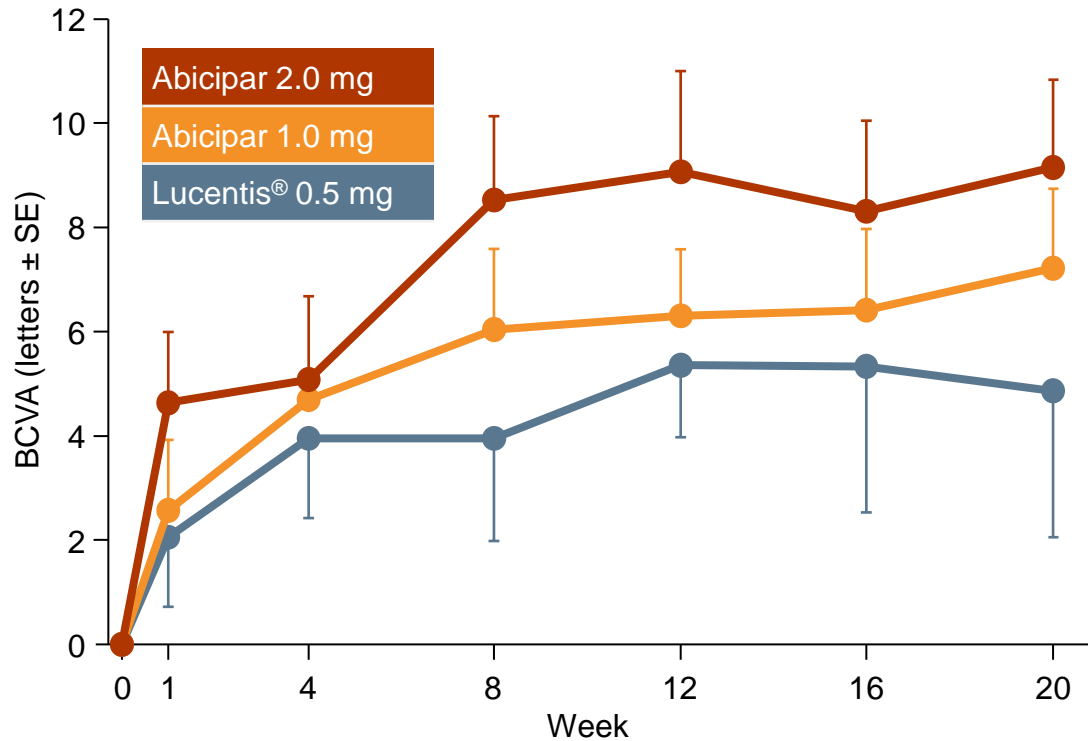
1. Reported by EvaluatePharma®, a service of Evaluate Ltd. (UK), www.evaluategroup.com. Accessed 27 Apr 2015.

*Avastin® is used off label.

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 phase 3

Dosing



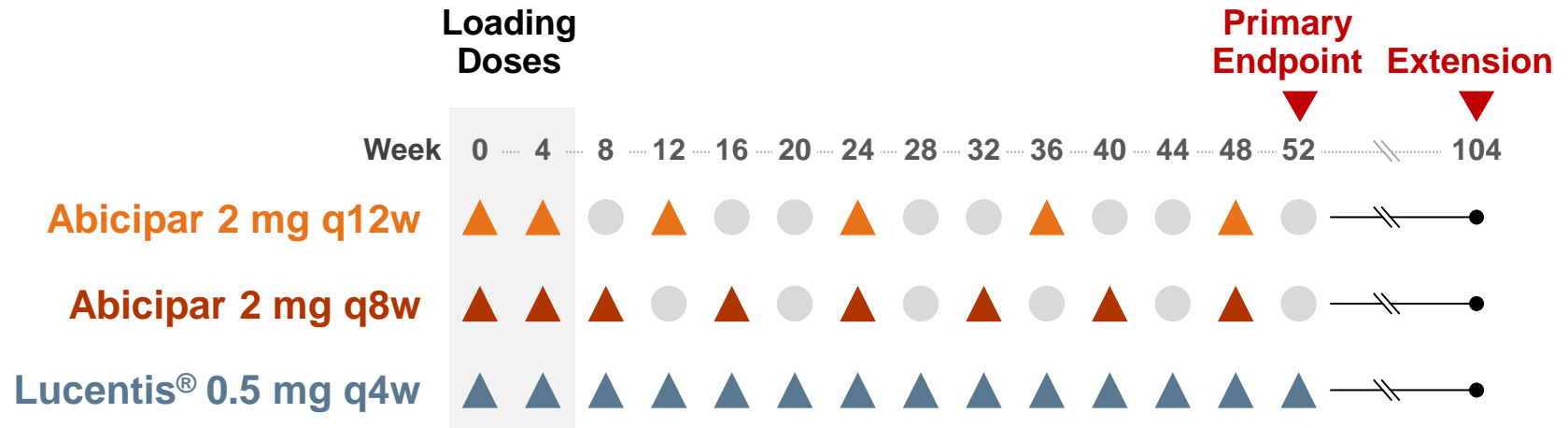
Allergan, 12 August 2014.

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

AE, adverse event.

CEDAR and SEQUOIA: Abicipar Registration Studies in Wet AMD

Abicipar

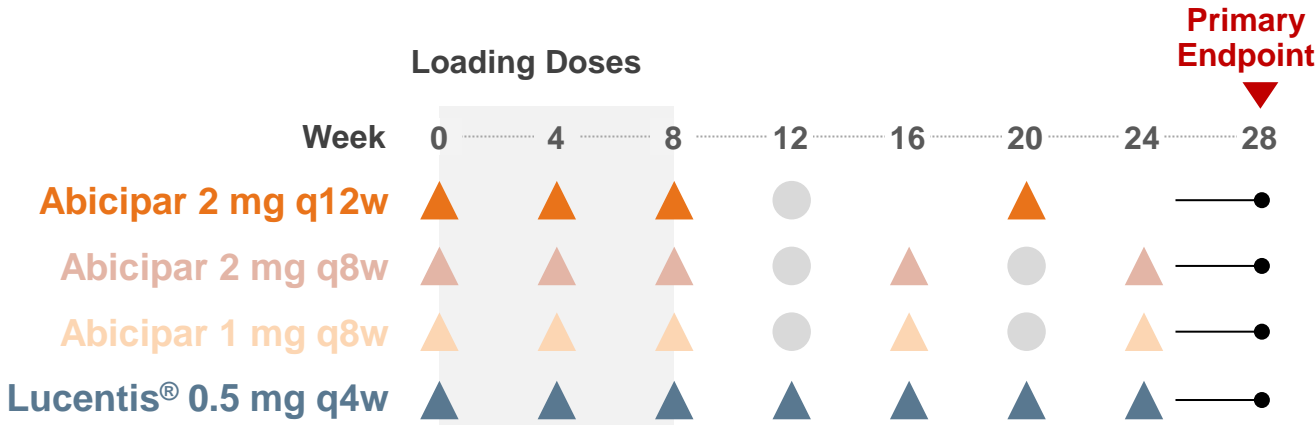


- 2 parallel, randomized, double-blind phase 3 studies
 - Expected global enrollment: 900 patients/study
 - Estimated study completion: Aug 2018

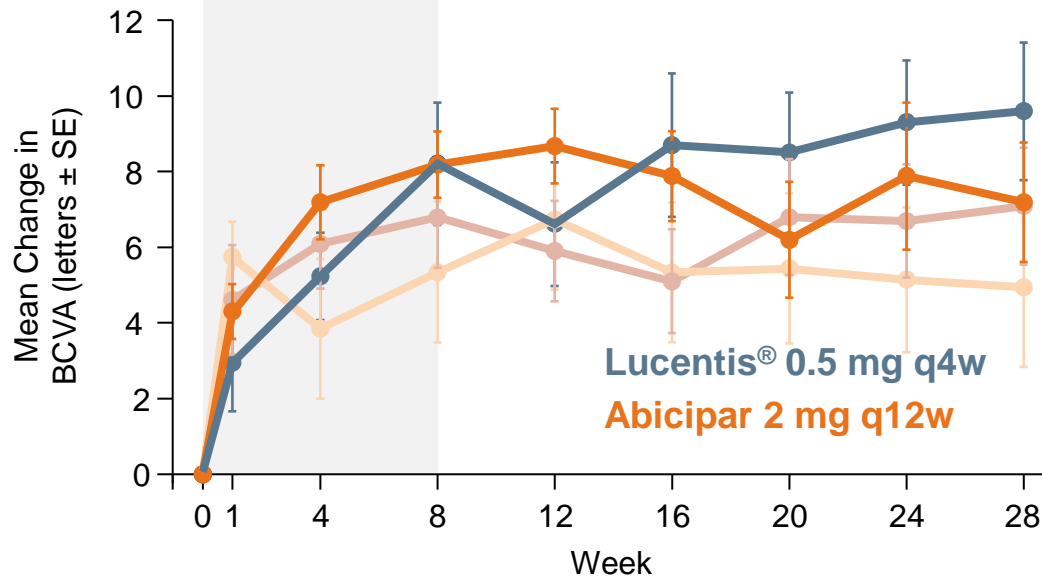
- Drug Safety Monitoring Committee (DSMC): no changes recommended Q4/16
- Next milestone: full study enrollment expected Aug 2017

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 Phase 3

Allergan 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 Partnership with Allergan



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		
Abicipar**: wet AMD	Full enrollment of Ph3	1-year efficacy data Ph3
Abicipar**: DME	Start of Ph3	

Cash CHF 180mn (Q4/16)

Financed well beyond key value inflection points

*Definition of the safe dose of MP0250 in combination with Velcade allowing transition to the efficacy part of the study

**Abicipar under development and control of Allergan. All costs borne by Allergan.

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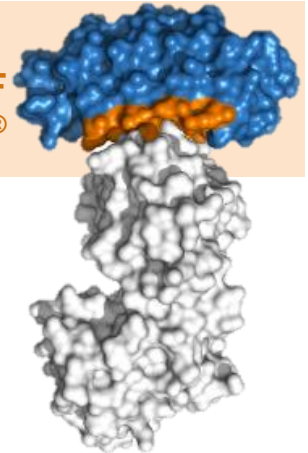
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anti-VEGF
DARPin®



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. Accessed 27 Apr 2015.