POLYPHOR

Corporate Strategy Update: **Focus Forward**

June 2020

Forward-looking statement

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Investment Highlights

1 Research driven clinical stage biopharmaceutical company with a Phase III immuno-oncology compound with fast path to market and a strong novel pipeline

Balixafortide

Potentially best-in-class CXCR4 inhibitor
Phase III first co-primary endpoint (ORR) in metastatic breast cancer expected in end Q1 2021
US$ 1.3 bn initial market potential with US$ 6-7 bn expanded potential

Antibiotics pipeline

First new class of antibiotics targeting WHO Priority 1 pathogens with very low resistance propensity
Lead candidate in Cystic Fibrosis P. aeruginosa infections: Phase 1 start planned for Q4 2020

Proprietary Macrocycle Technology Platform

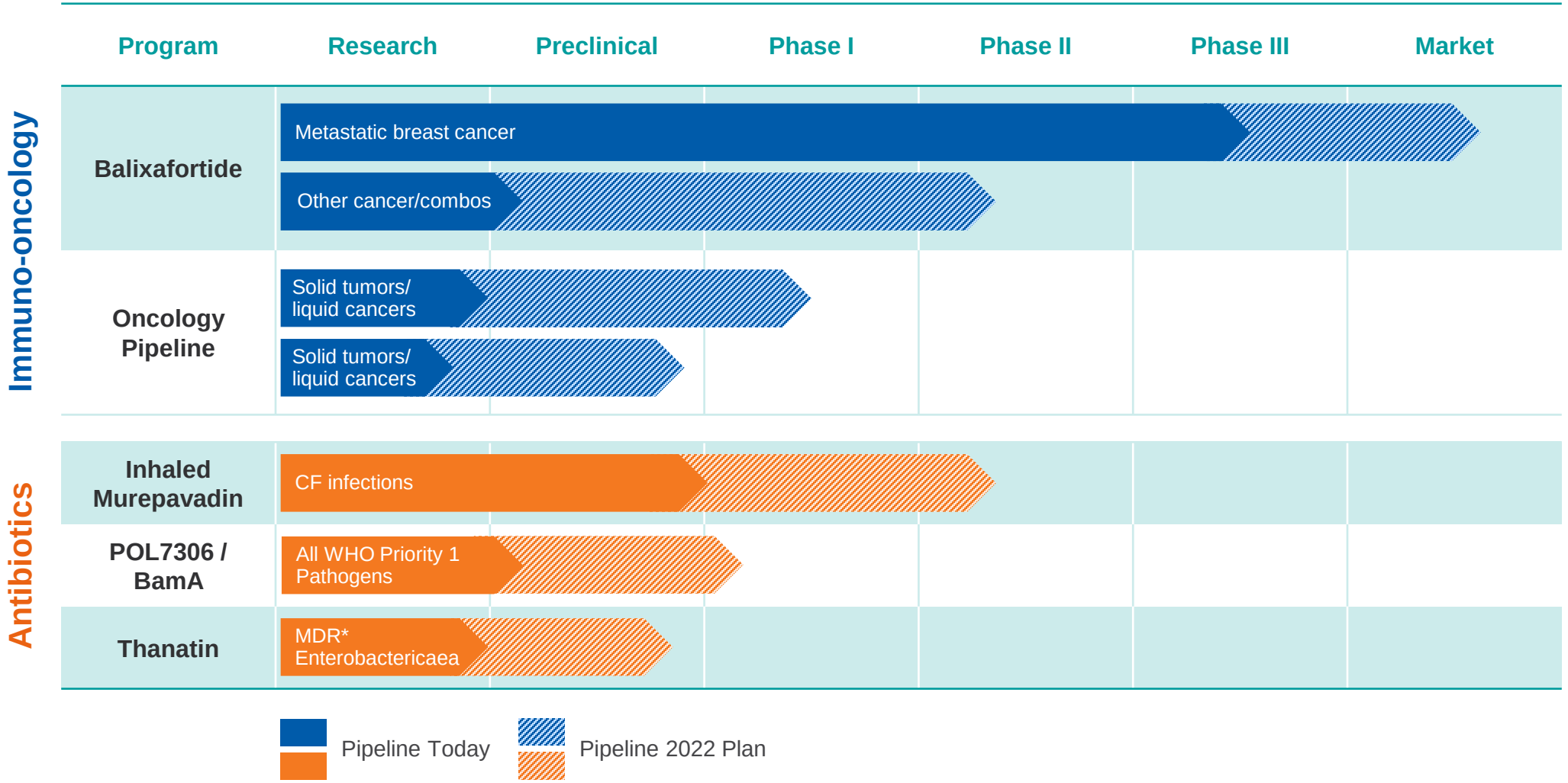
Discovery engine targeting oncology & antibiotics

2 Attractive valuation (CHF 95.1 M market cap, CHF 77.4 M cash and cash equivalents as of 31.12.2019, cash runway until end Q1 2021)

3 Polyphor provides multiple near-term pipeline progress and key value inflection points

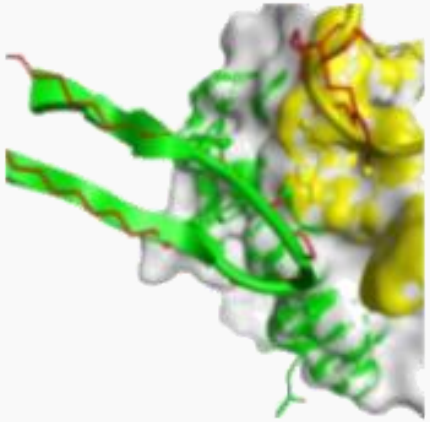
Polyphor Pipeline and Plan

Opportunity to provide multiple pipeline progress and key inflection points until 2022



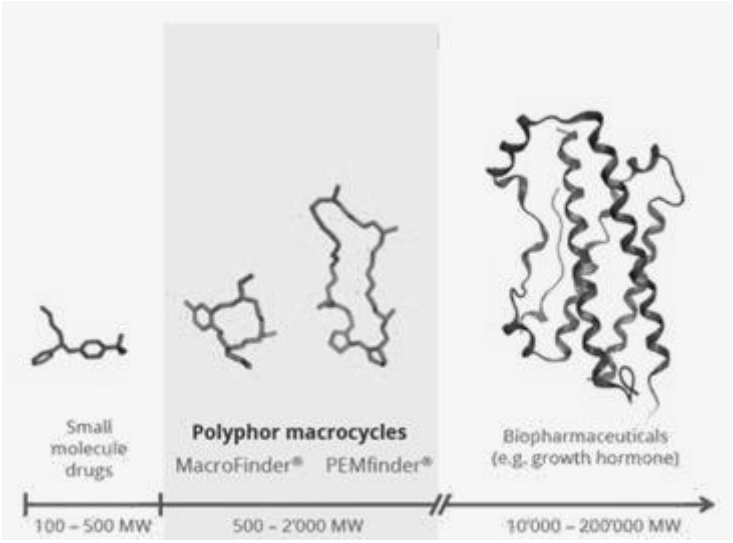
*Multidrug Resistant

Unique discovery & development engine



Macrocyclic Peptides: “Making the impossible possible”

- Peptides offer superior targeting vs. small molecules and large proteins against many targets
- The macrocyclic engineering approach potentially has two advantages over traditional peptides:
  - The compounds become more stable towards degrading enzymes
  - Become more selective and potent towards protein targets with therapeutic value
- Cost effective manufacturing

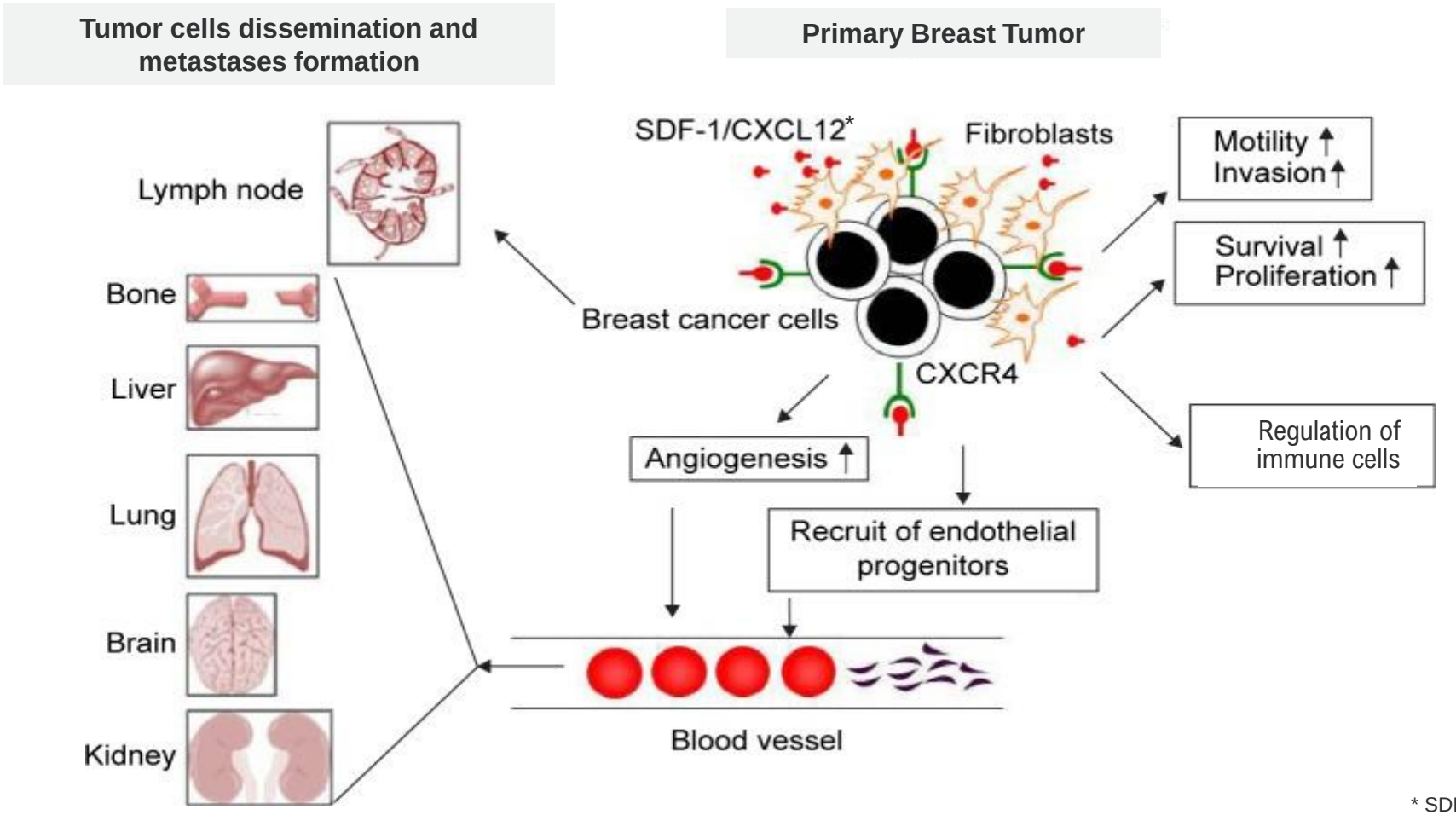


Delivering macrocyclic peptides in oncology and antibiotics

- Polyphor, a leader in macrocyclic peptide technology, the foundation of its pipeline
- One of the few companies with drug discovery to Phase 3 expertise while traditional approach is to license libraries to big pharma
- Our mission is to bring first-in-class molecules, focused in oncology and antimicrobial resistance
- Most advanced CXCR4 antagonist in clinical development for a solid tumor indication
- First new class of antibiotics targeting WHO Priority 1 pathogens with very low resistance propensity

CXCR4 overexpression is a key mechanism of cancer prognosis

CXCR4 promotes breast cancer growth through increased signalling pathways, angiogenesis, metastasis and immune cell modulation



* SDF-1/CXCL12: CXCR4 ligand

Xu *et al.*, 2015, modified

Balixafortide

Most advanced CXCR4 antagonist in clinical development for solid tumors

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Unlocking the potential of CXCR4 antagonism

- Highly selective and specific CXCR4 antagonist
- Clinically efficacious dose
- Clinical exposure 2000 fold above IC_{50}
- Not cytotoxic at clinical doses
- Low propensity of dose limiting toxicity with >5 fold safety margin*
- Potential to improve dose and schedule in various combinations

A novel immuno-oncology approach starting from a large indication

- First CXCR4 antagonist spearheading novel immuno-oncology approach in Phase III mBC**
- Large first indication in HER2 negative mBC 2nd and later lines of chemotherapy
- In combination with eribulin, the most recently approved chemotherapeutic in mBC
- Potential for:
  - Earlier lines of therapies in combination with other chemotherapies
  - Other tumor/oncology indications
  - Combination with checkpoint inhibitors

* comparing toxicology studies to current human doses

** Metastatic Breast Cancer

Balixafortide has potentially the best in class efficacy amongst CXCR4s*

Highest exposure among CXCR4 inhibitors – and importance of it shown by dose-response

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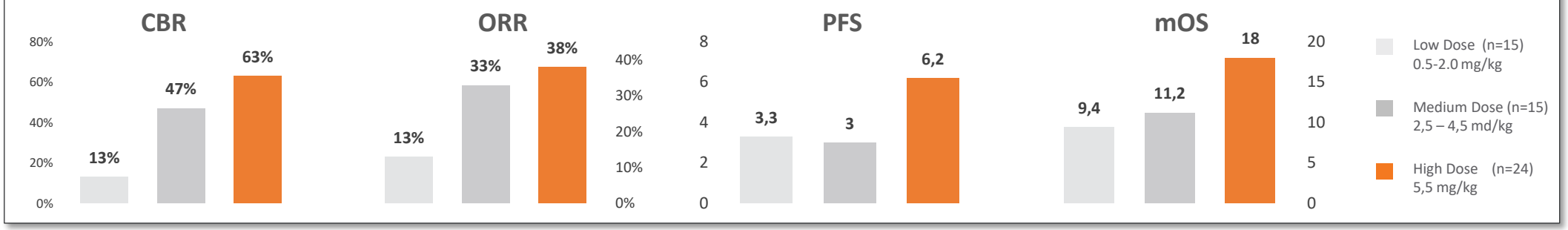
Molecule	Origin	Phase III Indication	Phase II Pipeline	Administration	Clinical Dose	IC50 coverage ratio by clinical exposure Cmax	IC50 coverage ratio by clinical exposure AUC
Plerixafor [1] *Sanofi*	Small molecule	**Hematopoietic stem cell mobilization** (Approved)		Subcutaneous	0.24 mg / kg	**1**	**1**
Mavorixafor [2] *X4 Pharma*	Small molecule	**WHIM syndrome**	**CC renal cell carcinoma** (combination with axitinib)	Oral	6-7 mg / kg (MTD)	**106**	**100**
Motixafortide [3] *BiolineRx*	Cyclic peptide 1st generation PD	**Mobilization of HSCs for autologous transplantation** (on top of G-CSF)	**Pancreatic Cancer** (comb. with pembro and chemo) **AML** (comb. with cytarabine)	Subcutaneous	1.25 mg / kg	**211**	**66**
Balixafortide [4] *Polyphor*	Cyclic peptide 3rd generation PD	**Metastatic Breast Cancer** (combination with eribulin)	**Metastatic Breast Cancer** (earlier lines in combination with chemo planned Q4 2020)	IV	5.5 mg / kg **(5-8 times safety margin) ****	**790**	**1064**

Impact of High Dose to Response Across all Efficacy Endpoints in Phase Ib Trial Balixafortide



* Compounds disclosed on company websites

1 FDA CDER Pharmacology Review: application number 22-311, FDA CDER Clinical Pharmacology Review: application number 22-311, mean of studies at 0.24 mg/kg dose

2 Wong, RS et al. Mol Pharmacol. 2008 Dec;74(6):1485-95. doi: 10.1124/mol.108.049775 Stone_Hendrix_2007, Antimicrob Agents Chemother 51(7):2351-2358

3 Tamamura H, et al. FEBS Lett. 2003 Aug 28;550(1-3):79-83, calculated from Abraham_Peled_2017, Clin Cancer Res 23(22); 6790–801 (supplemental table 2) From ClincalTrials.gov, accesed 23 January 2018, ongoing trials, e.g. COMBATà (NCT02826486)

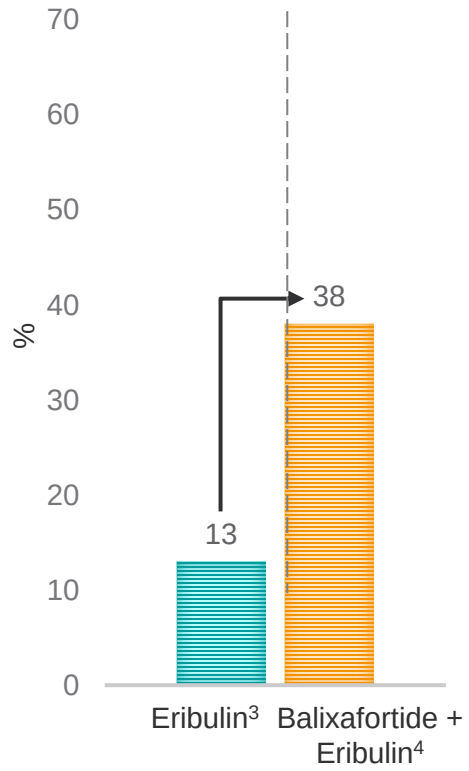
4 In-house unpublished study POL6326-07. Intra-experiment comparisons must always be interpreted with caution

** Safety Margins are calculated as multiples of Balixafortide plasma concentration at No Observed Adverse Effect Level (NOAEL) in 13 week NHP toxicology study compared to balixafortide plasma concentration in humans at 5.5mg/kg dose, which is the dose in the Phase 3 FORTRESS study.

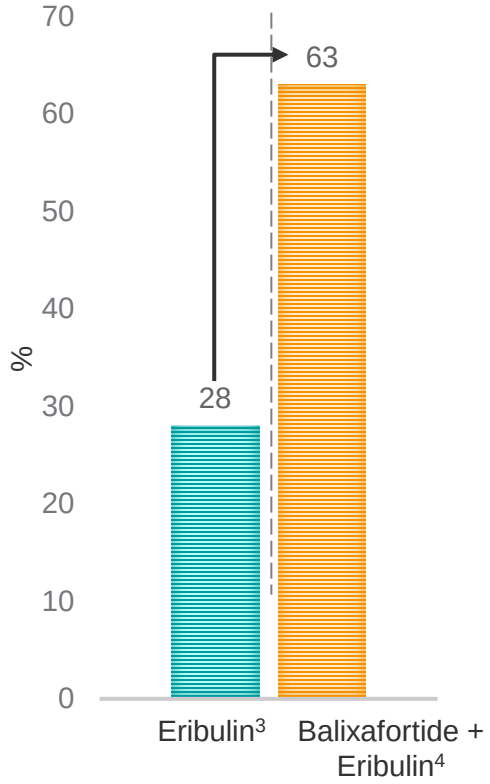
Balixafortide + eribulin: PoC demonstrated with strong results across all efficacy parameters

Balixafortide (Ph Ib / PoC) Proof of Concept[1]—Improving treatment of advanced HER2 negative mBC[2] (Open label, n=24)

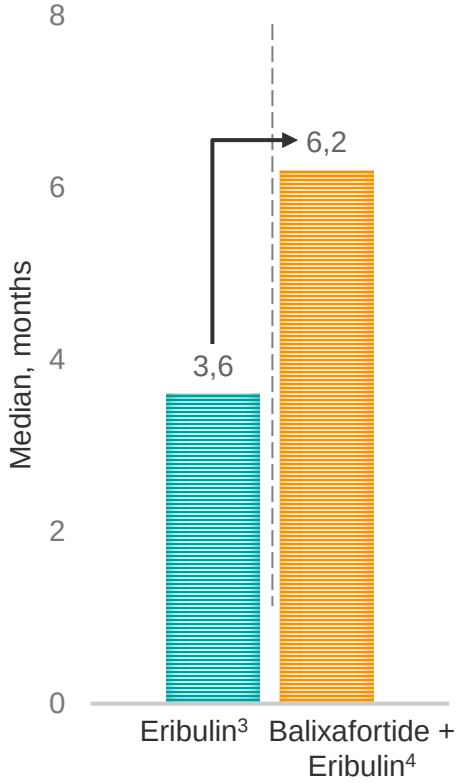
Overall Response Rate



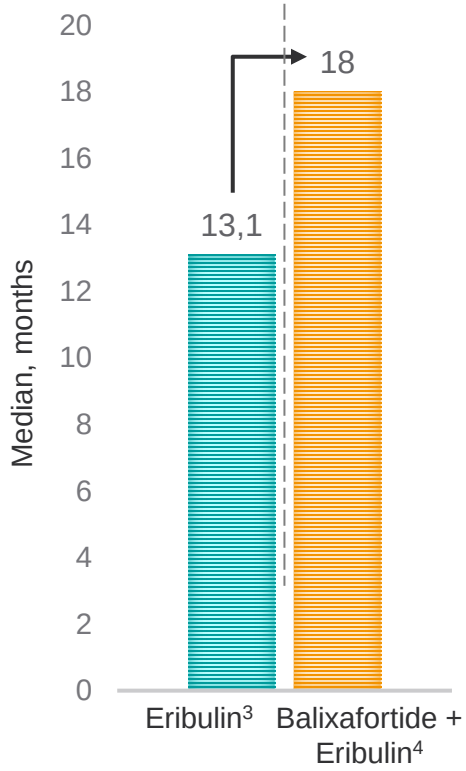
Clinical Benefit Rate



Progression Free Survival



Overall Survival



Notes:
1 Reflects an indirect comparison
2 Metastatic Breast Cancer
3 "Embrace" Registration Trial for Eribulin
4 Polyphor trial – results from dose expansion cohort

THE LANCET Oncology

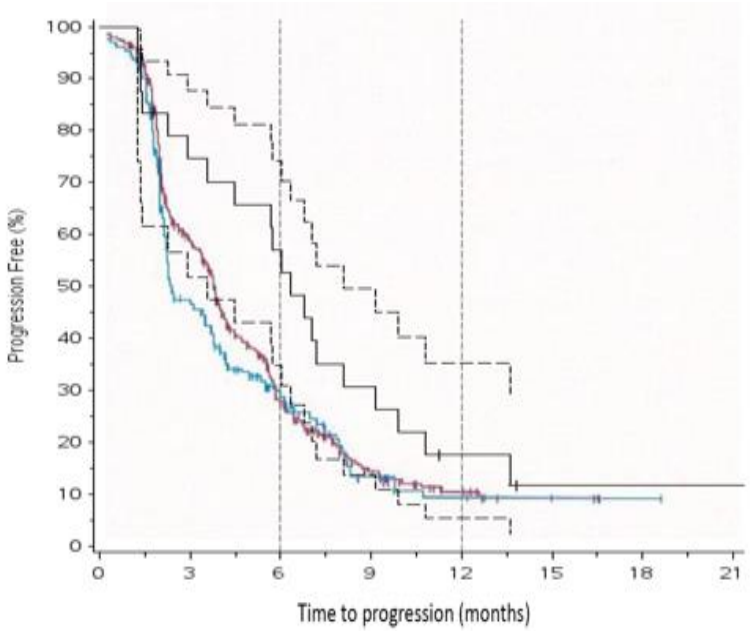
2017 ASCO ANNUAL MEETING JUNE 2-6, 2017

MUNICH 2018 ESMO congress

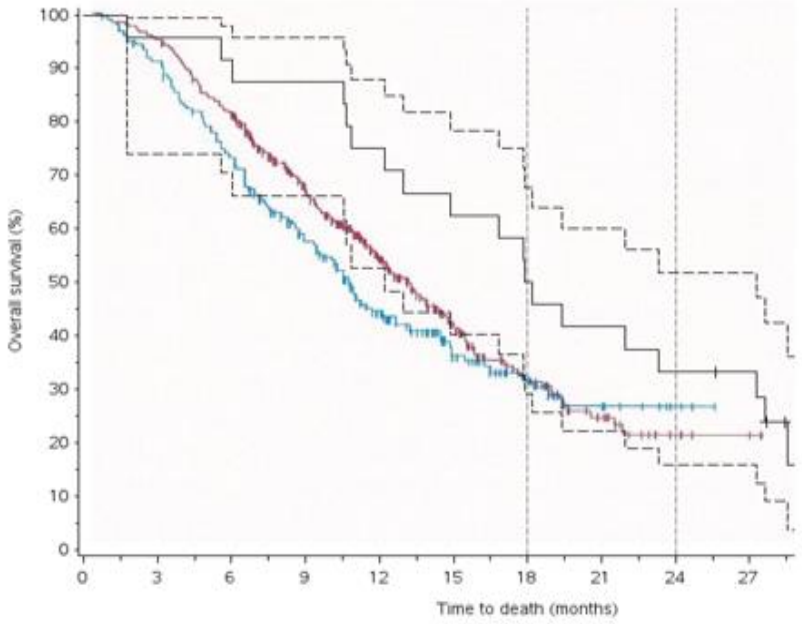
PFS and Overall Survival in Phase 1b Study

Balixafortide+ Eribulin vs EMBRACE studies – Rationale for Phase III

Progression Free Survival
High Dose patients



Overall Survival
High Dose patients



Eribulin (EMBRACE)
TPC (EMBRACE)
Balixafortide+ Eribulin Overall (Phase 1b)
Balixafortide+ Eribulin Confidence Interval (Phase 1b)

NOTE: Indirect comparison between studies.

Phase 3 Pivotal Study FORTRESS
Eribulin +/- Balixafortide in advanced BC

Study objectives and design: patient population & treatment scheme

Objectives:

- Confirm Phase 1b Clinical Proof of Concept results
- Improve patient outcomes in an area of highest medical need
- If positive enable a fast track to a very sizable market

Patient Population (n=384):

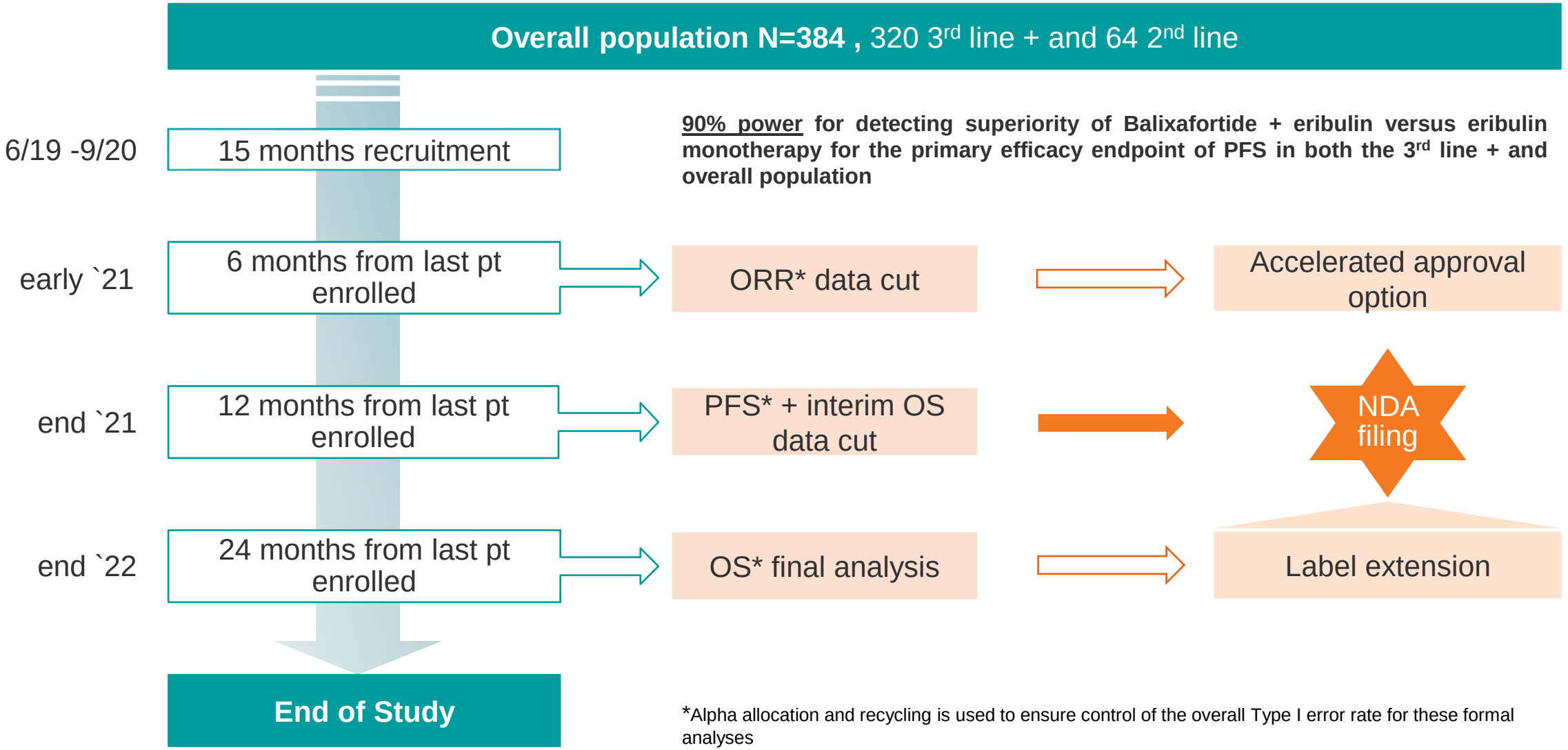
- locally recurrent (defined as unresectable locoregionally recurrent) or metastatic breast cancer (BC)
- HER2neg, with any ER/PR
- previously treated with 1−4 chemotherapeutic regimens for locally recurrent or metastatic BC
- previously received an anthracycline and a taxane in either the adjuvant or metastatic setting, unless contra-indicated for safety reasons

Treatment schedule:

Randomisation 1:1 ratio to either Balixafortide plus eribulin or eribulin alone

- Eribulin: 1.4 mg/m2 over appx 5 min (days 2 and 9 of 21 day cycle)
- Balixafortide: 5.5 mg/kg over 2 hours (or more if IRR, days 1,2,3 and 8,9,10 of 21 day cycle)

FORTRESS Study Timeline Flow Chart



*Alpha allocation and recycling is used to ensure control of the overall Type I error rate for these formal analyses

FORTRESS Recruitment is Ahead of Plan

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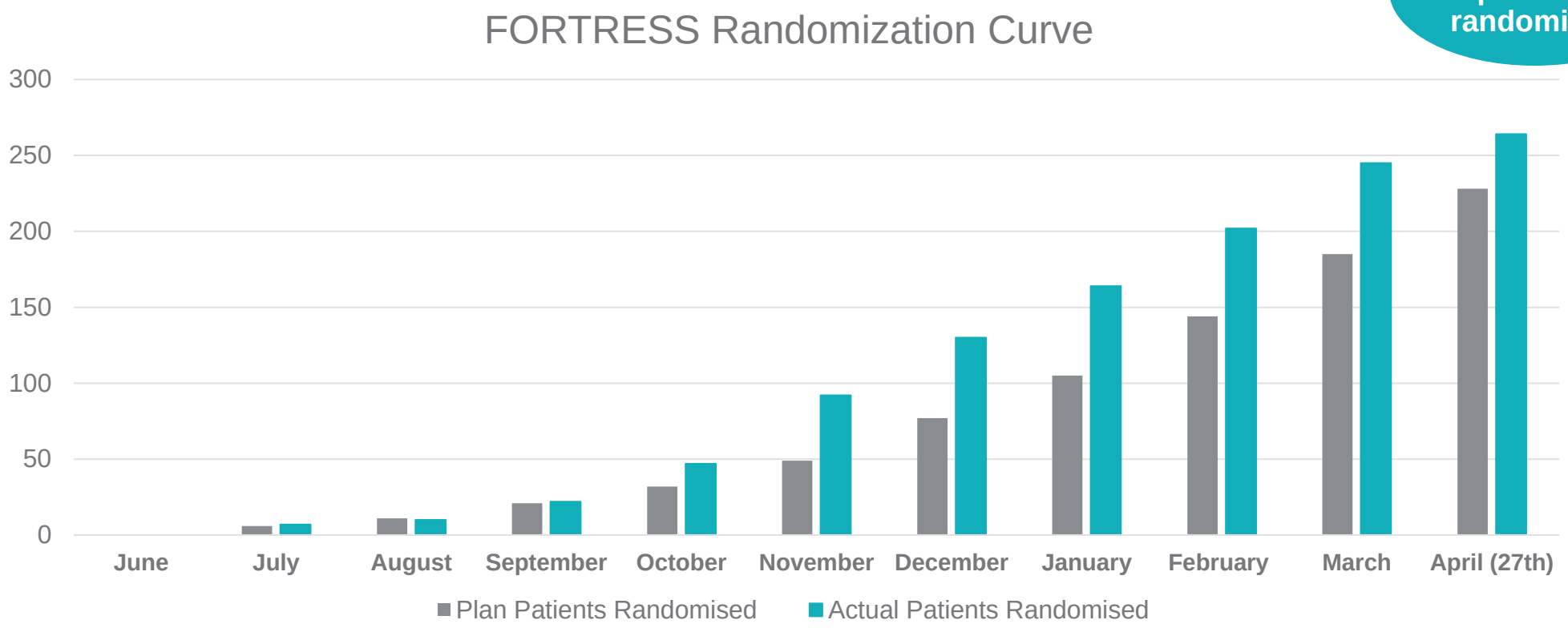
69% of patients randomized



- Today's randomization status n= 264 (69% of 384)
- Sites in all continents open.
- In the current situation with Covid 19 we are taking all possible measures to safeguard patients, study conductors and investigators and the study conduct in general.
- As of end of April, we are on plan to complete the recruitment of 384 patients in the Fortress study by end of September 2020.

Balixafortide Development Strategy

Near and midterm goals:

- **Completion of dossier for NDA filing ongoing:**
  - Clinical pharmacology package
  - CMC package
  - Non clinical safety and pharmacology package

- **Further development strategy beyond FORTRESS:**
  - Investigate improved dosing and scheduling
  - Define maximum tolerated dose (MTD)
  - Assess tolerance and preliminary efficacy in combination with other chemotherapies in mBC
  - Develop other formulations than IV
  - Develop a CXCR4 diagnostic test

Key enablers for expanding beyond the initial indication and building value for potential future partnerships

Oncology Pipeline Strategy

Long-term targets in expanding oncology opportunity

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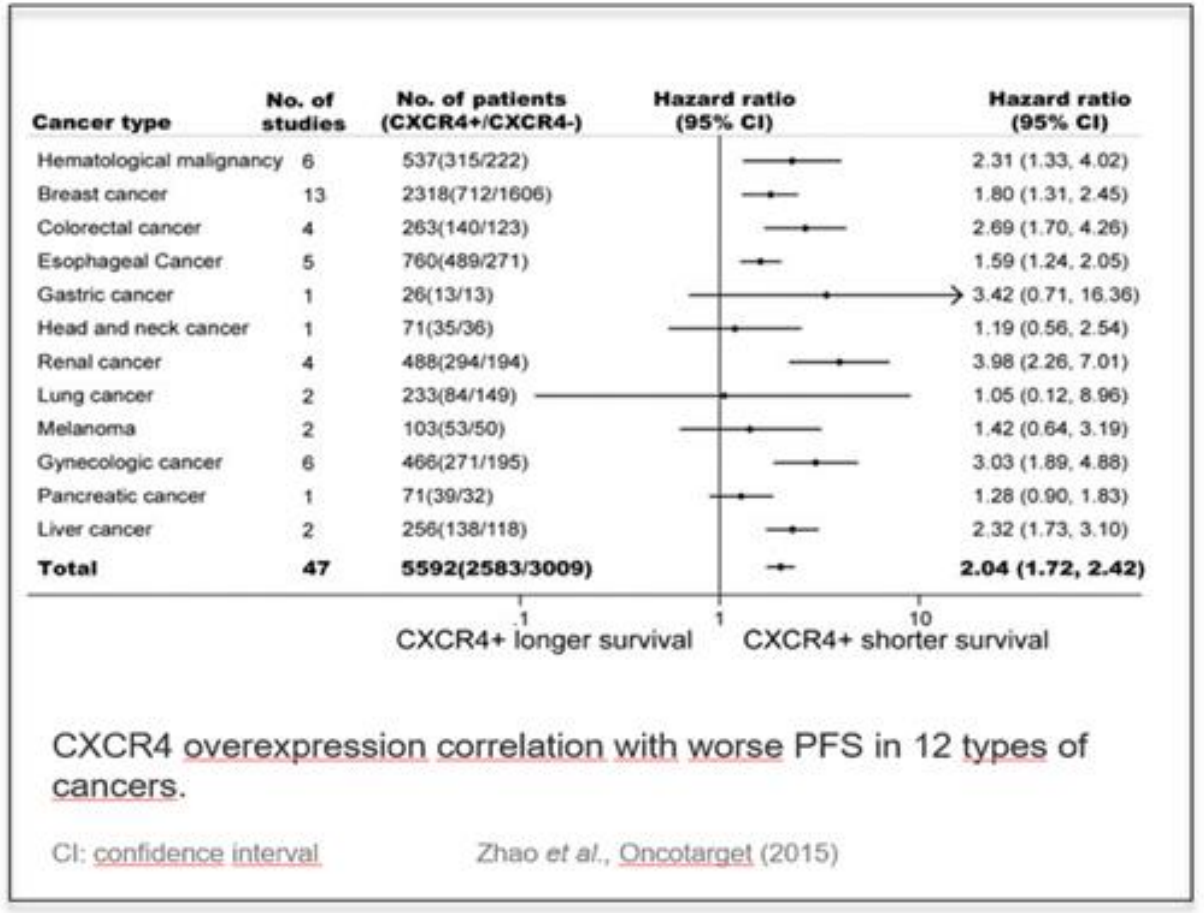
- CXCR4 expression has been validated as a negative prognostic factor for other cancer types
- Balixafortide has therefore a potential as a novel treatment option in tumors beyond mBCa
- Combinations with other immuno-oncology therapies and CXCR4 antagonists are promising and open further opportunities for balixafortide
- Identified novel immuno-oncology targets to be addressed by peptides from the macrocycle technology platform
- Post ORR results, intention to identify new lead compounds in the area of immuno-oncology to be nominated as development candidates



CXCR4 overexpression correlation with worse PFS in 12 types of cancers.

CI: confidence interval

Zhao *et al.*, Oncotarget (2015)

Balixafortide Strategy – Initial Indication and Expansion Plan

Initial Indication

- Today
- End of Recruitment
- ORR
- PFS
- Potential US approval (accelerated)
- EU Approval

2020			2021				2022				2023
Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1

Future Indication Expansion Plan

- Preclinical studies in other combinations / tumors
- Improved dose scheduling study
- Phase II Study in combination with other chemo in earlier mBC
- Non IV Formulation
- CXCR4 Diagnostic Test

Key enablers for expanding beyond the initial indication to earlier lines / other tumors and combos and building value for potential future partnerships.

2023 mBCa Market Projection (US and EU5)

Balixafortide is coming to a large market with limited competition especially in the HR+ Segment

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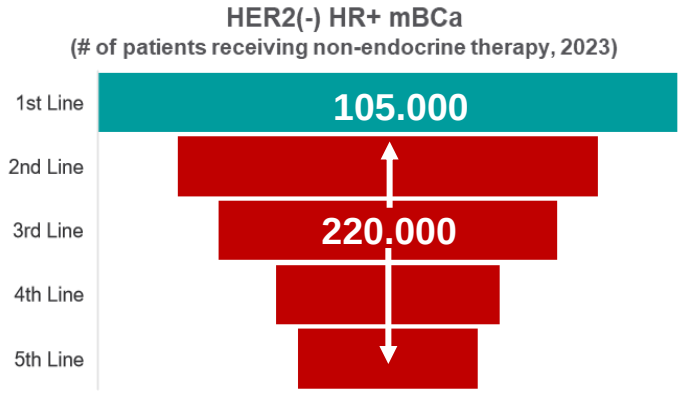
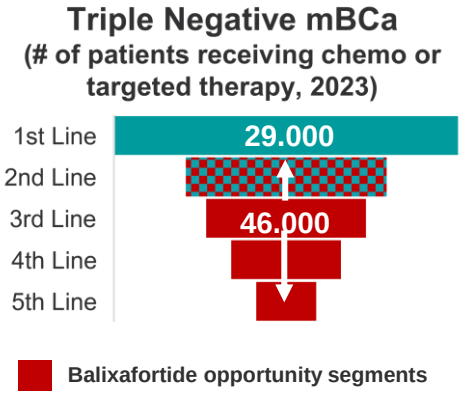
Large Total Addressable Patient Population Balixafortide Can Target

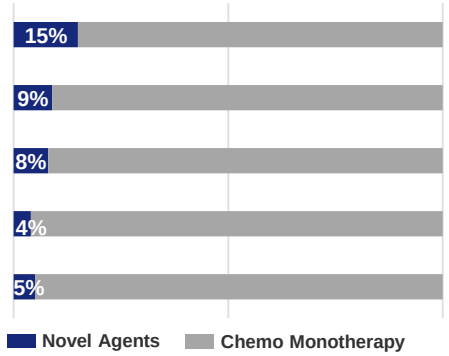




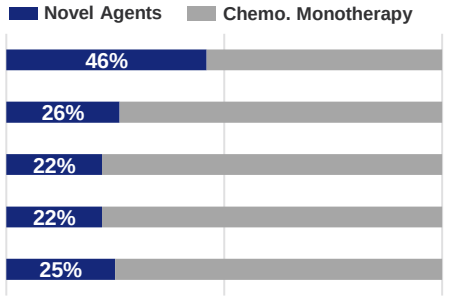
Source: Global Data HER2-Negative Breast Cancer: Market Analysis 2018–2028, Published February 2020

Limited Competition in HR+: Projected M. Share for Novel Options

2023 Projection On Treatment Share
(Novel agents are typically in combo with chemo)

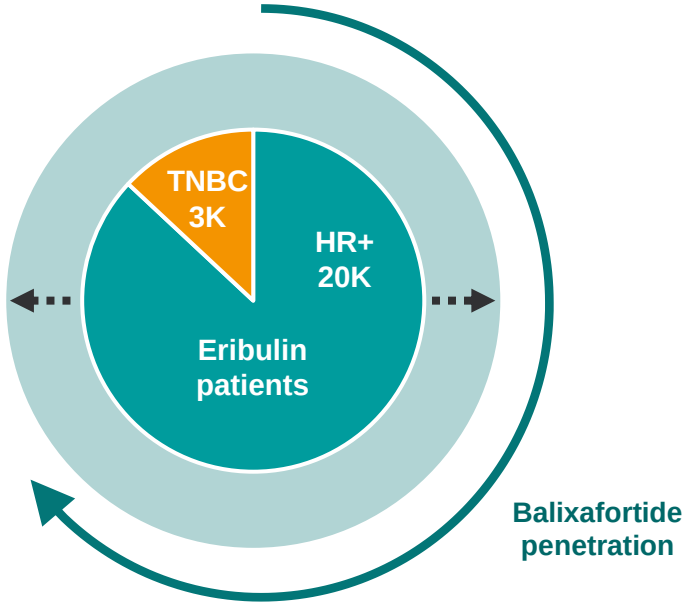


Earlier lines: Abemaciclib and AKT inhibitor
Later Lines: sacituzumab (primary balixa competitor)
BRCA+ patients across lines: PARP inhibitors



Earlier lines: Avastin, checkpoint inhibitors & AKT inhibitors in earlier lines in combination with chemo
Later Lines: sacituzumab (primary balixa competitor)
BRCA+ patients across lines: PARP inhibitors

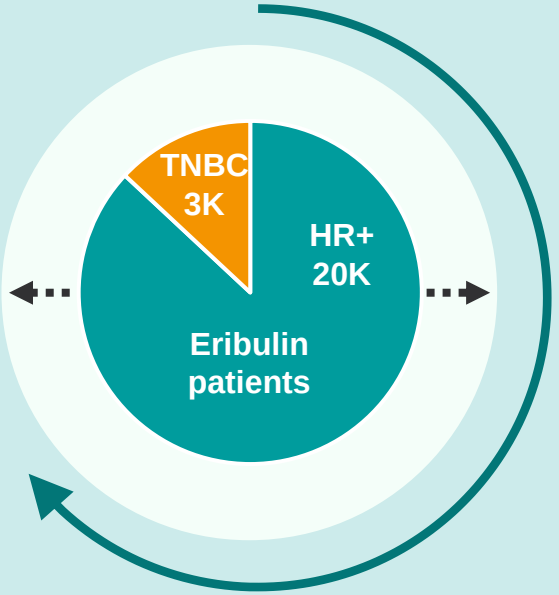
Balixafortide + eribulin to become new standard of care in later lines of HR+



- Large market (200K patients) in 2nd line and beyond in HR+
- Limited competition from novel treatments in HR+
- Eribulin is well established and can expand if PoC study results with balixafortide are replicated.
- Eribulin to become generic in 2023
- Competition mainly in earlier lines in TNBC

Balixafortide - US$ 1.3 Bn initial market potential and US$ 6-7 Bn additional midterm opportunity

Initial indication market potential

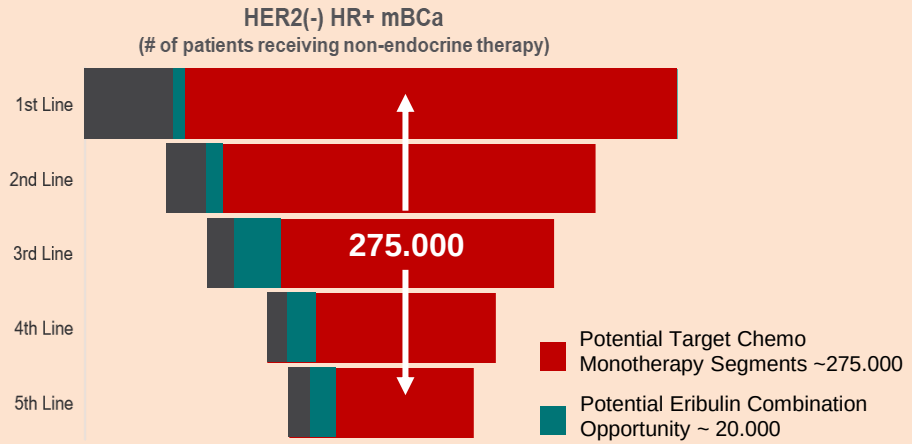


Balixafortide pricing: similar to targeted breast cancer therapies vs chemos inc. eribulin

Increased cycles due to better outcomes
vs. eribulin monotherapy

~ US$ 1.3 Bn Market Opportunity with eribulin market expansion in HR+ as upside

Midterm Opportunity for balixafortide in earlier lines of HR+ mBCa in combination with other chemotherapies



- Chemo will remain to be the SoC in earlier lines of HR+ mBCa. Novel combinations are needed to improve outcomes
- Opportunity to target earlier lines of HR+ mBCa with other chemos
- 14 times larger market than eribulin, e.g. 40% consist of taxanes

US$ 6-7 Bn Market Opportunity

Source: Global Data HER2-Negative Breast Cancer: Market Analysis 2018–2028, Published February 2020

Polyphor Portfolio Plan and Value Creation Journey

Immuno-oncology

1. Balixafortide Phase III program in HER2-metastatic breast cancer

- "A large and high unmet need" lead indication that can widen the opportunities in the field of immuno-oncology
- First co-primary endpoint ORR data cut in Q1 2021

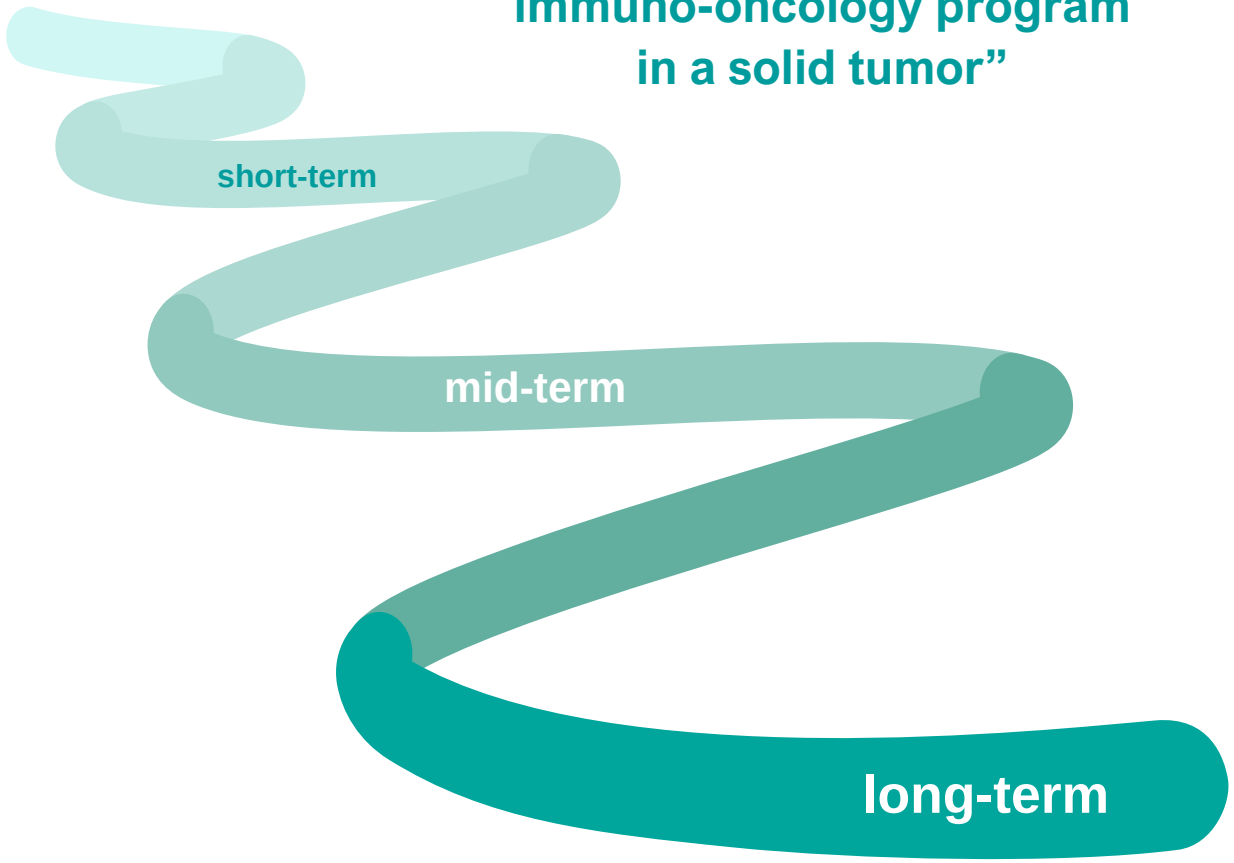
2. Balixafortide expansion in other indications / combos

- The success in the initial indication can significantly widen the opportunities in the field of immuno-oncology in following:
  - Earlier lines in mBCa
  - Other tumors / combo indications
  - Combination with checkpoint inhibitors

3. Oncology pipeline:

- Creating a pipeline of novel molecules based on our macrocycle platform in novel targets for solid/liquid tumors following potential positive ORR results in Q1 2021

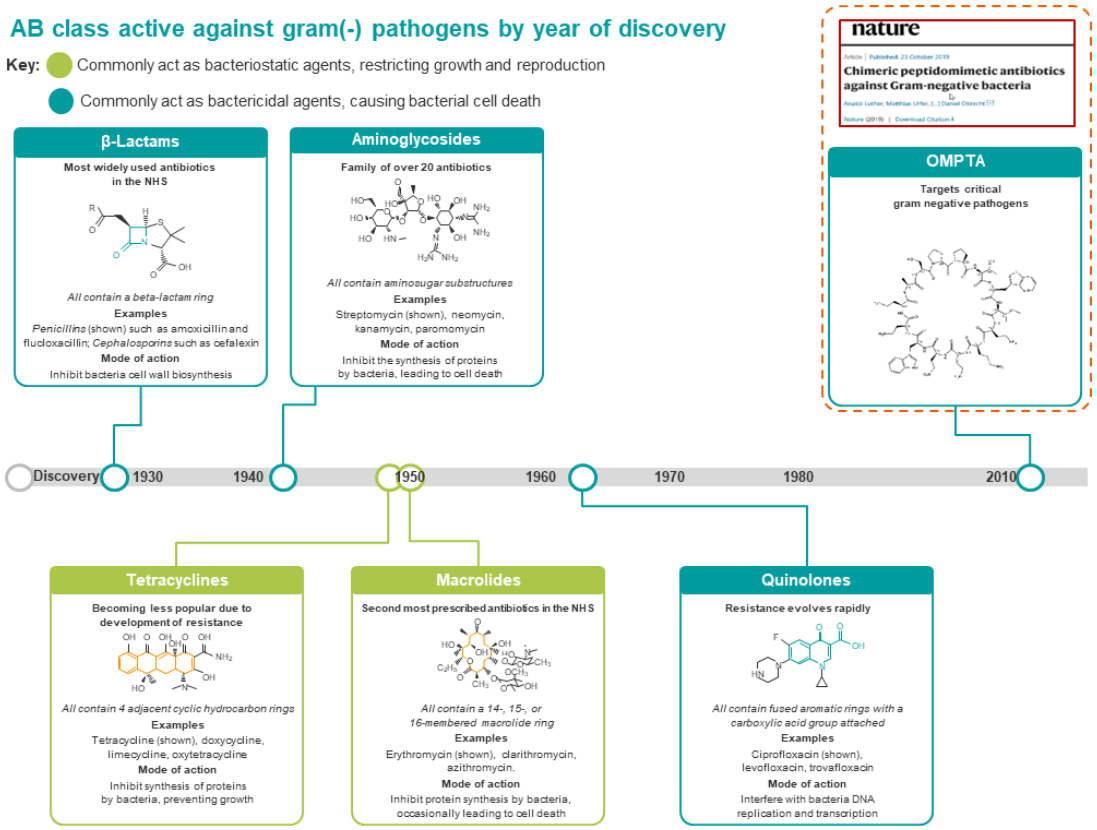
"Spearheading first-in-class immuno-oncology program in a solid tumor"



OMPTA Targets

Outer Membrane Protein Targeting Antibiotics constitute a novel class of antibiotics

"Polyphor's mission in tackling AMR is to bring first new class of gram-negative ABs after 50 years that are effective, safe and are durable against resistance"



Our innovation focuses on three targets within OMPTA class

LptD/E: Inhaled Murepavadin

LPS and BamA: POL7306 / New Generation BamA

LptA: Thanatin (a new target program)

- Truly a new class validated by Nature publication
- A unique spectrum of coverage targeting all, single or a group of specific WHO Priority 1 pathogens is possible
- Class of antibiotics with potential for lower propensity for resistance versus classical antibiotics
- Robust science enabling non-dilutive funding and external financing (CARBX, Welcome Trust, Novo, IMI)

Inhaled Murepavadin for Cystic Fibrosis

Expanding the clinical pipeline with a novel innovation in a rare disease

Infections will remain a major problem in Cystic Fibrosis post CFTR modulator era

- *Pseudomonas aeruginosa* accounts for 2/3 of the chronic infections in CF
- P. aeruginosa is the leading cause of exacerbations, lung function decline and mortality in CF
- Cystic Fibrosis Foundation has committed at least $100 million to the Infection Research Initiative in 2019

Current Inhaled antibiotics and the need for novel options:

- Tobramycin and aztreonam are most commonly used inhaled ABs for CF, developed nearly 10-20 years ago
- Both typically administered every other month in cycles to reduce AB resistance
- Inhaled colistin and levofloxacin also available in EU with similar broad spectrum
- Drug administration is usually 2-3 times daily
- Despite proven efficacy, exacerbation, lung function decline and mortality persist over time in CF due to *P. aeruginosa*
- Decreased microbial diversity is associated with more severe lung disease – relation to using broad spectrum ABs is not well established

An inhaled antibiotic targeting P. aeruginosa is urgently needed given patients suffer from lung function decline and frequent lung exacerbation over time

Inhaled Murepavadin for CF

Changing the treatment paradigm in treating chronic P. aeruginosa infections in Cystic Fibrosis

Inhaled Murepavadin – Novel Class Selective Inhaled AB for CF:

- Potentially first new class (OMPTA[1]) and *P. aeruginosa* specific inhaled AB for CF
- Best *in vitro* activity against *P. aeruginosa* including MDR / XDR [3] strains
- Biofilm activity (*in vitro)* and low resistance potential
- High safety margin (least 5-10 fold above IV application)[3] in preclinical GLP
- No cross-resistance with other antibiotics
- Potent activity in lung infection models
- Following attributes measured in clinical trials to potentially make Inhaled Murepavadin change the treatment paradigm:
  - Efficacy including refractory patients to standard of care (SoC)
  - Reduction in pulmonary exacerbations
  - Improvement in microbiome due to selectivity and its effect on long term lung function
  - Dosing vs. SoC

Excellent In-Vitro Activity

Vs. Approved Inhaled Antibiotics

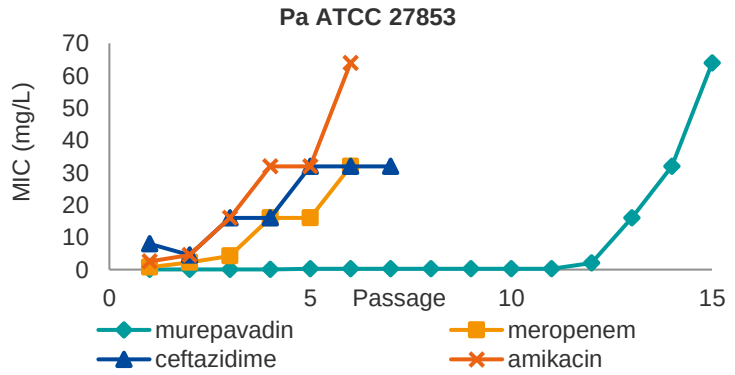
MICs (mg/L) of 414 *Pseudomonas aeruginosa* isolates from people with CF*

	MIC_{50}	MIC_{90}	Range
Murepavadin	**0.12**	**2**	**0.016->16**
Aztreonam	8	128	0.25->256
Ciprofloxacin	1	8	0.03->32
Tobramycin	1	16	0.12->128
Colistin	1	2	0.25->16

** Isolates collected between 2007- 2018, mostly from The Netherlands and Spain.*
Ref: Ekkelenkamp M. Report on in-vitro susceptibility of clinical isolates from cystic fibrosis and bronchiectasis patients against murepavadin (POL7080), part 1 of 2. The "inhaled Antibiotics in Bronchiectasis and Cystic Fibrosis" (iABC) consortium; 2018.

Low propensity of development of resistance

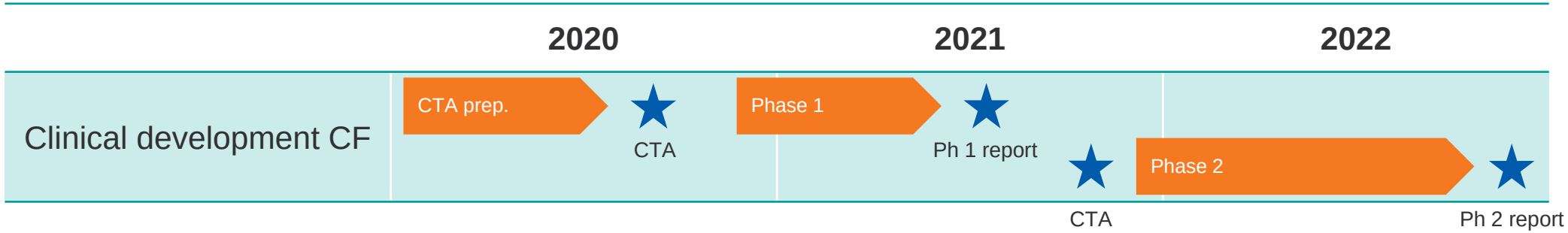
Resistance development: serial passage



1 OMPTA: Outer membrane protein targeting antibiotics
2 MDR: multidrug resistant, XDR: Extreme drug resistant
3 Safety margins based on available preclinical GLP Tox data

Inhaled Murepavadin for CF

Expanding the clinical pipeline with an attractive market opportunity



Clinical Program Plan and Timelines:

- Preclinical program complete suggesting broad safety margin and efficacy, plans to submit CTA for inhaled murepavadin and start Phase I program in Q4 2020
- Development of inhaled formulation ongoing
- Opportunity to be Phase II complete by end 2022 expanding Polyphor clinical pipeline
- Pursue additional external financing while the program already partly financed by IMI until 2021.

Targeted and attractive rare disease opportunity:

- Attractive orphan market opportunity
- Comparators' * peak sales (200-400m USD)
- Can be expanded from CF to Non Cystic Fibrosis Bronchiectasis and beyond

* Tobi and Cayston

Preclinical Antibiotics Program

Breakthrough science through the invention of new class of ABs provide long term opportunity

POLYPHOR

OMPTA
BamA

- New class of ABs after 50 years in gram negatives
- Unique medium Gram-negative spectrum of coverage targeting WHO priority 1 pathogens, *Enterobacteriaceae*, *P. aeruginosa*, *Acinetobacter b.*
- Very low propensity for resistance in in-vitro experiments
- Commercial potential of US$ 900 million
- POL7306 preclinical program complete however will switch to new formulation / new peptide design to improve therapeutic margins
- Learning from prior program will enable rapid optimization and progress
- **Current Phase: Hit to Lead / Lead Optimization**

Thanatin
(New Program)

- Narrow spectrum Gram-negative antibiotics for treatment of serious infections caused by carbapenem-resistant *Enterobacteriaceae*
- Potential gold standard in treating suspected/ confirmed XDR *Enterobacteriaceae*, in patients with limited treatment options
- Commercial potential of US$ 350 million
- **Current Phase: Hit to Lead**

OMPTA Program POL7306 MICs (µg/ml) against resistant isolates

- Polyphor firmly believes that new financial incentives (e.g. US DISARM, UK AMR plan) are a matter of time, given increased global awareness of infectious diseases, not least because of COVID-19. (50% of non-survivors with COVID had secondary infections vs. 1% in survivors according to a recent Lancet publication)
- Our science aligns well with proposed incentives and AB pipeline is a long term value generation opportunity.
- Programs are in early preclinical phase and will be continued provided they are largely funded through non-dilutive and/or external financing.

Polyphor Portfolio Plan and Value Creation Journey

Novel class antibiotics

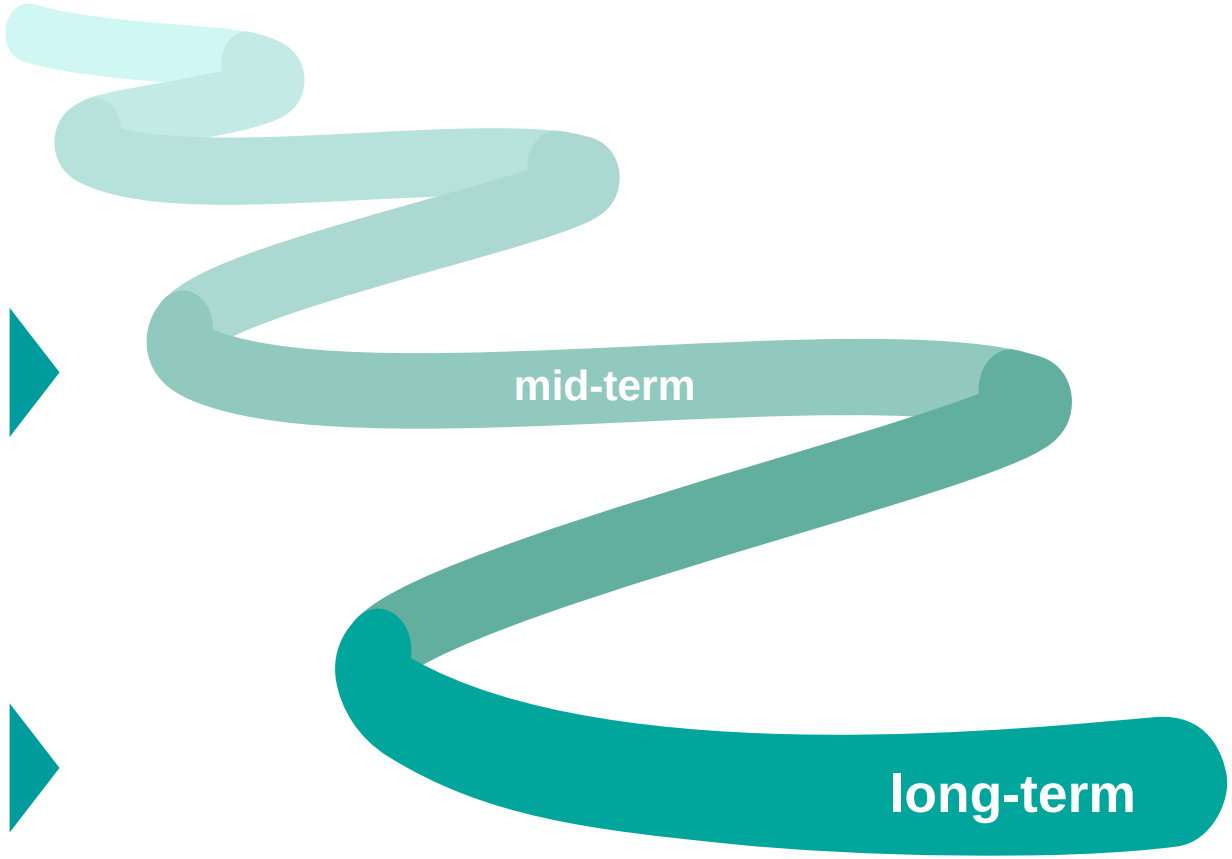
“First new class of antibiotics in gram negative space in 50 years targeting cystic fibrosis and hospital acquired infections”

1. Inhaled Murepavadin:

- Changing the treatment paradigm for people with cystic fibrosis (CF)
- Plan to move to Ph. I in Q4-20 to expand pipeline
- Orphan disease opportunity
- Program largely financed by IMI funding

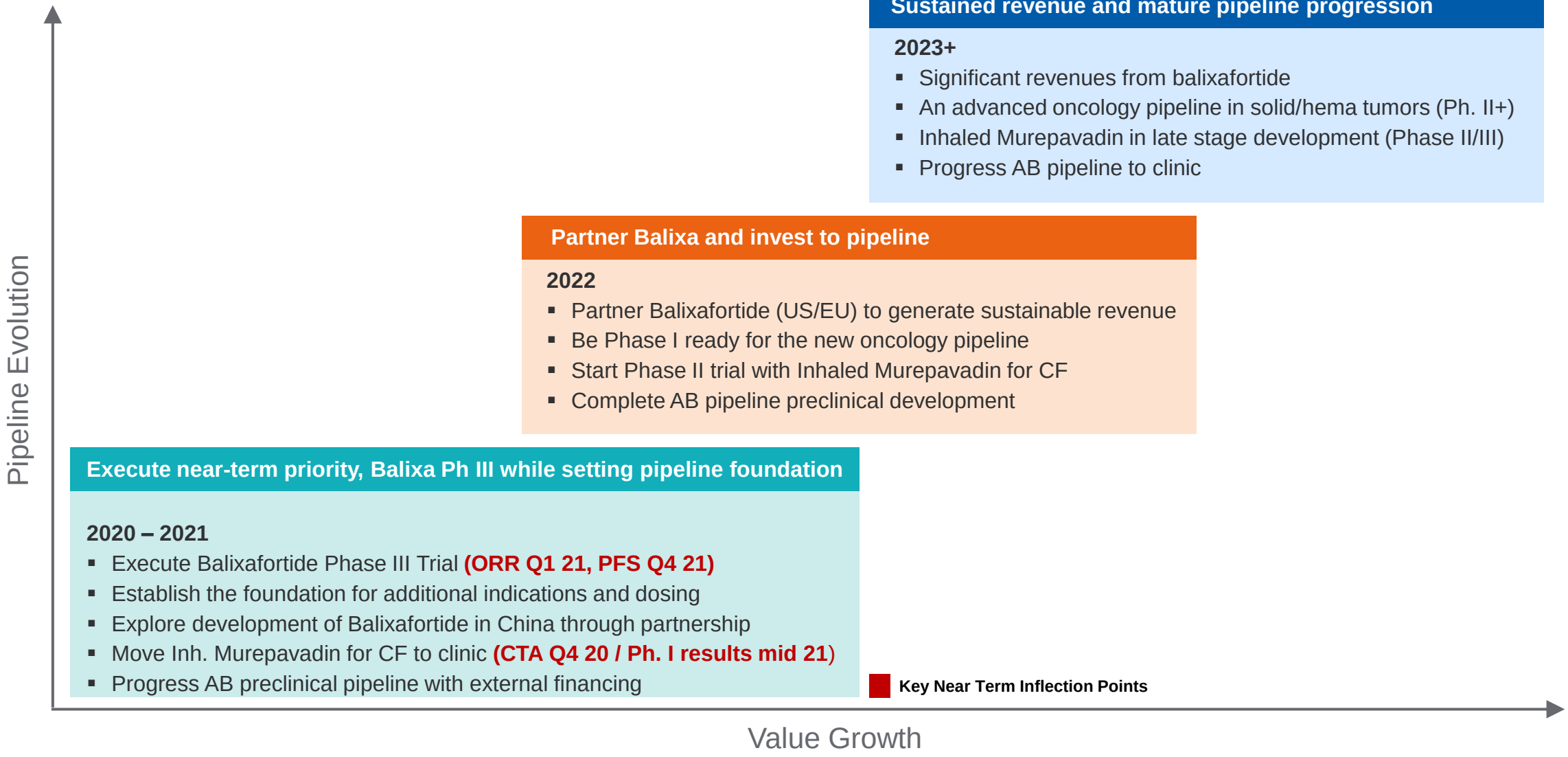
2. BamA / Thanatin Program:

- Bringing first new class of antibiotics targeting resistant WHO priority 1 gram(-) bacteria with low propensity for resistance
- Continue preclinical programs with external financing to ensure minimal cash burn impact until clinical stage
- Potential long term value driver following potential new AMR reward mechanisms



Strategy to Expand Shareholder Value

Polyphor provides multiple near-term pipeline progress and key value inflection points



Sustained revenue and mature pipeline progression

2023+

- Significant revenues from balixafortide
- An advanced oncology pipeline in solid/hema tumors (Ph. II+)
- Inhaled Murepavadin in late stage development (Phase II/III)
- Progress AB pipeline to clinic

Partner Balixa and invest to pipeline

2022

- Partner Balixafortide (US/EU) to generate sustainable revenue
- Be Phase I ready for the new oncology pipeline
- Start Phase II trial with Inhaled Murepavadin for CF
- Complete AB pipeline preclinical development

Execute near-term priority, Balixa Ph III while setting pipeline foundation

2020 – 2021

- Execute Balixafortide Phase III Trial **(ORR Q1 21, PFS Q4 21)**
- Establish the foundation for additional indications and dosing
- Explore development of Balixafortide in China through partnership
- Move Inh. Murepavadin for CF to clinic **(CTA Q4 20 / Ph. I results mid 21)**
- Progress AB preclinical pipeline with external financing

Key Near Term Inflection Points

Financials

Key Figures

(in CHF millions, except number of shares)

Profit & Loss	31.12.2019	31.12.2018
Revenue	-	6.5
R&D expenses	-60.7	-44.8
Net Loss	-64.7	-50.9
Avg. net cash burn	-4.6	-3.5
FTEs	63	59

Balance Sheet	31.12.2019	31.12.2018
Cash & Cash Equivalents	77.4	133.8
Total Assets	92.8	144.1
Total Equity	55.1	120.6

Share information	07.05.2020
Shares outstanding	11’063’207
52 week High / Low	CHF 14.20 / 4.18
Closing price - 07.05.2020	CHF 8.60
Market Capitalization	CHF 95.1 m

Guidance and outlook

- Opex 31.12.2020: CHF 61m to CHF 64m
- With existing cash, operations are financed until the end of Q1 2021.
- Under the current plan, the cash position will allow us to develop the balixafortide until the next value inflection point
- Early stage antibiotics programs partly financed through non-dilutive funding. On going discussions with key institutions in order to further support our antibiotics pipeline.

Investment Highlights

1 Research driven clinical stage biopharmaceutical company with a Phase III immuno-oncology compound with fast path to market and a strong novel pipeline

Balixafortide

Potentially best-in-class CXCR4 inhibitor
Phase III first co-primary endpoint (ORR) in metastatic breast cancer expected in end Q1 2021
US$ 1.3 bn initial market potential with US$ 6-7 bn expanded potential

Antibiotics pipeline

First new class of antibiotics targeting WHO Priority 1 pathogens with very low resistance propensity
Lead candidate in Cystic Fibrosis P. aeruginosa infections: Phase 1 start planned for Q4 2020

Proprietary Macrocycle Technology Platform

Discovery engine targeting oncology & antibiotics

2 Attractive valuation (CHF 95.1 M market cap, CHF 77.4 M cash and cash equivalents as of 31.12.2019, cash runway until end Q1 2021)

3 Polyphor provides multiple near-term pipeline progress and key value inflection points

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Corporate Update: **Focus Forward**

Q&A Session

Gökhan Batur

Chief Executive Officer

Frank Weber, M.D.

Chief Medical & Development Officer

Hernan Levett

Chief Financial Officer