oncopeptides

## Nomenclature

**International non-proprietary name (INN)**
Melphalan flufenamide

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

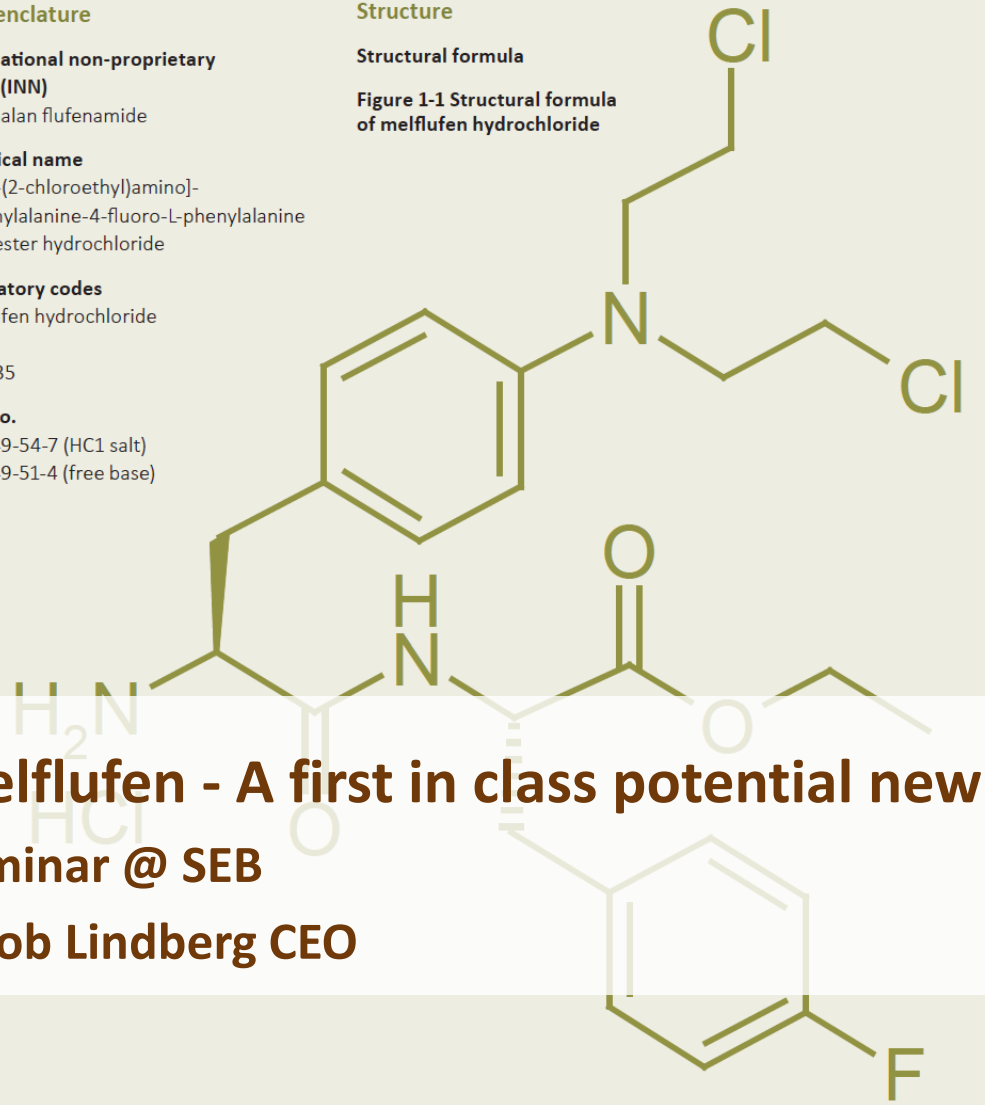
**Laboratory codes**
Melflufen hydrochloride
J1
CK 1535

**CAS No.**
380449-54-7 (HC1 salt)
380449-51-4 (free base)

## Structure

**Structural formula**

**Figure 1-1 Structural formula of melflufen hydrochloride**

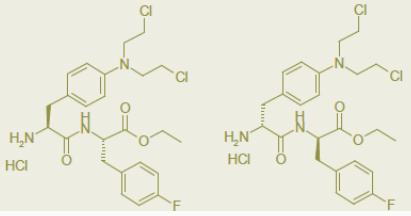



**Molecular formula**
C24 CH31C13FN3O3 (HC1 salt)

**Molecular weight**
534.9 (HC1 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]D 5.2° (c 1.9, CH3OH) 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 to be 205.4°C, as shown in

# Melflufen - A first in class potential new backbone for multiple myeloma

## Seminar @ SEB

## Jakob Lindberg CEO

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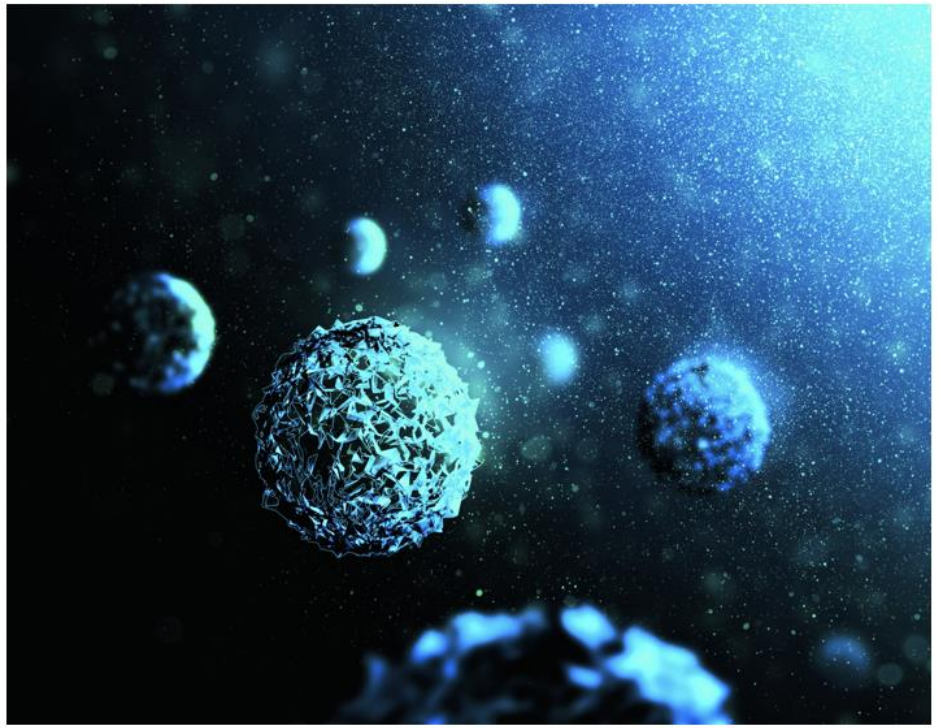
# Oncopeptides overview

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

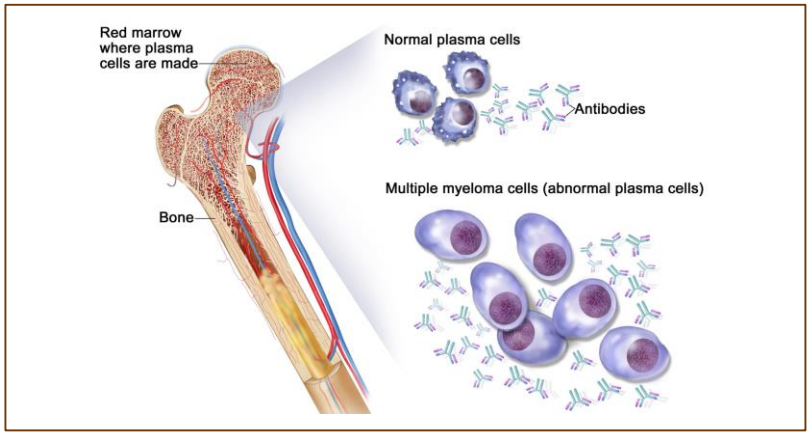
- **Develops targeted cancer treatments**
  - Proprietary peptidase-enhanced compounds
  - Lead compound Melflufen a peptide conjugated alkylator for Multiple Myeloma
- **Significant unmet needs in Multiple Myeloma**
  - Melflufen Phase 2 showed the best MM survival data to date
- **Melflufen Phase 3 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 650 MUSD
  - Cash position Sep. 30, 2018: 54 MUSD
- **New indications and NCEs in development**
  - Clinical trials expected to start in 2019



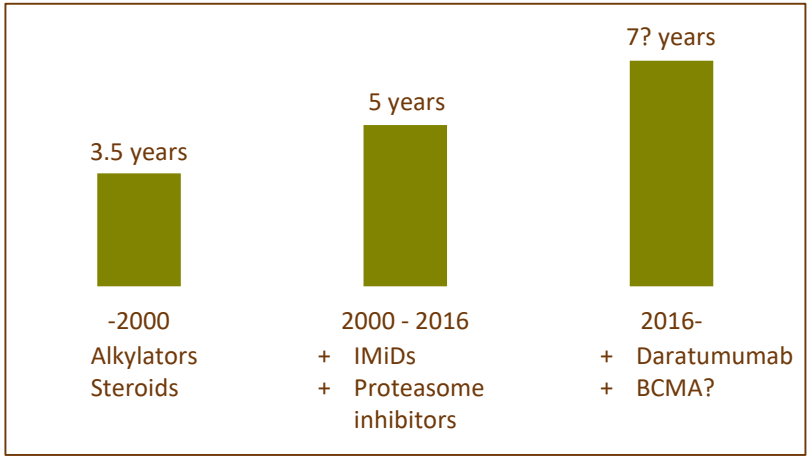
# Almost all multiple myeloma patients receive broad spectrum agents

## Treatment paradigm rapidly evolving with increased use of backbone agents

**Myeloma – Uncontrolled plasma cell proliferation**




**Median Survival increasing with more available treatment options**

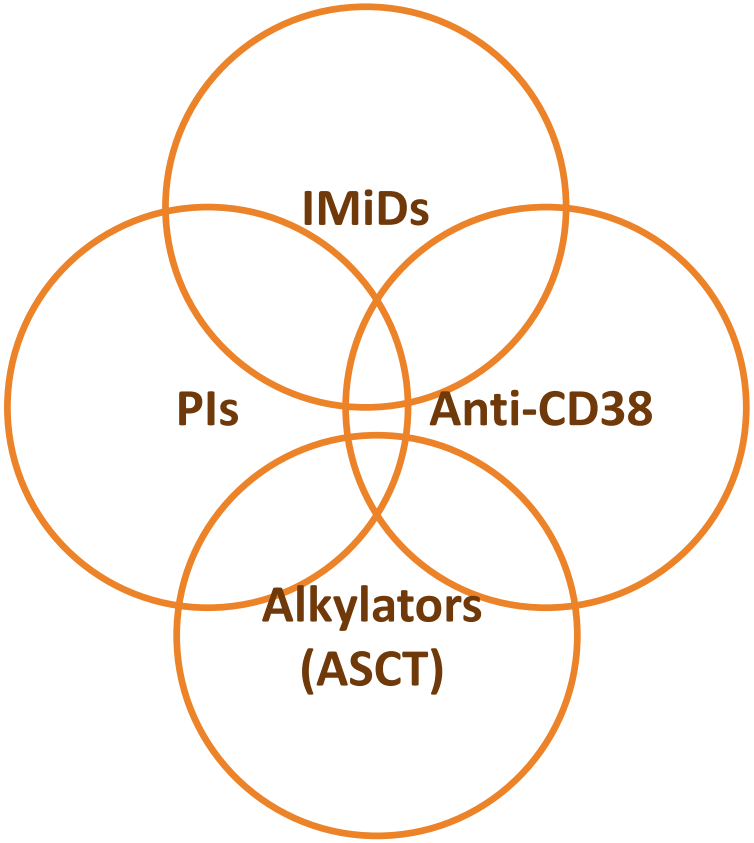



- Overall survival increasing but clonal selection results in inevitable relapse and treatment resistance
- 9 out of 10 patients receive broad spectrum agents (IMiDs, PIs and/or alkylators)
  - No ubiquitously expressed antigens in myeloma
  - Antibody-based therapies used in combination with IMiDs, 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

Source: IntrinsiQ and Kantar Health.

# Four classes of drugs form the back-bone of current myeloma care

Combination treatments are used aggressively in the frontline setting (+/- ASCT)



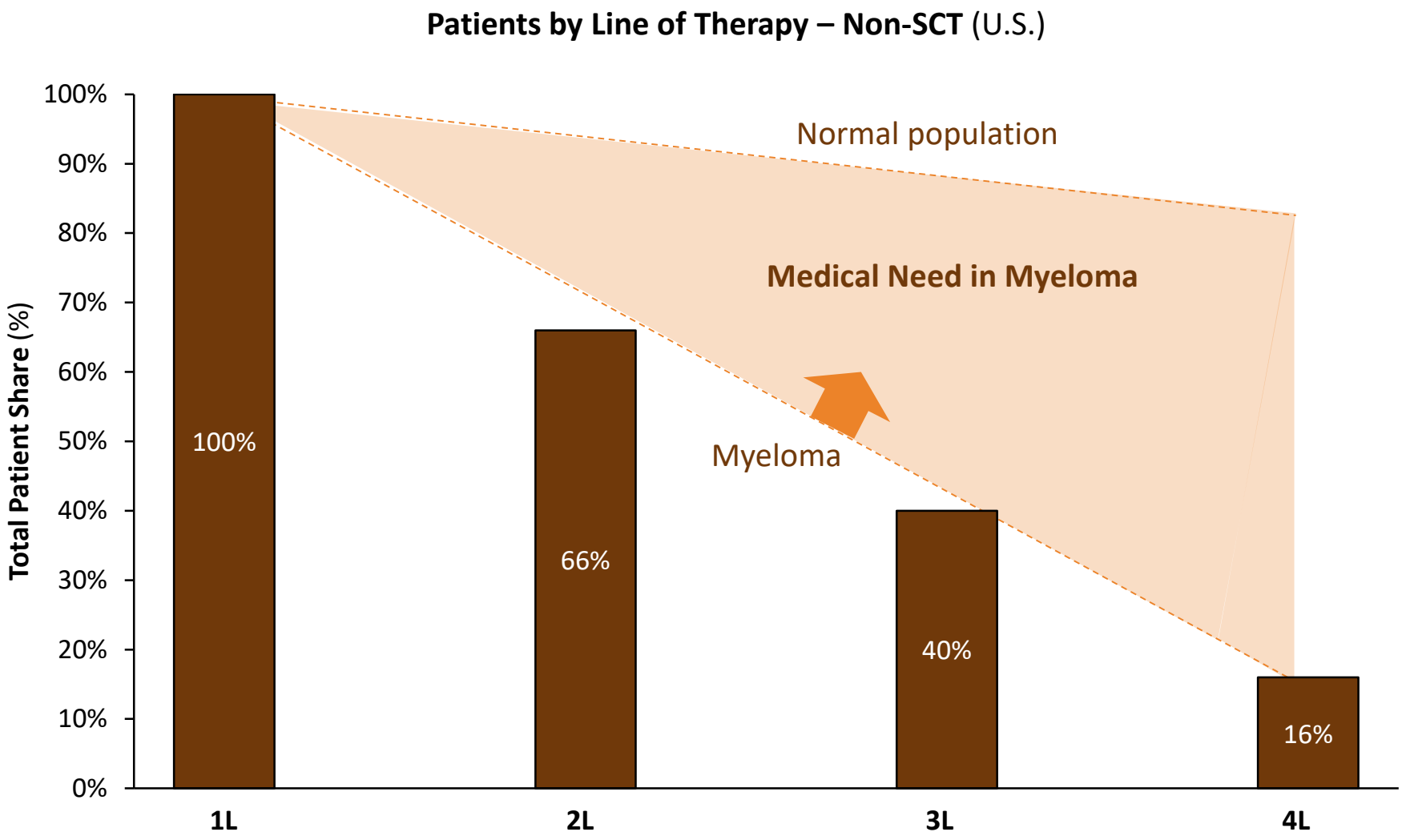

Current treatment algorithm development

- More aggressive use of combinations in frontline and 2nd line settings
- Treatment until disease progression – either continuously or as maintenance

Increased Progression Free Survival, trend towards increased Overall Survival, increased amount of tolerability issues and **increased number of patients in later lines of therapy with growing co-morbidity problems**

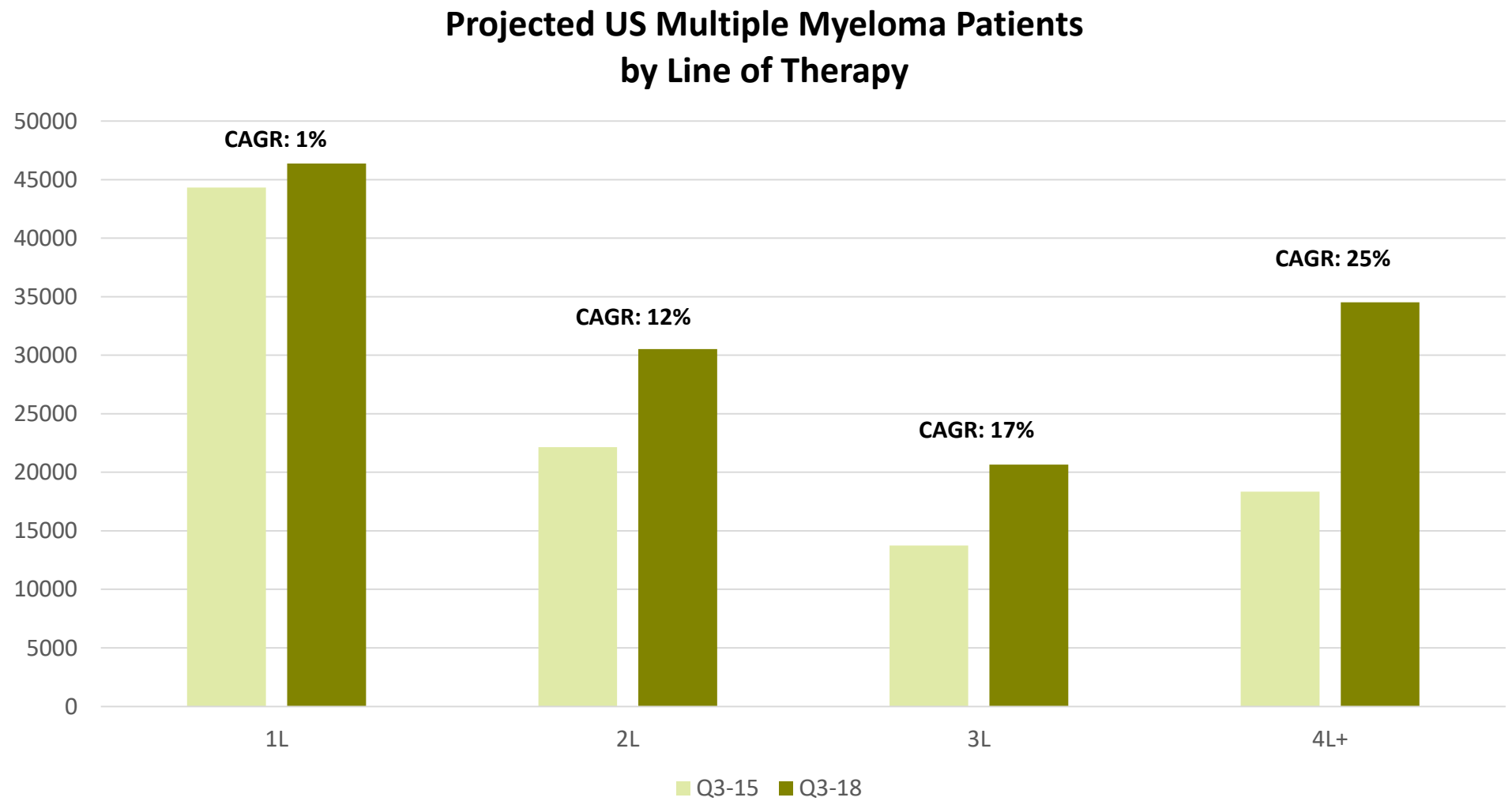
# We are still far from making myeloma a chronic disease

## Later line patient population growing with significant need for new treatments




Source: Kantar Health 2018

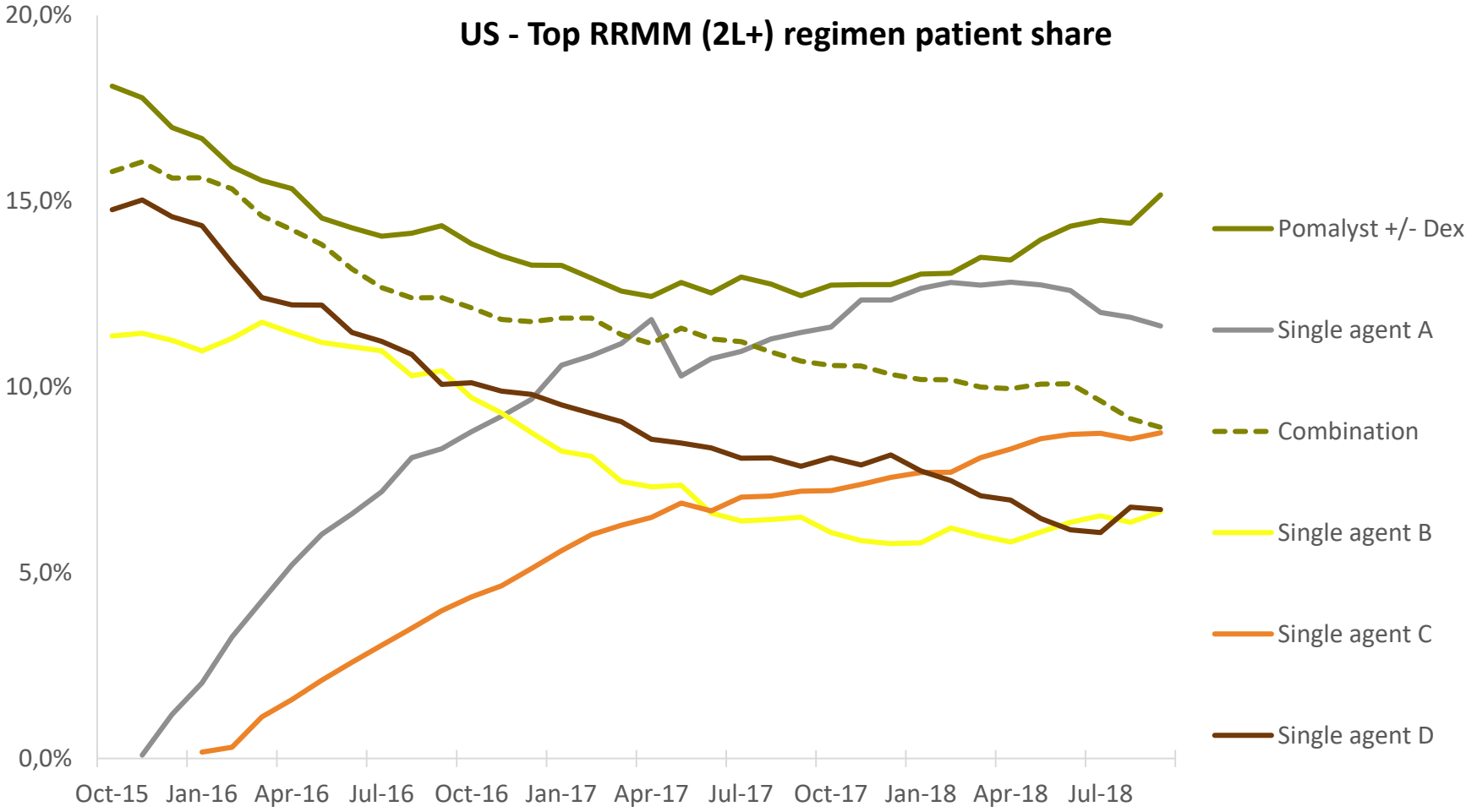
# Improved outcomes leads to fast growth in number of treated patients in later lines of therapy




Source: Intrinsiq Oct 2018, MAT
Note: 3-yr annual growth rate for 3Q15-3Q18

# Single agent +/- steroid predominantly used in 2 Line + despite guidelines

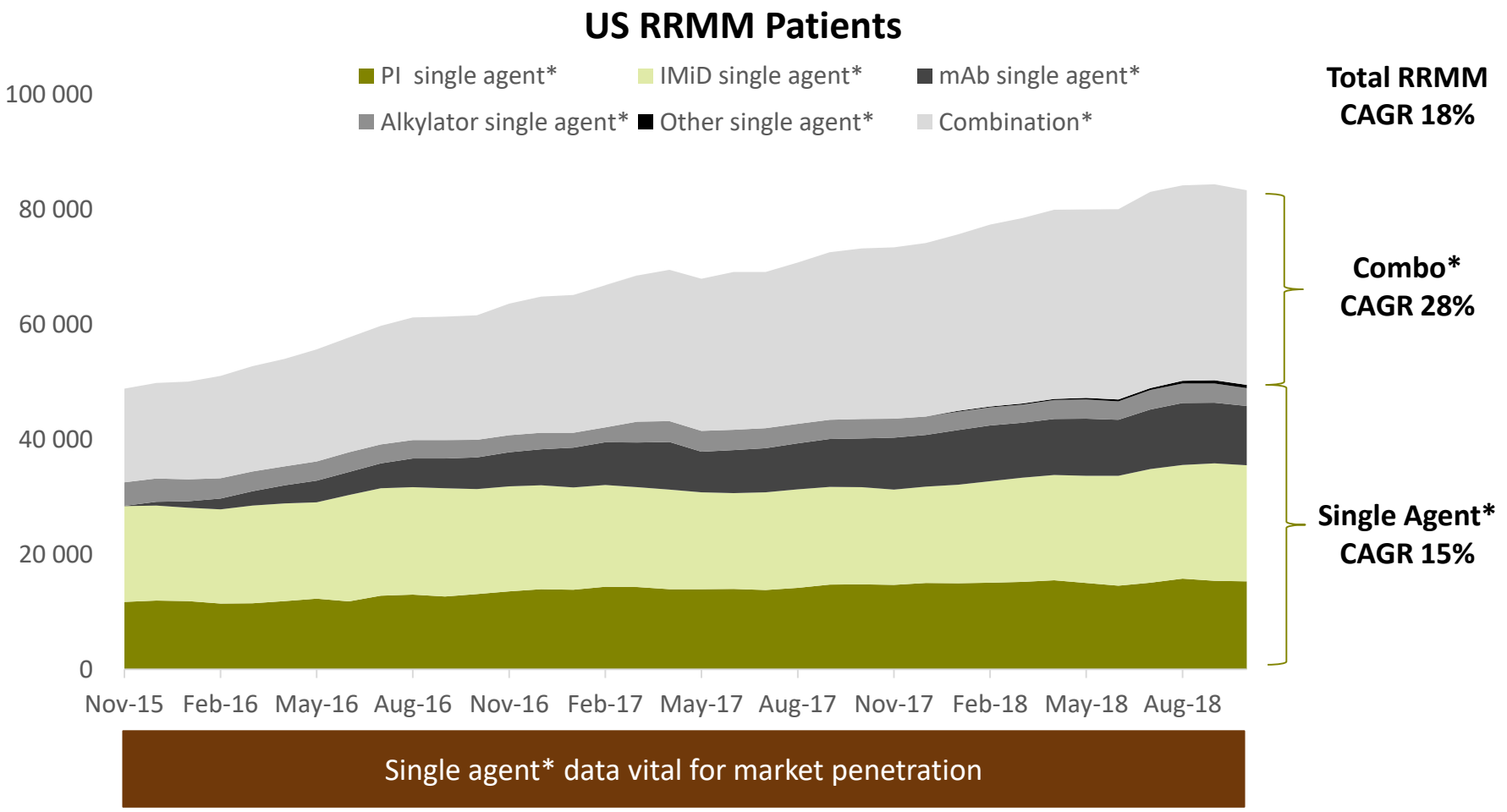
## Pomalyst is the most commonly used regimen in 2 Line + (US data)




Source: Intrinsiq, Sep MAT 2018
Note: Assume regimens include Dexamethasone although steroid use not reported. Regimens below 5% not shown.

# RRMM is the Fastest Growing Market Segment

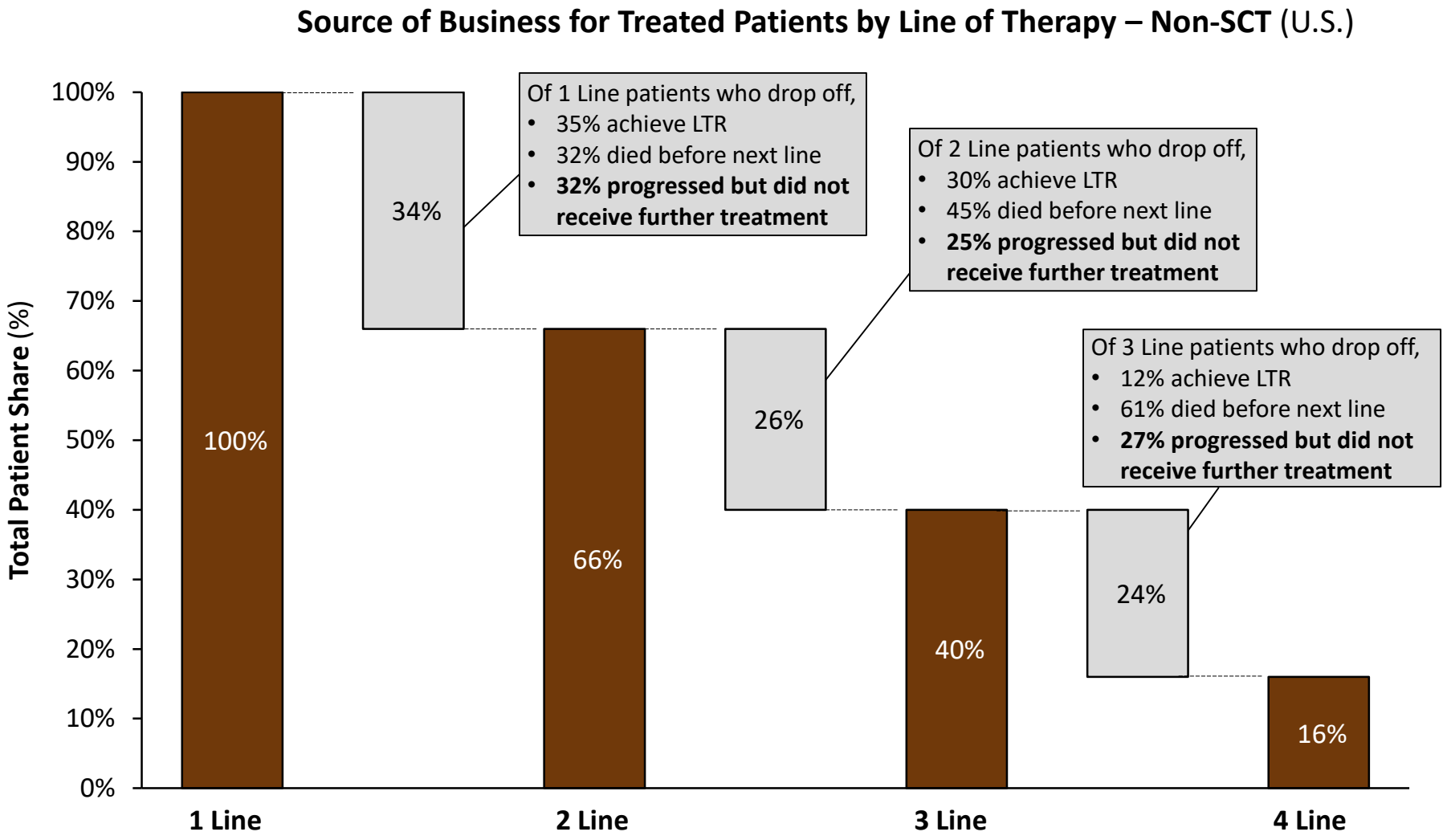
## Single Agents/dex used more although combination use is growing




Source: Intrinsiq Oct 2018, MAT
Growth shown as 3-yr CAGR
* Single agent is drug plus dexamethasone (± steroids)

# A significant number of patients do not tolerate additional therapy

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

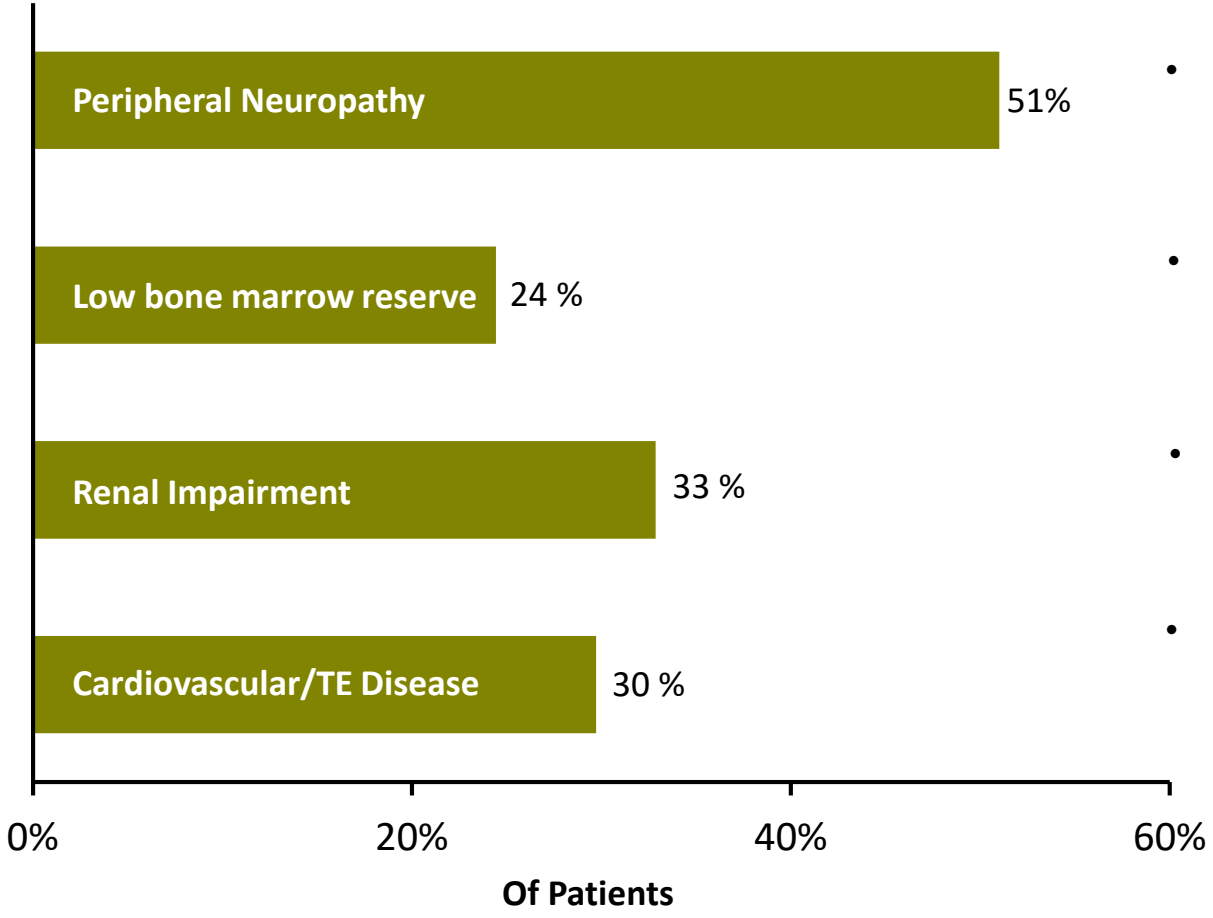



Source: Kantar Health
LTR: Long-Term Remission

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

## Comorbidity rates reflecting both qualitative research findings and literature reports

### Co-morbidities are common in Myeloma treatment



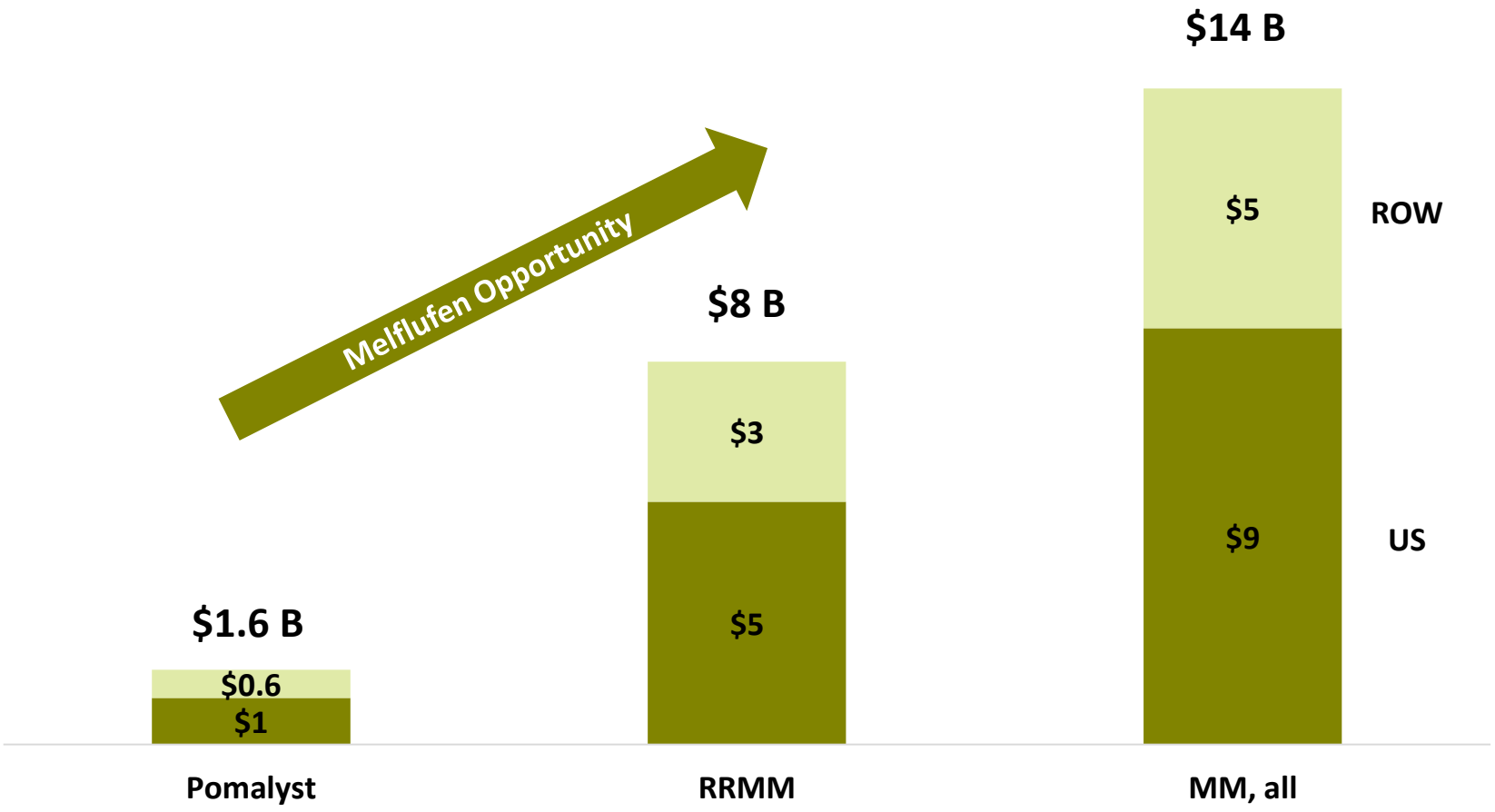

### Limits treatment options

- Acquired from protesome inhibitor treatment, diabetes and/or old age
- Acquired from disease progression or prior treatment
- Multiple Myeloma, age, diabetes, and/or cardiovascular related
- Acquired from prior therapy, age related (US population: 20% over 60 years, 25% over 80 years of age)

Source: Physician market research; Terpos, et al. *Eur J Haematol*, 2018.

# Melflufen opportunity in RRMM

## 2017 Multiple Myeloma Net Sales Breakdown

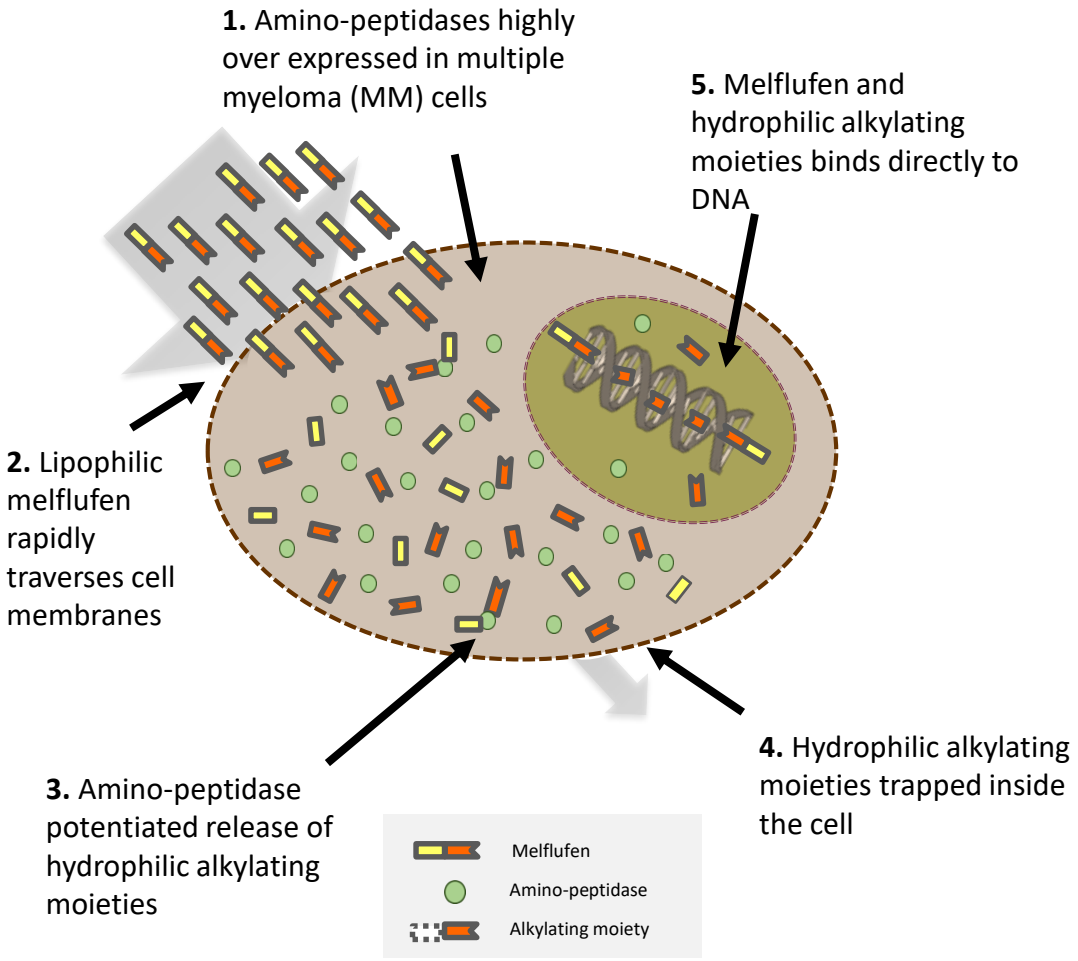



Source: EvaluatePharma, Intrinsiq, company analysis

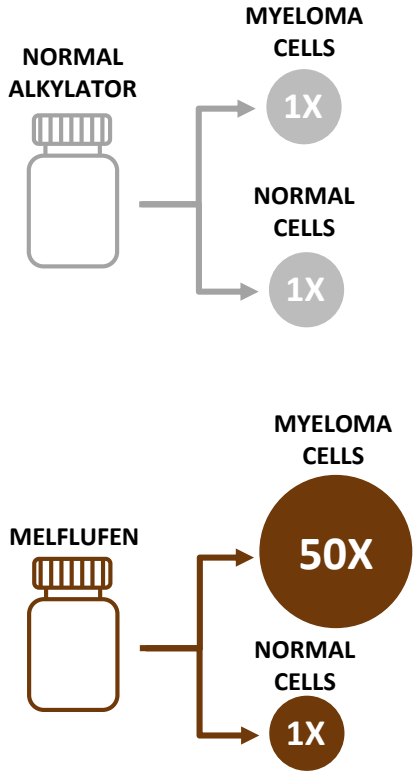
# Melflufen is a first in class peptide conjugated alkylator

## Aminopeptidases overexpressed up to 250x as part of transformation process

### Peptidase enhanced activity in Multiple Myeloma cells




### Results in 50-fold higher potency



# Melflufen is a highly differentiated selective compound

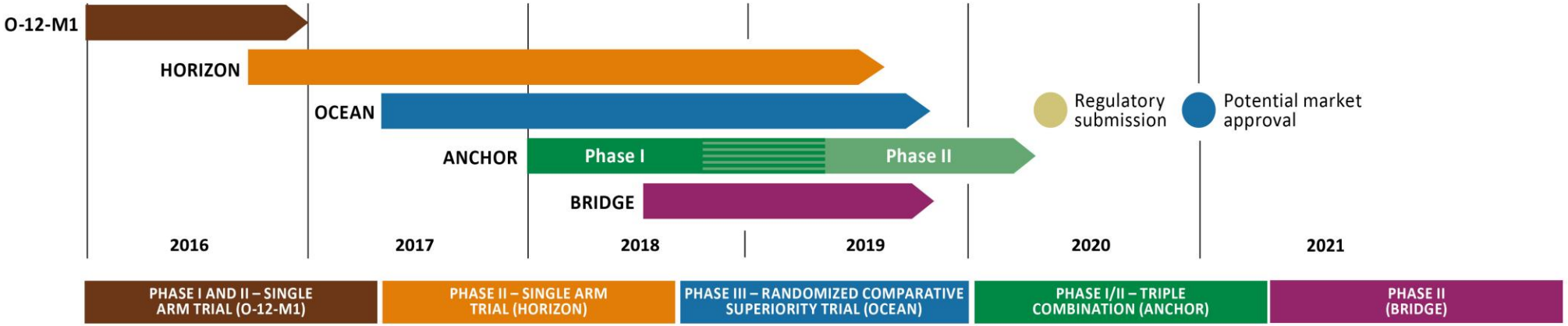
## Well positioned to become the next backbone agent in myeloma

- ✓ **Melflufen has a unique and well defined mechanism of action**
  - Does not share resistance mechanism with other classes
- ✓ **Phase 2 demonstrated the best overall survival data to date in late-stage myeloma**
  - Bone pain improvement seen in first-cycle of treatment
- ✓ **Well tolerated with limited adverse events negatively impacting patient quality of life**
  - Does not rely on renal excretion (renal function often severely impacted in myeloma)
- ✓ **Convenient once monthly 30 min infusion**
- ✓ **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

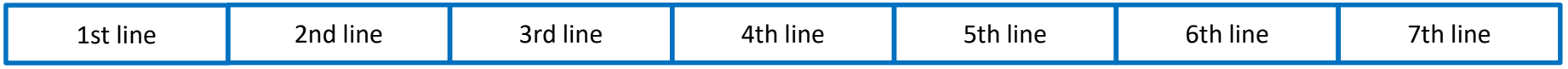
| Must have characteristics | Melflufen |
|---|---|
| • Single agent +/- steroid activity in multi-refractory patients of 20%+ ORR | • O-12-M1 showed an ORR of 31% and HORIZON an ORR of 32% in multi-refractory patients |
| • Single agent +/- steroid approval in refractory patients | • OCEAN is designed to give single-agent approval |
| • Efficacy synergy in combination with other main myeloma drugs with good tolerability | • ANCHOR, first dataset from ongoing trial was presented at ASH in December 2018 |
| • No major QoL tolerability issues | • Very good QoL with almost no non-hematological AEs |
| • No co-morbidity limitations | • No co-morbidity limitations, Drug-Drug Interaction |
| **Nice to have characteristics** | |
| • Easy administration schedule | • Once monthly 30min infusion |

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




| O-12-M1 | HORIZON | OCEAN | ANCHOR | BRIDGE |
|---|---|---|---|---|
| Show single-agent activity in RRMM | Show single-agent activity in RRMM | Show single-agent superiority over SoC in RRMM (pomalidomide) | Show combination synergy and tolerability with daratumumab and bortezomib | Show that melflufen can be used in patients with renal impairment |

# Overview of clinical data to date (ASH 2018)




ANCHOR

**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

O-12-M1

**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+)

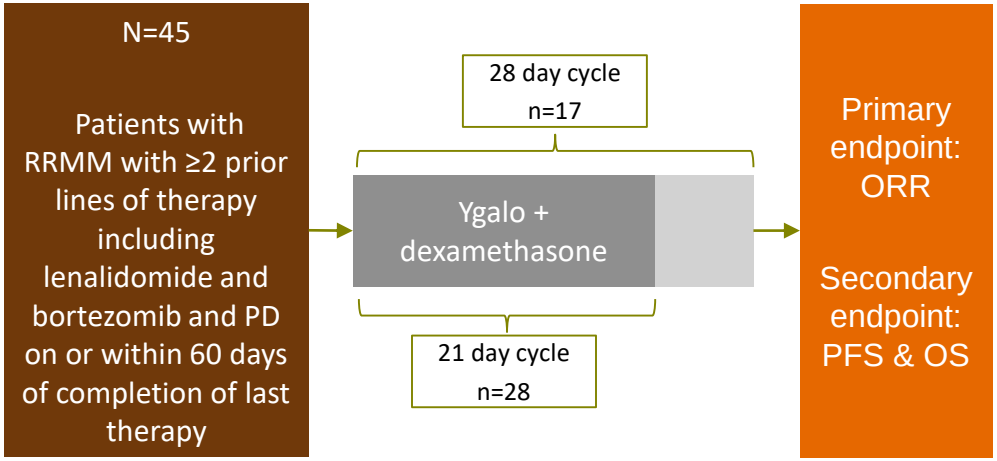
HORIZON

**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

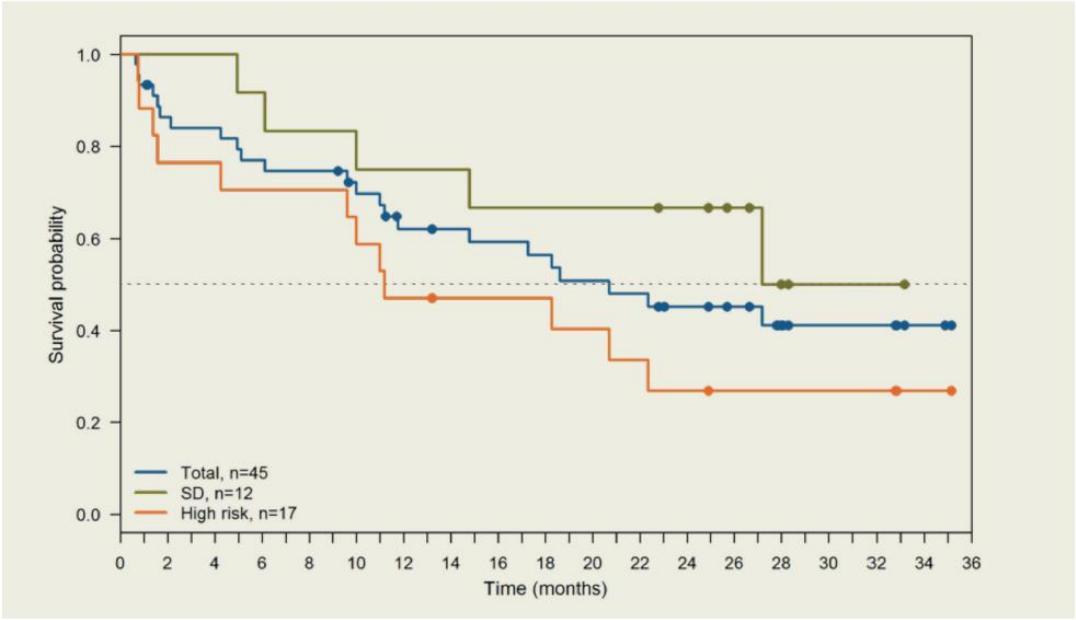



| | N = 45 |
|---|---|
| Median age, years (range) | 66 (47-78) |
| Years since diagnosis, median (range) | 5.1 (1.4 – 21.2) |
| Number of previous lines of therapy, median (range) | 4 (2-14) |
| ISS, stage at study entry, n (%) | |
| I | 15 (33) |
| II or III | 27 (60) |
| Unknown | 3 (7) |
| ECOG performance 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 demonstrated best-in-class survival data in late-stage RRMM




- >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)[1]** | 7 | 12 | 8 | 9 | 5 | 31% | 49% | 5.7 months (95% CI:3.7-9.3)[2] | 20.7 months (95% CI:11.8-∞)[3] |
| **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.

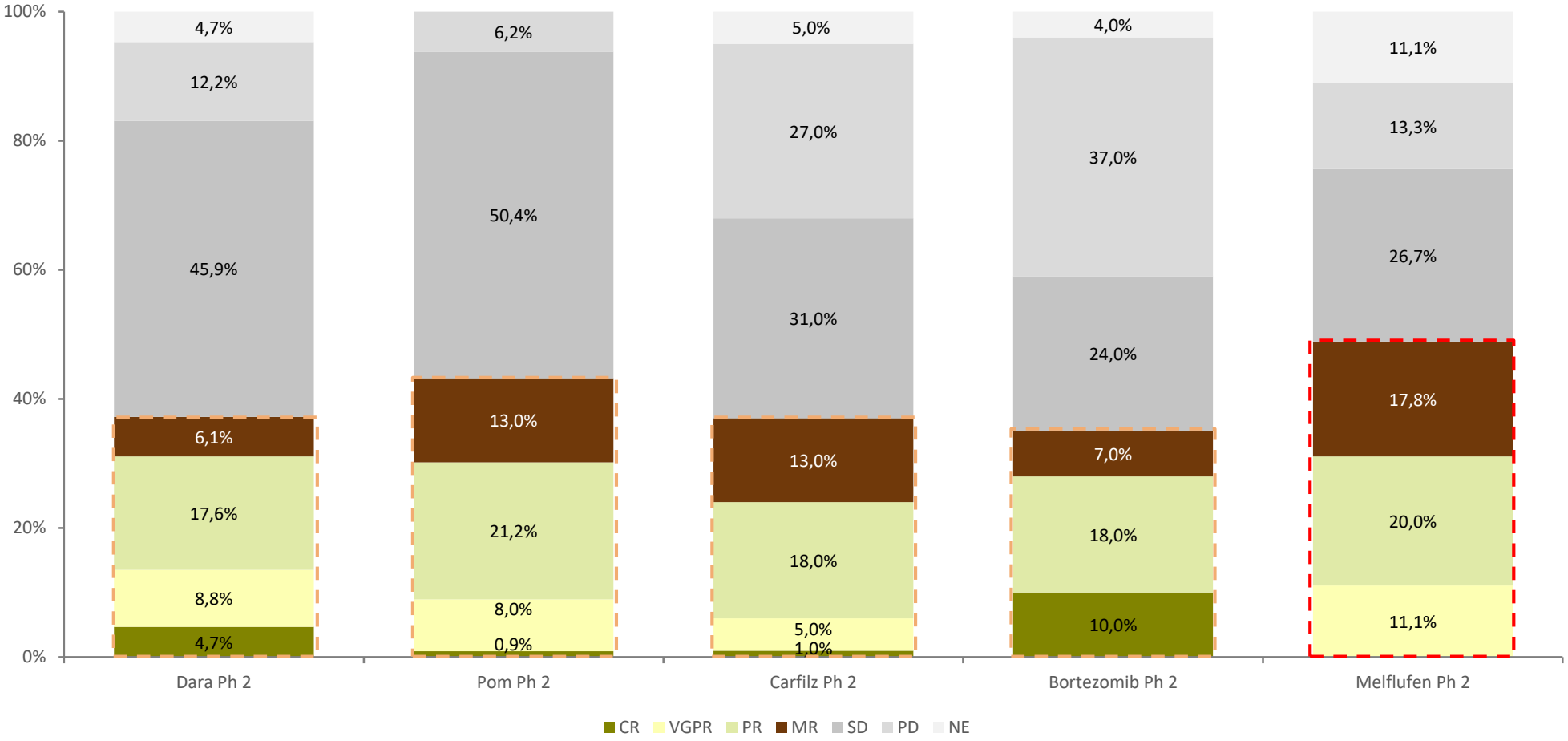
# Best overall survival data to date in late stage myeloma

| | Melflufen | Daratumumab | Pomalidomide* | Carfilzomib |
|---|---|---|---|---|
| **N** | 45 | 106 | 302 | 266 |
| **Year** | 2017 | 2016 | 2013 | 2012 |
| **Population** | 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 alklylator | >2 prior for relapsed including Bar, Len or thal, alk or anthra alone or in combo |
| **Time from diag.** | 5.0 years | 4.8 years | 5.3 years | 5.4 years |
| **High risk Cytog.** | 44% | 19% | ~30% | 28% |
| **Number of lines** | 4, 78% ≥3 lines | 5, 82% ≥3 lines | 5, 94 % ≥2 lines | 82% ≥4 lines |
| **Refract. to last** | 87% | 97% | 100.0% | 94.0% |
| **ORR** | 31.1% | 29.2% | 23.5% | 23.7% |
| **ORR high risk** | 25% | 20% | – | 29.6% |
| **Med. duration treat** | 3.7 months | - | Progressive Disease or Unacceptable Toxicity | 3.0 months |
| **Med. duration response** | 8.4 months | 7.4 months | 7.0 months | 7.8 months |
| **Median PFS** | 5.7 months (11.7 in ≥PR) | 3.7 months | 3.6 months | 3.7 months |
| **Median OS** | 20.7 months | 17.5 months | 12.4 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

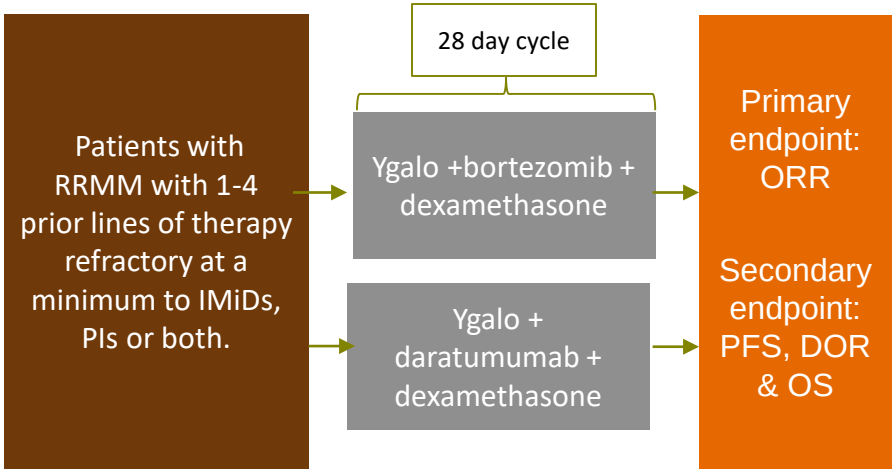
# Significant clinical benefit, in comparison with other approved drugs in late-stage RRMM




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

Source: ASH December 2018.

*Patients treated in combination with bortezomib can be bortezomib exposed but not refractory. Patients treated with daratumumab cannot be anti-CD38 exposed.

# ANCHOR – Interim data presented 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**

| | MELFLUFEN + DEX + BORTEZOMIB (N=3) | |
|---|---|---|
| CHARACTERISTICS | 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**

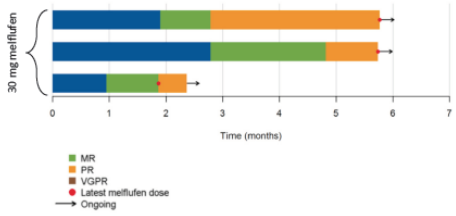
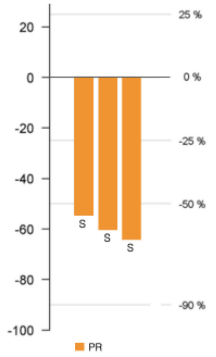



**Figure 5. Waterfall plot**




Source: ASH December 2018.

# ANCHOR – Interim data presented 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**

| | MELFLUFEN+BORTEZOMIB+DEX (N=9) | |
|---|---|---|
| CHARACTERISTICS | 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**

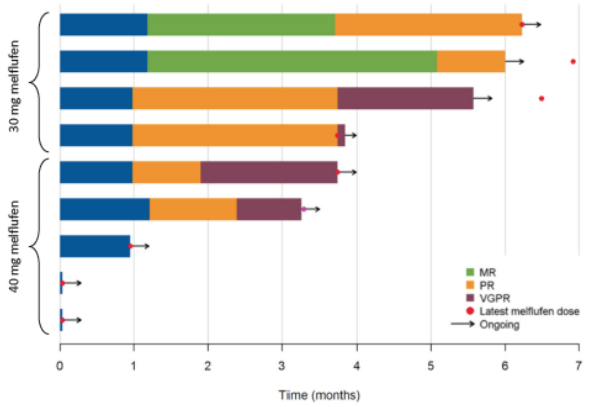
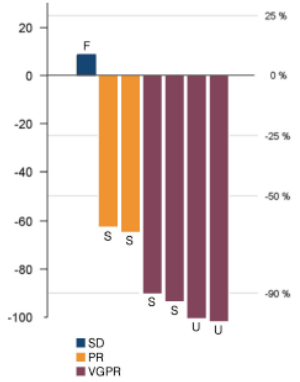


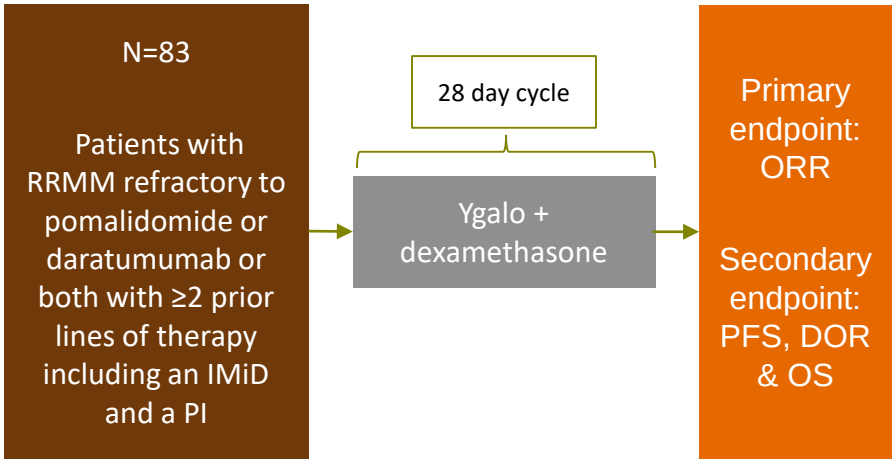

**Figure 7. Waterfall plot**




Source: ASH December 2018.

# HORIZON study overview

## Impact of Melflufen 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**

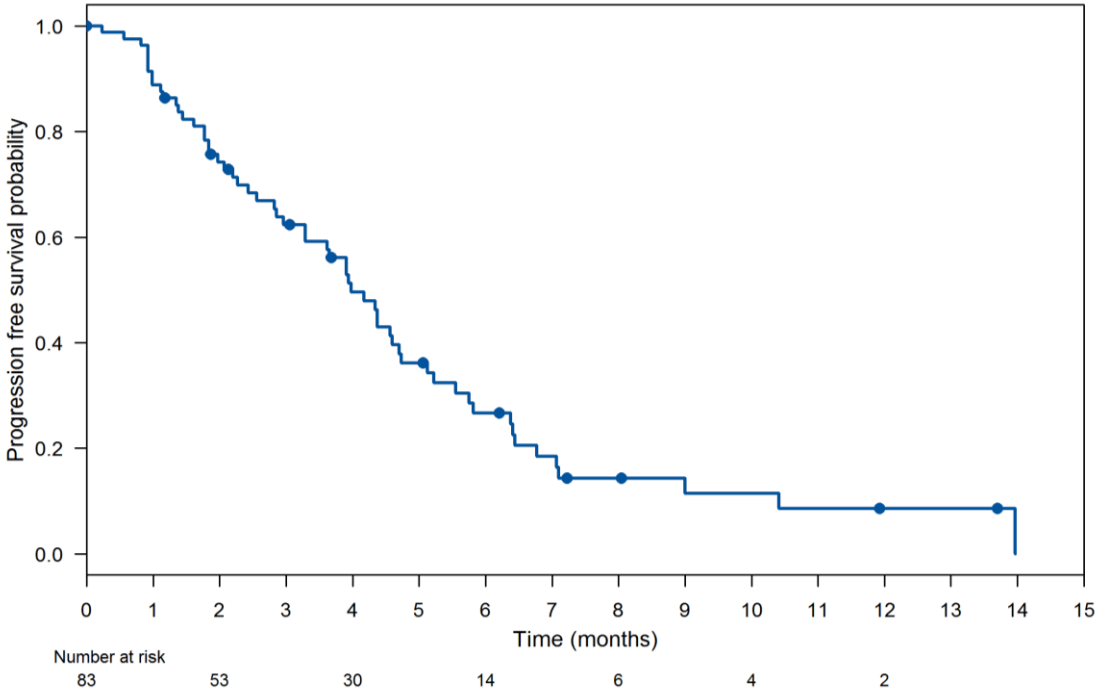
| | |
|---|---|
| Refractory to | % |
| Pom or dara | 100 |
| Pom and dara | 60 |
| Double refractory (PI+IMiD) | 86 |
| Double + anti-CD38 refractory | 60 |
| Monoclonal antibody (MoAb) | 80 |
| Alkylator exposed | 84 |
| Alkylator refractory | 55 |
| Received 1 ASCT / 2 ASCT | 69 / 25 |
| Refractory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

Source: ASH December 2018.
*Missing data for 3 patients.
** HR status data pending 7 missing in 23 patients

# Promising HORIZON results presented at ASH

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

| *sCR* | *VGPR* | *PR* |
|---|---|---|
| *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

Source: ASH December 2018.

# Very few non-hematological adverse events reported

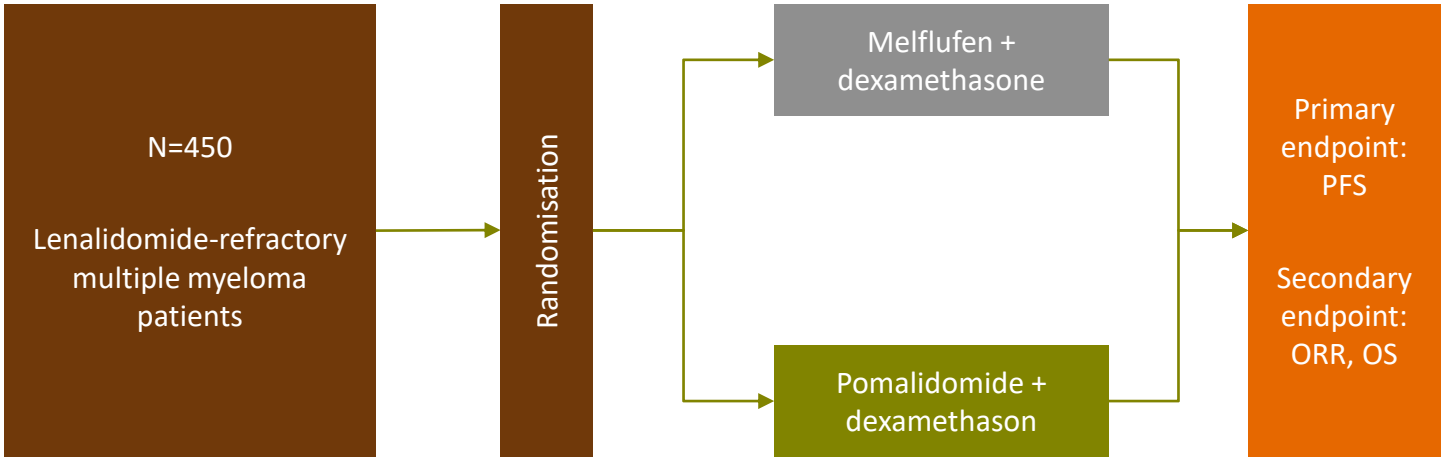
| | G3/G4 n (%) | G4 n (%) |
|---|---|---|
| Any treatment-related grade 3-4 AEs in ≥2 pts | 62 (75) | 42 (51) |
| Blood and lymphatic system disorders | 61 (73) | 41 (49) |
| Neutropenia | 51 (61) | 29 (35) |
| Thrombocytopenia | 49 (59) | 30 (36) |
| Anaemia | 21 (25) | 1 (1) |
| Febrile neutropenia | 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 Melflufen over standard-of-care in late-stage myeloma - a $8bn+ market opportunity




### Late-Stage Relapsed Refractory

OCEAN

| 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 |

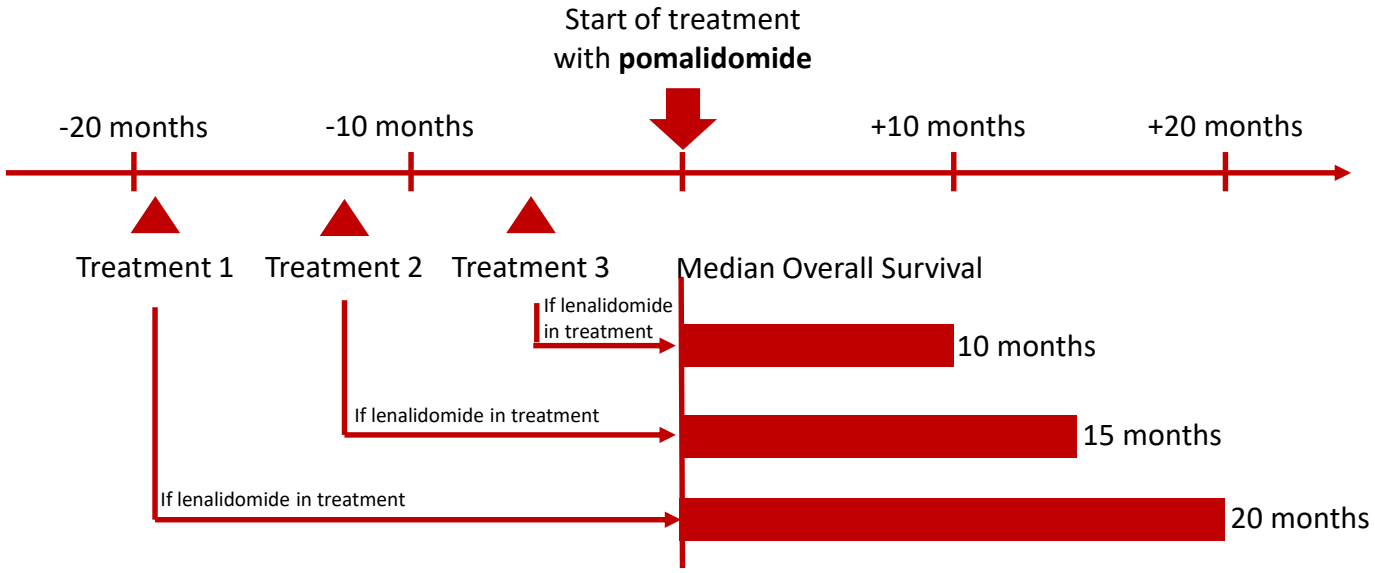
Note: NR=Not Reported. Ygalo® is not market approved.

Source: FDA Label.

# Pomalidomide shares resistance mechanism with lenalidomide

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

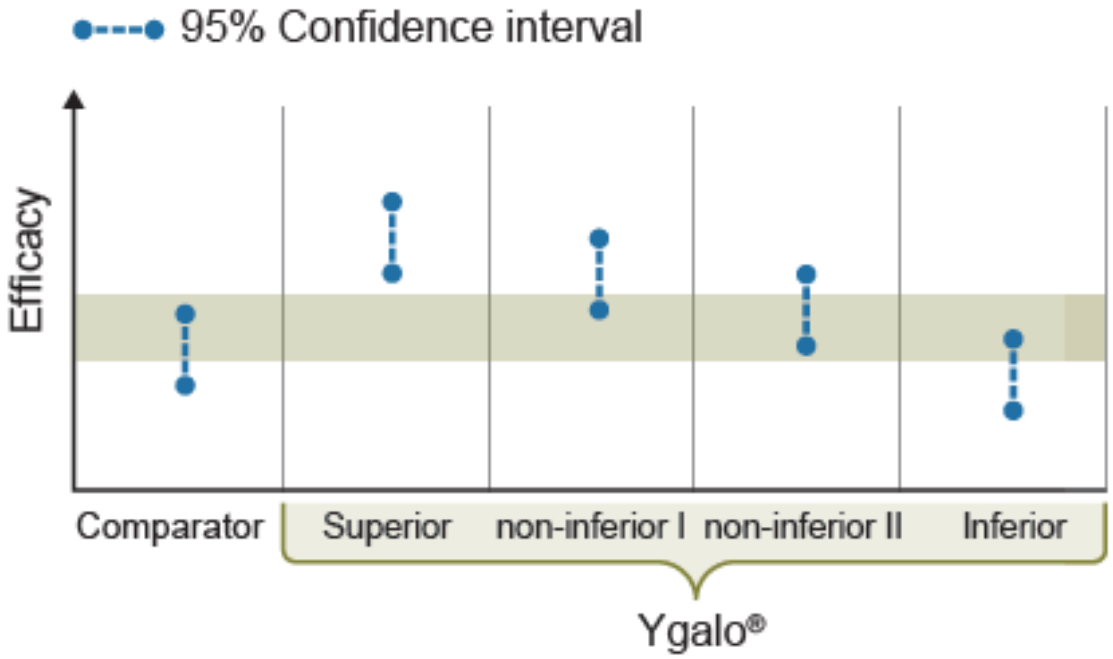
### Dimopoulos research supporting an IMiD free period




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

Source: Pomalidomide with Low Dose Dexamethasone Is Effective Irrespective of Primary or Secondary Resistance to Lenalidomide but the IMiD-Free Interval Is Important (Dimopoulos et. al. ASH poster 2016).

# 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 clearence not required for melflufen (Ygalo®) (BRIDGE)

Source: IntrinsiQ September 2017. US data.

# Patient recruitment across ANCHOR, HORIZON and OCEAN

- Patient recruitment in HORIZON is above forecast
- Patient recruitment in ANCHOR is above forecast
- In Q3 2018, the Company reported that patient recruitment was below forecast in OCEAN driven in part by the fact that pomalidomide is moving to a 2nd line treatment position (off-label)
  - Strong positive with regard to the addressable market
  - Negative for OCEAN patient recruitment
- Two measures have been implemented to be able to still meet the target of last-patient-in in Summer of 2019
  - Increasing the number of centers/hospitals that participate in OCEAN
  - Amend the OCEAN protocol to allow 2$^{nd}$ line patients to be included in the US (under certain conditions)
- The increase in number of hospitals that participate in OCEAN has been implemented slightly slower than plan
  - Forecast remains to deliver last-patient-in in Summer of 2019
  - Exact impact of the additional hospitals will be known first during the Spring of 2019

# Strategic Direction 2019

- Deliver on current plan and trials
  - Continue the build-up of commercial and medical relation capabilities to ensure stand-alone launch capacity
- Expand clinical trial footprint in multiple myeloma with melflufen
  - Explore more combination arms in ANCHOR where we will use melflufen as rescue after daratumumab failure (in addition to daratumumab and dexamethasone)
  - Evaluate randomized phase 2b trials with the ambition to initiate at least one combination treatment that includes melflufen for potential label extensions beyond OCEAN/ HORIZON
- Fully characterize melflufen's activity with regard to bone pain and extra medullary disease
- New indications, clinical trial synopsis already developed for amyloidosis, could potentially be initiated during H2 2019
- Initiate clinical trials in ASCT (bone marrow ablation) with OPD5 (new NCE) during H2 2019
- Further the pre-clinical development of our three NCEs