



**Ygalo - Targeted Alkylator for the Treatment of Myeloma** 

**JPM 2018** 

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# Oncopeptides is a phase 3 asset addressing a \$2bn+ market in myeloma

Phase 3 read-out mid 2019

Developing Ygalo: a nextgeneration broad spectrum agent for late stage RRMM

- Data so far supports superior efficacy over current standard of care in latestage myeloma
- First drug candidate is a PEnC class compound with an alkylating payload
- Overcomes resistance mechanisms that impact current therapies (IMiDs)

Significant and growing patient population

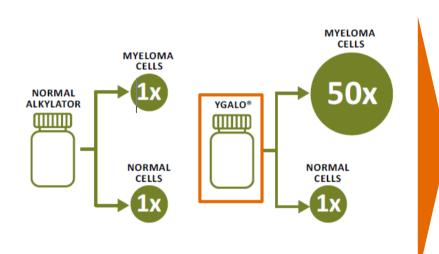
- Relapse is inevitable. New targeted therapies grow the market opportunity
- Prognosis is poor, with limited options available in late-stage disease
- Ygalo addressing a \$2bn+1 late-stage disease market with double digit % growth

Fully funded pivotal
Phase 3 trial underway;
broad development
program

- Agreement with FDA (SPA) and EMA on clinical trial design
- Orphan drug designation in EU and US
- Multiple paths to approval de-risk the development pathway
- New indications

# Phase 2 data supports superiority of Ygalo® over standard-ofcare in late-stage myeloma - a \$2bn+ USD market opportunity

Targeted broad spectrum mechanism underpins efficacy



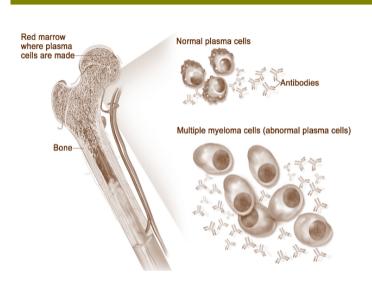
- >75% better Overall Survival (best survival data to date in late-stage myeloma)
- 30% better Progression Free Survival (by hazard ratio)
- 25%-35% better objective tumour response rates (ORR and CBR)
- Better tolerated by the patients

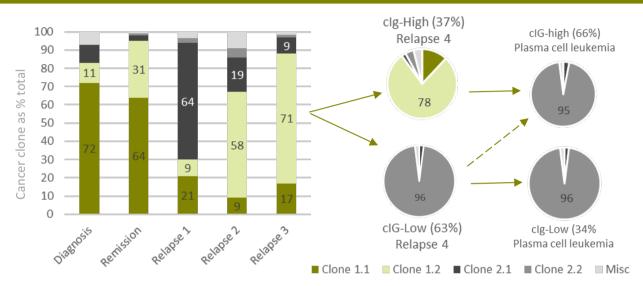
Phase 2 data: Comparison with data from patients that have not recently failed on lenalidomide

Strong foundation for Phase III program design where Ygalo® will be directly compared to current standard of care

## Multiple Myeloma is a hematologic cancer with no cure

## MM is a disease that is constantly evolving and becoming refractory / resistant to therapy is inevitable





## Broad Specturm agents are the bedrock of therapy

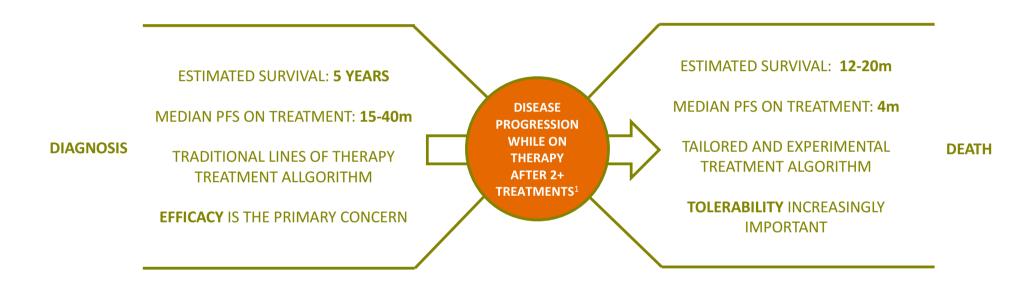
#### Myeloma Sales % US pts 2016 treated 2016 Pharmaceutical drugs Modality **Broad Spectrum Agents** Alylating agents Bendamustine, cyclophosphamide, melphalan **IMiDs** Revlimid, Pomalyst, thalidomide >10bn 93.9% **USD** Proteasome inhibitors Velcade, Kyprolis, Ninlaro Steroids Dexamethasone, prednisone **Targeted Agents** >0.7bn Anti-CD38 Darzalez 9.2% **USD** Anti-SLAMF7 **Empliciti**

### Late stage drugs limited: POM shares resistance with REV

Newly Relapsed / diagnosed Relapsed refractory	OCEAN HORIZON  Late-stage R/R
ASCT IF POSSIBLE (~45%) or COMBO THERAPY	2 COMBO THERAPY EXP. THERAPY
Reviimid "VELCADE" (bortezomib) ron ruerron	Pomalyst (pomalidomide)-upuss
Kyprolis. DARZALEX (daratumumab) (injection for intravenous inflation 10 mg/Set., 4.00 mg/20 mt.)	



There is one event that significantly changes the treatment/ prognosis in myeloma: Disease progression while on therapy (i.e. late-stage RRMM)



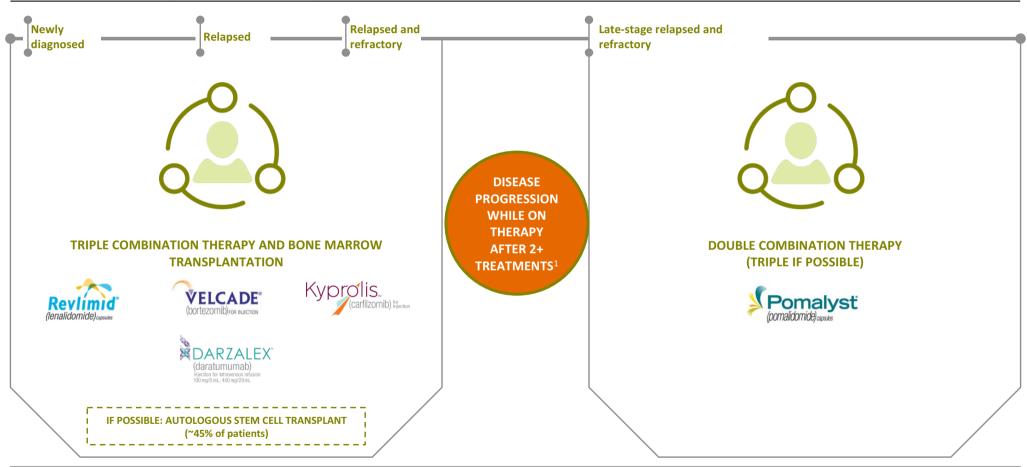
TIMING OF THE EVENT IS INDIVIDUAL

THE EVENT MEANS THE PATIENT HAS BECOME **MULTIRESISTANT** 

**CURRENTLY, 40,000 PATIENTS PER YEAR SUFFERS** FROM THE EVENT IN THE US AND EU-27

# There are limited number of treatment options for late-stage RRMM patients despite advances in treatment of early-stage MM

Lines of therapy throughout the disease stages<sup>1)</sup>



Limited number of treatment options for late-stage RRMM patients – Novel treatment options are necessary and demanded by patients and regulatory bodies

# Myeloma is primarily treated with single agents; lenalidomide and bortezomib are dominant (USA 2017)

Pomalidomide is the primary choice after lenalidomide and proteasome-inhibition failure

## Number of patients treated per 12m<sup>1</sup>

<u> </u>	
Lenalidomide	55,565
Bortezomib	52,289
Daratumumab	17,068
Carfilzomib	15,133
Pomalidomide	13,459
Ixazomib	10,843
Other	22,305
Total # of patients treated	132,829
	<u>"</u>

- Single agent treatment is by far the most common (combination treatment is only significant in the 1<sup>st</sup> line)
- Lenalidomide and proteasome inhibitors (Pis) are used in early in the treatment algorithm.
   Daratumumab is moving from last-line to 1<sup>st</sup> line/ 2<sup>nd</sup> line rapidly
- Pomalidomide is the primary choice after lenalidomide and PI failure (disease progression while on therapy)

## However, lenalidomide and pomalidomide originate from the same drug library...

Similar molecular structure from same library

LENALIDOMIDE

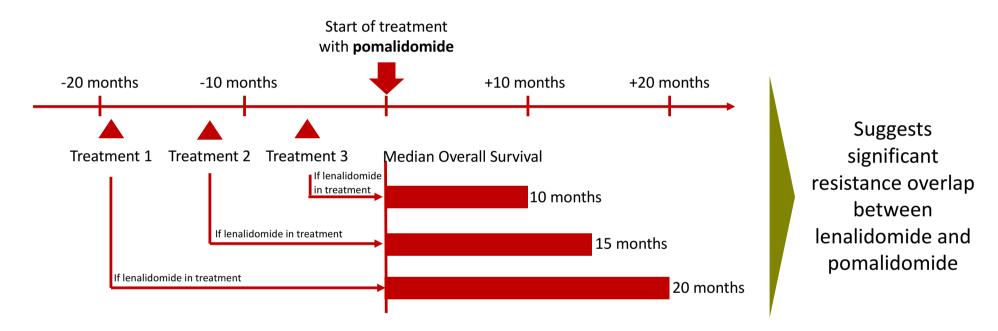
#### POMALIDOMIDE



Cross-resistance between lenalidomide and pomalidomide up for discussion based on pre-clinical data as well as FDA and EMA scrutiny of investigator reported clinical data

## ...and they seemlingy share resistance mechanism to a significant extent (ASH 2016)

## Dimopoulos research supporting an IMiD free period



# Phase 2 data supports superiority of Ygalo® over standardof-care in late-stage myeloma patients



TREATMENT	ORR	CBR	MEDIAN PFS	MEDIAN DOR	MEDIAN OS
Pomalidomide + dexamethasone	24%	NR	3.6 months	7.0 months	12.4 months
Ygalo® + dexamethasone	31%	49%	5.7 months	8.8 months	20.7 months

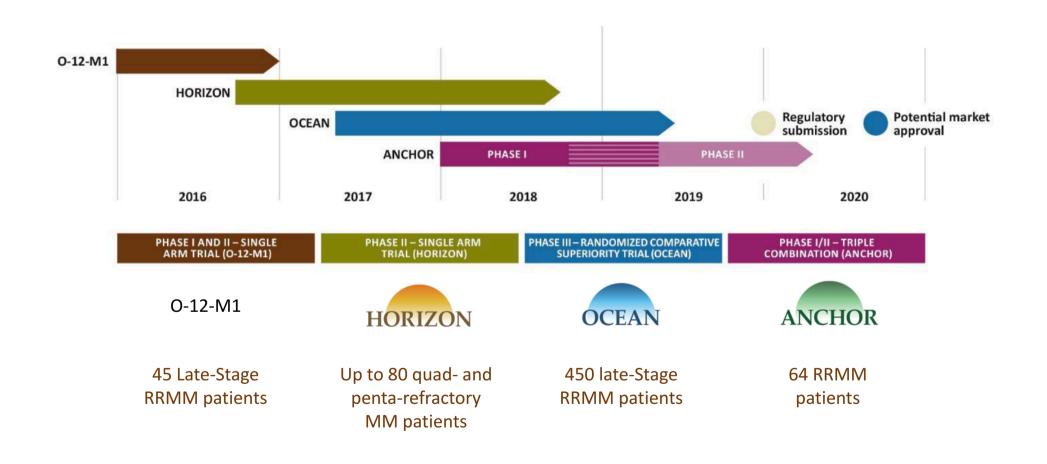
Note: NR=Not Reported. Ygalo® is not market approved.

Source: FDA Label

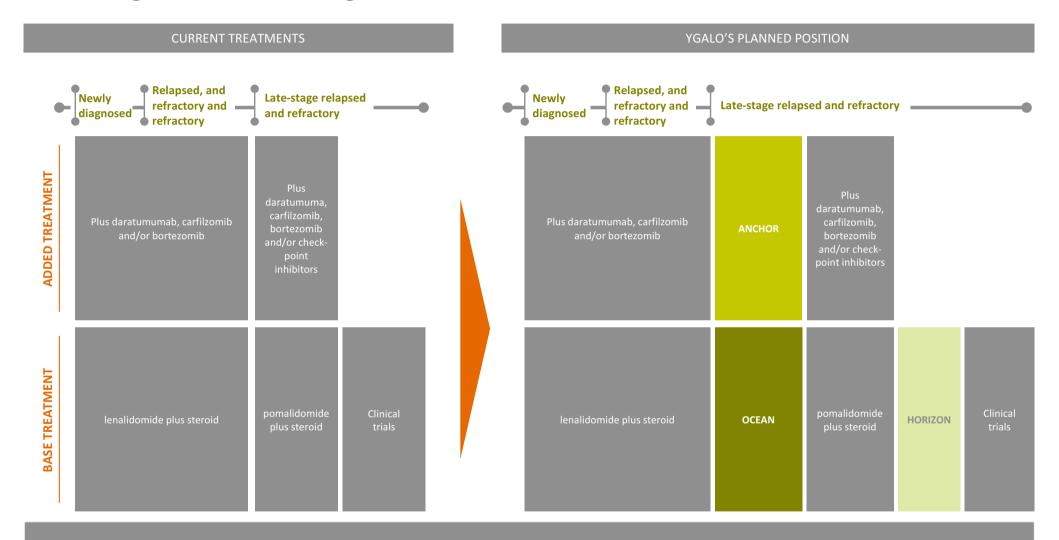
- >75% better Overall Survival (best survival data to date in late-stage myeloma)
- 30% better Progression Free Survival (by hazard ratio)
- 25%-35% better objective tumour response rates (ORR and CBR)
- Better tolerated by the patients

However, the cross-resistance between pomalidomide and lenalidomide puts pomalidomide at a disadvatnage in the real-world setting (see OCEAN trial design)

# Overview of Clinical Development Program in late-stage multiple myeloma



## Clinical development program provides a complete data set to show how to use Ygalo<sup>®</sup> in late-stage RRMM



Full characterization of Ygalo<sup>®</sup> as a complement in late-stage RRMM will help increase physicians willingness to prescribe

## Summary rationale for phase III program

- Ygalo has showed best-in-class efficacy with excellent tolerability in late-stage RRMM patients
- Phase III study is 90% powered to show superiority of Ygalo in late-stage RRMM comparing the phase II data of Ygalo with pomalidomides phase III data (MM-003)
- However, patients have been pre-treated with close to 10x as much lenalidomide today compared to when MM-003 was conducted
- Studies show that pomalidomide loses as much as 50% efficacy in patients that have received lenalidomide recently (i.e. when the tumor has recently learned how to grow in a lenalidomide rich environment)
- In OCEAN, all patients have been treated with, and progressed on, lenalidomide in their last line of therapy prior to study inclusion

## Clinical development program fully characterizes Ygalo<sup>®</sup> in myeloma De-risked development program with multiple paths to market approval

#### **Quad- and Penta-Refractory**



TREATMENT	ORR	CBR	MEDIAN PFS	MEDIAN DOR	MEDIAN OS
Selinexor + dexamethasone	21%	32%	2.1 months	5.0 months	9.3 months

Note: Selinexor is not market approved. Source: Blood 2016 128:491:

#### Late-Stage Relapsed Refractory



TREATMENT	ORR	CBR	MEDIAN PFS	MEDIAN DOR	MEDIAN OS
Pomalidomide + dexamethasone	24%	NR	3.6 months	7.0 months	12.4 months
Carfilzomib	23%	37%	3.7 months	7.8 months	15.6 months
Daratumumab	29%	34%	3.7 months	7.4 months	17.5 months
Ygalo® + dexamethasone	31%	49%	5.7 months	8.8 months	20.7 months

Note: NR=Not Reported, Ygalo® is not market approved Source: FDA Label

#### Relapsed and Relapsed Refractory

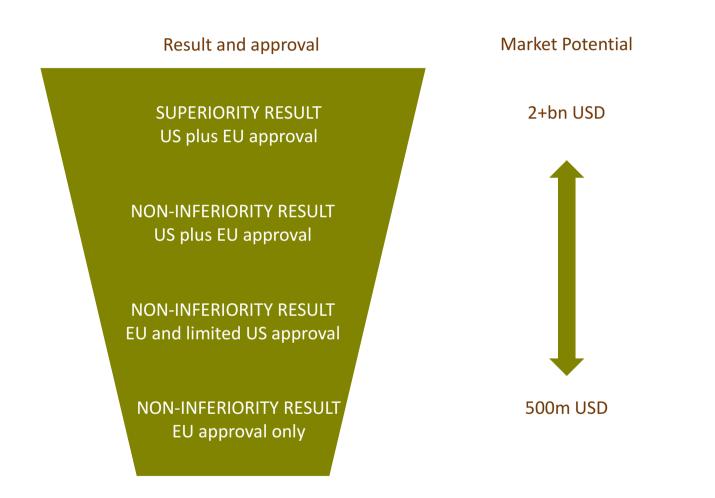


TREATMENT	ORR	MEDIAN PFS	MEDIAN DOR
Carfilzomib + lenalidomide + dexamethasone	87%	26.3 months	28.6 months
Lenalidomide + dexamethasone	67%	17.6 months	21.2 months

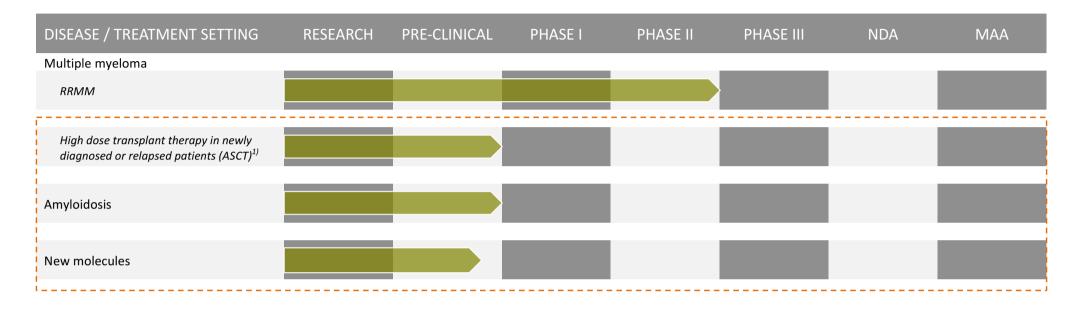
Note: Representative examples of recent clinical trials (triple and double combination therapy) Source: FDA Label.

- Patients who have failed other therapies
- Single- arm Phase 2 trial ongoing
- Supports OCEAN to receive market approval
- If data exceptionally convincing, potential for conditional marketing authorization
- Data due mid 2018
- Patients refractory to lenalidomide
- Phase III trial ongoing
- Superiority study vs. pomalidomide (noninferiority outcome results at least in market approval in the EU)
- Topline data due Q3 2019
- Evaluating potential for earlier line use in combination with other agents
- Phase 1/2 trial ongoing
- Could significantly expand market opportunity
- Data due 2019 (basic study) and 2020 (expansion cohorts)

## Clinical development program design enables multiple paths to approval with different labels



## Additional upside potential in pipeline – indication broadening as well as **NMEs**



## Expected news flow until regulatory submission

#### **CLINICAL DEVELOPMENT PROGRAM**

- Q1 2018: First patient in ANCHOR
- H2 2017: Patient enrollment rate OCEAN and ANCHOR
- During 2018: Patient enrollment rate OCEAN and ANCHOR
- Q2/Q3 2018: Last patient out HORIZON
- H1 2019: Last patient out OCEAN
- Summer 2019: Top-line data OCEAN
- H1 2020: Last patient out ANCHOR

#### **COMPANY RELATED**

H1 2018: Presentation of commercialization strategy

#### CONFERENCES WERE DATA COULD BE PRESENTED

- Dec 2017: American Society of Hematology (ASH)
- Jun 2018: European Hematology Association (EHA)
- Jun 2018: American Society of Clinical Oncology (ASCO)
- Dec 2018: American Society of Hematology (ASH)
- Jun 2019: American Society of Clinical Oncology (ASCO)
- Jun 2019: European Hematology Association (EHA)









## **Corporate Information**

## **Management Team**

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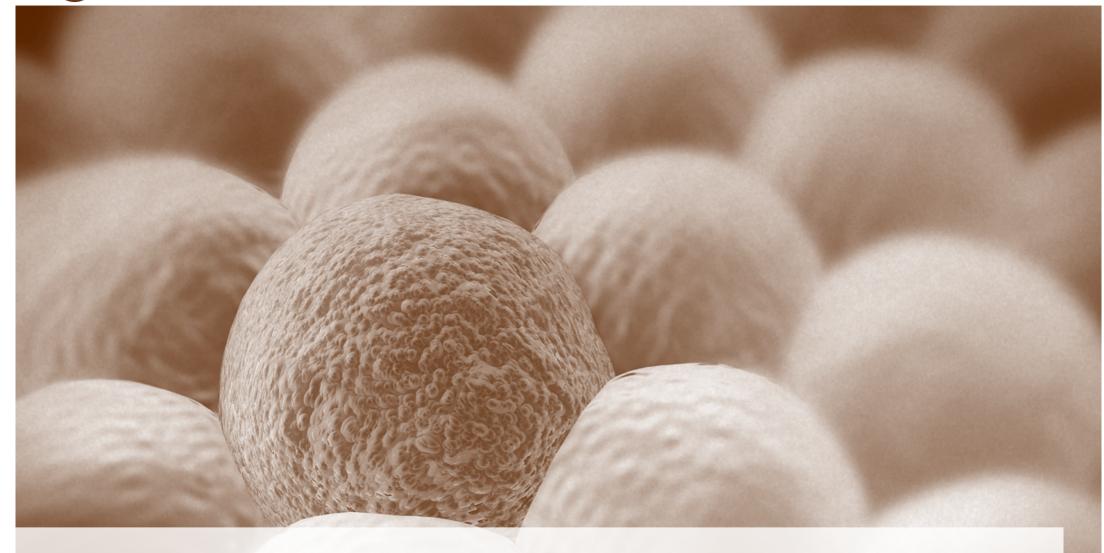
Ticker: ONCO (Stockholm) ISIN: SE0009414576

Analysts: ABG Sundal Collier, Carnegie Investment Bank, DNB

markets

## Contact

Rein Piir, Head IR Rein.piir@oncopeptides.se

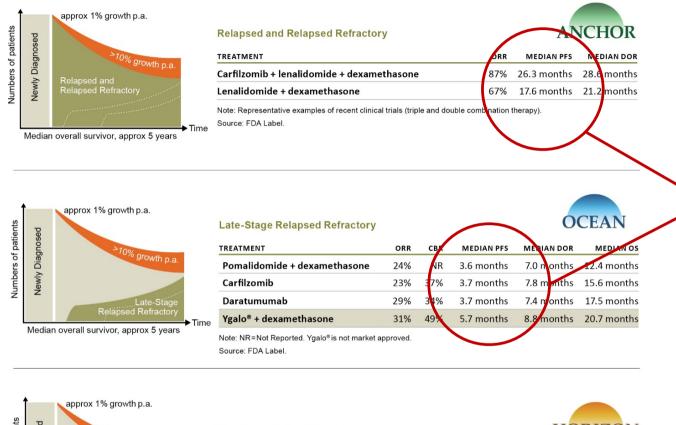


Thank you for your time

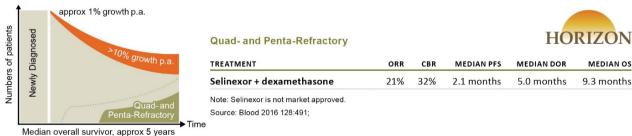
# **APPENDIX**

# **MULTIPLE MYELOMA**

## The medical need in treatment resistant patients is significant and growing



Significant reduction in efficacy after resistance development



## Different treatment modalities complement each other in myeloma care – but there is no cure

**Broad-spectrum Agents** (alkylators, PIs, IMiDs and HDAC inh.)

> **Targeted Agents** (CD38, BCMA, SLAM7)

> > **CAR-Ts**

- Back-bone in myeloma treatment
- Necessary treatment modality given heterogeneity of disease
- Resistance development is not on/off
- No (or limited) resistance pattern overlap with broadspectrum agents
- Single mutation resistance development
- Lack of good antigens in myeloma
- Best results together with broad-spectrum agents
- Lack of good antigens create limitations
- Good data in heavily pre-selected patients, but not better than antibody based therapies

# **YGALO**

# Ygalo<sup>®</sup> is a peptidase enhanced cytotoxic (PEnC) with an alkylating payload

1. Amino-peptidases highly over expressed in multiple myeloma (MM) cells 5. Melflufen and hydrophilic alkylating moieties binds directly to DNA 2. Lipophilic melflufen rapidly traverses cell membranes 4. Hydrophilic alkylating moieties trapped 3. Amino-peptidase potentiated inside the cell release of hydrophilic alkylating moieties

# Peptidase enhanced activity in MM cells results in:

- Approx. 50-fold higher intra-cellular exposure in MM cells<sup>1,5</sup>
- Approx. 50-fold higher anti-MM potency<sup>1,2,5</sup>
- Alkylation of DNA with limited or no induction of DNA repair<sup>3,5</sup>
- Strong anti-angiogenic properties 1,4,5
- Increase in therapeutic index of 20x 40x (MM cells compared with peripheral blood mononuclear cells)<sup>1,5</sup>



- 1. Chauhan et al. (2013) Clin Cancer Res 19(11): 3019-303.
- 2. Wickstrom et al. (2008) Invest New Drugs 26(3): 195-204.
- Ray et al. (2016) Br J Hematol 174: 397-409

- Strese et al. (2013) Biochem Pharmacol 86: 888–895.
- . Wickström et al. (2017) Oncotarget E-pub June 08.



# **CLINICAL DATA - YGALO**



## Melflufen is a targeted alkylator challenging the treatment paradigm in RRMM

Where: Omni Atlanta at CNN Center (Pecan Room/Foyer) 100 CNN Center, Atlanta, GA 30303

When: Sunday, December 10, 2017

Reception 8:00 - 8:30 PM and Scientific Program 8:30 -10:00 PM

By Invitation Only

Speakers: O-12-M1 - Long-term follow-up from phase-2 data and reflections around the role of

melflufen in multiple myeloma

Paul Richardson, MD

RJ Corman Professor of Medicine Harvard Medical School, Clinical Program Leader and Director of Clinical Research Jerome Lipper Multiple Myeloma Center Dana-Farber Cancer Institute Boston, Massachusetts

Horizon - Initial activity of melflufen after pomalidamide and daratumumab failure

María-Victoria Mateos, MD

Associate Professor of Medicine and Consultant Physician in the Hematology Department of the University Hospital

of Salamanca, Salamanca, Spain

Host: Bengt Gustavsson Dr Med Sci, MSc Pharm,

Medical Relations, Oncopeptides AB, Stockholm, Sweden



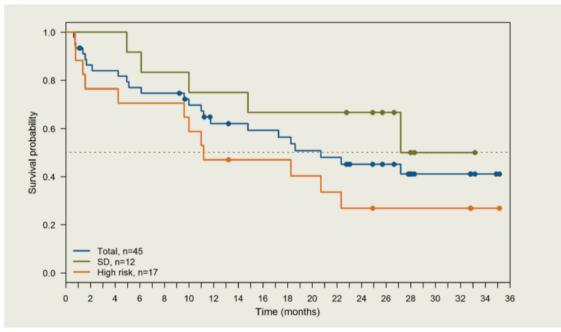




## Best-in-class survival data from Ygalo® in phase II in late-stage RRMM

Ygalo® has pronounced efficacy of its own and facilitates for further treatment following progression

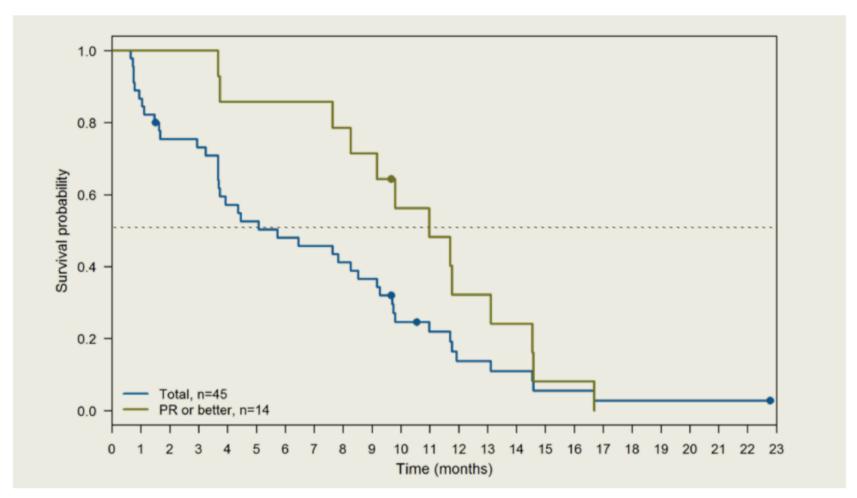
Figure 2. Overall survival



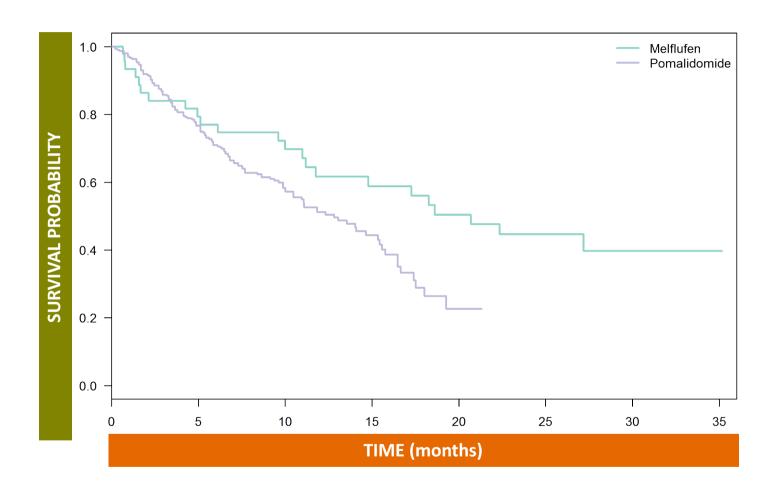
- Best-in-class survival data in late-stage RRMM
- Best PFS to date for a broad-spectrum agent in late-stage RRMM
- Tolerability profile very favorable with patients experiencing comparatively few side-effects that are detrimental to QoL (which in a palliative care setting with elderly patients is key)

# Best Progression Free Survival data from any broad-spectrum agent in late-stage RRMM

Data from O-12-M1 (Ygalo® + dex)



# Efficacy comparison between O-12-M1 (Ygalo®/melflufen + dex) and MM-003 (pomalidomide + dex) - Overall Survival



## Promising efficacy signal and excellent tolerability in patients with no remaining treatment options

## Interim data from HORIZON

Table 5. Overall response rate (N=30)

N	PD	SD	MR	PR	VGPR	ORR	CBR
Adjusted ITT, n (%)	11 (37)	9 (30)	2 (7)	6 (20)	2 (7)	26.7%	33.3%

Figure 1. Waterfall plot (N=30)

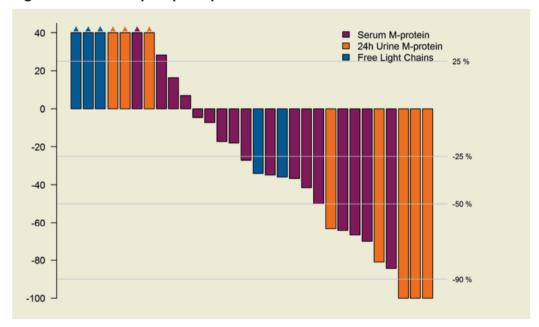
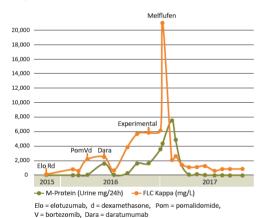


Table 6. Treatment-related G3/4 AEs occurring in ≥ 5% of the patients (N=38)

	GRADE 3 OR 4, n (%)	GRADE 4, n (%)
Any treatment-related AE	22 (58)	15 (39)
Blood and lymphatic system disorders	20 (53)	14 (37)
Thrombocytopenia	17 (45)	12 (32)
Neutropenia	15 (39)	9 (24)
Leukopenia	3 (8)	3 (8)
Anemia	8 (21)	0
Lymphopenia	3 (8)	0
Hemolytic anemia	2 (5)	0

Figure 2. Patient case study



42-year old man with ISS stage 3, MM diagnosed 2007. No detectable serum M-protein. Nine prior lines of therapy including ASCT X 2 and Allo-SCT. Refractory to R, Elo, V, Pom, Dara and an experimental drug. The patient only achieved PD to the last 4 lines of therapy.

Following 5 cycles of melflufen, the urinary M-protein was undetectable (Figure 2). The patient has received 9 cycles of melflufen, achieved VGPR and is ongoing as of Nov 2017.

# CLINICAL DEVELOPMENT PROGRAM

# Key Opinion Leaders and regulatory interactions provides strong foundation for planned pivotal development program

KOL network consisting of leading oncologists within the field of MM

#### SELECTION OF ONCOPEPTIDES CLINICAL ADVISORS AND INVESTIGATORS



#### Prof. Paul Richardson – Dana-Farber Cancer Institute, Harvard, USA

- Clinical program leader and Director of Clinical Research at Jerome Lipper Multiple Myeloma Center (Dana-Farber Cancer Institute)
- Lead clinical investigator for bortezomib
- Lead clinical investigator for pomalidomide





### Prof. Pieter Sonneveld - Erasmus University, Netherlands

- Professor and Head of Hematology at Erasmus University
- President-elect European Hematology Association
- Founder European Hematology Network
- Scientific advisory member for International Myeloma Foundation, International Myeloma Working Group and International myeloma Society

### Several regulatory interactions with meaningful authorities

#### FOOD AND DRUG ADMINISTRATION

Nov-12: Pre-IND type B meeting

Jan-13: IND application

Feb-13: IND approved

Mar-15: Orphan Drug Designation granted

Jun-15: Scientific Advice type C meeting

**Dec-15:** Scientific Advice type C meeting

**Apr-16:** Scientific Advice type C meeting

Jun-16: End of Phase II meeting

Jul-16: Application for exemption to conduct pediatric development under Pediatric Research

**Equity Act** 

Aug-16: Special Protocol Assessment Agreement Letter

#### KEY OPINION LEADERS WORKSHOPS

Jan-12: Boston, US

Dec-13: New Orleans, US

Jun-14: Stockholm, SE

Dec-14: San Francisco, US

Jan-15 to May-15: Individual Scientific Advice meetings with KOLs in EU and US

Sep-15: Rome, Italy

Dec-15: Orlando, US

### NATIONAL AUTHORITIES (MHRA & SMPA)

May-04: Scientific Advice meeting with Swedish MPA

Feb-06: First phase I study application granted by Swedish MPA

Jan-13 to Dec-13: Permission granted to conduct clinical trials in DK, NL and IT

Apr-13: Phase I/II study application granted by Swedish MPA

May-14: Scientific Advice meeting with Swedish MPA

Mar-15: EU Orphan Drug Designation granted by COMP / EMA

Apr-15 to Nov-15: Several Scientific Advice meetings with Swedish MPA

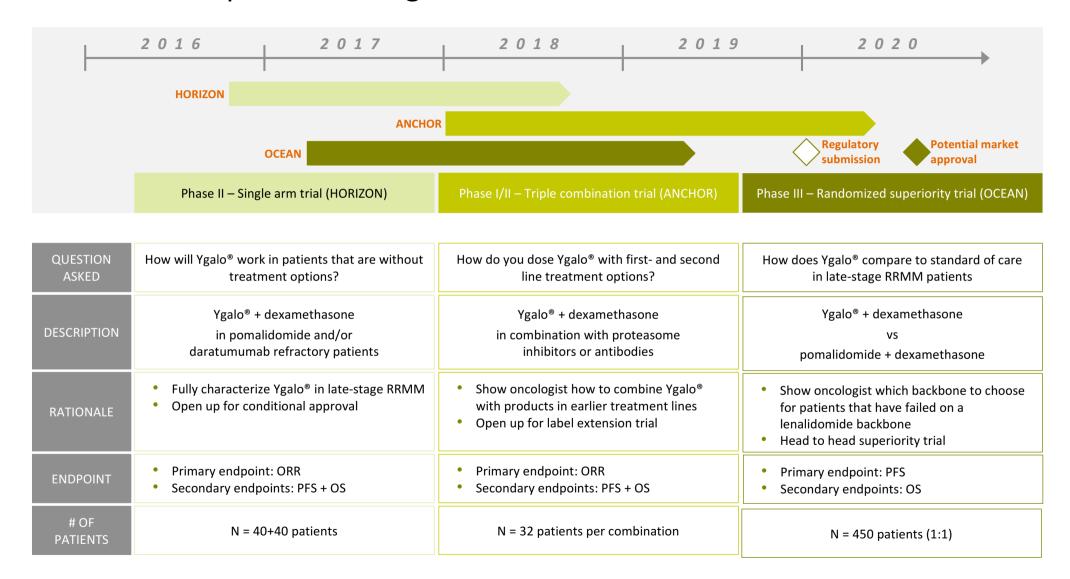
Mar-16: MHRA (British Medicines and Healthcare Products Regulatory Agency) gives positive feedback on design of phase III study





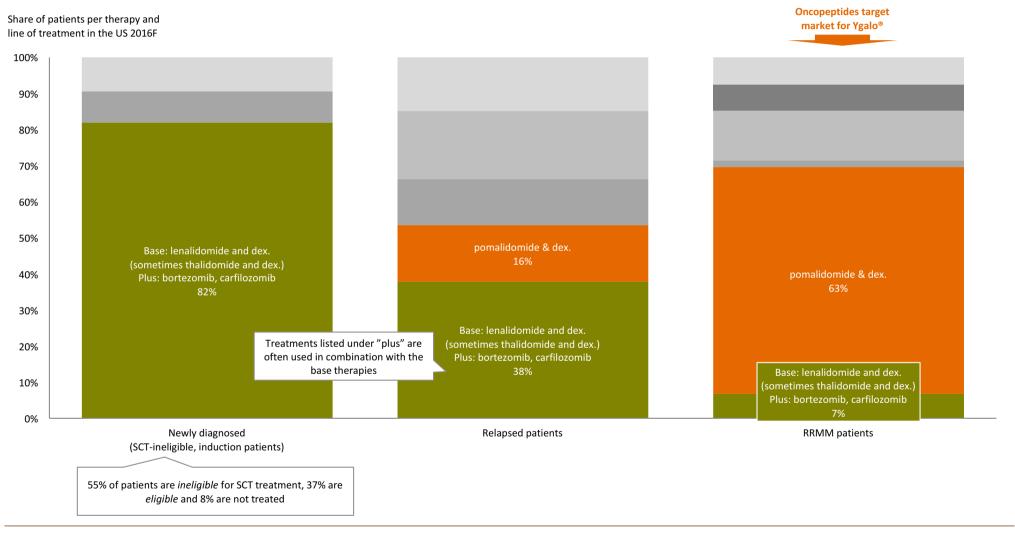
LÄKEMEDELSVERKET

## Regulatory approved and de-risked development program to characterize and maximize potential of Ygalo®



# However, 'continuous IMiD backbone' is standard of care – lenalidomide in newly diagnosed patients and pomalidomide in late-stage patients

Simplified overview of treatments used in different phases of multiple myeloma excluding stem cell transplantation





## CLINICAL DATA – NEW COMPOUNDS

## ASH 2017: BCMA clinically verified as a good target in myeloma

Study	NIH	Celgene/BB	Celgene/BB	Celgene/BB	Uni. Of Pen	Soochow Uni.	GSK
Source	ASH 2016	ASH 2016	ASCO 2017	ASH 2017	ASH 2017	ASH 2017	ASH 2017
Target	BCMA (CAR-T)	BCMA (CAR-T)	BCMA (CAR-T)	BCMA (CAR-T)	BCMA (CAR-T)	BCMA + CD19 (dual CAR-Ts)	BCMA ADCC
Patient Selection (% of total myeloma population)	50%	20-25%	20-25%	20-25%	50%	20-25%	100%
# of patients	16	6*	20*	20*	24	10	35
ORR	50%	100%	<b>7</b> 5%	85%	47%	80%	60%
Median PFS	<4 months	NA	4+ months	Est. at 11-12 months**	Roughly 4 months	Roughly 4 months	8 months

**Comment:** BCMA clinically verified as a good target in myeloma (still no cure). Currently no positive differentiating factor in terms of efficacy for CAR-T over antibody based BCMA therapies, meaning that BCMA CAR-Ts will struggle due to added cost, toxicity and overall complexity



<sup>\*</sup> Only what Celgene/BB considers as the right doses used in the comparison, i.e. the dose range that they state will be used in future studies

<sup>\*\*</sup> Estimated – median not reached after 9 months (61% without progression in ITT population)