POLYPHOR

Corporate Strategy Update: **Focus Forward**

November, 2020

Gökhan Batur

Chief Executive Officer

Frank Weber, M.D.

Chief Medical & Development Officer

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Chief Financial Officer

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 outcomes (ORR and PFS) in metastatic breast cancer expected in Q2 and Q4 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 90 M market cap, CHF 43.7 M cash and cash equivalents as of 30.06.2020, cash runway into Q3 2021)

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

ORR= Objective Response Rate PFS = Progression Free Survival

Polyphor Pipeline and Plan

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

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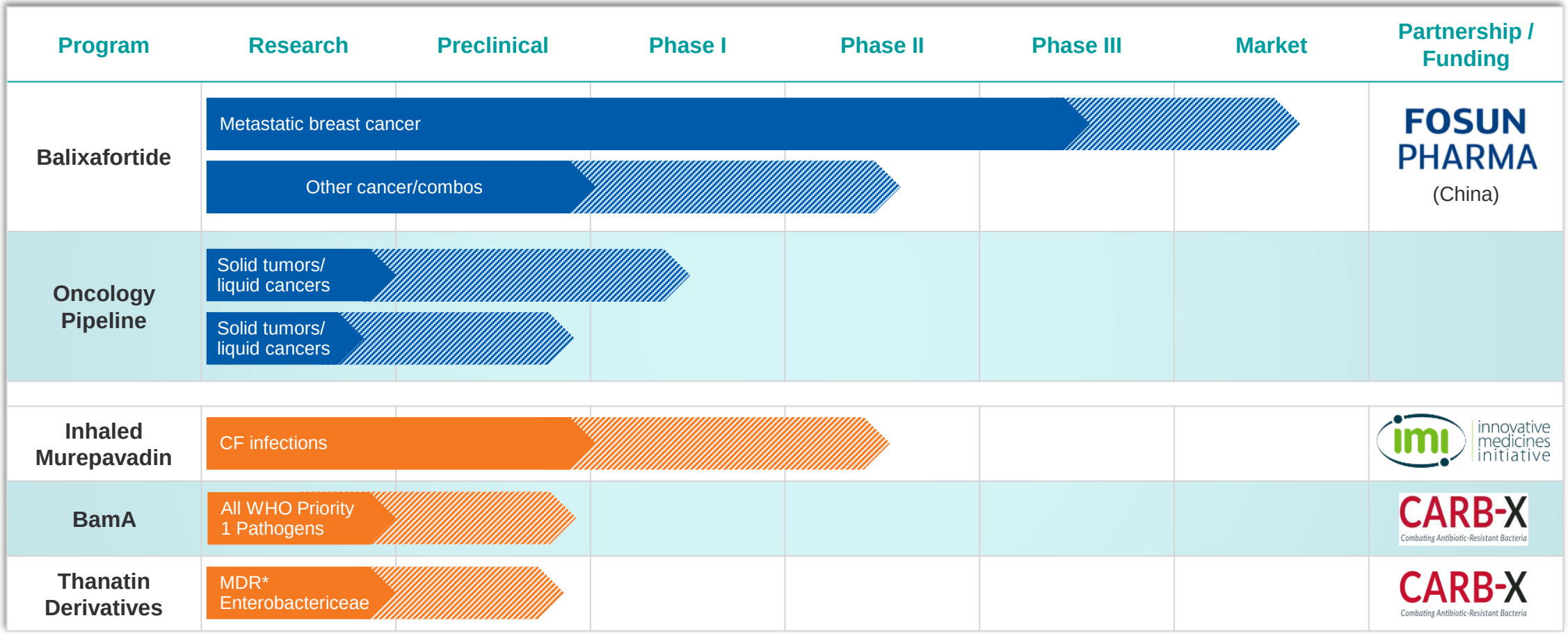


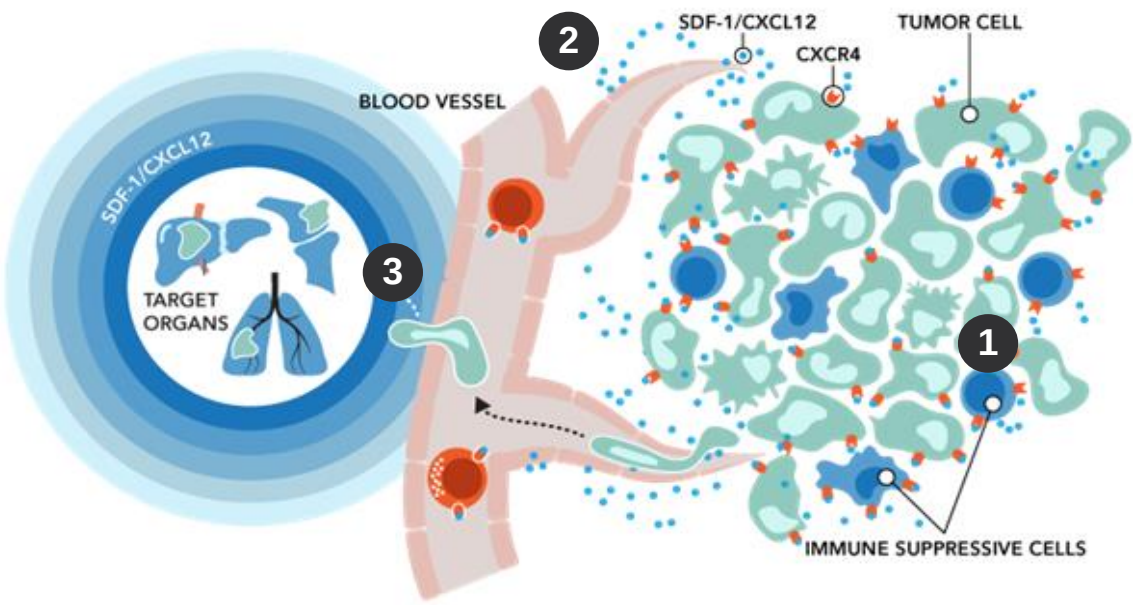
*Multidrug Resistant

Balixafortide

The only CXCR-4 antagonist in Phase III development in solid tumors

CXCR4 is a validated target in Oncology

CXCR4 overexpression is a key mechanism of cancer prognosis



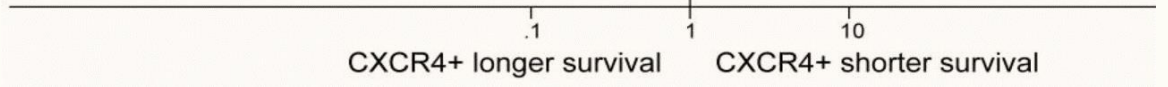
CXCR4 antagonist + Chemo

1 Immune suppression	Immune cell activation
2 Angiogenesis	Inhibited angiogenesis
3 Metastasis	Reduced metastasis

Xu *et al*., 2015, modified

CXCR4 is associated with poor prognosis in most cancers

Cancer type	No. of studies	No. of patients (CXCR4+/CXCR4-)	Hazard ratio (95% CI)	Hazard ratio (95% CI)
Hematological malignancy	7	764(413/351)		1.93 (1.33, 2.79)
Breast cancer	18	4125(1933/2192)		1.58 (1.29, 1.94)
Colorectal cancer	5	375(199/176)		1.83 (1.32, 2.53)
Esophageal Cancer	7	886(566/320)		1.65 (1.24, 2.19)
Gastric cancer	5	755(361/394)		1.94 (0.86, 4.35)
Head and neck cancer	7	577(283/294)		2.02 (1.37, 2.97)
Renal cancer	5	594(329/265)		2.93 (2.06, 4.15)
Lung cancer	6	573(248/325)		2.51 (1.64, 3.83)
Melanoma	3	136(52/84)		1.93 (0.88, 4.25)
Gynecologic cancer	7	796(530/266)		2.24 (1.11, 4.50)
Pancreatic cancer	2	320(254/66)		1.34 (0.63, 2.83)
Liver cancer	2	256(138/118)		2.75 (2.02, 3.75)
Prostate cancer	2	109(54/55)		2.67 (1.61, 4.42)
Sarcoma	2	168(97/71)		5.14 (0.64, 41.50)
Gallbladder cancer	1	72(50/22)		2.30 (1.10, 4.80)
Total	**79**	**10506(5507/4999)**		**1.94 (1.71, 2.20)**



- While first indication with Balixafortide in solid tumors is planned to be HER 2 negative metastatic breast cancer, Polyphor plans to expand to other solid tumors.

Zhao et al. Oncotarget. 2015 Mar 10;6(7):5022-40

HER2 Negative Metastatic Breast Cancer

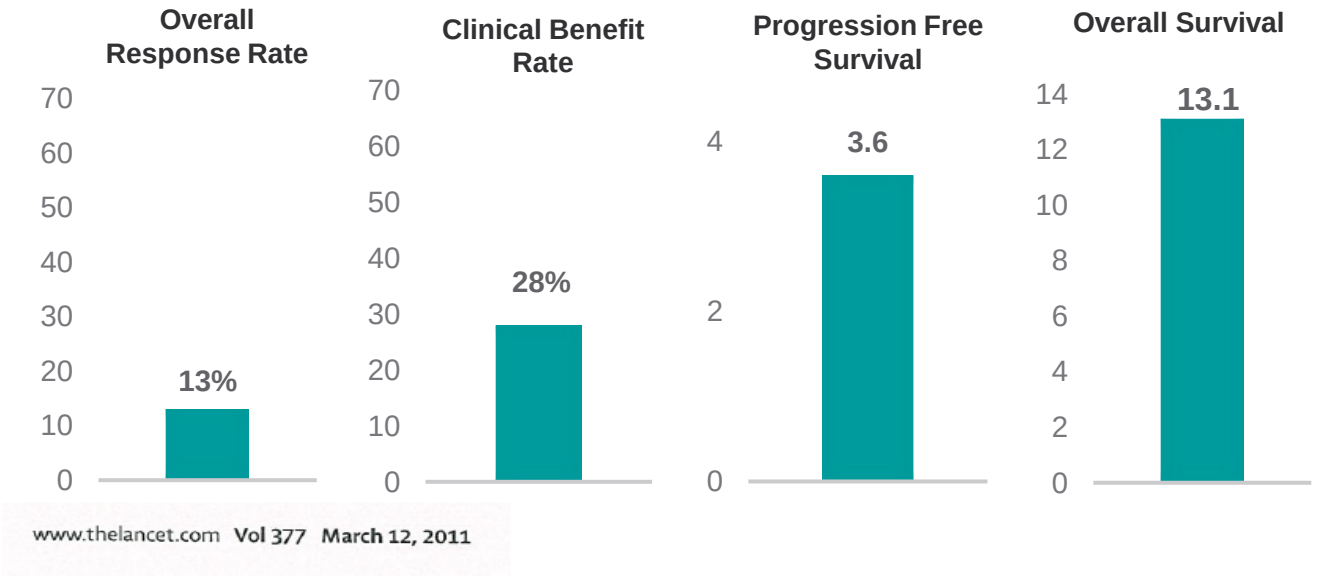
A large and high unmet medical need indication with limited options in later lines

- Breast cancer remains a high unmet medical need, particularly in HER2 Negative vs HER2+ where patients have lower rates of 5 year survival
- In HER2 - / HR+ metastatic breast cancer, mono-chemotherapy is the standard of care once the patients progress past hormone therapy. (In 2023, >90% patients to receive chemos in 2nd line and beyond)[1]
- No standard chemotherapeutic once patients have failed front line agents

Type of Breast Cancer	% of breast cancer cases	5 Yr survival (distant)
HER2 Positive / HR +	10%	44%
HER2 Positive / HR –	4%	37%
HER2 Neg / HR +	68%	30%
Triple Negative	10%	12%

Source: National Cancer Institute

Results of Standard of Care in 2nd/3rd line HER2- metastatic breast cancer: Eribulin Embrace study

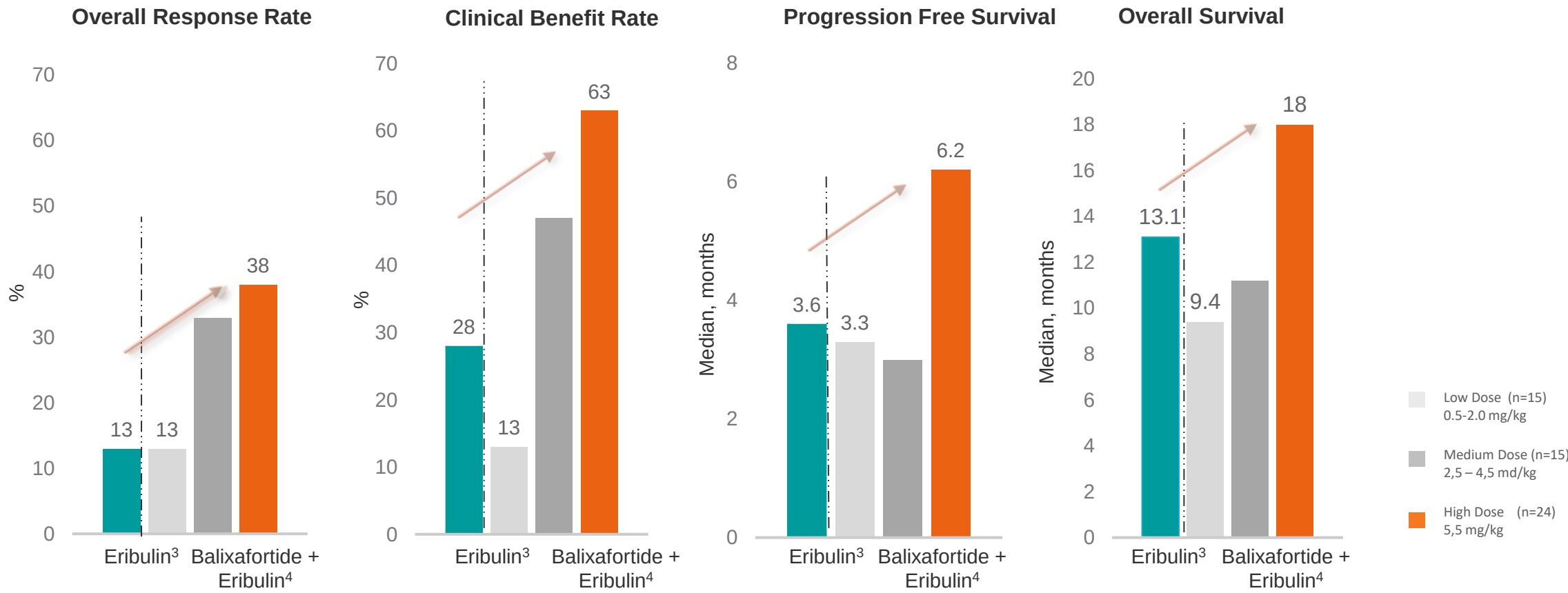


- Eribulin is the first and only single agent to show a significant overall survival benefit in patients with third-line metastatic breast cancer compared to other chemotherapies

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

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=56)



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

Analysis of Time and Duration of Response shows late responses typical for IO effect in Phase 1b Study

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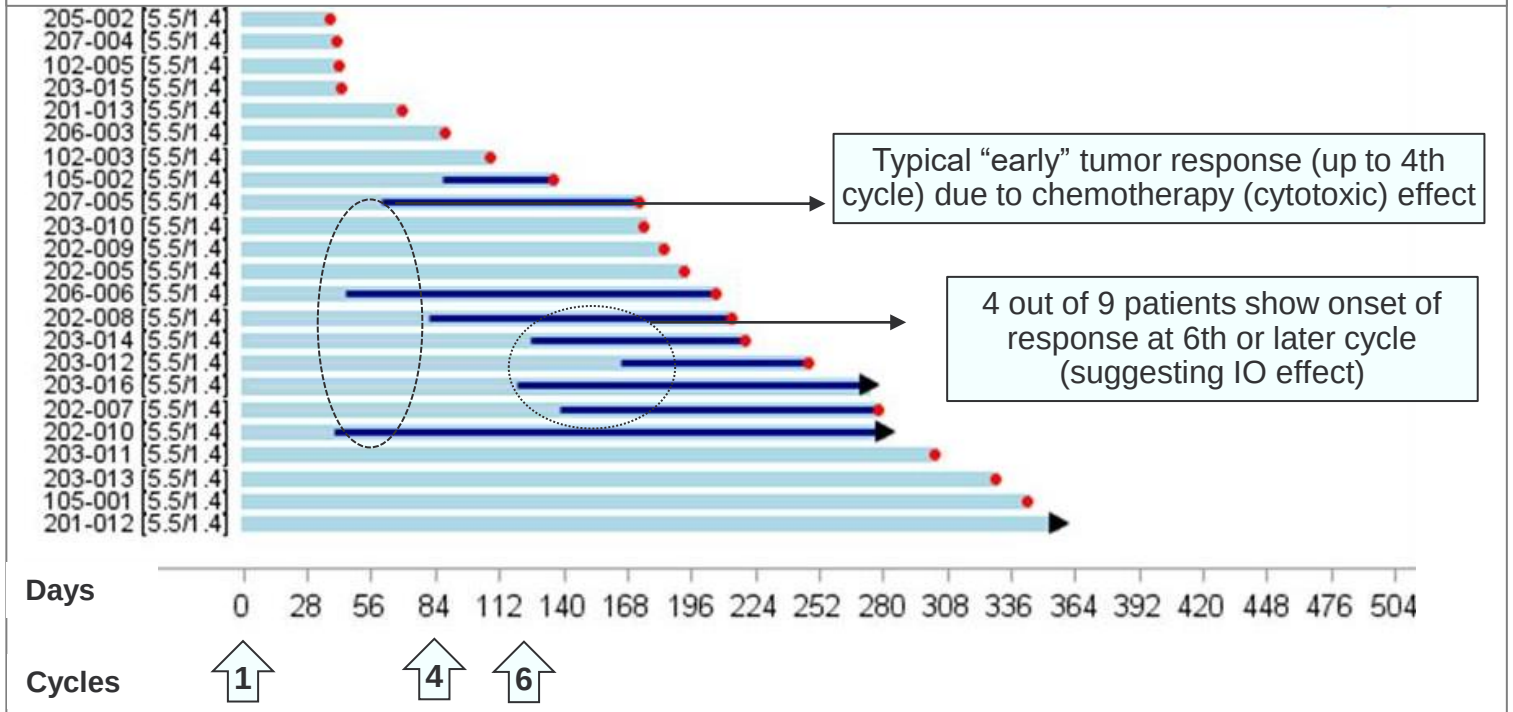
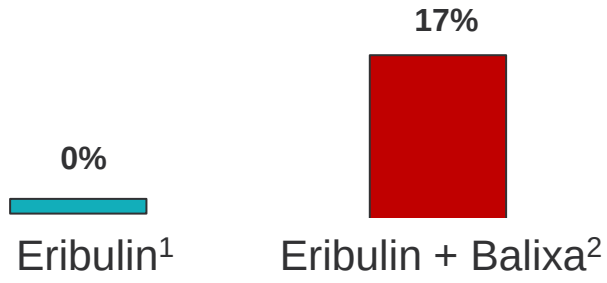
Analysis of individual tumor response in the expansion cohort (5.5mg/kg Balixafortide plus 1.4mg/m2 eribulin)

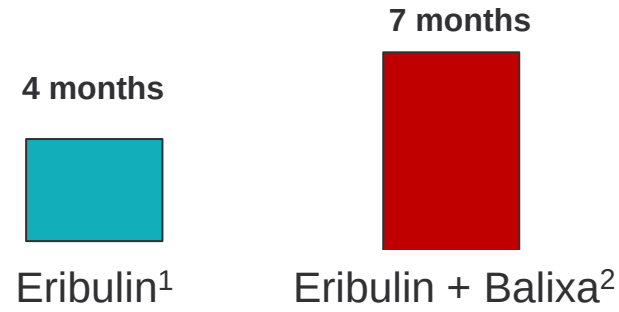


Patients Receiving Treatment > 5 cycles / 105 days [1,2,3]

Late onset responses



Duration of response and stable disease



1 "Embrace” Registration Trial for Eribulin
2 Polyphor trial – results from dose expansion cohort
3 Reflects an indirect comparison

Phase III FORTRESS Study Eribulin +/- Balixafortide in advanced BC

Study objectives, patient population & randomization status

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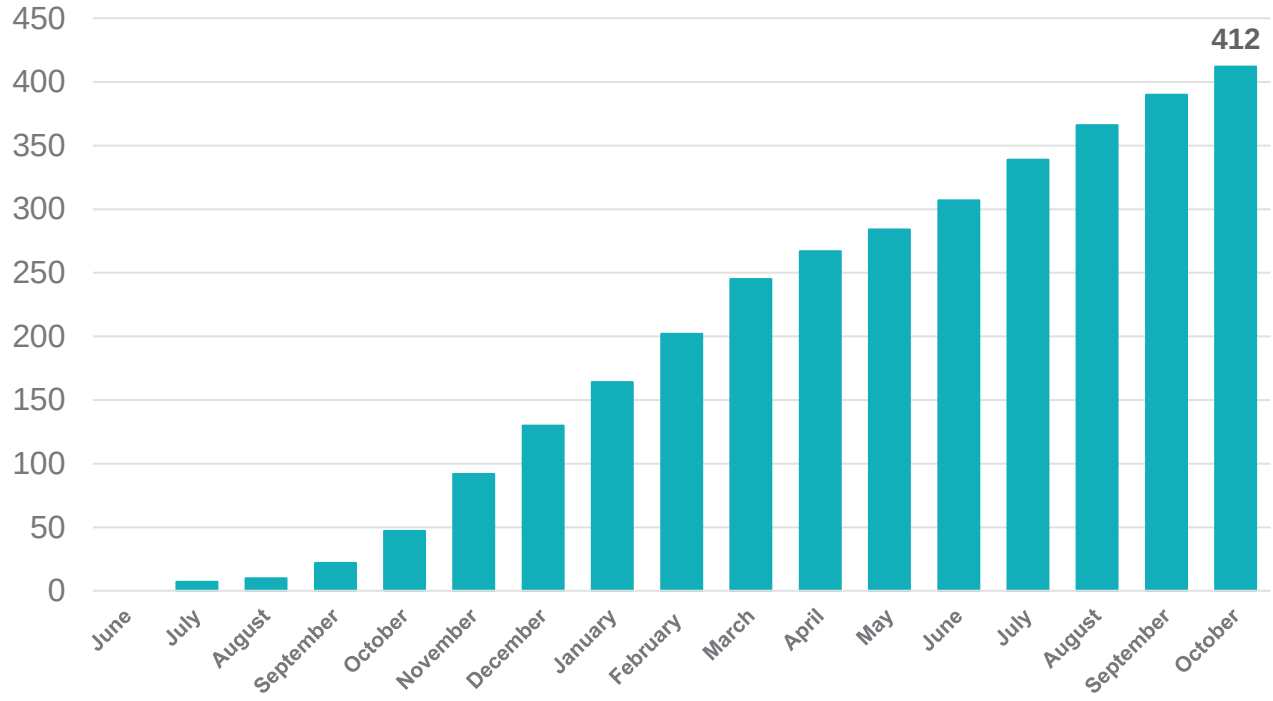
Objectives:

- **Key primary endpoint:** Progression free survival at 12 months after the last patient is randomized
- **Co-primary endpoint:** Objective Response Rate at 6 months after the last patient is randomized

Patient Population:

- Locally recurrent or metastatic breast cancer (BC)
- HER2 negative, 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

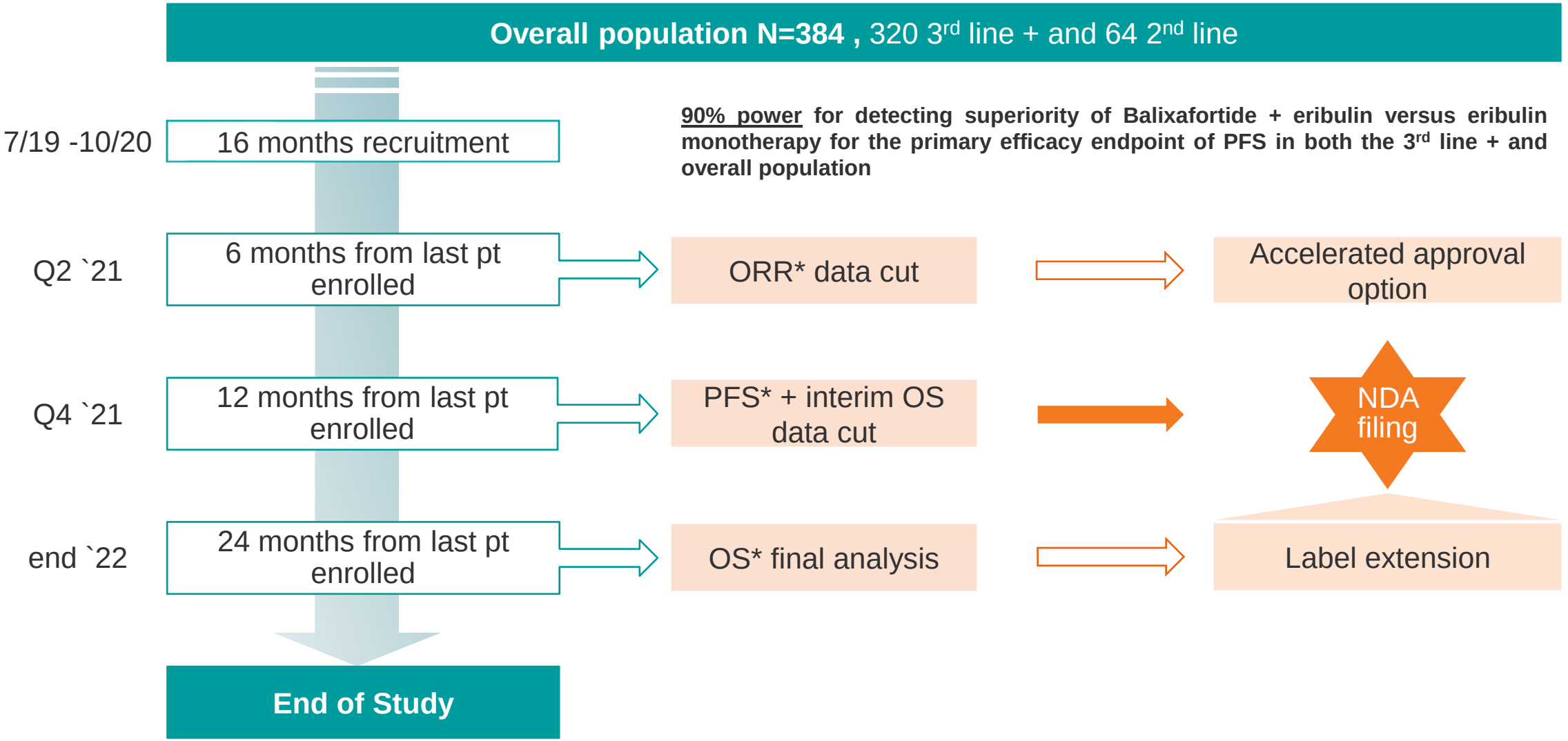
FORTRESS Randomization Curve (Oct 2020)



- 2 positive DSMB decisions to continue the trial without any modifications
- 3rd line+ patients: 324 / 320 recruited
- 2nd line patients: 88 / 64 recruited (mainly supports EU label) → complete
- Recruitment closed on October 29th

FORTRESS Study Timeline Flow Chart

Fast Track designation granted by FDA with potential breakthrough option



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

Balixafortide Strategy – Initial Indication and Expansion Plan

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Initial Indication

End of Recruitment

ORR in 3rd line+ patients

PFS in all patients

Potential US approval (accelerated)

US / EU Approval (PFS based)

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

Future Indication Expansion Plan

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

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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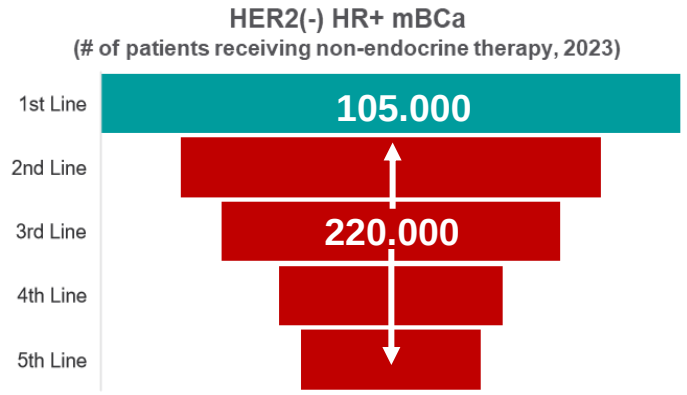
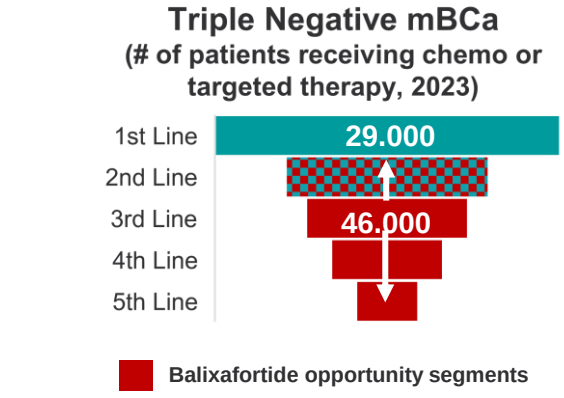
Large Total Addressable Patient Population Balixafortide Can Target

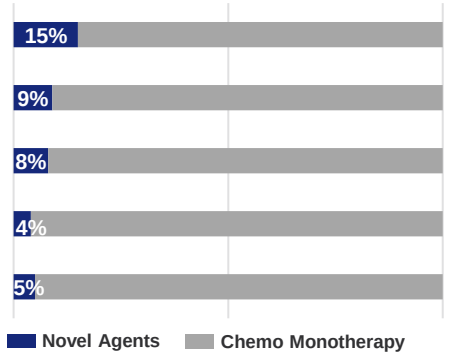




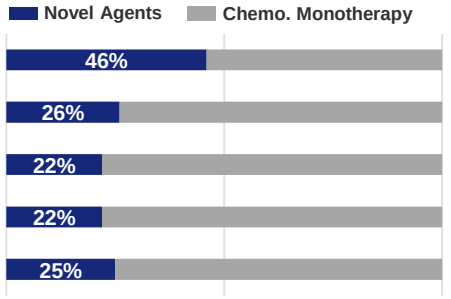
Source: Global Data HER2-Negative Breast Cancer: Market Analysis 2018–2028, Published February 2020

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

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

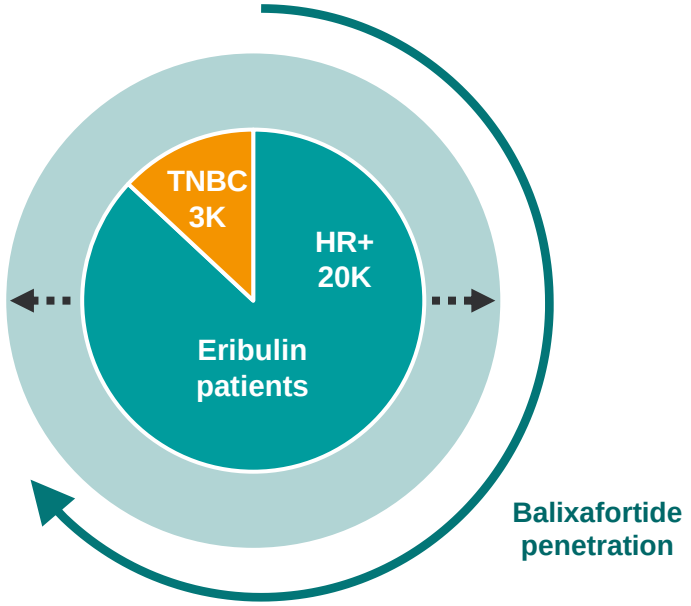


Earlier lines: Abemaciclib and AKT inhibitor
Later Lines: sacituzumab (primary balixa competitor)
BRCA+ patients across lines: PARP inhibitors



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

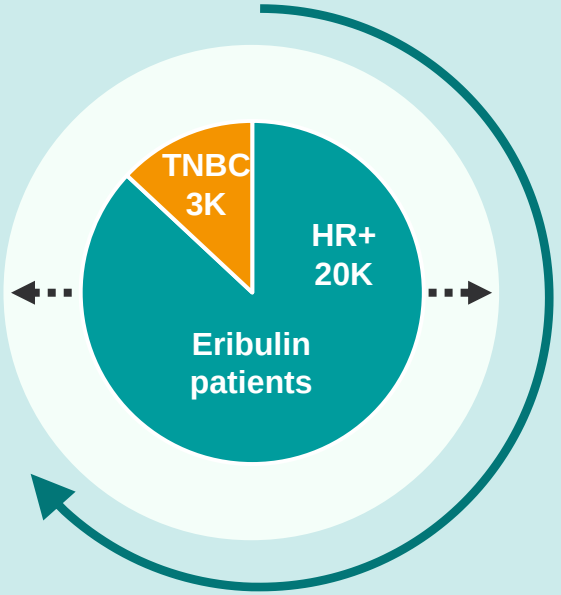
Balixafortide + eribulin to become new standard of care in later lines of HR+



- 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

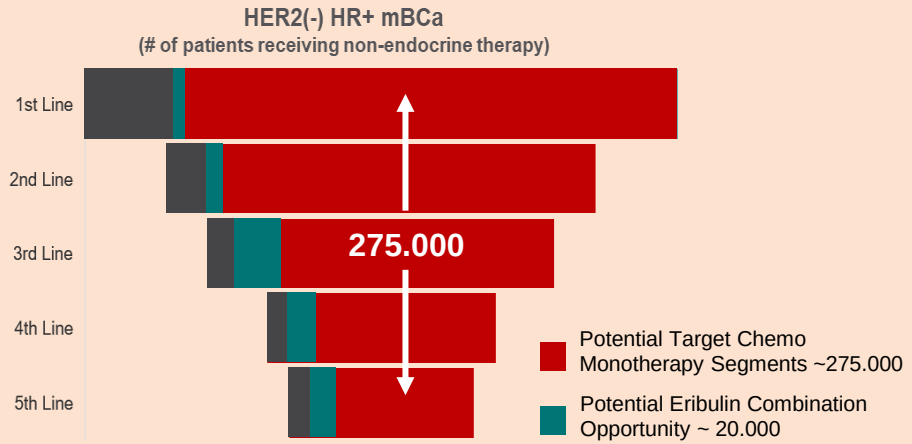


Balixafortide pricing: similar to targeted breast cancer therapies vs chemos inc. eribulin

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

Balixafortide China Licensing Agreement with Fosun Pharma

Strong validation to the scientific value and commercial potential of balixafortide

Balixafortide opportunity in China:

- China is expected to be the 2nd breast cancer market in the world expanding balixafortide opportunity in a large geography
- Fosun Pharma is a leading global Chinese company with:
  - Strong R&D capabilities to bring balixafortide to market in metastatic breast cancer and potentially additional indications / combinations
  - Strong commercial capabilities and oncology pipeline
  - Provides strong validation to the scientific value and commercial potential of balixafortide

Total deal value: Up to $182M plus royalties

- **$15M** upfront
- **Up to $19M** development milestones
- **Up to $148M** in sales milestones
- **Low to mid teen** royalties on net sales
- Strong value vs. benchmark Ph. III deals in China:
  - Average $12.0M upfront and $83.6M total deal size[1]

FOSUN PHARMA

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[1] https://torreya.com/publications/torreya-creating-value-through-china-partnering-oct2018.pdf

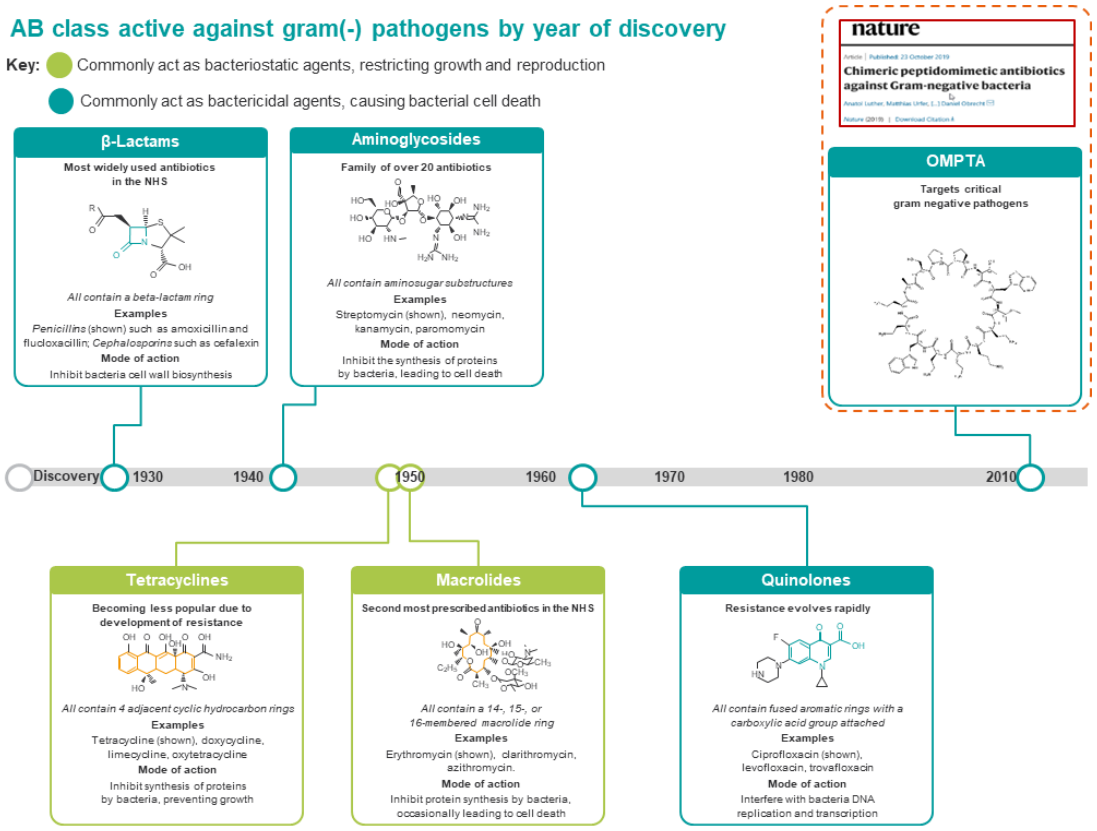
OMPTA Antibiotics

Novel class of antibiotics targeting WHO priority1 pathogens

OMPTA Antibiotics

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 covering all WHO priority 1 pathogens"



Our innovation focuses on three targets within OMPTA class

1. **LptD/E:** Inhaled Murepavadin Entering Phase I ***(IMI funding)***
2. **LPS and BamA:** Hit to Lead ***(CARBX funding)***
3. **LptA Thanatin Derivatives:** Hit to Lead ***(CARBX funding)***

- 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 are possible
- Strong 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

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

- P. aeruginosa is the leading cause of lung function decline and mortality in CF accounting for 2/3 of the chronic infections
- Tobramycin and aztreonam are commonly used inhaled ABs for CF, developed 10-20 years ago administered 2-3 times daily
- Despite proven efficacy, exacerbation, lung function decline and mortality persist over time in CF due to *P. aeruginosa*
- Cystic Fibrosis Foundation has committed at least $100 million to the Infection Research Initiative in 2019

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 [2] strains
- Biofilm activity (*in vitro)* and low resistance potential
- No cross-resistance with other antibiotics
- High safety margin (least 5-10 fold above IV application)[3] in preclinical GLP
- Potent activity in lung infection models

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.

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 Cystic Fibrosis

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

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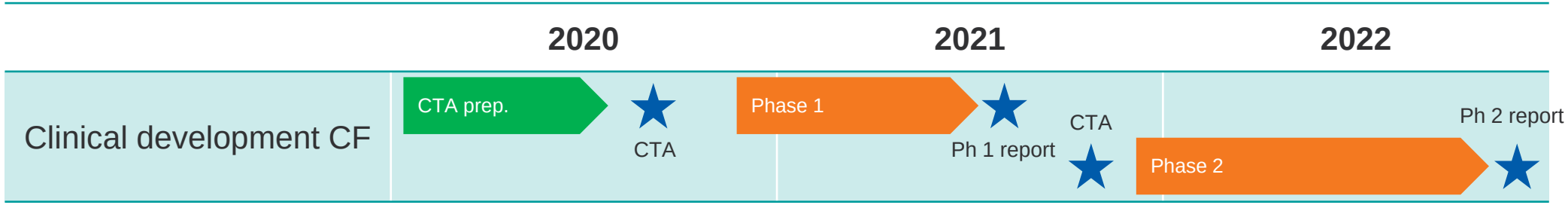
Potentially the first pathogen specific new class inhaled antibiotic for P. aeruginosa, leading cause of exacerbations, lung function decline and mortality in CF



Clinical Program Plan and Timelines:

- Preclinical program complete suggesting broad safety margin and efficacy; plans to submit CTA and start Phase I program in Q4 2020
- Phase I study plan to include single and multiple dosing in healthy volunteers up to 7 days
- 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

Financials

Financials

Key Figures

(in CHF millions, except number of shares)

Profit & Loss	30.06.2020	30.06.2019
Revenue	-	-
R&D expenses	-24.6	-25.3
Net Loss	-27.8	-27.9
Avg. net cash burn	-5.4	-5.9
FTEs	57	61

Balance Sheet	30.06.2020	31.12.2019
Cash & Cash Equivalents	43.7	77.4
Total Assets	57.7	92.8
Total Equity	29.6	55.1

Share information	30.10.2020
Shares outstanding	11’196’645
52 week High / Low	CHF 11.22 / 4.88
Closing price - 23.10.2020	CHF 8.20
Market Capitalization	CHF 91.8 m

Guidance and outlook

- Opex 31.12.2020: **CHF 57m to CHF 59m**
- With existing cash and USD 15m upfront from the partnering agreement with Fosun, operations are financed **well into Q3 2021**.
- Equity-linked financing arrangement in July 2020 with IRIS up to CHF 19.3 M providing flexibility to extend current cash if needed
- Next value inflection points for balixafortide are **ORR Q2 2021 and PFS Q4 2021**
- Early stage antibiotics programs primarily financed through non-dilutive funding.

Major shareholders	%
Ingro Finanz AG	11.2
Varuma AG	8.6
Credit Suisse Fund Management AG	6.0

Summary

Strategy to Expand Shareholder Value

Strong progress YTD and upcoming key inflection points

Strong Achievements YTD after renewed strategy and management team:

✓ Balixafortide Phase III Trial enrollment closed on time and 2 positive DSMBs

✓ Fosun Pharma China Partnership: strong deal size validating scientific and commercial value & non dilutive financing

✓ New CARB-X award to up to USD 18.4 M to develop new AB program – Thanatin derivatives

✓ Extended cash runway well into Q3 2021 through financial stewardship and upcoming China upfront

✓ Equity-linked financing arrangement with IRIS up to CHF 19.3 M providing flexibility to extend current cash if needed

Significant near-term value drivers at an attractive valuation:

- Prepare for ORR and PFS data readouts in **Q2 and Q4 2021** for balixafortide
- Expand balixafortide opportunity in additional indications prior to potential global licensing following PFS data
- CTA filing and plan to initiate Phase I for inhaled murepavadin in **Q4 2020** (results expected in 2021)
- Deliver on antibiotics pipeline milestones to continue to expand our pipeline.

Management Team

Gökhan Batur

Chief Executive Officer

Daniel Obrecht, Ph.D.

Chief Scientific Officer

Frank Weber, M.D.,

Chief Medical & Development Officer

Hernan Levett

Chief Financial Officer

Franziska Müller

Head of Human Resources

Q&A Session

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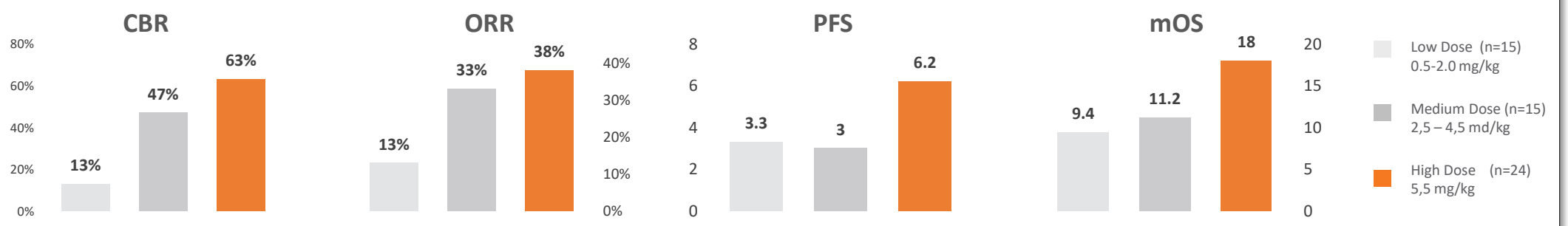
cover photo | © gettyimages.com

Balixafortide has potentially the best in class efficacy amongst CXCR4s*

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

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.