



**Focused on  
Growth and Innovation**

**“Patients are at the heart  
of what we do”**

Investor presentation  
October 2020



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## Executive summary





# Experienced leadership team



**David  
Veitch** CEO

Joined  
2014

Previous  
roles:



**Adesh  
Kaul** CFO

2009



**Marc  
Engelhardt**  
MD, Ph.D. CMO

2010



**Gerrit  
Hauck**  
Ph.D. CTO

2018



**Laurenz  
Kellenberger**  
Ph.D. CSO

2000



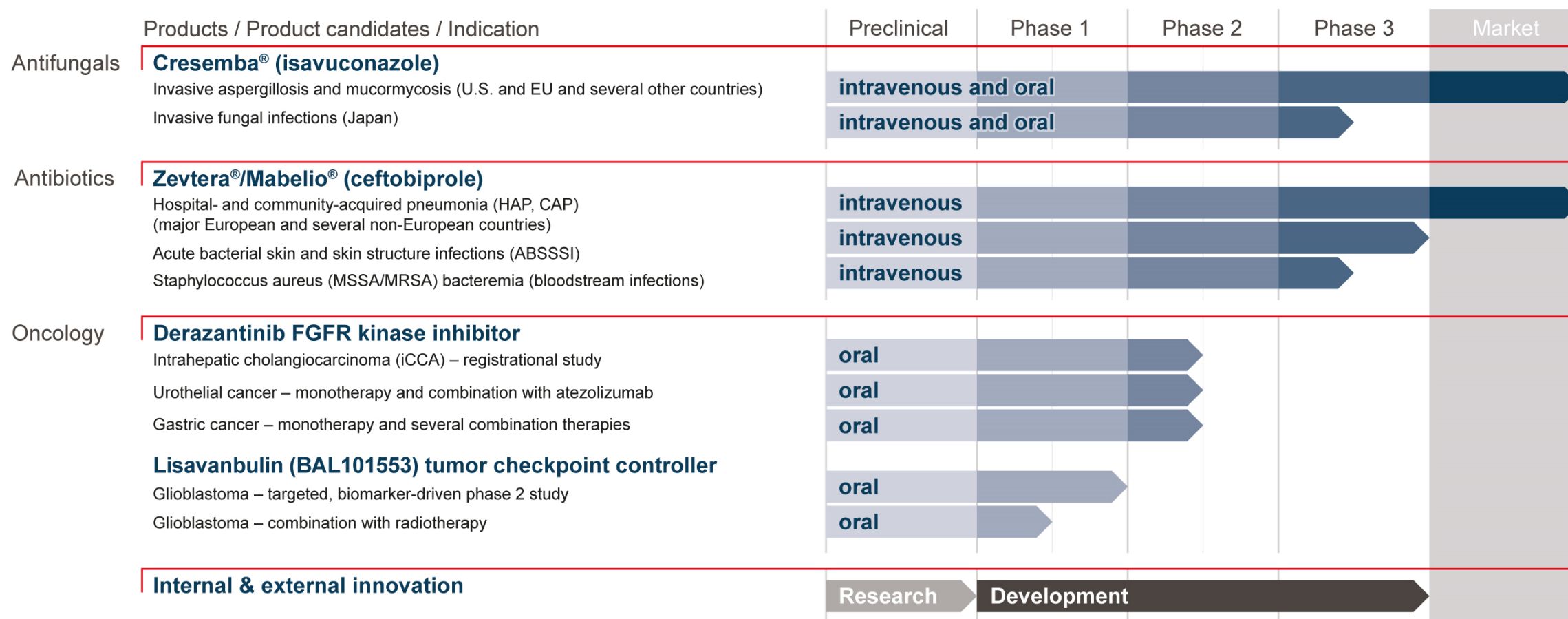


# At a glance

- Well funded, commercial-stage biotech company with significantly growing cash flows from commercialized products
- Focused in the areas of oncology and infectious diseases
- Potential for sustainable growth and value creation based on commercialized brands and an innovative pipeline
- Experienced people with the proven expertise to take compounds from research to market
- Two revenue generating hospital anti-infective brands, Cresemba® and Zevtera® and two clinical oncology drug candidates
- Recognized ability to establish and manage partnerships in both the development and commercial phase, providing access to international markets
- Listed on SIX Swiss Stock Exchange, SIX: BSLN
- Based in life sciences hub, Basel, Switzerland



# Potential for sustainable growth and value creation based on commercialized brands and innovative pipeline

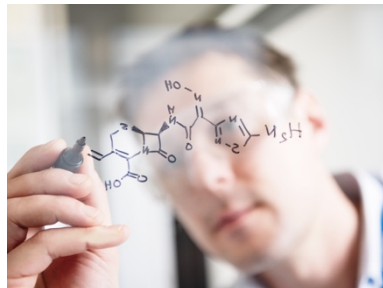


# Our strategy



## Foster

Foster an agile organisation based on a dynamic and open culture



## Focus

Focus on continuously increasing cash flow from our two commercial-stage hospital anti-infective brands, Cresemba® and Zevtera®



## Leverage

Leverage our expertise in bringing drugs from research to market by utilising appropriate partnerships with established organisations



## Invest

Invest in our clinical portfolio of targeted, small molecule, oncology drug candidates and the phase 3 ceftobiprole program

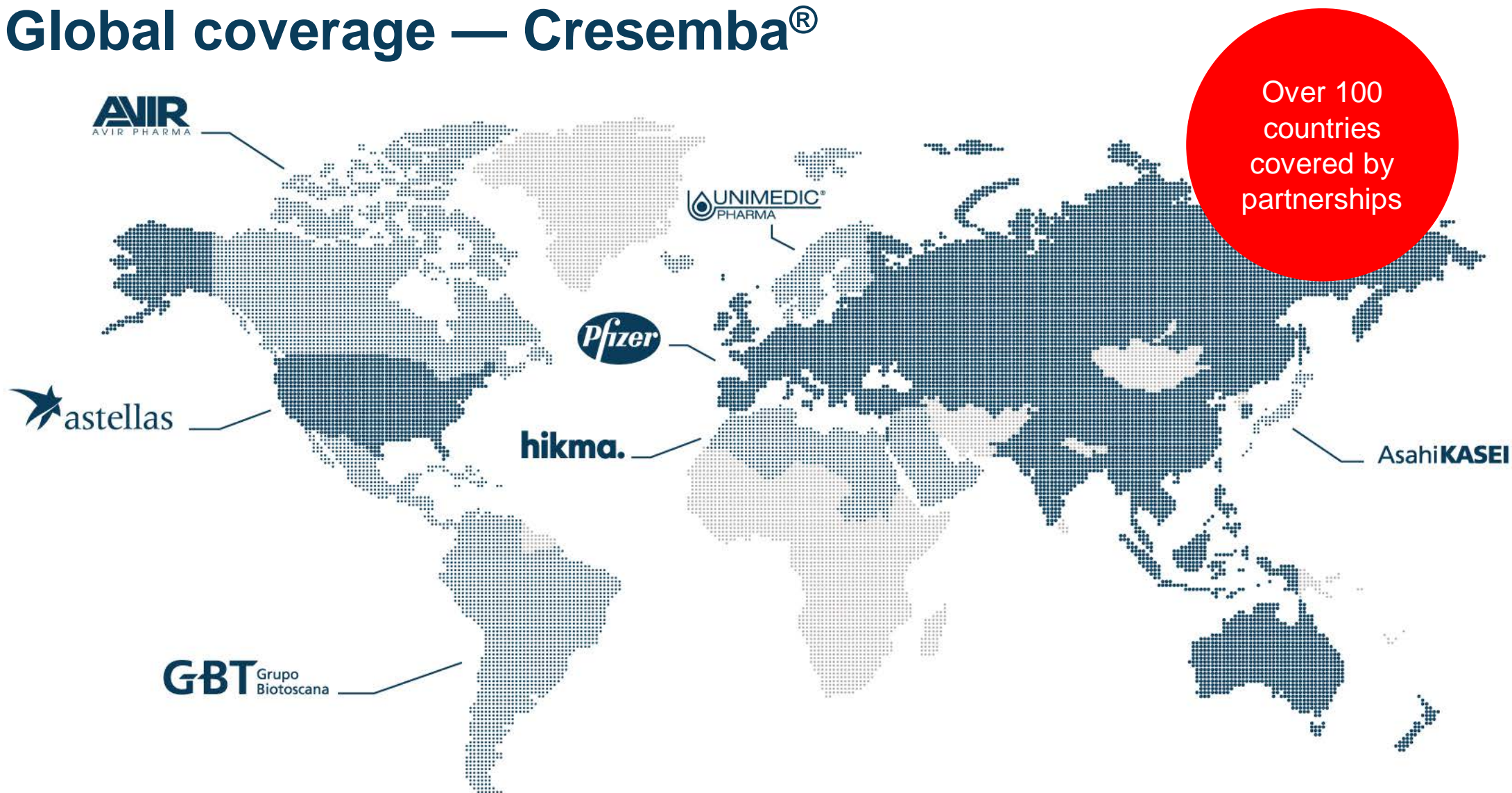


## Innovate

Continue to broaden our R&D pipeline through both internal and external innovation



# Global coverage — Cresemba®



# The company we keep — established strong partnerships

## License partners



Europe (excl. Nordics), China  
Asia-Pacific, Russia, Turkey  
and Israel (Cresemba®)



U.S. (Cresemba®)

**AsahiKASEI**

Japan (Cresemba®)



China (Zevtera®)

CR Gosun

## Distribution partners

**correvio**

Europe (excl. Nordics), Israel  
(Zevtera®)

**hikma.**

MENA region  
(Cresemba® and Zevtera®)

**GBT** Grupo Biotoscana

LatAm  
(Cresemba® and Zevtera®)



Nordics  
(Cresemba® and Zevtera®)



Canada  
(Cresemba® and Zevtera®)

Double digit  
percentage  
royalties on  
sales by  
license  
partners

USD 1.1 bn  
in potential  
milestones  
remaining

Participation  
in sales of  
distribution  
partners  
through  
transfer price

USD ~255 mn  
upfront and  
milestone  
payments  
received





## Five reasons to invest





# Five reasons to invest



## **Growth**

Well funded with increasing and sustainable cash flow through commercialized brands



## **Prospects**

Opportunity to share in pipeline value creation and proven approach to the successful commercialization of products around the world



## **Leadership**

Experienced team working in an agile culture able to turn pipeline projects into revenue generating brands



## **Partnerships**

Proven ability to build successful partnerships in research, development and commercialization with leading academic, governmental and industrial organisations



## **Focus**

One of the few biopharmaceutical companies in the world focused on the development and commercialization of targeted oncology small molecules and new antibiotics and antifungals

Antifungal

# **Cresemba® (isavuconazole)**

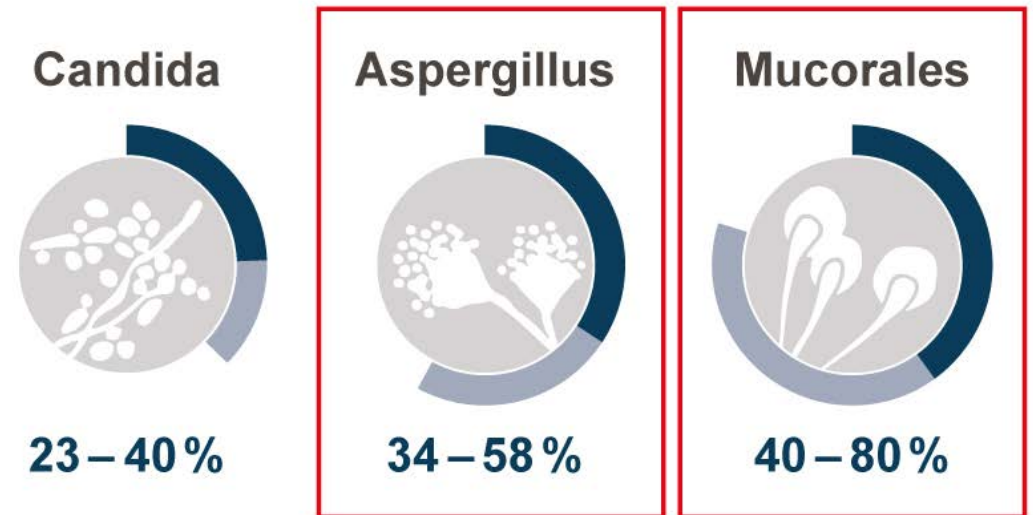
Invasive mold infections



# The market — Invasive fungal infections

- Severe, potentially life-threatening infections mainly affecting immunocompromised patients
- An important cause of morbidity and mortality in cancer patients undergoing intensive chemotherapy regimens
- Rising number of immunocompromised patients (cancer and transplantations) driving therapeutic demand
- Mucorales infections on the rise – doubled from 2000 to 2013
- Limitations of current therapies (spectrum of activity, toxicity, effective plasma levels) drive the need for new agents

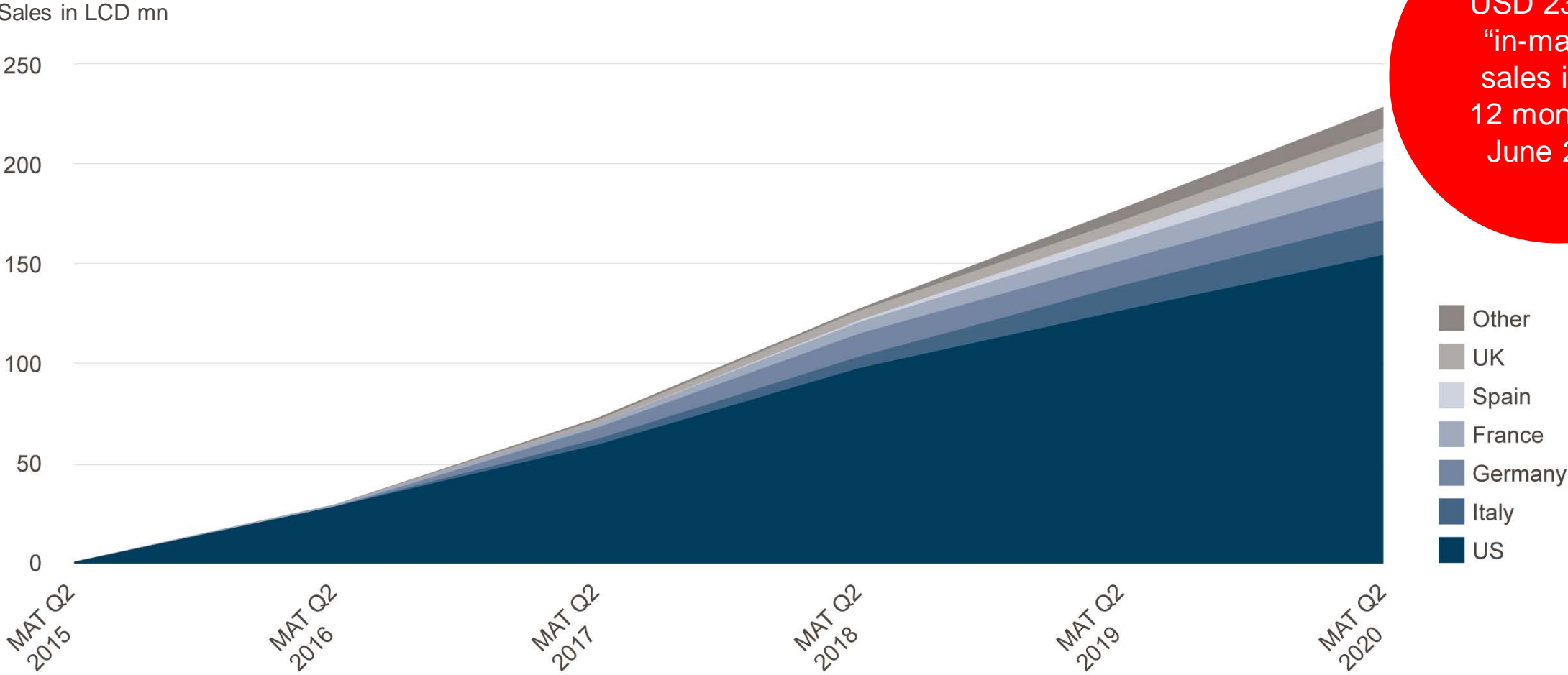
## Mortality rates for invasive fungal infections\*\*



\*\*Kullberg/Arendrup *N Engl J Med* 2015, Baddley *Clin Infect Dis* 2010, Roden *Clin Infect Dis* 2005, Greenberg *Curr Opin Infect Dis* 2004



# Cresemba continues strong in-market sales uptake



LCD: USD corrected for currency fluctuations; MAT: Moving annual total; Source: IQVIA, June 2020

# Sales of best-in-class antifungals\* by product

USD 2.9 bn sales (MAT Q2 2020)

- Potential to increase Cresemba® (isavuconazole) market share
  - Anticipate to be launched in 60 countries by end-2021
  - Exclusivity through 2027 in the U.S. and potential pediatric exclusivity extension to 2027 (from 2025) in the EU

\* Best-in-class antifungals: isavuconazole, posaconazole, voriconazole, AmBisome, anidulafungin, caspofungin, micafungin



MAT: Moving annual total; Sales figures in USD, corrected for currency fluctuations;  
Source: IQVIA, June 2020

# Cresemba® — Differentiated by spectrum, safety and tolerability

- Broad spectrum of activity against molds, including emerging molds (mucorales)
- Consistent plasma levels
- Statistically fewer drug-related adverse events and treatment-emergent adverse events (liver, skin, eye) in invasive aspergillosis patients vs. voriconazole in SECURE phase 3 study
- Can be administered without restriction in patients with renal impairment
- Manageable drug-drug interaction profile
- Once daily maintenance dose, i.v./oral treatment
- ECIL-6 guideline: Cresemba® recommended for the first-line treatment of invasive aspergillosis in leukemia and hematopoietic stem cell transplant patients. ECIL states that isavuconazole is as effective as voriconazole with a better safety profile.



Antibacterial

**Zevtera<sup>®</sup> / Mabelio<sup>®</sup>**  
**(ceftobiprole)**

Severe bacterial infections



# Zevtera® — An introduction

- Broad-spectrum anti-MRSA cephalosporin (including Gram-negative bacteria)
- Rapid bactericidal activity
- Potential to replace antibiotic combinations
- Early improvement in HAP, particularly in patients with MRSA, and CAP, including high-risk patients
- Cephalosporin class safety profile
- Marketed in selected countries in Europe, Latin America and the MENA-region as well as in Canada

Approved in major European countries & several non-European countries for both hospital-acquired pneumonia (HAP), excluding ventilator-associated pneumonia (VAP), and community-acquired pneumonia (CAP). Not approved in the U.S.

MENA: Middle East and North Africa

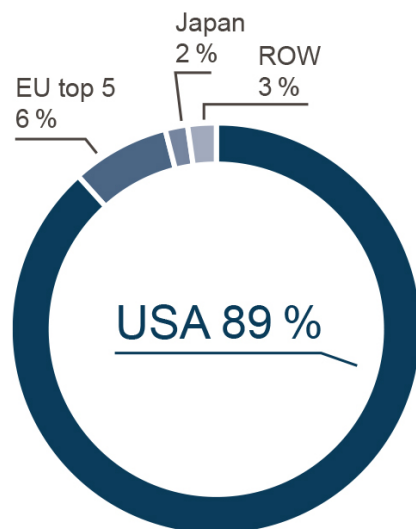


**Focused on Growth and Innovation**

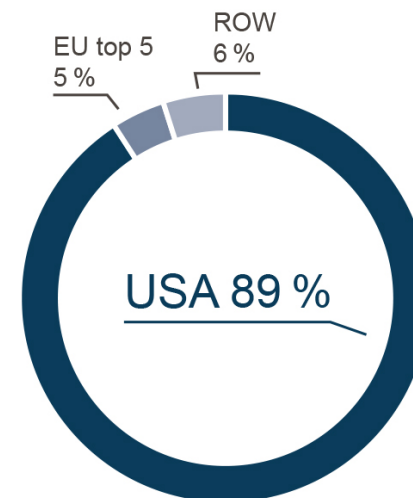


# The hospital anti-MRSA antibiotic market — A USD 2.8 bn market\* with the U.S. being the most important region

Daptomycin sales by region  
(2015, before LOE)



Ceftaroline sales by region  
(MAT Q2 2020)



\* Vancomycin, linezolid, teicoplanin, daptomycin, tigecycline, telavancin, ceftaroline, dalbavancin, oritavancin, and tedizolid

MRSA: Methicillin-resistant *Staphylococcus aureus*; LOE: Loss of exclusivity; ROW: Rest of world  
MAT: Moving annual total; Sales figures in USD, corrected for currency fluctuations; Source: IQVIA, June 2020



# Strategy for accessing the U.S. market

- Two cross-supportive phase 3 studies under FDA Special Protocol Assessment (SPA)
- Phase 3 program largely funded by BARDA (up to USD ~130 mn, ~70% of total program costs)

1. Acute Bacterial Skin and Skin Structure Infections (ABSSSI)<sup>1</sup> successfully completed



2. *Staphylococcus aureus* bacteremia (SAB)<sup>2</sup> ongoing, topline results from phase 3 study expected in Q1 2022



- Qualified Infectious Disease Product (QIDP) designation extends U.S. market exclusivity to 10 years from approval

<sup>1</sup> Overcash JS et al. ECCMID 2020, abstract 1594. (NCT03137173)

<sup>2</sup> Hamed K et al. Future Microbiol. 2020;15:35-48. (NCT03138733)

# SAB – an area with high medical need

- Nearly 120,000 *S. aureus* bloodstream infections in the US (in 2017)<sup>1</sup>
- ERADICATE targets complicated SAB, characterized by concomitant or metastatic infections such as bone, joint or heart valve infections; persistent bacteremia; or bacteremia in patients on dialysis
- Substantial morbidity and approximately 20% 30-day mortality<sup>2</sup>
- Limited antibiotic treatment options with only two approved treatments for SAB in the U.S. that cover both MSSA and MRSA, i.e. vancomycin and daptomycin

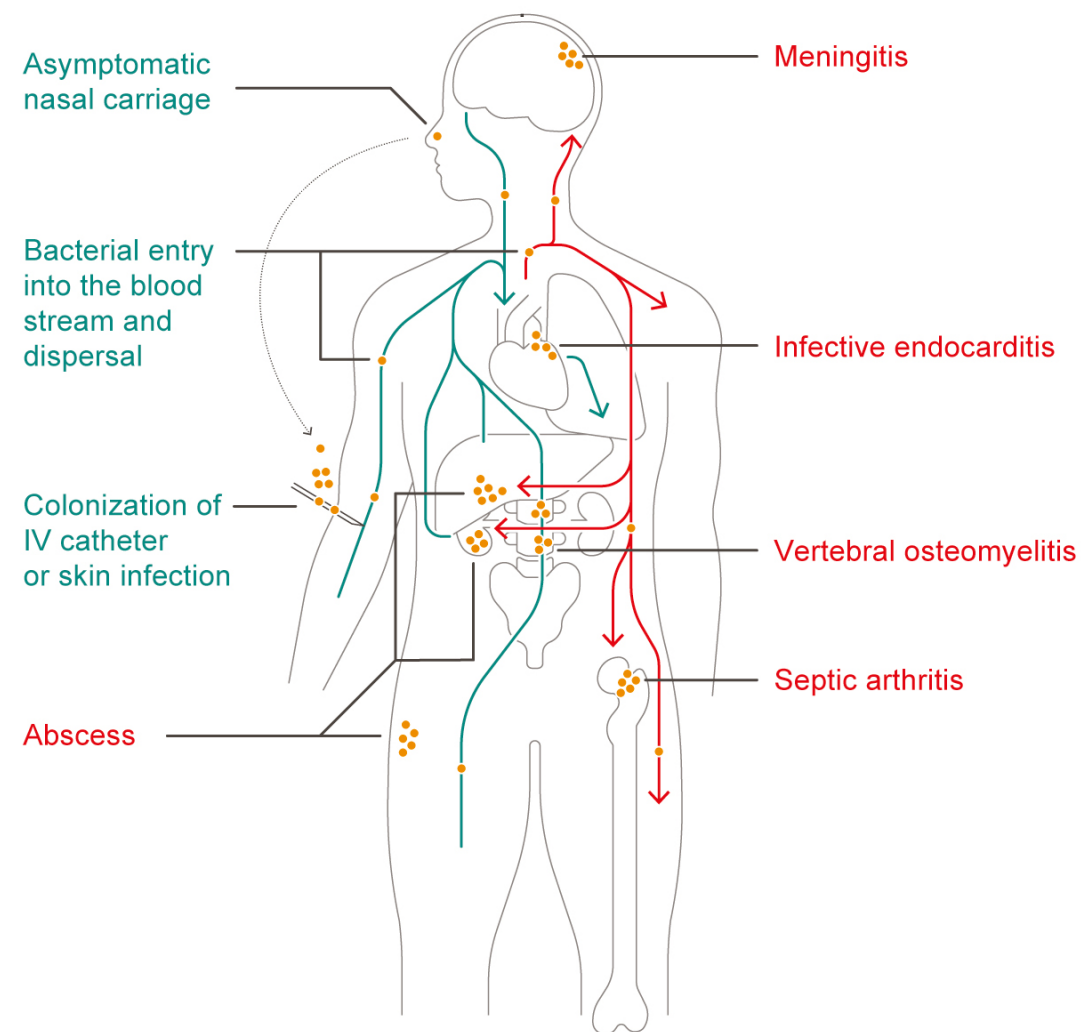
<sup>1</sup> MMWR, 2019;68:214–219.

<sup>2</sup> Hamed K et al. Future Microbiol. 2020;15:35-48.

MRSA: methicillin-resistant *Staphylococcus aureus*

MSSA: methicillin-susceptible *Staphylococcus aureus*

## Causes and consequences of SAB



Adapted from Edwards AM et al. Trends Microbiol. 2011;19:184-190.



A microscopic image of cells, likely cancer cells, with an orange overlay. The cells are spherical and have a textured surface. Some cells have long, thin, hair-like projections extending from them. The background is a solid orange color.

Oncology

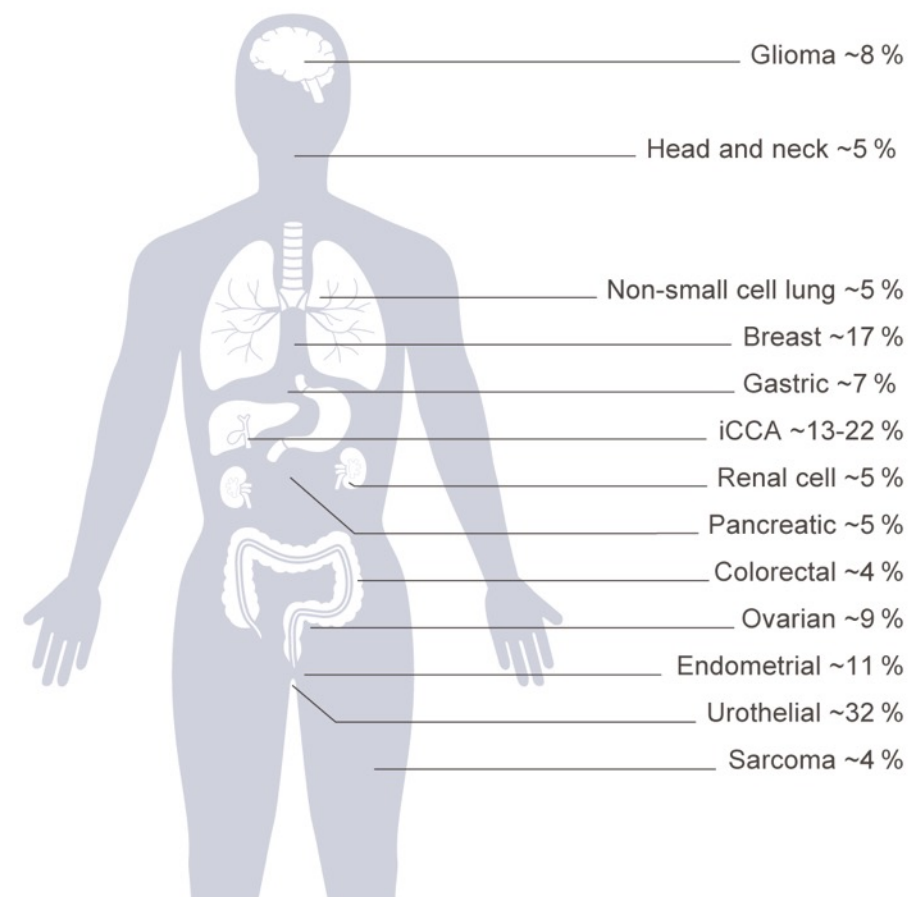
# Derazantinib

FGFR-driven tumors



# Targeting FGFR-driven tumors as single agent and in combination with immunotherapy

- Small molecule, oral inhibitor of FGFR family of kinases
- Development strategy focused on achieving differentiation by leveraging unique properties of derazantinib
  - Kinase inhibition profile: exploring therapeutic potential of additional targets of derazantinib such as CSF1R and VEGFR2 kinase
  - Safety profile: exploring relevance for potential combination therapies
- Three clinical studies ongoing
  - FIDES-01 (Ph 2) in intrahepatic cholangiocarcinoma (iCCA)
  - FIDES-02 (Ph 1/2) in urothelial cancer
  - FIDES-03 (Ph 1/2) in gastric cancer



Sources: Helsten et al., Clin Cancer Res 2016 (22), 257-267; FGFR2 fusions in iCCA: Graham et al. Hum Pathol 2014 (45), 1630-1638; Jain et al. JCO Precis Oncol 2018 (2) 1-12

# Registrational phase 2 study in iCCA (FIDES-01)<sup>1</sup>

## **Cohort 1:** Patients with FGFR2 gene-fusion expressing iCCA (2nd line)

- Encouraging interim results, consistent with earlier phase 1/2 data<sup>2</sup>
  - 21% ORR with six confirmed partial responses from 29 evaluable patients, 83% disease control rate
  - Manageable safety profile with low incidence of nail toxicity, retinal events, hand-foot syndrome and stomatitis
- Topline results expected H2 2020

## **Cohort 2:** Patients with FGFR2 gene mutations or amplifications

- Define the full therapeutic potential in iCCA with potential for differentiation
- Encouraging interim results - progression-free survival consistent with outcome in patients with FGFR2 gene-fusions<sup>3</sup>
  - Pooled data from 23 patients treated in clinical studies and from the early access and compassionate use programs
  - 7.2 months median progression free survival and 8.2 months median duration of treatment

<sup>1</sup> NCT03230318

<sup>2</sup> Droz Dit Busset et al. Annals of Oncology (2019) 30 (suppl\_5): abstract 3879 (NCT01752920)

<sup>3</sup> Droz Dit Busset et al. Annals of Oncology (2020) 31 (suppl\_5): abstract 45P (NCT01752920, NCT03230318)

# Clinical program in urothelial and gastric cancer

## FIDES-02<sup>1</sup> | Urothelial Cancer

*Multi-cohort Phase 1b/2 study of derazantinib monotherapy or in combination with atezolizumab in patients with urothelial cancer expressing activating molecular FGFR aberrations*

- Substudies (N≈300) in various treatment settings, including:
  - Post-chemotherapy/immunotherapy recurrence (second-line and post second-line)
  - First-line platinum-ineligible, PD-L1-low
  - Resistance to prior FGFR-inhibitor treatment
- Successful completion of phase 1b cohort
  - Recommended phase 2 dose for the combination at full standard doses of derazantinib and atezolizumab
  - No dose-limiting toxicities observed

## FIDES-03 | Gastric Cancer

*Multi-cohort Phase 1b/2 study of derazantinib as monotherapy or in combination therapy with standard of care or atezolizumab in patients with advanced HER2-negative gastric adenocarcinoma harboring FGFR genetic aberrations*

- Substudies using derazantinib monotherapy or combination treatment, including:
  - Derazantinib monotherapy in various molecular subtypes
  - Combination of derazantinib and standard of care
  - Combination of derazantinib with atezolizumab

<sup>1</sup> NCT04045613; Chaudhry A et al. Journal of Clinical Oncology 2020; 38, no. 6\_suppl. TPS590. (NCT04045613)



# FGFR-inhibitors show differences in safety profiles

	Cholangiocarcinoma				Urothelial cancer	
	DZB <sup>1</sup> (N=44)	INF <sup>2</sup> (N=71)	FUT <sup>3</sup> (N=67)	PEM <sup>4</sup> (N=146)	PEM <sup>5</sup> (N=108)	ERD <sup>6</sup> (N=87)
Dosing regimen	300mg QD	125mg Q4W QD for 3w	20 mg QD	13.5mg Q3W QD for 2w	13.5mg Q3W QD for 2w	8 mg QD (titration to 9mg)
Most frequent safety events	Phosphorus↑ Nausea Vomiting	Phosphorus↑ Fatigue Stomatitis	Phosphorus*↑ Diarrhea* Dry mouth*	Phosphorus↑ Alopecia Diarrhoea	Diarrhoea Alopecia Constipation	Phosphorus↑ Stomatitis Fatigue
Blood phosphorus↑†	59%	73%	88%	60%	31%	76%
Fatigue†	43%	49%	NR	42%	32%	54%#
Alopecia†	20%	38%	NR	49%	40%	26%
Dry eye/xerophthalmia†	16%	32%	NR	35%#	NR	28%#
Retinopathy†	0%	NR	9%	6%‡	NR	25%
Alanine aminotransferase (ALT) ↑	30%**	NR	NR	43%**	NR	41%**
Hand-foot syndrome/PPE	0%	27%	18%	15%	NR	26%
Nail toxicities	<5%	NR	42%	43%#	NR	41%#
Stomatitis	11%	45%	NR	35%	34%	56%

<sup>1</sup> Droz Dit Busset et al., ESMO 2019 and Basilea data on file, <sup>2</sup> Javle et al., ESMO 2018, <sup>3</sup> Goyal et al., ASCO 2020, <sup>4</sup> Pemazyre™ U.S. Prescribing Information (April 2020), <sup>5</sup> Necchi, et al., ESMO 2018,

<sup>6</sup> Balversa™ U.S. prescribing information (April 2019)

† assumed FGFR inhibitor class-effect; \*futibatinib treatment-related adverse events

# includes various and different adverse reactions; for details see Pemazyre™ U.S. Prescribing Information (April 2020) and Balversa™ U.S. prescribing information (April 2019);

† Refers to reported adverse events of Retinal Pigment Epithelial Detachment (RPED) for pemigatinib, Central Serous Retinopathy (CSR)/RPED for erdafitinib and CSR for futibatinib

‡ reported incidence is from 466 patients who received Pemazyre™ across clinical trials;

\*\* based on reported adverse events for DZB; based on reported laboratory abnormalities, regardless of causality for PEM and ERD.

Abbreviations: DZB: derazantinib, INF: infigratinib (BGJ398), FUT: futibatinib (TAS-120), PEM: pemigatinib (INCB54828), ERD: erdafitinib; PPES: Palmar-plantar erythrodysesthesia; NR: not reported; QD: daily; Q3W/Q4W: every 3/4 weeks; w: weeks

Oncology

# Lisavanbulin (BAL101553)

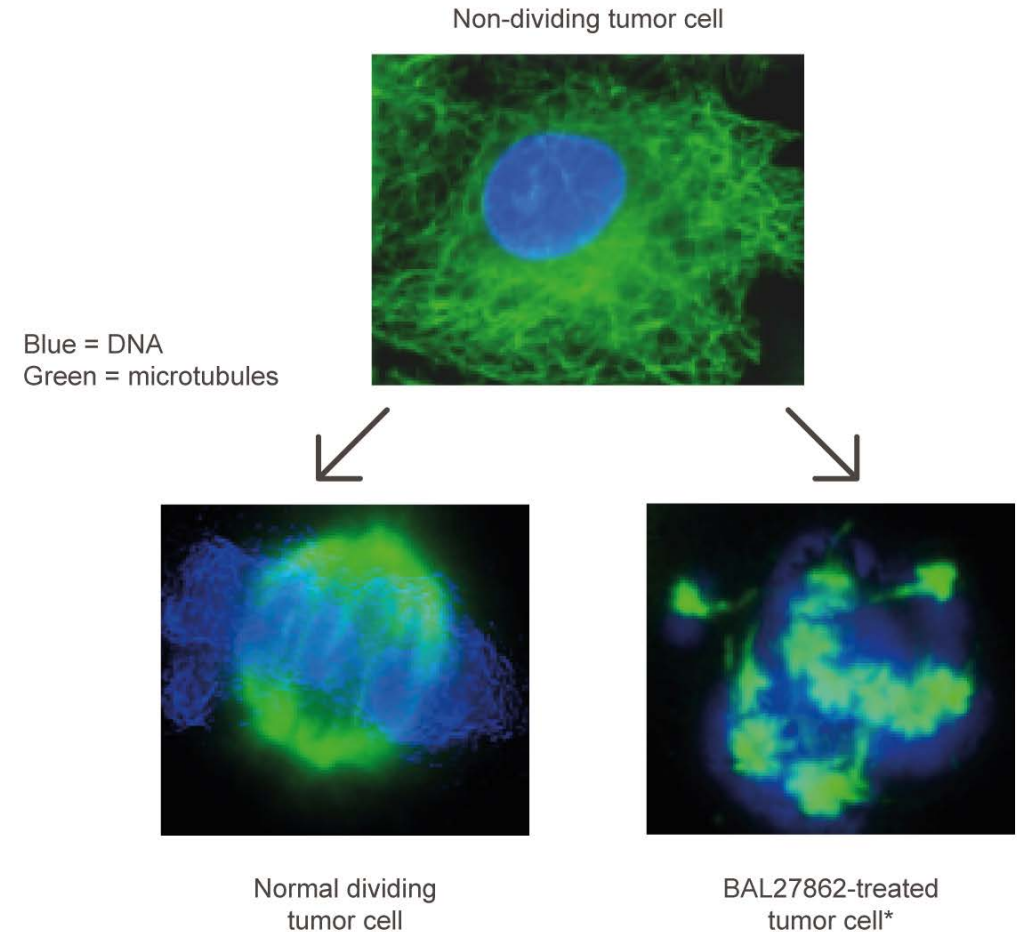
Glioblastoma  
and other solid tumors





# Novel tumor checkpoint controller crossing the blood-brain barrier

- Novel compound inducing tumor cell death through spindle assembly checkpoint activation
- Targeting diverse tumor types resistant to standard therapeutic approaches
- Flexible dosing potential, including daily oral dosing
- Comprehensive biomarker program to optimize patient selection
- Crosses the blood-brain barrier with potent activity in brain tumor models alone and in combination
- Biomarker-driven phase 2 study in patients with recurrent glioblastoma (GBM) using EB1-positivity as patient selection criterion ongoing



\* Lisavanbulin (BAL101553) is a prodrug of BAL27862

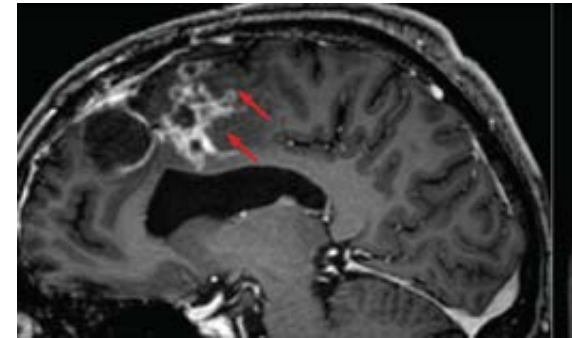


# EB1 — A potential response-predictive clinical biomarker for lisavanbulin

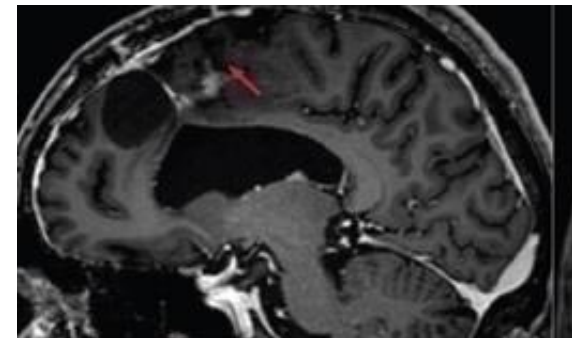
- EB1 (plus-end binding protein) is located on the microtubules and involved in microtubule dynamics and has been shown to be a response predictive marker for lisavanbulin in preclinical studies
- Strong EB1 staining was observed in a patient with an exceptional response to daily oral lisavanbulin in the phase 1 dose-escalation study in recurrent GBM<sup>1</sup>
  - Patient ongoing for more than two years
  - >80% reduction in GBM tumor size

<sup>1</sup> Lopez et al. Phase 1/2a study of once daily oral BAL101553, a novel tumor checkpoint controller, in adult patients with progressive or recurrent glioblastoma or high-grade glioma. JCO 2019;37:15 suppl, 2025 (NCT02490800)

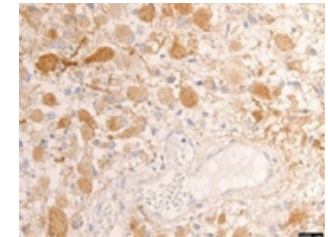
## GBM tumor size reduction in an exceptional responder and EB1 staining of GBM tissue compared to non-responding patients



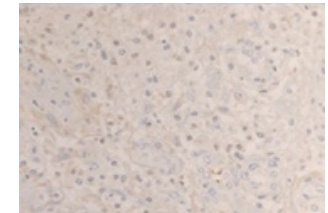
Baseline (May 2018)



Post Cycle 12 (April 2019)



Responder



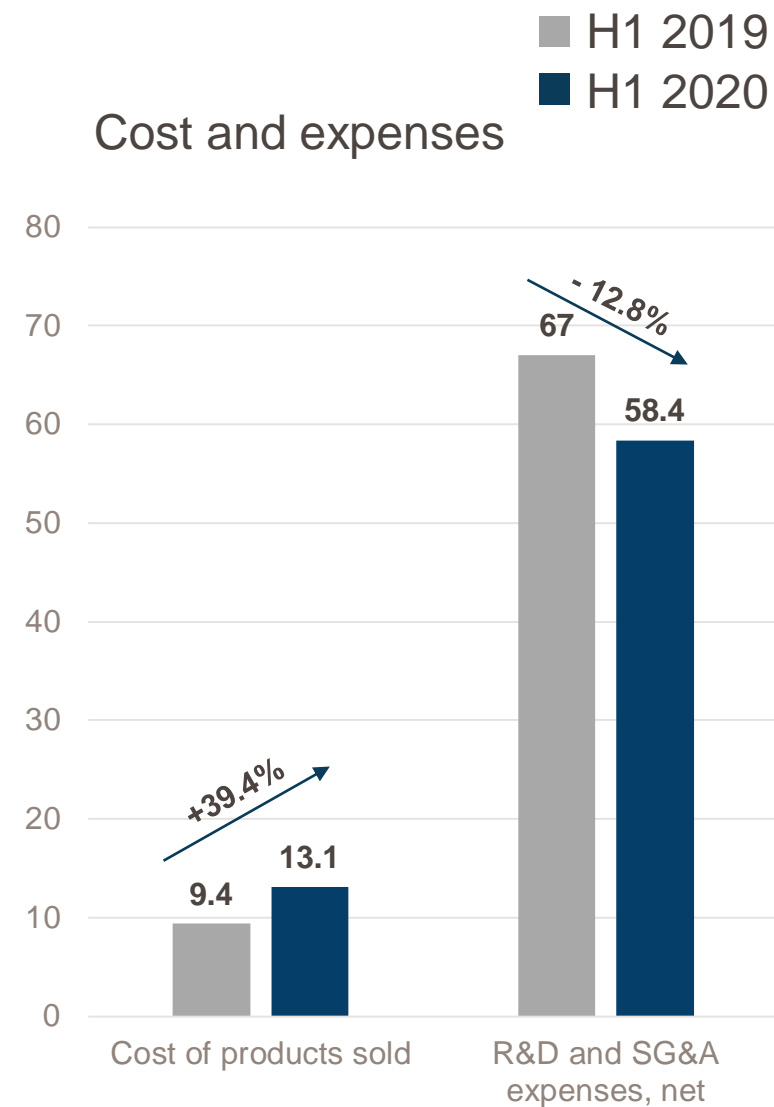
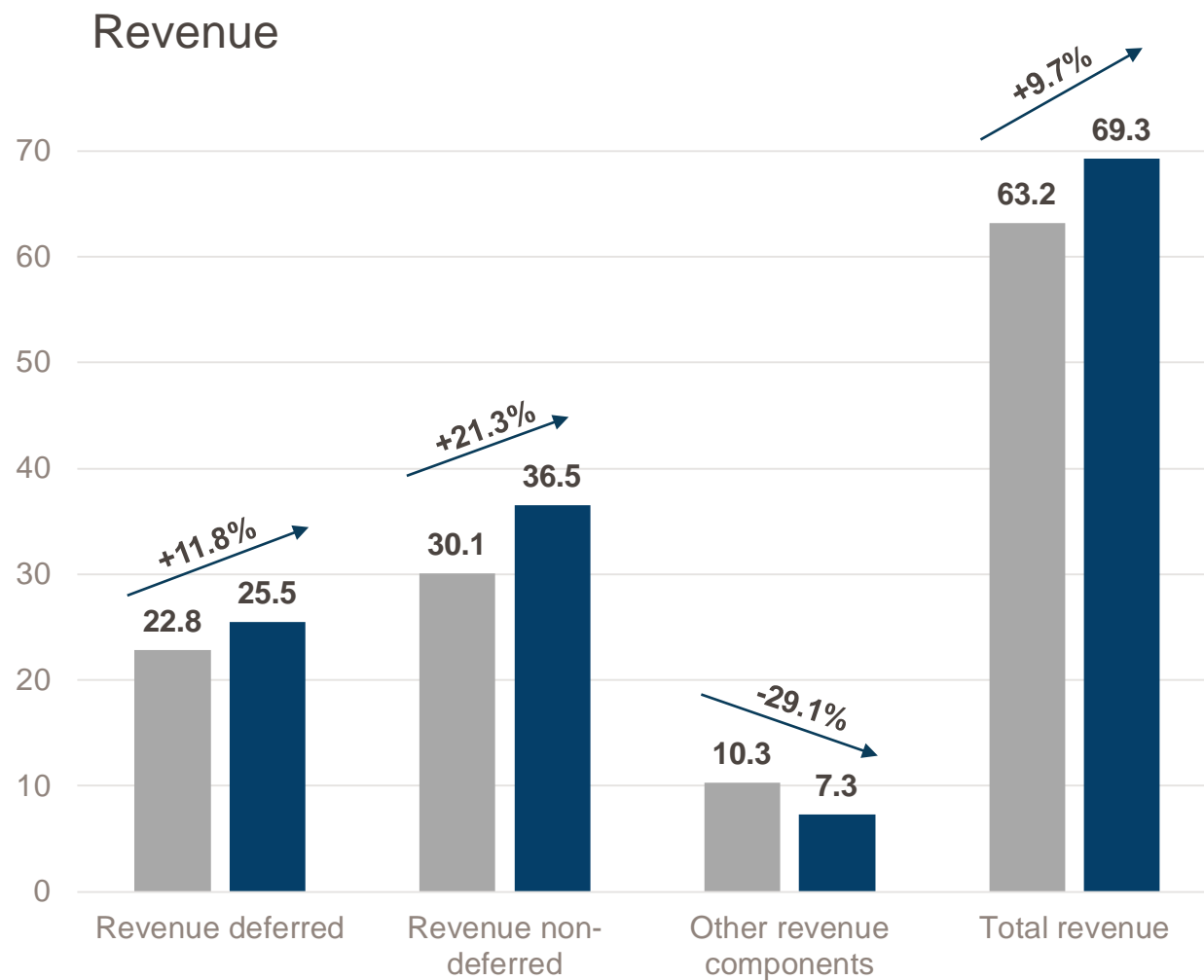
Non-responder



# Financials



# Financial summary, in CHF mn (1/2)

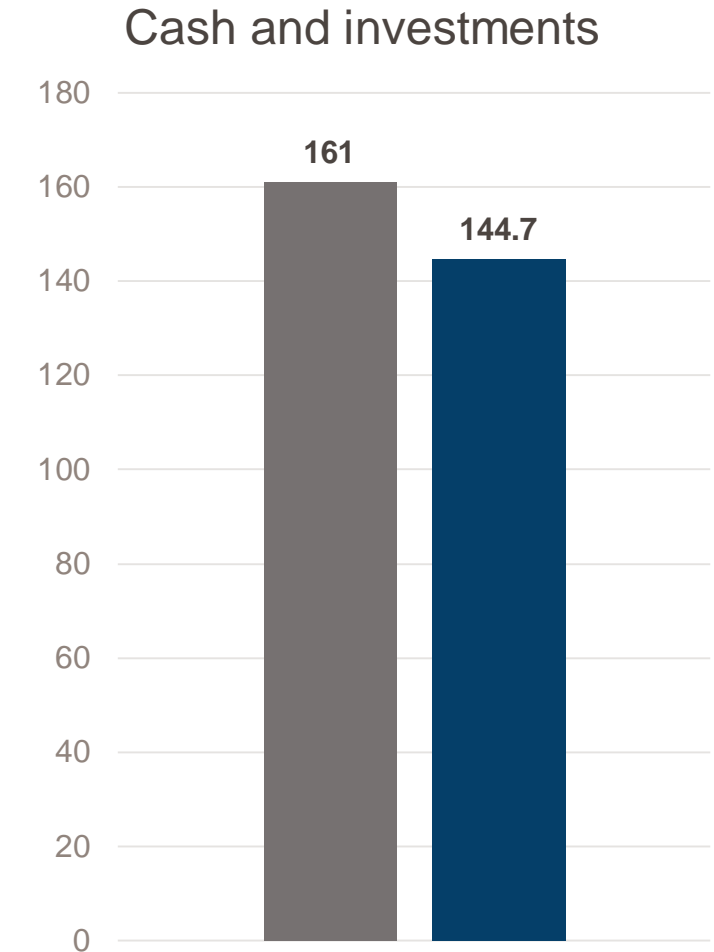
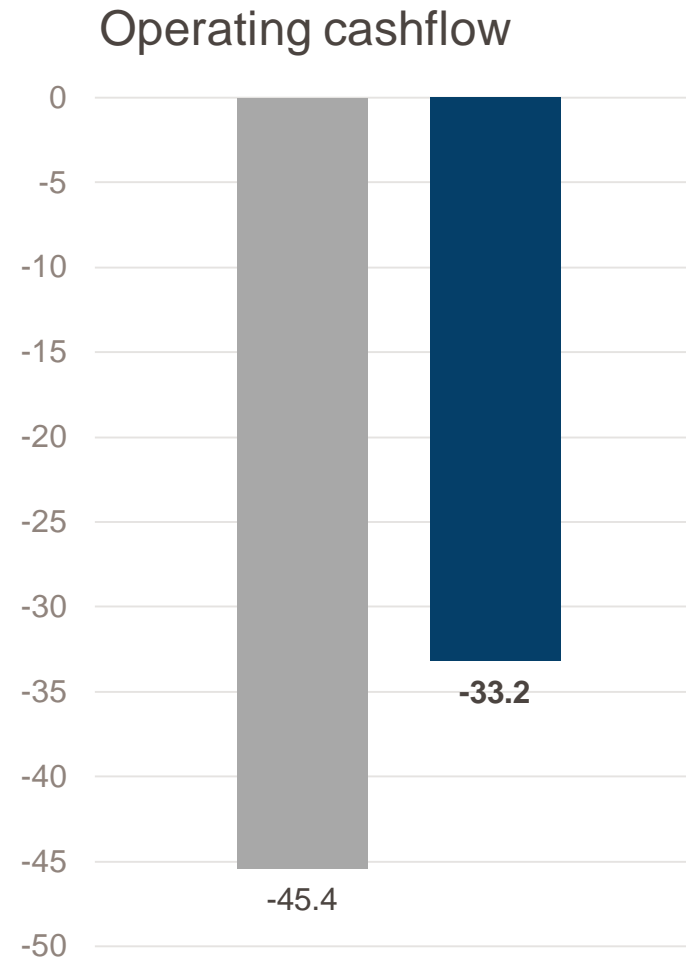
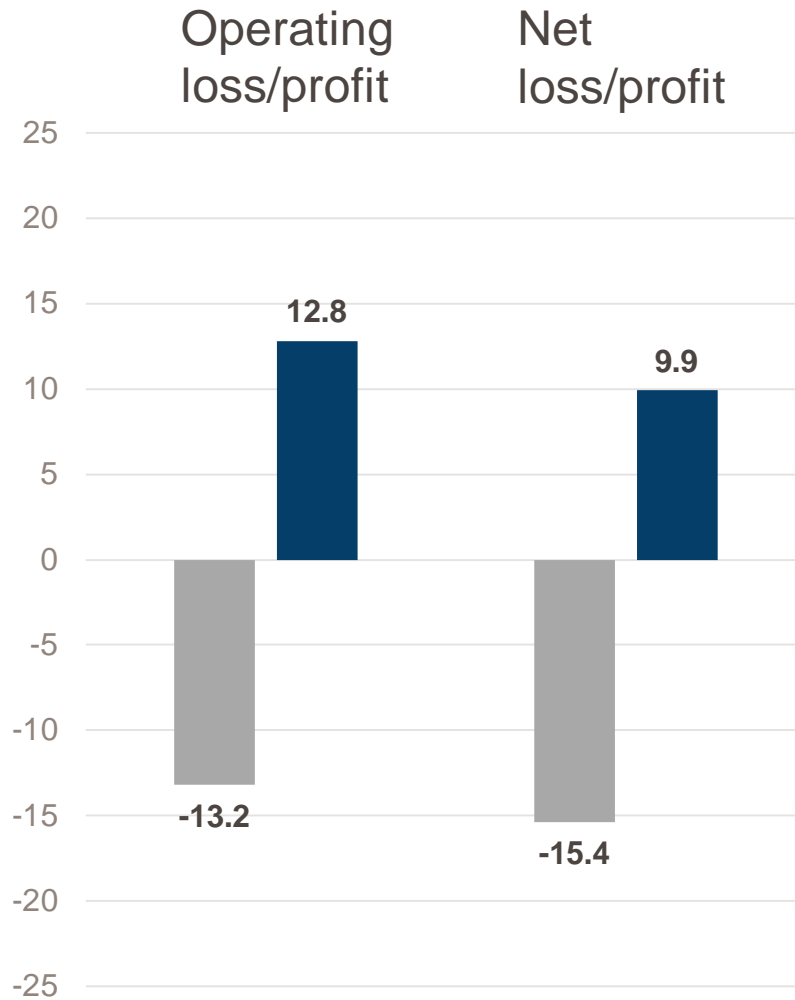


Note: Consolidated figures in conformity with U.S. GAAP; rounding applied consistently



# Financial summary, in CHF mn (2/2)

■ H1 2019  
■ H1 2020  
■ YE 2019

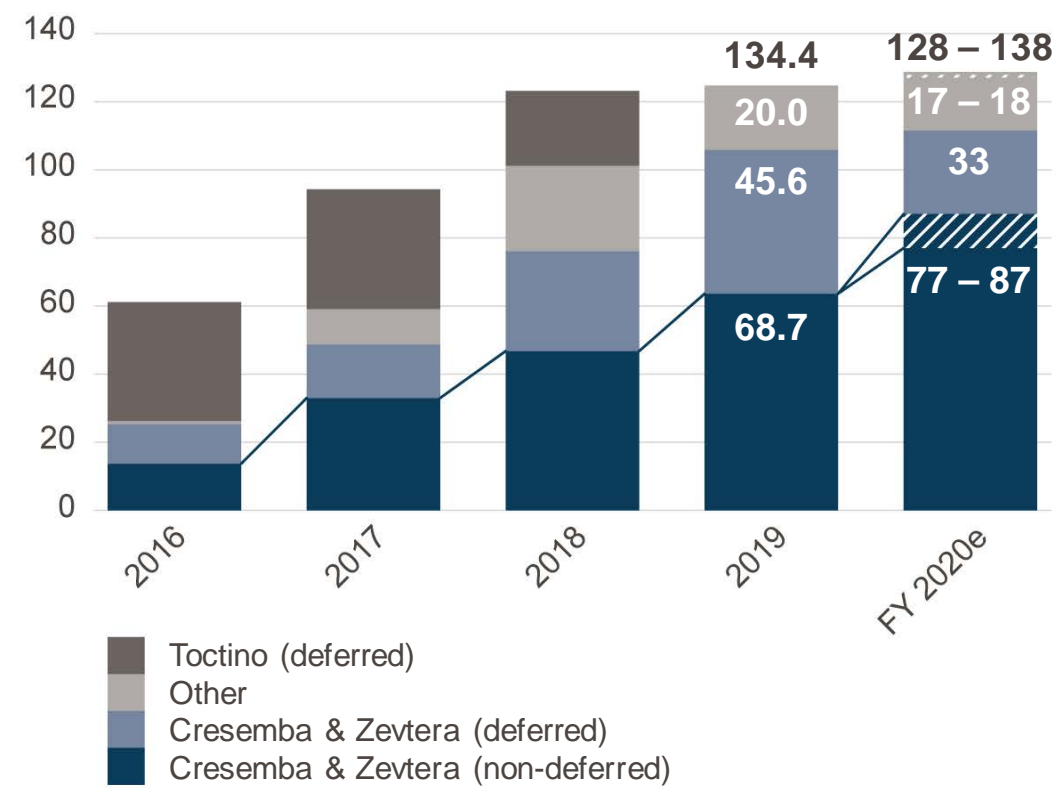


Note: Consolidated figures in conformity with U.S. GAAP; rounding applied consistently

# Financial guidance

In CHF mn	FY 2020e	FY 2019
Total revenue	128 – 138	134.4
thereof: Contributions Cresemba® & Zevtera® non-deferred deferred	77–87 33	68.7 45.6
Operating loss	5-15	17.2
Cash and investments	150	161.0

Strong increase in non-deferred revenue contributions  
Y-o-Y, CHF mn



# Outlook 2020 / 2021

## Cresemba® & Zevtera® — Increasing cash flows By the end of 2021, Cresemba to be on the market in 60 countries

	H1 2020	H2 2020	H1 2021	H2 2021
<b>Isavuconazole</b>	Complete patient enrolment in phase 3 study in Japan			Topline results from phase 3 study in Japan
<b>Ceftobiprole</b>				Complete patient enrolment in SAB phase 3 study
<b>Derazantinib</b>	FIDES-01 (iCCA)	✓ Complete patient enrolment in phase 2 registrational study (FGFR2 fusions)	Topline results (FGFR2 fusions)	
		✓ Interim results (other FGFR2 gene aberrations)		Topline results (other FGFR2 gene aberrations)
	FIDES-02 (urothelial cancer)	✓ Safety data and recommended phase 2 dose (RP2D) for derazantinib/atezolizumab combination and expansion into phase 2	Interim results in derazantinib monotherapy	Interim results in combination therapy with atezolizumab
	FIDES-03 (gastric cancer)	✓ Clinical supply agreement with Roche in gastric cancer	✓ Start of phase 1/2 study	Interim results
<b>Lisavanbulin (Oral)</b>	✓ Full results of phase 1 study in glioblastoma*	✓ Start phase 2 biomarker-driven glioblastoma study	Interim results from phase 2 biomarker-driven glioblastoma study	Topline results from phase 2 biomarker-driven glioblastoma study
			Complete patient enrolment in phase 1 study in newly diagnosed glioblastoma	

\* Accepted for ESMO poster presentation (Sept. 2020)

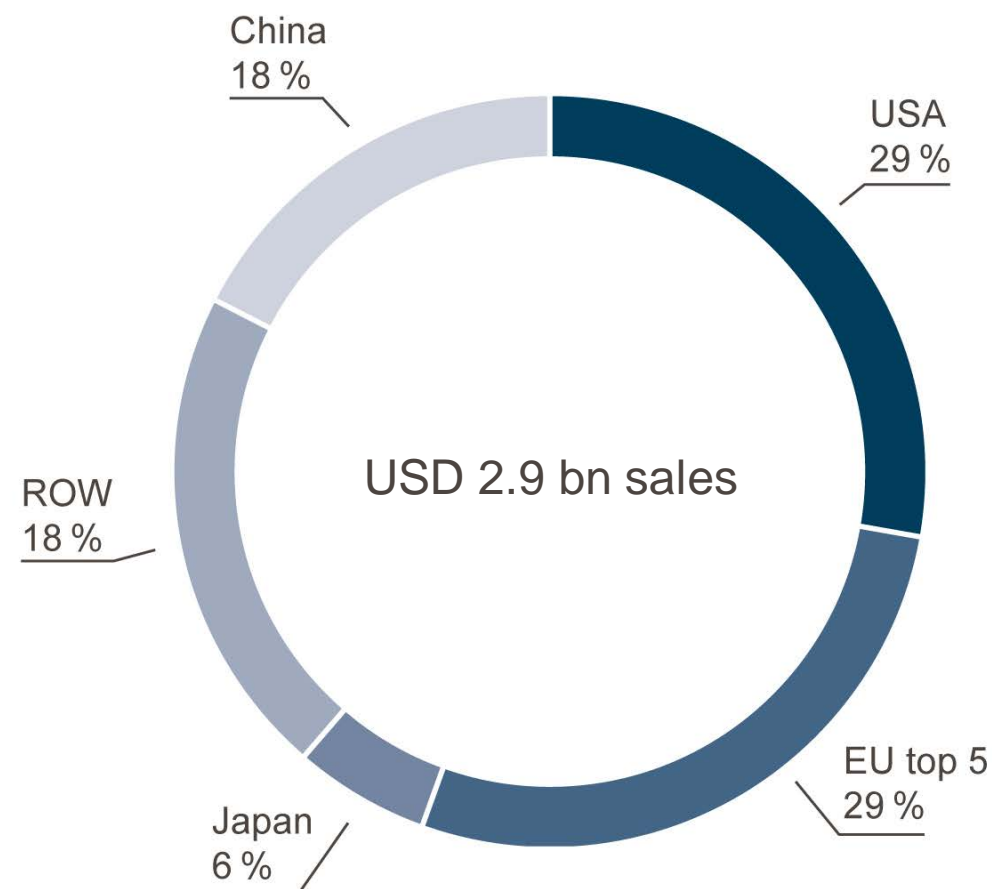


# Appendix

# Significant sales of best-in-class antifungals in all major regions — Covered by our partnerships

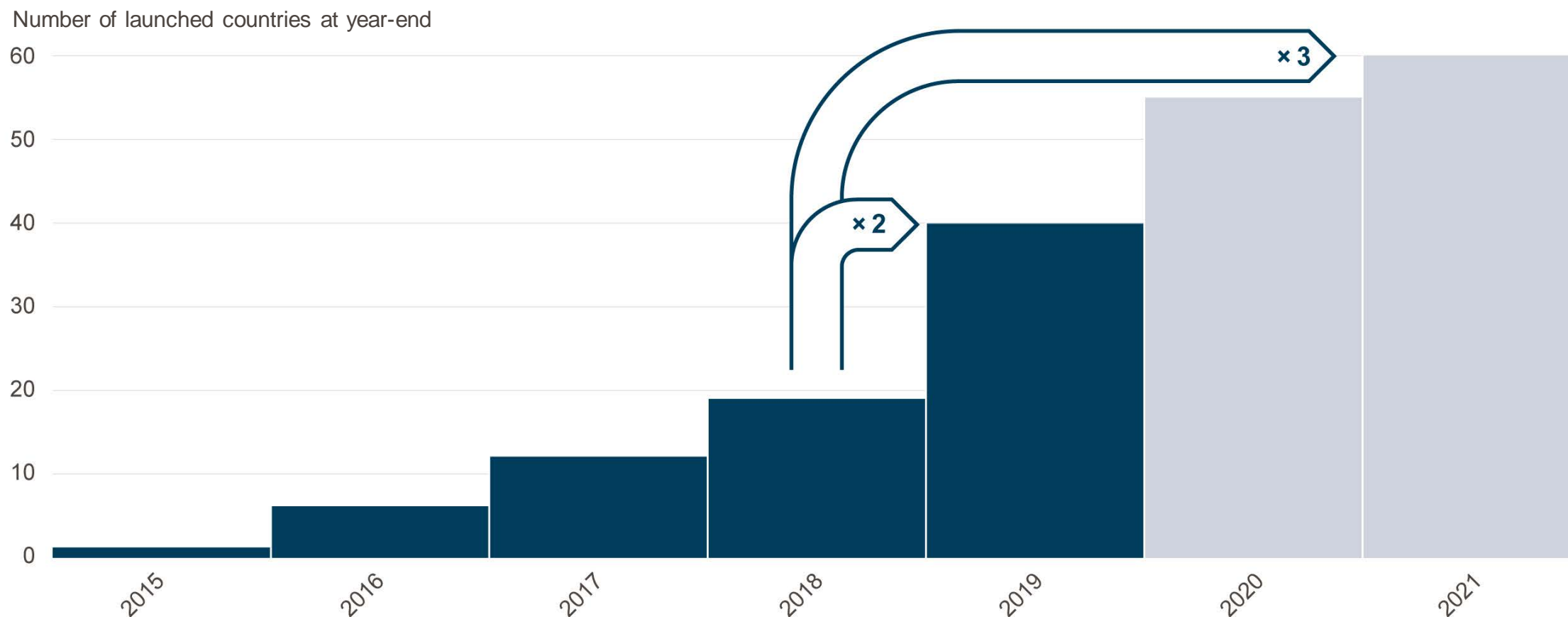
USD 2.9 bn sales of best-in-class antifungals\*  
(MAT Q2 2020)

\* Best-in-class antifungals: isavuconazole, posaconazole, voriconazole, AmBisome, anidulafungin, caspofungin, micafungin



MAT: Moving annual total; Sales figures in USD, corrected for currency fluctuations;  
Source: IQVIA, June 2020

# Cresemba® — Strong global roll out





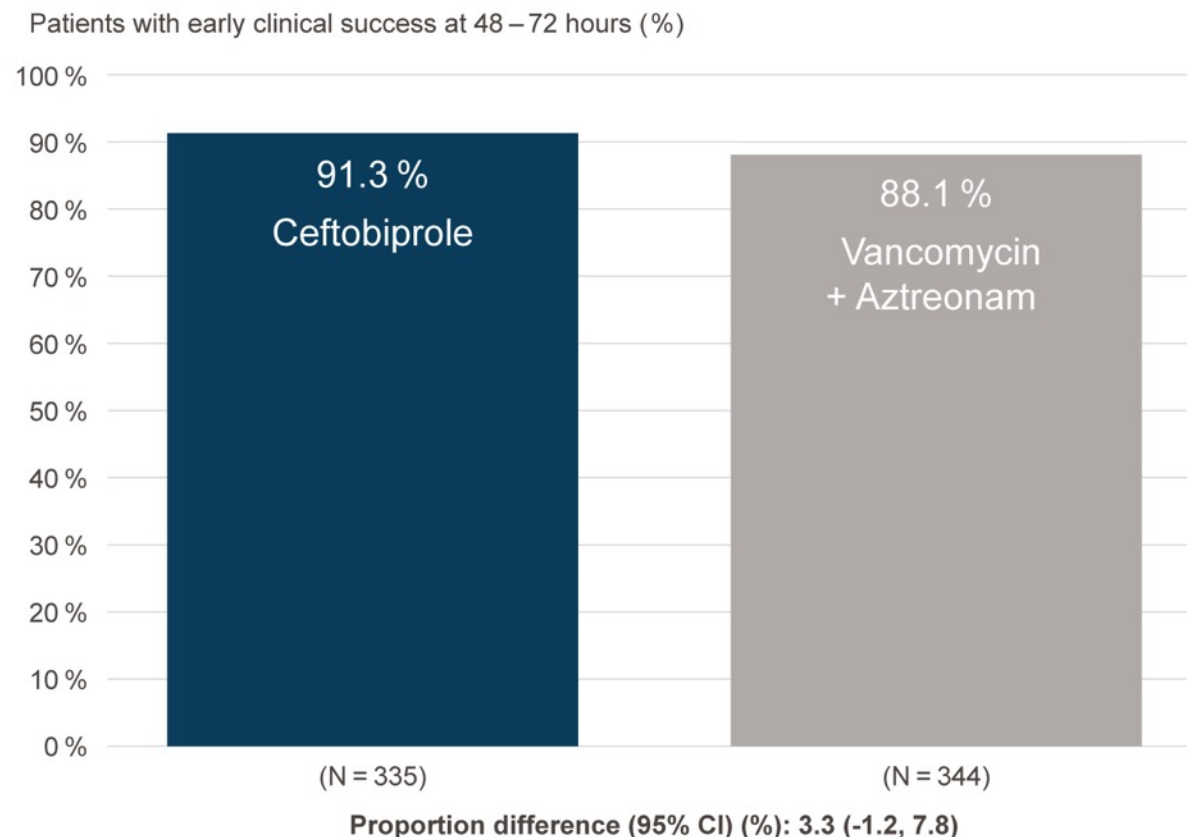
# Ceftobiprole — Positive topline phase 3 results reported in ABSSSI

Key topline study<sup>1</sup> results showing non-inferiority of ceftobiprole to vancomycin plus aztreonam for the primary and secondary endpoints



<sup>1</sup> NCT03137173  
ABSSSI: Acute bacterial skin and skin structure infections

## Early clinical response at 48–72h after start of treatment (ITT population)



ITT: intent-to-treat  
Pre-defined limit of non-inferiority = lower limit of 95 % CI for difference > -10 %

# Ceftobiprole — Positive topline phase 3 results reported in ABSSSI

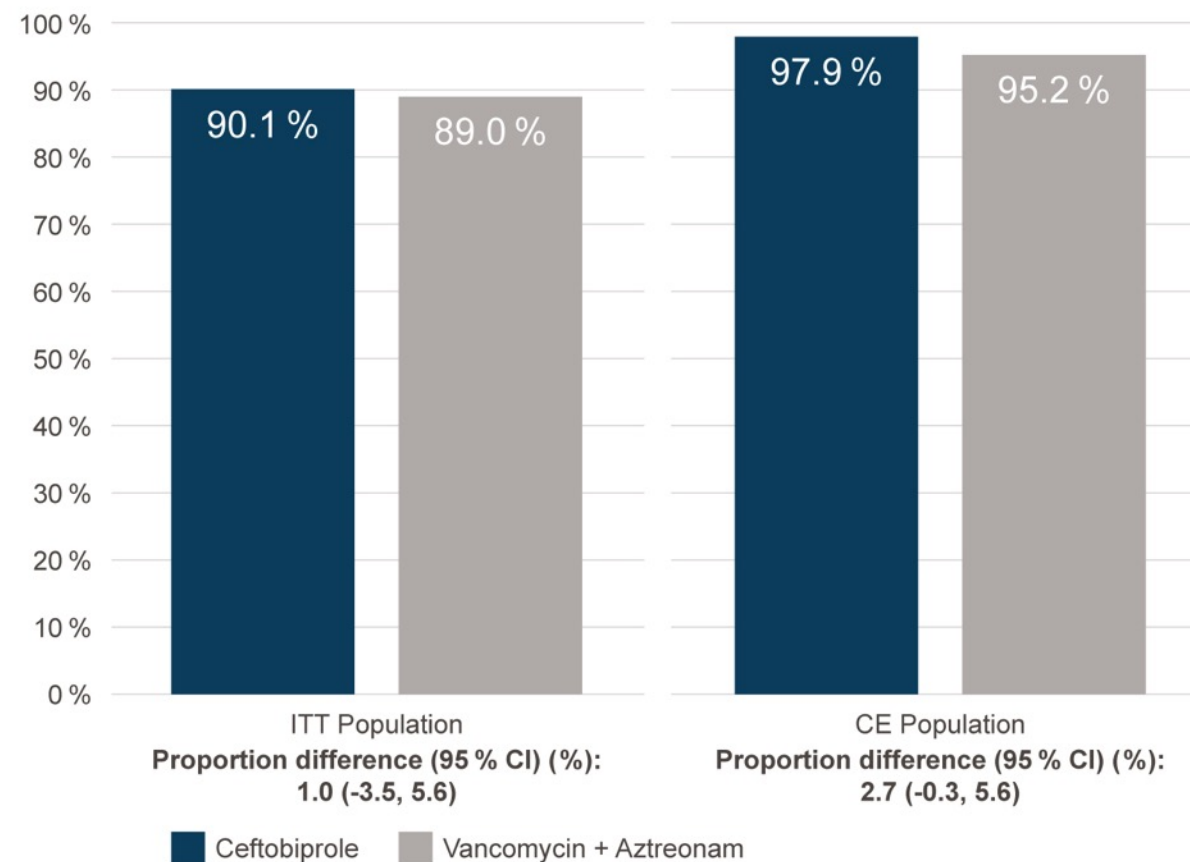
Key topline study<sup>1</sup> results showing non-inferiority of ceftobiprole to vancomycin plus aztreonam for the primary and secondary endpoints



<sup>1</sup> NCT03137173  
ABSSSI: Acute bacterial skin and skin structure infections

## Investigator-assessed clinical success at test-of-cure (TOC) 15-22 days after randomization (ITT, CE populations)

Patients with clinical success at the TOC visit (%)



CE: clinically evaluable; ITT: intent-to-treat

# Ceftobiprole key attributes for SAB treatment

- Beta-lactam antibiotic with rapid bactericidal activity against MSSA and MRSA<sup>1</sup>
- Superior activity profile in preclinical models of endocarditis compared to vancomycin and daptomycin<sup>2</sup>
- Low propensity for resistance development<sup>1</sup>
- Gram-negative coverage<sup>1</sup> in cases with polymicrobial infections
- Efficacy demonstrated in Phase 3 clinical trials in pneumonia and complicated skin and soft tissue infections<sup>1,3,4</sup>
- Established safety profile consistent with the cephalosporin class<sup>1,3</sup>

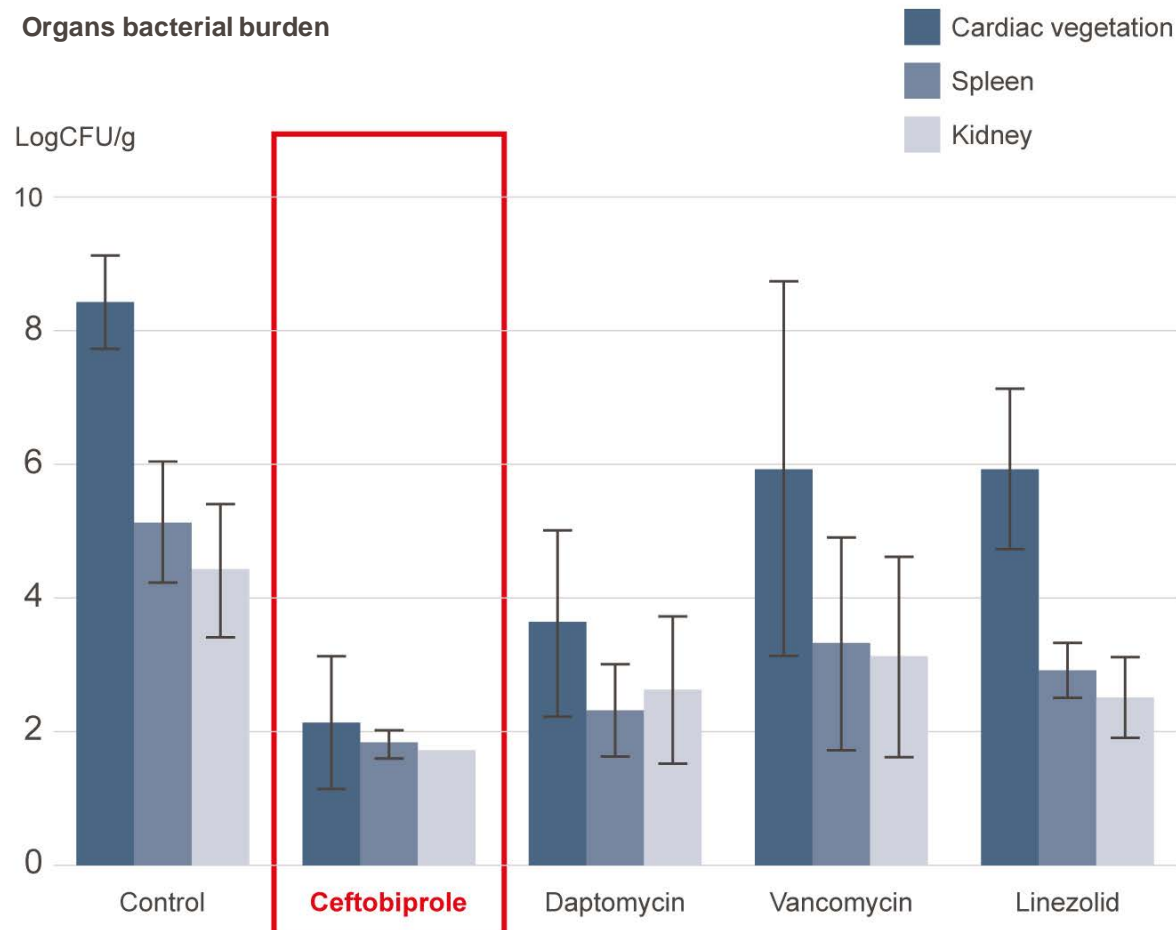
<sup>1</sup>Syed YY. Drugs. 2014;74:1523-1542.

<sup>2</sup>Tattein P et al. Antimicrob Agents Chemother. 2010;54:610-613.

<sup>3</sup>Giacobbe DR et al. Expert Rev Anti Infect Ther. 2019;17:689-698.

<sup>4</sup>Overcash JS et al. ECCMID 2020, abstract 1594

## Comparative efficacy in a rabbit model of endocarditis



Organism titers in cardiac vegetations, spleens and kidneys of untreated and antibiotic treated rabbits infected with MRSA<sup>2</sup>



# Phase 3 study with ceftobiprole in the treatment of patients with SAB



- **Design:** randomized, double-blind, multi-center
- **Enrolment:** approximately 390 adult patients (male and female)
- **Indications:** *Staphylococcus aureus* bacteremia (SAB), including endocarditis (IE) and other forms of complicated SAB
- **Main inclusion criteria:** Positive *S. aureus* blood culture and signs & symptoms for SAB
- **Intervention:** ceftobiprole medocaril i.v.; comparator daptomycin i.v. or daptomycin plus aztreonam to cover Gram-negative bacteria
- **Primary endpoint:** overall success as assessed by an independent Data Review Committee (DRC) in the treatment of SAB, including IE, at the post-treatment evaluation (PTE) visit (70 days after randomization) in the modified intent-to-treat (mITT) population.
- **Secondary endpoints:** includes all-cause mortality at Day 28 and Day 70 (PTE visit) in the intent-to-treat (ITT) and mITT populations; and time to *S. aureus* bloodstream clearance

# FGFR-inhibitors show differences in kinase-inhibition profiles<sup>1</sup>

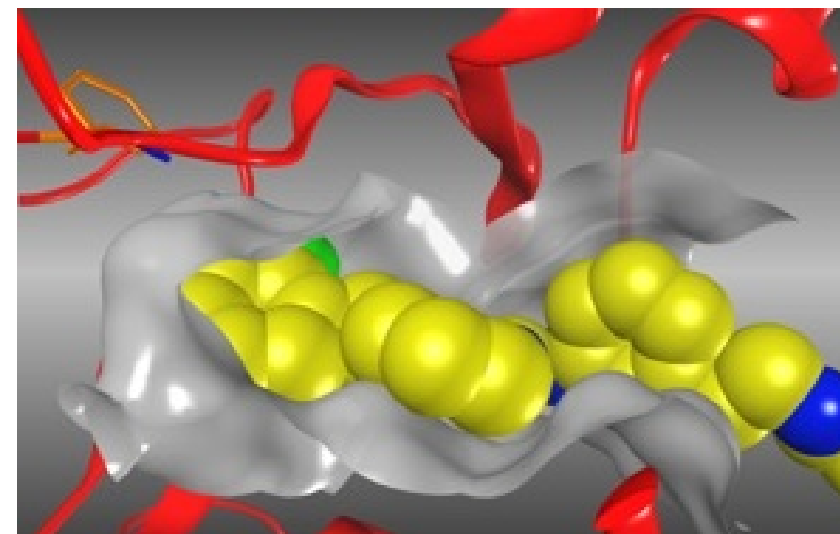
FGFR-inhibitor compound (Sponsor)	Parameter	FGFR1	FGFR2	FGFR3	FGFR4	CSF1R	VEGFR2
<b>Derazantinib</b> (Basilea)	Ratio to FGFR2 activity	4	1	4	77	3	6
<b>Pemigatinib</b> (Incyte)	Ratio to FGFR2 activity	3	1	4	39	231	62
<b>Erdafitinib</b> (Janssen)	Ratio to FGFR2 activity	2	1	2	13	95	6
<b>Rogaratinib</b> (Bayer)	Ratio to FGFR2 activity	5	1	6	18	116	48
<b>Infigratinib</b> (QED)	Ratio to FGFR2 activity	2	1	2	47	86	55
<b>Futibatinib</b> (Taiho)	Ratio to FGFR2 activity	2	1	2	18	NA	NA

<sup>1</sup> McSheehy et al. Derazantinib (DZB): A dual FGFR/CSF1R-inhibitor active in PDX-models of urothelial cancer. Mol Cancer Ther. 2019 (18) (12 Supplement) LB-C12

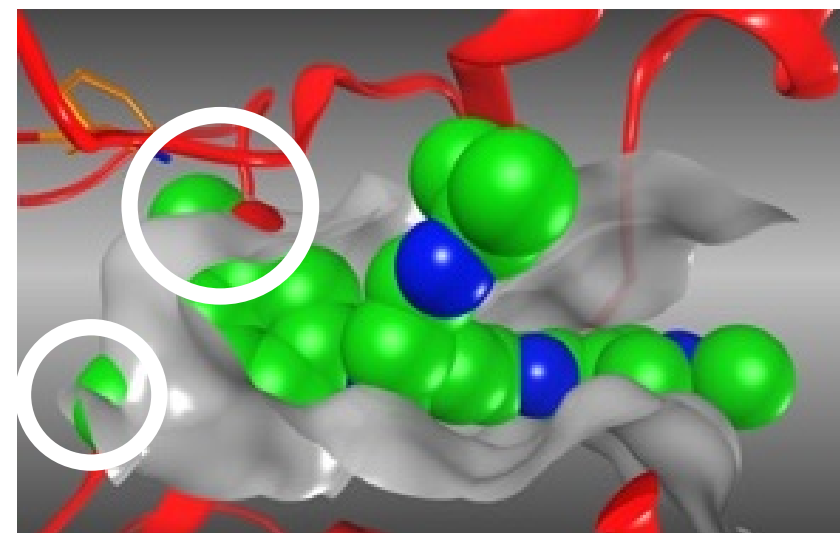
# In-silico analysis of derazantinib binding to CSF1R

- Crystal structures indicate differences in inhibitor binding sites of FGFR and CSF1R kinases
- Improved kinase inhibition activity of derazantinib against CSF1R versus other FGFR-inhibitors can be explained by the unique chemical structure of derazantinib<sup>1</sup>

<sup>1</sup> McSheehy et al. Derazantinib (DZB): A dual FGFR/CSF1R-inhibitor active in PDX-models of urothelial cancer. Mol Cancer Ther. 2019 (18) (12 Supplement) LB-C12



**Derazantinib** (yellow) fits to smaller active site pocket of CSF1R (grey/red)



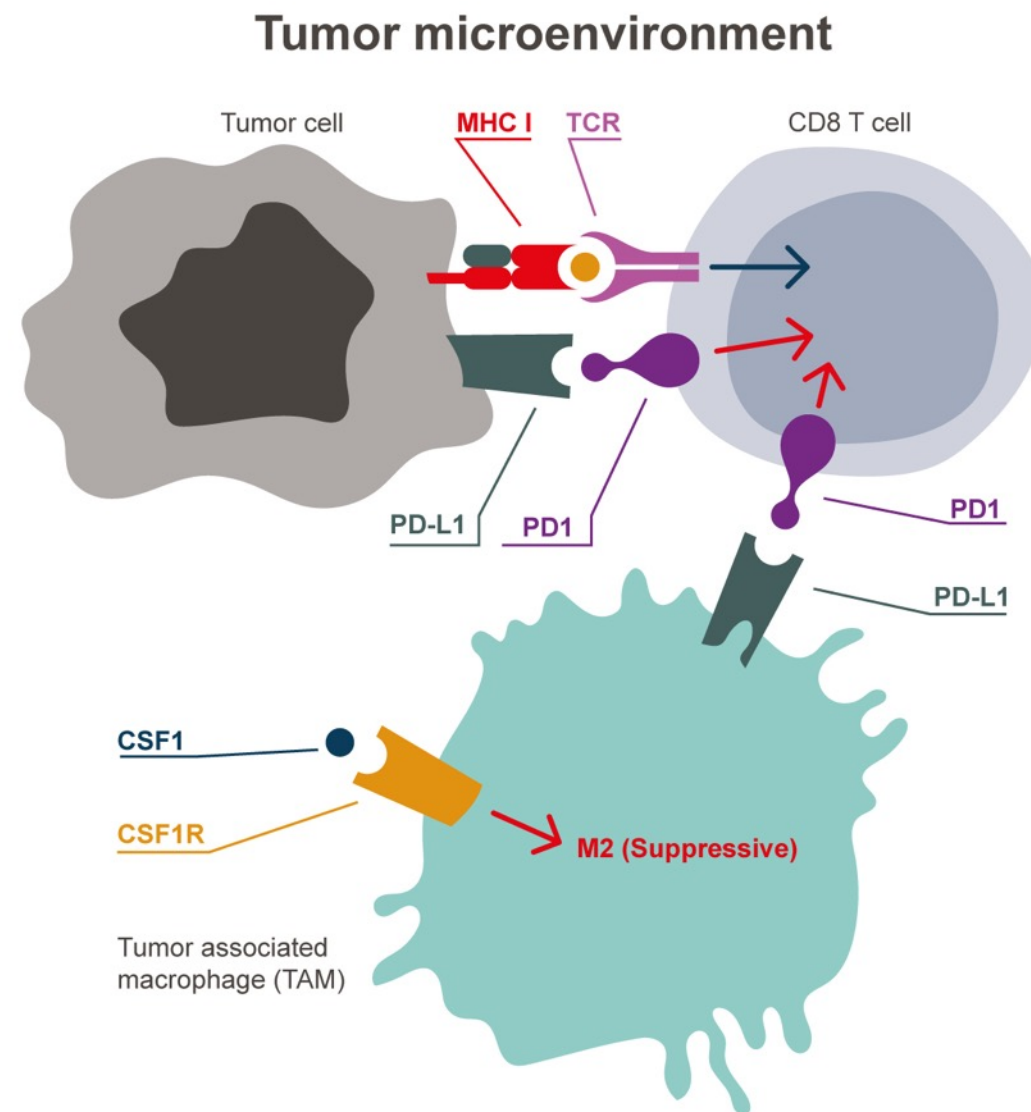
**Erdafitinib** (green) is too large (white circles) for the active site pocket of CSF1R (grey/red)



# Potential therapeutic relevance of CSF1R-inhibition

- Derazantinib is active in inhibiting FGFR kinases and CSF1R (Colony-stimulating factor-1 receptor)
- CSF1R-inhibition may reprogram immunosuppressive tumor-infiltrating macrophages, restore T-cell activity and thereby improve the susceptibility to PD1/PD-L1 inhibitors<sup>1</sup>
- Derazantinib may address several oncogenic mechanisms at the same time, i.e. inhibiting FGFR and making the tumor more susceptible to immunotherapy
- Basilea entered into a clinical supply agreement with Roche to study a combination of derazantinib and Roche's PD-L1-blocking immune-checkpoint inhibitor atezolizumab in patients with urothelial and gastric cancer

<sup>1</sup> X. Zheng et al. Redirecting tumor-associated macrophages to become tumoricidal effectors as a novel strategy for cancer therapy. *Oncotarget*. 2017;8(29):48436-48452

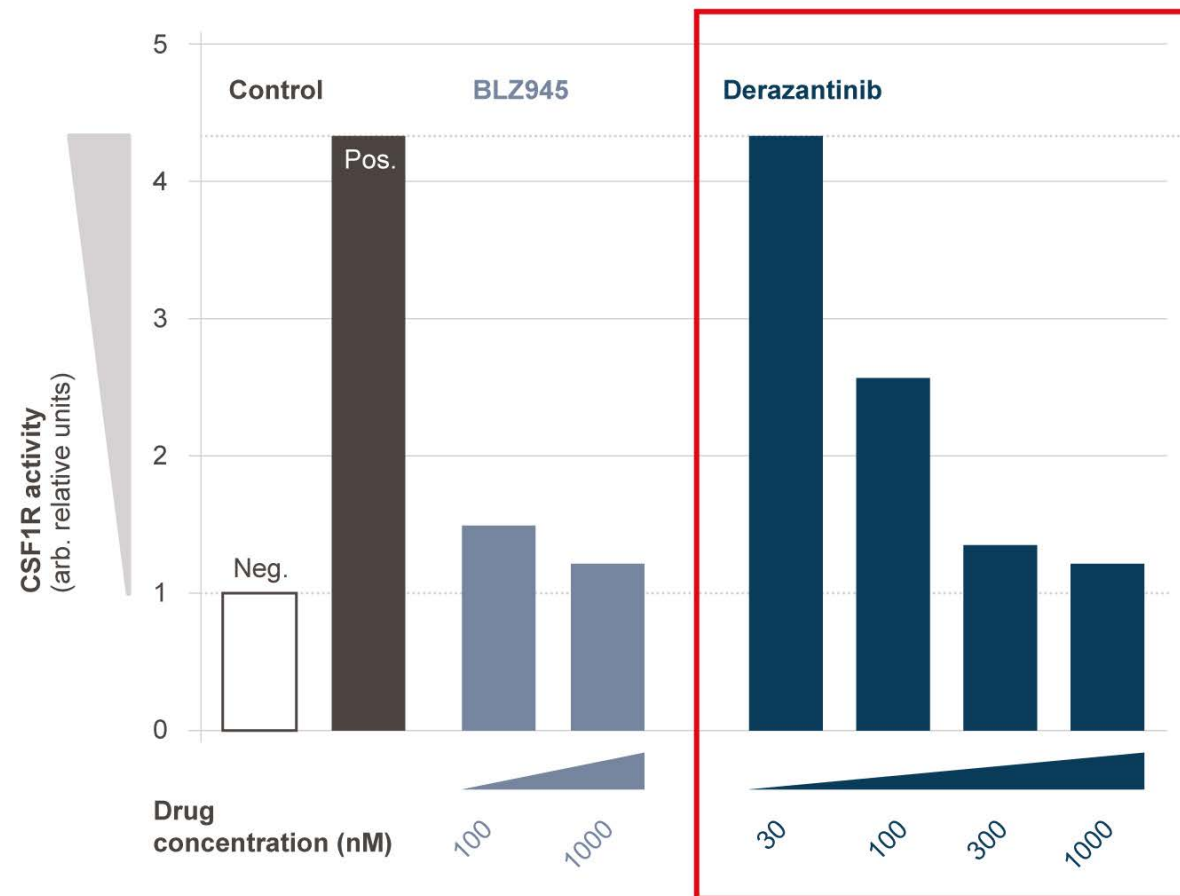


Graph adapted from: A. Ghasemzadeh et al. New Strategies in Bladder Cancer: A Second Coming for Immunotherapy. *Clin Cancer Res*. 2016;22(4):793-801

# Derazantinib inhibits mouse macrophage CSF1R activity

- Derazantinib treatment reduced CSF1-stimulated CSF1R activation (pCSF1R) in a concentration-dependent manner
- The maximum effect is similar to the specific CSF1R inhibitor BLZ945
- Derazantinib active-concentration is achievable in patients

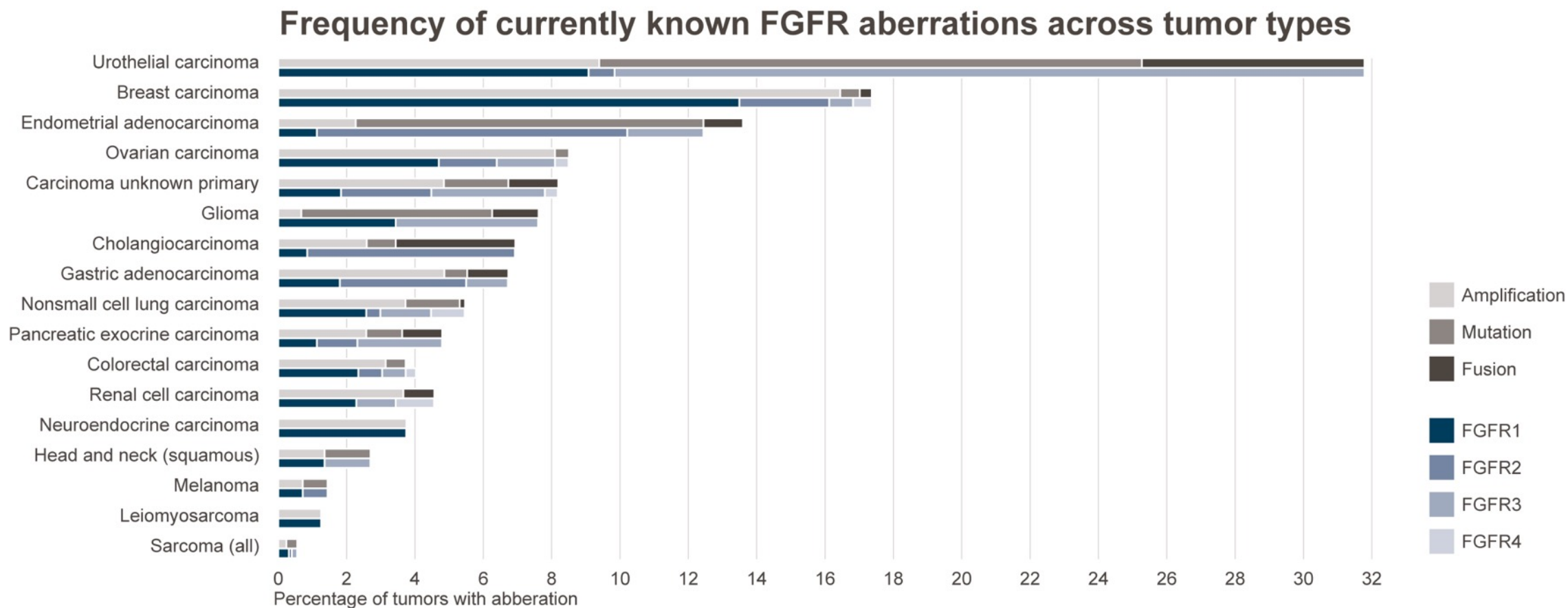
## Inhibition of CSF1R activity



*Method: bone-marrow-derived mouse macrophages were starved overnight, treated with CSF1 for 3 min, with or without pre-incubation with BLZ945 or DZB, and then extracted for subsequent immunoblot. The graph shows the quantification of the experiment based on densitometric analysis of the immunoblots*

<sup>1</sup> McSheehy et al. Derazantinib (DZB): A dual FGFR/CSF1R-inhibitor active in PDX-models of urothelial cancer. Mol Cancer Ther. 2019 (18) (12 Supplement) LB-C12

# Derazantinib — Significant potential beyond iCCA



Source: Helsten et al., Clin Cancer Res. 2016;22:259-67



# Derazantinib — Multi-cohort phase 1/2 study in advanced urothelial cancer (FIDES-02)<sup>1</sup>

- Derazantinib as single agent and in combination with atezolizumab in patients with advanced urothelial cancer testing positive for mutations or fusions of FGFR1, FGFR2 or FGFR3 genes
- The subgroup of patients with low PD-L1 expression have limited clinical benefit from the treatment with PD1/PD-L1 inhibitors. This subgroup, however, shows frequent FGFR genomic abnormalities (mainly FGFR3 fusions)
- Derazantinib combined with PD1/PD-L1 inhibitors may provide benefits related to multiple mechanisms (FGFR-inhibition, macrophage modulation, enhanced response to immunotherapy), in particular in the low PD-L1 expression subgroup
- Across a total of four sub-studies, FIDES-02 potentially can enroll up to approximately 300 patients
- Patient cohorts in various treatment settings, including:
  - Post-chemotherapy/immunotherapy recurrence (second-and post second-line)
  - First-line platinum-ineligible
  - Resistance to prior FGFR-inhibitor treatment
- Study conducted in multiple centers in Asia-Pacific, Europe and North America
- Clinical supply agreement with Roche for the immune-checkpoint inhibitor atezolizumab

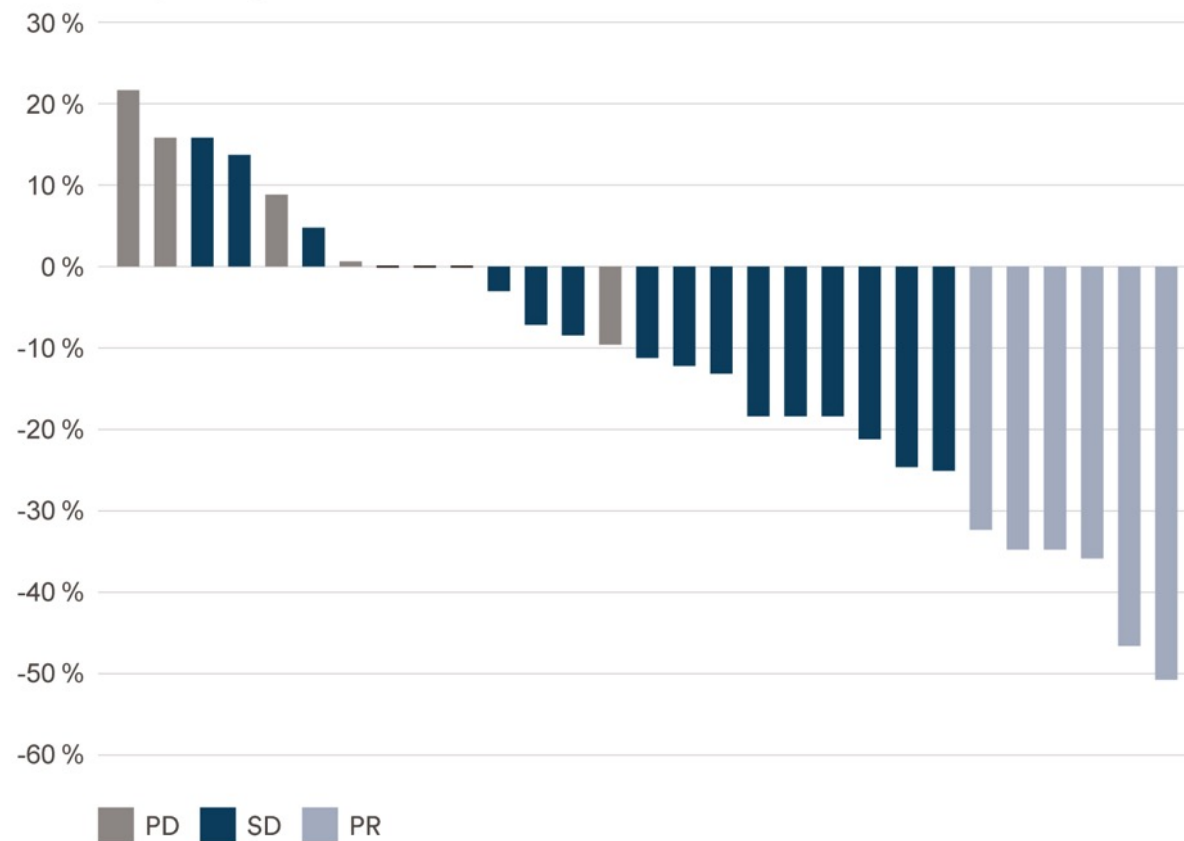
<sup>1</sup> NCT04045613

# Derazantinib — Established proof-of-concept in iCCA in phase 1/2a study

- Subgroup analysis of 29 patients with FGFR2-fusion positive iCCA:
  - Objective response rate of 21%
  - In 72% of patients, tumor response or disease stabilization for  $\geq 16$  weeks was achieved\*
- Compares favorably to Standard-of-Care (SoC) chemotherapy (cross-trial comparison)
  - Objective Response Rate (ORR) 21% for derazantinib<sup>1</sup> versus  $<10\%$  for SoC<sup>2, 3</sup>
  - Progression-Free Survival (PFS) approx. 6 months<sup>1</sup> versus 3 months for SoC<sup>2, 3</sup>
- Manageable safety profile<sup>1, 4</sup>

<sup>1</sup> V. Mazzaferro et al. Derazantinib (ARQ 087) in advanced or inoperable FGFR2 gene fusion-positive intrahepatic cholangiocarcinoma. British Journal of Cancer 2018 <sup>2</sup> A. Lamarca et al. Second-line chemotherapy in advanced biliary cancer: a systematic review. Annals of Oncology 2014 (25), 2328-2338; <sup>3</sup> L. Fornaro et al. Second-line chemotherapy in advanced biliary cancer progressed to first-line platinum-gemcitabine combination: a multicenter survey and pooled analysis with published data. Journal of Experimental & Clinical Cancer Research 2015 (34), 156 <sup>4</sup> K. P. Papadopoulos et al. A phase 1 study of ARQ 087, an oral pan-FGFR inhibitor in patients with advanced solid tumors. British Journal of Cancer 2017, 1-8

Best change of target lesion from baseline



Sources: Mazzaferro et al. British Journal of Cancer 2018;  
\* Mazzaferro et al. J Clin Oncol 2017;35 suppl: abstract 4017

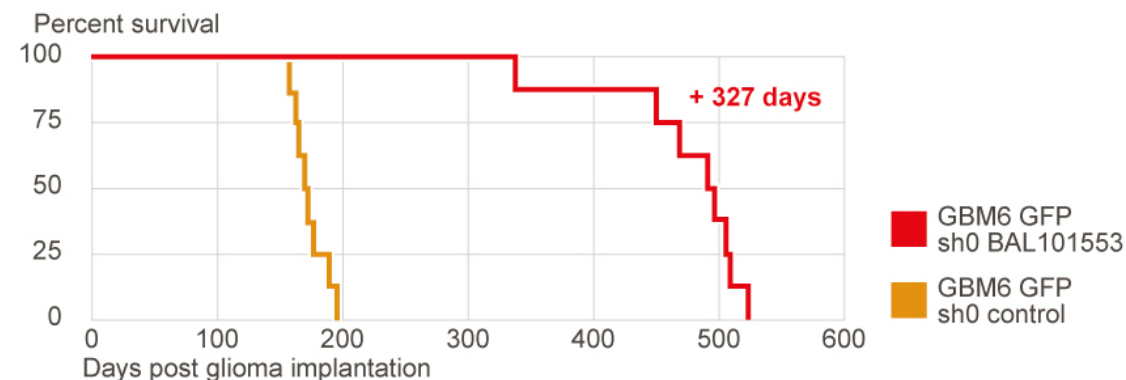
# EB1 — A potential response-predictive clinical biomarker for lisavanbulin

- EB1 (plus-end binding protein)<sup>1</sup> is located on the microtubules and involved in microtubule dynamics
- Predictive of response to lisavanbulin in mouse models<sup>1</sup>

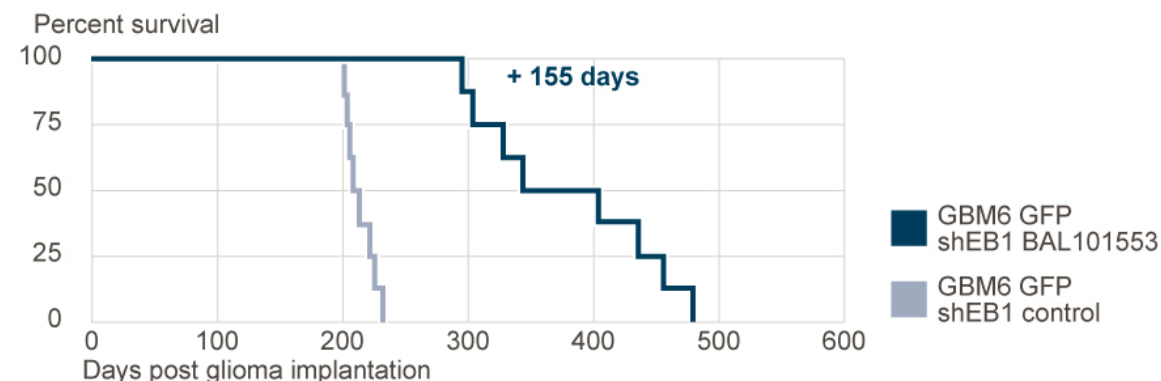
<sup>1</sup> Berges et al. EB1-dependent long survival of glioblastoma cancer stem-like cell tumor-bearing mice after oral treatment with the novel tubulin-binding checkpoint activator BAL101553. Eur. J. Cancer 2018, 103, E61-62, A166

## Effect of lisavanbulin (BAL101553) on survival in mice with EB1-expressing or EB1 downregulated GBM

### EB1-expressing GBM



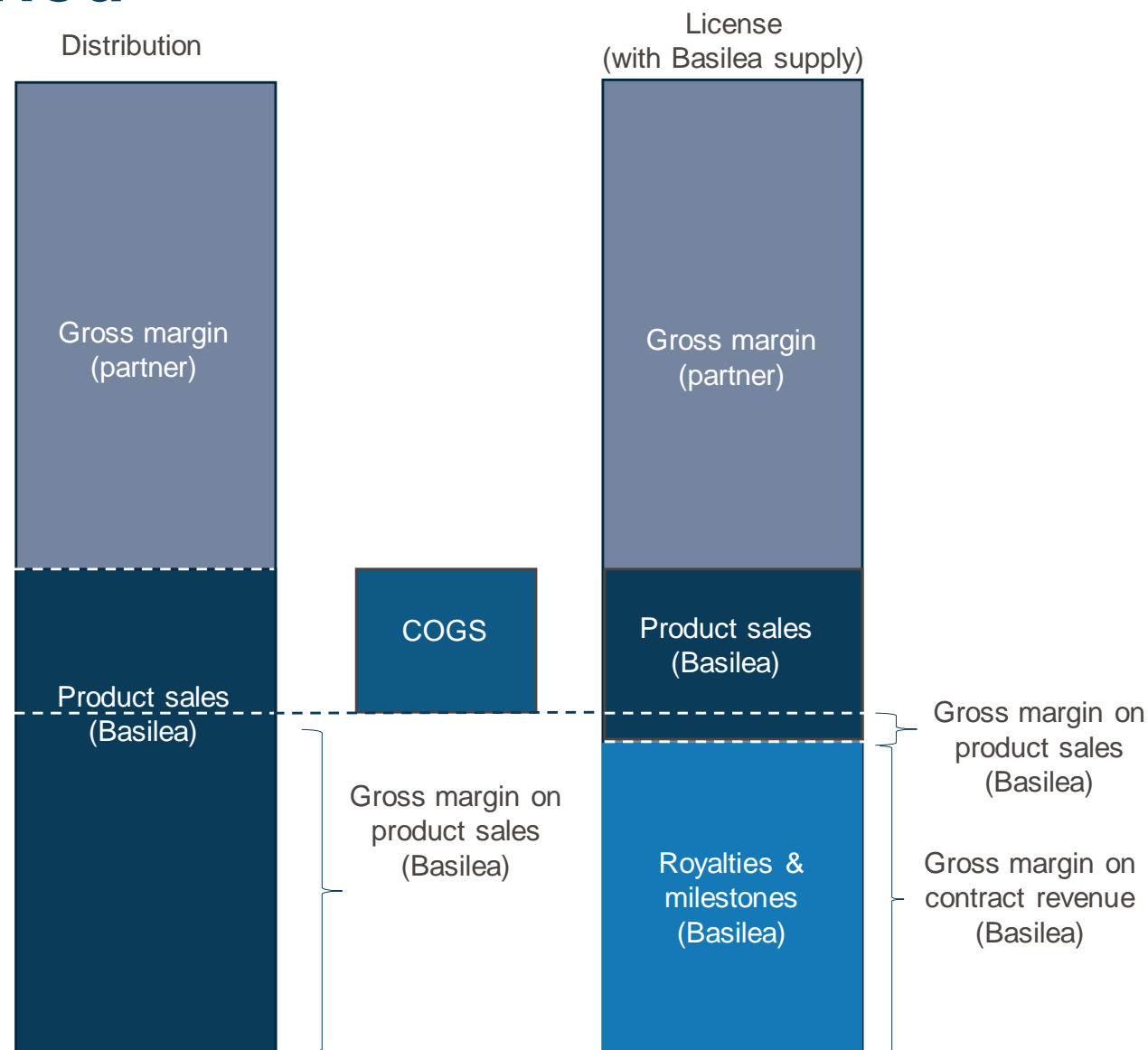
### EB1-downregulated GBM



# Extension of Pfizer supply period

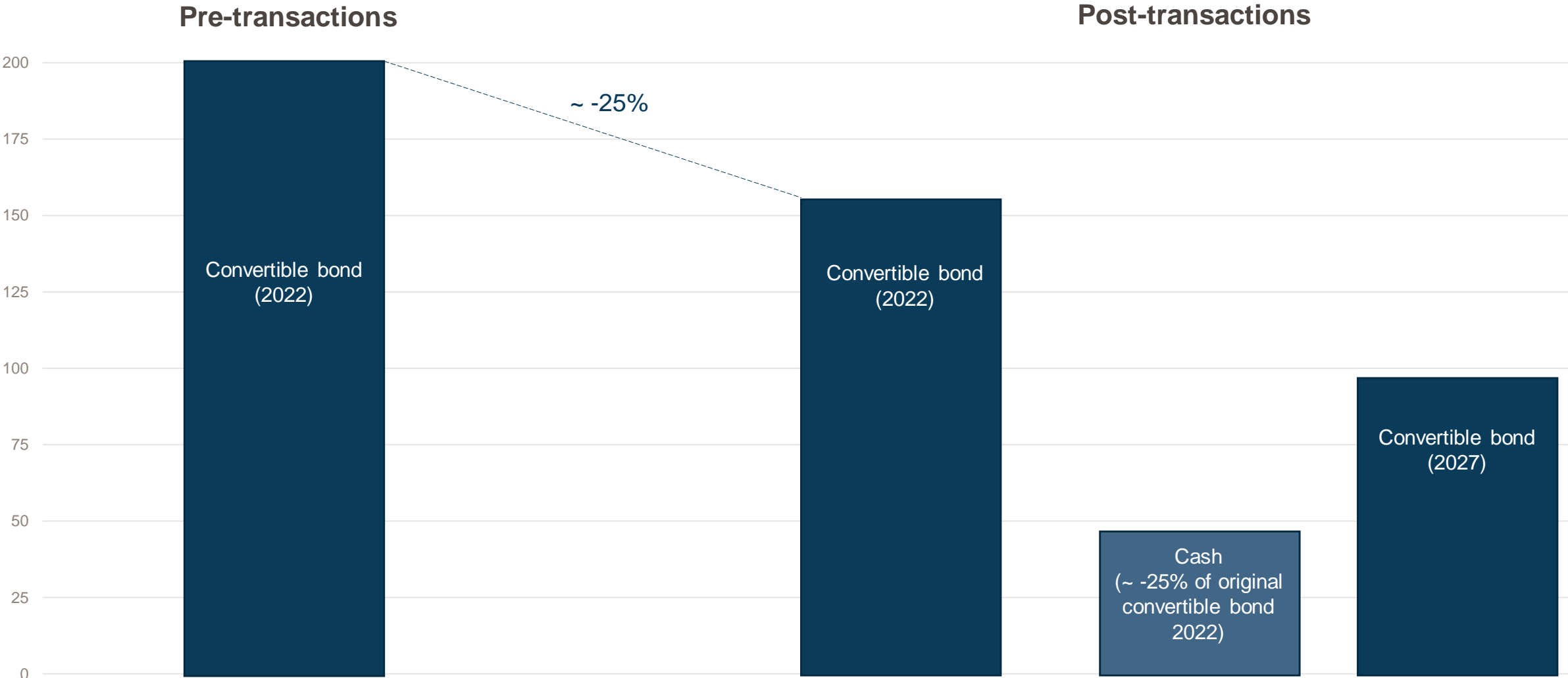
- Supply API and bulk Cresemba vials 2020/2021
  - Increase in product sales (in CHF)
  - Increase in cost of products sold (in CHF); economies-of-scale in supply to other partners
  - Lower gross margin (in % of product sales)
  - Temporary increase in working capital

=> Net positive cash flow over 2020/2021





# Convertible bond transactions — successfully improved debt maturity profile (in CHF mn)



# Glossary

- ABSSSI: Acute bacterial skin and skin structure infections
- CSF1R: Colony-stimulating Factor 1 Receptor
- FGFR: Fibroblast Growth Factor Receptor
- GBM: Glioblastoma multiforme
- iCCA: Intrahepatic cholangiocarcinoma
- MRSA: methicillin-resistant *Staphylococcus aureus*
- MSSA: methicillin-susceptible *Staphylococcus aureus*
- SAB: *Staphylococcus aureus* bacteremia
- VEGFR2: Vascular Endothelial Growth Factor Receptor 2

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