

## Nomenclature

### International non-proprietary name (INN)

Melphalan flufenamide

### Chemical name

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

### Laboratory codes

Melflufen hydrochloride

J1

CK 1535

### CAS No.

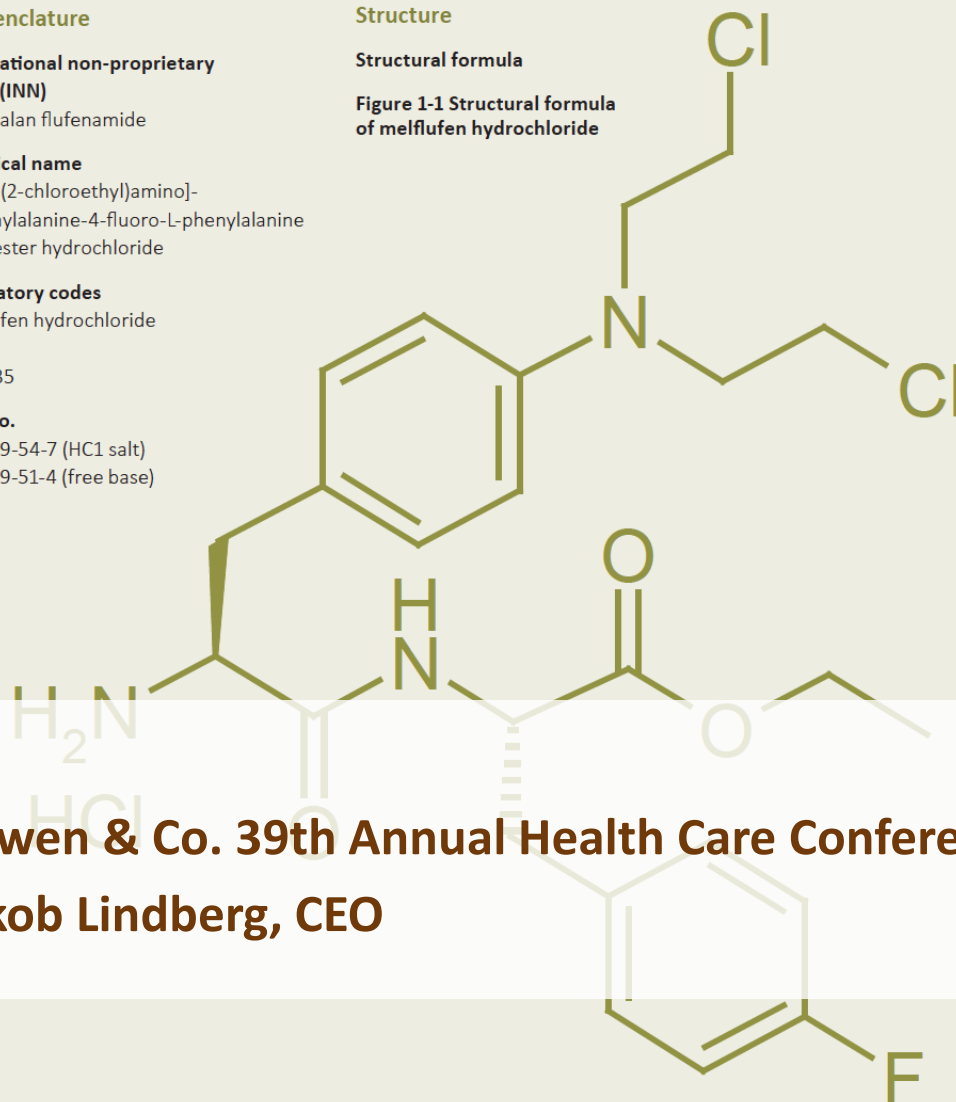
380449-54-7 (HCl salt)

380449-51-4 (free base)

## Structure

### Structural formula

Figure 1-1 Structural formula  
of melflufen hydrochloride



### Molecular formula

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

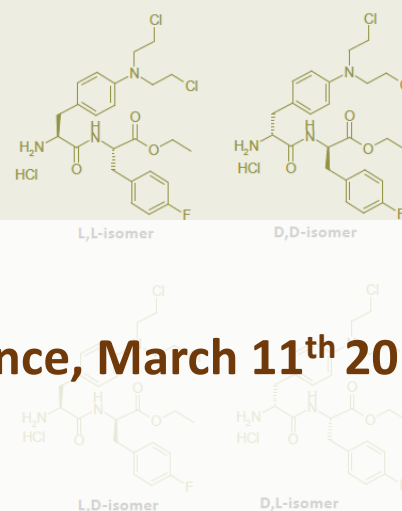
### Molecular weight

534.9 (HCl Salt)

### Stereochemistry

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

Figure 1-2 Structure of melflufen  
hydrochloride isomer



## General properties

### Appearance

White to slightly yellowish powder

### Solubility

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

### Partition coefficient

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

### Dissociation constant

pKa 10.0 (determined in ethanol solution)

### Optical rotation

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

### Thermal behaviour

Differential scanning calorimetry (DSC) was performed using a Mettler Toledo DSC 822 instrument and a scanning rate of 2(tecken)C/minute. The melting temperature was measured using batch GF404528 and determined from the DSC thermogram to be 205.4°C, as shown in Figure 1-3.

Cowen & Co. 39th Annual Health Care Conference, March 11<sup>th</sup> 2019  
Jakob Lindberg, CEO

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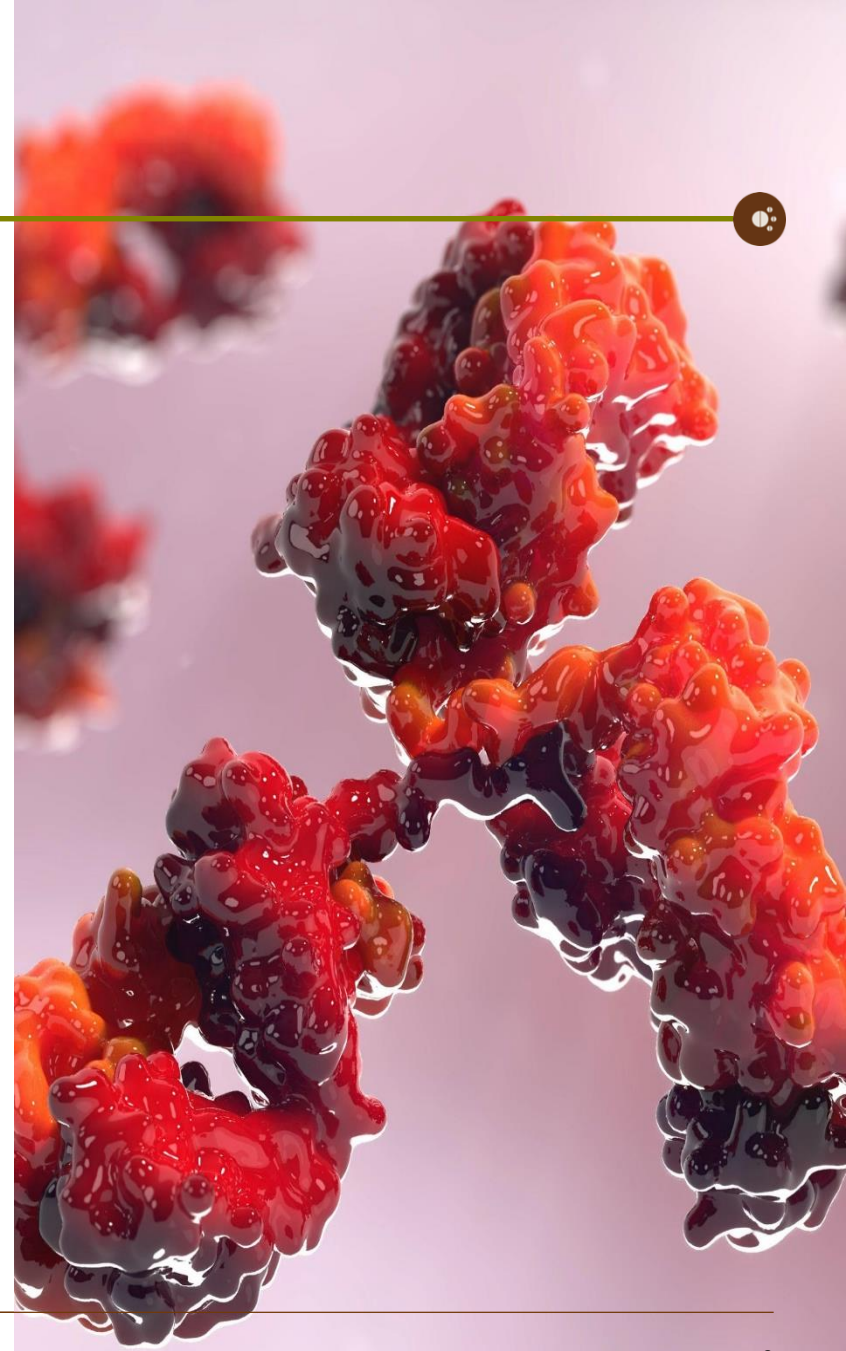
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# Oncopeptides at a glance

- **Develops targeted cancer treatments**
  - Proprietary peptidase-enhanced compounds
  - Lead compound Melflufen a peptide conjugated alkylator
- **Initial focus on Multiple Myeloma**
  - Significant market opportunity in orphan indication
  - Melflufen Phase 2 showed the best MM survival data to date
- **Phase 3 expected to be fully enrolled in the summer of 2019**
  - Approximately 450 patients at 140 sites
  - Three additional supporting trials ongoing, additional Phase 3 to be started 2019
- **Listed on NASDAQ Stockholm, strong financial position**
  - Market cap: ~\$700 M
  - Cash position Dec. 31, 2018: \$40 M, raised an additional \$55 M in January
- **New indications and NCEs in development**
  - Clinical trials expected to start in 2019



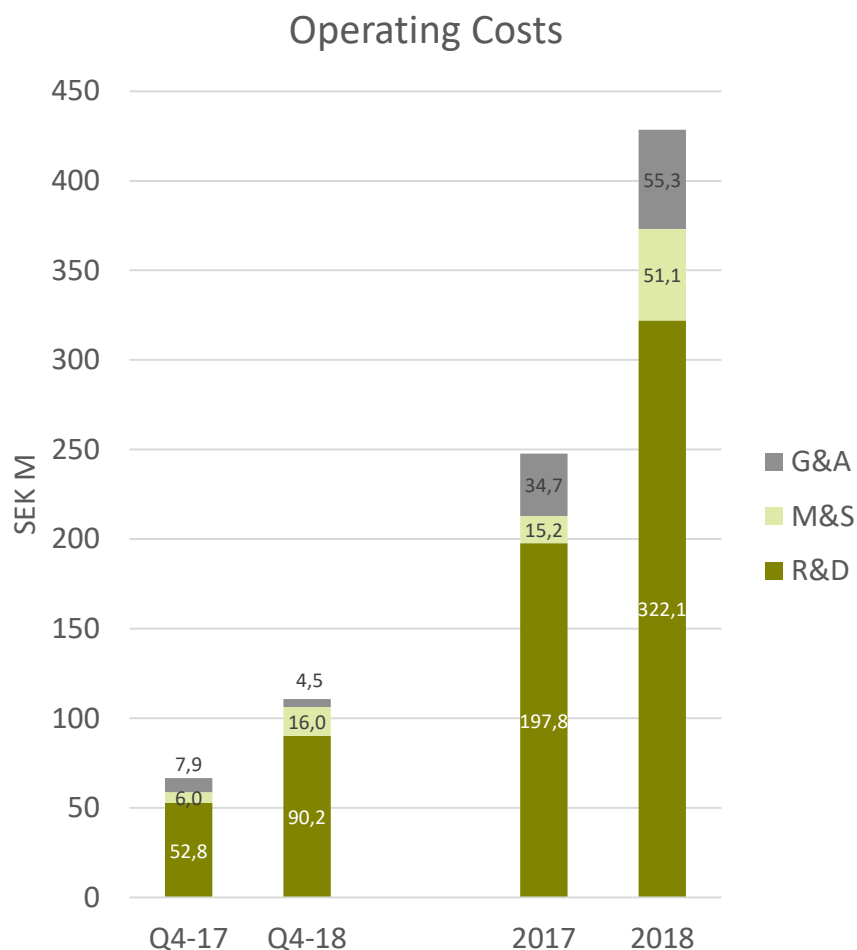
# Highlights 2018

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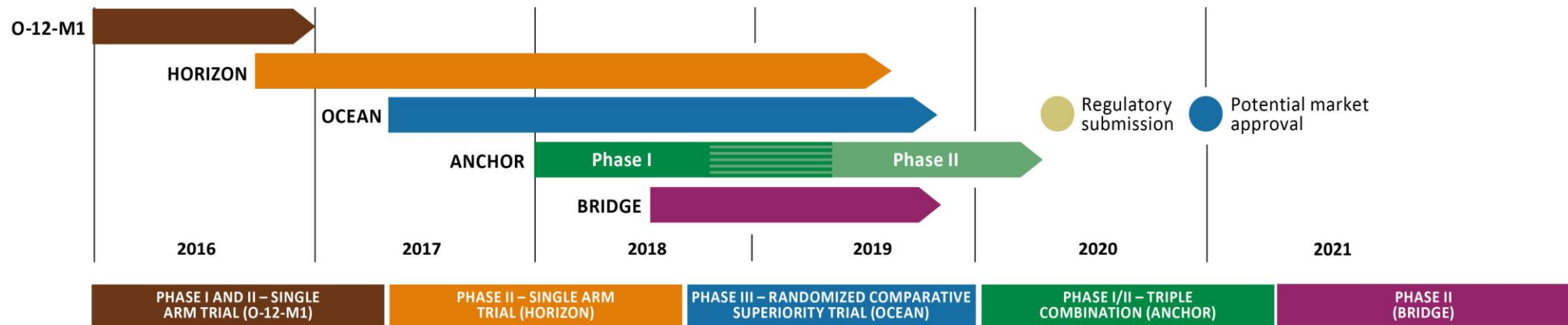
- Capital raise of SEK 314 M in March 2018 (around USD 38 M)
- Expanded the amount of clinics in pivotal OCEAN trial with continued enrollment of patients
- HORIZON study in patients without remaining options expanded based on good results
- Initiated ANCHOR trial studying combinations with Velcade and Darzalex
- Initiated the positioning study BRIDGE in patients with renal impairment
- Presented strong interim results from the HORIZON trial at EHA and later at ASH
- Strong interim results from the ANCHOR trial presented for the first time at ASH
- Capital raise of SEK 546 M in January 2019 (around USD 55 M)

# Financial results for the period Jan –Dec 2018



- Operating loss increased to SEK 419.3 M (loss:247.6)
  - R&D increased primarily due to increase in Clinical: SEK 260.3 M (146.2)
    - OCEAN costs SEK 132.1 M (79.8)
  - Build-up of commercial and medical relations
- Operating costs include non-cash costs related to incentive programs
  - SEK 45.7 M (30.5) for the year, -7.1 M (7.5) for q4
- Cash flow from operating activities neg. SEK 333.7 M (neg. 271.5)
  - Cash flow from financing activities SEK 304.9 M (636.8)
- Cash position was SEK 375.6 M (404.1) as of December 31, 2018
  - Directed share issue raised SEK 514.8 M after issue costs in January, 2019

# Overview of our present clinical development program in multiple myeloma



O-12-M1



Show single-agent activity in RRMM

Show single-agent activity in RRMM

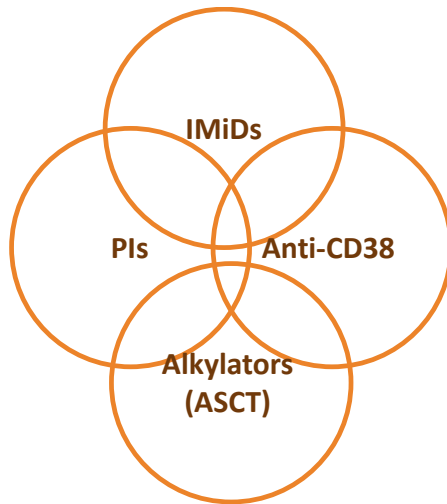
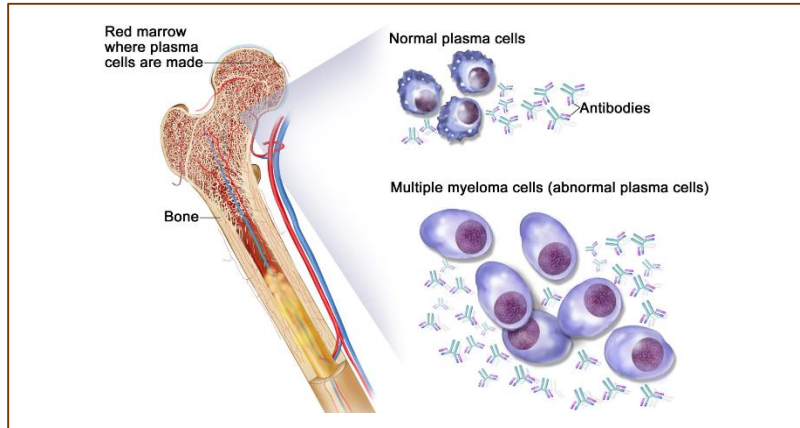
Show single-agent superiority over SoC in RRMM (pomalidomide)

Show combination synergy and tolerability with daratumumab and bortezomib

Show that melflufen can be used in patients with renal impairment

# Multiple Myeloma is a hematological cancer without cure and significant medical need

## Myeloma – Uncontrolled plasma cell proliferation



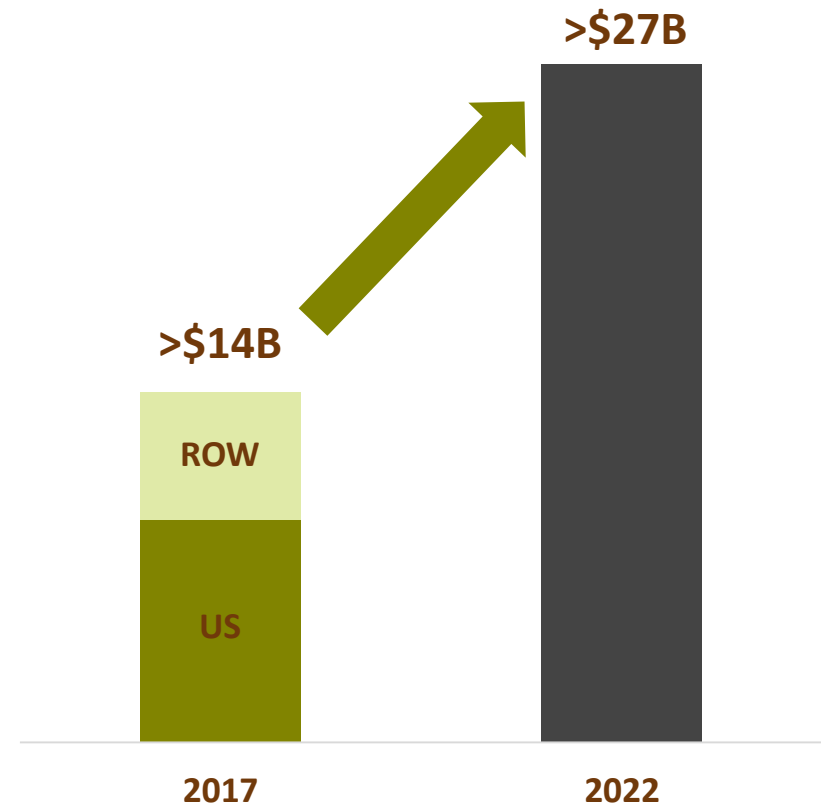
- Overall survival of around 5 years
- Four treatment modalities used with inevitable resistance development
- Currently, the majority of patients have been treated with all four modalities after 2-3 lines of therapy with limited treatment options left
- Frequent co-morbidities further compounding the problem with limited treatment options
- Growing USD 14B market
- Strong underlying growth beyond 1<sup>st</sup> line with 2-4<sup>th</sup> line patients growing with 12-25% CAGR (2015-2018)

# Multiple Myeloma is a Fast Growing Market –

## Approvals of novel agents have expanded market

- IMiDs and PIs will continue to be the foundation of early myeloma care
- 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 - an increased number of treatment months per patient
- The multiple myeloma market is expected to almost double in size before Revlimid patent expiry

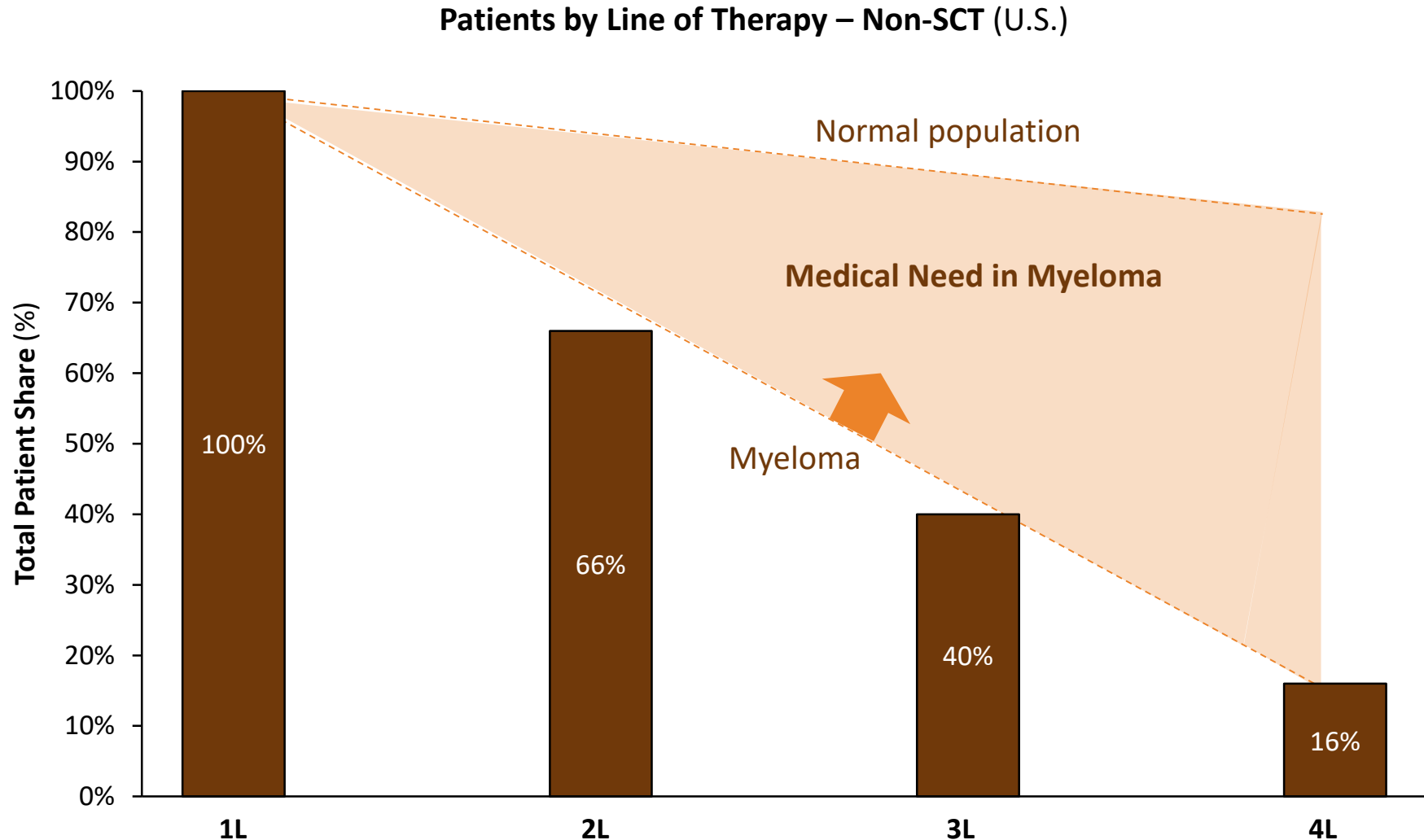
### Market Value Expected to Double





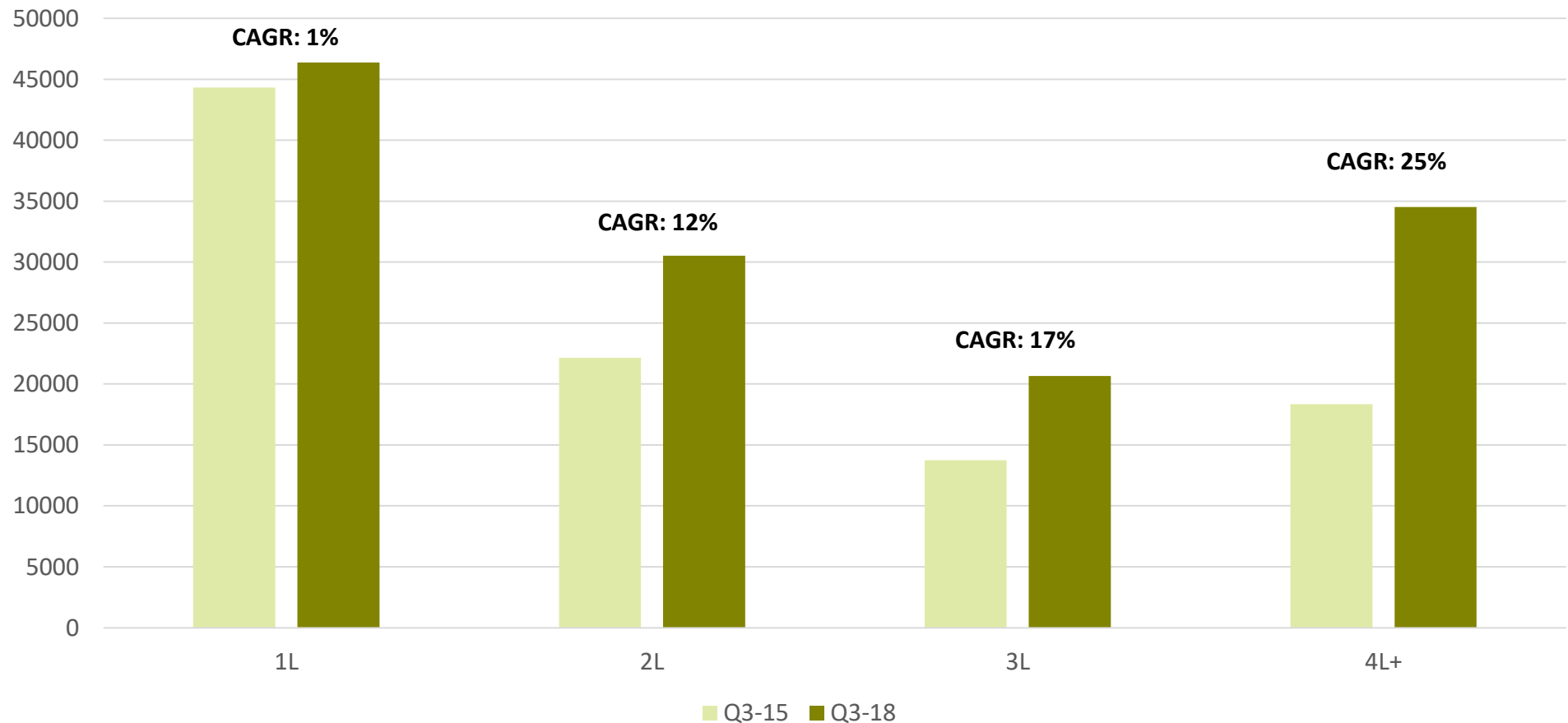
# We are still far from making myeloma a chronic disease –

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



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

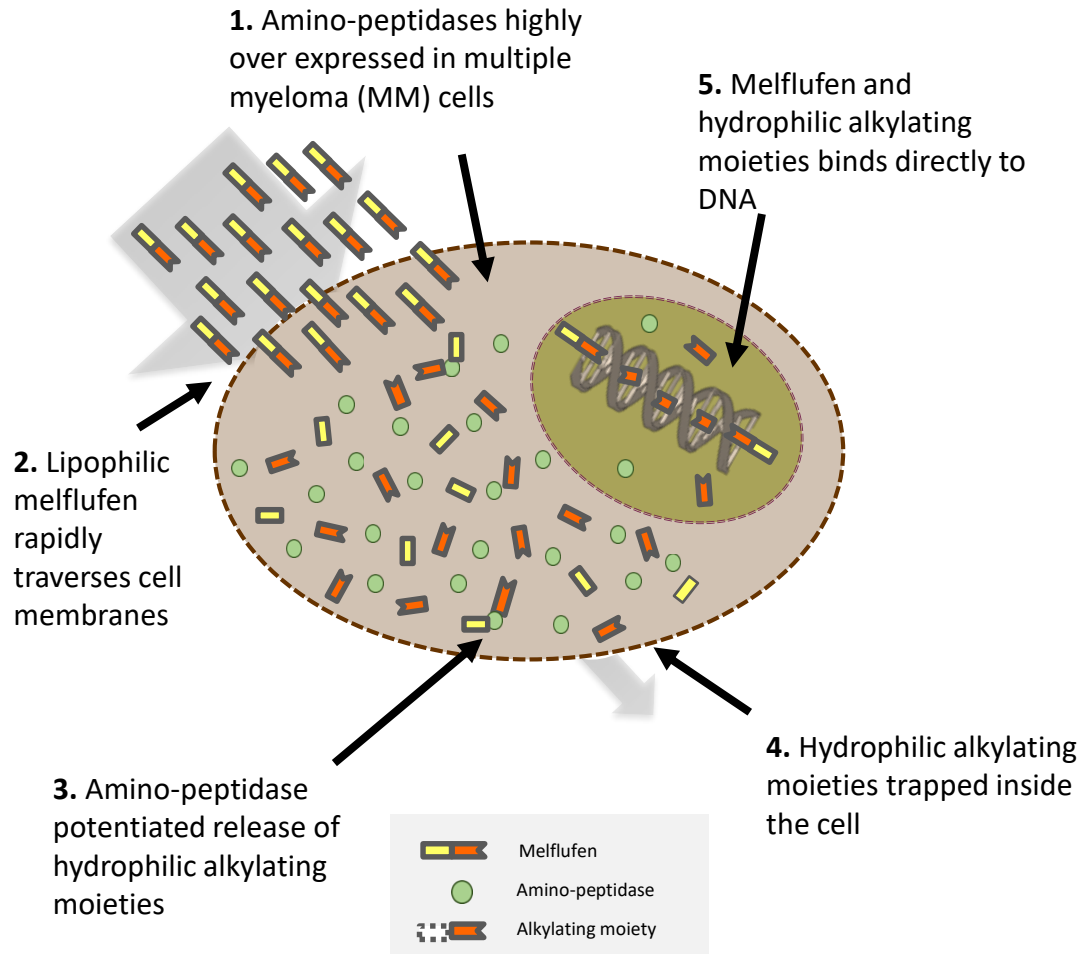
Projected US Multiple Myeloma Patients  
by Line of Therapy



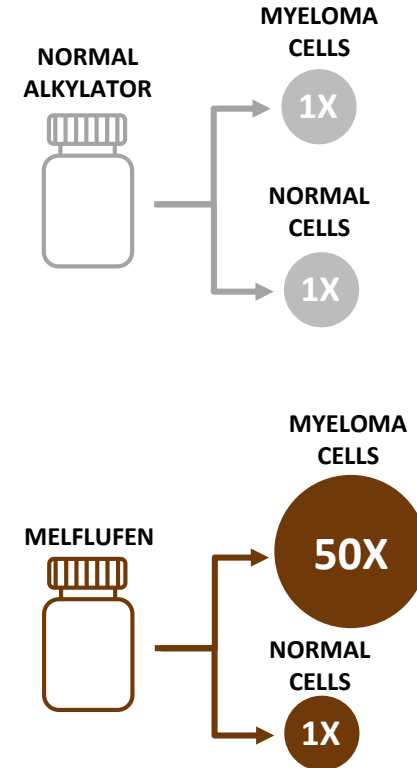
# Melflufen is a first in class peptide conjugated alkylator –

## Aminopeptidases activity increased up to 250x as part of transformation process

### Peptidase enhanced activity in Multiple Myeloma cells



### Results in 50-fold higher potency



# 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

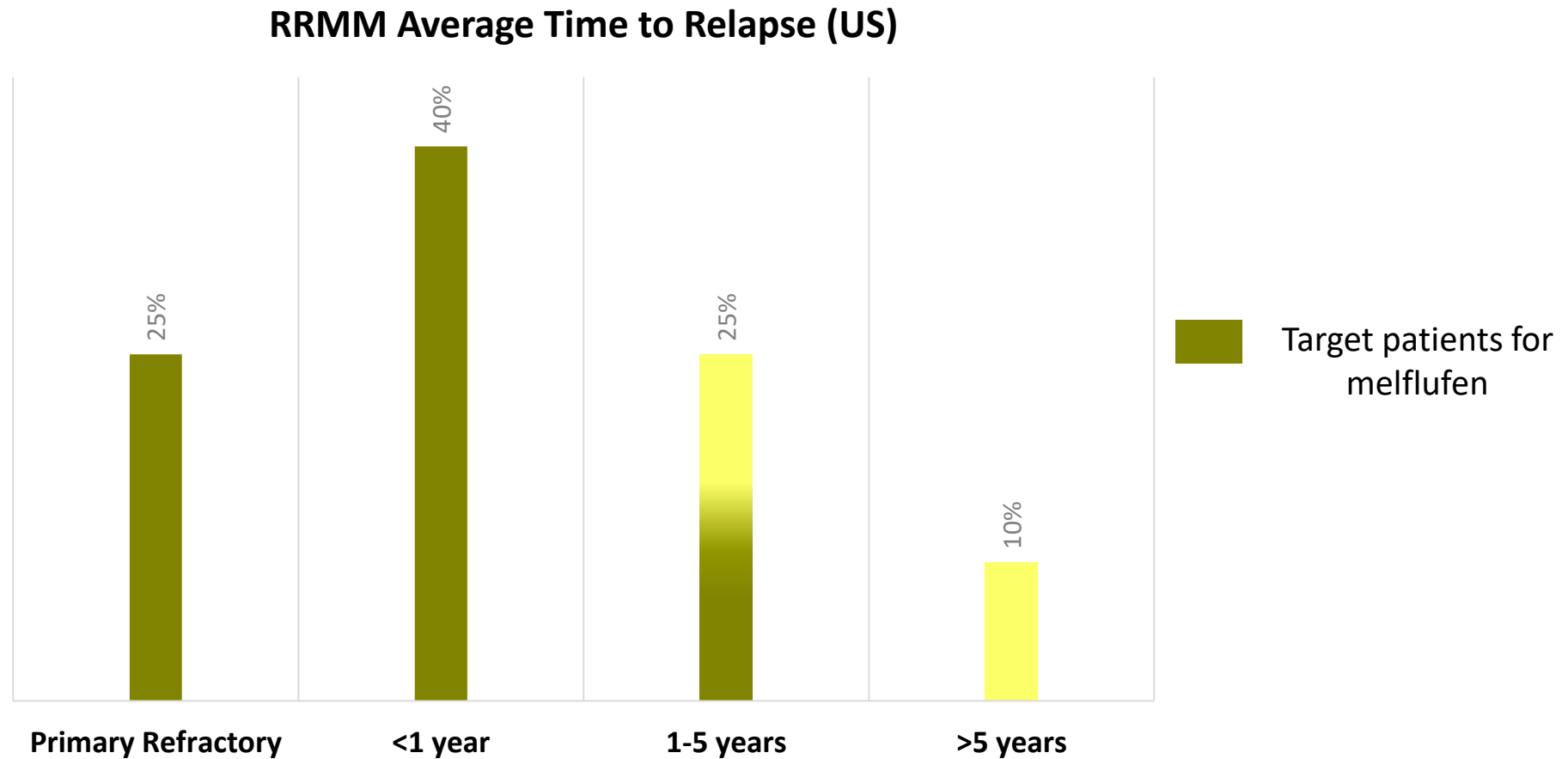
 **NINLARO**

 **Empliciti**  
(elotuzumab)

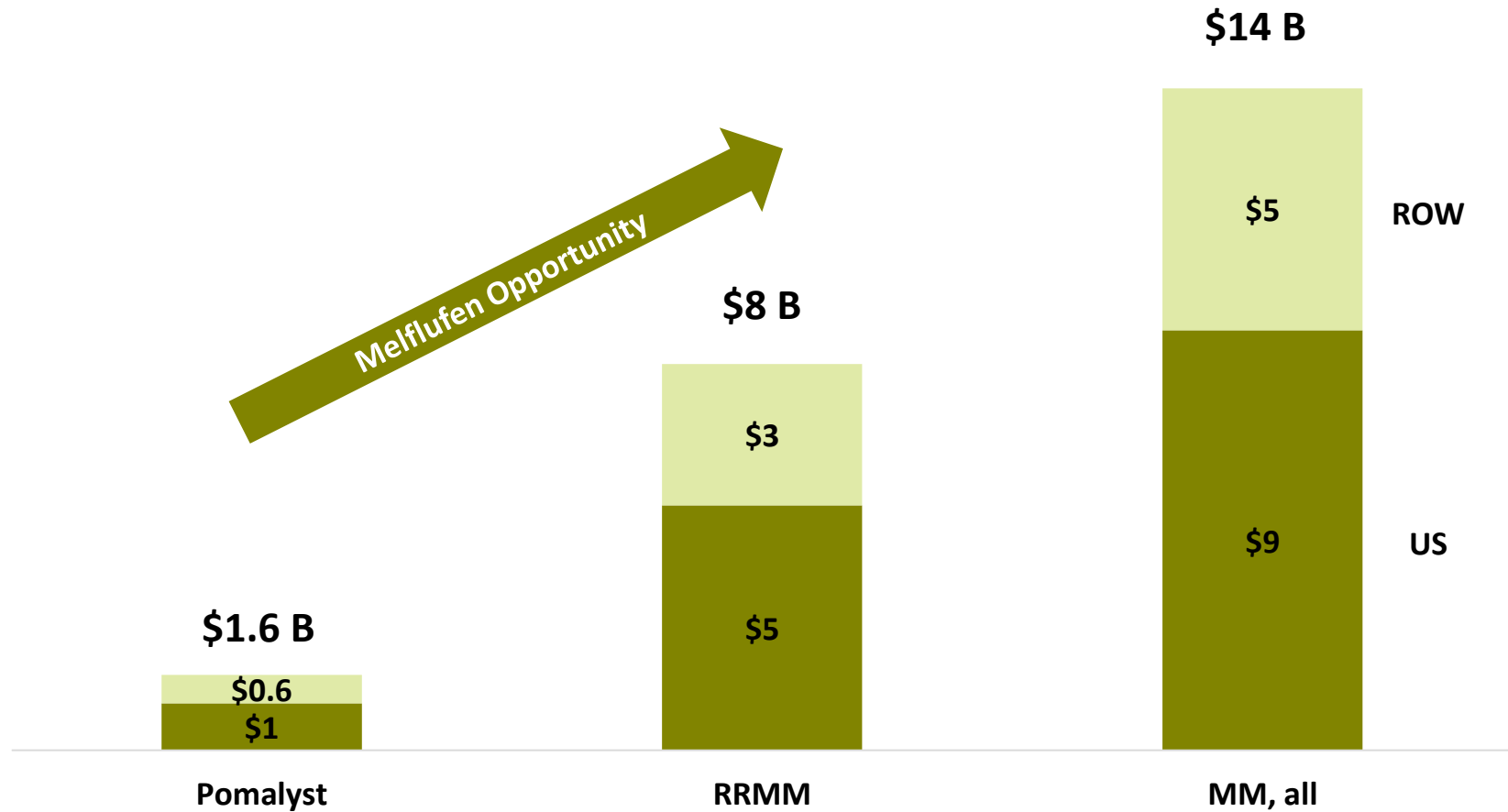
# Development Program for Melflufen is Designed to Support its Potential as a New Agent after IMiD and PI Failure

Must have characteristics		Melflufen
<ul style="list-style-type: none"><li>Single agent +/- steroid activity in multi-refractory patients of &gt;20% ORR</li></ul>	➤	<ul style="list-style-type: none"><li>O-12-M1 showed an ORR of 31% and HORIZON an ORR of 33% in multi-refractory patients</li></ul>
<ul style="list-style-type: none"><li>Single agent +/- steroid approval in refractory patients</li></ul>	➤	<ul style="list-style-type: none"><li>OCEAN head to head study vs. Pomalyst/dex is designed for approval</li></ul>
<ul style="list-style-type: none"><li>Efficacy synergy in combination with other main myeloma drugs with good tolerability</li></ul>	➤	<ul style="list-style-type: none"><li>ANCHOR shows excellent synergy and good tolerability with daratumumab and bortezomib (limited number of patients so far)</li></ul>
<ul style="list-style-type: none"><li>No major QoL tolerability issues</li></ul>	➤	<ul style="list-style-type: none"><li>Good QoL with almost no non-hematological AEs</li></ul>
<ul style="list-style-type: none"><li>No co-morbidity limitations</li></ul>	➤	<ul style="list-style-type: none"><li>No co-morbidity or drug-drug interactions limitations</li></ul>
Nice to have characteristics		
<ul style="list-style-type: none"><li>Easy administration schedule</li></ul>	➤	<ul style="list-style-type: none"><li>One 30 minute infusion every 28 days</li></ul>

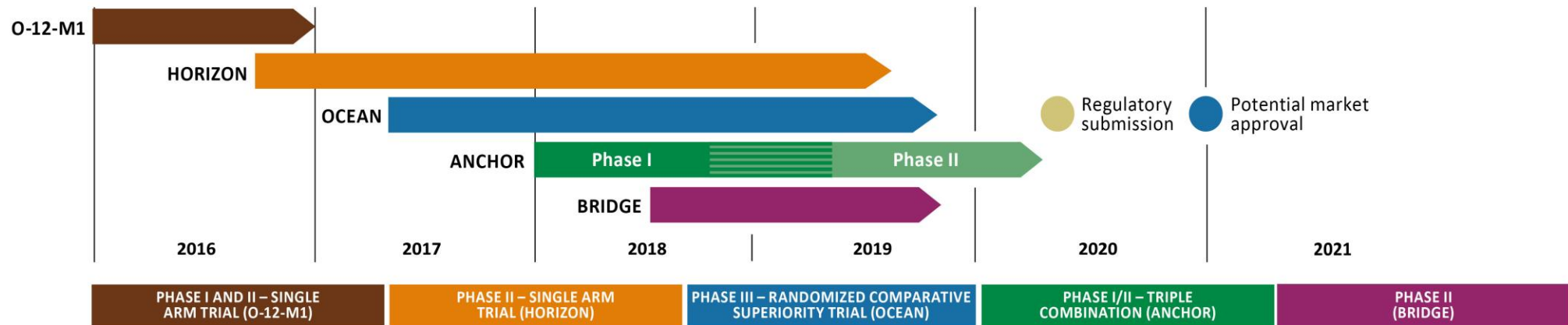
# Melflufen Ideal Patients are Refractory or Relapsing within 1-2 Years of Therapy



# Melflufen opportunity in RRMM – 2017 Multiple Myeloma Net Sales Breakdown



# Overview of our present clinical development program in multiple myeloma



O-12-M1



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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



# O-12-M1 phase 2 study generated best overall survival data to date in late stage myeloma

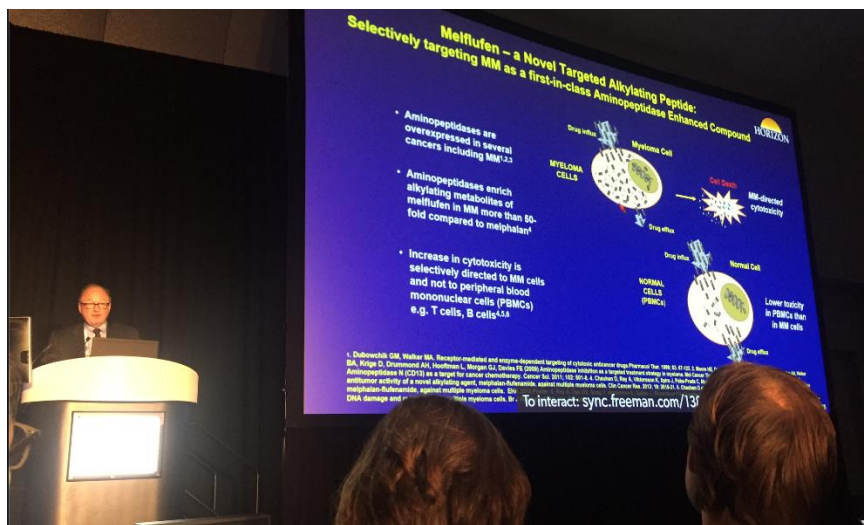
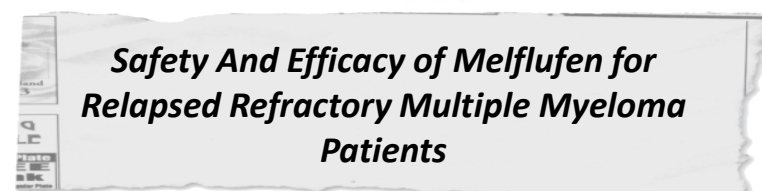
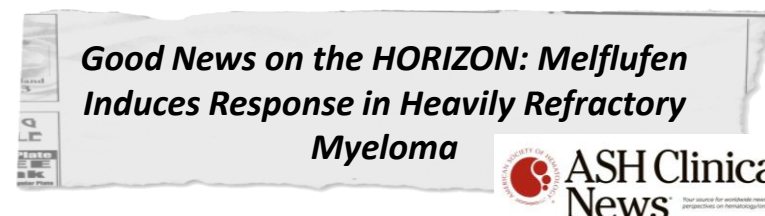
	Melflufen	Daratumumab	Pomalidomide*	Carfilzomib
<b>N</b>	45	106	302	266
<b>Year</b>	2017	2016	2013	2012
<b>Population</b>	Refractory to last, exposed to iMiD, PI and alkylator, IMiD and PI refractory	Refractory to last, ≥3 lines with IMiDs and PI, double refractory to PI and IMiD	Refractory to last, at least 2 lines with bort and len and received alkylator	>2 prior for relapsed including Bar, Len or thal, alk or anthra alone or in combo
<b>Time from diag.</b>	5.0 years	4.8 years	5.3 years	5.4 years
<b>High risk Cytog.</b>	44%	19%	~30%	28%
<b>Number of lines</b>	4, 78% ≥3 lines	5, 82% ≥3 lines	5, 94 % ≥2 lines	82% ≥4 lines
<b>Refract. to last</b>	87%	97%	100.0%	94.0%
<b>ORR</b>	31.1%	29.2%	23.5%	23.7%
<b>ORR high risk</b>	25%	20%	—	29.6%
<b>Med. duration treat</b>	3.7 months	-	Progressive Disease or Unacceptable Toxicity	3.0 months
<b>Med. duration response</b>	8.4 months	7.4 months	7.0 months	7.8 months
<b>Median PFS</b>	5.7 months (11.7 in ≥PR)	3.7 months	3.6 months	3.7 months
<b>Median OS</b>	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

# Strong data presented at ASH 2018

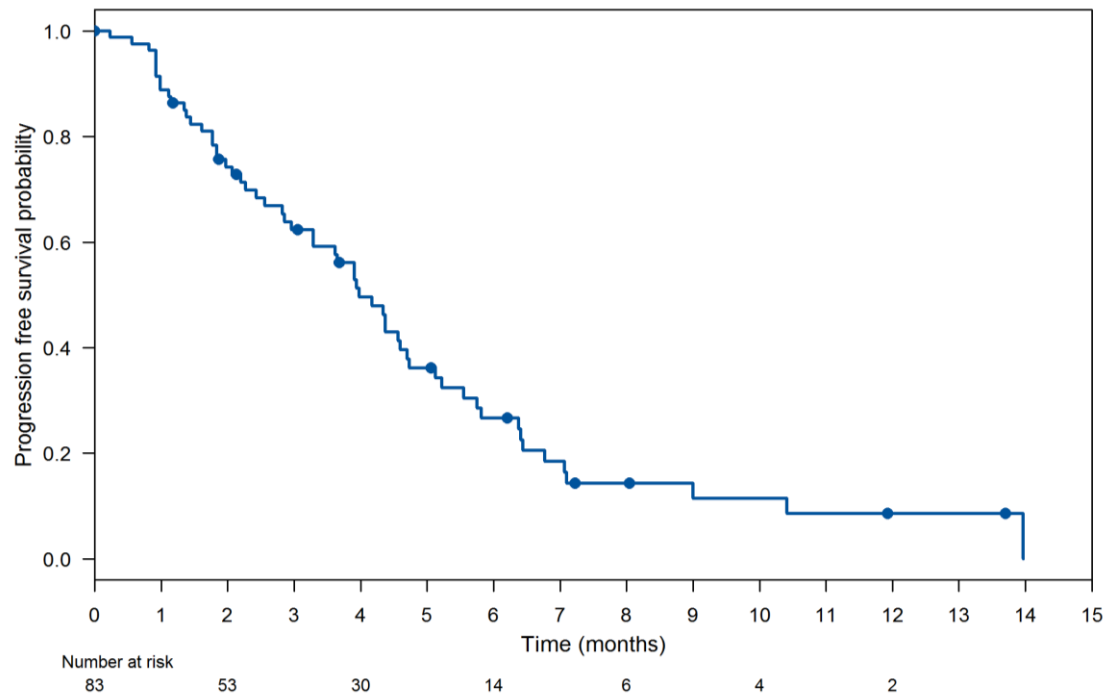
- Interim HORIZON data in patients with no or limited treatment options presented by Prof. Paul Richardson
- Melflufen in combination with bortezomib and daratumumab presented from the ANCHOR trial



# Promising efficacy data for patients without remaining treatment options presented at ASH

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

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



- n= 83, 5-6 prior lines of therapy (median of 5)
- Strong overall response rate with 33%
- Median PFS of 4.0 months
- Strong activity in triple refractory (IMiD, PI and daratumumab) refractory patients

# Safety indicates a very good quality of life profile for patients



Grade 3 and 4 TEAEs occurring in >5% of patients	
	HORIZON
<b>SAE rate</b>	37%
<b>Hematological</b>	
Anemia	26%
Leukopenia	
Lymphopenia	
Neutropenia	55%
Thrombocytopenia	52%
Febrile neutropenia	5%
<b>Infections and infestations</b>	
Pneumonia	5%

- Absence of grade 3 and 4 TEAEs outside of the hematological system and infections and infestations
- Low infection rate in comparison with other myeloma drugs
- Hematological toxicity clinically manageable – 73% of patients in HORIZON maintains the full 40mg dose while on treatment despite low bone marrow reserves

# Upcoming discussion with the FDA with regard to HORIZON data



- HORIZON is a study in myeloma patients with no or limited treatment options
- Potential for accelerated approval path in the USA – but not certain
- ODAC meeting regarding selinexor (a competitor) on February 26th confirmed the target population and efficacy hurdle in late-stage myeloma (i.e. triple-class refractory myeloma patients)
- FDA meeting before the summer regarding HORIZON with input from the ODAC as well as updated HORIZON data will guide Oncopeptides for the possibility to apply for accelerated approval

# Encouraging data for Melflufen and Dex in Combination with bortezomib presented at ASH



## Summary of 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

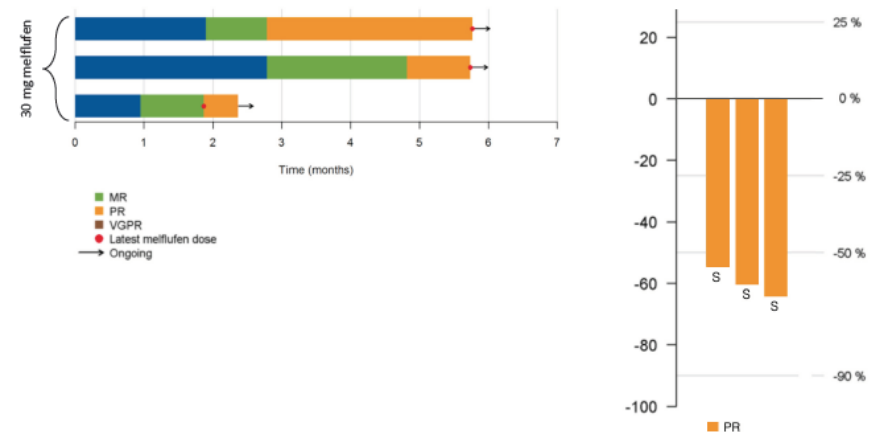
## Few non-hematological AEs

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

## 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)

## Overall response rate 100%



# Data indicates synergistic effect of Melflufen and Dex in combination with daratumumab

## Summary of 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.

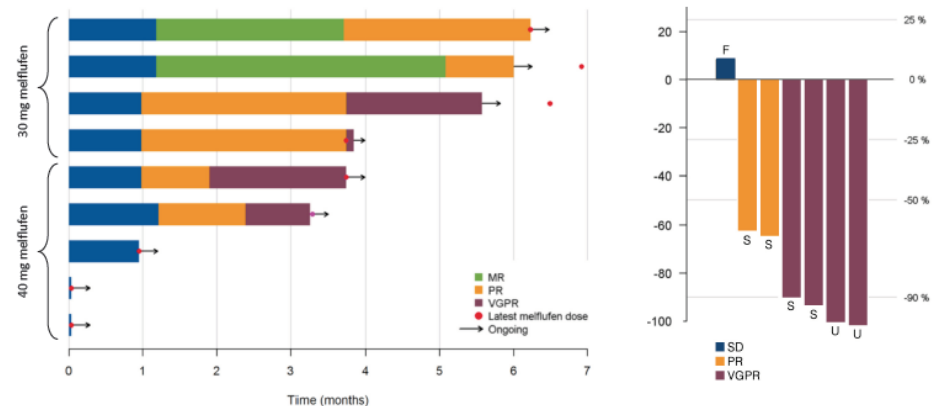
## Manageable hematological AEs and very few non-hematological AEs

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

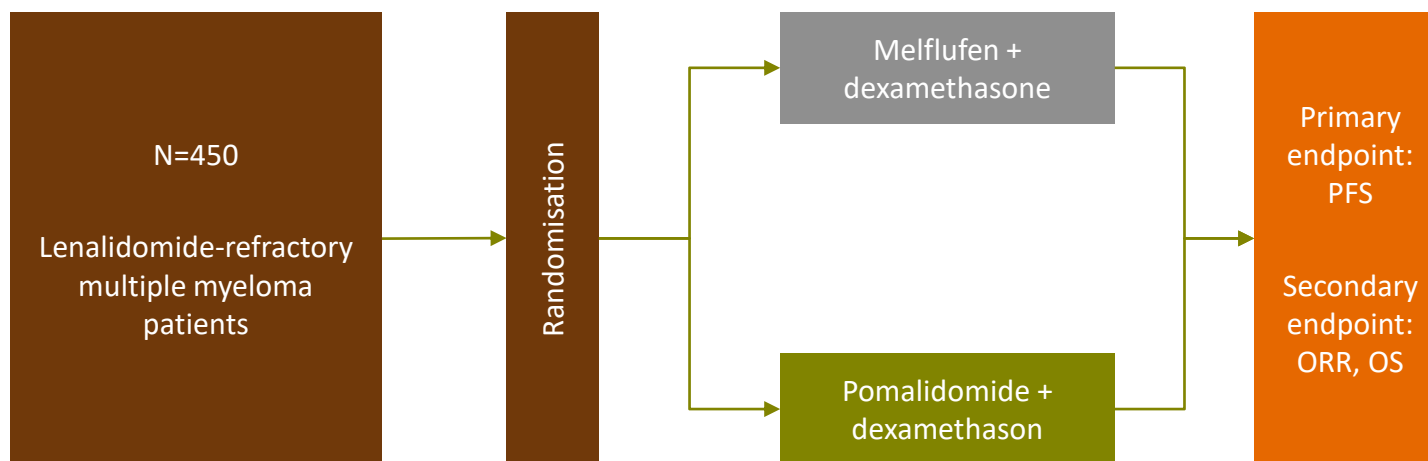
## Patient Characteristics

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)

## Overall response rate 86%



# Data to date provides high conviction for success in pivotal trial OCEAN



## RRMM data from pomalidomide FDA label and O-12-M1 study

Treatment	ORR	CBR	Median PFS	Median DOR	Median OS
Melflufen + Dexamethasone	31%	49%	5.7 months	8.8 months	20.7 months
Pomalidomide + Dexamethasone	24%	NR	3.6 months	7.0 months	12.4 months

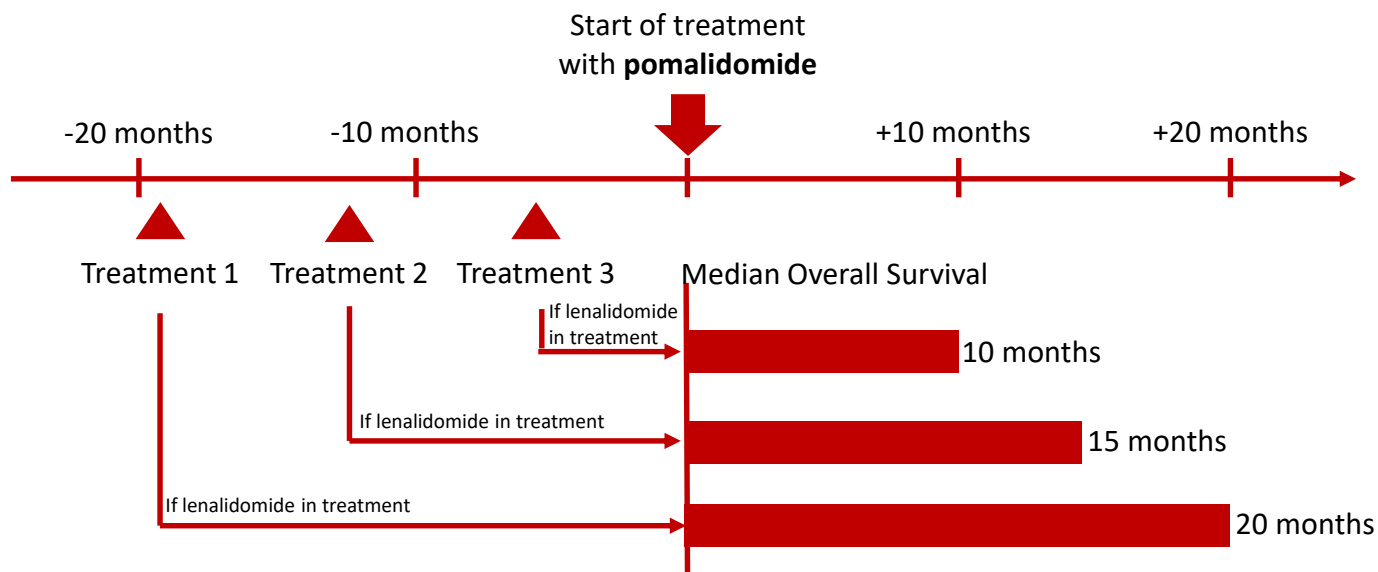


# Pomalidomide shares resistance mechanism with lenalidomide

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



## Dimopoulos research supporting an IMiD free period

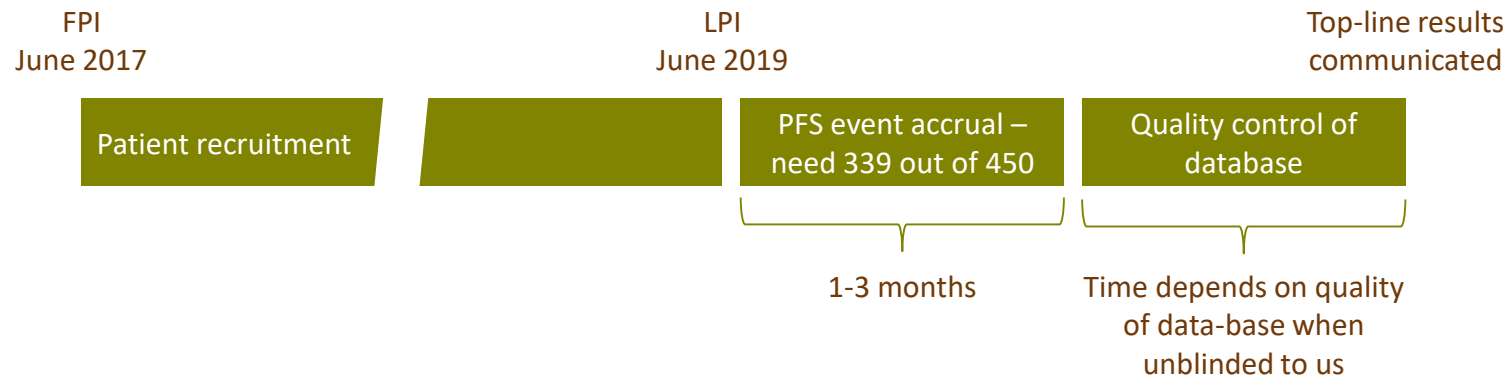


50% reduction in efficacy if patient recently failed on lenalidomide - suggests significant resistance overlap between lenalidomide and pomalidomide

# OCEAN recruitment update



- Last patient in (LPI) estimated for summer of 2019 (no change)
- Previous communication has stated that there is an increased risk of delay to last patient in
  - More than 40 hospitals added to the trial to increase patient recruitment
  - Amendment discussions ongoing with the FDA
- Early 2019 has performed well in terms of patient recruitment
- Process and time-line from last patient in to top-line results:



# Our new pivotal combination trial LIGHTHOUSE of high strategic importance

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- Second pivotal phase III trial with melflufen in multiple myeloma
- Two objectives:
  - Expand market potential in myeloma by label extension to include treatment with melflufen in combination with daratumumab in earlier line patients
  - De-risk the melflufen clinical development program in myeloma by adding a third trial that can result in market registration in the EU and US
- Melflufen+daratumumab+dexamethasone vs daratumumab+dexamethasone randomized 2:1
- We are preparing the study and aiming for having the first patient in H2 2019

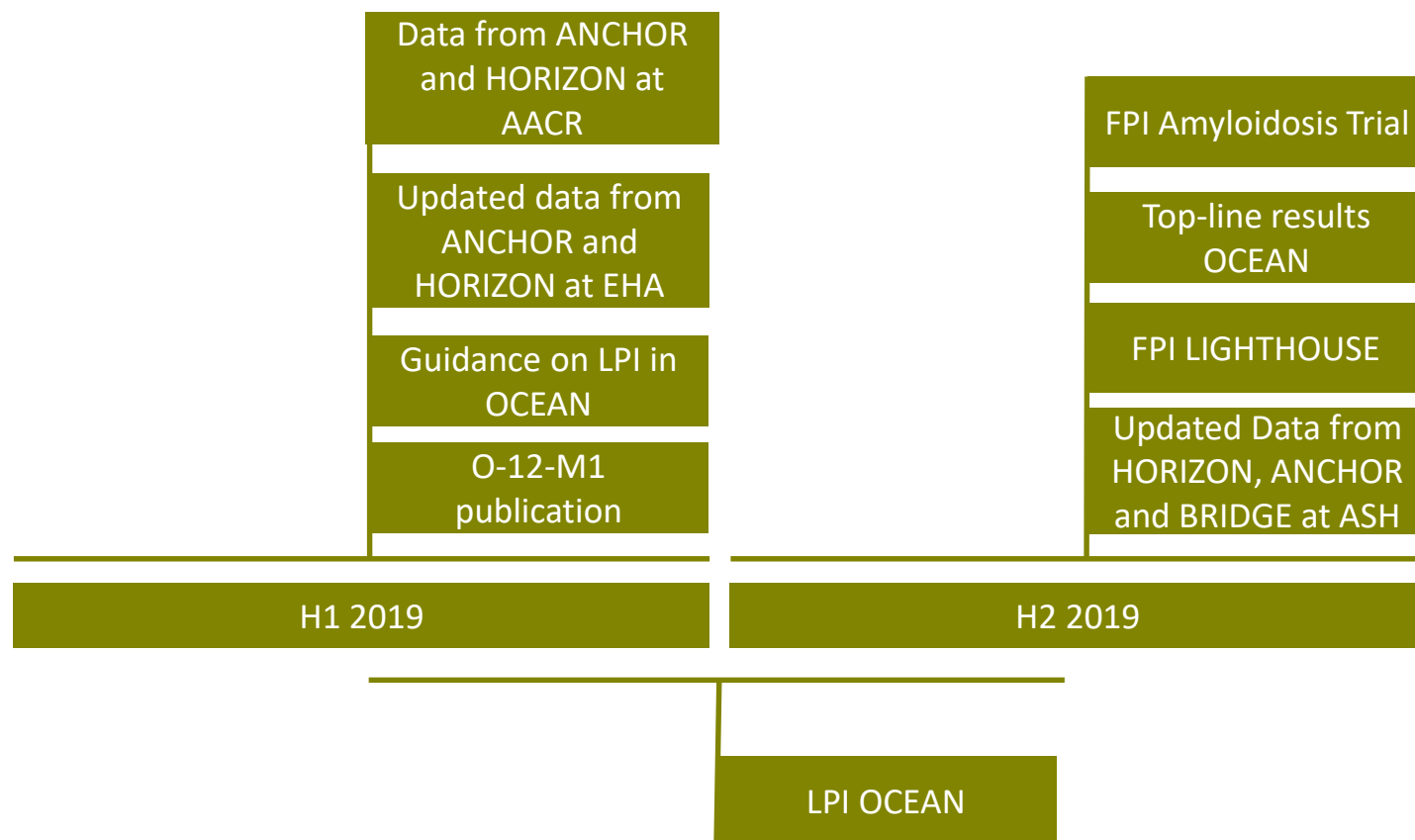
# Our new indication AL AMYLOIDOSIS

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- Similar to myeloma, AL amyloidosis is a disease of the B-cell system
  - Antibody light-chains misfold and form deposits in multiple organs with organ dysfunction as a result
  - Orphan disease - 30-45,000 patients in the USA and the EU<sup>1</sup>
  - Majority of patients >65 years old
- Similar drug use as for myeloma – drugs that are efficacious in myeloma are also most of the time efficacious in AL amyloidosis
- Limited treatment options with median overall survival of 1.5-2.0 years (1995-2013) with a trend towards improved survival (3.5 years for the period 2010-2013)<sup>2</sup>
- Phase I+II study with first-patient-in H2 2019 – up to 30 patients across both phases

# Upcoming newsflow – highly exciting year ahead of us



# 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.

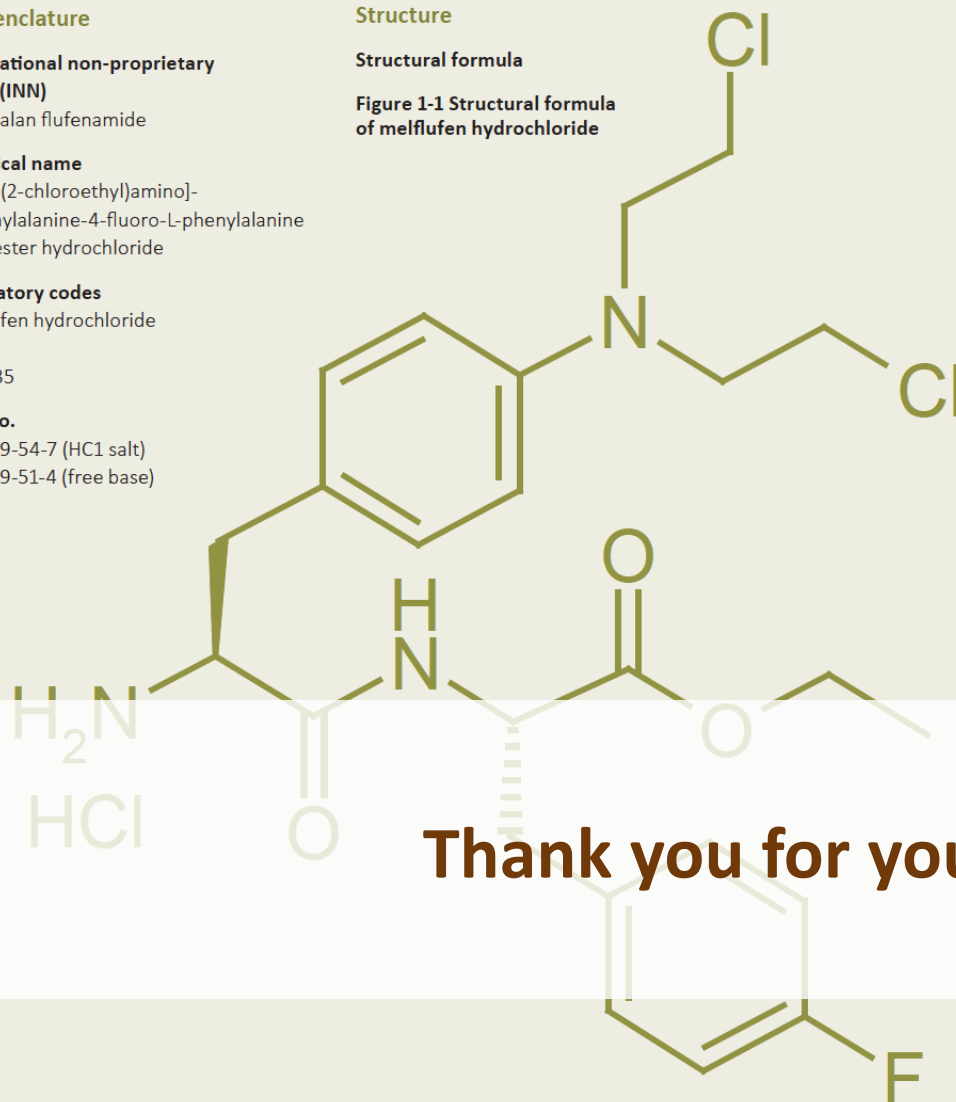
380449-54-7 (HCl salt)

380449-51-4 (free base)

## Structure

### Structural formula

Figure 1-1 Structural formula of melflufen hydrochloride



### Molecular formula

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

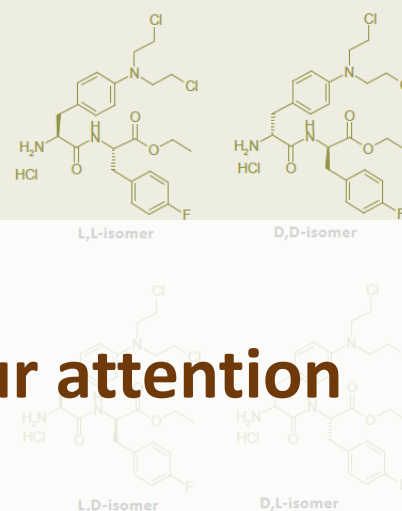
### Molecular weight

534.9 (HCl Salt)

### Stereochemistry

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

Figure 1-2 Structure of melflufen hydrochloride isomer



## General properties

### Appearance

White to slightly yellowish powder

### Solubility

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

### Partition coefficient

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

### Dissociation constant

pKa 10.0 (determined in ethanol solution)

### Optical rotation

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

### Thermal behaviour

Differential scanning calorimetry (DSC) was performed using a Mettler Toledo DSC 822 instrument and a scanning rate of 2(tecken)C/minute. The melting temperature was measured using batch GF404528 and determined from the DSC thermogram to be 205.4°C, as shown in Figure 1-3.

Thank you for your attention