

POLYPHOR

Corporate Strategy Update: **Focus Forward**

20th February 2020

Forward-looking statement



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Our Agenda Today And The Polyphor Team



- 1** Polyphor Strategy Update
- 2** Balixafortide Immuno-Oncology Program Progress
- 3** Inhaled Murepavadin and Antibiotics Pipeline
- 4** Financial Outlook
- 5** Summary and Q&A



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

1

Polyphor: a research based clinical stage biopharmaceutical company, targeting first in class molecules, focused in oncology and antimicrobial resistance, two of the most critical health problems.

2

Strong execution with the Phase III immuno-oncology program with balixafortide. Enrollment ahead of plan with 192 patients (50% of total) and reaffirming first co-primary endpoint, ORR (Overall Response Rate) timelines of end Q1 2021.

3

Given strong Phase III trial progress, Polyphor intends to complete the package for MA (Marketing Authorization) filing and expand balixafortide future opportunity beyond the initial indication.

4

Successfully completed the preclinical package and plans to move inhaled murepavadin for cystic fibrosis to Phase Ia in Q4 2020.

5

New strategy for antibiotics research and development applying the learning from our experience to enhance future clinical success. Restructured existing programs and initiated a new target program within the OMPTA class.

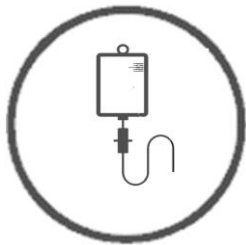
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Financed to achieve the next value inflection points – specifically balixafortide ORR, expected around end of Q1 2021.



Polyphor Strategic Priorities

Deliver near term value driver while building beyond the major inflection point **POLYPHOR**



Delivering on balixafortide Phase III trial



Unlocking the full value potential of balixafortide



Advancing Inhaled Murepavadin for CF to clinic



New strategy for antibiotics research and development **applying past learning**



Becoming a **leaner, more efficient, research-driven clinical stage company** to deliver near term opportunities while expanding the pipeline

 Near term priority

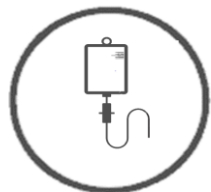
 Pipeline plan

Balixafortide Fortress Trial

Deliver Phase III trial by continuing strong performance



Delivering on
balixafortide Phase III
trial



Organizational focus to continue strong Phase III trial (Fortress) execution for balixafortide

- 192 patients randomized to-date (50% of total) and enrollment is progressing ahead of plan to be complete end Q3 2020.
- Reaffirming first co-primary endpoint, ORR timelines of end Q1 2021.
- ORR results could lead to an accelerated approval in the US or PFS (Q4 2021) will be the basis for regular MA submission in EU and US.

Balixafortide Development Strategy

Expanding balixafortide program beyond first co-primary endpoint



Unlocking the full value potential of balixafortide



- **Given strong Phase III trial progress, Polyphor plans to complete the package for MA filing and expand balixafortide future opportunity beyond the initial indication**
- **Projects planned to be initiated second half of 2020:**
 - Initiate additional studies to complete balixafortide package for potential MA filing.
 - Investigate additional dosing and scheduling options for broader use leveraging broad safety margin findings.
- **Projects currently planned and to be initiated post ORR results:**
 - Initiate studies to pursue additional combinations in MBC (earlier lines) and enhance its characterization in CXCR4 driven immune pathway.
 - Expand activities to further profile balixafortide activity in other combinations and tumors.
 - Identify additional novel development candidates in the field of immuno-oncology will be a strategic consideration moving forward.
- **The company will actively pursue broadening academic and industry collaboration in the mid-term.**

Inhaled Murepavadin for CF

Expanding the clinical pipeline with an attractive market opportunity



Advancing inhaled murepavadin for CF to clinic



Opportunity to be the first new class inhaled antibiotics targeting specifically chronic Pseudomonas A. infections, a major cause of disease progression and death in people with cystic fibrosis

- Following the successful completion of the preclinical program suggesting broad safety margin and efficacy, plans to submit CTA (Clinical Trial Application) for inhaled murepavadin and start Phase Ia program in Q4 2020.
- Safety margins based on available preclinical GLP Tox data are at least 5-10 fold above IV application.
- Pursue additional external financing while the program already partly financed by IMI until Phase I.

New Antibiotics Research Strategy

Apply the learning and experience to enhance future clinical success



New strategy for
antibiotics research
and development
applying the learning



Continue the antibiotics research and development supported by the existing and future non-dilutive and/or external financing

- Strong focus on formulation and peptide design optimization in reprioritizing programs applying lessons learned from the murepavadin IV program, which the company has decided to terminate.
- Despite the promising efficacy package after completion of its preclinical program, the company will not continue POL7306 program to clinical research as is. Polyphor plans to focus on a new formulation of POL7306 and peptide design optimization of its OMPTA program achieve broader therapeutic margins before moving into clinical trials.
- Initiated a new target program within OMPTA class, thanatin derivatives targeting specifically Enterobacteriaceae inc. most resistant strains, one of the most common and resistant pathogens.

Organizational Transformation

Establish a lean high-performing organization while creating operational efficiency



Organizational Transformation



In line with the renewed strategy, organization and resources will be focused on greatest opportunities innovation and value creation.

- A planned restructuring by up to 17 positions is expected to create operational efficiencies and help become a leaner and high-performance organization in progressing breakthrough science and innovation. A consultation process with employees is initiated.
- New organization will be equipped to deliver balixafortide and inhaled murepavadin clinical studies while maintaining the core in research in antibiotics and oncology.

Unlocking the potential of CXCR4 antagonism

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

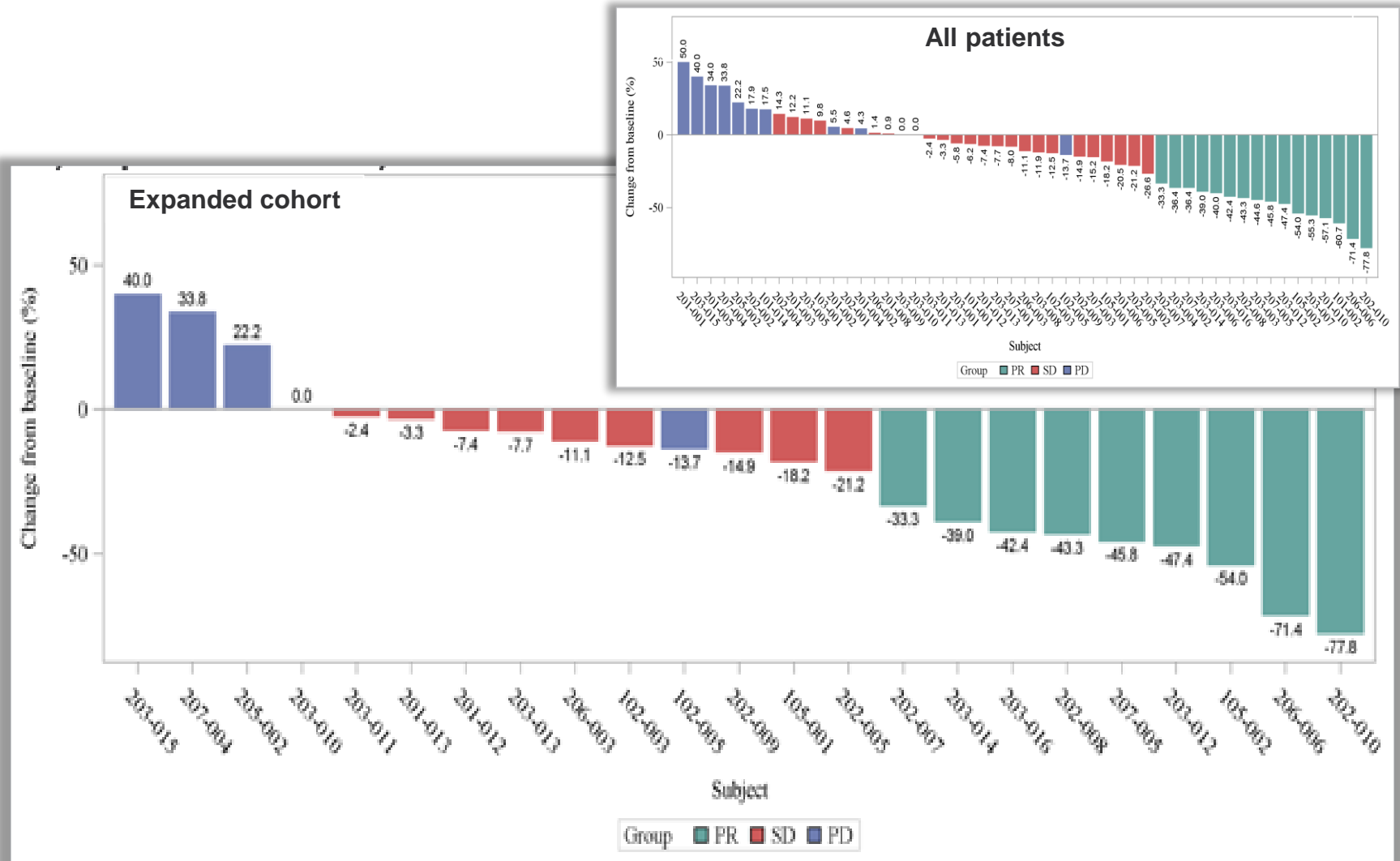
A novel immuno-oncology approach starting from a large indication

- First CXCR4 antagonist spearheading novel immuno-oncology approach in Phase III MBC
- Large first indication in HER2negative 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 ctx
 - Other tumors / oncology indications
 - Combination with checkpoint inhibitors

Phase Ib Clinical proof of Concept in HER2-negative MBC on top of Eribulin



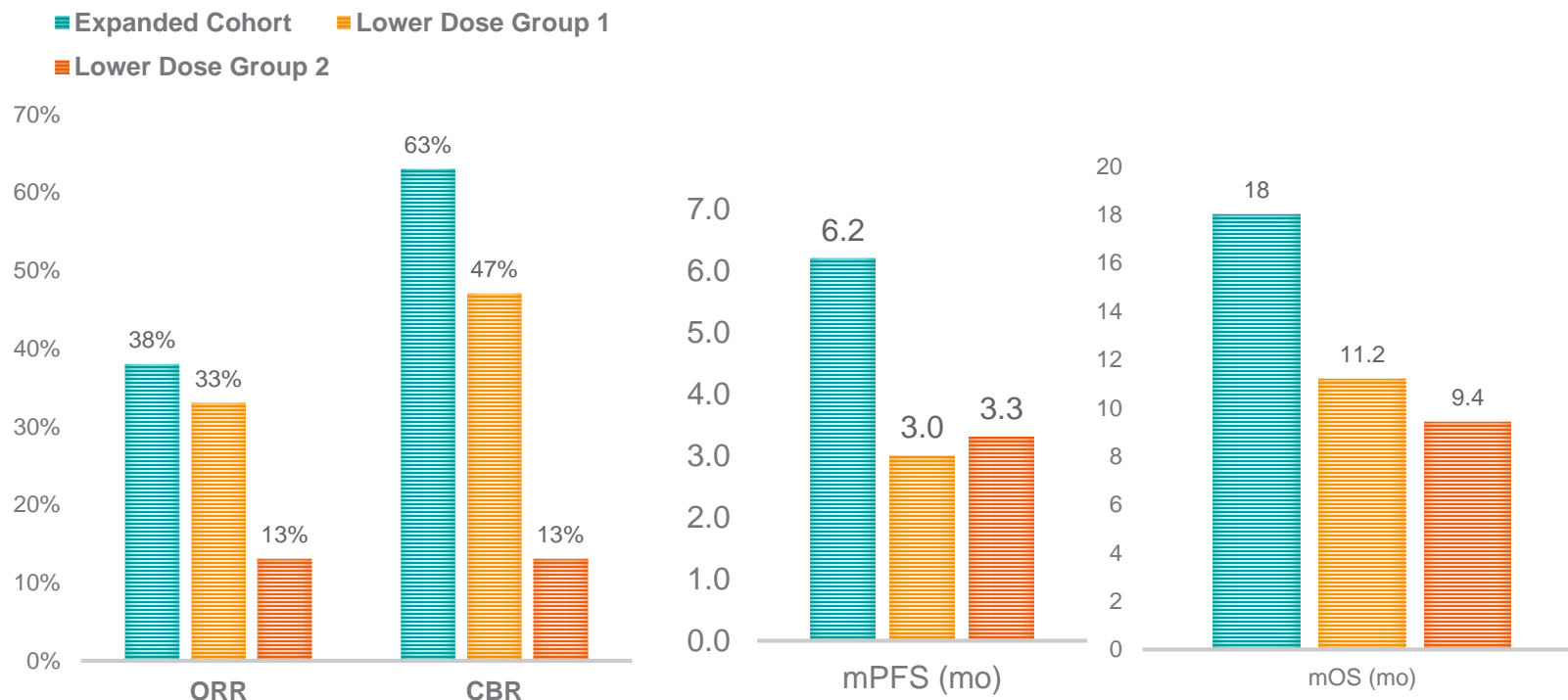
Best overall response by maximal percent reduction in tumor size for target lesion



Phase Ib Clinical Proof of Concept in HER2-negative MBC on top of Eribulin



THE LANCET
Oncology



- All groups have approved dose of eribulin
- On top balixafortide shows a clear dose response across all efficacy endpoints

“An International, Phase III, Multicenter, Randomized, Open-Label Trial Comparing BalixaFORTide in combination with ERibulin versus Eribulin alone in PatientS with Locally Recurrent or MetaStatic Breast Cancer”.

Objectives:

- Confirm Phase Ib 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

Phase III Pivotal Study FORTRESS

Eribulin +/- Balixafortide in advanced MBC

Study design: patient population & treatment scheme



Patient Population (n=384):

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

Treatment schedule:

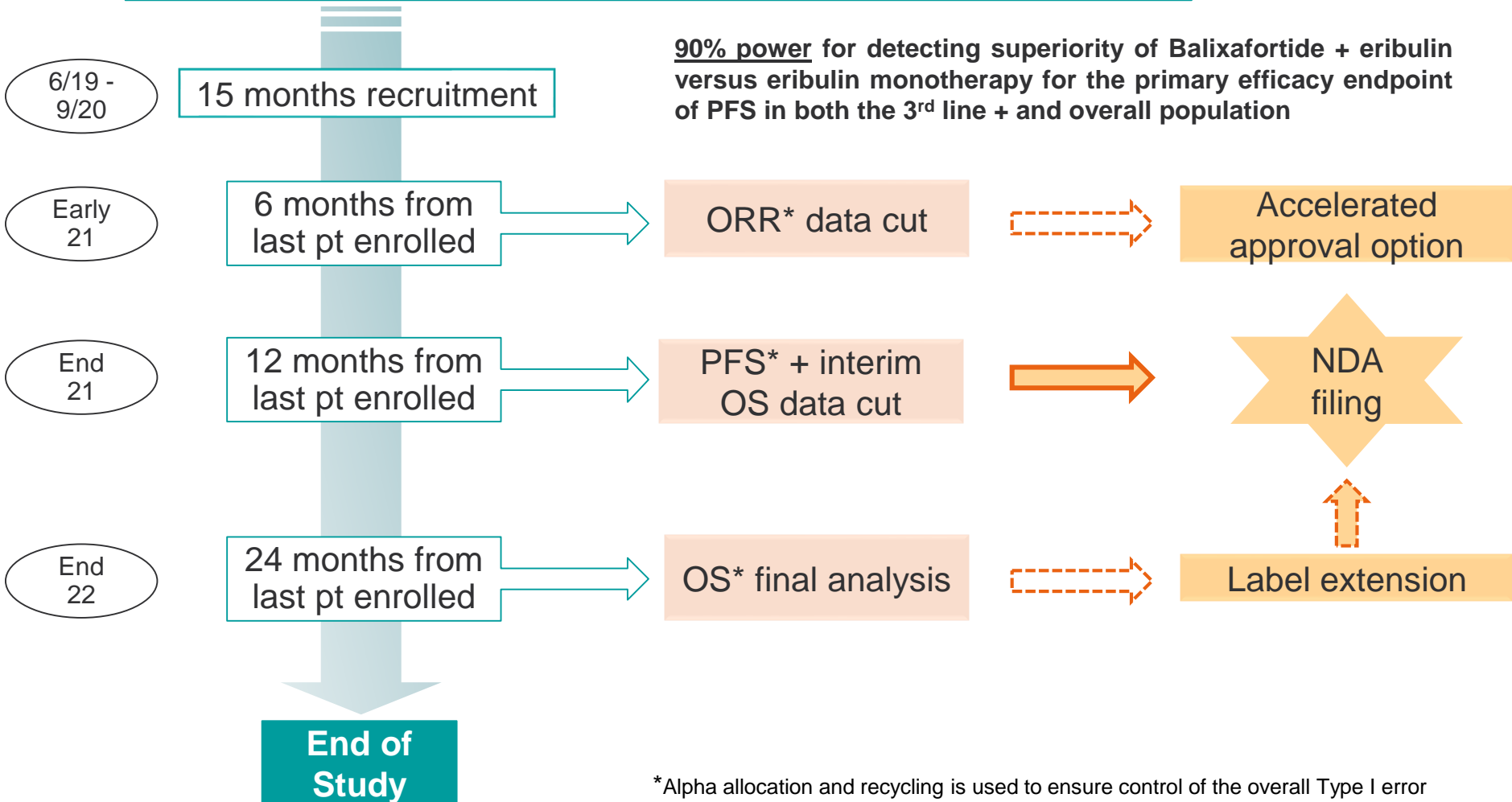
Randomisation 1:1 ratio to either balixafortide plus eribulin or eribulin alone

- 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

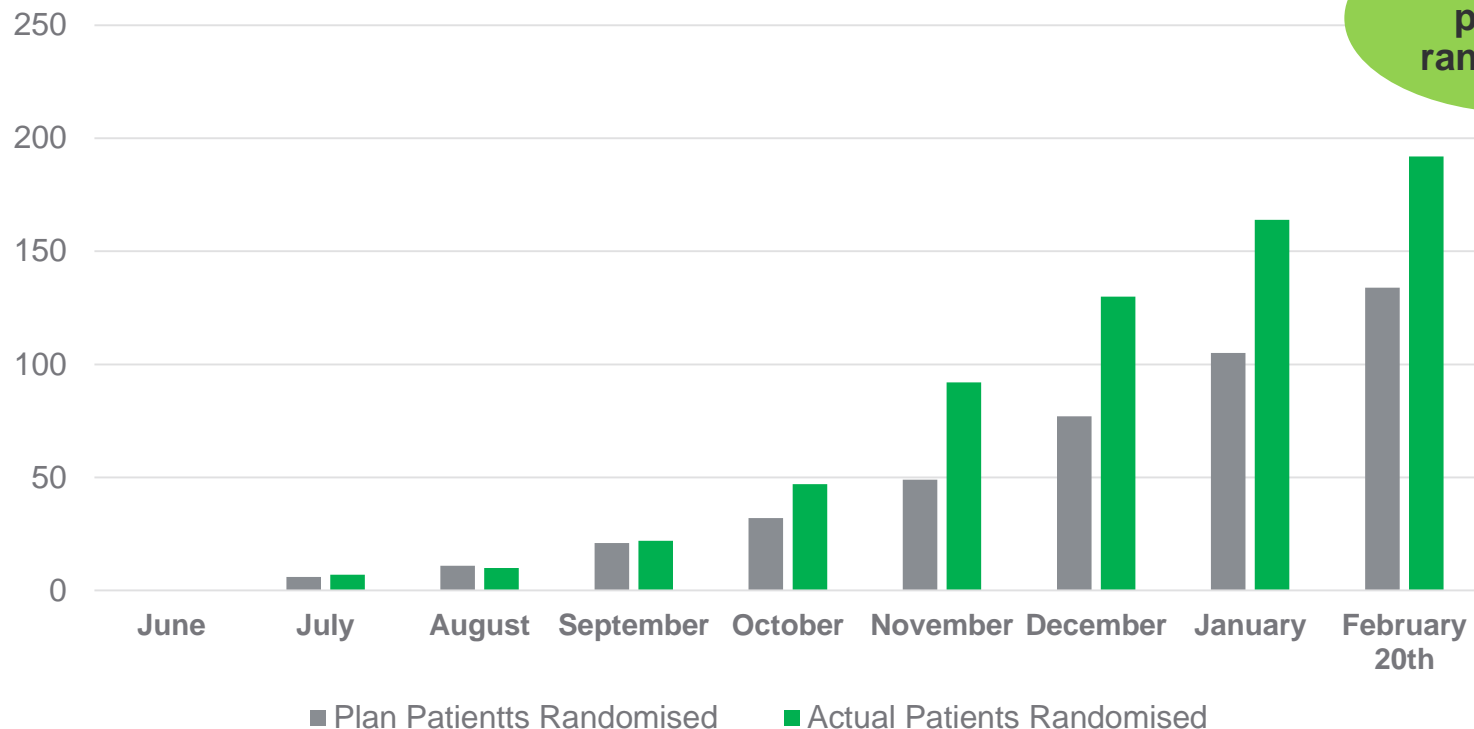


Overall population N=384 , 320 3rd line + and 64 2nd line



FORTRESS Recruitment is ahead of Plan

FORTRESS Randomisation Curve



- Today's Randomisation status n= 192 (50% of 384)
- Study recruits well with currently > 30 patients / months
- Sites in all continents open, Spain is currently leading recruitment country
- New sites opening planned until April 20

Balixafortide Development Strategy



Near and midterm goals:

- **Planning to complete dossier for NDA filing ongoing:**
 - Clinical pharmacology package
 - CMC package
 - Non clinical safety and pharmacology package

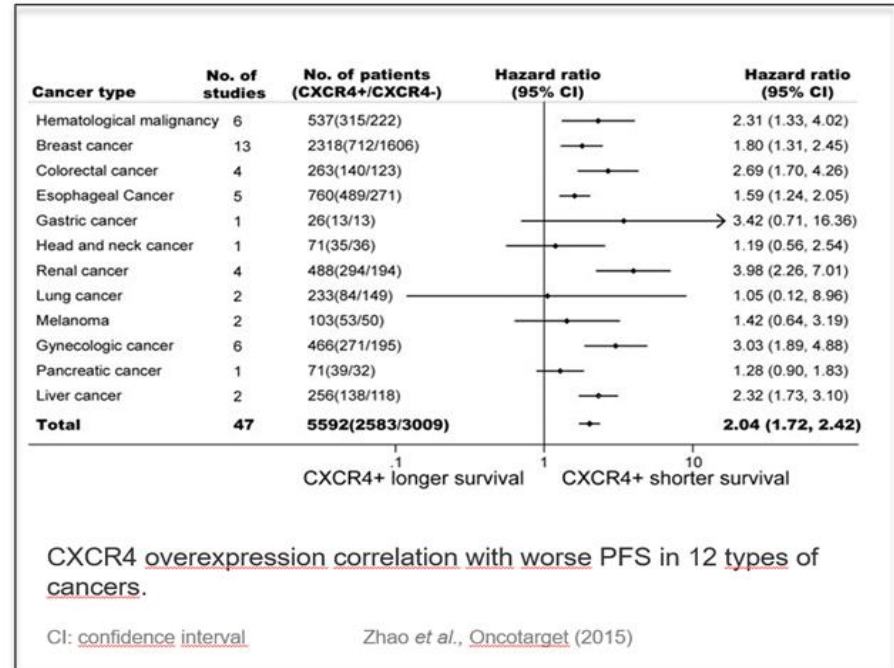
- **Further development strategy beyond FORTRESS:**
 - Investigate improved dose and scheduling
 - Define maximal tolerated dose (MTD)
 - Assess tolerance and preliminary efficacy in combination with other chemotherapies in MBC
 - Develop other formulations than IV
 - Develop a CXCR4 diagnostic test

Oncology Pipeline Strategy

Longterm targets in expanding oncology opportunity



- 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 MBC
- Combinations with other immuno-oncology therapies and CXCR4 antagonists are promising and open further opportunities for balixafortide



- Beyond balixafortide Polyphor has identified a number of novel targets in the area of immuno-oncology which are very suitable for being addressed by peptides from the macrocycle technology platform
- Polyphor is currently assessing the opportunity to identify new lead compounds in the area of immuno-oncology to be nominated as development candidates

Inhaled Murepavadin:

Treatment of chronic *Pseudomonas a.* infection in people with cystic fibrosis



Plan to move to human trials after the successful completion of the preclinical program

■ Inhaled Murepavadin could change the treatment paradigm for CF patients

- 2/3 of CF patients have a *Pseudomonas* infection
- The need for effective *Pseudomonas* control has not changed after introduction of CFTR modulators
- Murepavadin exhibits strong preclinical efficacy, incl. resistant strains, and exposure
- A mono-pathogen would be the most rational treatment vs broad spectrum agents (e.g microbiome impact)

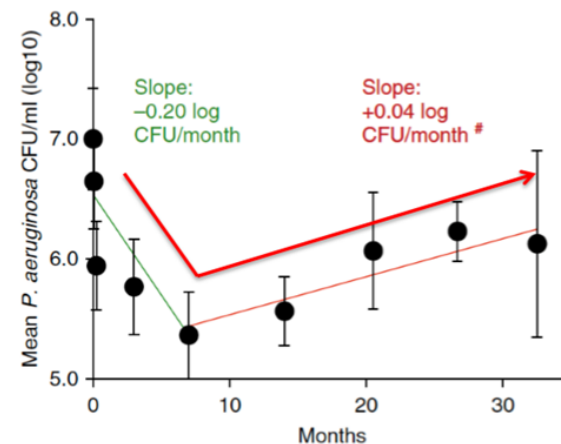
■ Targeted and attractive orphan opportunity

- Attractive orphan market opportunity where innovation is rewarded
- Comparators' * peak sales (200-400m USD)
- Can be expanded from CF to NCFB** and beyond
- IMI Contribution up to Ph I included

■ Development Status

- Non clinical package for CTA nearly completed
- Safety margins based on available preclinical GLP Tox studies at least 5-10 fold above IV application.
- Development of inhaled formulation ongoing
- Clinical trial application planned for Q4 2020

Evolution of PA colonization after ivacaftor treatment



ACRCCM 2017, 195 ; 12:1617-28

* Tobo and Cayston ** Non Cystic Fibrosis Bronchiectasis

OMPTA Targets

OMPTA is a novel class of antibiotics with a mission



“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 Derivatives (a new target program)

Polyphor has shown:

- It’s truly a new class validated by Nature Journal publication
- A unique spectrum of coverage targeting all, single or a group of specific WHO Priority 1 pathogens is possible
- This class of antibiotics have the potential for lower propensity for resistance versus classical antibiotics
- Our science is robust to attract non-dilutive funding and external financing

nature

Article | Published: 23 October 2019

Chimeric peptidomimetic antibiotics against Gram-negative bacteria

Anatol Luther, Matthias Urfer, [...] Daniel Obrecht

Nature (2019) | Download Citation

Positive external validation to the target and class

New strategy in research and development of ABs

Applying the learning to our research and development efforts



- Polyphor will transform its antibiotics research strategy based on lessons learned from the murepavadin IV program, which the company has decided to terminate.
- OMPTA programs have strong efficacy and durability (against resistance) potential however strong focus on formulation and peptide design optimization is required to improve therapeutic margins to improve late stage clinical development POS.
- Inhaled murepavadin, planned to move to Ph. Ia, is a positive example of the approach (formulation).
- Despite the promising efficacy within completed preclinical package, decision to not continue POL7306 program to clinical research as is. Polyphor plans to focus on a new formulation of POL7306 and peptide design optimization of its OMPTA program to improve therapeutic margins before going into clinical.
- Polyphor initiated a new target program within OMPTA class, thanatin derivatives, targeting specifically Enterobacteriaceae including multidrug resistant strains, one of the most common and resistant pathogens. Initial program profile aligns with the optimization targets of the new strategy.
- Polyphor with its OMPTA platform, has one of the most innovative approaches to tackle antimicrobial resistance. We believe our science and targets align well with the objectives of currently discussed financial incentives which intends to increase the attractiveness of this therapeutic area.
- Polyphor will continue the research and development with careful consideration and largely supported by the existing and future non-dilutive and/or external financing.

Financial Outlook



- The company reconfirms its guidance for 2019 in terms of operating expenses of CHF 60m to CHF 65m and cash of 68m to CHF 72m.
- The company reconfirms its guidance that with existing cash, operations are financed until the end of Q1 2021.
- Under the current plan, the cash position will allow Polyphor to develop the balixafortide program towards the next value inflection point (ORR, around end of Q1 2021).
- Early stage antibiotics programs partly financed through non-dilutive funding and external financing. On-going discussions with key institutions in order to further support the antibiotics pipeline.
- Polyphor plans to release its FY 2019 financial results on April 28th 2020.

Summary and Conclusion



- ✓ With a focused new strategy and a lean organization, Polyphor continues its focus in two key areas, oncology and antimicrobial resistance.
- ✓ Near-term priority is to deliver our Phase III immuno-oncology program with balixafortide continuing strong trial execution.
- ✓ Given strong trial progress, balixafortide strategy now extends beyond ORR, plans to complete the package for MA filing and expand the future opportunity beyond the initial indication.
- ✓ Planning to expand the clinical stage pipeline with inhaled murepavadin for CF in Q4 2020.
- ✓ New antibiotics strategy applying the learning from our experience will help enhance pipeline evolution and future clinical success. Will utilize existing and future non-dilutive and external financing.
- ✓ Financed to achieve the next value inflection points – specifically balixafortide ORR.

Focus Forward: Delivering balixafortide Ph. III trial while establishing a clear strategy on progressing its pipeline in oncology and antibiotics

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Corporate Strategy Update: **Focus Forward**

Q&A Session



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