



# Pharma Business - Gaining Momentum



Outperforming market growth in 9M 2013



Sales growth driven by strong uptake of new products



Life-cycle management for new launch products in place

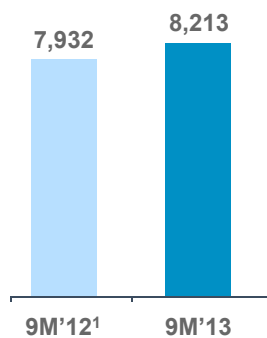


Development of 5 early/mid-stage pipeline assets accelerated

## 9M 2013 – Dynamic Business Development at Pharma

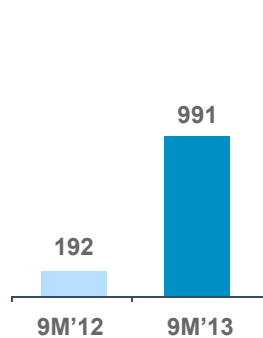


**Sales**  
in € million  
% currency & portfolio adj.



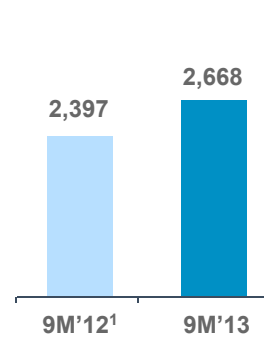
+9%

**New Product Sales**  
in € million



●

**EBITDA**  
before special items  
in € million

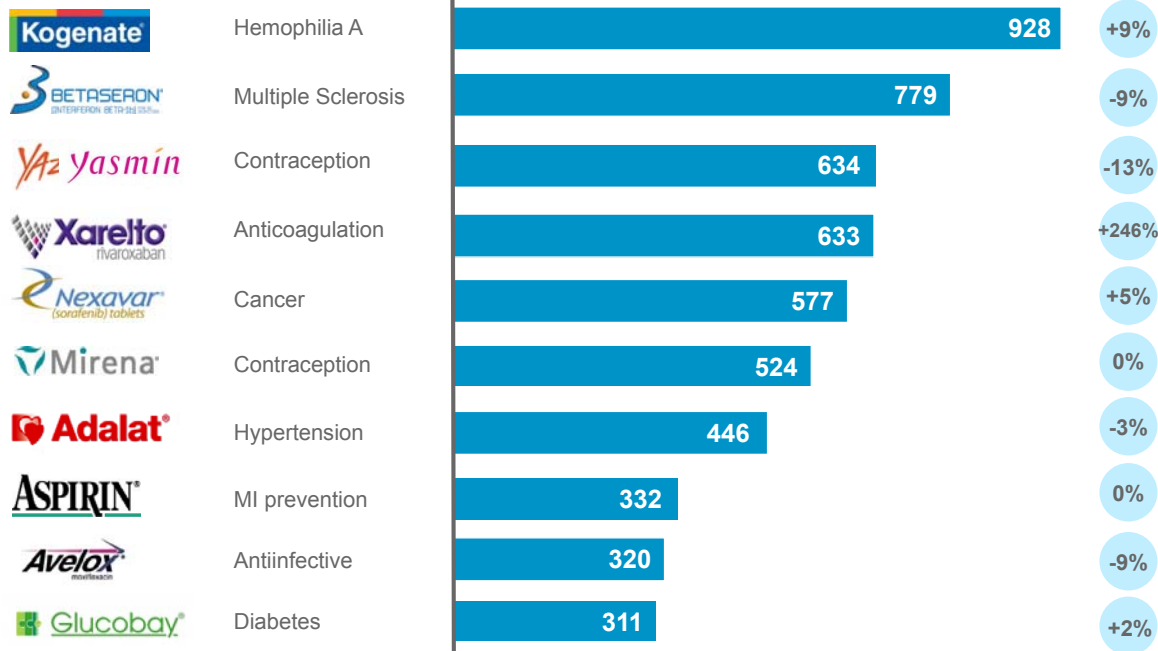


+11%



# 9M Performance of Top 10 Pharma Products

9M 2013 sales in € million ( $\Delta\%$  yoy Fx-adj.)



MI: Myocardial infarction



# Pharma – 2013 Financial Outlook

Sales  $\Delta$  Fx and portfolio adjusted

	2012 <sup>1</sup>	$\Delta$ vs. 2011	2013E
Sales	€10.8bn	+4%	High-single-digit % increase*
Sales of New Launch Products	€368m	●	>€1.4bn
EBITDA before special items	€3.2bn	+9%	Improve
Margin	29.9%	0 bp	Improve

# 7% 2012 CAGR 2015e

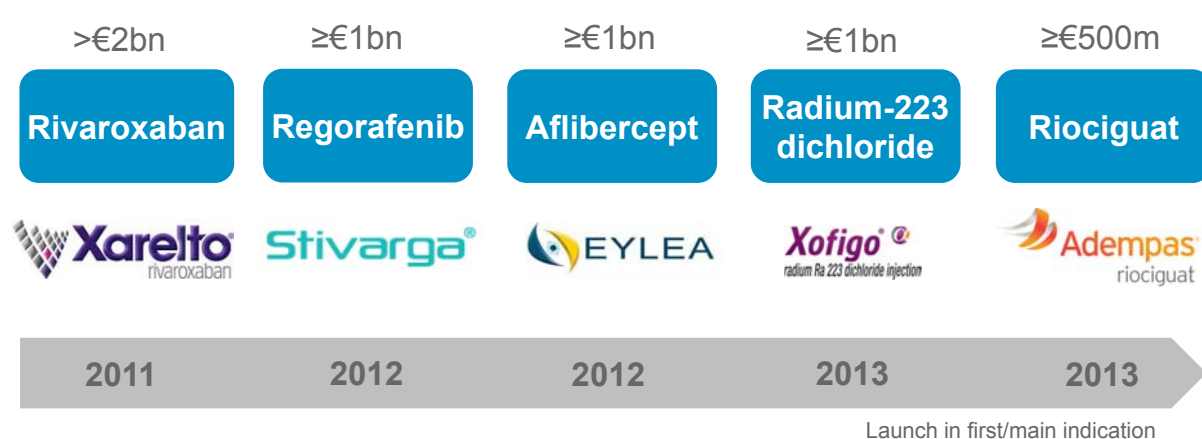
## Pharma: Sales Growth Acceleration Driven by New Products

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### New Launch Products Have a Business Transforming Potential



**Combined\* Peak Sales Potential >€5.5bn**



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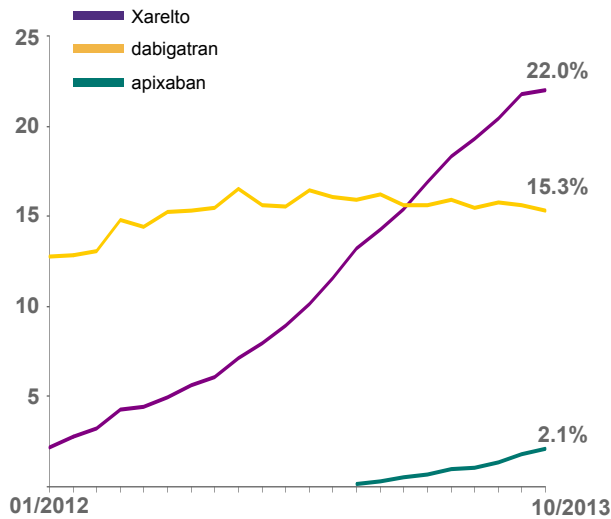
\*Combined peak sales potential for Xarelto, Stivarga, Eylea, Xofigo and Adempas assuming approvals and launches as planned

# Xarelto – Outperforming Competition, Exceeding Expectations



## Xarelto – Leading Novel OAC<sup>1</sup> Globally

Sales market share in % (retail & hospital combined)



- World-class launch, achieved leading position in the novel anticoagulants segment in key markets
- Uptake significantly exceeding expectations
- New sales target 2013: >€800m (prev.: ~€600m)
- Broadest label of novel oral anticoagulants with once-daily-dosing advantage<sup>2</sup>

<sup>1</sup> Oral anticoagulant; <sup>2</sup> Exception 15mg BID dosing for treatment of acute DVT/PE or 2.5mg BID for ACS sec. prevention

# Eylea – Excellent Launch Trajectory



## Eylea wAMD Market Share in Selected Countries\*



40 – 50%



40 – 50%



40 – 50%

- Clinically developed for the treatment of various back-of-the-eye diseases
- Fixed every-other-month dosing for wAMD after initial loading doses
- Roll-out in ex-US markets ongoing
- Expansion into back-of-the-eye diseases beyond wAMD underway:
  - CRVO (approved in EU [8/13], Jp [11/13])
  - mCNV (filed in Jp [11/13])
  - DME (filed in EU [11/13])

\*) Market share as of October 2013 (Source IMS)

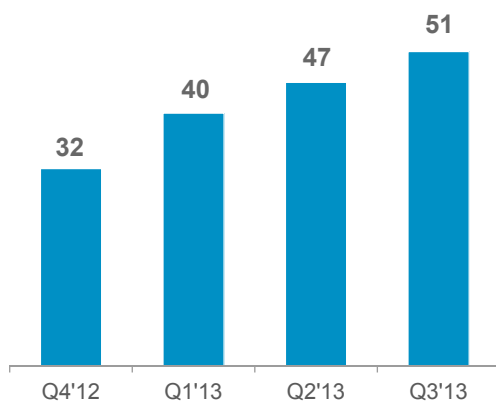
wAMD: Wet age-related macular degeneration, CRVO: Central retinal vein occlusion; mCNV: Myopic choroidal neovascularization; DME: Diabetic macular edema

# Stivarga – Treatment of Gastro-intestinal Cancers



## Quarterly Sales Development (€m)

Stivarga®



- Oral cancer drug, potently blocking multiple protein kinases
- Launched for treatment of mCRC and mGIST in the US & Japan
- Launched for treatment of mCRC (8/13) and filed for mGIST (9/13) in Europe
- Encouraging initial uptake

# Xofigo – A New Treatment for CRPC Patients with Bone Metastases

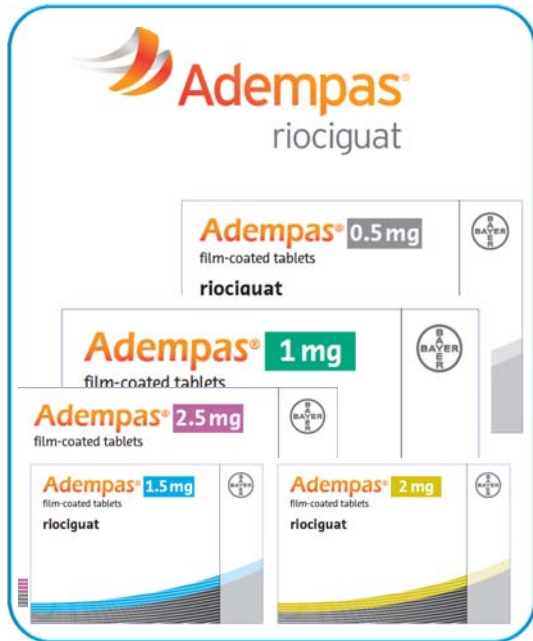


**Xofigo®**  
radium Ra 223 dichloride injection



- First in class alpha-pharmaceutical
- Treatment of CRPC with symptomatic bone metastases and no known visceral metastatic disease
- Launched in the US (06/13)
- Approved in Europe (11/13) – launch underway
- High awareness among oncologists and urologists

# Adempas – First Approved Drug for Two Forms of Pulmonary Hypertension

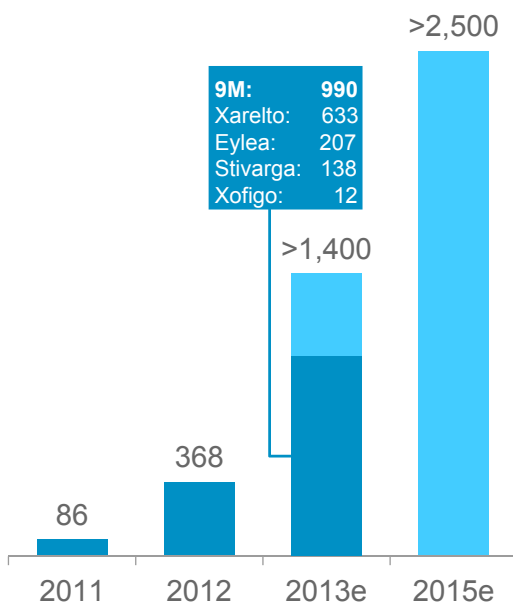


- Oral soluble guanylate cyclase (sGC) stimulator with exciting phase III results in PAH and CTEPH
- First and only drug receiving marketing authorization for the treatment of CTEPH
- Approved in the US for treatment of PAH and CTEPH (10/13)
- Encouraging early launch feedback
- Filed in Europe (2/13) and Japan (5/13)

# New Products Drive Growth and Rejuvenate Portfolio

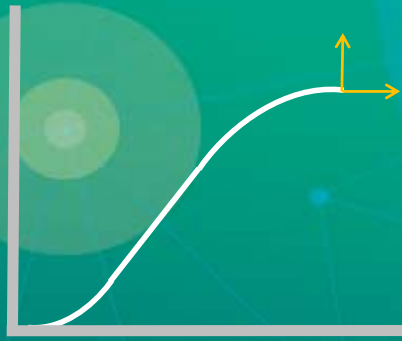


Sales in €m



- Executing world class launches
- New product sales significantly exceeding expectations
- Incremental investment into marketing & sales to further drive growth
- Additional R&D funding to fully exploit life-cycle management opportunities





# Life-cycle Management

## Maximizing the Value of New Launch Products

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### Expanding and Strengthening the Profile of Xarelto



- Significant medical need in thromboembolic disease areas
- Heterogeneous patient population with atrial fibrillation deserves further characterisation
- Two-dimensional approach in life-cycle management

#### Expansion into additional thromboembolic disease areas

- Peripheral arterial disease / coronary arterial disease
- Chronic heart failure with coronary arterial disease

#### Strengthening the clinical profile in patients with atrial fibrillation

- Patients with percutaneous coronary intervention
- Patients who undergo cardioversion
- Patients undergoing ablation

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# Entering Additional Cancers of the Gastro-Intestinal Tract with Stivarga



- Positive clinical data in metastatic colorectal cancer and 2nd-line hepatocellular carcinoma
- Mode of action suggesting activity in a broad range of tumor types
- Life-cycle management targets:

Expand in HCC and CRC	Expand to additional tumor types
<ul style="list-style-type: none"> <li>● Phase III in 2nd-line hepatocellular carcinoma underway</li> <li>● Phase III in colorectal cancer after resection of liver metastases</li> </ul>	<ul style="list-style-type: none"> <li>● Signal generating phase I studies in various cancer types</li> </ul>

# Addressing Multiple Life-Cycle Opportunities for Xofigo (Radium-223 dichloride)



Life-Cycle Opportunities	Addressed Through
Repeat dosing in CRPC	Phase II trial assessing the short and long-term safety of re-treatment
Higher dose in CRPC	Phase II trial with dose higher than the approved 50 kBq/kg
Earlier disease stages of CRPC	Phase III combination trial with abiraterone in chemo-naïve patients with asymptomatic or mildly symptomatic bone metastases
Combination study in CRPC	
Expansion into additional cancer types	Phase I and/or II studies in breast cancer, osteosarcoma and potentially in additional cancer types





## Pulmonary hypertension with idiopathic interstitial pneumonia (PH-IIP)

- Positive phase II data in PH-ILD prompt initiation of phase IIb in PH-IIP (a specific sub-segment of PH-ILD)
- Majority of PH-IIP patients suffer from pulmonary hypertension due to idiopathic pulmonary fibrosis
- No approved treatment option

## Diffuse systemic sclerosis (SSc)

- Chronic systemic autoimmune disease characterized by fibrosis
- No approved treatment
- Strong preclinical antifibrotic data



## Accelerating the Development of 5 early/mid-stage Pipeline Assets

# Five New Molecular Entities Selected For Accelerated Development



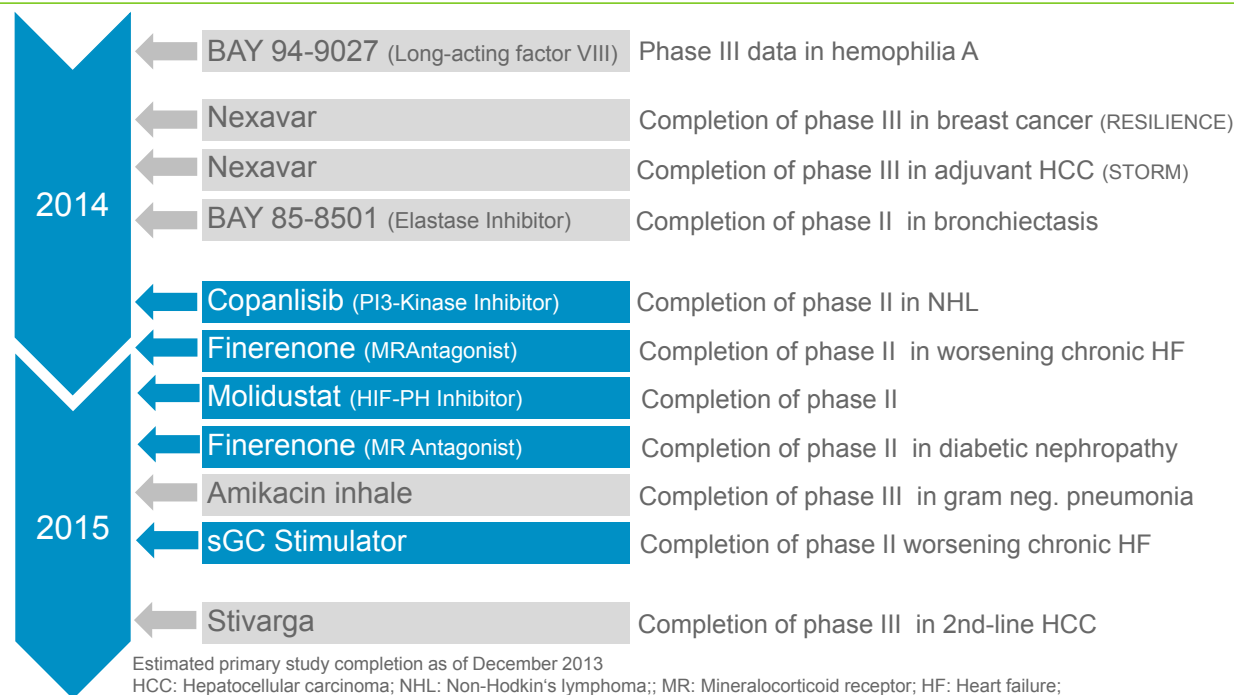
Project	Mechanism	Indication	Status
<b>Copanlisib</b> (BAY 80-6946)	PI3-Kinase Inhibitor	Cancer	Phase IIa in NHL ongoing
<b>Finerenone</b> (BAY 94-8862)	MR Antagonist	Chronic heart failure (CHF) Diabetic nephropathy	Phase IIb in CHF ongoing
<b>Molidustat</b> (BAY 85-3934)	HIF-PH Inhibitor	Anemia	Phase IIb ongoing
<b>sGC-Stimulator</b> (BAY 1021189)	sGC Stimulator	Worsening chronic heart failure	Phase IIb ongoing
<b>sPRM (S-PRAnt)</b> (BAY 1002670)	Progesterone Receptor Antagonist	Symptomatic uterine fibroids	Phase I completed

# Positive Proof-of-Concept Increases Confidence in NME-quality



<b>Copanlisib</b>	▶ 100% of patients (6/6) with follicular lymphoma achieved a partial response as best response in phase I
<b>Finerenone</b>	▶ Phase II results in CHF patients suggest improved safety with at least similar efficacy compared to spironolactone
<b>Molidustat</b>	▶ Significant increase in levels of endogenous EPO and reticulocytes demonstrated in phase I
<b>sGC-Stimulator</b>	▶ Improvement in important cardiological parameters observed in phase I
<b>sPRM (S-PRAnt)</b>	▶ Phase I data demonstrated reversible induction of amenorrhea

# Major Expected Pharma Pipeline Newsflow 2014/2015

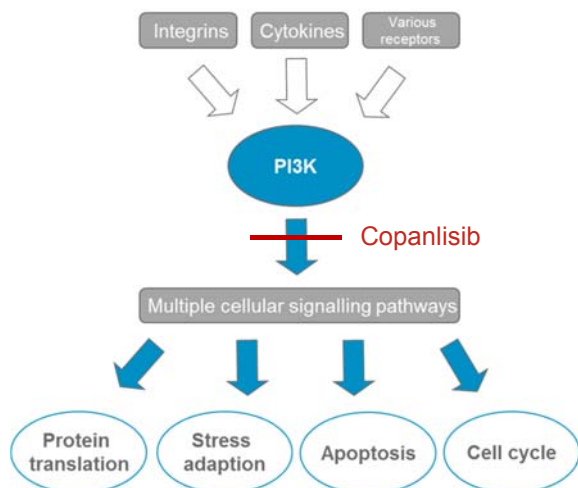


## Appendix – Pharma Pipeline

# Copanlisib (BAY 80-6946) – A PI3K-Inhibitor in Phase II in Cancer



Phosphatidylinositol-3 kinases (PI3K) play a central role in cellular signal transduction processes

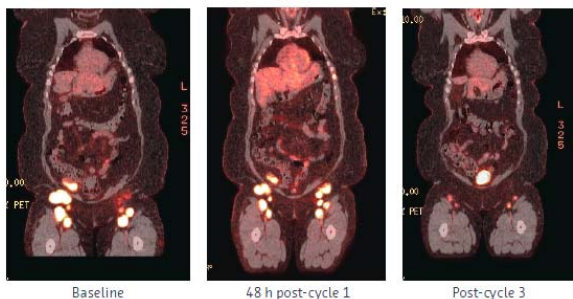


- In most tumor cells, the PI3K-signaling cascade is activated and provides important tumor growth and survival signals
- Copanlisib is a pan class I PI3K-inhibitor with dominant  $\alpha/\delta$  activity
- Copanlisib has shown a broad anti-tumor spectrum in preclinical tumor models
- Phase IIa in Non-Hodgkin's lymphoma is ongoing; completion expected end of 2014

# Copanlisib Has Shown Substantial Activity in Follicular Lymphoma



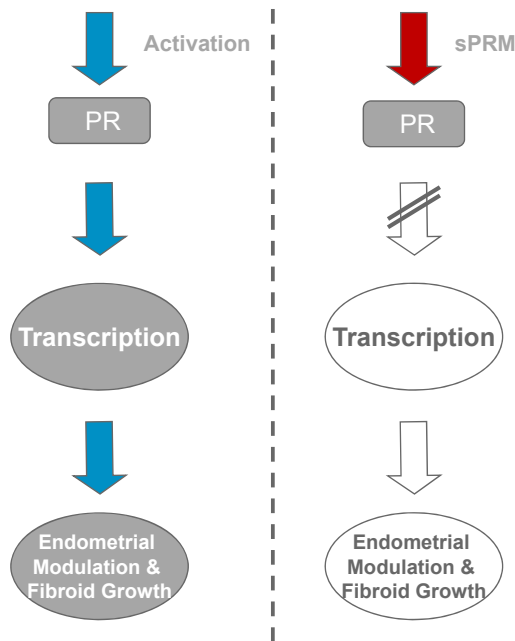
<sup>18</sup>FDG-PET scans of a follicular lymphoma patient with partial response



52-year-old female with FL, grade 1-2, diagnosed stage IVa

- Phase I trial successfully completed
  - 100% of patients (6/6) with follicular lymphoma (FL) responded to therapy achieving a partial response as best response\*
  - Maximum response duration > 840 days
  - Encouraging signals in diffuse large B cell lymphoma patients
- <sup>18</sup>FDG-PET data suggest that Copanlisib has rapid antitumor activity

# Selective Progesterone Receptor Modulation for Treatment of Uterine Fibroids

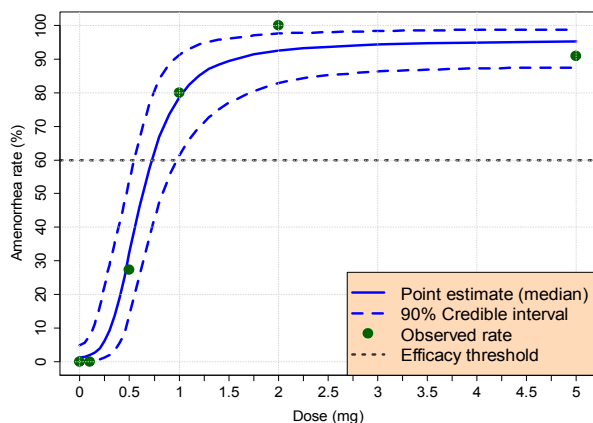


- Uterine fibroids are the most common benign tumors in women of reproductive age: 5-10% of premenopausal population suffers from symptomatic fibroids
- Symptoms may include heavy menstrual bleeding and tumor size related symptoms
- Current therapies include surgical procedures or short-term use of GnRH analogs for estrogen depletion
- Growth of fibroids strongly depends on progesterone and estrogen
- Progesterone receptor modulation may offer long-term treatment of uterine fibroids without estrogen depletion side effects of GnRH analogs

# sPRM (BAY 1002670) – For the Treatment of Symptomatic Uterine Fibroids

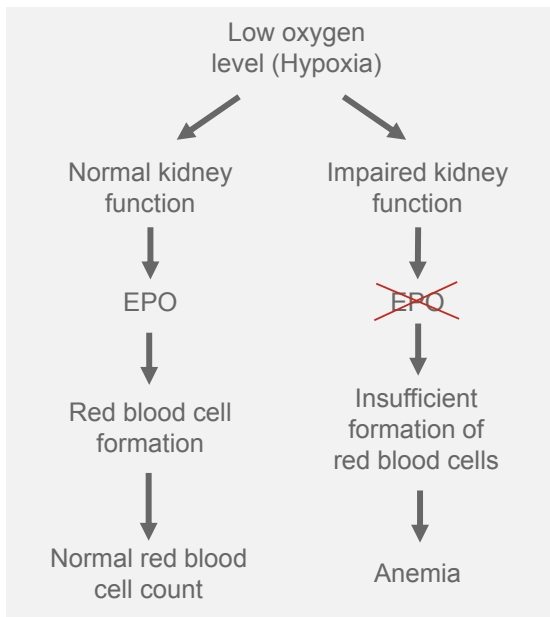


**Phase I data BAY 1002670**  
Dose effect curve for amenorrhea rate



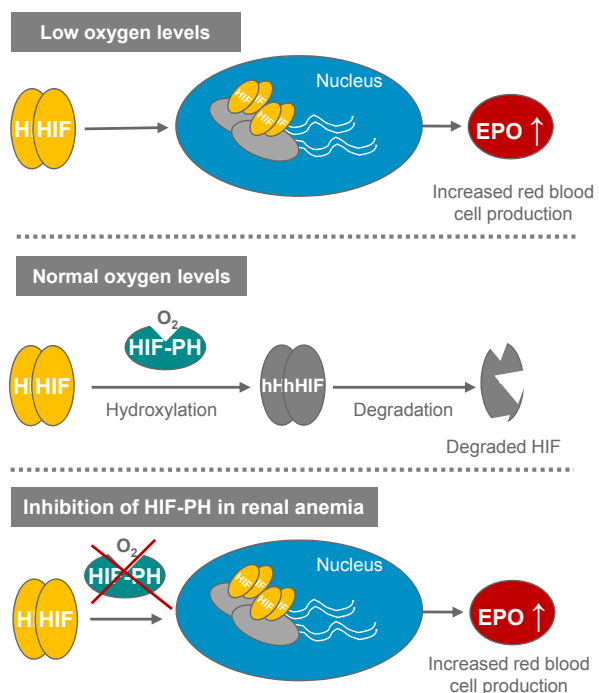
- BAY 1002670 is a novel oral, highly potent and selective progesterone receptor modulator
- Exhibits marked efficacy in an innovative humanized fibroid disease model<sup>1</sup>
- Phase I data (N=67) showed proof of concept including:
  - Reduction of bleeding: induced amenorrhea (non-bleeding) in >60% of women treated with dosages >1mg/day
  - Reversal of amenorrhea after treatment cessation
  - No prohibitive safety findings

# Renal Anemia is an Important Area of Unmet Medical Need



- Diseased kidneys do not produce sufficient levels of erythropoietin (EPO) in response to hypoxia, leading to anemia
- CKD/ESRD is the leading cause of anemia in industrialized countries
- Substitution with parenteral EPO is standard of care – however, unphysiologically high EPO doses correlate with significant side effects
- There is a need for novel therapies that lack the side effects of high doses of EPO-substitution

# Molidustat – An Oral HIF-PH Inhibitor for Treatment of Renal Anemia



Under hypoxia conditions, HIF is activated and induces the synthesis of erythropoietin (EPO) in the kidneys which stimulates red blood cell formation

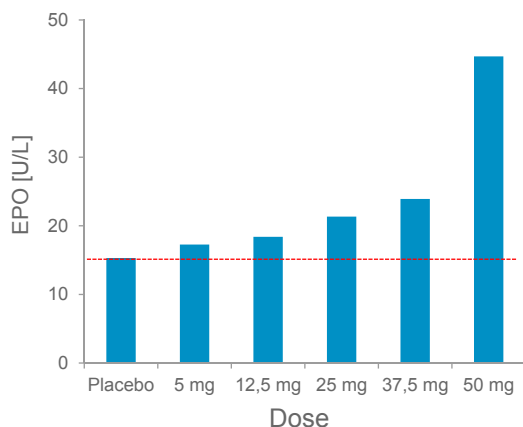
Under normal oxygen conditions, HIF gets hydroxylated by HIF-PH and then degraded

Inhibition of HIF-PH increases the stability of HIF resulting in production of endogenous EPO - potential novel therapeutic approach for the treatment of renal anemia

# Molidustat (BAY 85-3934) – Proof of Concept Demonstrated



## Maximal EPO concentration after single dose administration of Molidustat (Phase I)

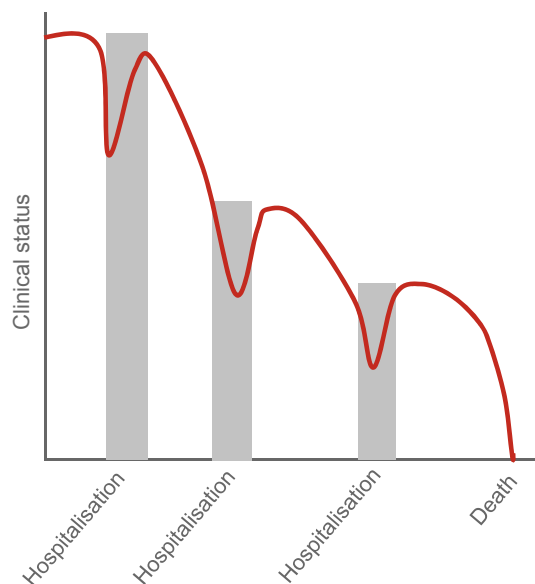


- Molidustat is a novel oral inhibitor of the enzyme HIF-PH
- In development for the treatment of anemia associated with chronic kidney disease
- Phase I in healthy subjects showed:
  - Significant increase of EPO levels after  $\geq 12.5$  mg
  - Significant increase of reticulocytes for doses  $\geq 37.5$  mg
  - No prohibitive safety findings

# sGC Stimulation to Address Unmet Medical Need in Patients with Heart Failure



Patients who require hospitalization due to HF (worsening HF) have a poor prognosis with high rates of re-hospitalization and death

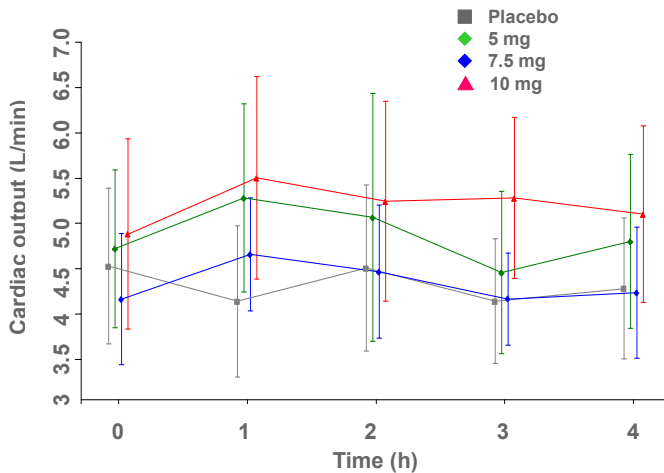


- Worsening chronic heart failure is an established indication with high medical need
- Limitations of standard of care include tolerance, oxidative stress, endothelial dysfunction and venoselectivity
- sGC stimulation can improve hemodynamics via restoration of cardiac and vascular cGMP signaling
- sGC stimulation may provide a new principle to reduce event rates in patients with worsening chronic heart failure

# sGC Stimulator (BAY 1021189) – Improvement of Cardiovascular Function

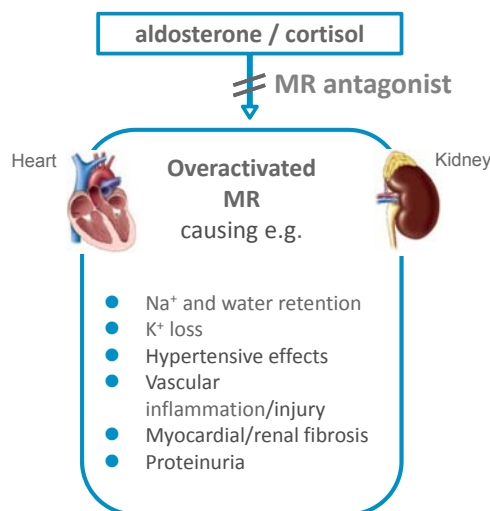


Phase I of BAY 1021189 show improved cardiac output (n = 36)



- BAY 1021189 is a novel sGC stimulator suitable for once-a-day dosing
- Phase I successfully completed – improvement observed in important cardiological parameters, including:
  - Cardiac output / index (“volume of blood pumped by the heart”)
  - Systemic vascular resistance
  - Stroke volume
- No untoward safety findings in phase I
- BAY 1021189 may offer a new treatment modality for HF

# MR-Inhibition is a Proven Principle in the Treatment of Heart Diseases



- MR has multiple functions:
  - Regulation of salt, fluid homeostasis and blood pressure
  - Mediator of oxidative stress, subsequent inflammation, fibrosis and cardiorenal disease
- Steroidal MR antagonists spironolactone and eplerenone have been shown to be effective in reducing cardiovascular mortality in patients with HF but are underutilized due to the risk of hyperkalaemia, renal dysfunction and anti-androgenic / progestogenic side effects
- Steroidal MR antagonists are not approved for kidney diseases eg. diabetic nephropathy



# Finerenone – A Novel Non-Steroidal and Selective MR-Antagonist



## Key phase II findings in patients with CHF and moderate\* (part B) CKD :

Data at Day 29 +/- 2 in part B of the study with 392 pts in total; Spironolactone was given at an initial dose of 25mg o.d. and uptitrated to 50mg o.d. on day 15±1 if sodium potassium concentration remained ≤4.8mmol/L; \* eGFR 30-60 ml/min/1.73m<sup>2</sup>

### Mean increases in serum potassium concentration

Finerenone 10mg o.d.:	0.21 mmol/l
Spironolactone:	0.45 mmol/l
	<i>P</i> < 0.001

Indicates lower incidence of hyperkalaemia

### Mean change in estimated glomerular filtration rate

Finerenone 10mg o.d.:	-2.69 ml/min/1.73m <sup>2</sup>
Spironolactone:	-6.70 ml/min/1.73m <sup>2</sup>
	<i>P</i> < 0.05

Indicates lower incidence of worsening of renal function

### Median change from baseline in NT-proBNP

Finerenone 10mg o.d.:	-193 pg/mL
Spironolactone:	-170 pg/mL
	(descriptive analysis)

Decreased BNP/NT-proBNP – a key parameter for cardiac stress

Phase II results suggest improved safety with at least similar efficacy on key cardiac and renal parameters compared to spironolactone