

## Nomenclature

### International non-proprietary name (INN)

Melphalan flufenamide

### Chemical name

4-[Bis-(2-chloroethyl)amino]-L-Phenylalanine-4-fluoro-L-phenylalanine ethyl ester hydrochloride

### Laboratory codes

Melflufen hydrochloride

J1

CK 1535

### CAS No.

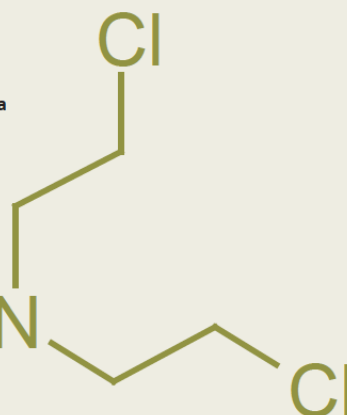
380449-54-7 (HCl salt)

380449-51-4 (free base)

## Structure

### Structural formula

Figure 1-1 Structural formula of melflufen hydrochloride



### Molecular formula

C<sub>24</sub>H<sub>31</sub>Cl<sub>3</sub>N<sub>3</sub>O<sub>3</sub> (HCl salt)

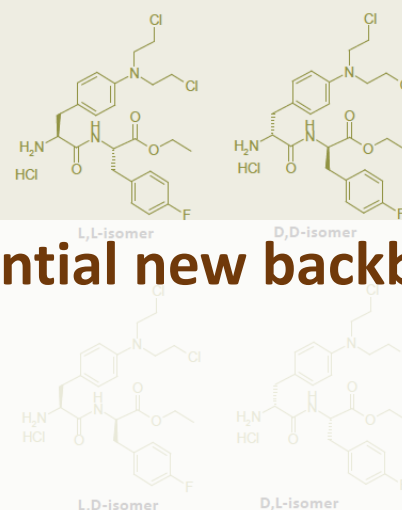
### Molecular weight

534.9 (HCl Salt)

### Stereochemistry

Melflufen hydrochloride contains two stereogenic centers giving rise to four possible stereoisomers. Melflufen hydrochloride drug substance is the L,L-isomer. The structures are outlined in Figure 1-2.

Figure 1-2 Structure of melflufen hydrochloride isomer



## General properties

### Appearance

White to slightly yellowish powder

### Solubility

Melflufen hydrochloride is soluble in most organic solvents. The solubility in water and buffers is limited.

### Partition coefficient

ClogP = 4.04 (tecken) 0.66, calculated using ACD logP DB, v.6.0 (from Advanced Chemistry Development)

### Dissociation constant

pKa 10.0 (determined in ethanol solution)

### Optical rotation

[α]<sub>D</sub> 5.2° (c 1.9, CH<sub>3</sub>OH) at 20°C

### Thermal behaviour

Differential scanning calorimetry (DSC) was performed using a Mettler Toledo DSC 822 instrument and a scanning rate of 2(tecken)C/minute. The melting temperature was measured using batch

GF404528 and determined from the DSC thermogram (see Figure 1-3).

# Melflufen (Ygalo®) - A first in class potential new backbone for multiple myeloma

## Corporate Presentation December 2018

## Jakob Lindberg CEO

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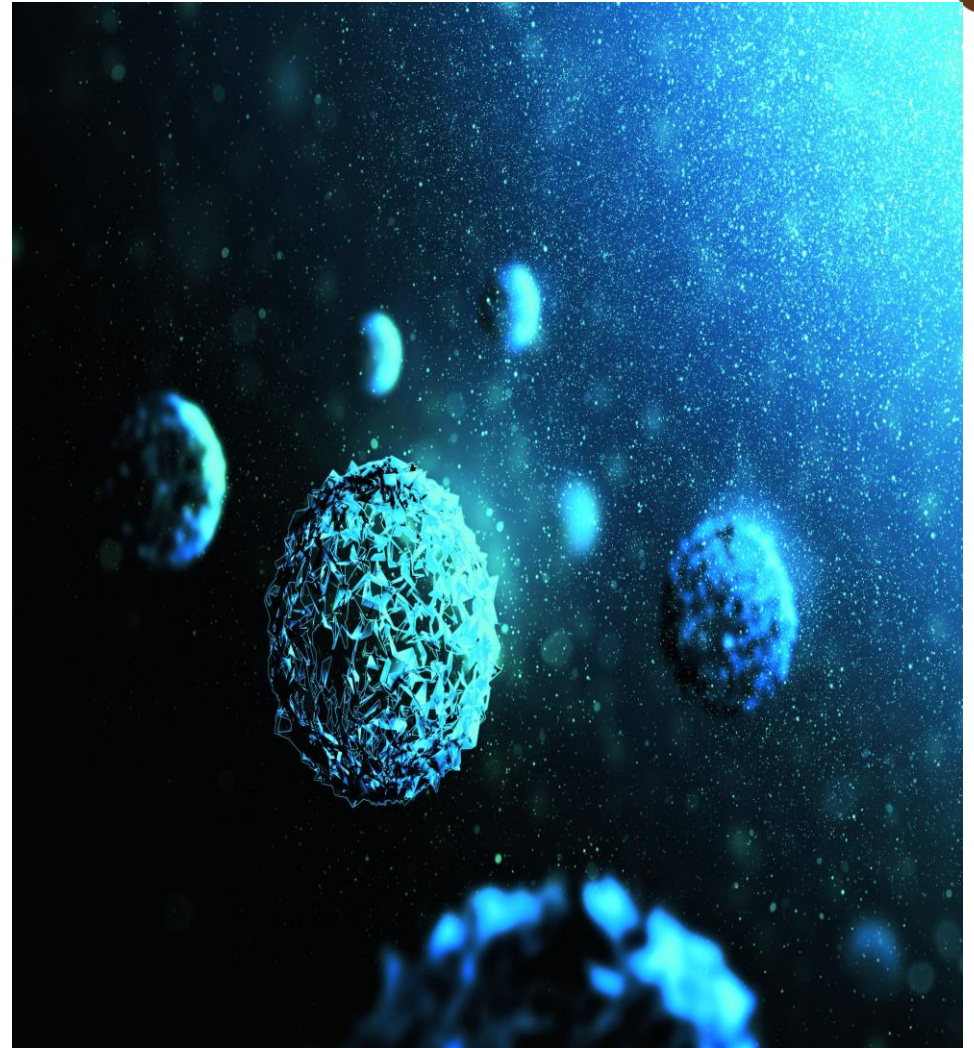
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# Oncopeptides overview

Ongoing Phase 3 program addressing a \$8bn+ market opportunity in myeloma

- **Develops targeted cancer treatments**
  - Proprietary peptidase-enhanced compounds
  - Lead compound Melflufen a peptide conjugated alkylator for Multiple Myeloma
- **Significant unmet needs in Multiple Myeloma**
  - Melflufen Phase 2 showed the best MM survival data to date
- **Melflufen Phase 3 readout expected in Q3 2019**
  - Pivotal program running at 140 sites
  - Three additional supporting trials ongoing
- **Based in Sweden, listed on NASDAQ Stockholm**
  - Market cap: approximately 825 MUSD
  - Cash position Sep. 30, 2018: 54 MUSD
- **New indications and NCEs in development**
  - Clinical trials expected to start in 2019



# Melflufen (Ygalo®) - Potential new backbone agent in multiple myeloma

Phase III read-out Q3 2019

**Significant unmet need for novel backbone agent**

- Relapse in multiple myeloma inevitable despite approval of novel agents
- Treatment paradigm evolving rapidly – resistance and tolerability remain key challenges
- 9 out of 10 patients receive broad spectrum (“backbone”) agents (IMiDs/PIs/Alkylators)
- Majority of patients receive single agent (+/- steroid) treatments after 1L
- Once refractory, prognosis is poor, with limited options (pomalidomide de facto SoC)

**Melflufen (Ygalo®):  
With a novel mechanism of action**

- Melflufen is an alkylating peptide developed with Oncopeptides proprietary Peptidase Enhanced Cytotoxic (PEnC) platform
- Highly selective for transformed cells, with significant increase in therapeutic index
- 50+x activity increase in transformed cells with no increase against PBMCs
- Does not share resistance mechanisms with other classes of agents including alkylators

**Best-in-class efficacy seen in Phase 2**

- Phase 2 demonstrated the best overall survival data to date in late-stage myeloma
- Well tolerated with limited adverse events negatively impacting patient quality of life
- Bone pain improvement seen in first-cycle of treatment
- Data provides high level conviction for success in Phase 3 OCEAN head-to-head comparison with polamidomide

**Ygalo well positioned to address \$8bn+ market opportunity**

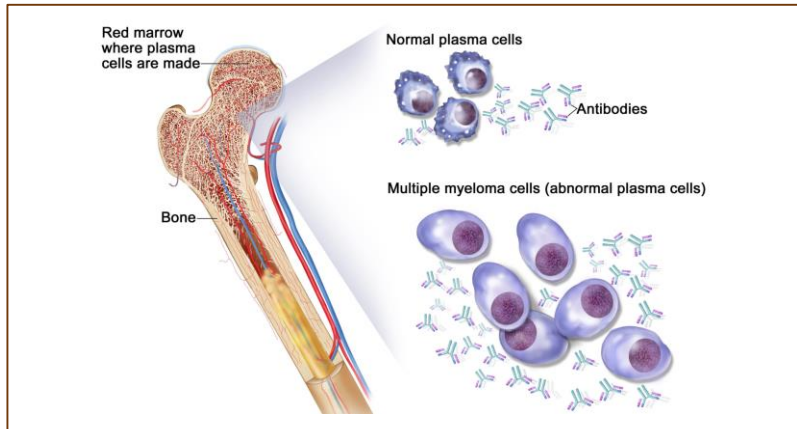
- Melflufen (Ygalo®) addresses \$8bn+ market opportunity with double digit % growth
- Agreement with FDA (SPA) and EMA on P3 clinical trial design
- Orphan drug designation in EU and US
- Multiple paths to approval de-risk the development pathway
- Good activity signal in a broad range of oncology indications

# Almost all multiple myeloma patients receive broad spectrum agents

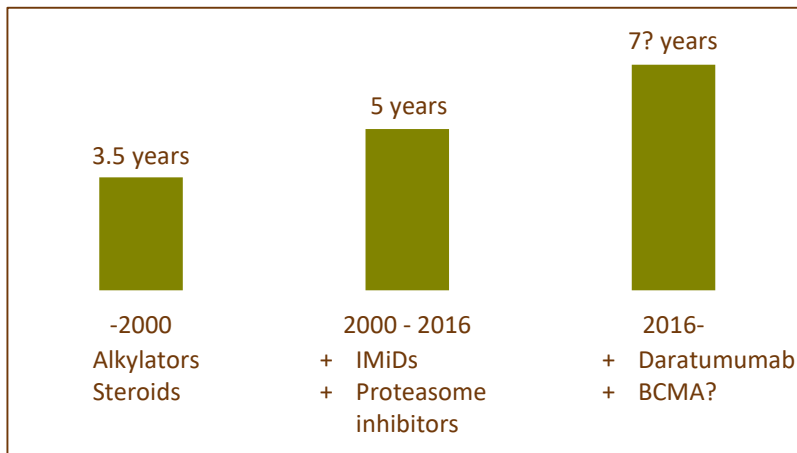
Treatment paradigm rapidly evolving with increased use of backbone agents



## Myeloma – Uncontrolled plasma cell proliferation



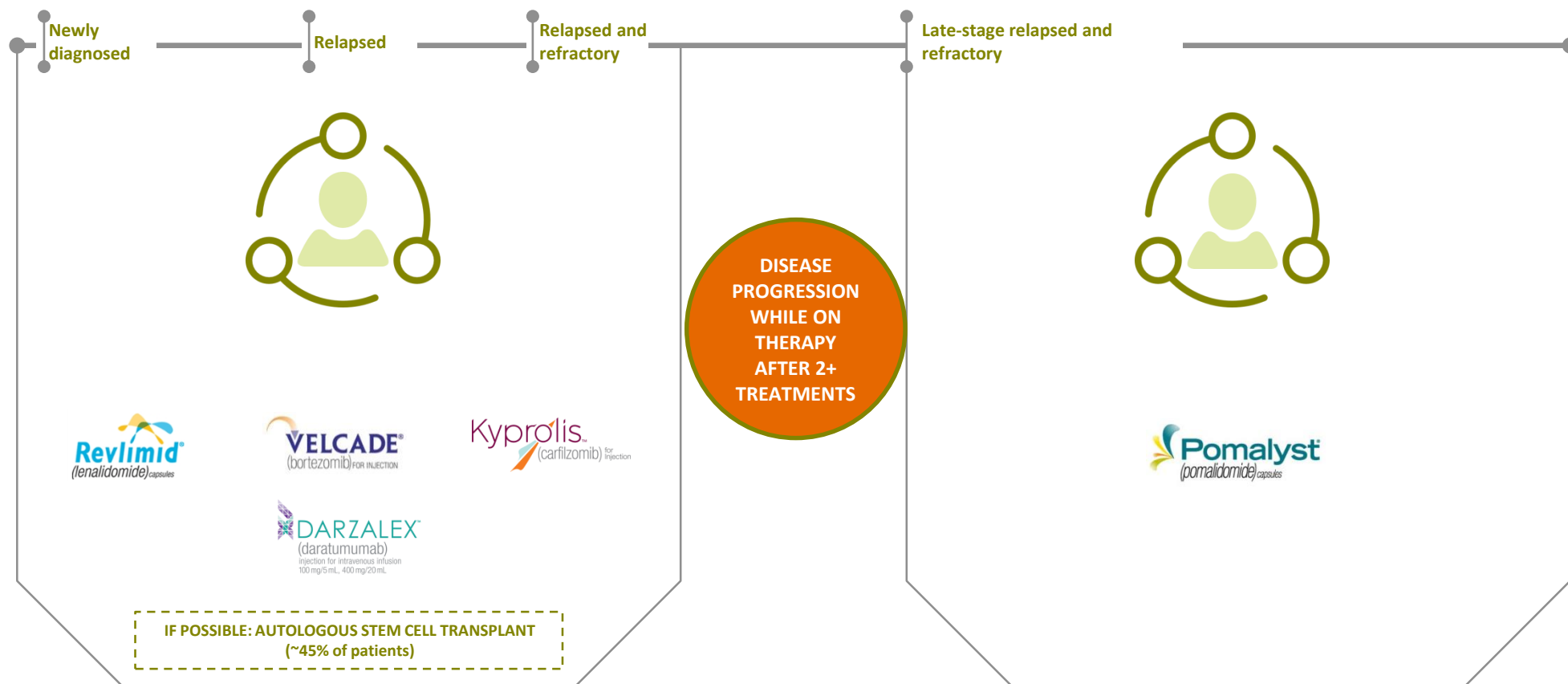
## Median Survival increasing with more available treatment options



- Overall survival increasing but clonal selection results in inevitable relapse and treatment resistance
- 9 out of 10 patients receive broad spectrum agents (IMiDs, PIs and/or alkylators)
  - No ubiquitously expressed antigens in myeloma
  - Antibody-based therapies used in combination with IMiDs, PIs and alkylators
- New targeted agents are growing the patient population
  - 4th+ line patients receiving treatment in the US grew by >40% in 2017
- Rapidly shifting treatment landscape
  - Lenalidomide and proteasome inhibitors are used early in the treatment algorithm
  - Daratumumab is moving from last-line to 1st line/ 2nd line rapidly

# Late-stage myeloma patients are well defined from both a regulatory and clinical point of view

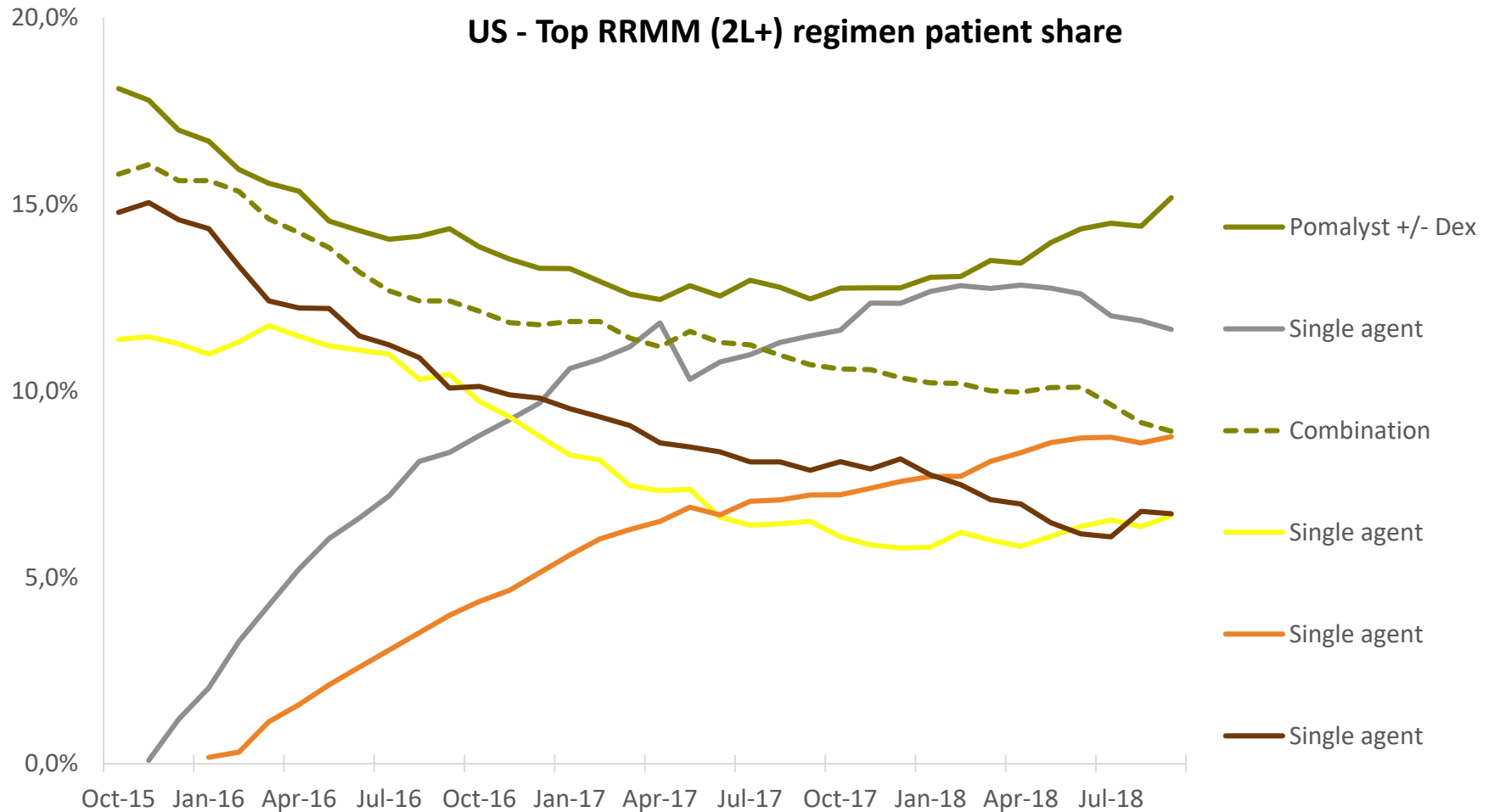
Lines of therapy throughout the disease stages



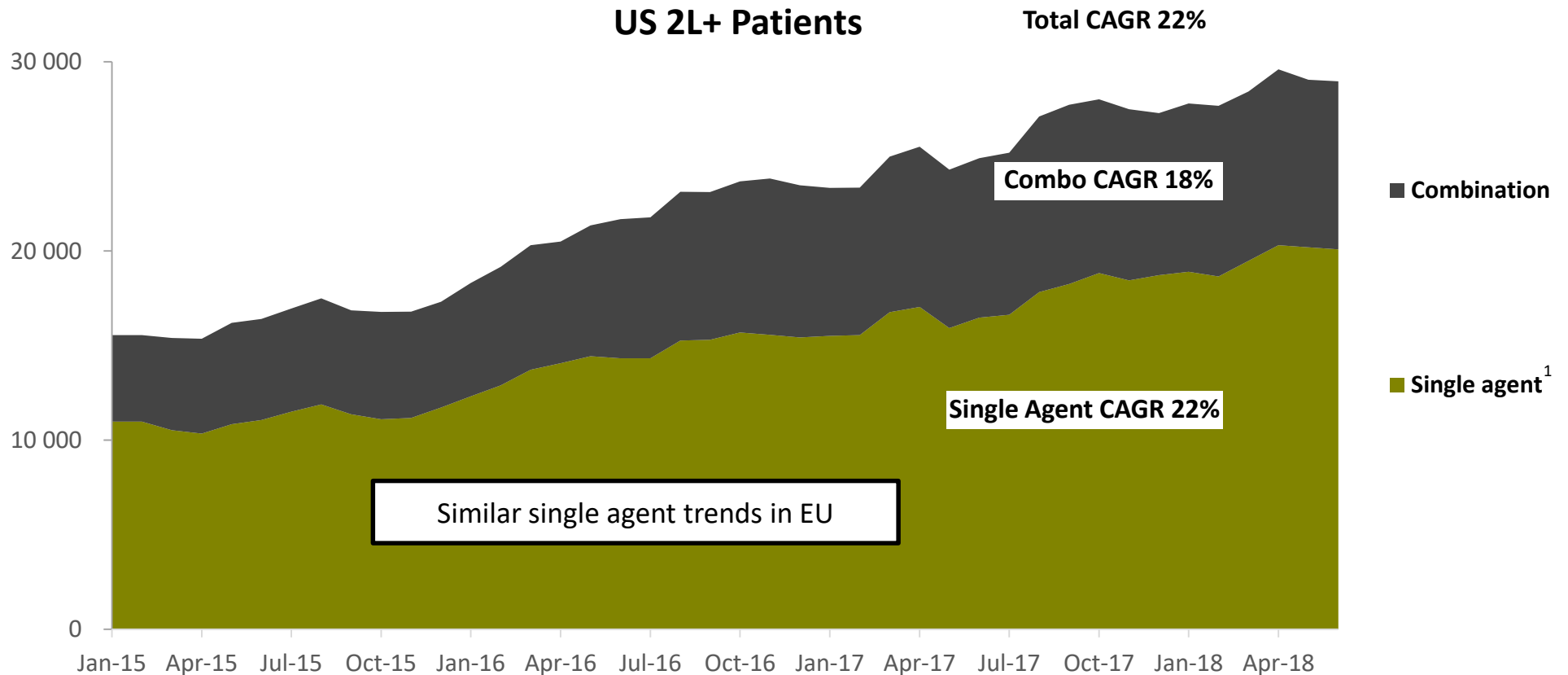
Limited number of treatment options for late-stage RRMM patients –  
Novel treatment options are necessary and demanded by patients and regulatory bodies

# Despite guidelines, single agent +/- steroid predominantly used in 2L+

## Pomalyst is the most commonly used regimen in 2L+



# Single agent regimens are growing faster than combinations in 2L+, seemingly cementing the rise of single agent +/- steroid



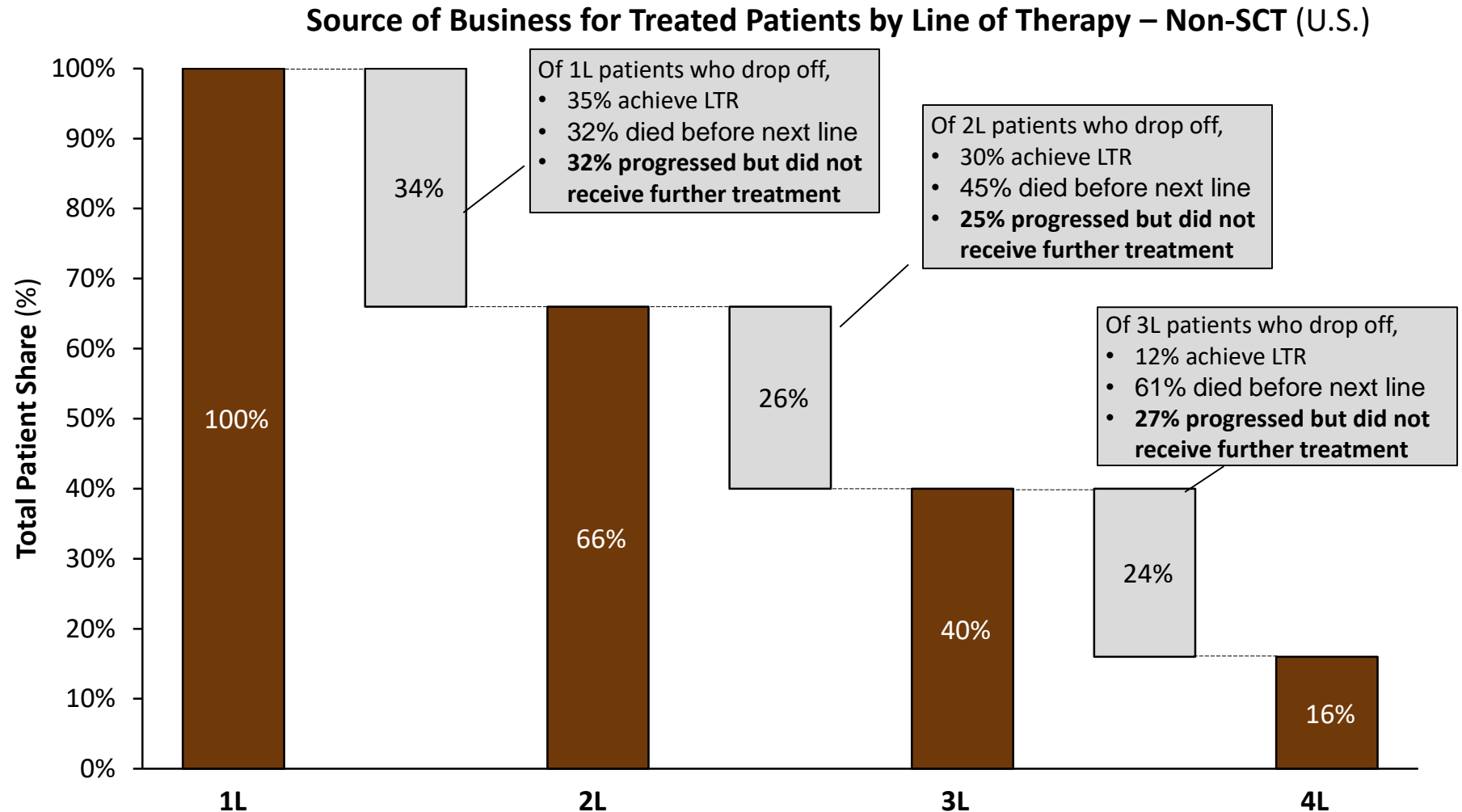
Limited use of Antibodies with combination data only, single agent data vital for market penetration

Source: Intrinsiq, Mar 2018, CAGR for YE15-17, EU trend based on Kantar Health report.

1. Single agent is drug plus dexamethasone ( $\pm$  steroids)

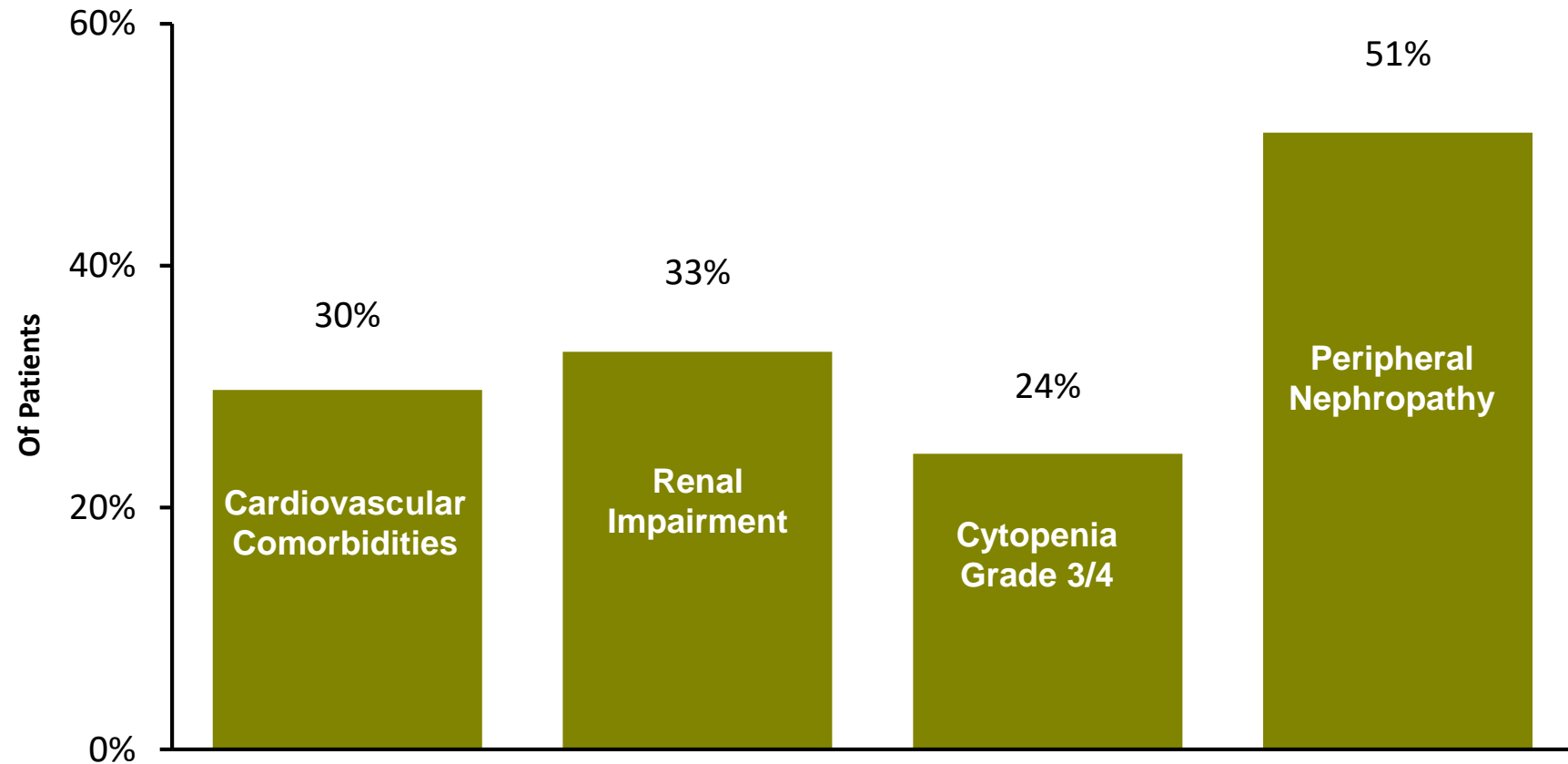
# A significant number of patients do not tolerate additional therapy

One in four patients drop out of treatment - mainly due to tolerability



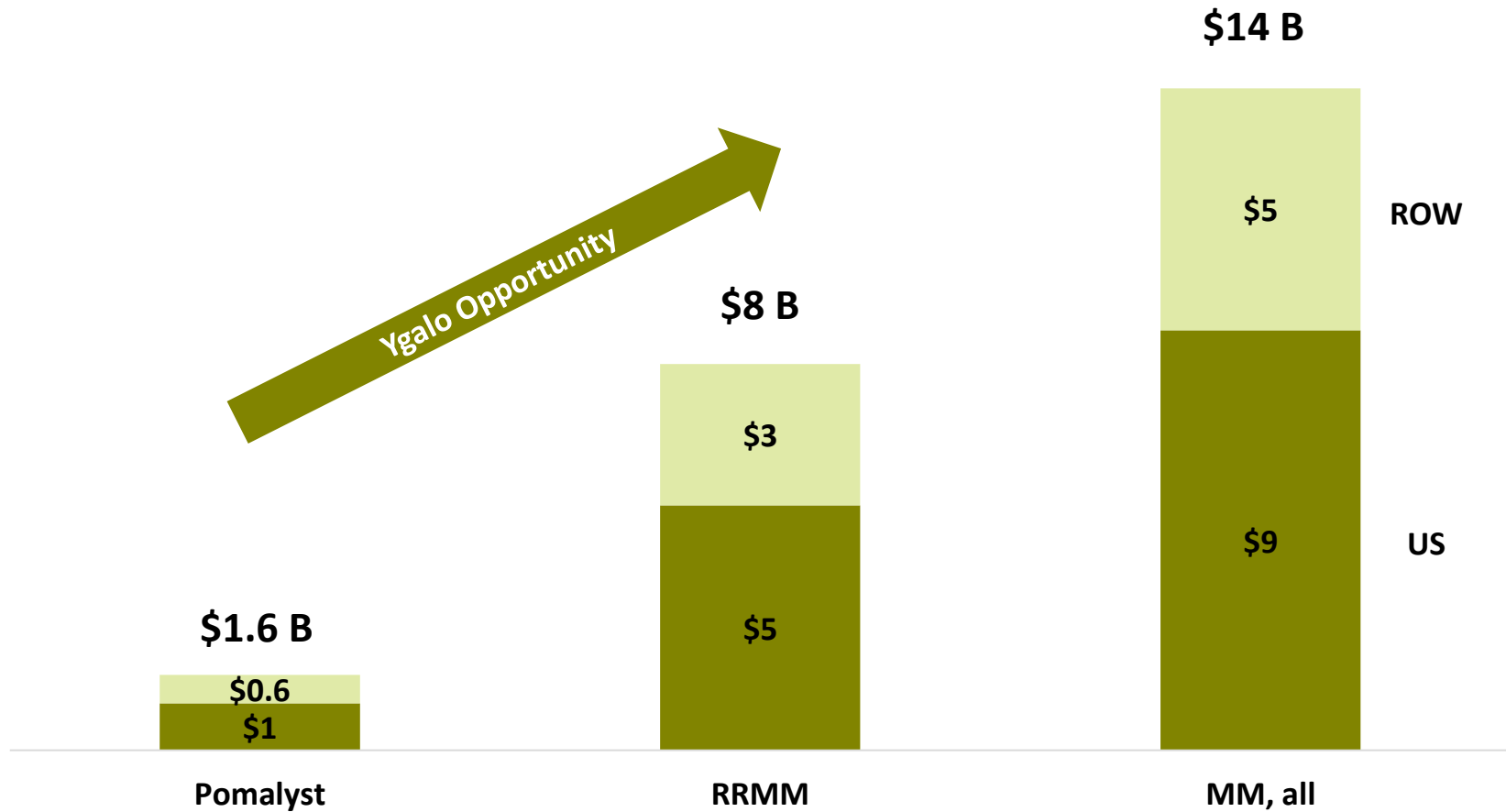
# Co-morbidities restrict treatment selection in all stages of treatment

Comorbidities significantly restrict therapy choice, with surveyed comorbidity rates reflecting both qualitative research findings and literature estimates



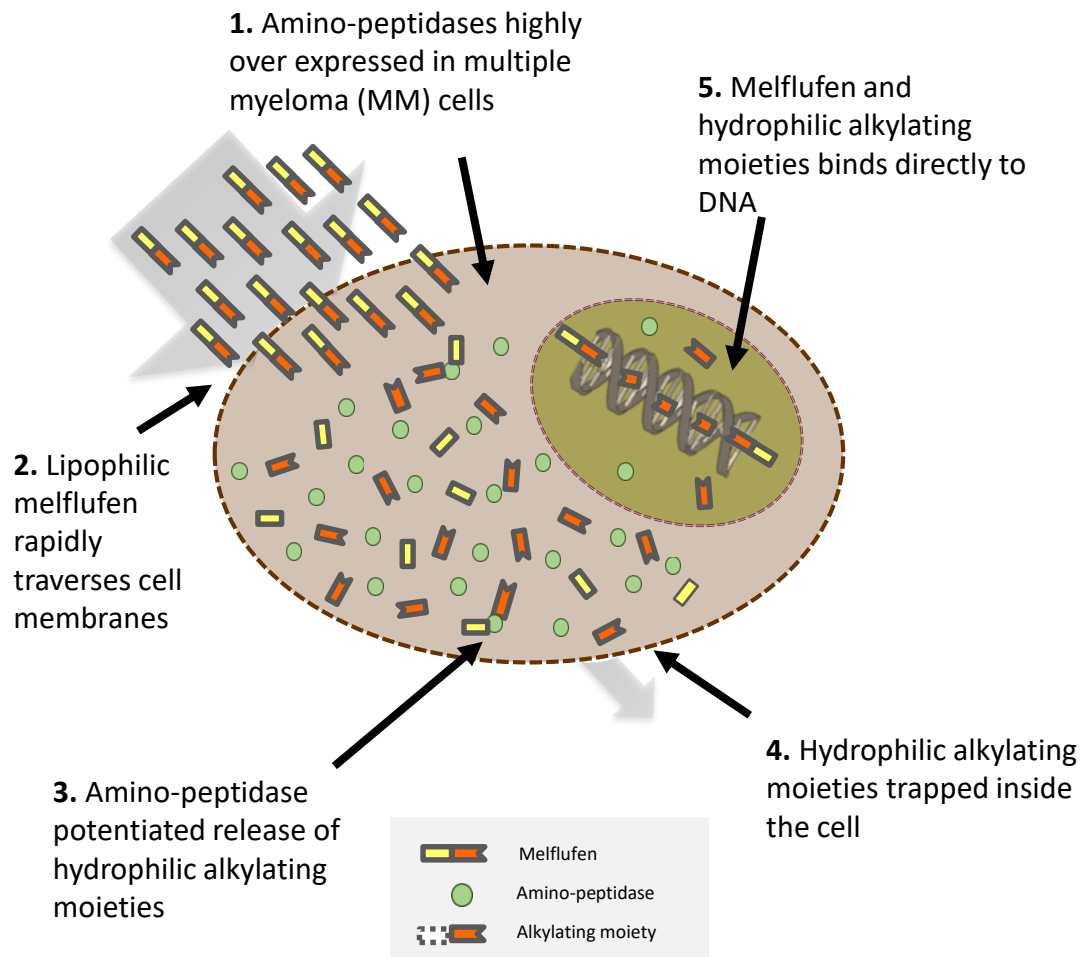
# Melflufen (Ygalo®) opportunity in RRMM

## 2017 Multiple Myeloma Net Sales Breakdown



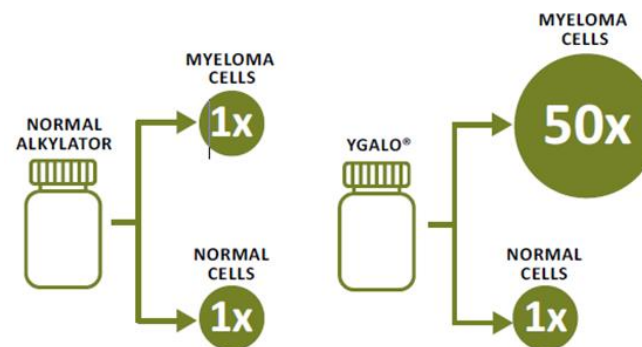
# Melflufen is a first in class peptidase enhanced compound (PEnC)

Amino-peptidases overexpressed up to 250x as part of transformation process



## 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<sup>1,4,5</sup>
- 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.  
3. Ray et al. (2016) Br J Hematol 174: 397-409.

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

# Melflufen (Ygalo®) is a highly differentiated selective compound

Well positioned to become the next backbone agent in myeloma

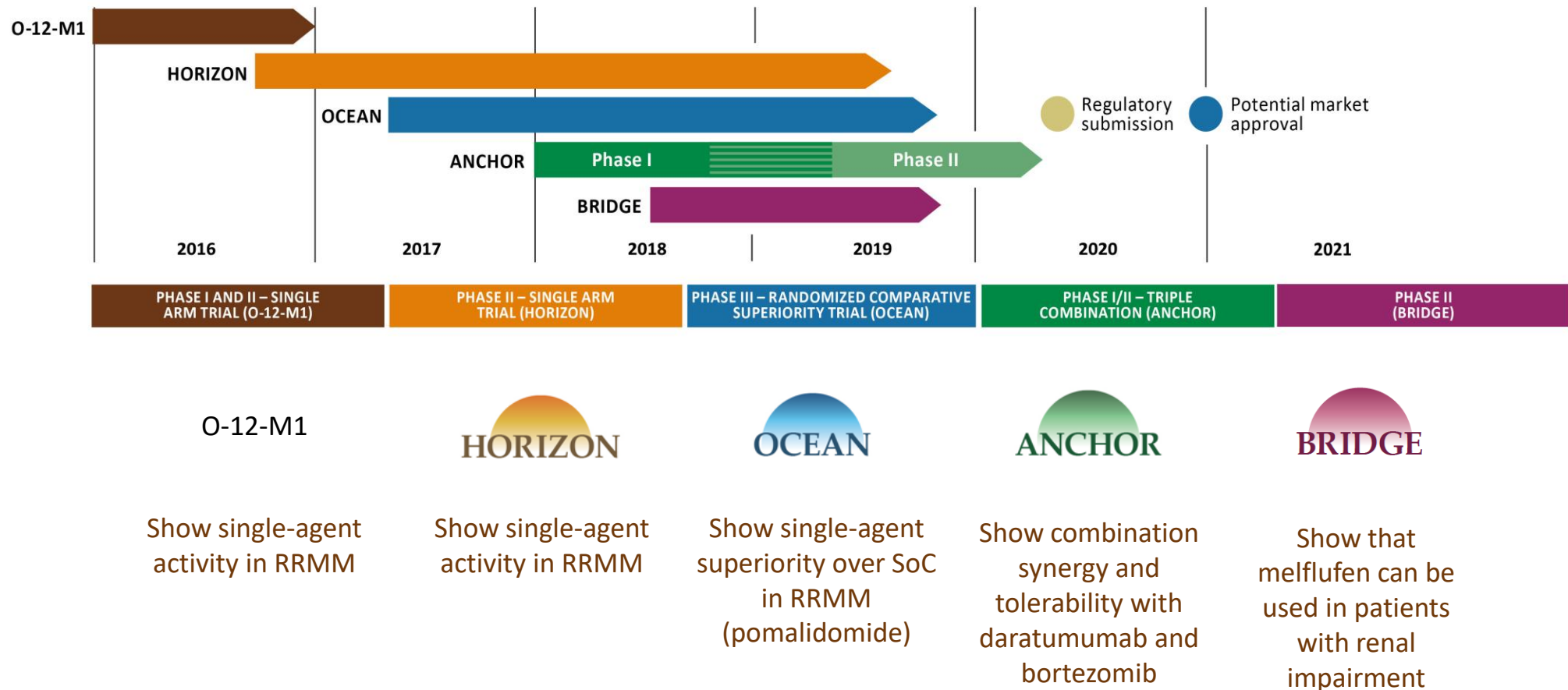
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- Ygalo® is peptide conjugated alkylator belonging to a novel class of peptidase-enhanced compounds, an PEnC peptide with a well-defined mechanism of action
- Ygalo® is highly selective for transformed cells, with significant increase in therapeutic index with a 50x+ activity increase in transformed cells with no increase against bone-marrow cells
- Ygalo® does not share resistance mechanisms with other classes of agents
- Phase 2 demonstrated the best overall survival data to date in late-stage myeloma
- Well tolerated with limited adverse events negatively impacting patient quality of life
- Bone pain improvement seen in first-cycle of treatment
- Does not rely on renal excretion (renal function often severely impacted in myeloma)
- Convenient once monthly 30 min infusion (simplifying community hospital use where majority of patients treated)
- Covered by Medicare Part B vs Part D

# Development program for melflufen is designed to support its potential as a new broad spectrum backbone agent after IMiD and PI failure

Must have characteristics		Melflufen
<ul style="list-style-type: none"><li>Single agent +/- steroid activity in multi-refractory patients of 20%+ ORR</li></ul>	➤	<ul style="list-style-type: none"><li>O-12-M1 showed an ORR of 31% and HORIZON an ORR of 32% in multi-refractory patients</li></ul>
<ul style="list-style-type: none"><li>Single agent +/- steroid approval in refractory patients</li></ul>	➤	<ul style="list-style-type: none"><li>OCEAN is designed to give single-agent approval</li></ul>
<ul style="list-style-type: none"><li>Efficacy synergy in combination with other main myeloma drugs with good tolerability</li></ul>	➤	<ul style="list-style-type: none"><li>ANCHOR, first dataset from ongoing trial was presented at ASH in December 2018</li></ul>
<ul style="list-style-type: none"><li>No major QoL tolerability issues</li></ul>	➤	<ul style="list-style-type: none"><li>Very good QoL with almost no non-hematological AEs</li></ul>
<ul style="list-style-type: none"><li>No co-morbidity limitations</li></ul>	➤	<ul style="list-style-type: none"><li>No co-morbidity limitations, Drug-Drug Interaction</li></ul>
Nice to have characteristics		
<ul style="list-style-type: none"><li>Easy administration schedule</li></ul>	➤	<ul style="list-style-type: none"><li>Once monthly 30min infusion</li></ul>

# Our clinical development program is designed to establish a tier 1 drug in RRMM



# Overview of clinical data to date (ASH 2018)

1st line	2nd line	3rd line	4th line	5th line	6th line	7th line
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O-12-M1



**Inclusion criteria: 1-4 prior lines of therapy and at a minimum refractory to IMiDs, PIs or both (RRMM)**

- Early interim data (n=12)
- All patients ongoing
- 2-3 prior lines of therapy
- ORR of 100% in combination with bortezomib
- ORR of 86% in combination with daratumumab
- Not enough follow-up for DOR, PFS and OS

**Inclusion criteria: 2+ prior lines of therapy, IMiD and PI exposed and refractory to last line of therapy**

**21-day and 28-day cycle tested**

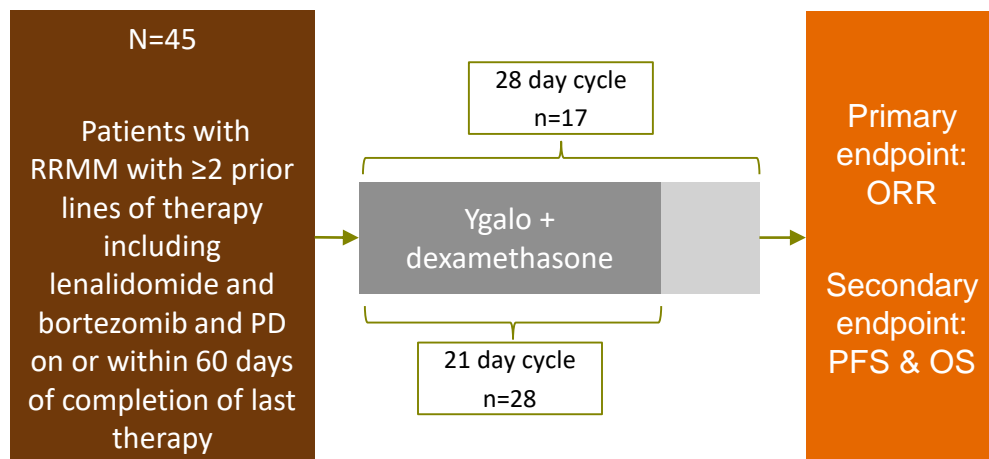
- n=45
- 4-5 prior lines of therapy (median 4)
- ORR of 31.1%
- DOR of 8.4m
- mPFS of 5.7m (11.7m in PR+)
- OS of 20.7m (27.2m in SD+)

**Inclusion criteria: 2+ prior lines of therapy, PI and IMiD exposed as well as pom and/or dara refractory**

- n=83
- 5-6 prior lines of therapy (median of 5)
- ORR of 33%
- mPFS of 4.0m (6.3m in PR+)

# Phase II (O-12-M1) study design and patient disposition

Patients were IMiD and PI exposed with refractory disease

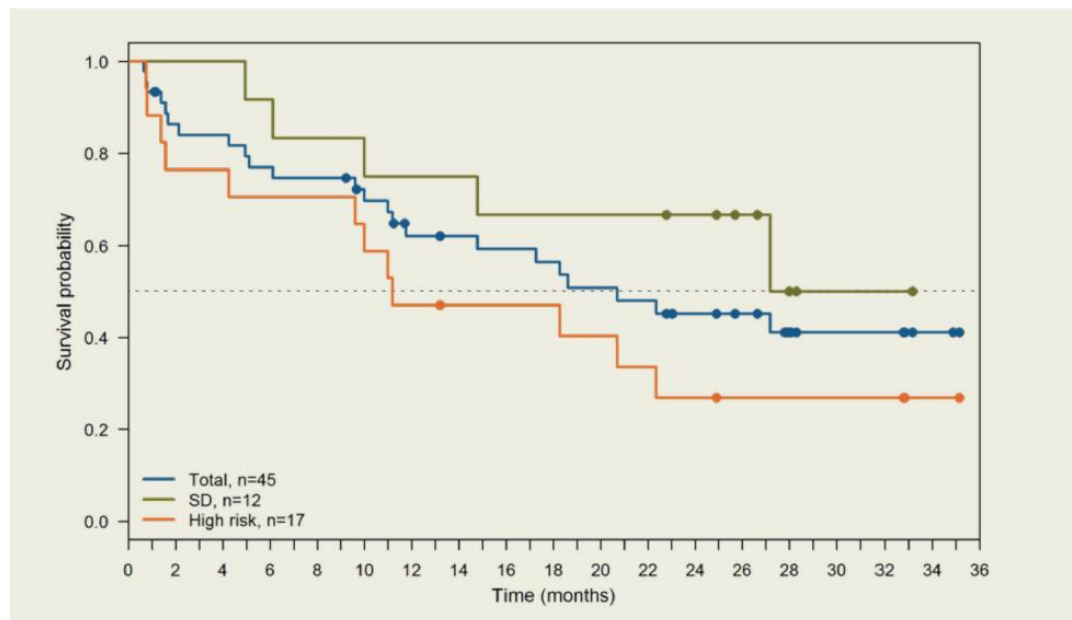


	N = 45
Median age, years (range)	66 (47-78)
Years since diagnosis, median (range)	5.1 (1.4 – 21.2)
Number of previous lines of therapy, median (range)	4 (2-14)
ISS, stage at study entry, n (%)	
I	15 (33)
II or III	27 (60)
Unknown	3 (7)
ECOG performance status, n (%)	
0	23 (51)
1	22 (49)
2	0
High-risk cytogenetic risk factors by FISH, n (%)*	17 (38)
Double-refractory, n (%) (IMiD +PI)	29 (64)
Last line refractory, n (%)**	42 (93)
Pomalidomide refractory, n (%)	20 (44)
Refractory to an alkylator (melphalan, cyclophosphamide or bendamustine), n (%)	24 (53)

\* t(4;14), t(14;16), t(14;20), del(17/17p) or gain(1q)

\*\* 3 patients had PR or better in the last line of therapy and PD within 180 days of last dose

# Melflufen (Ygalo®) demonstrated best-in-class survival data in late-stage RRMM with good tolerability



- >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 tumor Response Rates (ORR and CBR)
- Better tolerated by the patients – non-hematological toxicity is rare
- Ygalo demonstrated a larger benefit on OS than PFS suggesting that Ygalo may improve response to subsequent treatments. A possible mechanism for this is clonal resetting which requires further exploration in ongoing studies

N	PD	SD	MR	PR	VGPR	ORR	CBR	PFS	OS
ITT (N=45) <sup>1</sup>	7	12	8	9	5	31%	49%	5.7 months (95% CI: 3.7-9.3) <sup>2</sup>	20.7 months (95% CI: 11.8-∞) <sup>3</sup>
Efficacy evaluable (N=34)	1	11	8	9	5	41%	65%		

1. 4 patients did not have a response assessment.

2. Based on 41 events in 45 pts. In pts with ≥PR, the median PFS was 11.7 months (95% CI: 9.8 – ∞, event rate 93%). The median DOR was 8.4 months (95% CI: 5.8 – ∞).

3. Based on 23 events in 45 pts. Among the 12 pts that achieved stable disease, the mOS was 30.2m (95% CI: 14.8 – ∞, event rate 42%), and in pts with high-risk cytogenetics the mOS was 11.2 m (10.0 – ∞, event rate 71%). Fourteen (31%) pts were alive 24m after end of treatment, including 4 pts with high-risk cytogenetics.

# Best overall survival data to date in late stage myeloma

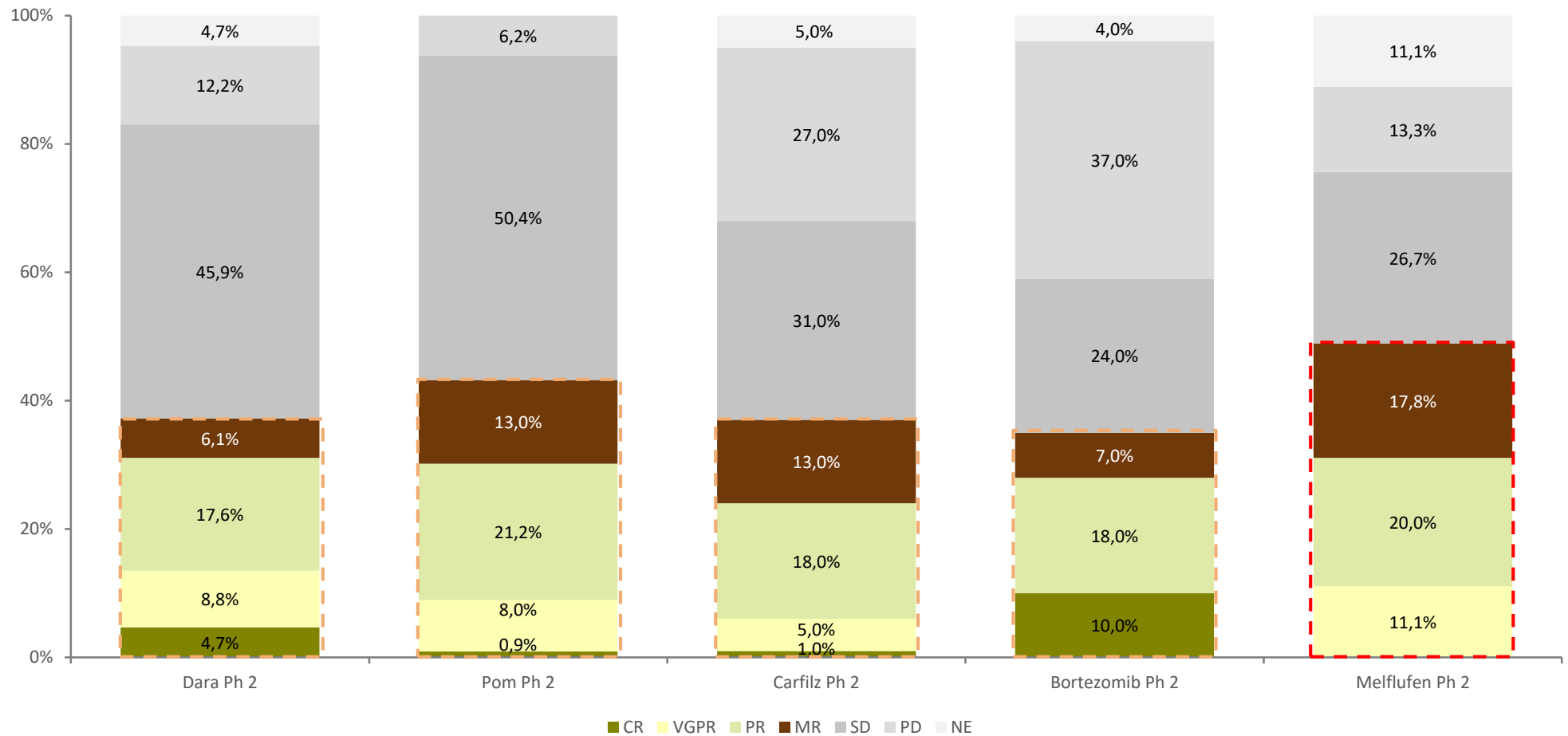


	Melflufen	Daratumumab	Pomalidomide*	Carfilzomib
<b>N</b>	45	106	302	266
<b>Year</b>	2017	2016	2013	2012
<b>Population</b>	Refractory to last, exposed to iMiD, PI and alkylator, iMiD and PI refractory	Refractory to last, ≥3 lines with iMiDs and PI, double refractory to PI and iMiD	Refractory to last, at least 2 lines with bort and len and received alkylator	>2 prior for relapsed including Bar, Len or thal, alk or anthra alone or in combo
<b>Time from diag.</b>	5.0 years	4.8 years	5.3 years	5.4 years
<b>High risk Cytog.</b>	44%	19%	~30%	28%
<b>Number of lines</b>	4, 78% ≥3 lines	5, 82% ≥3 lines	5, 94 % ≥2 lines	82% ≥4 lines
<b>Refract. to last</b>	87%	97%	100.0%	94.0%
<b>ORR</b>	31.1%	29.2%	31.0%	23.7%
<b>ORR high risk</b>	25%	20%	—	29.6%
<b>Med. duration treat</b>	3.7 months	-	Progressive Disease or Unacceptable Toxicity	3.0 months
<b>Med. duration response</b>	8.4 months	7.4 months	7.0 months	7.8 months
<b>Median PFS</b>	5.7 months (11.7 in ≥PR)	3.7 months	4.0 months (TTP 4.7 months)	3.7 months
<b>Median OS</b>	20.7 months	17.5 months	12.7 months	15.6 months

Source: Richardson PG *et al.*, ASH 2017; Usmani SZ *et al.*, 2016; Miguel JS *et al.*, 2013; Siegel DS *et al.*, 2012

\* = source FDA label

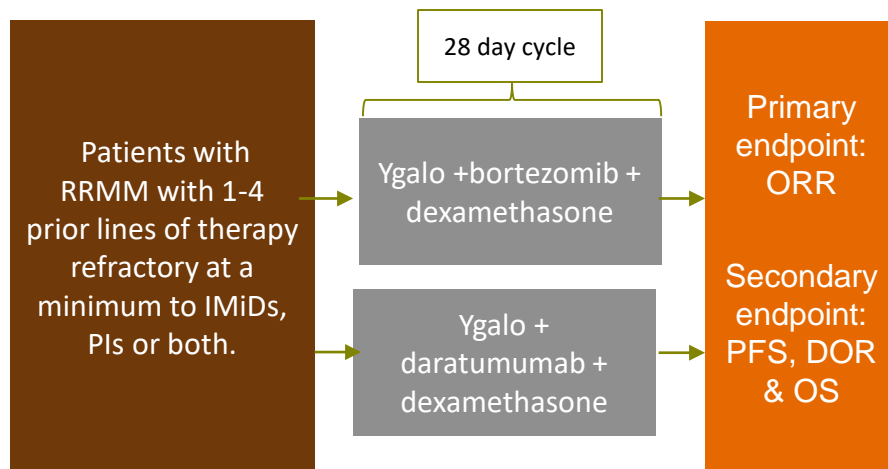
# Significant clinical benefit, in comparison with other approved drugs in late-stage RRMM



NE: Non-evaluable. PD: Progressive Disease. SD: Stable Disease. MR: Minimal Response.  
PR: Partial Response. VGPR: Very Good Partial Response. CR: Complete Response.

# ANCHOR study overview

The ability to combine melflufen with bortezomib or daratumumab in RRMM



- While single agent treatment is most common in 2L+, combination regimens are not infrequent, especially at academic centers
- All major treatment options in myeloma are possible to combine with other modalities for synergistic effects on efficacy
- ANCHOR aims to show that melflufen has treatment synergies with bortezomib and daratumumab in the treatment of patients with RRMM

# ANCHOR – Interim data reveal at ASH 2018

## Melflufen and dexamethasone in combination with bortezomib in RRMM (n=3)

### In combination with bortezomib – n=3

- Elderly population – 3 prior lines of therapy
- True RRMM population (not maintenance refractory) – 2/3 had disease progression while on last line of therapy
- 3/3 responded on therapy (ORR 100%) – all pts ongoing with good tolerability

**Table 1. Patient characteristics**

CHARACTERISTICS	MELFLUFEN+BORTEZOMIB+DEX (N=3)
Median age, years (range)	81 (70-82)
Median time since diagnosis, years (range)	6.9 (5.7-7.3)
Number of previous lines (range)	3 (2-4)
ISS at study entry, n (%)	
I	3 (100)
II	0
III	0
High-risk, cytogenetic risk factor by FISH*, n (%)	0
Median albumin, n (range)	3.9 (3.6-4.2)
High LDH (1.5 x UNL), n (%)	2 (67)
IMiD refractory, n (%)	3 (100)
Dara refractory, n (%)	1 (33)
Alkylator refractory, n (%)	1 (33)
Last line refractory, n (%)	2 (67)

\*t(4;14), t(14;16), t(14;20), del(17;17p) or gain(1q)

Note: PI refractory status was an exclusion criterion in this trial arm.

### SAFETY

No DLTs were observed at the 30 mg melflufen dose level. The regimen was well tolerated with clinically manageable G3/4 hematological AEs and the low number of non-hematological AEs was noteworthy. The highest cohort of melflufen 40 mg has been opened for enrolment.

**Table 2. Treatment-related (possible/probable) G3/G4 AEs**

CHARACTERISTICS	MELFLUFEN + DEX + BORTEZOMIB (N=3)	
	GRADE 3 n (%)	GRADE 4 n (%)
Any treatment-related AE	2 (67)	0
Neutropenia	2 (67)	0
Thrombocytopenia	2 (67)	0
Pneumonia pneumococcal	1 (33)	0

One patient experienced 3 treatment-related SAEs (G2 pneumonia, G3 neutropenia, G3 pneumonia pneumococcal).

### EFFICACY

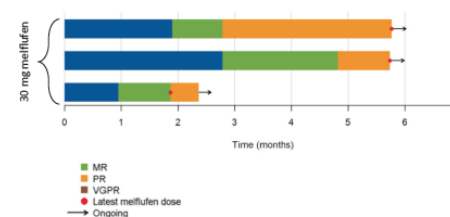
All 3 patients were still ongoing with a median treatment duration of 5.8 months (2.3-6.1). The patients received a total of 17 cycles of treatment with a median of 7 (3-7). All 3 patients achieved partial response (PR) (Table 3).

**Table 3. Response assessment**

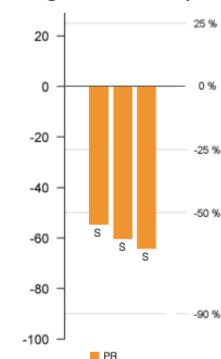
	ORR	CR	VGPR	PR	MR	SD	PD
Total (N=3)	100%	0	0	3*	0	0	0

\* 1 unconfirmed PR

**Figure 4. Swim-lane plot**



**Figure 5. Waterfall plot**



# ANCHOR – Interim data reveal at ASH 2018

## Melflufen and dexamethasone in combination with daratumumab in RRMM (n=9)

### In combination with daratumumab – n=9

- 2-3 prior lines of therapy
- True RRMM population (not maintenance refractory) – 5/9 had disease progression while on last line of therapy
- 6/7 patients responded to therapy (ORR 86%) with good tolerability and deepening responses. All patients ongoing.

**Table 4. Patient characteristics**

CHARACTERISTICS	MELFLUFEN + DEX + DARA (N=9)
Median age, years (range)	63 (35-78)
Median time since diagnosis, years (range)	4.0 (1.8-6.6)
Number of previous lines (range)	2.0 (1-3)
ISS at study entry, n (%)	
I	8 (89)
II	0
III	1 (11)
High-risk cytogenetic risk factor by FISH*, n(%)	3 (33)
Median albumin (range)	4.1 (3.1-4.5)
High LDH (1.5 x UNL)	3 (33)
IMiD refractory, n (%)	6 (67)
PI refractory, n (%)	2 (22)
IMiD + PI refractory, n (%)	1 (11)
Alkylator, n (%)	2 (22)
Last line refractory, n (%)	5 (56)

\*t(4;14), t(14;16), t(14;20), del(17;17p) or gain(1q)

Note: Daratumumab refractory status was an exclusion criterion in this trial arm.

### SAFETY

Four\* patients were treated with 30 mg melflufen and no DLTs were observed. Five patients were treated with 40 mg melflufen with no DLTs observed (6 patients on 40 mg melflufen required to confirm dose level). The combination of melflufen, dexamethasone and daratumumab was well tolerated with clinically manageable G3/4 hematological AEs and the low number of non-hematological AEs was noteworthy.

\* First patient in the 40 mg cohort erroneously received 30 mg.

**Table 5. Treatment-related (possible/probable) G3/G4 AEs**

CHARACTERISTICS	MELFLUFEN+BORTEZOMIB+DEX (N=9)	
	GRADE 3/4 n (%)	GRADE 4 n (%)
Any treatment-related AE	7 (78)	4 (44)
Neutropenia	6 (67)	0
Thrombocytopenia	3 (33)	1 (11)
Lymphocyte count decrease	3 (33)	3 (33)
White blood cell count decrease	1 (11)	1 (11)

No treatment-related SAEs were reported.

### EFFICACY

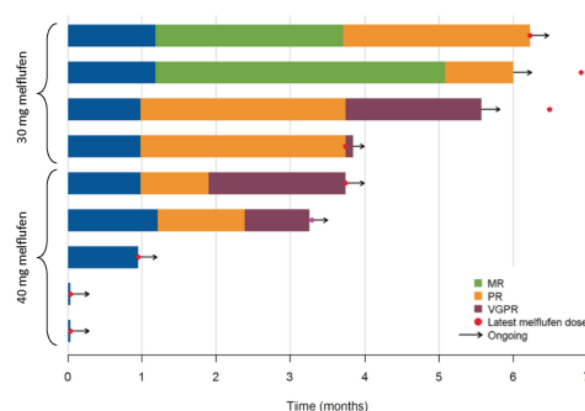
All 9 patients were still ongoing with a median treatment duration of 3.9 months (0-6.9). They received a total of 39 cycles of treatment with a median of 4 (1-8). Best response for the 9 treated patients is described in Table 6.

**Table 6. Response assessment**

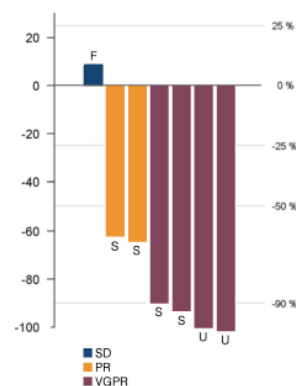
	ORR	CR	VGPR	PR	MR	SD	PD	N/A**
Total (N=9)	86%	0	4*	2	0	1	0	2

\* 1 unconfirmed VGPR \*\* 2 pts were still in their first cycle of treatment and were therefore not evaluable for response

**Figure 6. Swim-lane plot**

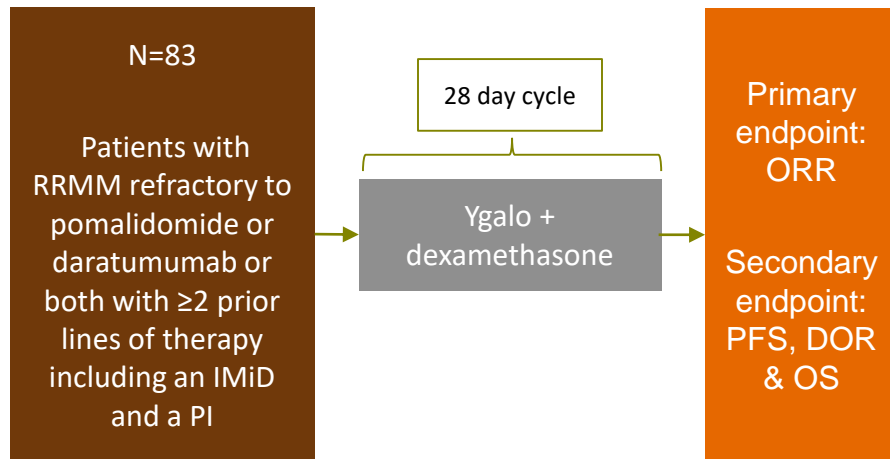


**Figure 7. Waterfall plot**



# HORIZON study overview

## Impact of Melflufen (Ygalo®) on patients with very limited treatment options



- Once patients become IMiD/PI/Dara refractory, they have an extremely poor prognosis
- Growing evidence that dara refractory patients are extremely difficult to treat
- Very ill patient population (61% High-risk patients, 36% ISS stage III patients)

### Baseline characteristics

	RANGE
Age (median)	63 yrs (35-86)
Male / Female	59 / 41 %
Median time since diagnosis	6.5 yrs (0.7-25)
Median prior lines of therapy	5 (2-13)
ISS stage I / II / III*	33 / 29 / 36 %
ECOG 0 / 1 / 2	27 / 58 / 16 %
High-risk cytogenetics** / 2 or more high risk abnormalities	61 / 20 %
Received ASCT (%) / Relapsed within 1 year after ASCT (%)	69 / 17 %
Albumin < 3.5 g/dl	35%
Baseline β2 microglobulin > 3.5 mg/l	50%

### Prior lines of therapy

	%
Refractory to	
Pom or dara	100
Pom and dara	60
Double refractory (PI+IMiD)	86
Double + anti-CD38 refractory	60
Monoclonal antibody (MoAb)	80
Alkylator exposed	84
Alkylator refractory	55
Received 1 ASCT / 2 ASCT	69 / 25
Refractory in last line	93

Source: ASH December 2018.

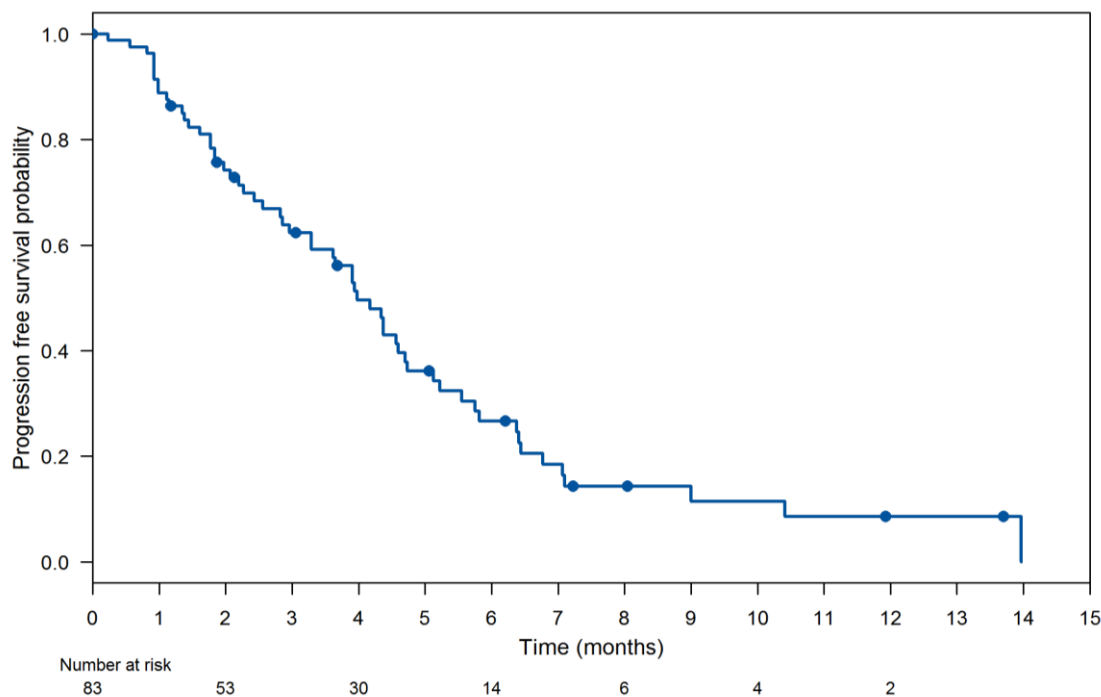
\*Missing data for 3 patients.

\*\* HR status data pending 7 missing in 23 patients

# Promising results in patients without treatment options (HORIZON)

Response	NE	PD	SD	MR	ORR
% (n)	1% (1)	15% (12)	45% (37)	6% (5)	33% (27)

<i>sCR</i>	<i>VGPR</i>	<i>PR</i>
1% (1)	11% (9)	21% (17)



Median PFS of 4.0 months

- Strong overall response rate with 33%
- Median PFS of 4.0 months
- Strong activity in triple refractory (IMiD, PI and daratumumab) refractory patients

## Promising results in patients without treatment options (HORIZON)

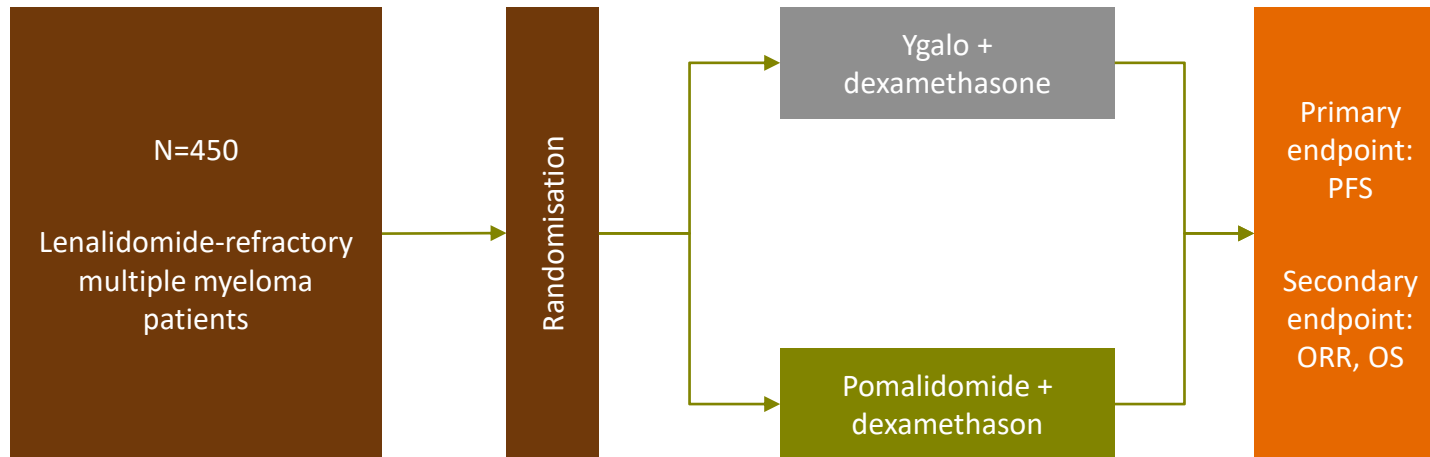
	G3/G4 n (%)	G4 n (%)
Any treatment-related grade 3-4 AEs in ≥2 pts	62 (75)	42 (51)
Blood and lymphatic system disorders	61 (73)	41 (49)
Neutropenia	51 (61)	29 (35)
Thrombocytopenia	49 (59)	30 (36)
Anaemia	21 (25)	1 (1)
Febrile neutropenia	5 (6)	2 (2)
Leukopenia	4 (5)	3 (4)
Lymphopenia	4 (5)	1 (1)
Infections and infestations	6 (7)	0 (0)
Pneumonia	2 (2)	0 (0)
Treatment-related SAEs	14 (16)*	5 (6)

\*Most frequent: febrile neutropenia (5 of 14), neutropenia (3 of 14) and thrombocytopenia (2 of 14).

- No treatment-related deaths.
- The patients had G4 lab thrombocytopenia at Day 29 in 4% of the cycles.
- 3 pts (4%) experienced treatment-related bleeding: G1 in 2 patients, and G3 in 1 patient.
- Incidence of non-hematologic adverse events low.
- Incidence of infections low (7.2%).
- Discontinuation rate due to AEs was 13% (8 of 11 due to thrombocytopenia).

# Data to date provides high conviction for success in OCEAN

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



## Late-Stage Relapsed Refractory



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

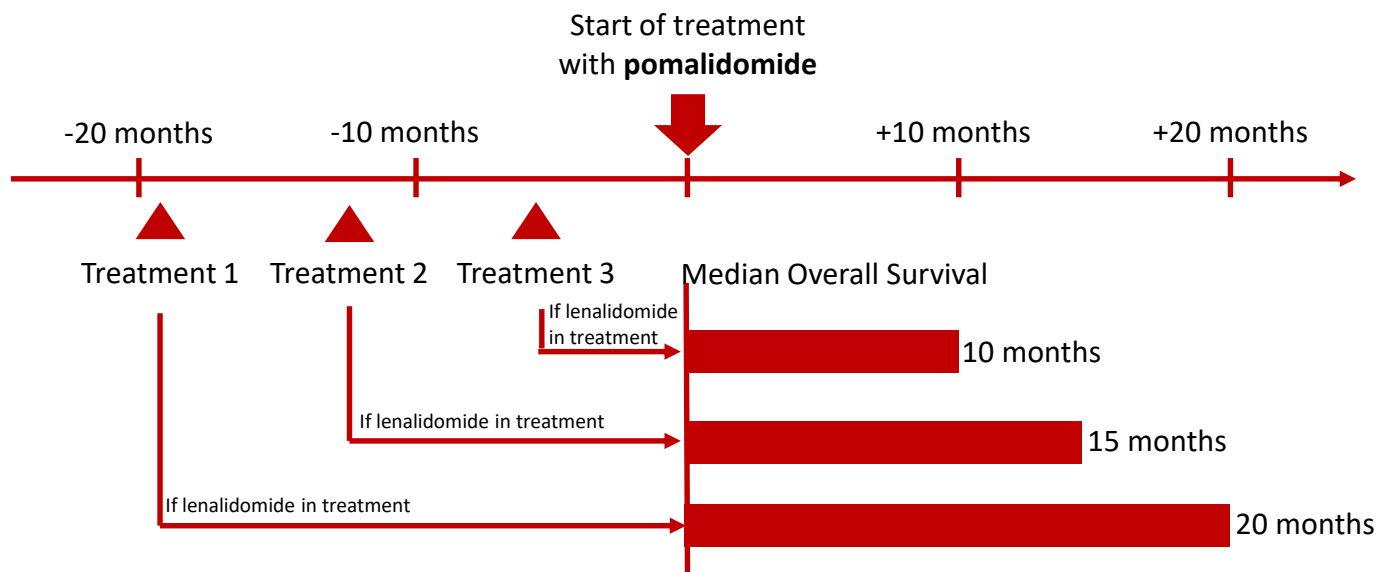
Note: NR=Not Reported. Ygalo® is not market approved.

Source: FDA Label.

# Pomalidomide shares resistance mechanism with lenalidomide

No assumption has been made in OCEAN power calculation about this factor

## Dimopoulos research supporting an IMiD free period



50% reduction in efficacy if patient recently failed on lenalidomide - suggests significant resistance overlap between lenalidomide and pomalidomide

# Pomalidomide shares resistance mechanism with lenalidomide (cont'd.)

No assumption has been made in OCEAN power calculation about this factor

## Siegel data of pom+dex in len-refractory patients


Median prior lines of 2, 91% len-refractory,  
median 4.5 years since diagnosis, 5.4% ISS III,

- 33.9% ORR
- 9.6m PFS

## Len-registration data as 2nd line agent together with dex

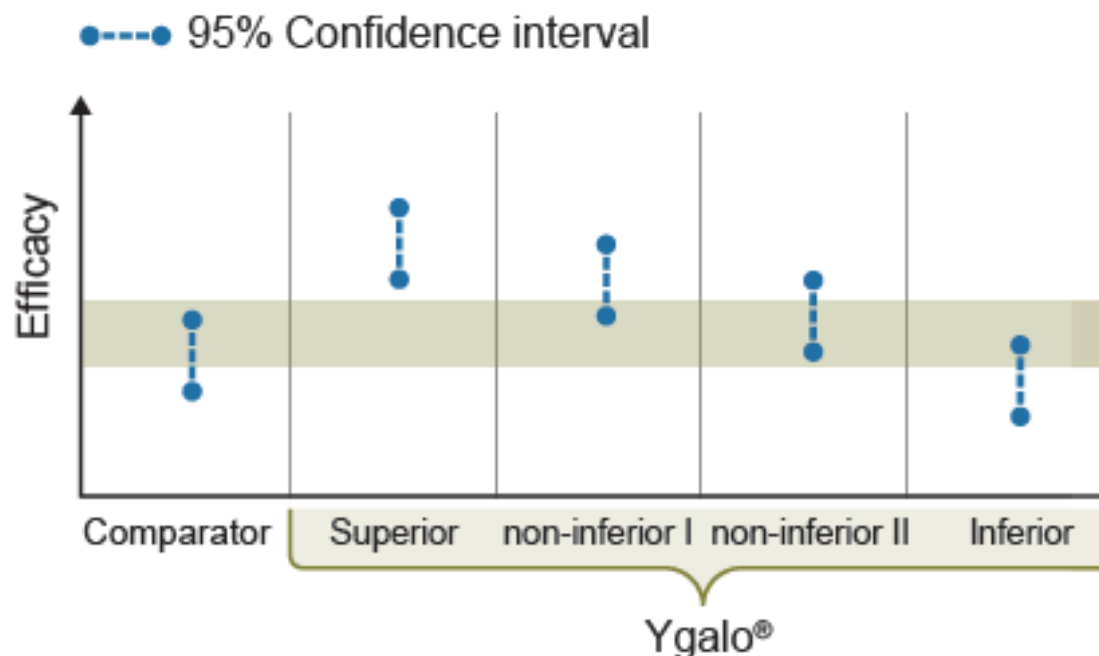
Median prior lines of 2, 30.1% thalidomide exposed, median  
3.4 years since diagnosis, 65.3% Durie-Salmon III

- 60.2% ORR (includes thalidomide exposed patients)
- 13.5m PFS



29-44% reduction in efficacy in a significantly healthier population (the difference in staging should be based on data resulting in a 39% difference to the benefit of pom) in len-refractory patients

# HORIZON and BRIDGE support the result in OCEAN



**In a non-inferiority outcome scenario, differentiation is key, e.g.**

- Better tolerability (OCEAN)
- No overlap in resistance mechanism (HORIZON)
- Renal clearance not required for Ygalo® (BRIDGE)

# Executive summary

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- Relapse in MM is inevitable despite advances with novel agents
- Fundamentally only four treatment modalities available – IMiDs, PIs, alkylators and anti-CD38
- 9 out of 10 patients treated with broad spectrum backbone agents due to heterogeneity of the tumor
- Aggressive front line use of IMiD/PI combinations until disease progression results in need to switch treatment already in 2L patients. With only four available treatment modalities this drives a heterogeneous 2L+ treatment landscape
- As a consequence, there is a significant need for novel MoAs in relapsed-refractory MM patients
- Treatment with single-agent +/- steroid most common in 2L+ patients with pomalidomide +/- dex having the largest market share
- QoL is a key factor for patients – one MM patient out of four opt out of treatment mainly due to tolerability
- Melflufen's clinical profile to date and current clinical development program addresses a significant clinical need in myeloma with its level of efficacy, tolerability profile, administration schedule, lack of co-morbidity drug/drug interaction limitations and expected label.
- Initial market revenue will be generated from a USD 8bn+ opportunity.