



# *Driving Performance and Delivering New Growth Opportunities*



**Capital Markets Day  
London, December 5, 2018**

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# The Pharma Market Will Remain Attractive



## Major market dynamics

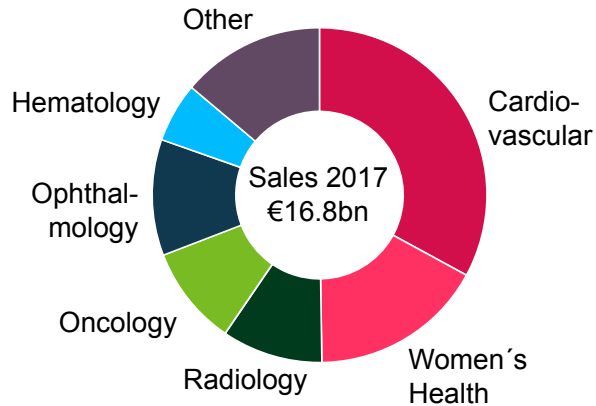
- // Aging population
- // Accelerating pace of innovation
- // Declining R&D productivity
- // Technological disruption by breakthrough science
- // Digitalization across the value chain
- // Pressure on price for value continues to increase
- // Non-traditional new entrants

Source: IQVIA Market Prognosis Update 2018-22 incl. Radiology

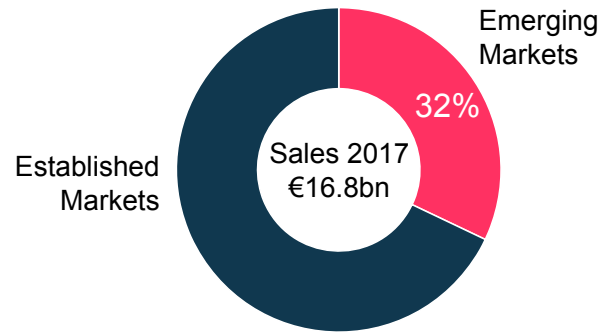


# Innovative Medicines in Areas of High Unmet Medical Need

## Therapeutic area focus



## Emerging markets exposure



## Global leadership in important therapeutic areas

- // **No. 1** in Retinal Diseases
- // **No. 1** in Women's Health
- // **No. 1** in Radiology
- // **No. 2** in Cardiovascular
- // **No. 2** in Hematology

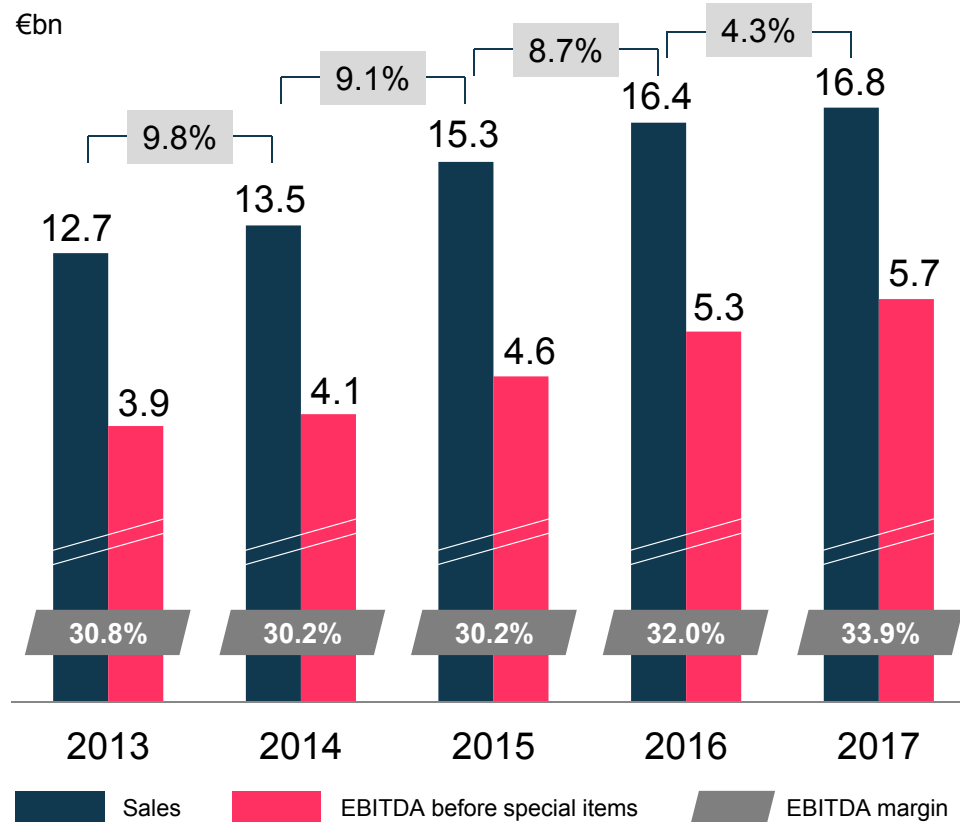
## Leading Brands



Emerging markets include Latin America, Asia (w/o Japan, Australia, New Zealand), Africa and Middle East incl. Turkey, Eastern Europe



# Continued Sales Growth and Margin Expansion

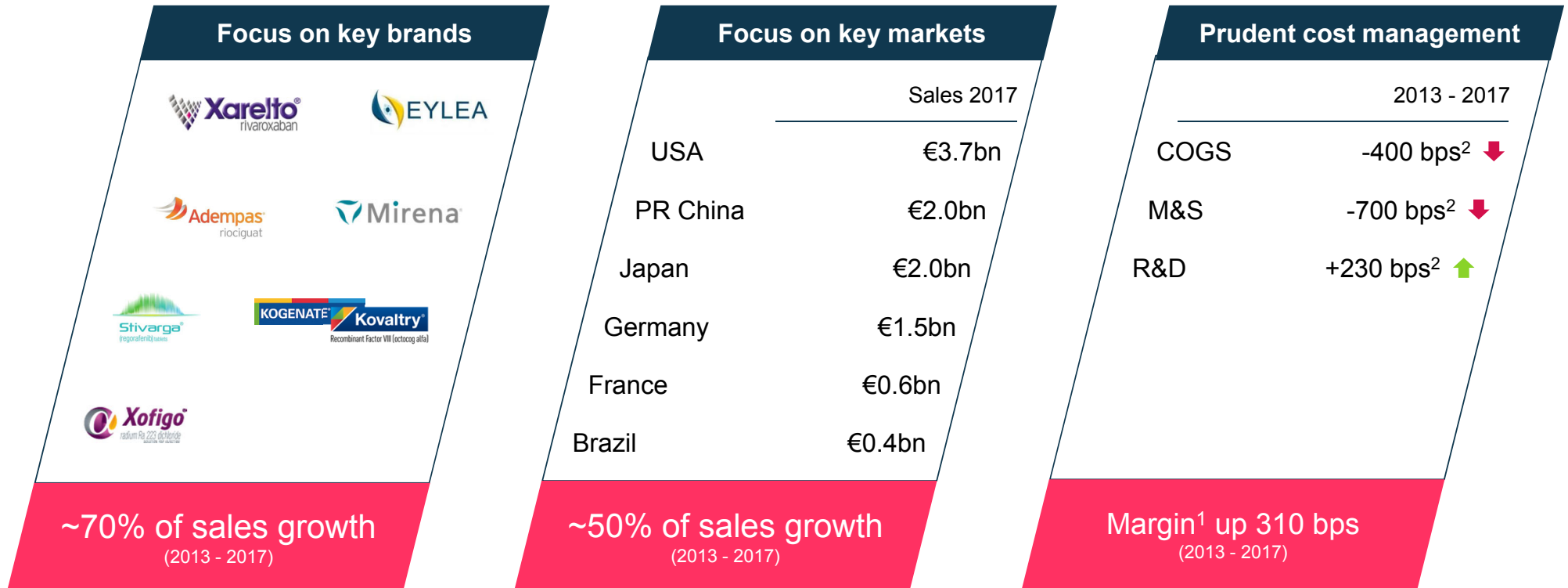


Including Radiology; Sales growth currency and portfolio adjusted; EBITDA margin before special items

- // Sales growth above industry level
- // Successfully launched and commercialized innovative products, with Xarelto and Eylea becoming blockbuster brands
- // Disciplined resource allocation
- // 2017 EBITDA margin at upper end of guidance corridor of 32-34% – achieved one year earlier than originally planned
- // Increase in R&D investment by ~€1 billion p.a. to c.17% of sales



# Key Drivers for Growth and Margin Expansion



<sup>1</sup> EBITDA margin before special items; bps: Basis points, <sup>2</sup> as percentage of sales



# Focused Leadership Strategy to Deliver Mid-term Targets and to Ensure Long-term Success

## 2022 Targets for Pharma

**Sales CAGR 4 - 5%**  
(Basis 2018e of ~€16.8bn)

**EBITDA-margin >35%**

## Focused Leadership



### Relentless Focus

- // Stringent focus on **key brands** and **markets incl. China**
- // Achieve **category/segment leadership** within **Oncology** and **Cardiovascular**



### Innovation

- // Supplement organic pipeline with select **in-licensing** and **bolt-on M&A options**
- // **Transform innovation model** to ensure long-term success beyond LoEs



### Excellence in Execution

- // Maintain **operational focus**
- // Deliver on **mid-term growth and margin aspirations**
- // Execute **efficiency measures**

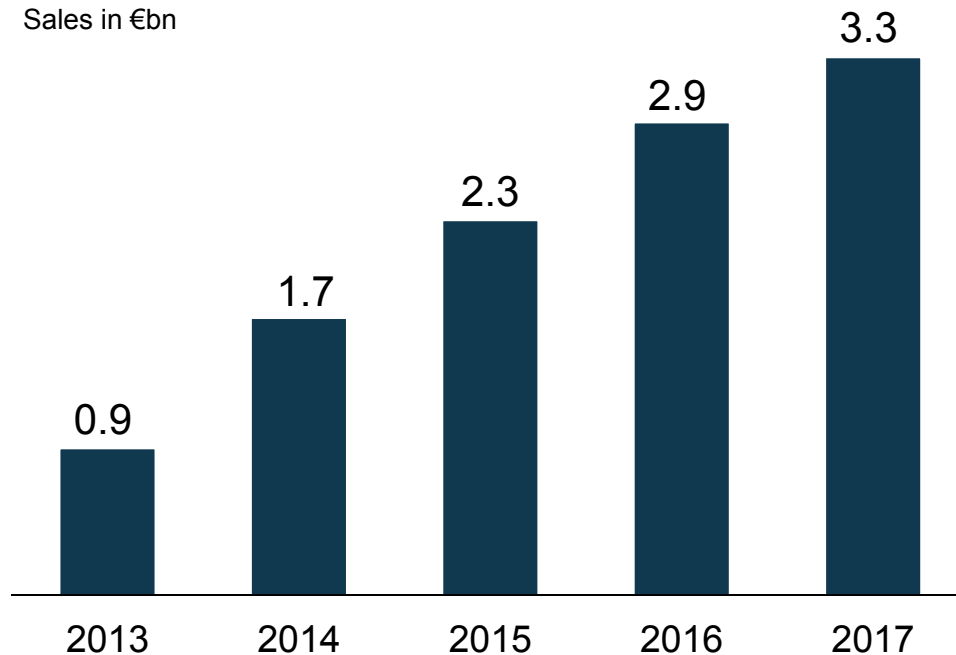
2022 targets at constant currencies, not including portfolio measures; EBITDA margin before special items; LoE: Loss of exclusivity



# Xarelto – Continued Growth of a Leading Anticoagulant



Sales in €bn



- // Most broadly indicated anticoagulant for use in venous and arterial thromboembolic conditions
- // A leading pharma brand with global sales of €5.0bn in 2017 incl. sales at Johnson & Johnson
- // New CAD/PAD indication launching in EU and the US
- // Peak sales potential: >€5.0bn<sup>1</sup>
- // Further growth driven by:
  - // Under-served patient populations
  - // Demographics
  - // Shift from warfarin
  - // New indications targeting patients currently not treated with anticoagulants

CAD: Coronary artery disease; PAD: Peripheral artery disease  
<sup>1</sup>Ex-US sales plus royalty from J&J as reported by Bayer

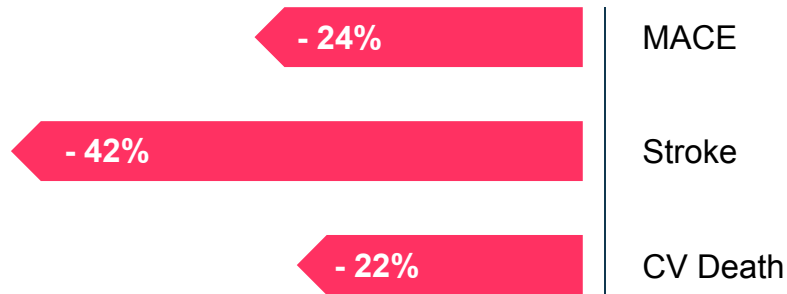




# Xarelto Demonstrates Significant Therapeutic Benefits in CAD/PAD

Potential for Changing the Current Standard of Care

## Efficacy (RRR)



// Combination of Xarelto 2.5 mg bid + aspirin 100 mg od compared to aspirin 100 mg od alone (COMPASS)

// Significant reduction in the relative risk for the primary composite of stroke, myocardial infarction and cardiovascular death (MACE)

// 20% improvement in net clinical benefit<sup>1</sup>

## Safety

// Low overall bleeding incidence rates, although major bleeding was increased

// No significant increase in fatal or intracranial bleeding

// Provides a larger relative risk reduction than dual anti-platelet strategies

// Xarelto is the only oral anticoagulant that is approved for the prevention of atherothrombotic events in patients with CAD or PAD

Eikelboom et al., N Engl J Med 2017; 377: 1319-1330

CAD: Coronary artery disease; PAD: Peripheral artery disease; MACE: Major adverse cardiovascular events; CV: Cardiovascular; RRR: Relative risk reduction

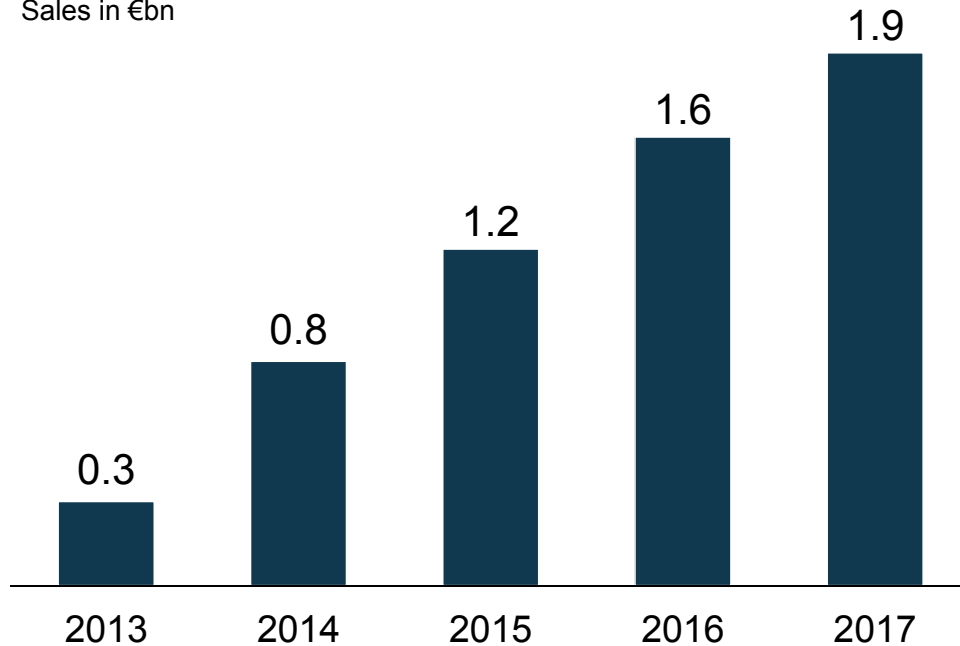
<sup>1</sup> Net clinical benefit was defined as the composite of stroke, cardiovascular death, myocardial infarction, fatal bleeding or symptomatic bleeding in a critical organ



# Eylea – A Leader in Retinal Diseases



Sales in €bn



// A leader in retinal diseases with global brand sales of €5.2bn in 2017 incl. sales at Regeneron<sup>1</sup>

// Approved for the treatment of 5 retinal diseases: wAMD, DME, BRVO, CRVO, mCNV

// Treat and extend dosing regimen with injection intervals of up to 12 weeks or more for wAMD

// Peak sales potential: >€2.5bn<sup>2</sup>

// Further growth driven by:

// Continued generation of real-life experience in wAMD across key markets and treatment-naïve patient share gains

// Market expansion in DME

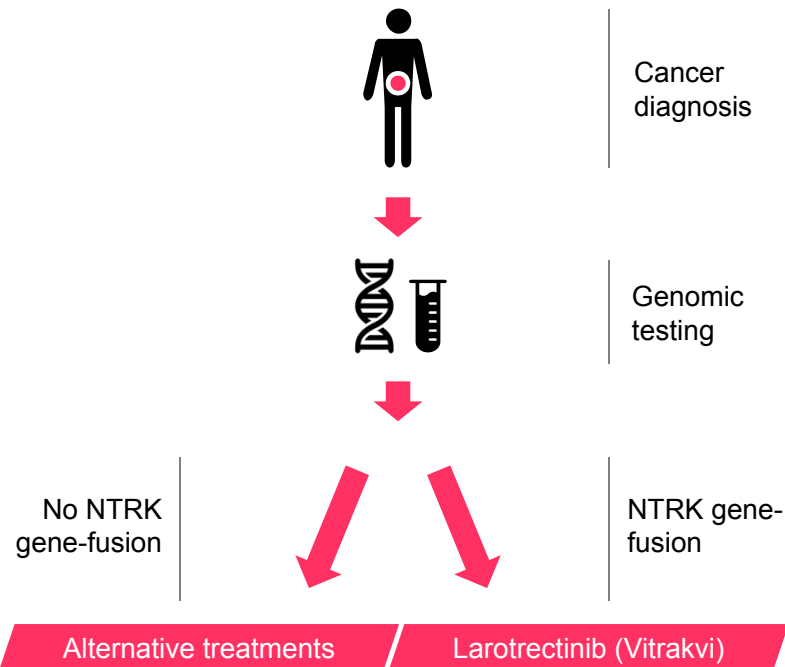
<sup>1</sup> Marketed by Bayer ex-US only; <sup>2</sup> As reported by Bayer

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



# Larotrectinib Provides Novel Tumor-Agnostic Precision Medicine Cancer Therapy

Precision medicine, identifying the right patient for the right treatment



// Larotrectinib (Vitrakvi) is an oral, small molecule, highly selective inhibitor of tropomyosin receptor kinases (TRKs)

// NTRK gene fusions can lead to cancer and are facilitating tumor growth as oncogenic drivers

// Relevant genetic alteration is estimated to occur in about 0.5 - 1.0% of patients with solid tumors

// FDA approved for the treatment of adult and pediatric patients with solid tumors that have a neurotrophic receptor tyrosine kinase gene fusion

// Distinguished science, in-licensed from Loxo Oncology together with 2<sup>nd</sup> generation TRK inhibitor LOXO-195

// Peak sales potential of >€750 million

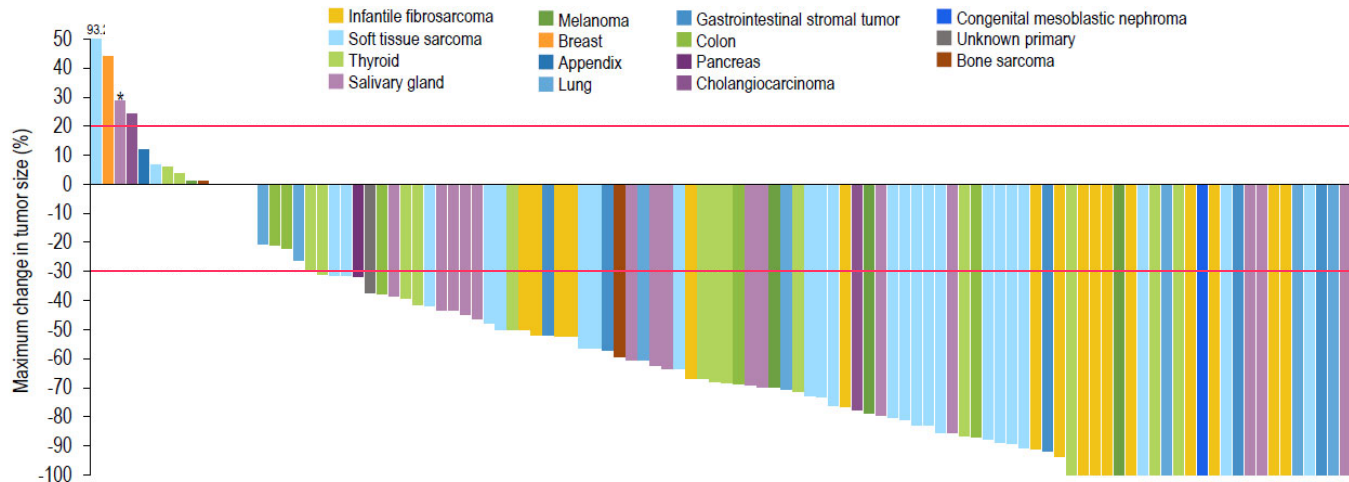
NTRK: Neurotrophic receptor tyrosine kinase  
Full labeling information available at [http://labeling.bayerhealthcare.com/html/products/pi/vitrakvi\\_PI.pdf](http://labeling.bayerhealthcare.com/html/products/pi/vitrakvi_PI.pdf)



# Larotrectinib Demonstrates Impressive Anti-Tumor Activity

Activity in a Wide Range of Tumors Associated with NTRK Gene Fusions

## Maximum change in tumor size according to tumor type (RECIST)



## Objective response rate

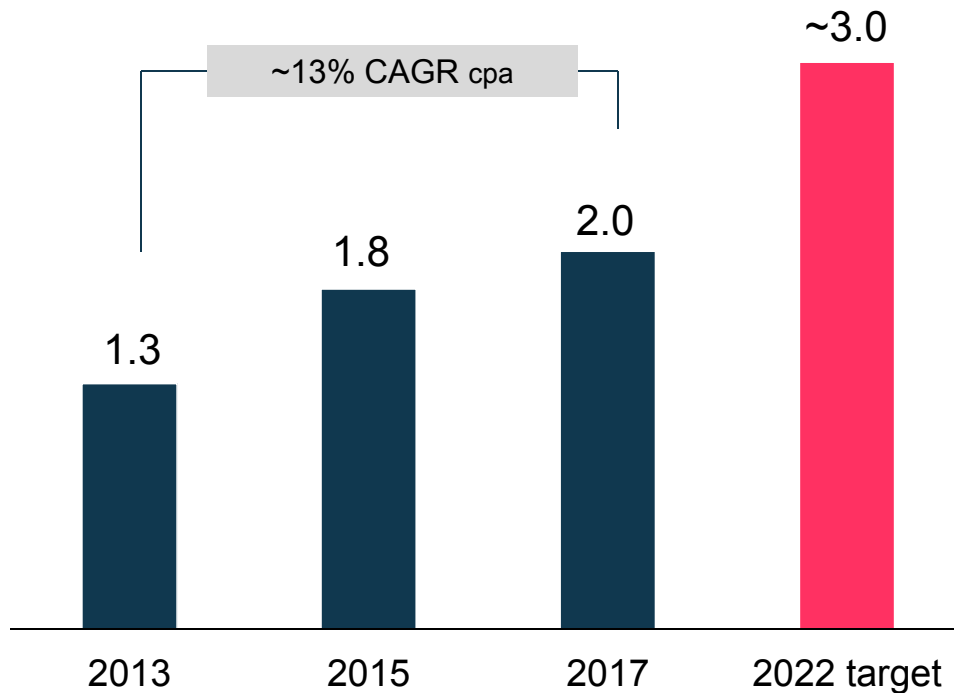
Assessment (N=109)	
Objective response rate (95% CI)	81% (72-88%)
Best response	
// Partial response	63%
// Complete response	17%

Lassen, U. et al., ESMO 2018  
 NTRK: Neurotrophic receptor tyrosine kinase; RECIST: Response evaluation criteria in solid tumors



# China is a Growth Engine for Pharma

Sales in PR China in €bn



- // Ranked among the top 5 multi-national pharma companies in China
- // Targeting sales of ~€3bn in PR China by 2022
- // Portfolio of established and innovative drugs matches China's needs
- // Strong growth of key products
- // Xarelto and Nexavar entered the National Reimbursement Drug List in 2017
- // Glucobay, Adalat, Nimotop, Bayaspirin and Ciprobay listed on China's Essential Drug List

cpa: Currency and portfolio adjusted



# Successful Track Record in Innovation



## Growth driver

- // Above industry average output in terms of product sales from pipeline assets launched over last 10 years



## Pipeline quality

- // 100% success rate for phase III development of new molecular entities since 2008
- // ~50 projects in clinical development
- // More than 70 clinical trials underway with ~28,000 patients enrolled



## Scientific leadership

- // Major success with state-of-the-art anticoagulant Xarelto
- // Pioneering sGC-modulators with Adempas as first-in-class product
- // Delivered first marketed targeted alpha-therapy, Xofigo



## Stringent focus

- // Focus on areas with greatest potential for breakthrough impact on the lives of patients - Cardiovascular Diseases and Cancer
- // Selective R&D activities in Hemophilia, Women's Health, and Ophthalmology

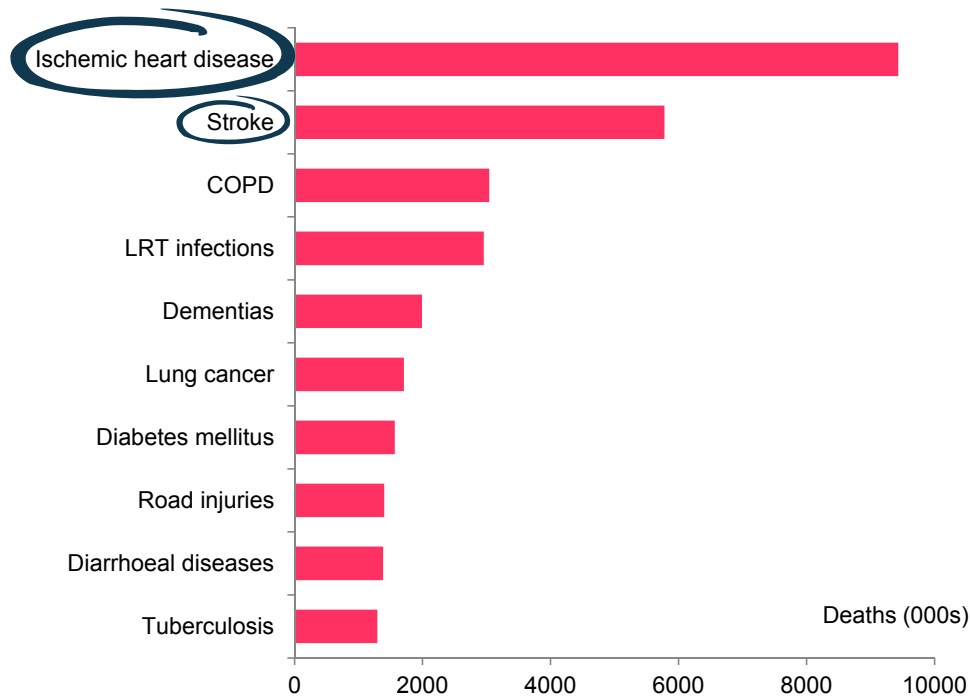
sGC: Soluble guanylate cyclase



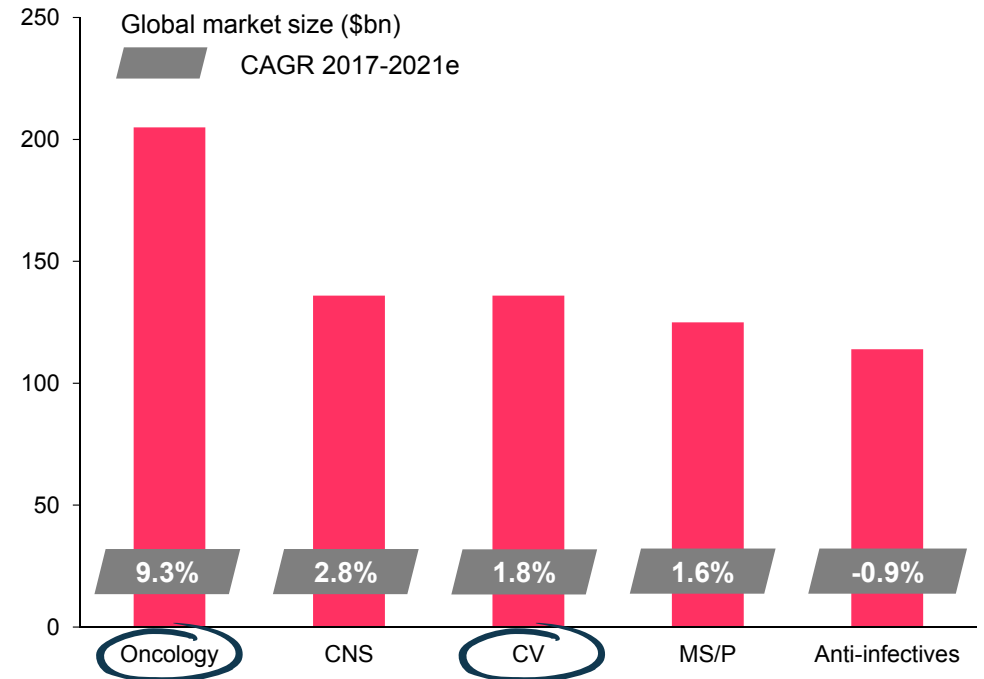
# Addressing High Unmet Medical Need and Attractive Markets

Cardiovascular Diseases are Still the “Biggest Killers”, While Oncology is the Fastest Growing Market

Main causes of death (2016)



Top 5 therapeutic categories



WHO Global Health Observatory Data 2018; Decision Resources Group  
 COPD: Chronic obstructive pulmonary disease; LRT: Lower respiratory tract; CNS: Central nervous system; CV: Cardiovascular; MS/P: Musculoskeletal/Pain



# Late-stage Pipeline with Progress in Oncology

Darolutamide met Primary Endpoint in Phase III-trial and FDA-approval of Larotrectinib

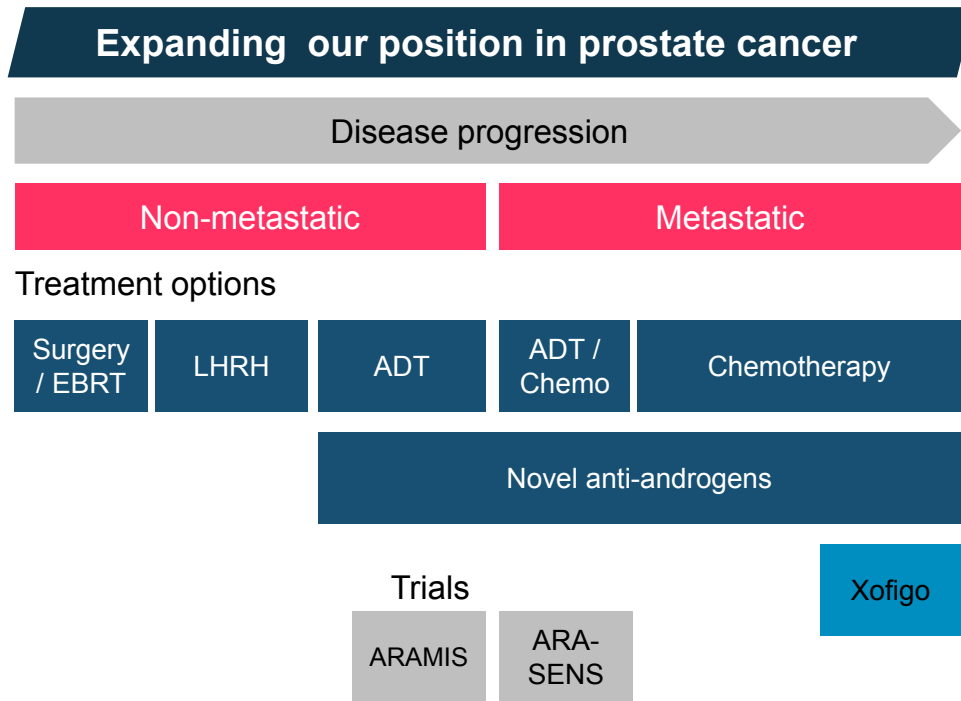
	Larotrectinib	Darolutamide	Copanlisib	Finerenone	Vericiguat
Indication	// <i>TRK-fusion Cancer</i>	// <i>Prostate Cancer</i>	// <i>Lymphoma</i>	// <i>Diabetic Kidney Disease</i>	// <i>Chronic Heart Failure</i>
Status	// <i>FDA approved / in registration</i>	// <i>Phase III (nmCRPC)</i> // <i>Phase III (mHSPC)</i>	// <i>Launched in the US</i> // <i>Phase III</i>	// <i>Phase III</i>	// <i>Phase III (HFrEF)</i> // <i>Phase II (HFpEF)</i>
Commercial Potential	// <i>PSP &gt;€750m</i>	// <i>PSP ≥€1bn</i>	// <i>PSP ≥€0.5bn</i>	// <i>PSP ≥€1bn</i>	// <i>PSP ~€0.5bn</i>
Clinical Completion	// <i>Clinical program ongoing</i>	// <i>Completed (ARAMIS, nmCRPC)</i> // <i>Aug 2022e (ARASENS, mHSPC)</i>	// <i>May 2020e (CHRONOS-3)</i> // <i>Sep 2021e (CHRONOS-4)</i>	// <i>May 2020e (FIDELIO-DKD)</i> // <i>Jul 2021e (FIGARO-DKD)</i>	// <i>Jan 2020e (VICTORIA, HFrEF)</i> // <i>Oct 2019e (VITALY, HFpEF)</i>

NTRK: Neurotrophic receptor tyrosine kinase; nmCRPC: Non-metastatic castration resistant prostate cancer; mHSPC: Metastatic hormone sensitive prostate cancer; HFrEF: Heart failure with reduced ejection fraction; HFpEF: Heart failure with preserved ejection fraction; PSP: Peak sales potential





# Darolutamide Significantly Extended Metastasis-free Survival in Men with Castration Resistant Prostate Cancer

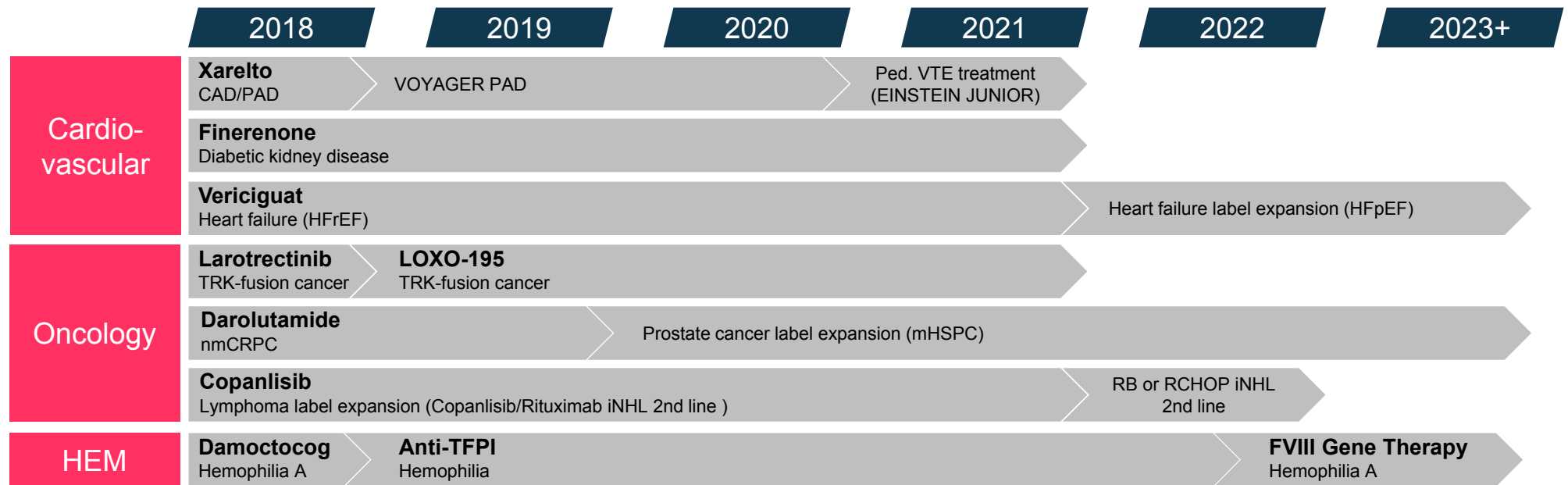


- // Darolutamide is a novel non-steroidal androgen receptor antagonist in development for the treatment of prostate cancer
- // Met primary endpoint of metastasis-free survival in the ARAMIS trial in non-metastatic CRPC
- // Phase III trial in metastatic HSPC (ARASENS) ongoing
- // Potential for differentiation:
  - // Differentiated chemical structure
  - // Higher binding affinity
  - // Negligible blood-brain barrier penetration<sup>1</sup>

CRPC: Castration resistant prostate cancer; HSPC: Hormone sensitive prostate cancer; EBRT: External beam radiation therapy; LHRH: Luteinizing hormone-releasing hormone; ADT: Androgen deprivation therapy; <sup>1</sup> based on pre-clinical data In collaboration with Orion Pharmaceuticals



# Expected Launches of Key Pipeline Assets

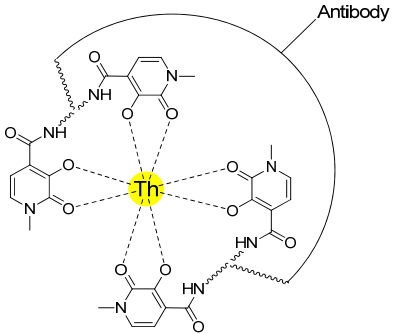


First launch in first indication

NTRK: Neurotrophic receptor tyrosine kinase; nmCRPC: Non-metastatic castration resistant prostate cancer; mHSPC: Metastatic hormone sensitive prostate cancer; HFrEF: Heart failure with reduced ejection fraction; HFpEF: Heart failure with preserved ejection fraction, iNHL: Indolent Non-Hodgkin Lymphoma TFPI: Tissue factor pathway inhibitor; WH: Women's Health; HEM: Hematology



# Bayer Has Unique Access to Targeted Thorium Conjugates, a New Approach for Cancer Treatments



**Components:**

- Antibody** Targeting the tumor cell
- Chelator** Forming highly stable complexes with Thorium
- Thorium-227** Killing the tumor cell through  $\alpha$ -radiation

- //  $\alpha$ -radiation is highly energetic and may induce DNA damage leading to cell death
- // Other than  $\beta$ -radiation,  $\alpha$ -radiation is active over a very short distance only which may increase tissue specificity
- // Targeted Thorium conjugates direct  $\alpha$ -radiation to tumor cells by specific antibodies
- // Thorium-227 is the only commercially viable  $\alpha$ -radionuclide for antibody targeted therapy
  - // Thorium-227 forms highly stable complexes with chelators
  - // Efficacy is independent of antibody internalisation
  - // No known mechanism for resistance to  $\alpha$ -radiation



# Targeted Thorium Conjugate Platform May Have Potential in Several Oncology Settings

Project	Indication	Status	Comment
CD-22-TTC	CD-22 <sup>+</sup> NHL	Phase I	Significant need for new therapeutic options for the treatment of r/r NHL (DLBCL, FL)
Mesothelin-TTC	Solid tumors expressing mesothelin	Phase I	Mesothelin is overexpressed in the vast majority of pancreatic adenocarcinomas, mesotheliomas and adenocarcinomas of the lung, ovary and the stomach
PSMA-TTC	mCRPC	Phase I ready	PSMA as a predictive biomarker with high and specific overexpression in prostate cancer cells
HER2-TTC	HER2 <sup>+</sup> cancer	Pre-clinical	Potential for treatment of patients resistant/refractory to approved HER2-targeting therapies

// Novel approach for radio-immunotherapies with local effect at the tumor

// Tumor specificity defined by antigen/antibody selection, making TTC a flexible technology platform

// Potential to leverage experience with Xofigo

TTC: Targeted Thorium conjugate; NHL: Non-Hodgkin's lymphoma; DLBCL: Diffuse large b-cell lymphoma; FL: Follicular lymphoma; mCRPC: Metastatic castration resistant prostate cancer; PSMA: Prostate specific membrane antigene; HER2: Human epidermal growth factor receptor 2



# Re-alignment of R&D-activities to Increase Sustainable R&D Productivity

## From

- // **Broad set of indications** in Oncology, Cardiovascular Diseases and Gynecological Therapies
- // Focus on **functional and technical expertise**
- // Strong reliance on **small molecules**
- // Majority of **assets sourced internally**
- // Highly **concentrated geographical footprint**
- // **Internally oriented** resource model

## To

- // **Focus on select areas** with high unmet medical need in Oncology, Cardiovascular Diseases and Gynecological Therapies
- // Focus on **deep disease understanding**
- // **Broader mechanistic approach** beyond therapeutic area focus
- // Invest in **new technologies and capabilities**
- // Continue to explore potentially **game-changing innovations** through LEAPS
- // Increased portion of R&D **assets to be sourced externally** in the future
- // Evolve footprint with **more co-location in science hubs**
- // Adapt internal cost base to **free up funds for sourcing inorganic opportunities**



# External Innovation and Partnering are Essential Components of Success at Pharma

## Joint Labs

// Joint Labs: e.g. German Cancer Research Center (DKFZ), Broad Institute



## Consortia

// Innovative Medicines Initiative



// Structural Genomics Consortium SGC



## Arm's Length

// Accelerator:  
e.g. Grants4-Initiatives



// Incubator:  
CoLaborator



## Research Collaborations

// Multiple projects: e.g., Evotec, Tsinghua University, Peking University, Vanderbilt University, MD Anderson



## License Agreements

// Pipeline assets:  
Darolutamide, Larotrectinib, Loxo-195, Vericiguat, FXI-Antisense



// Launched products:  
Nexavar, Stivarga, Eylea, Adempas



Examples only



# First Wave of Breakthrough Investments by LEAPS



- // Biotech with Bayer and CRISPR Therapeutics as major investors
- // \$300 million over 5-6 years, associated with \$70 million equity of Bayer in CRISPR Therapeutics
- // Awarded “No. 1 Most Valuable Pharma Deal 2016” by Pharma Dive

- // Biotech with Bayer and Versant Ventures as major investors
- // \$225 million over 4-5 years
- // BlueRock selected to Top-30 World Game Changer companies (CB Insights Game Changer Report)

## TECHNOLOGIES

- // CRISPR/Cas-based DNA-editing
- // Research focus:
 

I. Cardiology	IV. Autoimmune diseases
II. Ophthalmology	V. Ear diseases
III. Hematology (non-malignant)	VI. Metabolic diseases

## TECHNOLOGIES

- // Best-in-class induced pluripotent stem cell therapies using an industry-leading platform
- // Vision is to cure diseases with significant cell loss and diminished self-repair potential
- // (Initial) research focus on:
 

I. Cardiology (heart muscle regeneration after MI or with HF)
II. Neurology (Parkinson’s disease)

MI: Myocardial infarction; HF: Heart failure



## Further Growth in Sales and Profitability

Pharma	2018e	Indicative Guidance 2019	Target 2022
<b>Sales/Sales growth</b>	~€16.8bn	~4%	CAGR 4-5%
<b>EBITDA/EBITDA margin</b>	~€5.6bn	~34%	>35%

2022 targets at constant currencies, not including portfolio measures  
EBITDA / EBITDA margin based on EBITDA before special items





# We Are Confident for Pharma Also Beyond 2022



LoE: Loss of exclusivity



# Key Takeaways

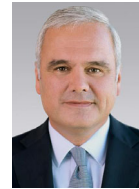
Driving Performance and Delivering New Growth Opportunities

- 1** Mid-term targets project further growth and margin improvement
- 2** China is a growth engine for Pharma
- 3** Late-stage pipeline with progress in Oncology
- 4** Re-alignment of R&D activities to increase sustainable R&D productivity
- 5** Accelerating sourcing of external innovation

LoE: Loss of exclusivity; nmCRPC: Non-metastatic castration resistant prostate cancer



# Experienced Pharmaceuticals Executive Leadership Team



**Stefan Oelrich**  
President, Pharmaceuticals



**Reinhard Franzen**  
Commercial Operations  
Europe, Middle East & Africa



**Sebastian Guth**  
Commercial Operations  
Americas



**Wei Jiang**  
Commercial Operations  
China & Asia Pacific



**Heike Prinz**  
Commercial Operations Japan



**Robert LaCaze**  
SBU Oncology



**Stefan Oelrich<sup>1</sup>**  
Strategic Marketing



**Joerg Moeller**  
Research & Development



**Michael Devoy<sup>2</sup>**  
Medical Affairs &  
Pharmacovigilance



**Wolfram Carius**  
Product Supply



**Julio Triana**  
Finance



**Christoph Bertram**  
Human Resources  
Business Partner



**Stefan Gehring**  
Law, Patents and Compliance  
Business Partner

<sup>1</sup> Stefan Oelrich will additionally take over the lead for PH Strategic Marketing on an interim basis; <sup>2</sup> Additional role as Chief Medical Officer for Bayer AG



Capital Markets Day

# *Pharmaceuticals*

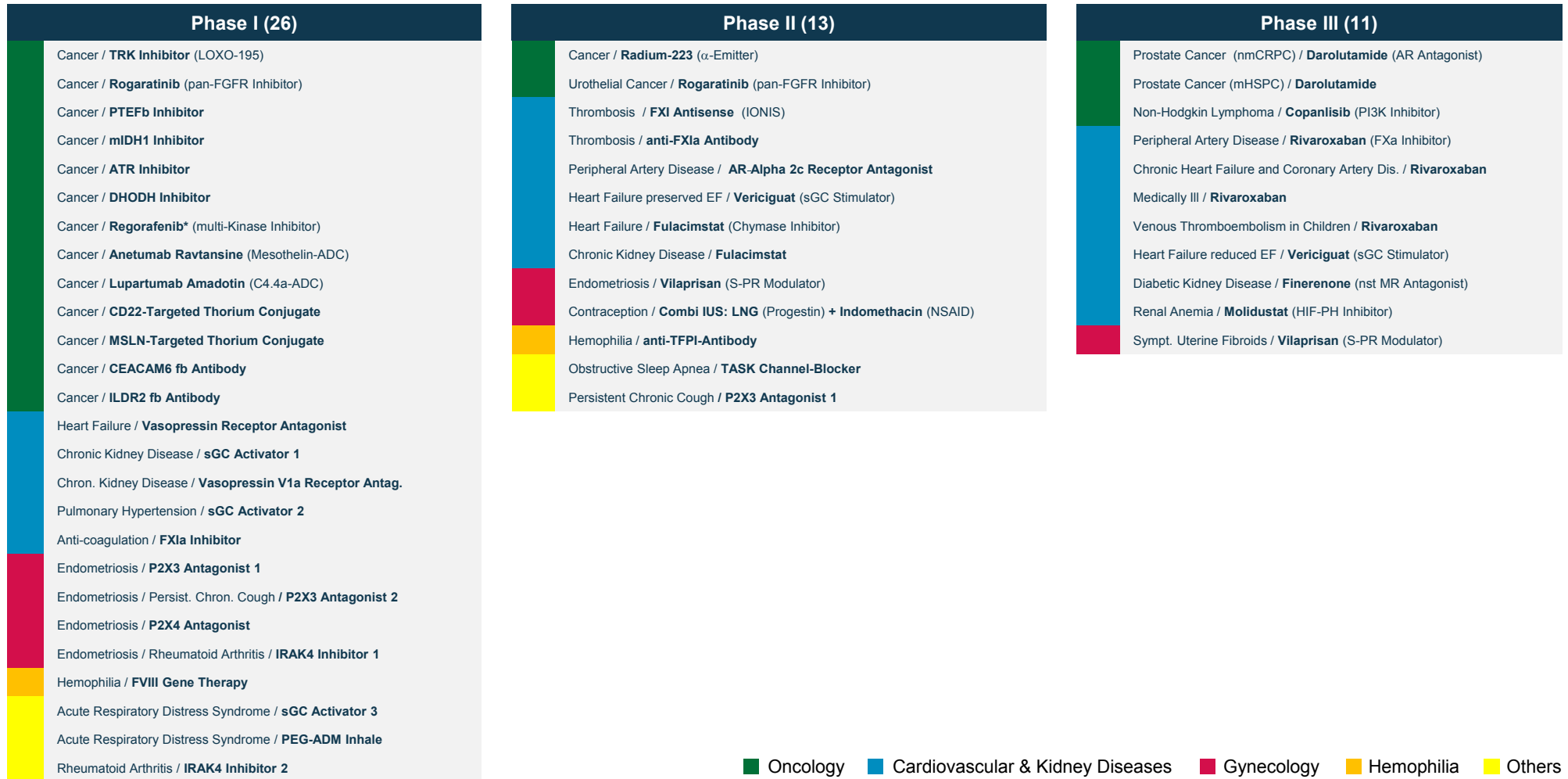


**Appendix**





# Our Pipeline Contains ~50 Projects in Clinical Development

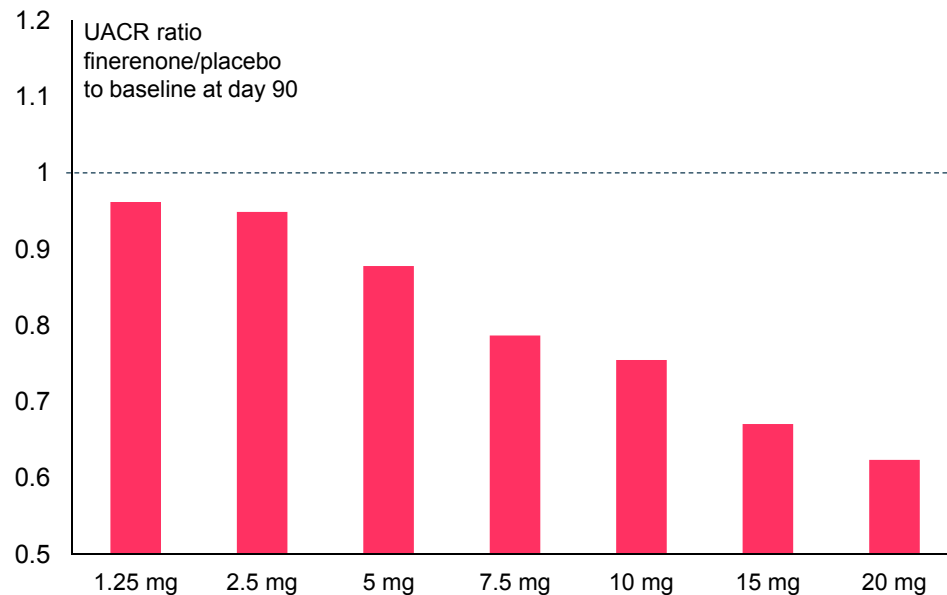


■ Oncology
 ■ Cardiovascular & Kidney Diseases
 ■ Gynecology
 ■ Hemophilia
 ■ Others



# Finerenone May Reduce the Risk of CV-mortality and the Progression of Kidney Disease in Patients with Diabetic Kidney Disease

## Key phase II data (ARTS-DN<sup>1</sup>)



**Dose dependent reduction of proteinuria by finerenone when added to RAS blocker therapy in patients with DKD**

// Finerenone is a novel non-steroidal MRA that has greater receptor selectivity and better receptor affinity than existing MRAs (e.g. spironolactone, eplerenone)

// Addressing high unmet medical need

// Two phase III trials in diabetic kidney disease underway: FIDELIO DKD (CV study) and FIGARO DKD (renal study)

// Potential for differentiation:

// First-in-class MRA for treatment of DKD

// Non-steroidal structure, no interaction with steroid hormone receptors compared to existing MRAs

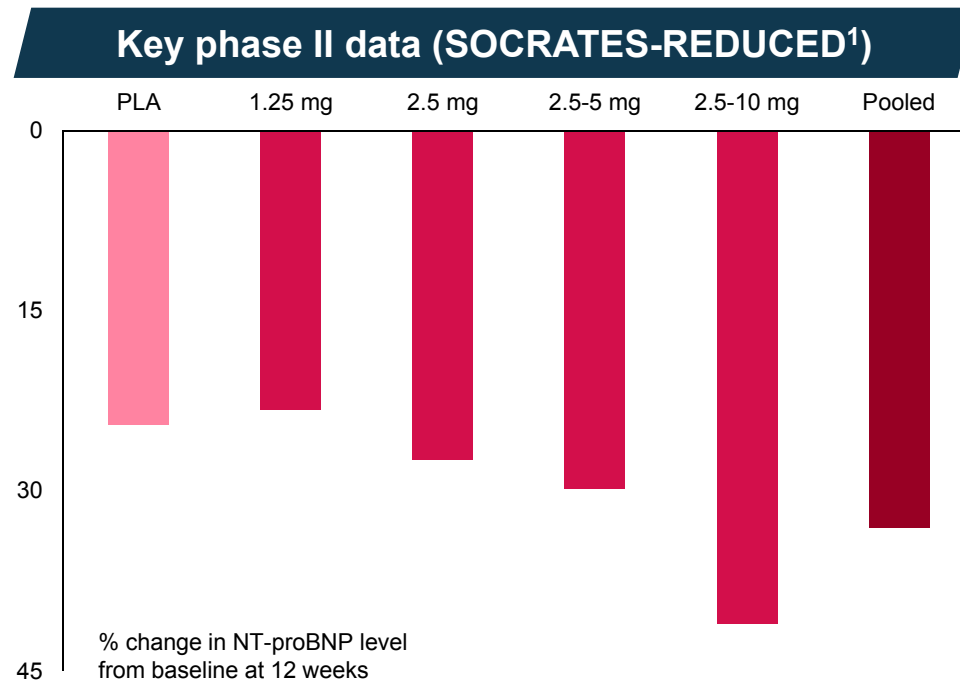
// Low risk of hyperkalemia which prohibits the use of marketed MRAs in DKD

MRA: Mineralocorticoid receptor antagonist; RAS: Renin-angiotensin system; CV: Cardiovascular; DKD: Diabetic kidney disease; UACR: Urinary albumin-creatinine ratio

<sup>1</sup> Bakris, G.L. et al., JAMA 2015; 314:884-894.



# Vericiguat is a Potentially New Treatment Option on Top of Standard of Care for Patients with Heart Failure



- // First-in-class, direct sGC stimulator addressing the NO-sGC-cGMP pathway, a relevant mechanism in heart failure
- // Heart failure is still associated with significant mortality risk despite the availability of new therapeutic options
- // Potential for differentiation:
  - // New mode of action to be positioned on top of standard of care
  - // OD dosing and overall favorable safety and tolerability profile
- // Development in collaboration with Merck & Co.

## Dose-response relationship between vericiguat dose and reduction in NT-proBNP, a surrogate marker for cardiac function

sGC: Soluble guanylate cyclase; NO: Nitric oxide; cGMP: Cyclic guanosinmonophosphate; OD: Once daily; PLA: Placebo; NT-proBNP: N-terminal prohormone of brain natriuretic peptide  
<sup>1</sup> Gheorghiadu, M. et al: JAMA 2015; 314: 2251-2262



# Copanlisib is a Differentiated PI3K-inhibitor for the Treatment of Lymphoma

## Key phase II data (CHRONOS-1)<sup>1</sup>

Overall response rate in patients with follicular B-cell non-Hodgkin's lymphoma who had relapsed disease following at least two prior treatments:

n=104	Copanlisib
Overall response rate	59%
// Complete response	14%
// Partial response	44%

Copanlisib had a favorable safety profile with a low rate of severe toxicities overall.

- // Phosphatidylinositol-3-kinase (PI3K) inhibitor blocking cellular signal transduction processes crucial for cancer progression
- // In development for various forms of lymphoma
- // Potential for differentiation:
  - // Inhibits different isoforms of PI3K
  - // Intravenous administration, thus lower propensity for serious gastrointestinal toxicity
  - // Intermittent once weekly dosing
- // Launched in the US in 2017 for the treatment of relapsed follicular lymphoma. Registration granted under accelerated FDA approval based on phase II data

<sup>1</sup> Dryling M. et al.: Blood 2017; 130: 2777





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