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

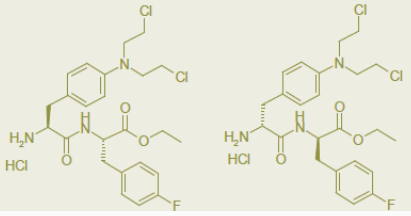
Figure 1-1 Structural formula of melflufen hydrochloride

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

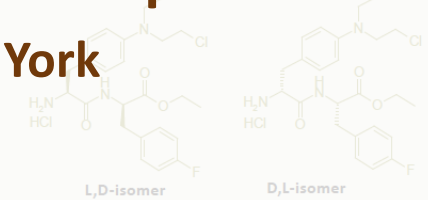
Solubility
Melflufen hydrochloride is soluble in most organic solvents. The solubility in water and buffers is limited.

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 figure



Melflufen - A new potential backbone for relapsed multiple myeloma

Capital Markets Day | 14 December 2018 | New York

Jakob Lindberg CEO

Disclaimer

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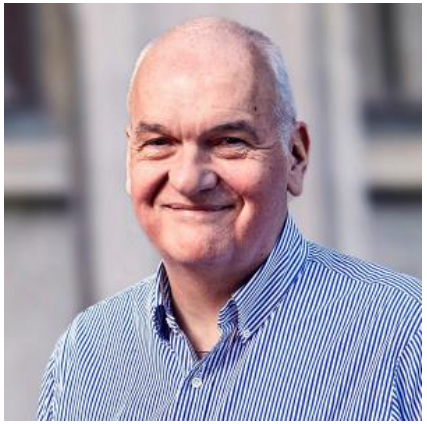
Oncopeptides Capital Markets Day Program, December 14th, 2018

8.30 – 09.00	**Introduction to Oncopeptides including a Clinical Trials Overview** *Jakob Lindberg, CEO of Oncopeptides*
9.00 – 09.45	**HORIZON and ANCHOR Trials Data Update** *Professor Paul G Richardson, Dana-Farber Cancer Institute*
9.45 – 9.50	**Short Break**
09.50 – 10.10	**The Evolving Myeloma Treatment Landscape and the Position of Melflufen** *Paula Boultbee, CCO at Oncopeptides*
10.10 – 10.40	**Panel discussion and Q&A** *Professor Paul G Richardson, Dana-Farber Cancer Institute* *Jakob Lindberg, CEO of Oncopeptides* *Christian Jacques, MD, MSc, EVP Clinical Strategy and Chief Scientific Officer* *Paula Boultbee, CCO at Oncopeptides*
10.40 – 11.00	**Summary and Conclusions** *Jakob Lindberg, CEO of Oncopeptides*

Today’s presenters

Oncopeptides’ Capital Markets Day – December 14th

Professor Paul G Richardson, Dana-Farber Cancer Institute



Christian Jacques, MD, MSc, EVP Clinical Strategy and Chief Scientific Officer

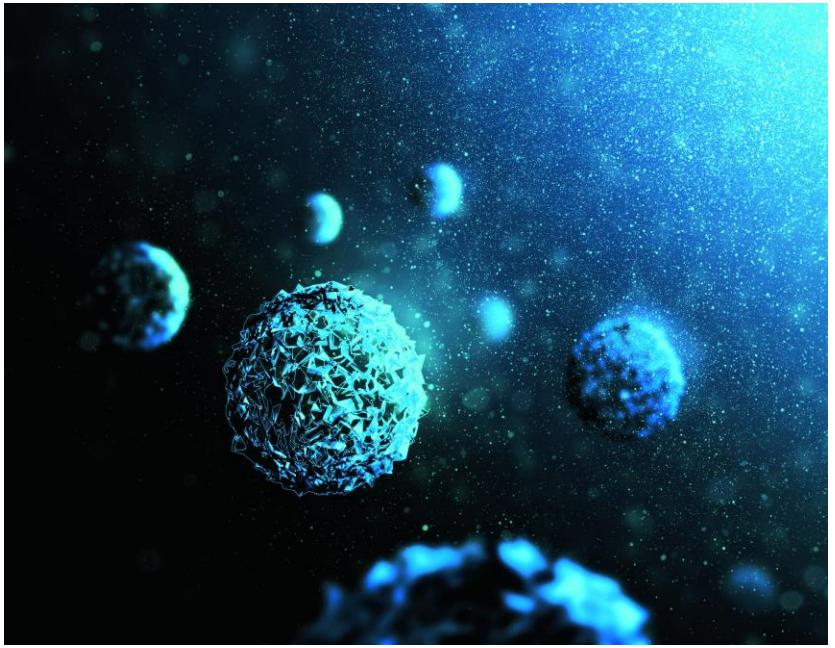
Jakob Lindberg, CEO of Oncopeptides

Paula Boultbee, CCO at Oncopeptides

Oncopeptides overview

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

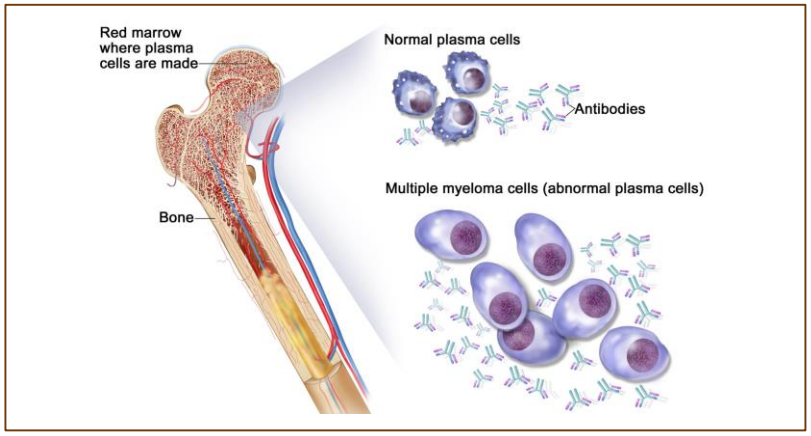
- **Develops targeted cancer treatments**
  - Proprietary peptidase-enhanced compounds
  - Lead compound Melflufen a peptide conjugated alkylator for Multiple Myeloma
- **Significant unmet needs in Multiple Myeloma**
  - Melflufen Phase 2 showed the best RRMM survival data to date
- **Melflufen Phase 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 $725 M
  - Cash position Sep. 30, 2018: $54 M
- **New indications and NCEs in development**
  - Clinical trials expected to start in 2019



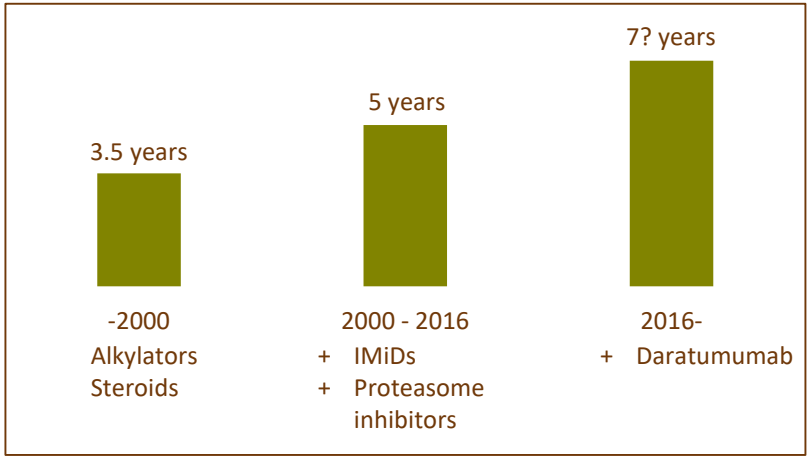
Almost all multiple myeloma patients receive broad spectrum agents

Treatment paradigm rapidly evolving with increased use of backbone agents

Myeloma – Uncontrolled plasma cell proliferation



Median Survival increasing with more available treatment options

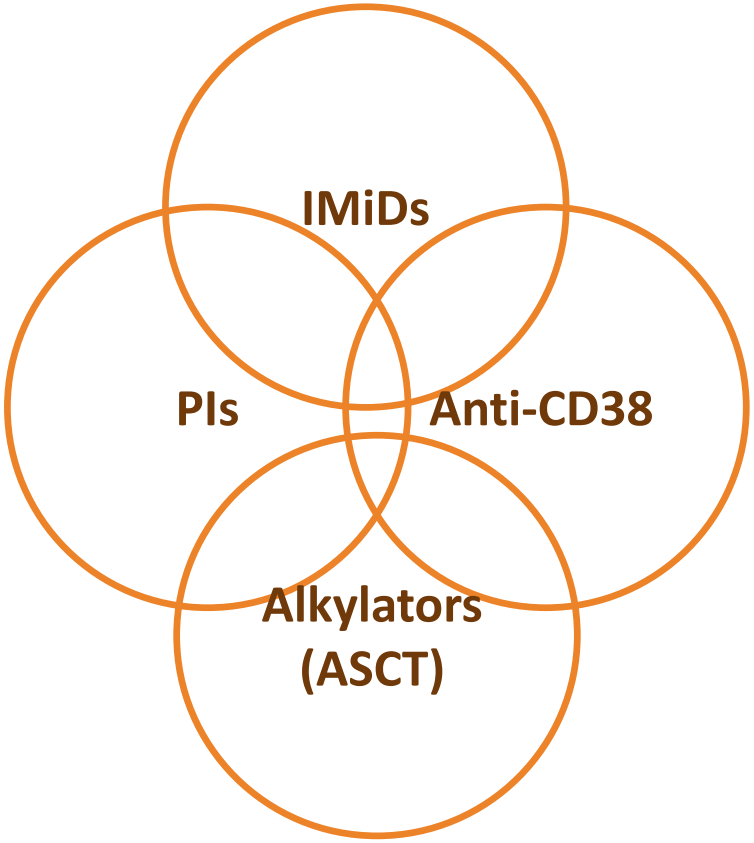


- Overall survival increasing but clonal selection results in inevitable relapse and treatment resistance
- 9 out of 10 patients receive broad spectrum agents (IMiDs, PIs and/or alkylators)
  - No ubiquitously expressed antigens in myeloma
  - Antibody-based therapies used in combination with IMiDs, PIs and alkylators
- New targeted agents are growing the patient population
  - 4th+ line patients receiving treatment in the US grew by >20% 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)



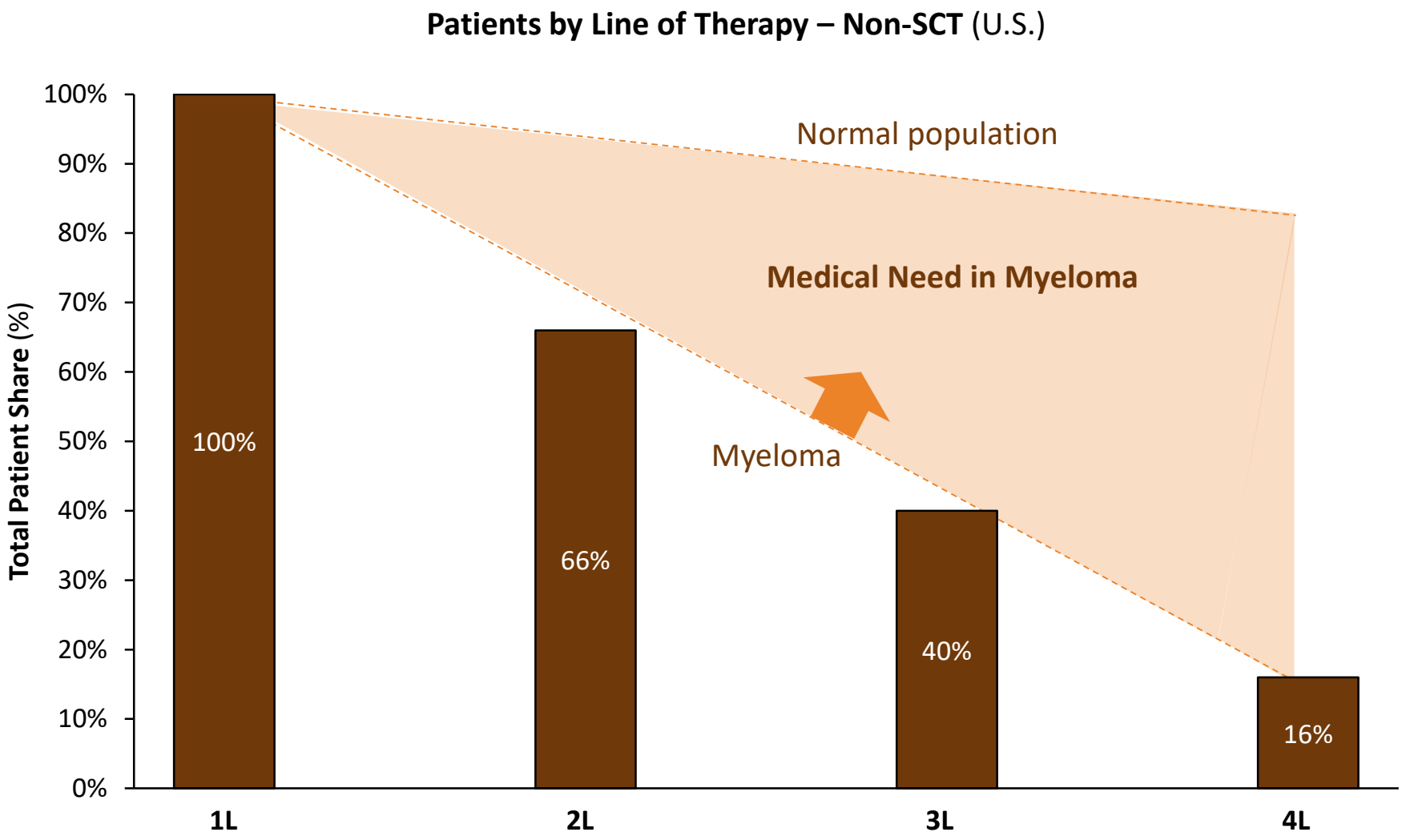
Current treatment algorithm development

- 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

The medical need in myeloma

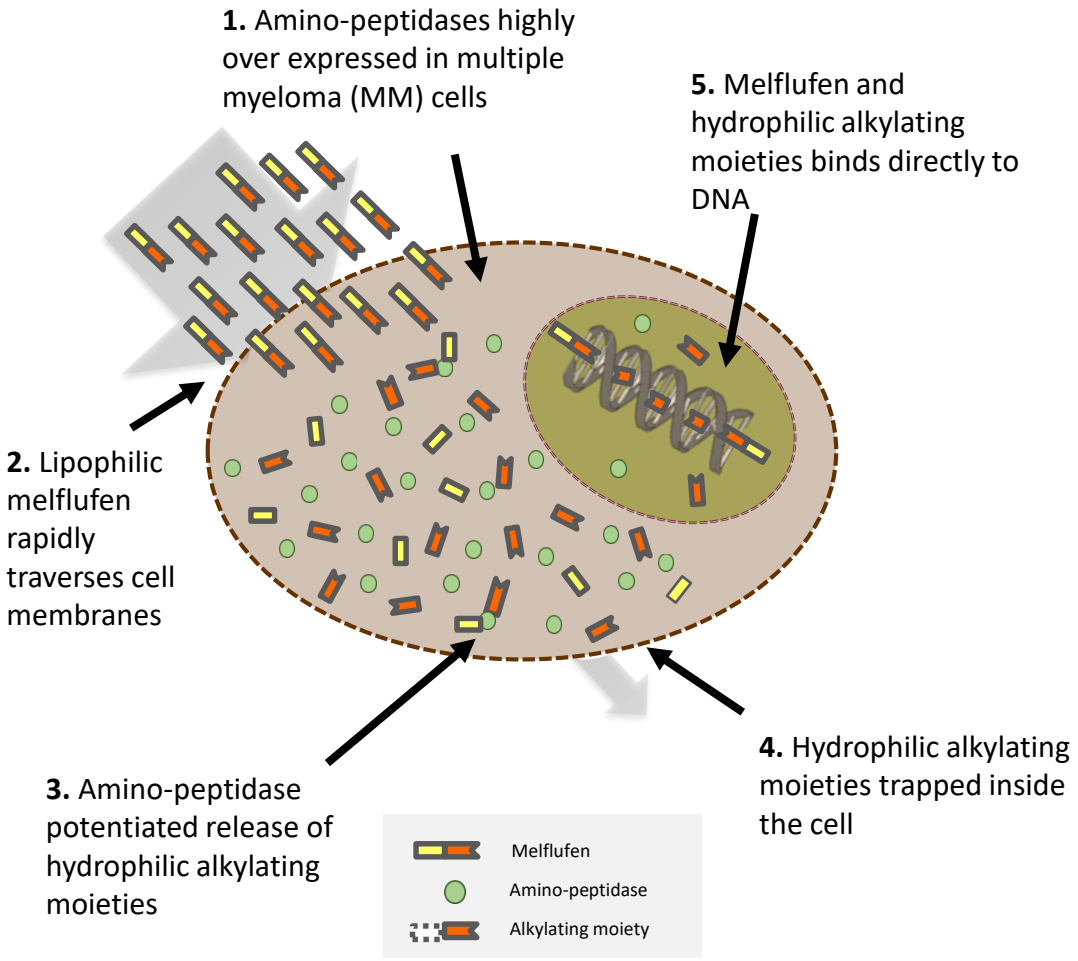
A patient that has been exposed to IMiDs, PIs, and anti-CD38 with increasing signals of intolerance and/or drug resistance

- Rapidly growing patient population
- No real options outside clinical trials apart from retreatment with IMiDs, PIs and anti-CD38

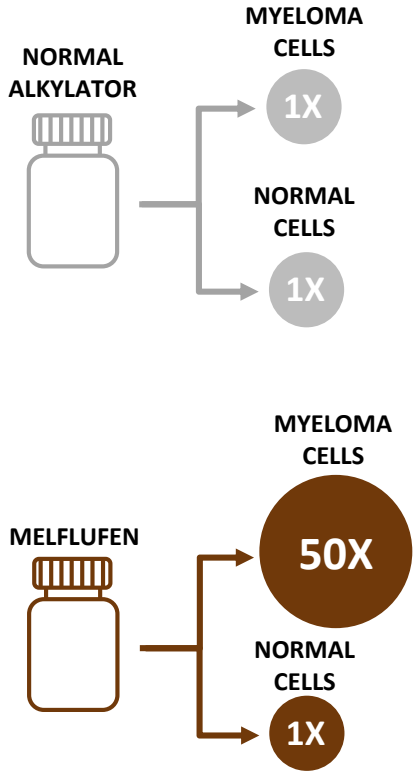
Melflufen is a first in class peptide conjugated alkylator

Aminopeptidases overexpressed up to 250x as part of transformation process

Peptidase enhanced activity in Multiple Myeloma cells



Results in 50-fold higher potency

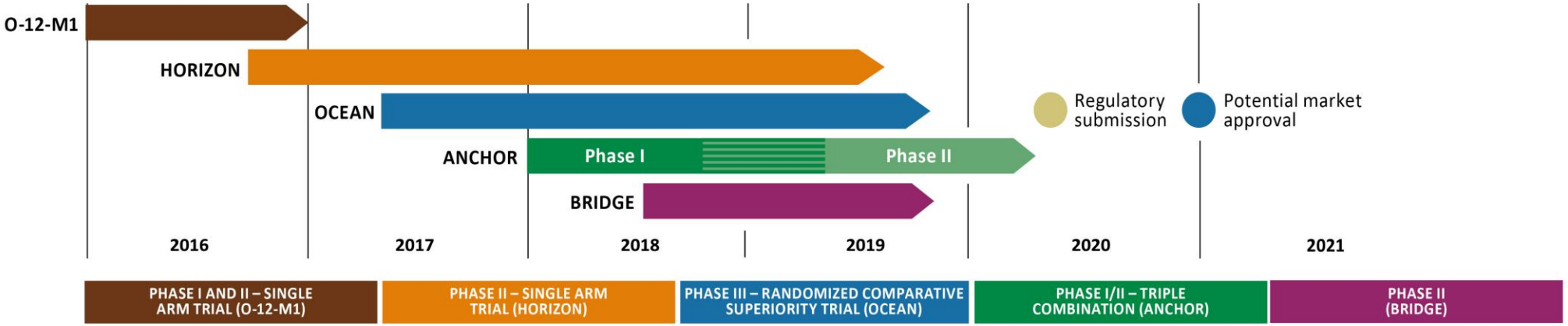


Melflufen (Ygalo®) is a highly differentiated selective compound

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
  - Clear signal in patients with extramedullary disease
- ✓ **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**

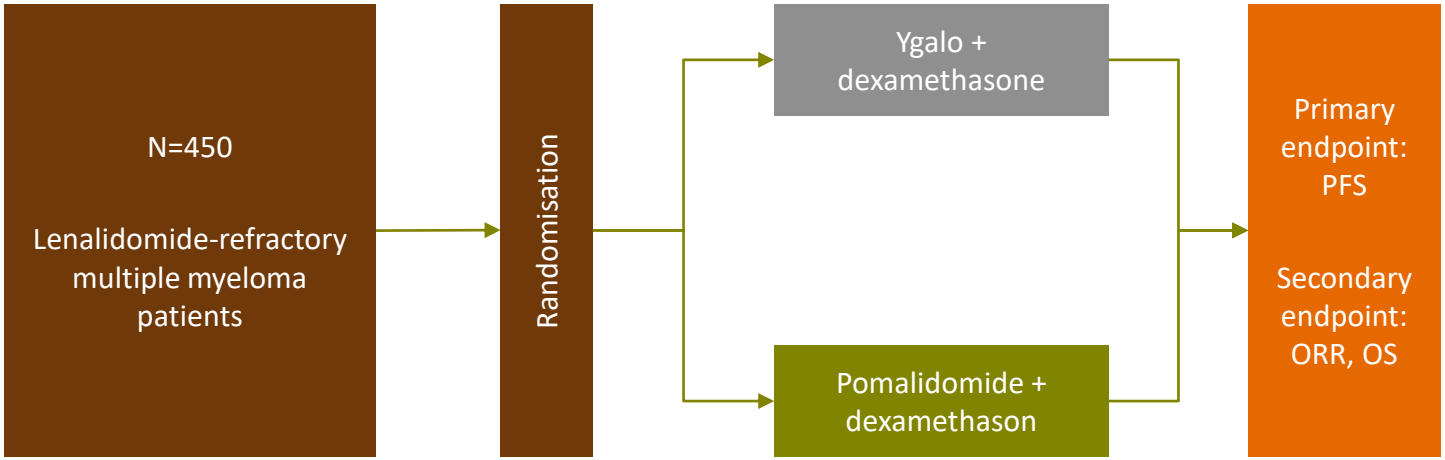
Our clinical development program is designed to establish a potential new back-bone in RRMM



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 backbone in RRMM (pomalidomide)	Show combination synergy and tolerability with daratumumab and bortezomib	Show that melflufen can be used in patients with renal impairment

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 $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

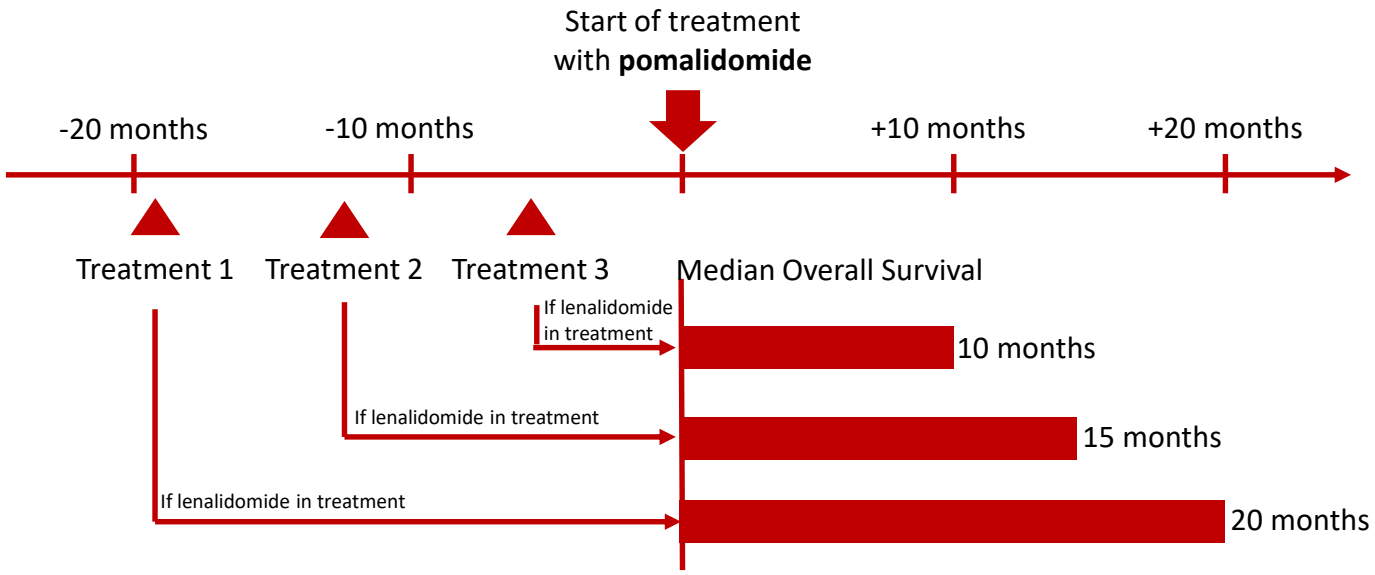
Note: NR=Not Reported. Ygalo® is not market approved.

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).

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

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

Pomalidomide+dex in lenalidomide-refractory pts

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

Source: Dimopolous et al, 2014. Siegel et al, 2017 .

Competitive landscape in multiple myeloma

Less competition than what meets the eye

IMiDs	Thalidomide	Lenalidomide	Pomnalidomide	Cellmods
PIs	Bortezomib	Carfilzomib	Ixazomib	New ones?
Anti-CD38	Daratumumab	Sub-cut. dara	Isatuximab	
Anti-BCL2	Venetoclax			
Anti-BCMA	bb2121(7)	GSK916	AMG420	Legend/J&J CAR-T
Nuclear Pore inh.	Selinexor			
Check-point inh.	Nivolumab	Pembrolizumab		

Competitive landscape in multiple myeloma (cont.)

Less competition than what meets the eye

Venetoclax

- Anti-BCL2 agent that inhibits one of the main proteasome inhibition pathways
- Strong data in BCL2+ myeloma once induced (patient sub-population)
- *Key question: How strong will the data be together with a PI before BCL2+, i.e. should it be given together with a PI upfront or together with a PI in a subset of patients after BCL2+ resistance development?*

Selinexor

- Nuclear pore inhibitor with activity as a single agent (+steroid) in multi-refractory patients
- Multiple studies ongoing
- Tolerability issues due to common GI toxicity and fatigue/asthenia
- *Key question: What impact will the GI toxicity have on the use of the drug?*

Competitive landscape in multiple myeloma (cont.)

Less competition than what meets the eye

Anti-BCMA

- BCMA is a very good target in myeloma – there will be an anti-BCMA therapy in myeloma. No data to suggest anything else than shared resistance between the various investigational new drugs.
- Very good response data across different investigational drugs
- Responses have durability problems across different investigational drugs
- Seemingly no difference between cell-based (bb2121(7) and Legend) and anti-body based approaches (GSK916 and AMG420)
- The CAR-T programs have a complexity and cost challenge due to comparable data with the antibody based approaches
- The antibody based approaches have challenges due to toxicity (GSK916 and AMG420) and administration (AMG420)
- *Key question: With no perfect approach in development, what anti-BCMA approach will succeed?*

Future treatment landscape in myeloma

- **Overall thoughts regarding the field of myeloma treatment**
- **Reflections from ASH2018**

Expanding our development program – Multiple Myeloma

Positive data should result in more clinical studies

Expanded Combination Studies

- Explore more combinations in ANCHOR in addition to bortezomib and daratumumab
- MERMAID to be initiated where we will use melflufen as rescue after daratumumab failure (in addition to daratumumab and dexamethasone)
- Explore randomized phase 2b studies (e.g. melflufen+daratumumab+dex vs. daratumumab+dex) for potential label extensions beyond OCEAN/ HORIZON

Explore Activity with Regard to Bone Pain and Extramedullary Disease

- Collate data from all current and historical trials regarding bone pain and extramedullary disease (ongoing)
- Potentially initiate small trials to specifically explore the observed activity

Expanding our development program – Multiple Myeloma

Positive data should result in more clinical studies

New Indications

- Clinical Trial synopsis already developed for amyloidosis. Clinical trial can be initiated in 2019

New Molecular Entities

- Focus on hematological oncology
- OPD5 – Novel peptide conjugated alkylator designed for ASCT (bone marrow ablation). Trials can be initiated in H2 2019.
- Three NCEs in pre-clinical development with aim to have at least one additional NCE ready for clinical development in 2020

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
  - Evaluate randomized phase 2b trials with the ambition to initiate at least one combination treatment that includes melflufen
- Fully characterize melflufen's activity with regard to bone pain and extra medullary disease
- Initiate clinical trials in ASCT with OPD5 (new NCE)
- Further the pre-clinical development of our three NCEs

Clinical Results in Multiple Myeloma (MM) with Melflufen: Current Status and Future Directions

Paul G. Richardson, MD
RJ Corman Professor of Medicine
Harvard Medical School

Clinical Program Leader, Director of Clinical Research
Jerome Lipper Multiple Myeloma Center
Dana-Farber Cancer Institute
Boston, Massachusetts

NYC, December 2018

DISCLOSURES

- Advisory Boards/Educational Symposia
  - Celgene Corporation, Novartis, Takeda, Oncopeptides, Karyopharm
- Consultant
  - None
- Honoraria
  - None
- Research Funding
  - Celgene, Takeda, Oncopeptides, Bristol-Myers Squibb

Key Targets in MM 2018

Genomic abnormalities:

- Target and Overcome Mutations
- Critical Role of Combination Therapy
- Evolving Position and Timing of ASCT

Excess Protein Production:

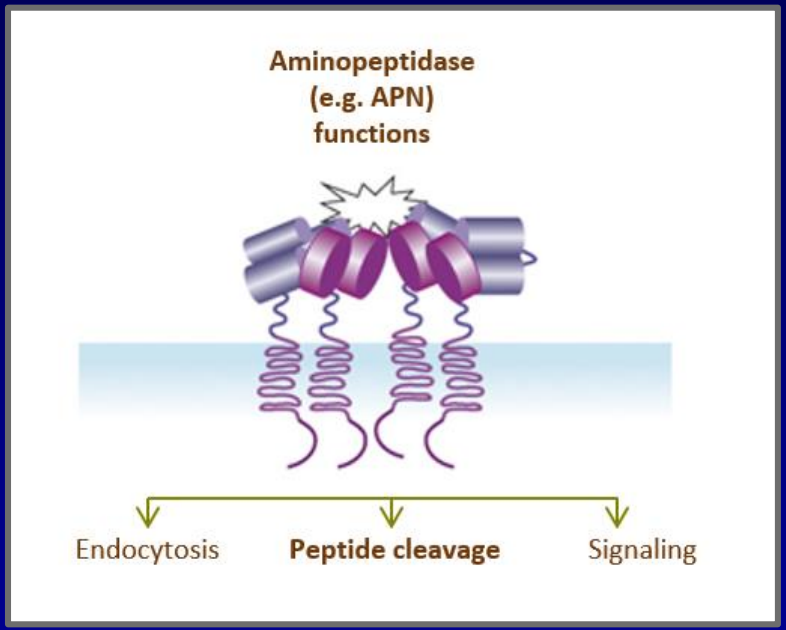
- Target Protein Degradation and Related Pathways

Immune Suppression:

- Restore anti-MM immunity

Aminopeptidases in MM
Key Functional Role in Multiple Myeloma

- Aminopeptidases (APs) are Zn2+ metalloenzymes that catalyze the cleavage of amino acids at the N-terminus of peptides and proteins by hydrolysis of peptide bonds
- APs operate downstream of ubiquitin-proteasome pathway and play a key role in protein homeostasis
- APs are also involved in key processes such as DNA repair, cell-cycle progression, signal transduction, transcriptional regulation, gene expression essential for immune response, development and programmed cell death



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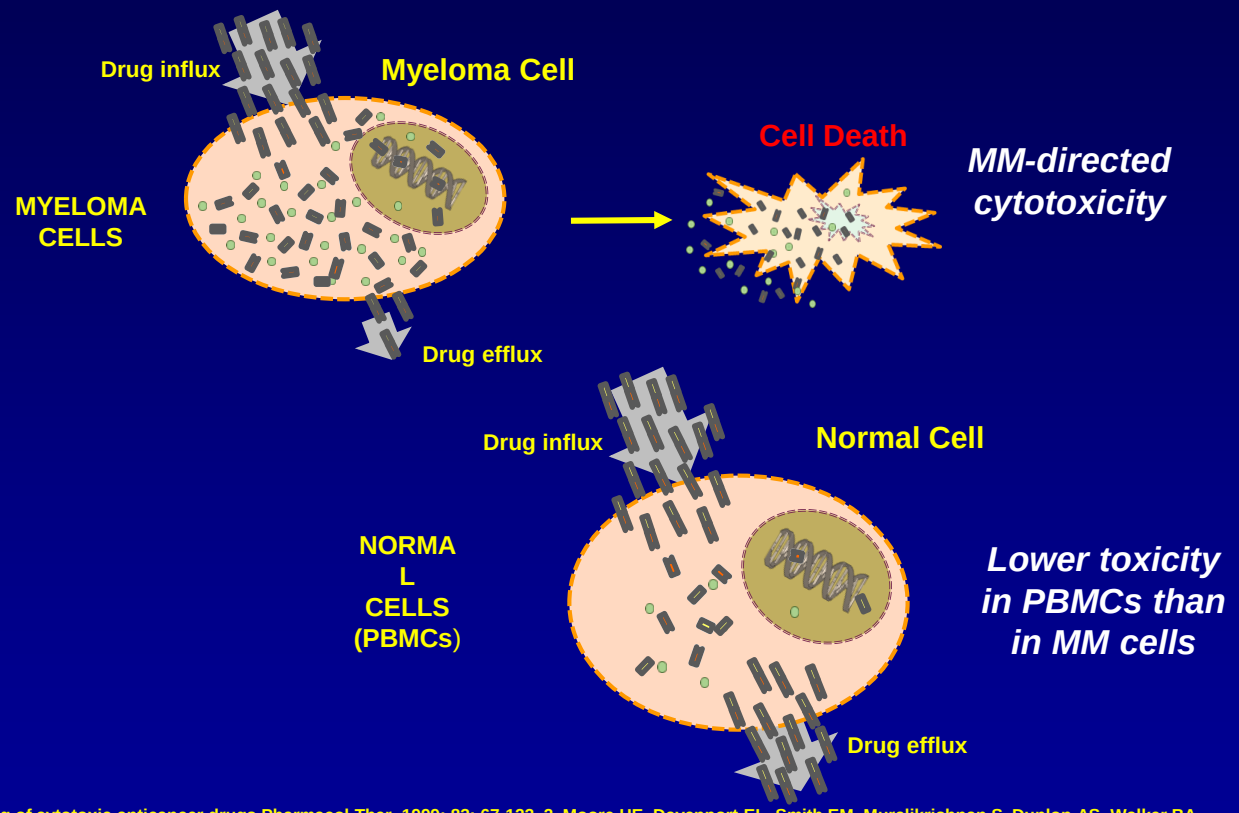
Melflufen – a Novel Targeted Alkylating Peptide: Mechanism of Action

Selectively targeting Myeloma as a first in class Aminopeptidase Enhanced Compound

- Aminopeptidases are overexpressed in several cancers including MM[1,2,3]
- Aminopeptidases enrich alkylating metabolites of melflufen in MM more than 50-fold compared to melphalan[4]
- Increase in cytotoxicity is selectively directed to MM cells and not to peripheral blood mononuclear cells (PBMCs)
  e.g. T cells, B cells[4,5,6]



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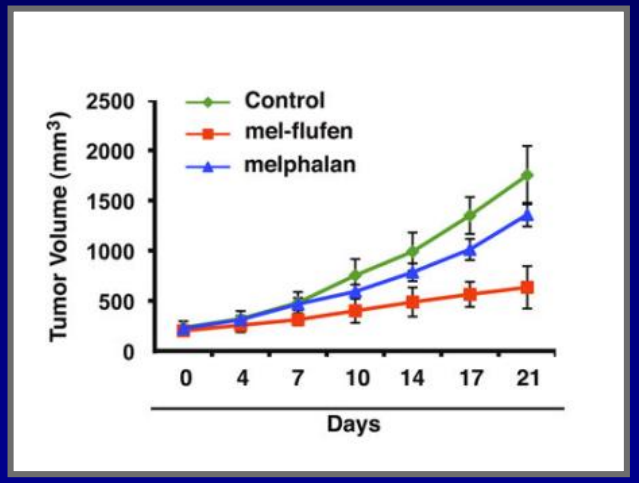
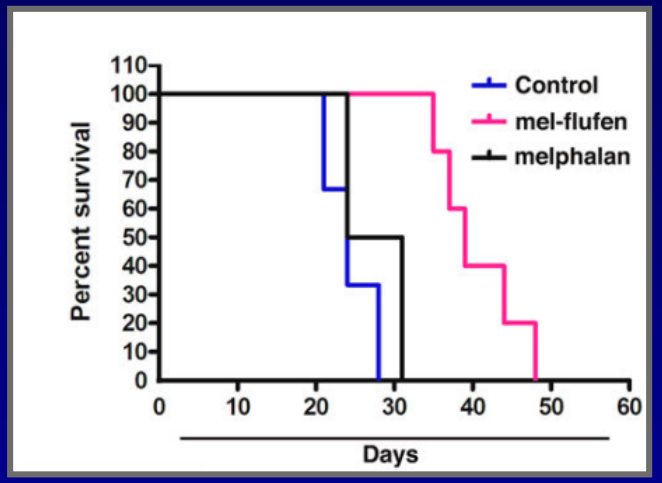
Melflufen Selective Cytotoxicity:
In vivo Efficacy

- ***In vivo*** **human xenograft mouse models treated with melflufen showed**
  - **Higher inhibition of tumor growth**
  - **Prolonged survival than those treated with alkylators such as melphalan alone**



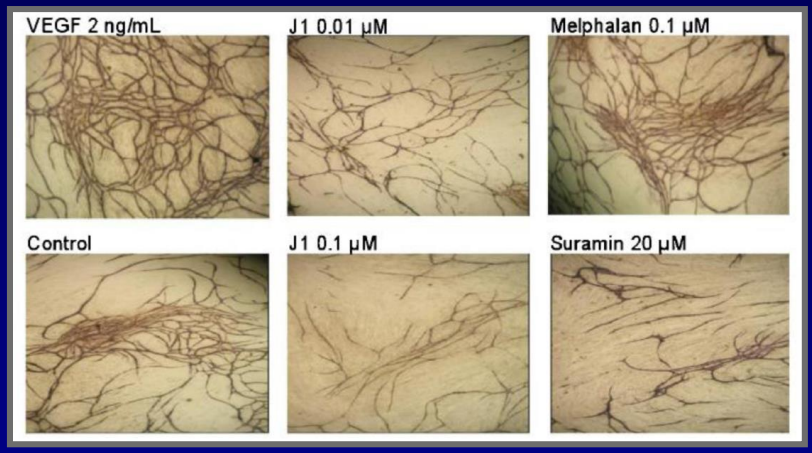


In vivo **efficacy of melflufen shown using a human plasmacytoma MM.1S xenograft mouse model. Treatment of tumor-bearing mice with melflufen intravenously significantly inhibited A) MM tumor growth (P = 0.001) and B) prolonged survival (P < 0.001) of these mice**

Chauhan D, Ray A, Viktorsson K, et al. In vitro and in vivo antitumor activity of a novel alkylating agent, melphalan-flufenamide, against multiple myeloma cells. Clin Cancer Res 2013;19:3019-31.

Selective Cytotoxicity of Melflufen:
Anti-angiogenesis

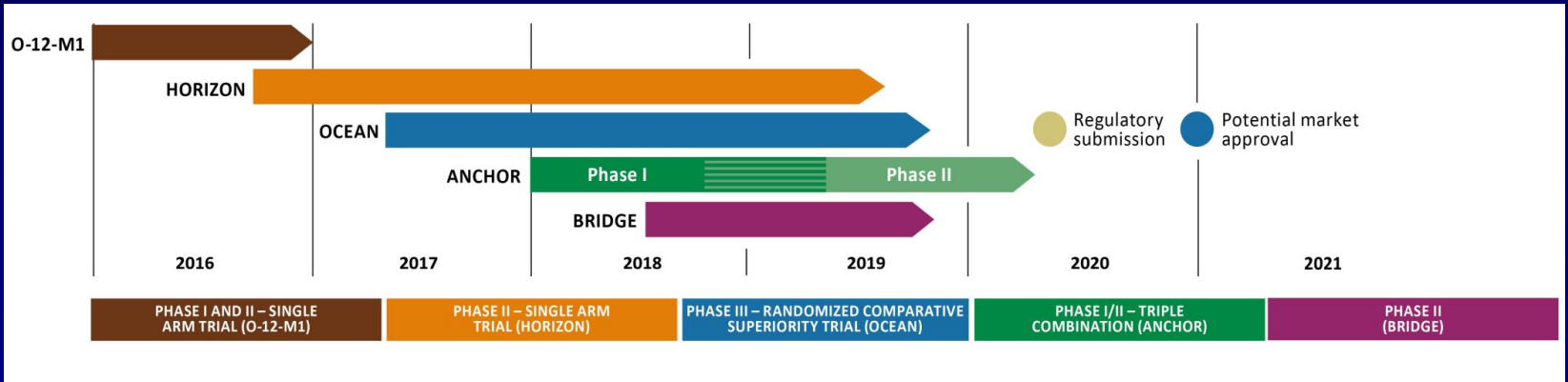
- Melflufen is cleaved by aminopeptidases such as APN which is also known to be overexpressed in angiogenic endothelial cells in the tumor microenvironment
- Melflufen itself is shown to have strong anti-angiogenic properties
- In xenografted mice models, melflufen not only showed cytotoxic effects but also decreased vasculature within the tumors
- Melflufen showed pronounced anti-angiogenic activity (> 100-fold in some assays) at lower doses than the existing alkylator, melphalan alone



Decrease in both tubule length and vessel junctions shown for melflufen and melphalan in a dose response manner compared to the positive control VEGF (2 ng/ml)

Strese S, Wickstrom M, Fuchs PF, et al. The novel alkylating prodrug melflufen (J1) inhibits angiogenesis in vitro and in vivo. Biochem Pharmacol 2013;86:888-95.

Overview of Current Clinical Development Program for Melflufen in Multiple Myeloma



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

Overview of Clinical Results to Date

MM line of therapy

1st line	2nd line	3rd line	4th line	5th line	6th line	7th line

ANCHOR

O-12-M1

HORIZON

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 (3/3)**
- **ORR of 86% in combination with daratumumab (7/8)**
- **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 pomalidomide and/or daratumumab refractory

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

Melflufen/dex in RRMM O-12-M1 Study Summary (n=45)

- Melflufen 40 mg every 28 days with 40 mg dex weekly identified as recommended dose and schedule
- Melflufen/dex demonstrated high response rate and durable response activity in heavily pretreated RRMM patients with a median of 4 prior lines (IMiD- and PI-exposed and disease progression while on therapy or within 60 days of last dose in their last line of therapy)
- ORR was 31% and CBR 49% in ITT population: similar results were seen across patient subgroups, regardless of refractory status
- Benefit of treatment durable, with median DOR of 8.4 months, median PFS of 5.7 months, and median OS of 20.7 months
- Favorable tolerability - hematologic toxicity, mostly thrombocytopenia was common but clinically manageable; non-hematologic AEs were infrequent

Richardson PG, Bringhen S, Voorhees P et al., First report on OS and improved PFS in a completed phase 2 study (O-12-M1) of melflufen in advanced RRMM. Presented at the 2017 American Society of Hematology Annual Meeting, Atlanta, December 9-12, 2017.

Response in Alkylator Refractory pts (O-12-M1)

Time of progression on alkylator treatment in relationship to melflufen	ORR on melflufen + dex
Within 12 months	42%
Within 60 days	38%

Richardson PG, Bringhen S, Voorhees P et al., First report on OS and improved PFS in a completed phase 2 study (O-12-M1) of melflufen in advanced RRMM.

Presented at the 2017 American Society of Hematology Annual Meeting, Atlanta, December 9-12, 2017.

Patients that progressed while on alkylator therapy within 12m in O-12-M1

Alkylator regimen	Time on alkylator regimen treatment (mos)	Best response on regimen	Time between last dose of alkylator and first dose of melflufen (mos)	Best subsequent response to melflufen
CyKd	13	PR	0.7	VGPR
Cy	2	PD	1.1	NE
CyVD, CyP	16	VGPR	1.2	NE
CyVD	2	PD	1.4	SD
CyP	1	PD	1.5	PR
MP / Cy	1.5 / 6	SD / SD	1.5 / 5.5	SD
Mel200, Cy	ASCT/ 3	SD	1.6 / 2.9	PR
Cy	15	SD	1.7	SD
CyTD	12	SD	3.5	VGPR
MPR	5	PD	9.8	PR
CyRVdDox	4	PR	11.2	MR
Mel30	1	SD	11.3	SD

Efficacy in RRMM

	Melflufen+Dex	Daratumumab	Pomalidomide+Dex	Carfilzomib	FOCUS (Cy+steroid)
N	45	106	113	266	158
Year	2017	2016	2013	2012	2016
Population	≥2 prior lines incl bortezomib and lenalidomide, refractory to last tx	≥3 prior lines incl PI and IMiD or double refractory (PI and IMiD)	≥2 prior lines incl lenalidomide and bortezomib, refractory to last tx	≥2 prior lines for relapsed disease incl bortezomib, thalidomide or lenalidomide, alkylator, or anthracycline	≥3 prior lines incl bortezomib, lenalidomide or thalidomide, alkylator, steroids, anthracycline and relapsed to last tx
Time from diag.	5.0 years	4.8 years	5.3 years	5.4 years	5.0 years
High risk Cytog.	44%	19%	27%	28%	18%
Median number of lines	4, 78% ≥3 lines	5, 82 % >3 lines	5, 95 % >2 lines	5, 82% ≥ 4 lines	5, 100% ≥ 3 lines
Refract. to last	87%	97%	100%	95%	99%
ORR	31.1%	29.2%	33.0%	23.7%	11.0%
ORR high risk	25.0%	20.0%	-	29.6%	-
Med duration treat	3.7 months	-	-	3.0 months	2.5 months
Med. Dur response	8.4 months	7.4 months	8.3 months	7.8 months	9.4 months
Median PFS	5.7 months (11.7 in ≥ PR)	3.7 months	4.2 months	3.7 months	3.3 months
Median OS	20.7 months	17.5 months	16.5 months	15.6 months	10.0 months

Richardson PG, Bringhen S, Voorhees P et al., First report on OS and improved PFS in a completed phase 2 study (O-12-M1) of melflufen in advanced RRMM. Presented at the 2017 American Society of Hematology Annual Meeting, Atlanta, December 9-12, 2017; Lonial S, Weiss BM, Usmani SZ et al., Daratumumab monotherapy in patients with treatment-refractory multiple myeloma (SIRIUS): an open-label, randomized, phase 2 trial. The Lancet 2016;387:1551-60; Richardson PG, Siegel DS, Vij R et al., Pomalidomide alone or in combination with low-dose dexamethasone in relapsed and refractory multiple myeloma: a randomized phase 2 study. Blood 2014;123(12):1826-32; Siegel DS, Martin T, Wang M et al. A phase 2 study of single-agent carfilzomib (PX-171-003-A1) in patients with relapsed and refractory multiple myeloma. Blood 2012;120:2817-25. Hájek R, Masszi T, Petrucci MT et al. A randomized phase III study of carfilzomib vs low-dose corticosteroids with optional cyclophosphamide in relapsed and refractory multiple myeloma (FOCUS). Leukemia 2017;31(1):107-114.

OP-106 Melflufen therapy for RRMM patients refractory to daratumumab and/or pomalidomide

Updated Results and First Report on PFS

Paul G. Richardson, MD[1], Enrique M. Ocio, MD[16], Albert Oriol, MD[2], Alessandra Larocca, MD[3], Paula Rodríguez Otero, MD[4], Jan S. Moreb, MD[5], Joan Bladé, MD[6], Hani Hassoun, MD[7], Michele Cavo, MD[8], Adrián Alegre, MD[9], Amitabha Mazumder, MD[10], Christopher Maisel, MD[11], Agne Paner, MD[12], Nashat Gabrail, MD[13], Jeffrey Zonder, MD[15], Dharminder Chauhan, PhD[1], Johan Harmenberg, MD[15], Sara Thuresson, MSc[15], Hanan Zubair, MSc[15] and María-Victoria Mateos, MD[16]

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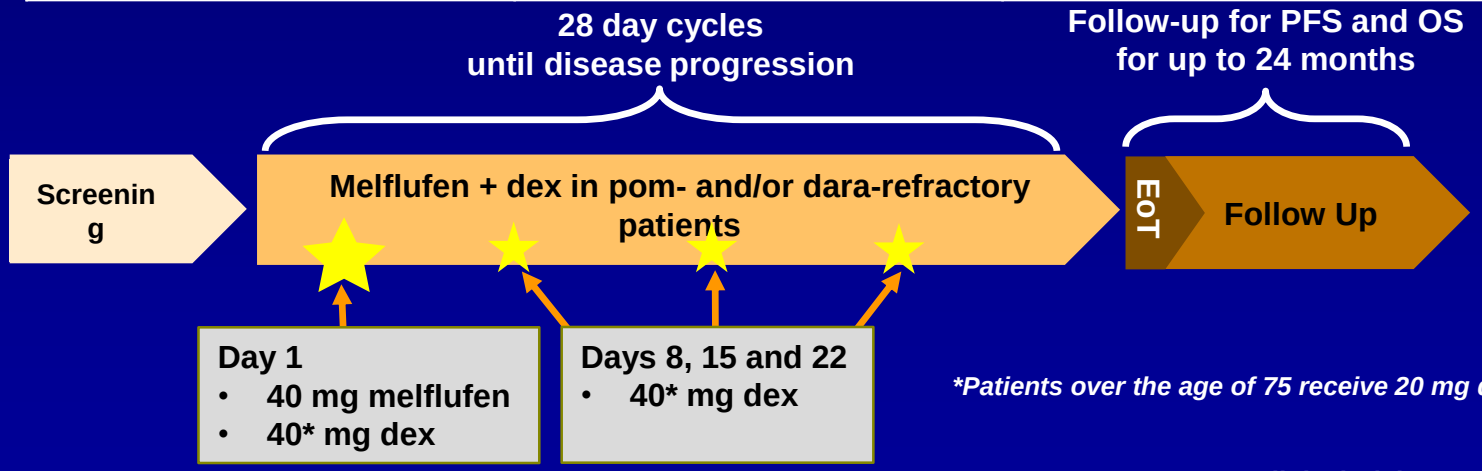
American Society of Hematology Annual Meeting San Diego 2018

OP-106 HORIZON: Phase 2 of Safety and Efficacy of Melflufen in Pomalidomide- and/or Daratumumab-refractory RRMM Patients

HORIZON

Background	HORIZON Design	Potential Outcomes
• Patients who are daratumumab (dara) and/or pomalidomide (pom) refractory have limited options • Introducing a class change with an effective compound may represent a new best treatment strategy • Data suggests patients could derive clinical benefit if administered Melflufen in this setting	• Single arm, open-label, phase II multicenter study • ≥2 lines of prior therapy and pts are refractory to pomalidomide and/or daratumumab • Primary endpoint: ORR • Secondary endpoints: PFS, DOR, OS, CBR, TTR, TTP, safety and tolerability	• Supports OCEAN to receive regulatory approval



**Patients over the age of 75 receive 20 mg dex*

ClinicalTrials.gov Identifier: NCT02963493

Study Design and Disposition

Primary endpoint ORR (n=83)

HORIZON

Key Inclusion Criteria

- Refractory to pom and/or dara
  - Relapsed on therapy or within 60 days of last dose of pom or dara in any line
  - ≥2 prior therapies including an IMiD and a PI
- Measurable disease (at least one of the following)
  - Serum M protein >0.5 g/dL
  - Urine M protein >200 mg/24hrs
  - SFLC: Involved FLC >10mg/dL and abnormal FLC ratio (<0.26 or >1.65)
- ANC ≥ 1000 cells/mm^3 (1.0x10^9/L)
- Platelets ≥75,000 cells/mm^3 (75x10^9/L)

Study treatment:

Melflufen 40 mg i.v. Day 1 +

Dex 40 mg (20 mg for patients ≥75 yrs) Day 1, 8, 15, 22

Treatment up to PD, withdrawal of consent or unacceptable AE

PFS follow-up monthly until progression/ start of new therapy

OS follow-up every 3 months for up to 24 months*

*In the event that we would like to determine the OS status of patients following 24 months, future inquiries about their health status may be conducted.

- At data cut-off (22 Oct 2018):
  - 83 patients (pts) treated; 82 evaluable for response (80 with M-protein data)
  - 19 pts (23%) ongoing on treatment and
  - 64 pts (77%) discontinued treatment;
    57% due to PD, 13% due to AEs and 7% due to other reasons
- Study is ongoing and will recruit up to approximately 150 pts (including Quality of Life data for 50 pts)

Patient Characteristics at Study Entry (n=83)

HORIZON

		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 β_2 microglobulin $\geq$ 3.5 mg/l	50 %	

*ISS at study entry unknown for 3 pts **HR status data pending/missing in 23 pts

Prior Treatment and Refractory Characteristics (n=83)

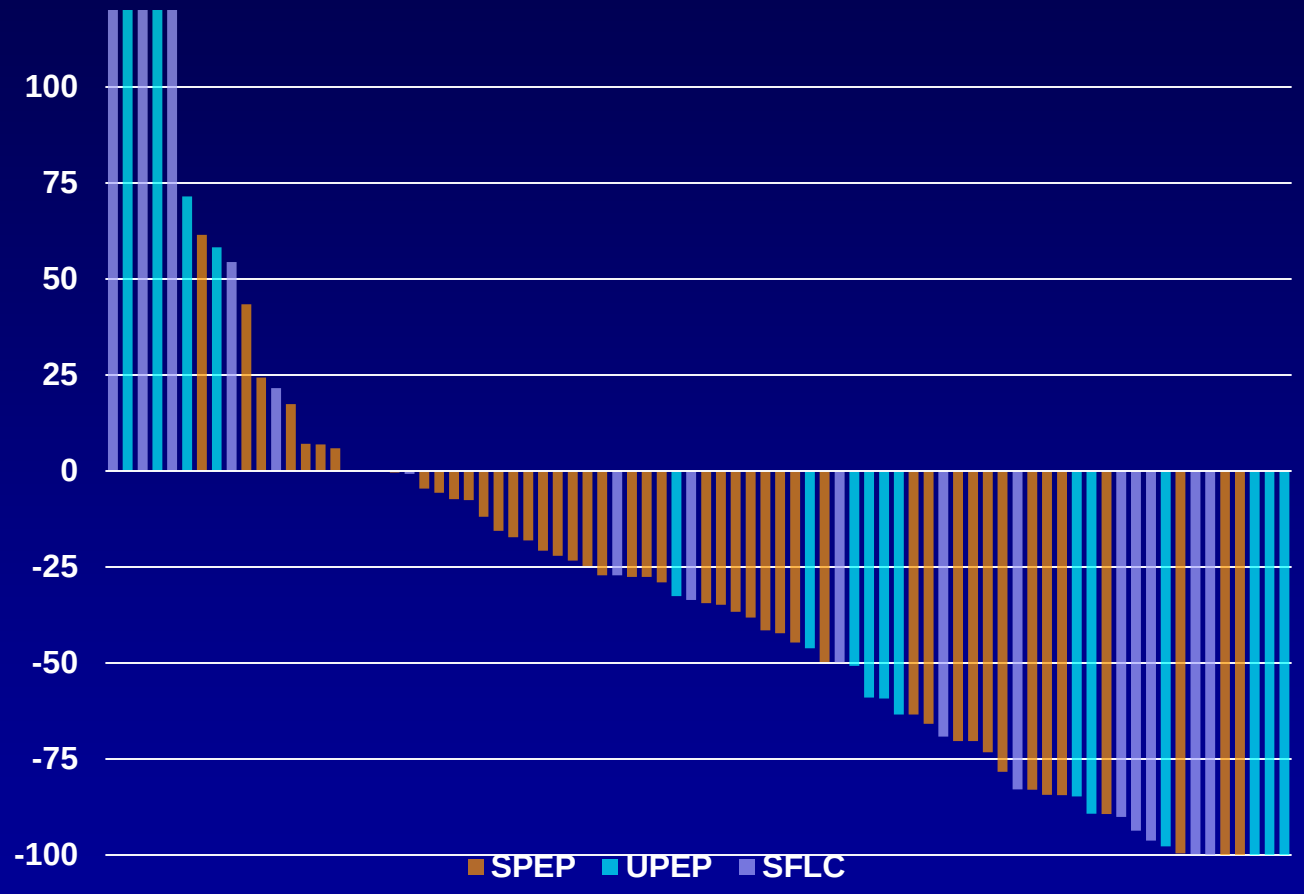
HORIZON

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

- All 83 (100%) pts received prior PIs + IMiDs
- 46% used ≥3 treatment regimens in the last 12 months

- IMiDs include lenalidomide, thalidomide and pomalidomide
- PIs include bortezomib, carfilzomib and ixazomib
- MoAbs include daratumumab, elotuzumab, isatuximab

Best M-Protein Response: Majority of Patients show Disease Stabilization and/or Reduction of Tumor Burden (n=80)



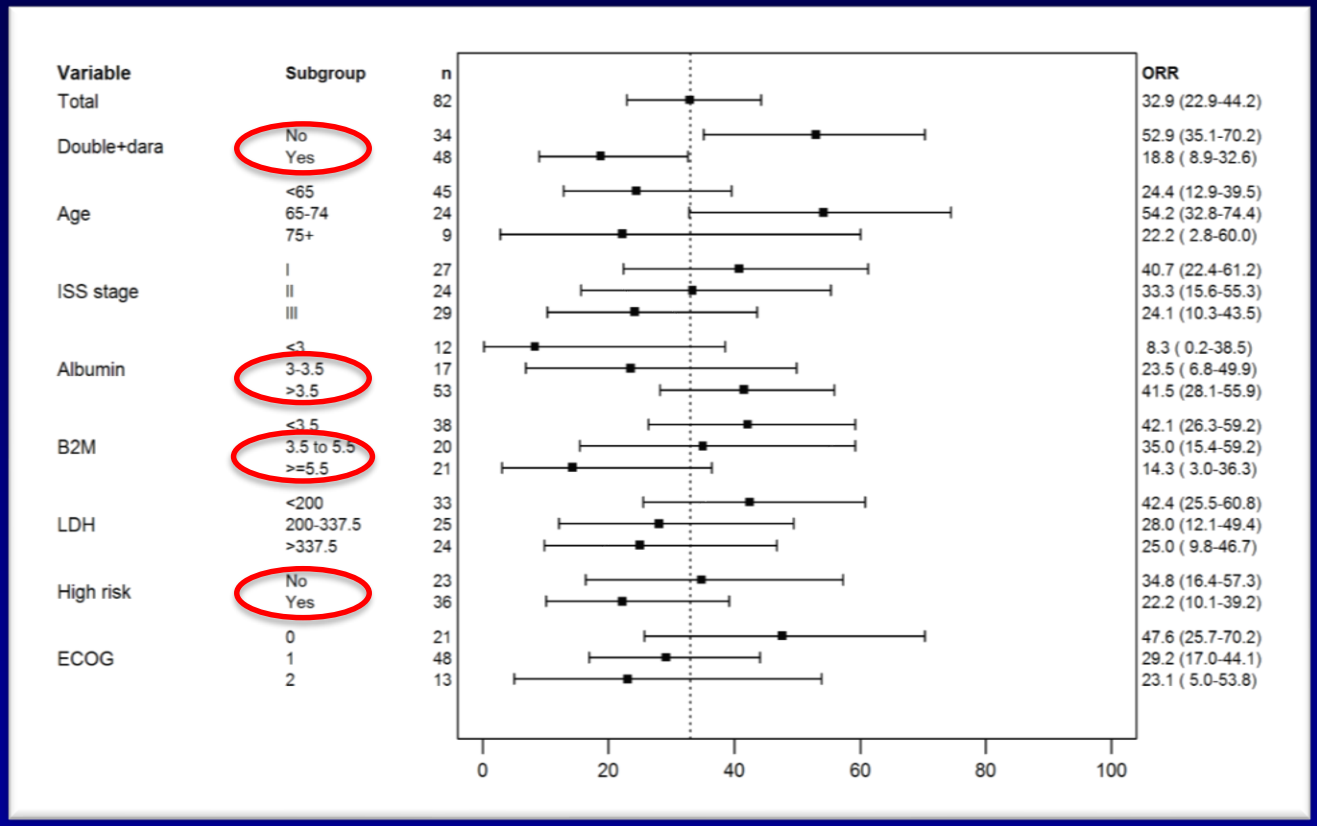
ORR in Multi-Refractory RRMM patients (n=83)

HORIZON

	n	%
Overall response	27	33
sCR	1	1
CR	0	0
VGPR	9	11
PR	17	21
MR	5	6
SD	37	45
PD	12	15
Not evaluable	1	1
Data pending	1	1

- Overall response rate (≥PR) 33%
- Clinical Benefit Rate (≥MR) 39%
- Disease stabilization (≥SD) 84%

Overall Response Rate in Patient Subgroups (n=82)



Areas of further investigation:

- **Good signal in extramedullary disease**
- **Alkylator exposed/ refractory/ disease stage**
- **Detailed refractory status breakdown**

Prognostic Factors Associated with Response
Albumin and β_2 microglobulin in Response Evaluable Pts

	n	Overall Response Rate	Albumin ≥3.5 g/dL	Albumin ≥3.5 g/dL and β_2 microglobulin <3.5 mg/L
ITT	82	33%	42%	49%
Pom refractory	74	30%	38%	43%
Dara refractory	57	25%	34%	40%
Pom + Dara refractory	49	19%	28%	29%
Dara + double refractory	48	19%	28%	36%

Important to know underlying biological performance status to evaluate response data in late-stage RRMM pts

Serum Albumin: Strongest Predictor of ORR (β_2M and LDH lose significance once adjusted for albumin)

HORIZON

	n	Odds ratio	95% CI	P-value
Albumin	79	2.62	(0.91-7.56)	0.075
β_2M	79	0.92	(0.73-1.15)	0.460
LDH	79	0.96	(0.80-1.15)	0.648
ISS at study entry	79	0.95	(0.49-1.84)	0.872

- In an exploratory multivariable logistic regression model, only baseline albumin emerged as a prognostic factor for ORR.

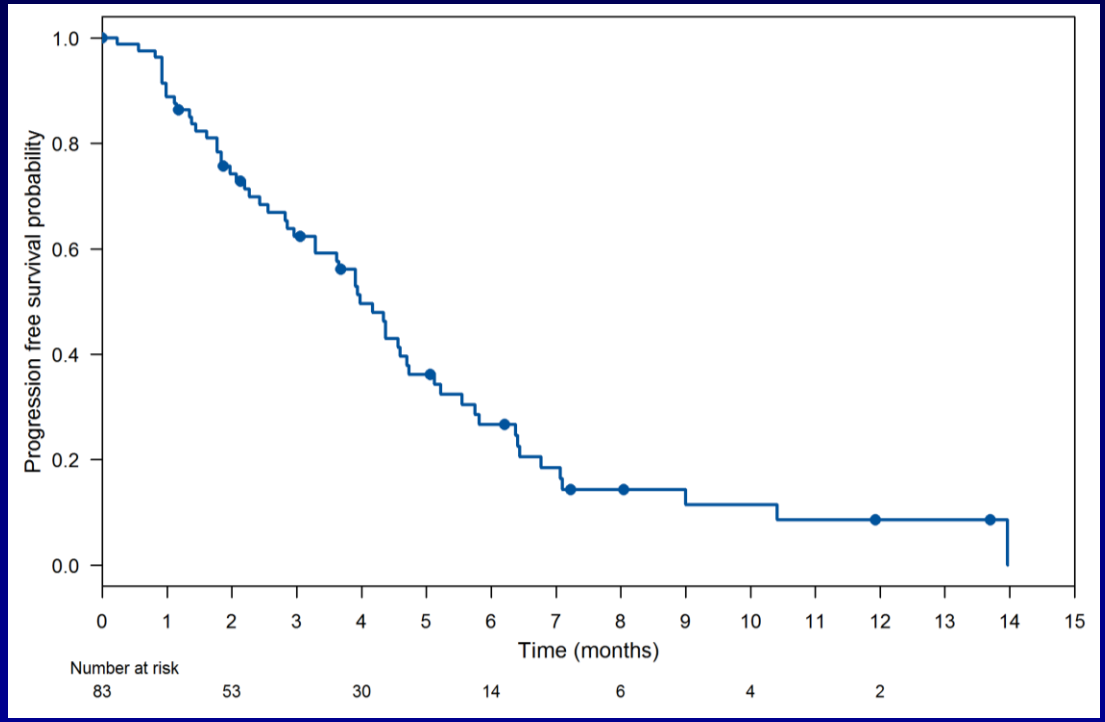
  Baseline LDH, β_2M and ISS at study entry did not add additional information.

- Further verified after a stepwise selection process where albumin remained only independent factor.

	n	Odds ratio	95% CI	P-value
Albumin	79	3.21	(1.19-8.69)	0.021

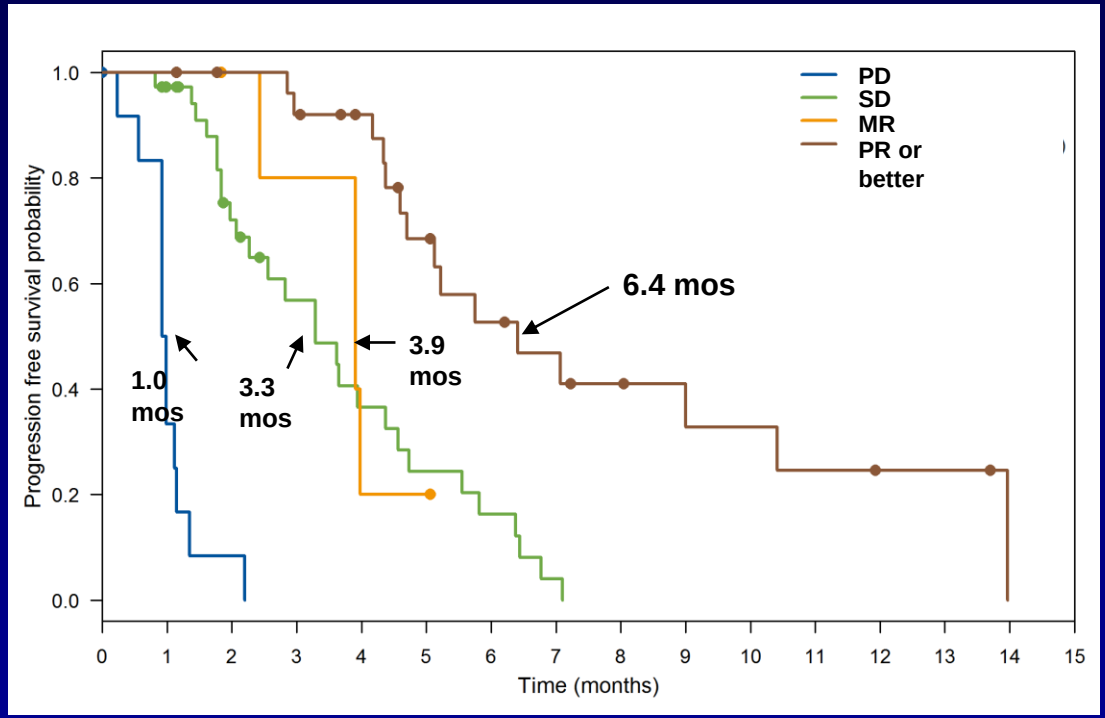
- Further evaluation ongoing, but caution warranted given relatively low number of events, non pre-specified analysis

Progression-Free Survival (n=83)



Median PFS: 4.0 months (95% CI: 3.3-5.1)

PFS by Response Category (n=83)



Overview of Safety and Tolerability (n=83)

	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)

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

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

HORIZON: Patient Case

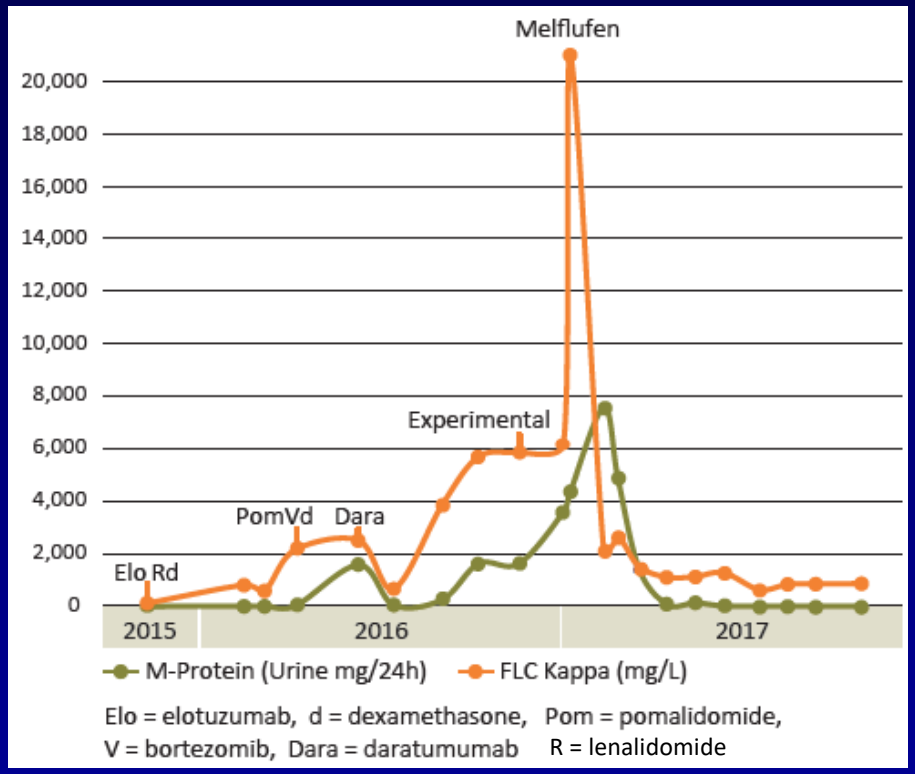
Treatment History
(Initial Treatment and Salvage from 2007-2015)

MM BJ Kappa LC MM
42 year gentleman at diagnosis

Prior lines:
1. Thalidomide, Dex + ASCT → CR
2. Bortezomib, Dex + 2nd ASCT → CR
3. Lenalidomide, Dex → VGPR
4. VTD x2, DCEP x2, PomDex → PR
5. VBCMP/VBAD + Allo-SCT → PR

6. Elo Rd → PD
7. Pom Dex, Bortezomib (PVD) → PD
8. Dara → PD
9. Experimental drug (ADC targeting CS1) → PD

PD with RR MM (2015-2016)
Refractory to last 4 lines, with 9 lines of treatment overall



- **Started 40 mg melflufen/dex (2017)**
- **Received 9 cycles per protocol VGPR as best response in cycle 3**
- **Experienced treatment-related G4 thrombocytopenia, G3 anemia, G3 neutropenia, otherwise well tolerated**
- **EOT due to PD after 9 cycles completed**
- **PFS: 10.4 months**

Mateos MV, Rocafiguera AO, Otero PR, et al. The HORIZON study: a preliminary report on efficacy and safety of melflufen in late stage relapsed-refractory myeloma (RRMM) patients refractory to pomalidomide and/or daratumumab. Presented at the 2018 European Hematology Association Annual Meeting, Stockholm, June 14-17, 2018.

HORIZON Conclusions

- Melflufen/dex has promising activity in multi-resistant RRMM patients, with an ORR of 33% (≥PR), CBR of 39% (≥MR), disease stabilization (≥SD) in 84% and PFS of 4.0 months

- Activity regardless of underlying refractory status, but serum albumin is a strong predictor of ORR

- Treatment was generally well tolerated with manageable toxicity
  - Non-hematological adverse events were infrequent – absence of alopecia, mucositis, GI toxicity, cardiac toxicity and PN noteworthy
  - Infection rate 7.2%

- Study is ongoing with robust accrual – planned total N =150

A Phase 1/2 Study of Safety and Efficacy of Melflufen and Dexamethasone in Combination with either Bortezomib or Daratumumab in Patients with RRMM; First Report on Phase 1 Data

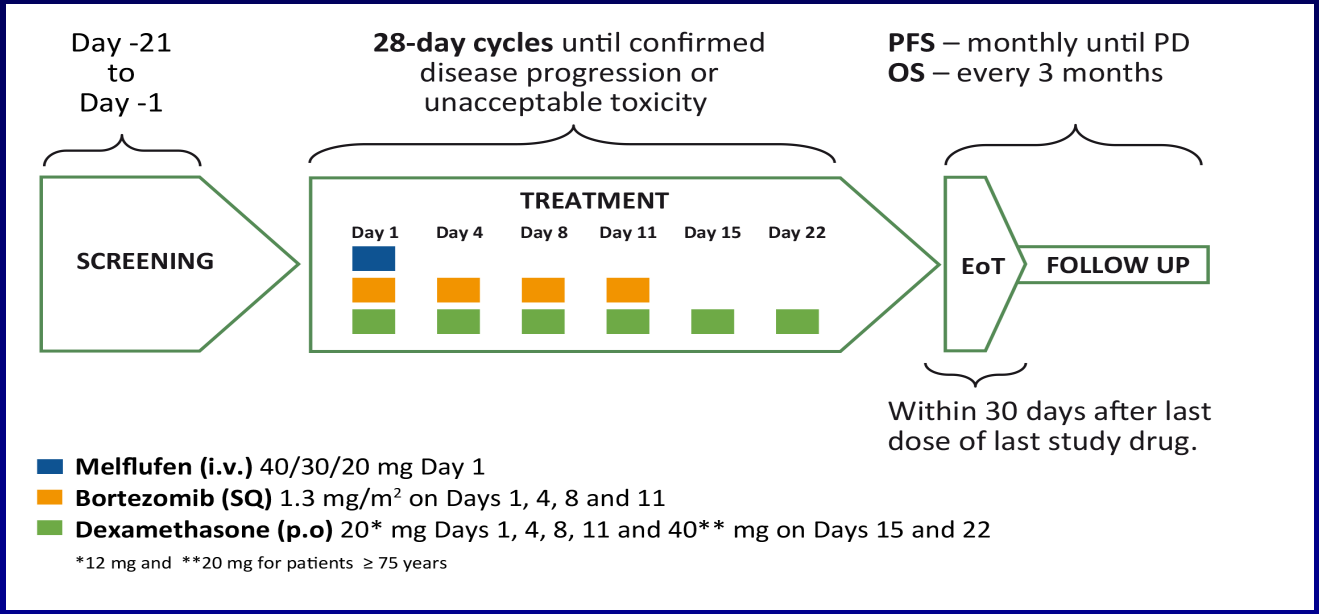
Ludek Pour, MD, Yvonne Efebera, MD, Miquel Granell, MD, Roman Hajek, MD, Albert Oriol, MD, Jacques Delaunay, MD6 Katell Le Du, MD, Jean-Richard Eveillard, MD. Lionel Karlin, MD, Vladimir Maisnar, MD10 Joaquín Martinez-Lopez, MD, María-Victoria Mateos, MD, Jan Moreb, MD, Vincent Ribrag, MD, Paul G. Richardson, MD, Jan Straub, MD, Catriona Byrne, RN, Christian Jacques, MD, Hanan Zubair, MSc and Enrique M. Ocio, MD

ASH 2018 San Diego

ANCHOR Study Design

- Phase 1/2 trial of melflufen in combination with either bortezomib or daratumumab (NCT03481556)
- Patients must have had 1-4 prior lines of therapy and be refractory (or intolerant) to an IMiD or PI or both.
- In combination with bortezomib patients cannot be refractory to a PI.
- In combination with daratumumab patients cannot be previously exposed to any anti-CD38 monoclonal antibody.
- Patients treated until documented disease progression or unacceptable toxicity.
- Primary objective of phase 1: to determine the optimal dose of melflufen, up to a maximum of 40 mg. Once the optimal dose has been established, an additional 20 patients per regimen will be recruited in the phase 2 part of the study where the primary objective is ORR (investigator assessed according to IMWG criteria).
- Up to three dose levels of melflufen are being tested starting at 30 mg and either increasing to 40 mg or decreasing to 20 mg based on observed dose limiting toxicity (DLT). Melflufen is given i.v. on Day 1 of each 28-day cycle in the 2 different combinations.
- Regimens are evaluated separately.

Melflufen and Dexamethasone in Combination with Bortezomib



ANCHOR

Patient Characteristics of Melflufen and Dex in Combination with Bortezomib

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)

At the time of data cut-off (12 Nov 2018), 3 pts had been treated with 30 mg melflufen and dex in combination with bortezomib. Median age was 81 years with a median of 3 prior lines of therapy. All pts were relapsed-refractory and 2/3 pts were last line refractory (disease progression while on therapy). All pts were ongoing with a median of 7 cycles on treatment.

Safety of Melflufen and Dex in Combination with Bortezomib

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

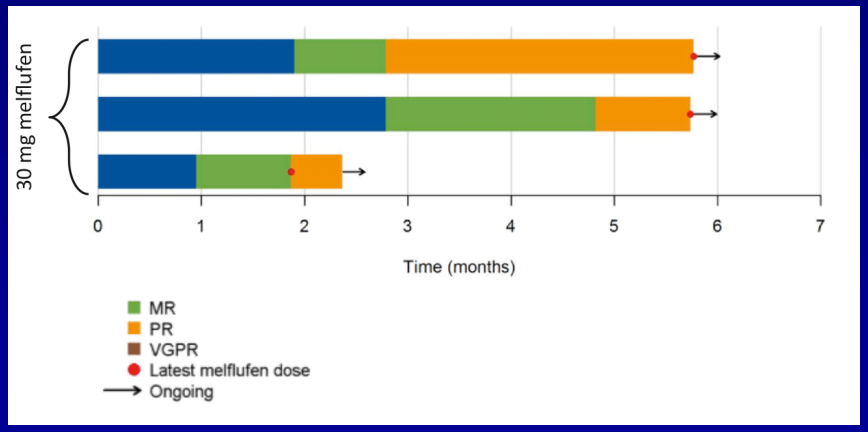
- **No DLTs were observed at the 30 mg melflufen dose level.**
- **Regimen was well tolerated with clinically manageable G3/4 hematological AEs with limited non-hematological AEs.**
- **Highest cohort of melflufen 40 mg has been opened for enrolment.**
- **One patient experienced a treatment-related SAE (G3 neutropenia, G3 pneumonia - pneumococcal).**

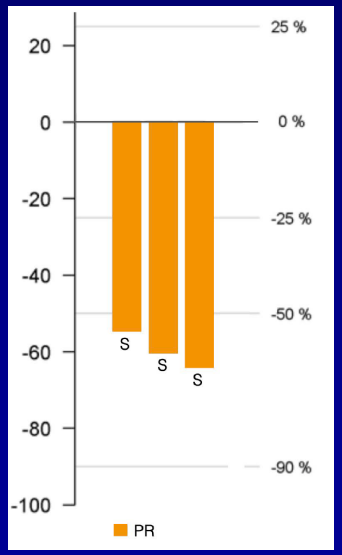
Efficacy of Melflufen and Dex in Combination with Bortezomib

- 3 patients ongoing with a median treatment duration of 5.8 months (2.3-6.1).
- Patients received a total of 17 cycles of treatment with a median of 7 (3-7).
- All 3 patients responded, with responses ongoing at data cutoff

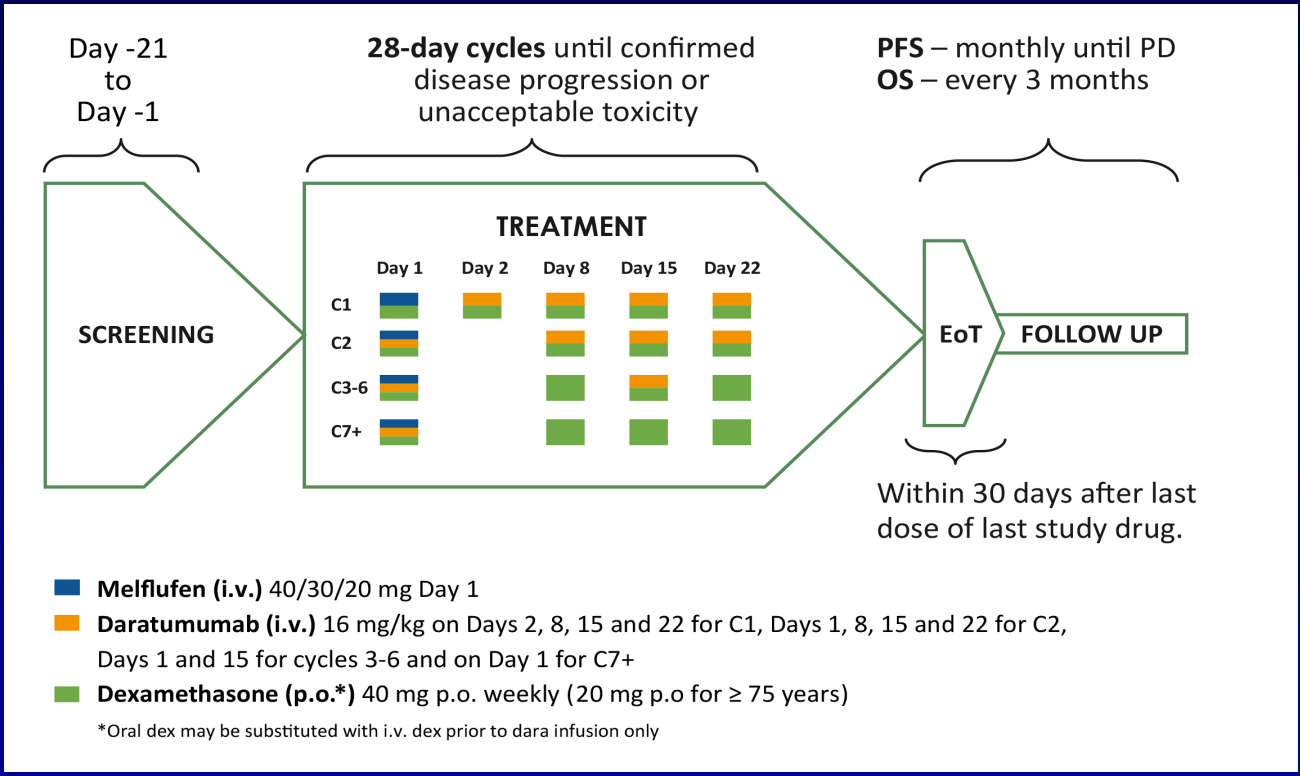
	ORR	CR	VGPR	PR	MR	SD	PD
Total (N=3)	100%	0	0	3*	0	0	0

*** 1 unconfirmed PR**





Melflufen and Dexamethasone in Combination with Daratumumab



ANCHOR

Patient Characteristics of Melflufen and Dex in Combination with Daratumumab (n=9)

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.

At the time of the data cut-off (12 Nov 2018), 9 pts had been treated with melflufen and dex in combination with daratumumab. Median age was 63 years with a median of 2 prior lines of therapy. No pt had achieved CR in any previous line of therapy, 67% were IMiD refractory and 56% were last line refractory (disease progression while on therapy). All pts were on-going with a median of 4 cycles on treatment.

Safety of Melflufen and Dex in Combination with Daratumumab (n=9)

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)

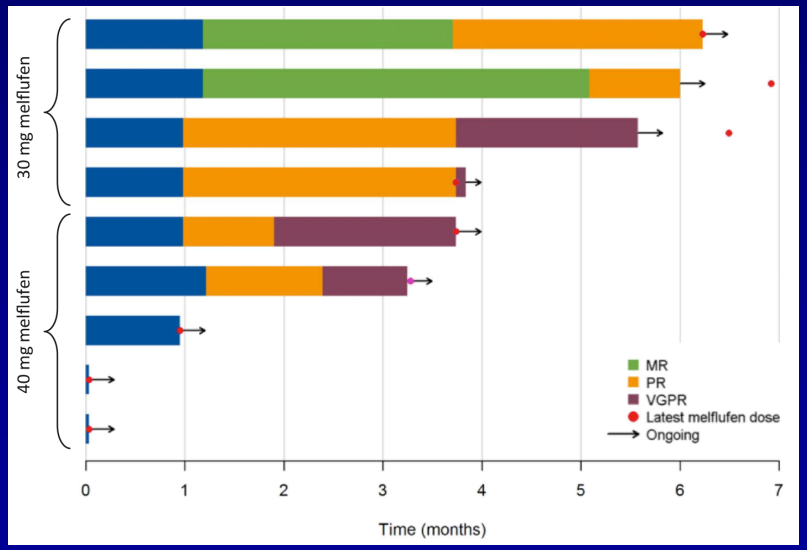
- **Four* patients were treated with 30 mg melflufen and no DLTs were observed.**
- **Five patients were treated with 40 mg melflufen with no DLTs observed**
- **Combination of melflufen, dexamethasone and daratumumab generally well tolerated with clinically manageable G3/4 hematological AEs and low number of non-hematological AEs**
- **No treatment related SAEs reported**

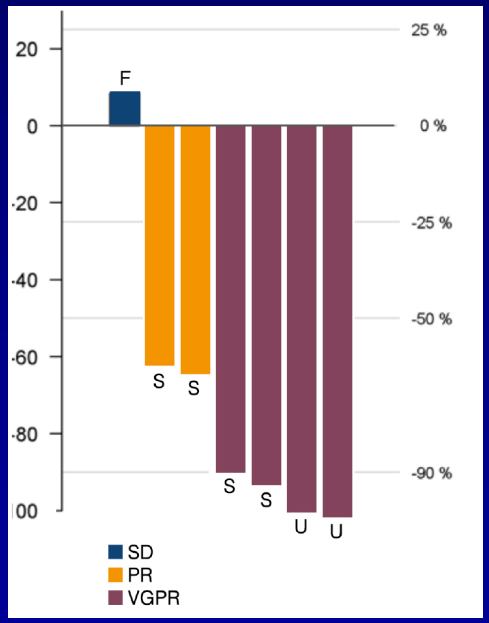
Efficacy of Melflufen and Dex in Combination with Daratumumab (n=9)

- All 9 patients 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).

	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 still in their first cycle of treatment and were therefore not evaluable for response**





ANCHOR Conclusions

- Combination of melflufen and dexamethasone with either bortezomib or daratumumab is well tolerated in this preliminary data-set
- Efficacy is encouraging in both combinations. All patients are still on treatment. Response rate is favorable in combination with bortezomib (3/3 responses) and 86% in combination with daratumumab (6/7), with a median treatment duration of 5.8 and 3.9 months respectively.
  - All patients but 1 across the two regimens responded to treatment (achieved SD after 1 cycle, still ongoing).
  - 3 PR/uPR in combination with bortezomib
  - 4 VGPR, 2 PR and 1 SD in combination with daratumumab
- No DLTs observed across both regimens and dose levels, with 40 mg dose level now recruiting.
- Grade 3/4 AEs mostly hematological, clinically manageable.
- Study is ongoing

Future Directions for Melflufen in Multiple Myeloma

- Phase 3 study (NCT03151811) comparing melflufen/dexamethasone and pomalidomide/dexamethasone in RRMM ongoing (OCEAN)
- Further enrollment in HORIZON and ANCHOR; safety profile and low incidence of non-heme toxicity noteworthy
- Expanded combination studies (larger studies and more combinations) – given that current early data is encouraging, especially in triple class refractory patients (pts.)
- Potential use of peptidase conjugated alkylators in ASCT (for BM ablation and anti-MM effect); chemotherapeutic of choice in older non- SCT eligible pts.

Oncopeptides Capital Markets Day
December 14th

5 minute break

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

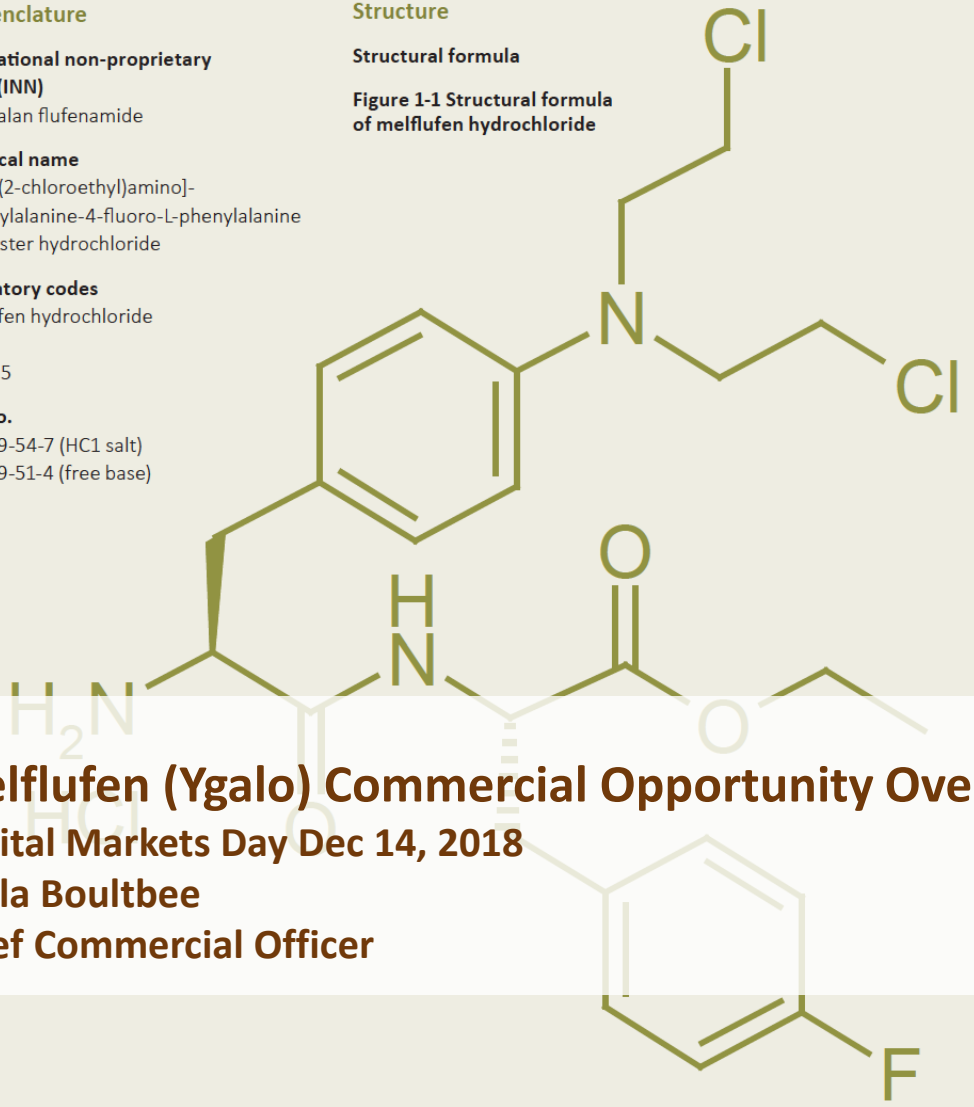
Laboratory codes
Melflufen hydrochloride
J1
CK 1535

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

Structure

Structural formula

Figure 1-1 Structural formula of melflufen hydrochloride

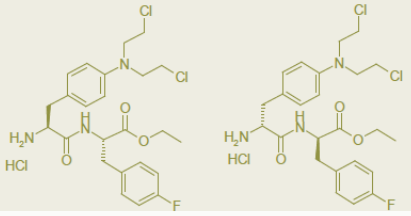


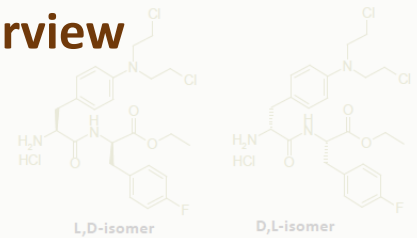
Molecular formula
C24 CH31C13FN3O3 (HC1 salt)

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 Figure 1-3.

Melflufen (Ygalo) Commercial Opportunity Overview

Capital Markets Day Dec 14, 2018

Paula Boultbee
Chief Commercial Officer

Commercial Success Factors for Ygalo® (melflufen)

- Growing patient pool of relapsed refractory multiple myeloma patients
- Relapsed refractory multiple myeloma treatment patterns are fragmented
- A new mechanism of action, is in high demand by treating physicians

Ygalo® is a “peptide conjugated alkylator” that show promising efficacy and safety in relapsed and refractory multiple myeloma

Commercial Opportunity Summary

Situation

Multiple Myeloma is a fast growing global market

- $14B market today expected to grow to $27B by 2022
- Four treatment classes – IMiDs, PIs, alkylators and antibodies- (CD38, SLAM-7)
- Aggressive front line combination regimens and ASCT have led to better outcomes
- Majority of patients are treated with single agent, due to tolerability issues
- Relapse is still inevitable despite recent advances – no cure in sight

Unmet Need

In demand novel MoA treatments in relapsed and refractory MM patients

- Marketed products have shortcomings :
  - compounding toxicities
  - dosing limited by patient comorbidities
  - drug /drug interactions limits treatment choice
- Lack of good treatments for MM patients with bone pain, extra medullary disease, and CNS involvement
- No real standard of care exists in relapsed refractory multiple myeloma due to overlapping efficacy and toxicities

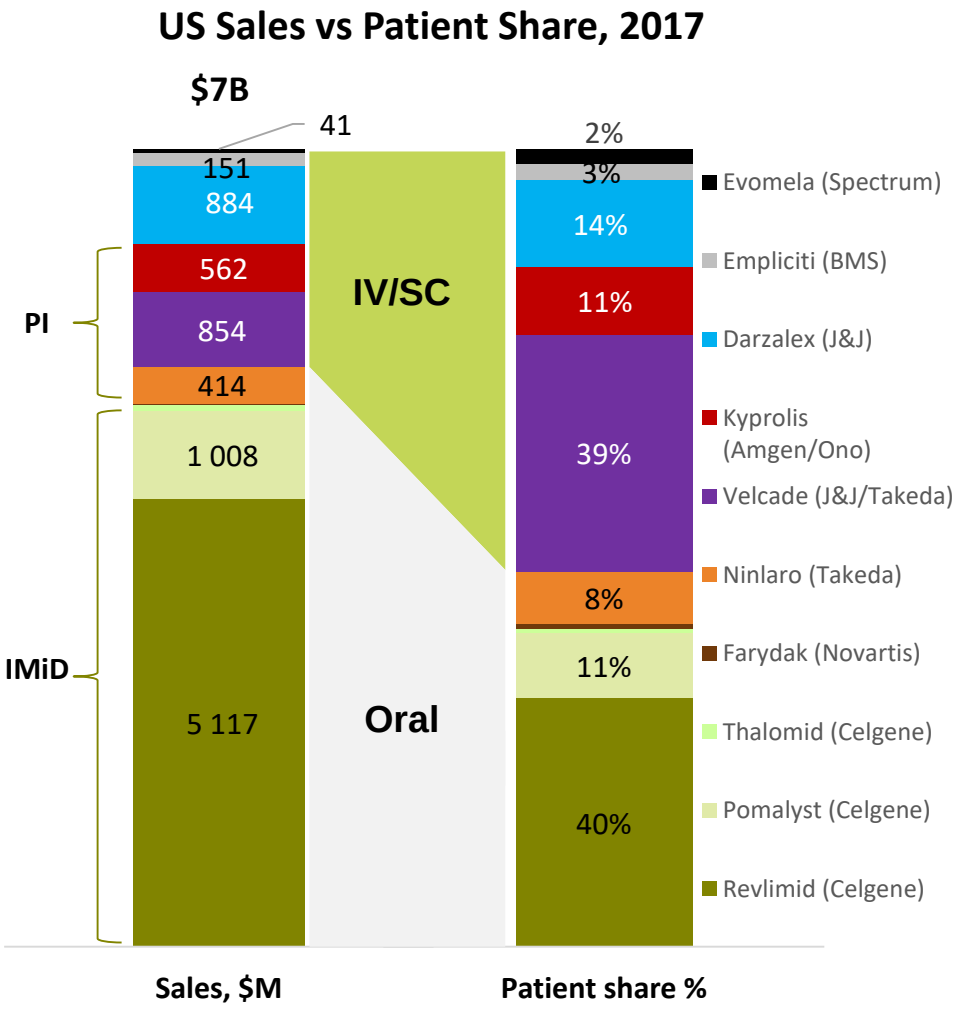
Program

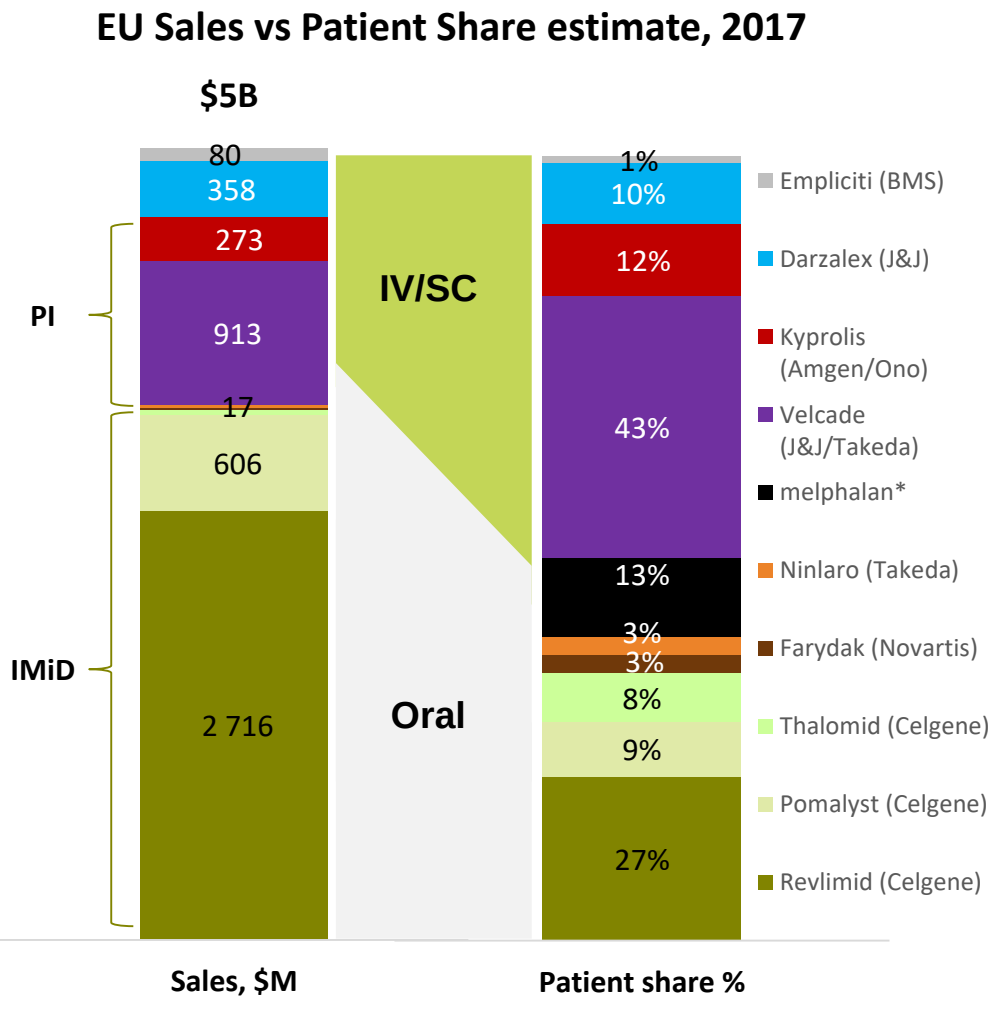
Melflufen's clinical development is addressing a patient population after IMID and PI failures

- RRMM treatment choice need to have:
  - single agent efficacy
  - be well tolerated
  - easy administration schedule
  - lack of co-morbidity and no drug/drug interaction limitations
- Promising efficacy and tolerability in combination therapy
- Melflufen has the potential to make a real difference in the $8B RRMM opportunity and beyond

Similar Patient Shares for IMiDs and PIs, IMiD Sales Significantly Higher

Revlimid revenue is likely to be impacted by upcoming loss of patent

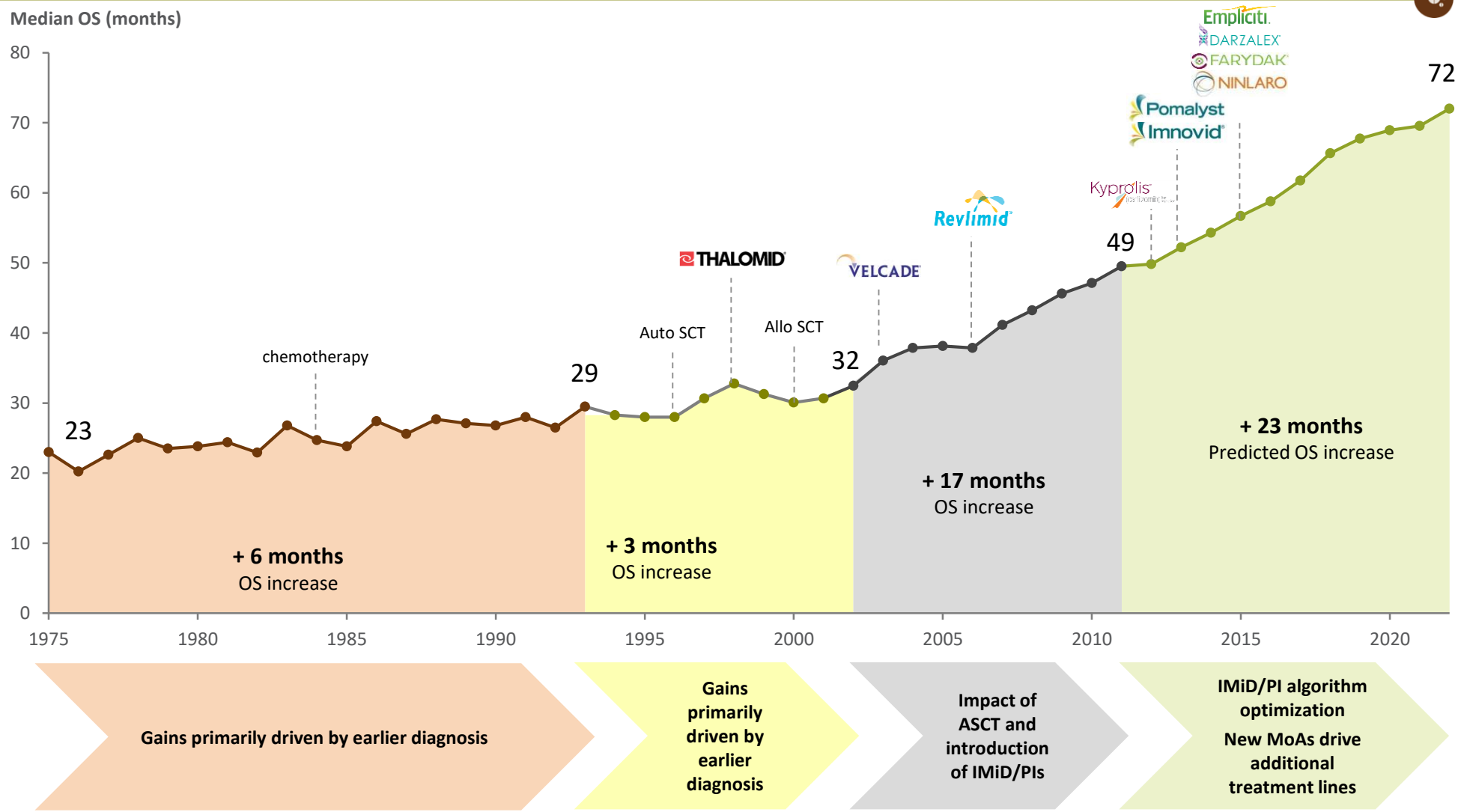




Source: EvaluatePharma, Intrinsiq, Kantar Health, company analysis

Novel Therapies Have Improved Outcomes for Patients

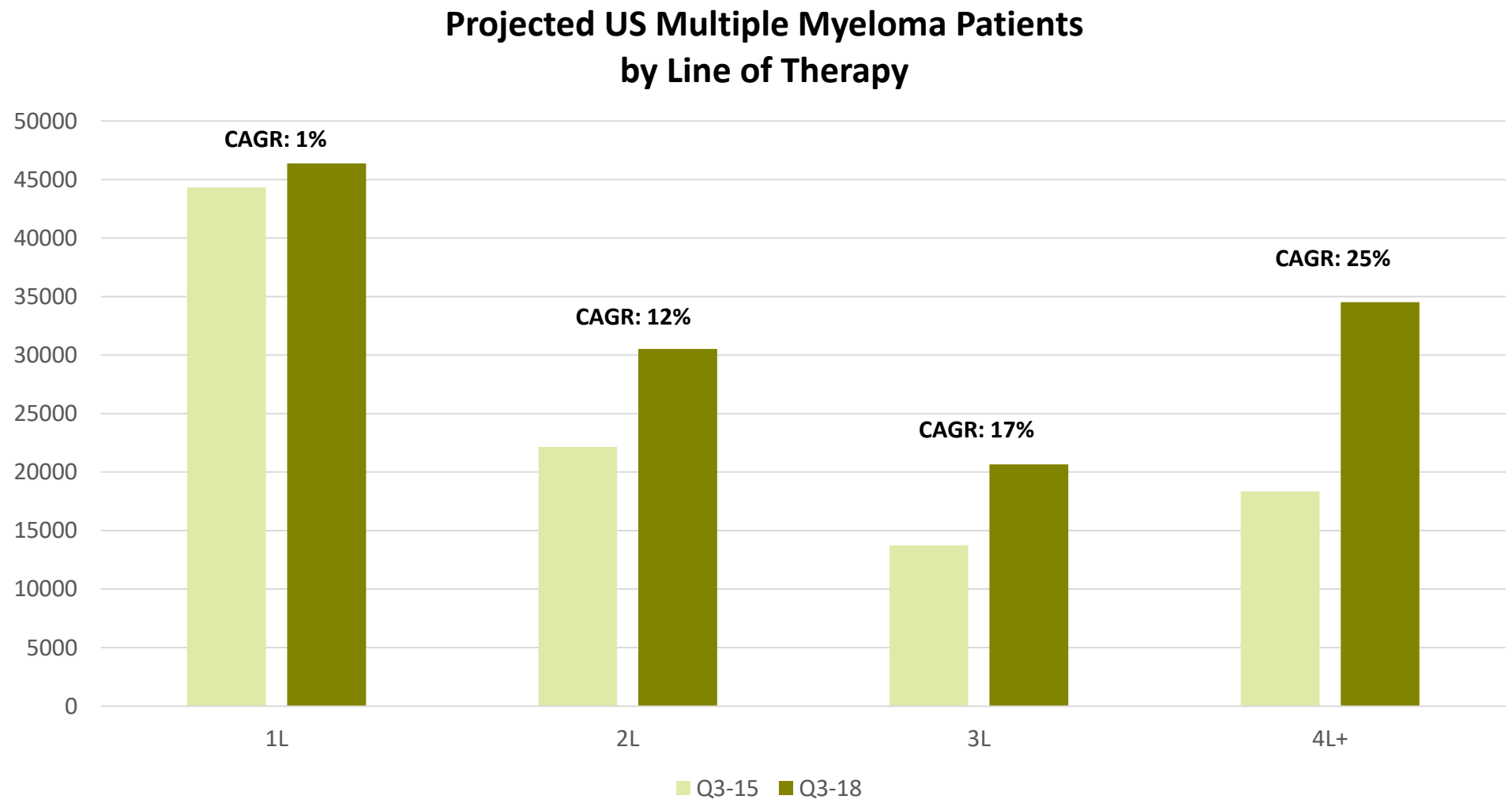
Clonal selection results in inevitable relapse & development of resistance to treatment



Source: Drawid A et al. Impact of Novel Therapies on Multiple Myeloma – Current and Future Outcomes. Poster presented at the 20th Congress of the European Hematology Association; Vienna, Austria, June 11-14, 2015.

Note: From 2017, OS benefit are projections based on estimated 5 year survival.

Improved Outcomes Leads to Fast Growth in Number of Treated Patients in Later Lines of Therapy



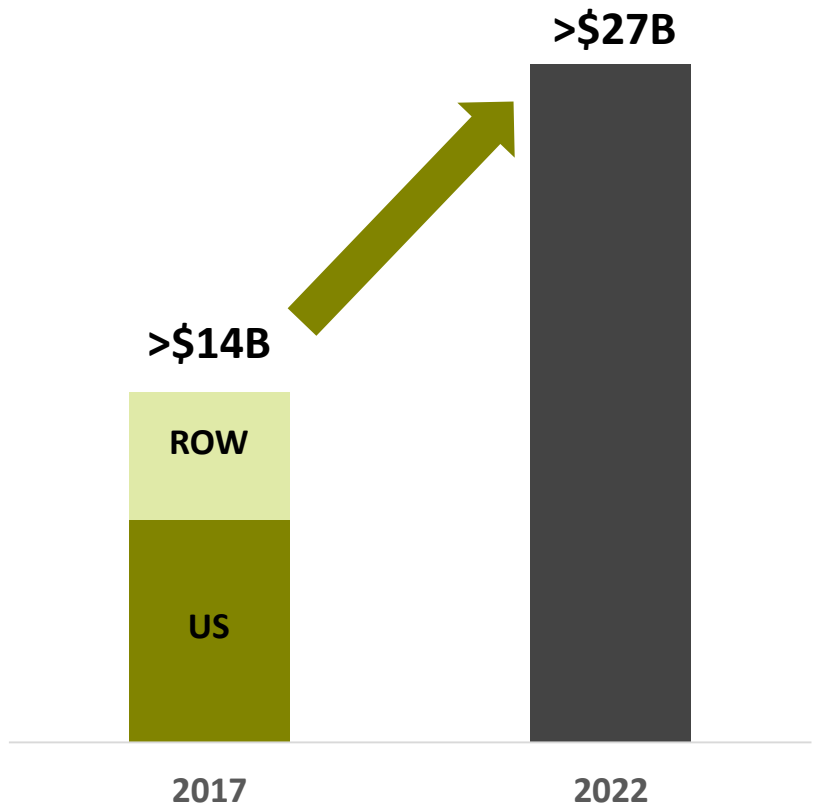
Source: Intrinsiq Oct 2018, MAT
Note: 3-yr annual growth rate for 3Q15-3Q18

Multiple Myeloma is a Fast Growing Market

Approvals of novel agents have expanded market

- IMiDs and PIs will continue to be used at least once during the course of the disease
- Daratumumab has driven market growth in both number of patients treated and duration on therapy
- Late stage multiple myeloma patient pool is growing due to improved therapies, more treatment months per patient
- The multiple myeloma market is expected to almost double in size before Revlimid patent expires

Market Value Expected to Double



Source: EvaluatePharma

Refractory Patients Represent Significant Unmet Need

Physicians cite novel MoA agents as a critical unmet need in multiple myeloma

Impact of Guidelines and treatment patterns

Guidelines

- Treat until disease progression
- Relapse patients should be treated with a different class of drug
- Re-treatment if treatment-free interval is at least 6–9 months

Treatment patterns

- Front line patients may be out of treatment options at relapse (when combinations used)
- Patients with triple refractory (IMiD, PI, CD38) disease have extremely poor prognoses

Physician surveys highlight additional MoA options for RRMM patients as one of the most critical unmet needs

Treatment Guideline Recommendations

"In patients who experience a high quality, prolonged response with minimal toxicity to initial therapy, re-treatment can be considered if they have obtained at least a 6–9 months treatment-free interval. The alternative is to change to a different class of drug and reserve the original treatment scheme for second relapse. "

"We recommend patients in second relapse or beyond receive a salvage regimen incorporating at least one agent to which there has not been prior evidence of resistance or intolerability"

Physicians Desire Novel MoAs

"While OS of patients with MM has improved, the survival of patients progressing after treatment with the IMiDs and bortezomib remains dismal"

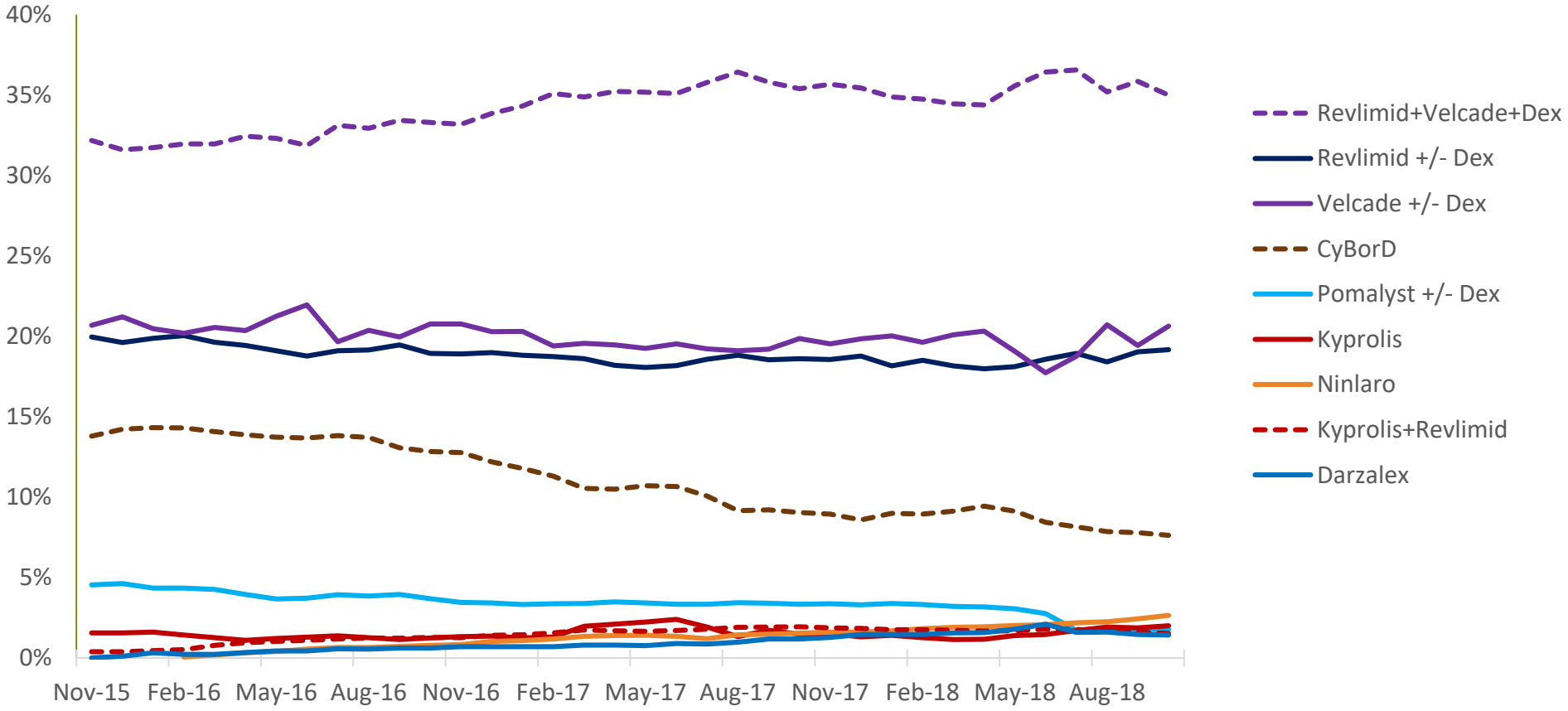
"There are a ton of PI and IMiD options, but patients become resistant. I'd really like some new MoAs to try"

Source: IMWG Guidelines, Physician market research

The Majority of Patients Receive IMiD and PI Combinations in 1st Line

In Accordance with Treatment Guidelines (US data), trend likely to continue

Newly Diagnosed MM Treatment Patient Shares



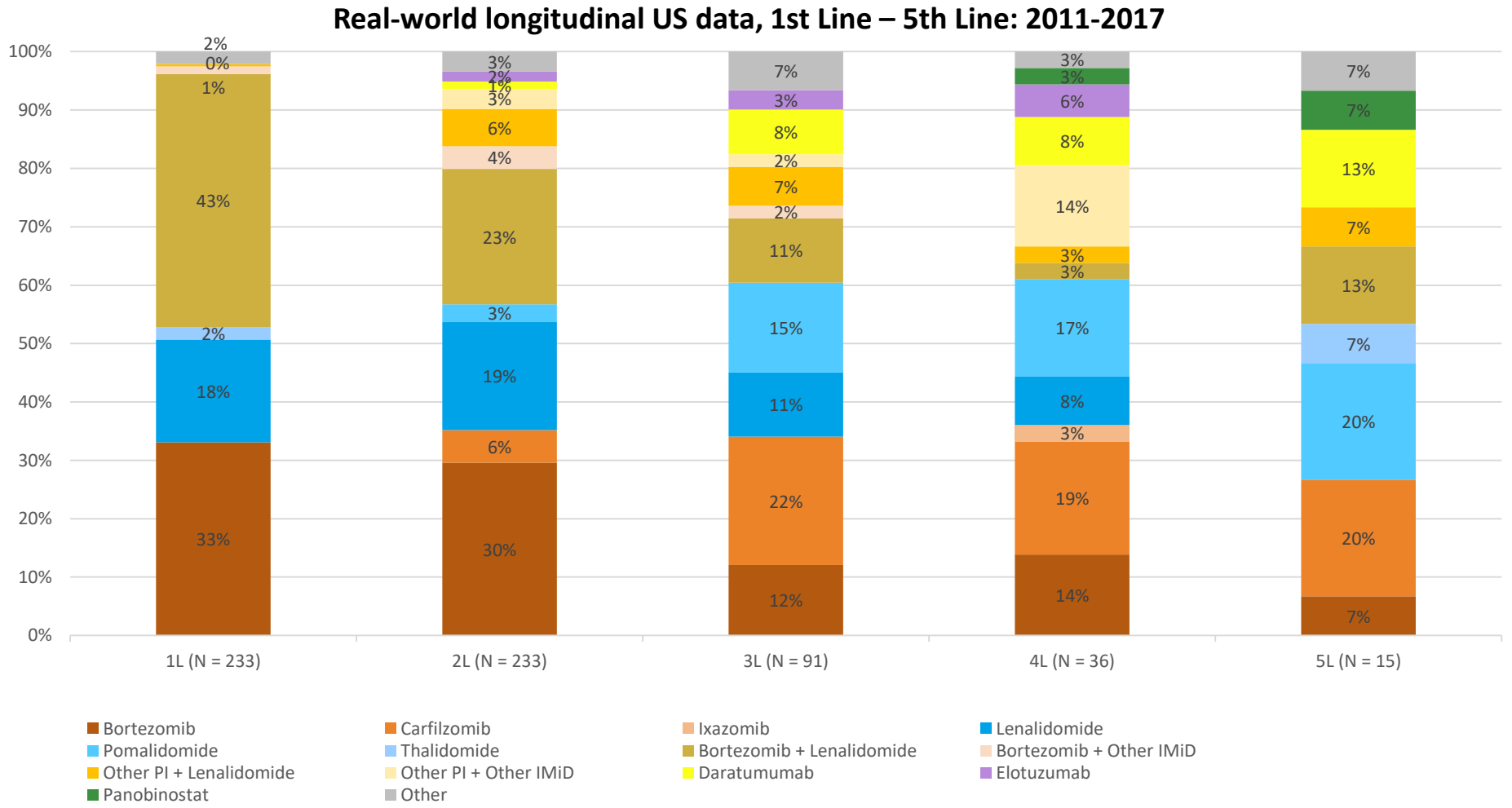
Source: IntrinsiQ Oct 2018, MAT

Note: Assume regimens include Dexamethasone although steroid use not reported in Intrinsiq data.

Single agent

Combination

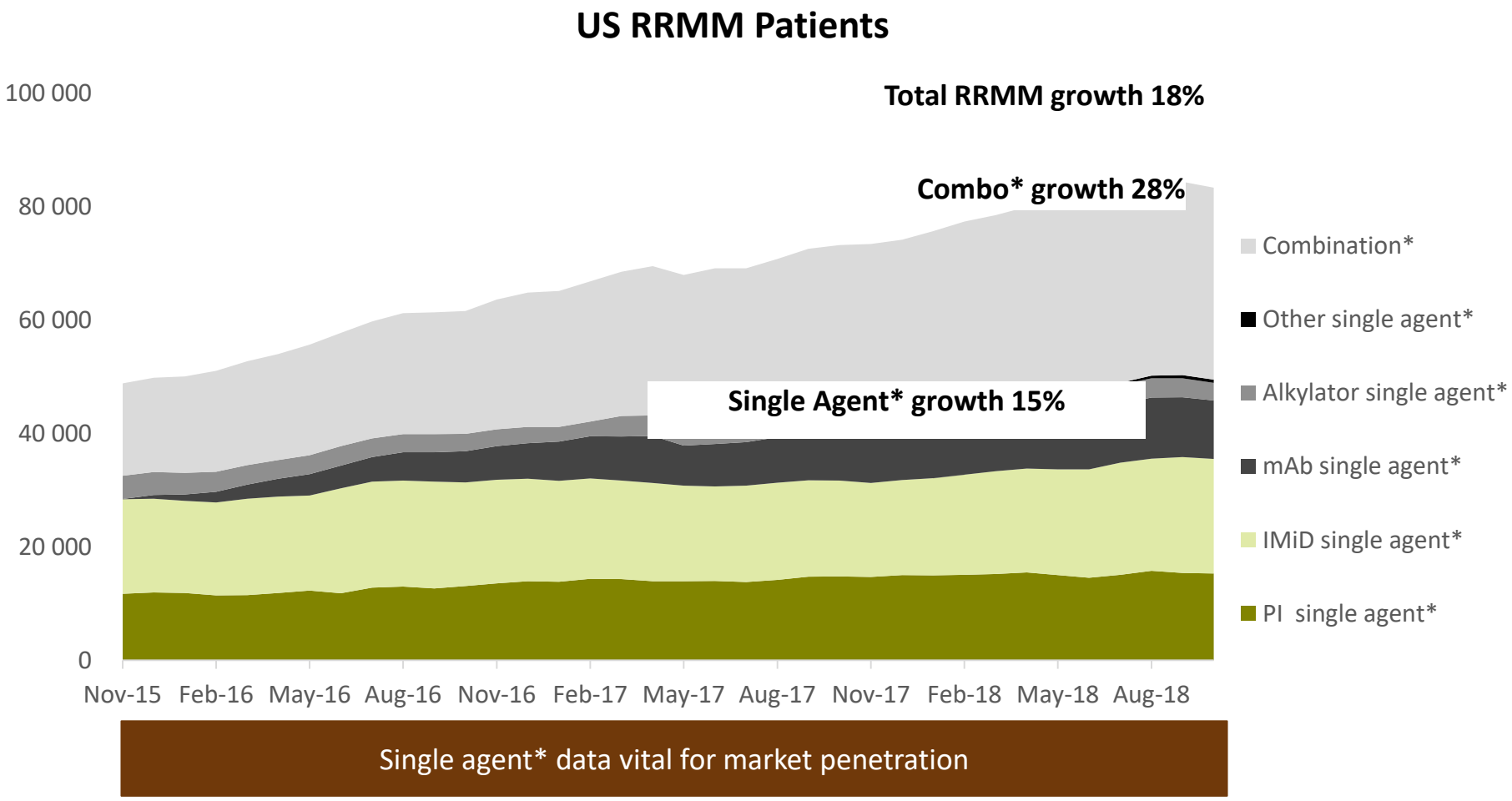
Lack of Treatment Options Drive Fragmentation in 2nd Line+ Patients
Same drugs are used multiple times over course of disease progression



Source: Wilson et al., ASCO Abstract. 2018; e20038 (Chart review from EMR).

RRMM is the Fastest Growing Market Segment

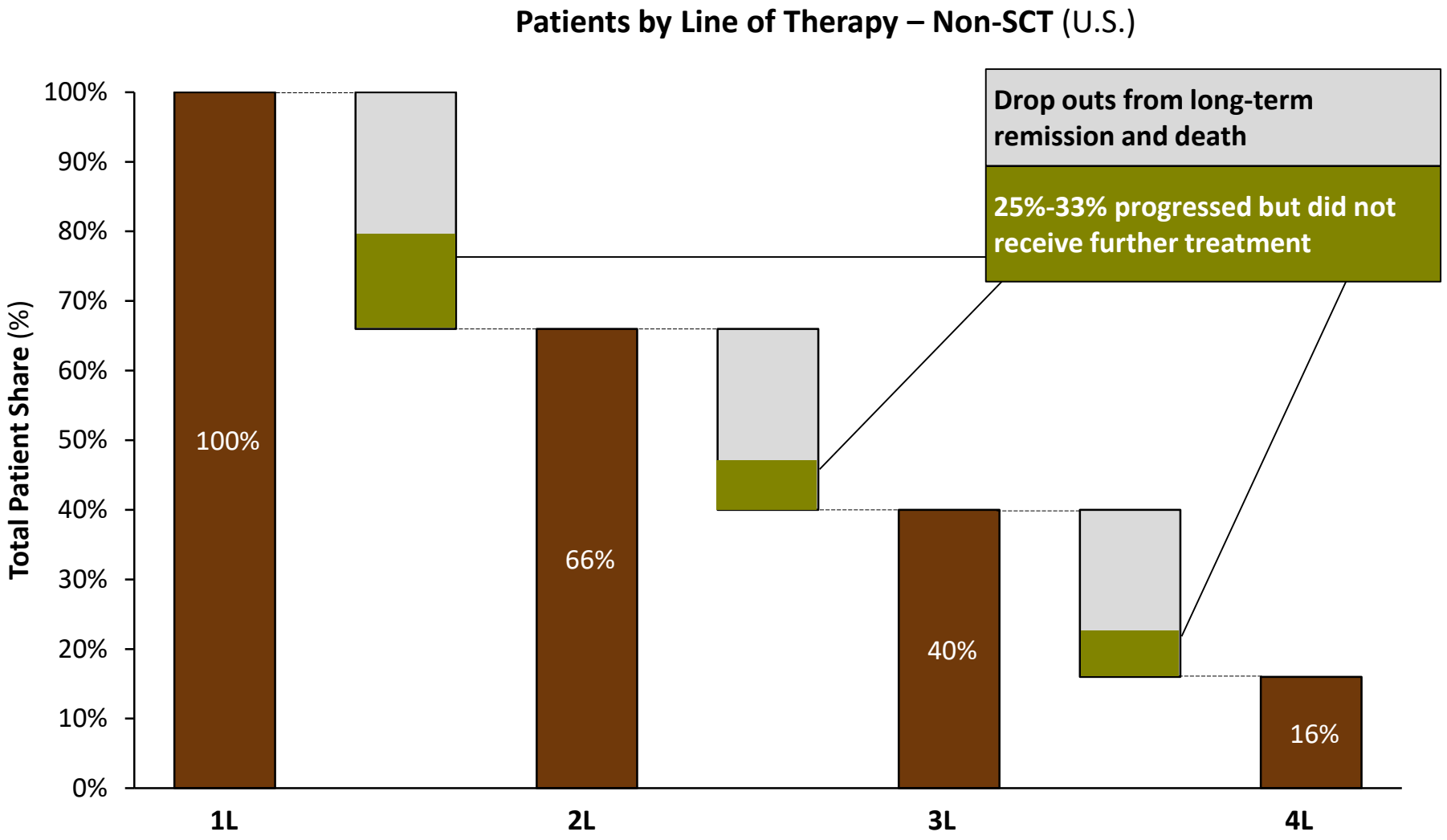
Single Agents/dex used more although combination use is growing



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

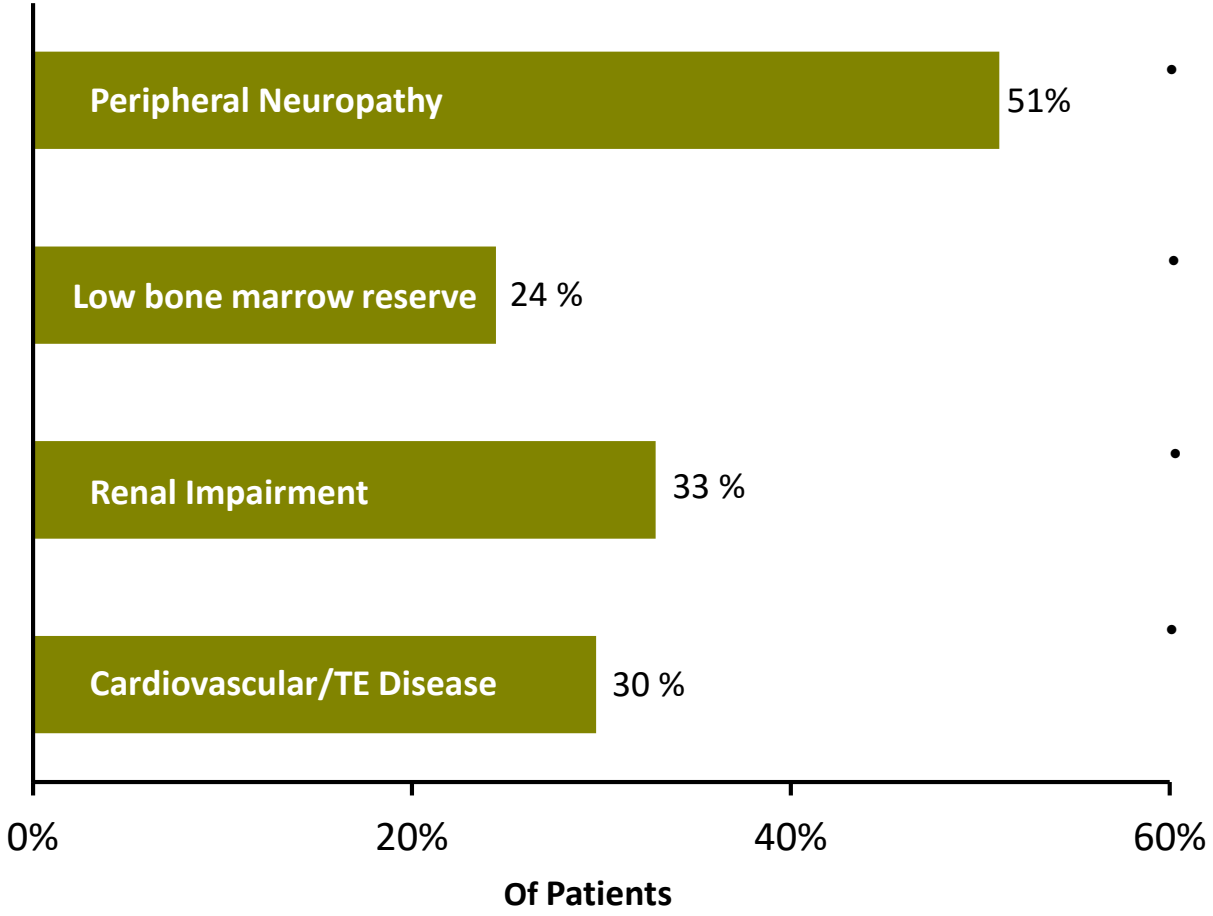


Source: Kantar Health 2018

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.

Requirements for Success in Relapsed Refractory Multiple Myeloma Approvals after Revlimid and Velcade

Must have characteristics

- Single agent +/- steroid activity in multi-refractory patients of 20%+ ORR
- Single agent +/- steroid approval in refractory patients
- Efficacy synergy in combination with other main myeloma drugs with good tolerability
- No major QoL tolerability issues
- No co-morbidity limitations
- Easy administration schedule

Requirements for Success in Relapsed Refractory Multiple Myeloma Approvals after Revlimid and Velcade

Must have characteristics	Pomalyst	DARZALEX	Kyprolis	FARYDAK (panobinostat) capsules 10mg/15mg/20mg	NINLARO	Empliciti (elotuzumab)
Single agent +/- steroid activity in multi-refractory patients of 20%+ ORR	☑	☑	☑	☐	☐	☐
Single agent +/- steroid approval in refractory patients	☑	☑	☑	☐	☐	☐
Efficacy synergy in combination with other main myeloma drugs with good tolerability	☑	☑	☑	☑	☑	☑
No major QoL tolerability issues	☑	☑	☐	☐	☑	☑
No co-morbidity limitations	☑	☑	☐	☑	☑	☑
Easy administration schedule	☑	☐	☐	☑	☑	☐

Requirements for Success in Relapsed Refractory Multiple Myeloma

Must have characteristics

- Single agent +/- steroid activity in multi-refractory patients of >20% ORR
- Single agent +/- steroid approval in refractory patients
- Efficacy synergy in combination with other main myeloma drugs with good tolerability
- No major QoL tolerability issues
- No co-morbidity limitations

Nice to have characteristics

- Easy administration schedule

Proven single agent activity

Pomalyst®

DARZALEX™

Comorbidity or tolerability limitations

Kyprolis™

FARYDAK® (panobinostat) capsules 10mg/15mg/20mg

Limited to no single agent data

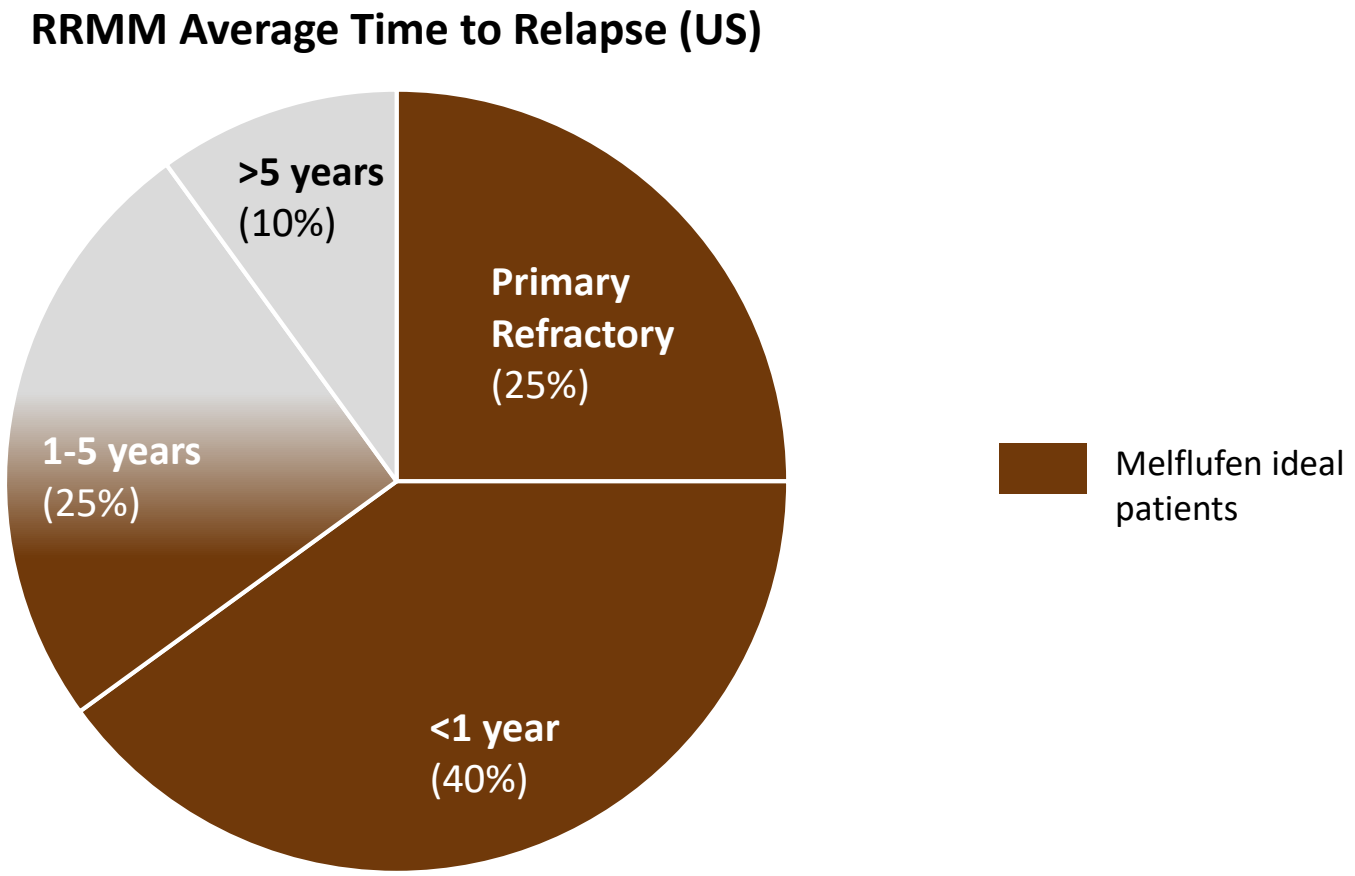
NINLARO®

Empliciti™ (elotuzumab)

Development Program for Melflufen is Designed to Support its Potential as a New 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 head to head study vs. Pomalyst/dex is designed for approval
• Efficacy synergy in combination with other main myeloma drugs with good tolerability	• ANCHOR shows excellent synergy and good tolerability with daratumumab and bortezomib (limited number of patients so far)
• No major QoL tolerability issues	• Good QoL with almost no non-hematological AEs
• No co-morbidity limitations	• No co-morbidity or drug-drug interactions limitations
Nice to have characteristics	
• Easy administration schedule	• One 30 minute infusion every 28 days

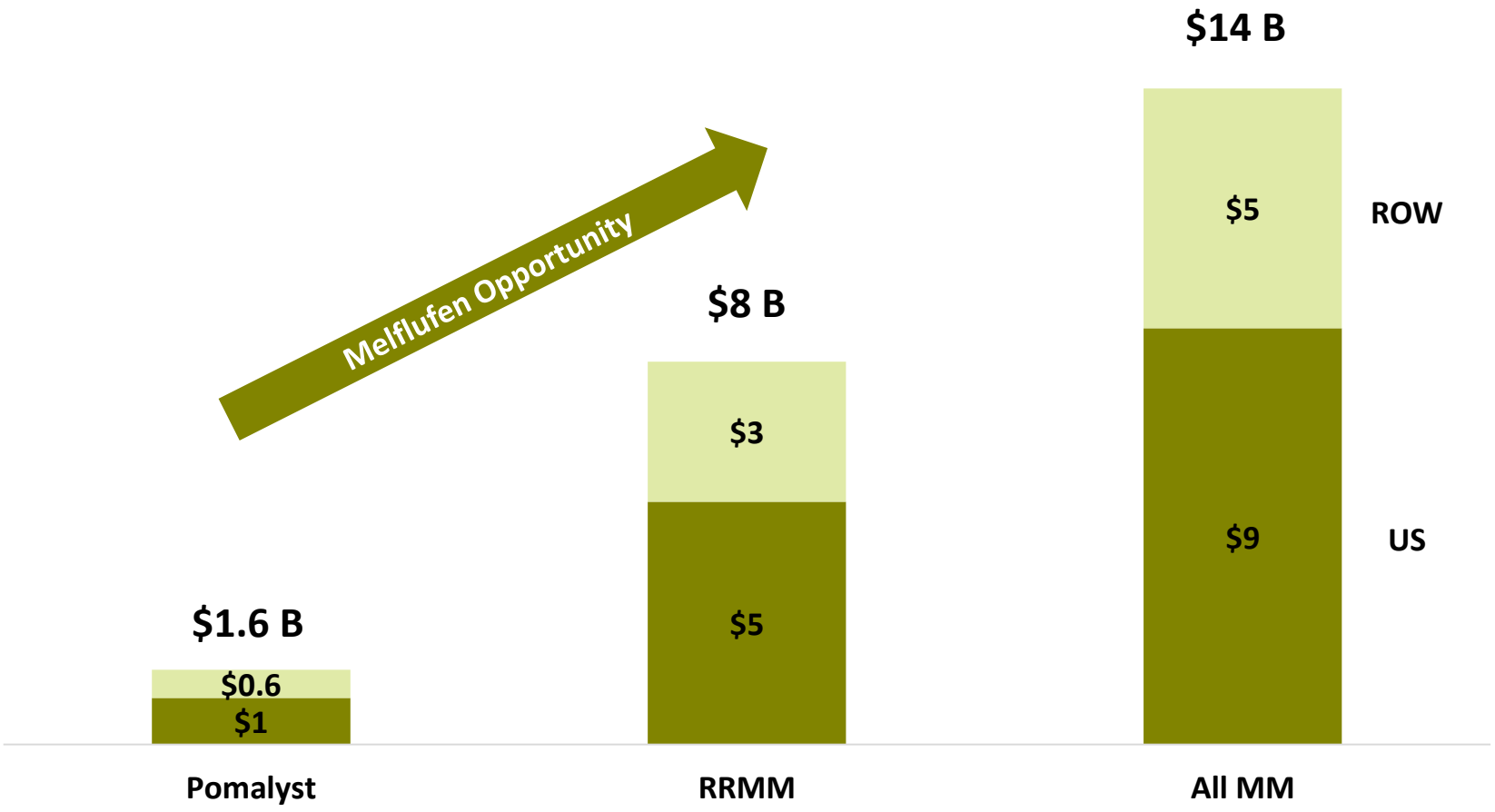
Melflufen Ideal Patients are Refractory or Relapsing within 1-2 Years of Therapy



Source: Kantar Health, IntrinsiQ

Melflufen Opportunity in RRMM

2017 Multiple Myeloma Net Sales Breakdown



Source: EvaluatePharma, Intrinsiq, company analysis

Commercial Opportunity Summary

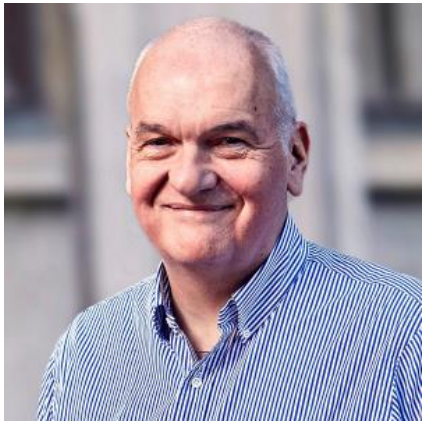
- RRMM market is $8B (2017)
- Pomalyst revenue 2017A of $1.6B and 2018F of $1.9B
- Focusing on US myeloma market only:
  - RRMM patient pool of 80K+ patients per year of which 60K+ patients per year should switch class/treatment due to rapid disease progression after or on previous line of therapy
  - Price band of $7,500 to $15,000 per month (US)

- **Melflufen's emerging profile offers potential to capture significant market share**
  - ✓ Excellent activity with no cross-resistance with other modalities
  - ✓ Single agent approval
  - ✓ Well tolerated and synergistic in combination with PIs and anti-CD38
  - ✓ Excellent tolerability
  - ✓ No co-morbidity or drug/drug interaction limitations
  - ✓ Easy administration schedule

Panel discussion and Q&A

Oncopeptides CMD – December 14th

Professor Paul G Richardson, Dana-Farber Cancer Institute



Christian Jacques, MD, MSc, EVP Clinical Strategy and Chief Scientific Officer

Jakob Lindberg, CEO of Oncopeptides

Paula Boultbee, CCO at Oncopeptides

Oncopeptides Capital Markets Day
December 14th

Summary and Conclusions

Jakob Lindberg, CEO of Oncopeptides