# POLYPHOR

## Corporate Update and 2019 Financial Results

April 28th 2020

# Forward-looking statement

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# 2019 Highlights and the Outlook

*After 2019 turnaround, 2020 is focused on Balixafortide execution and pipeline expansion*

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## 2019 Highlights:

- Balixafortide – Start FORTRESS Phase III trial, followed by strong progress
- Decision to halt murepavadin I.V. clinical program
- Inhaled Murepavadin – Completion preclinical program
- POL7306 preclinical program complete - decision to not submit IND, but continue formulation / peptide design
- New leadership and board of directors changes
- CHF 77.4 million in cash and cash equivalents as of December 31, 2019

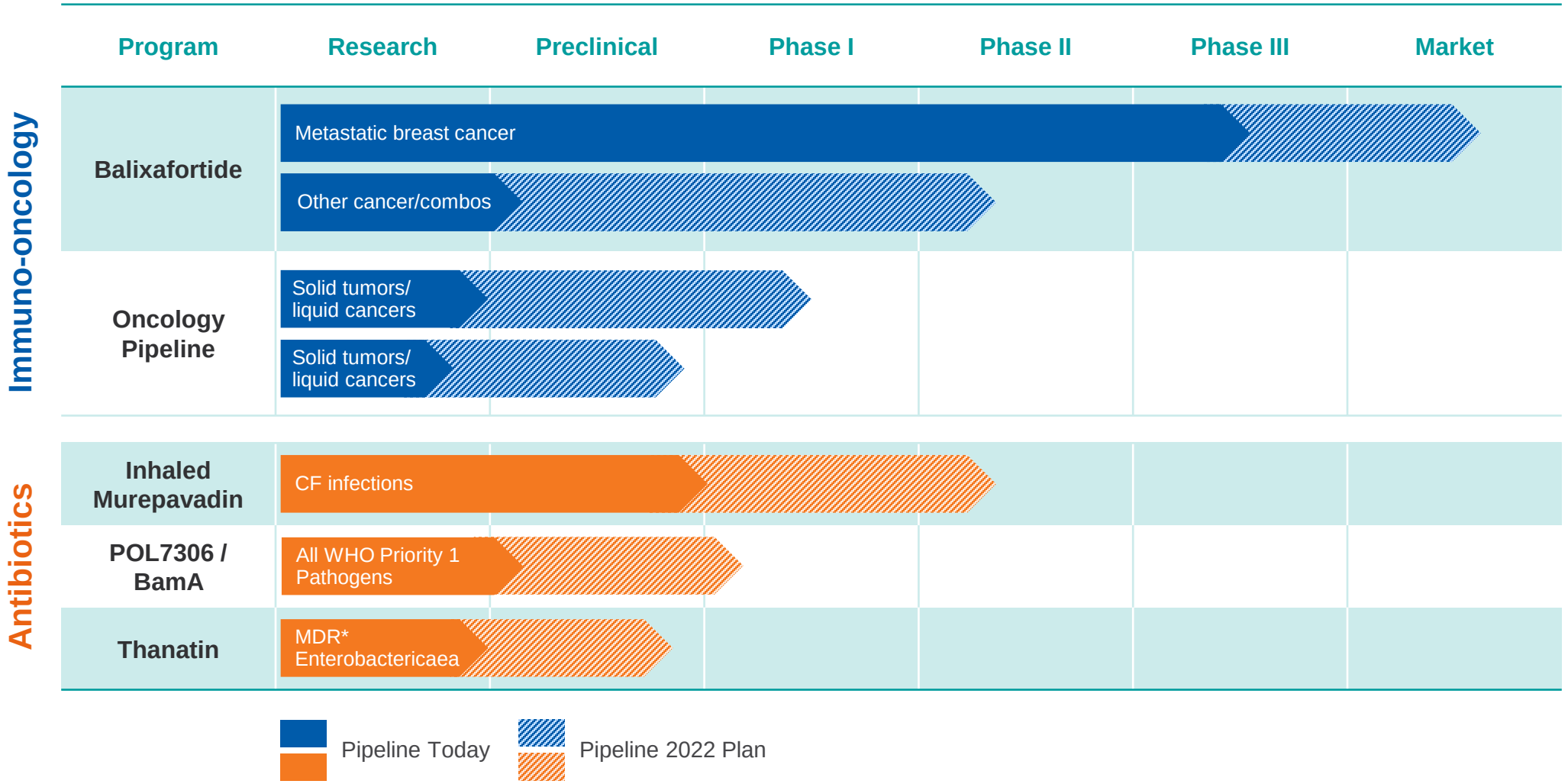
## Outlook:

- Balixafortide – Strong Phase III trial progress in metastatic breast cancer with enrollment ahead of plan and positive first DSMB. First co-primary endpoint (ORR*) data-cut expected end Q1 2021
- Plans to expand balixafortide opportunity with new dosing schedule, non IV formulation, earlier lines of mBCa, other tumor types and combinations
- Explore new oncology candidates from our platform following ORR data in Q1 2021
- Inhaled Murepavadin – Plan to submit CTA in Q4 2020
- Renewed strategy for our research and preclinical antibiotic programs with strong focus on formulation and peptide design optimization

*Objective Response Rate

# Polyphor Pipeline and Plan

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




*Multidrug Resistant

# 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

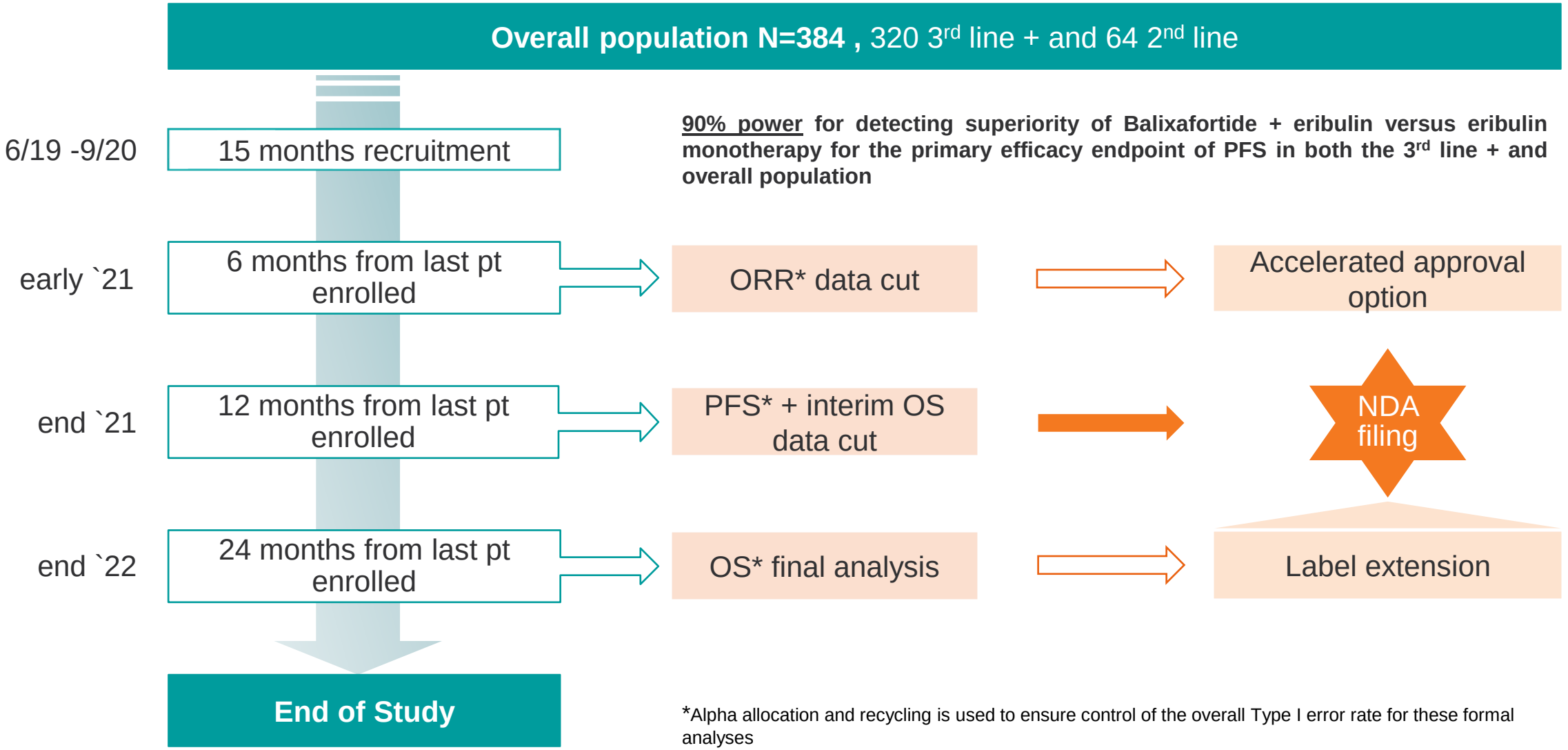
## A novel immuno-oncology approach starting from a large indication

- 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

# 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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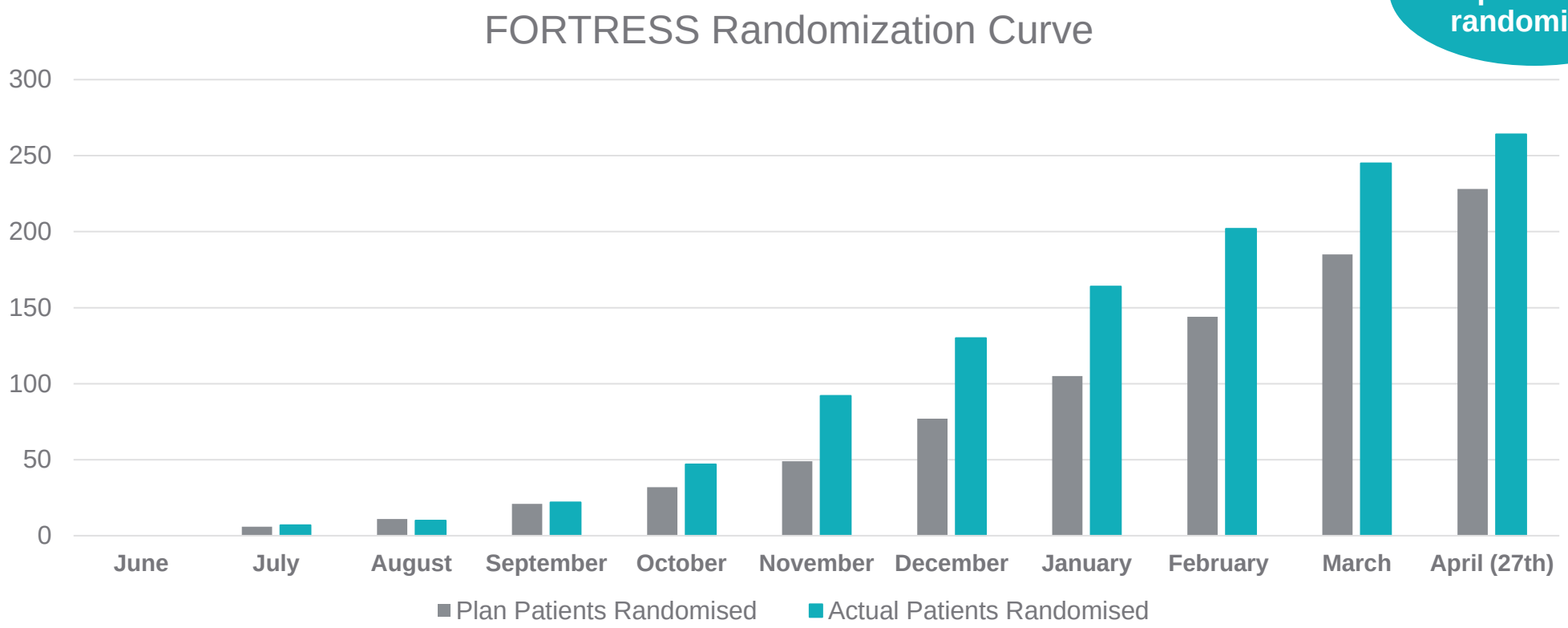
**69% of patients randomized**




- 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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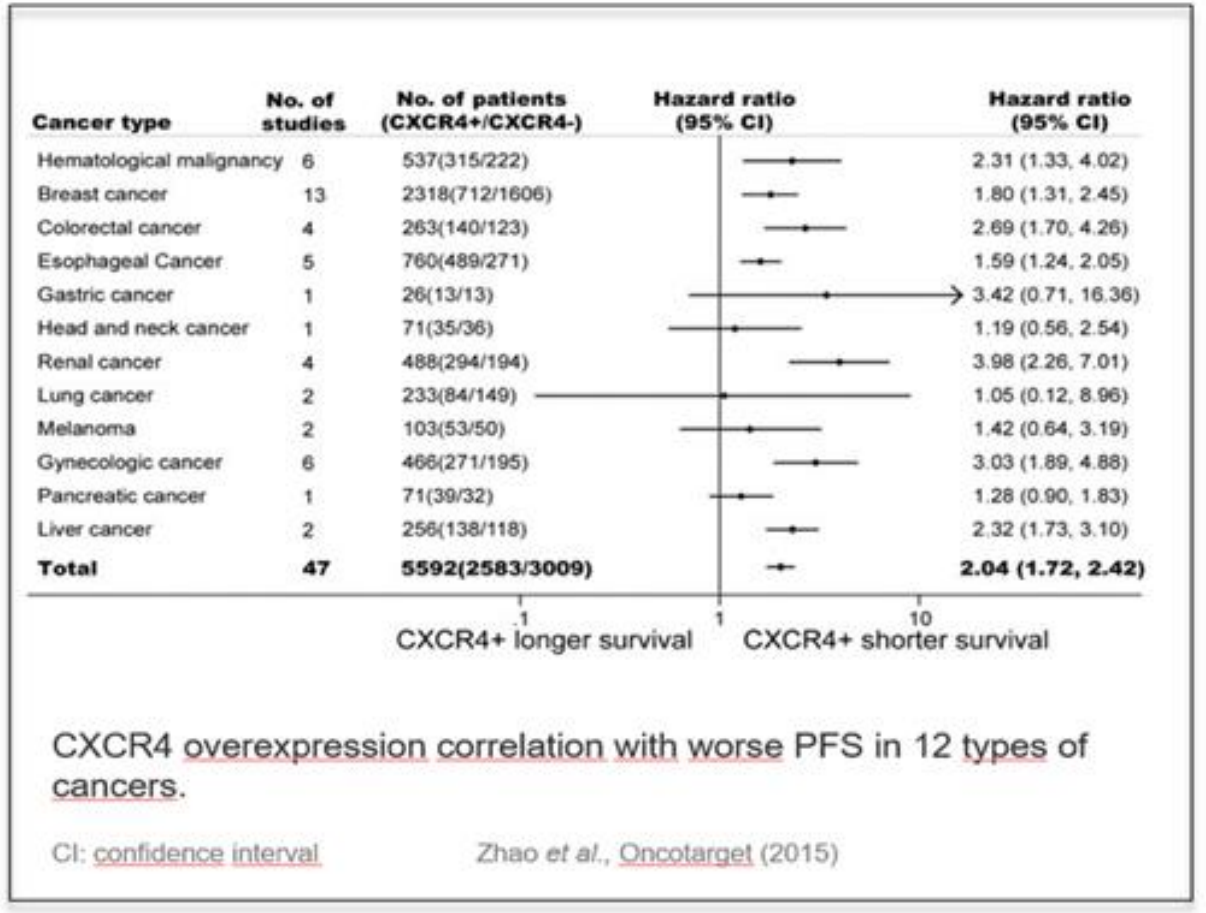
- CXCR4 expression has been validated as a negative prognostic factor for other cancer types
- Balixafortide has therefore a potential as a novel treatment option in tumors beyond mBCa
- Combinations with other immuno-oncology therapies and CXCR4 antagonists are promising and open further opportunities 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**

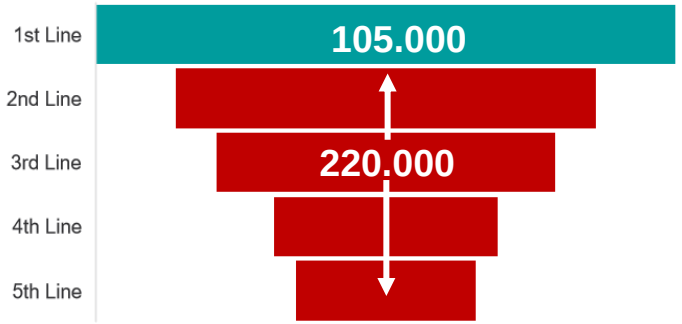
- Preclinical studies in other combinations / tumors
- Improved dose scheduling study
- Phase II Study in combination with other chemo in earlier mBC
- Non IV Formulation
- CXCR4 Diagnostic Test

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

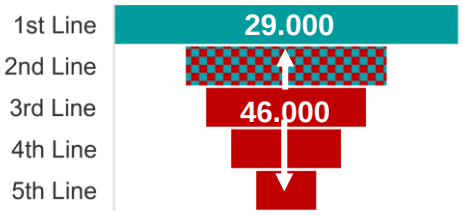
# 2023 mBCa Market Projection and Initial Opportunity (US and EU5)

## Large Total Addressable Patient Population Balixafortide Can Target

HER2(-) HR+ mBCa
(# of patients receiving non-endocrine therapy, 2023)




## Triple Negative mBCa
(# of patients receiving chemo or targeted therapy, 2023)

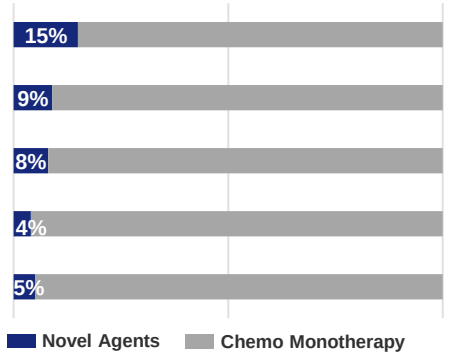



Balixafortide opportunity segments

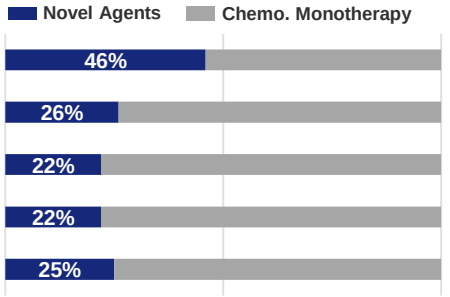
Source: Global Data HER2-Negative Breast Cancer: Market Analysis 2018–2028, Published February 2020

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

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

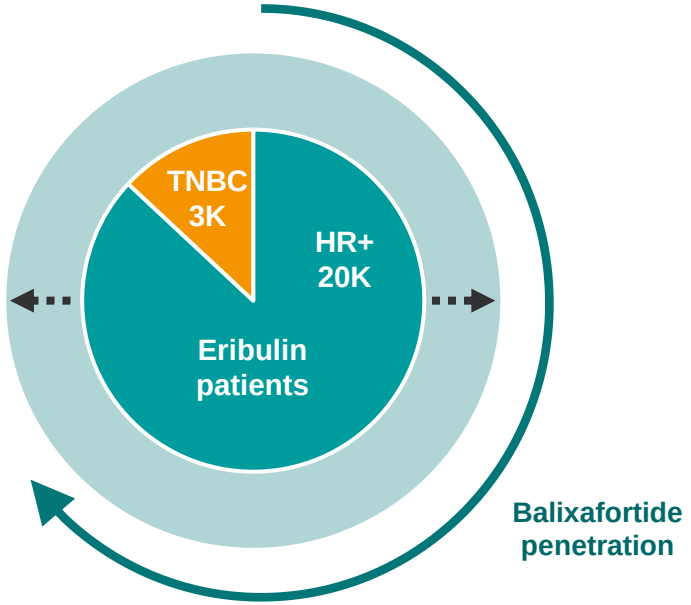



**Earlier lines:** Abemaciclib and AKT inhibitor
**Later Lines:** sacituzumab (primary balixa competitor)
**BRCA+ patients across lines:** PARP inhibitors




**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

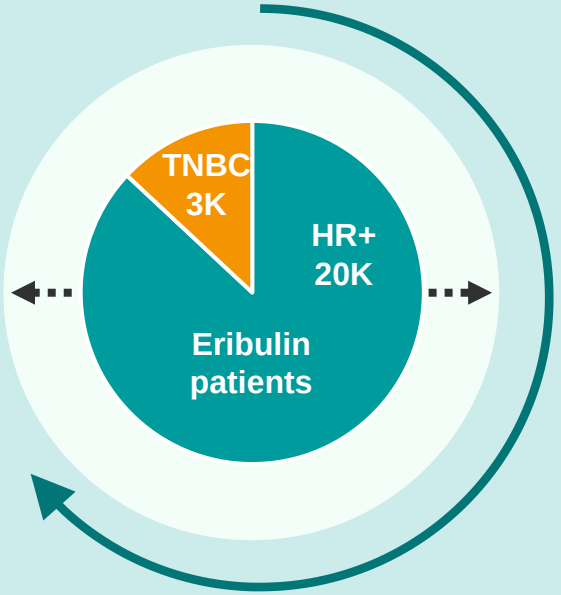
## Balixafortide + eribulin to become new standard of care in later lines of HR+




- 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

# US$ 1.3B Initial Market Potential; US$ 6-7B Mid-term Opportunity

## Initial indication market potential

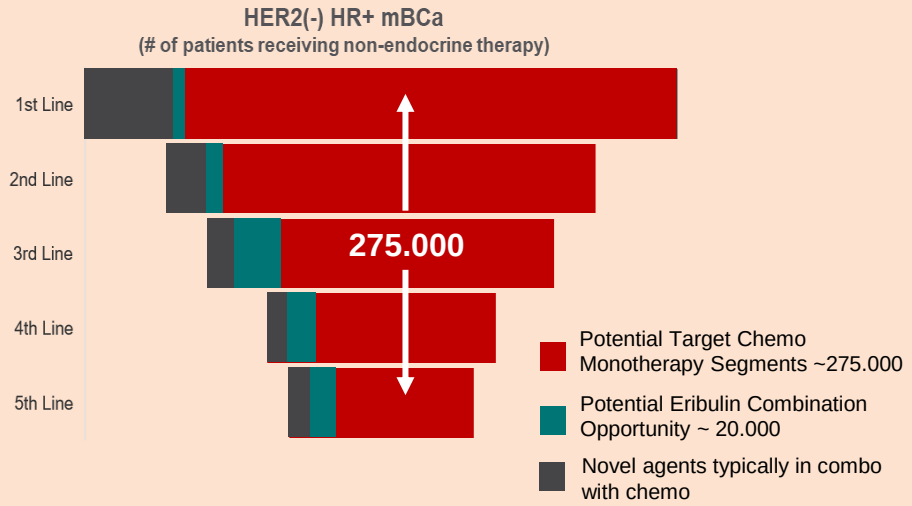



**Balixafortide pricing:** similar to targeted breast cancer therapies vs chemos inc. eribulin

**Increased cycles due to better outcomes**
vs. eribulin monotherapy

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

## Mid-term 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$ 6-7B 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

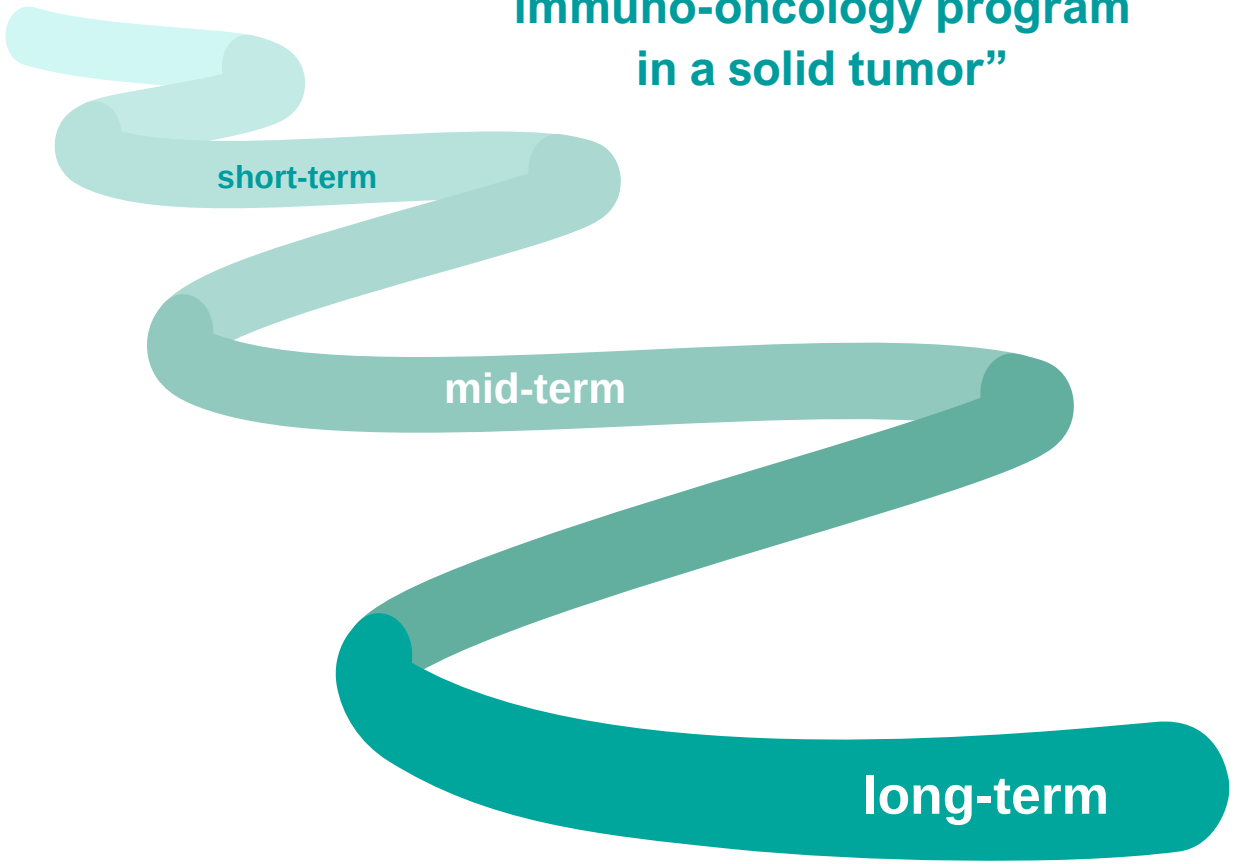
**2. Balixafortide expansion in other indications / combos**

- 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"**



# 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 [2] 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

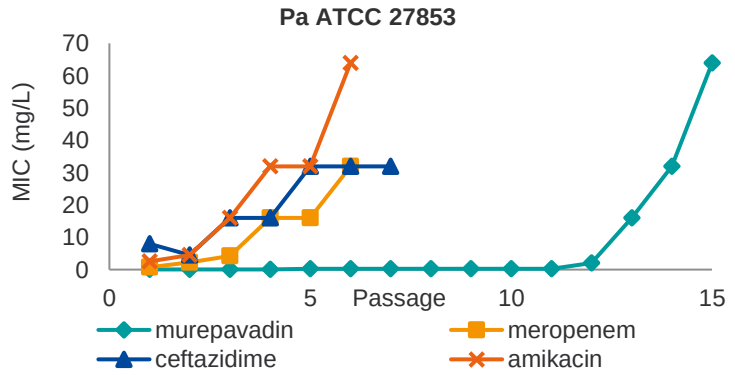
**MICs (mg/L) of 414 *Pseudomonas aeruginosa* isolates from people with CF***

| | $MIC_{50}$ | $MIC_{90}$ | 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

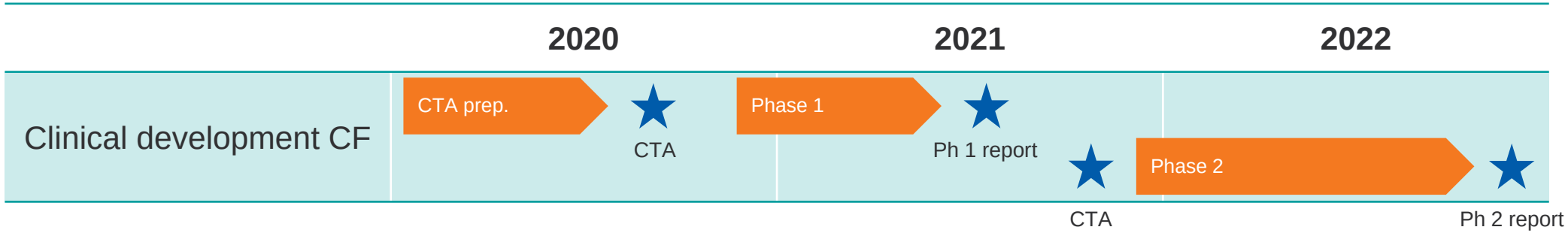
Resistance development: serial passage




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*

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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*

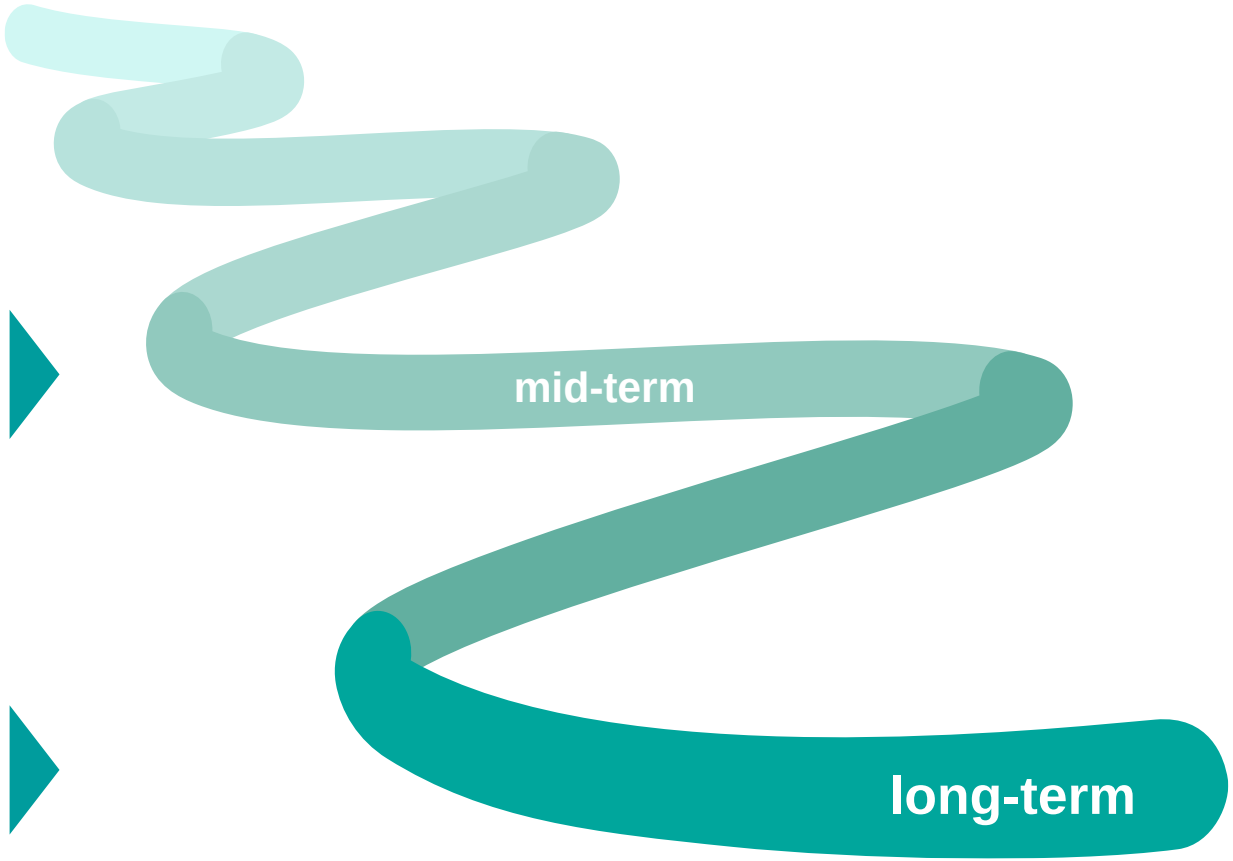
**“First new class of antibiotics in gram negative space in 50 years targeting cystic fibrosis and hospital acquired infections”**

### 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:

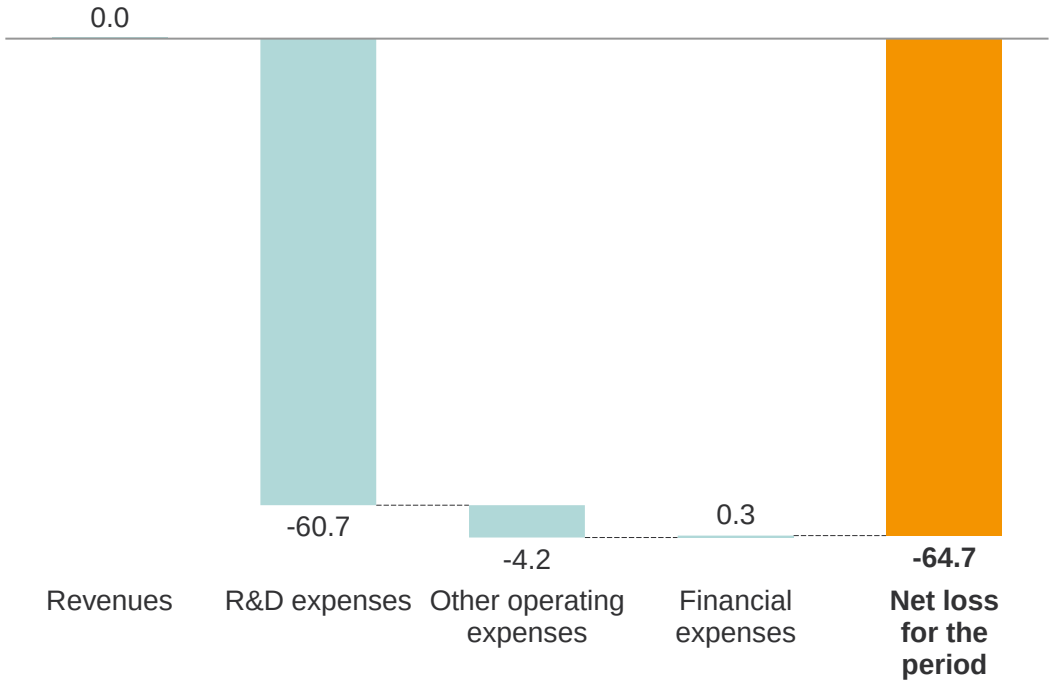
- Bringing first new class of antibiotics targeting resistant WHO priority 1 gram(-) bacteria with low propensity for resistance
- Continue preclinical programs with external financing to ensure minimal cash burn impact until clinical stage
- Potential long term value driver following potential new AMR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



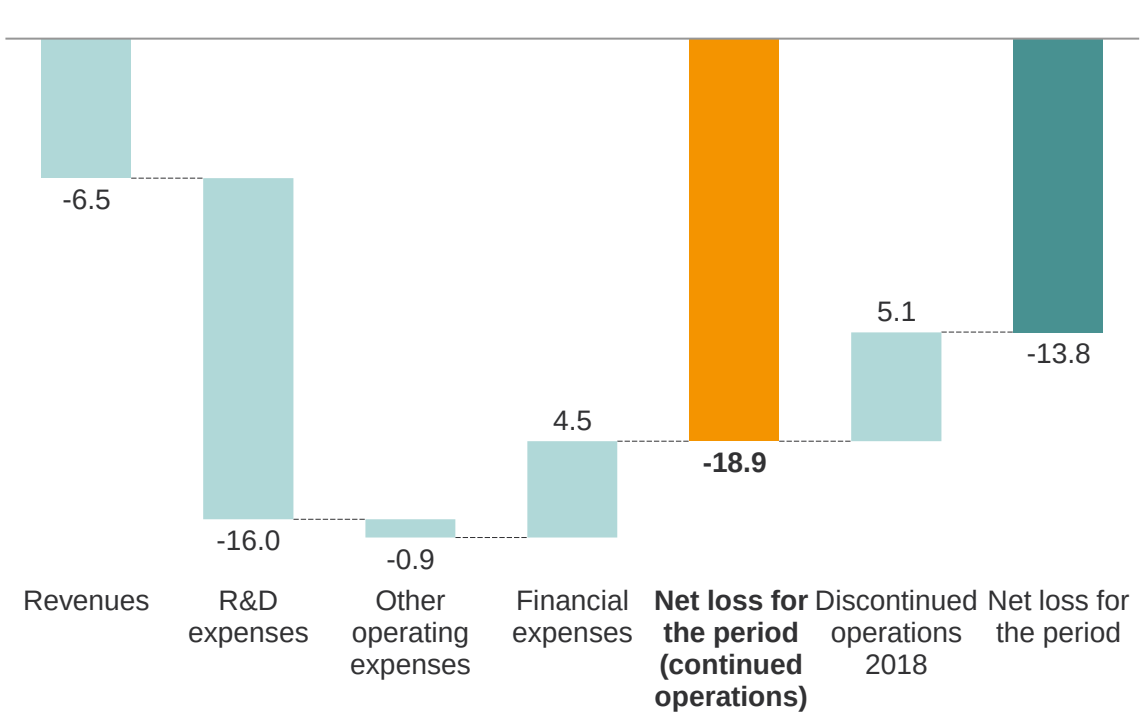
# Financial Highlights – Net loss

*In CHF million (based on consolidated IFRS financial statements)*

## Results 2019



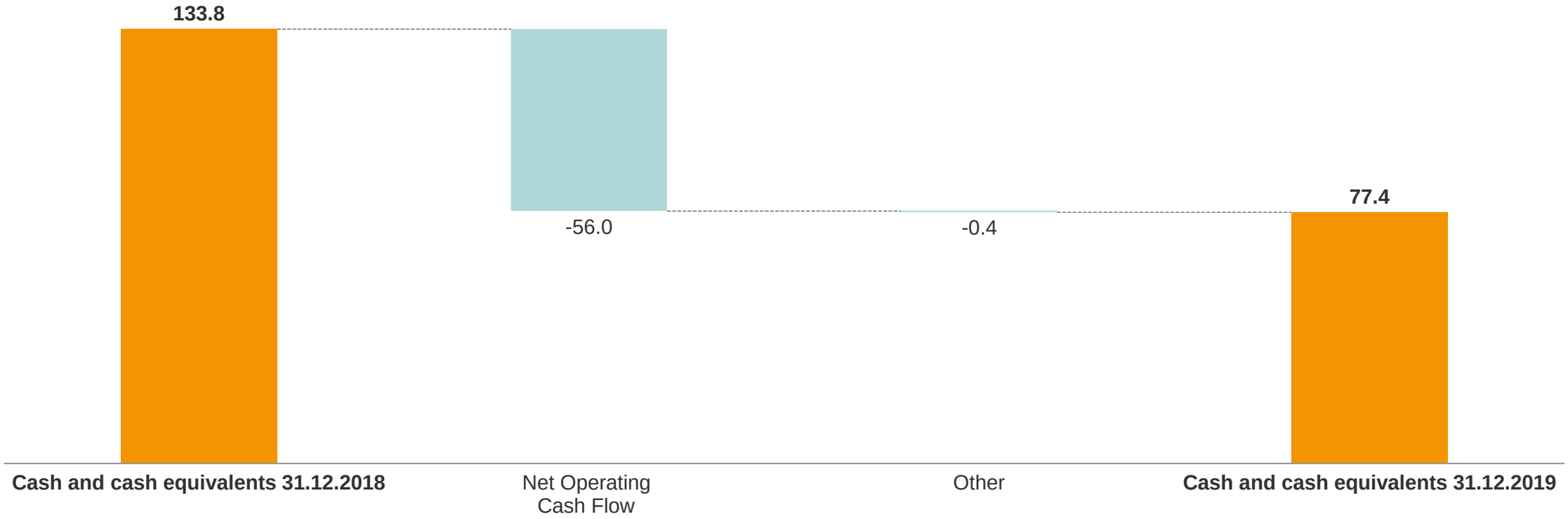

## Change vs 2018




- FY 2019 Net loss of CHF 64.7 million, within the range of guidance provided during our H1 2019 results conference call
- Overall expenses driven by R&D costs invested in our pipeline
- Increase in net loss driven versus 2018 driven by increase in R&D expenses, specifically wind-down of the Murepavadin pivotal trials, progress in Balixafortide Fortress Trial and further build-up of the pipeline
- Other operating expenses includes G&A (CHF -4.7m), M&S (CHF -1.4m) and other income for (CHF 1.9m)
- Revenues decreased by CHF 6.5 million from the last reporting period which included a licensing agreement with Santhera

# Financial highlights - Cash Flow

*In CHF million (based on consolidated IFRS financial statements)*



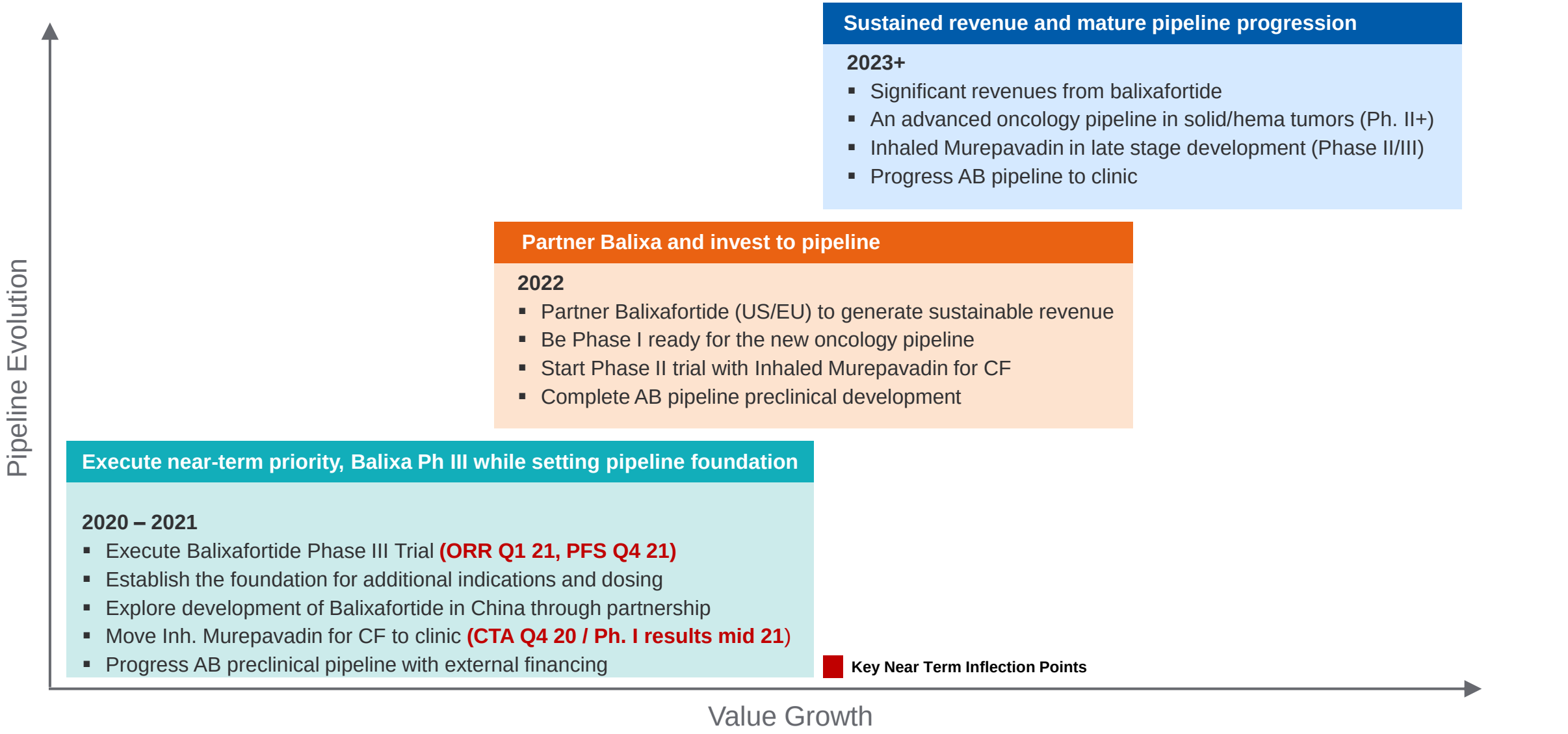

- Cash and cash equivalents at the end of 2019 were CHF 77.4 million.
- Cash was deployed to our operating activities, mainly driven by the closure of the PRISM and UDR trials for murepavadin I.V. and the initiation and execution of the FORTRESS trial for balixafortide
- Other includes proceeds form the disposal of financial investment (CHF +1.4m), net financing includes repayment of the loan on leasehold improvements and related interest (CHF -1.5m), and CHF -0.3m relates to the net effect of exchange rates movements.

# Guidance for 2020

- For 2020 we expect that operating expenses (excluding share-based payments and IAS 19 pension adjustments) to be in the range of CHF 61 - 64 million.
- Company’s operations funded into Q1/2021
- Continue to attract non-dilutive funding for antibiotics and explore partnering opportunities in oncology.
- Next AGM will be held on June 4$^{th}$ 2020

# Strategy to Expand Shareholder Value

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



# Summary

1 Despite a challenging 2019, Polyphor is committed in developing first-in-class molecules for oncology and antimicrobial resistance leveraging our innovative macrocyclic peptide platform.

2 Strong progress in 2020 executing near term priority and pipeline expansion plan in oncology and ABs

## Balixafortide

Phase III trial in metastatic breast cancer ahead of plan (69% enrolled) with positive first DSMB decision
First co-primary endpoint (ORR) data-cut expected in end Q1 2021
US$ 1.3B initial market potential with US$ 6-7B expanded potential

## Pipeline expansion plan in oncology

Planning to expand balixafortide into earlier mBCa indications, new tumors and combinations
Identify novel oncology development candidates from our macrocyclic platform following ORR results

## Antibiotics pipeline

Inhaled Murepavadin in Cystic Fibrosis P. aeruginosa infections: Phase I start planned for Q4 2020
Progress early AB programs, OMPTA BamA and Thanatin, largely with external financing given evolving landscape

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

# POLYPHOR

## Corporate Update and 2019 Financial Results

## **Q&A Session**

Gökhan Batur

Chief Executive Officer

Frank Weber, M.D.

Chief Medical & Development Officer

Hernan Levett

Chief Financial Officer