Updated Results of a Phase 1 First-in-Human Study of Cemsidomide (CFT7455), a Novel MonoDAC® Degrader, with Dexamethasone in Patients with Relapsed/Refractory Multiple Myeloma

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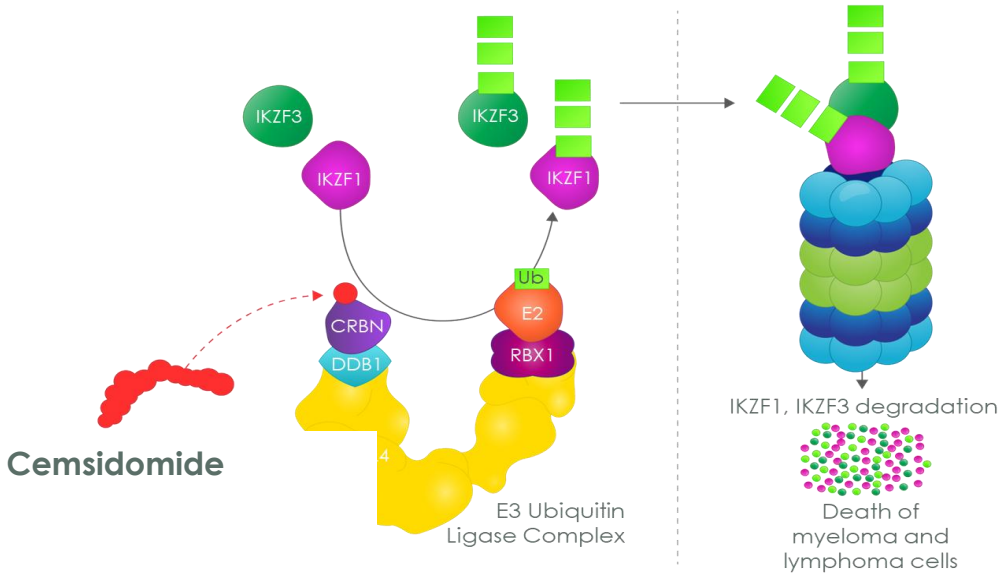
Cemsidomide (CFT7455) Background

- Cemsidomide is a novel, potent, cereblon-based IKZF1/3 MonoDAC® degrader with:
  - Catalytic activity enabling rapid and deep target degradation
  - High binding affinity to overcome resistance due to low cereblon levels
  - Pharmacologic profile to promote tumor residence time and sustained IKZF1/3 degradation

Mechanism of Action for Cemsidomide



- Cemsidomide binds to cereblon to facilitate the recruitment and ubiquitination of IKZF1 and IKZF3, leading to the proteasomal degradation of both proteins

IKZF1/3 Degradation Induces:

- Multiple myeloma cell death
- Stimulation of the immune system
  - Activates fully differentiated T-cells, preventing T-cell exhaustion
  - Promotes secretion of key immune stimulating cytokines (e.g., IL-2)
- On-target neutropenia
  - Disrupts hematopoietic stem cell differentiation

IKZF 1/3, Ikaros zinc finger protein 1/3

CFT7455-1101 Study Design: Arm B2 in RRMM

- Open-label, multicenter, phase 1/2 clinical trial with dose escalation and expansion phases (NCT04756726)
- Dose escalation phase, with a starting oral dose of 50 µg MWF 14 days on/14 days off, following a Bayesian logistic regression model until determination of the MTD and/or RP2D
  - Escalation cohorts enrolled 3-6 patients; following determination of safety by SRC, additional patients were eligible to enroll at the dose deemed safe
    - G-CSF and transfusions were not allowed in cycle 1 for dose escalation subjects
    - Once a dose was declared safe, additional patients at each dose level were allowed G-CSF use at any timepoint

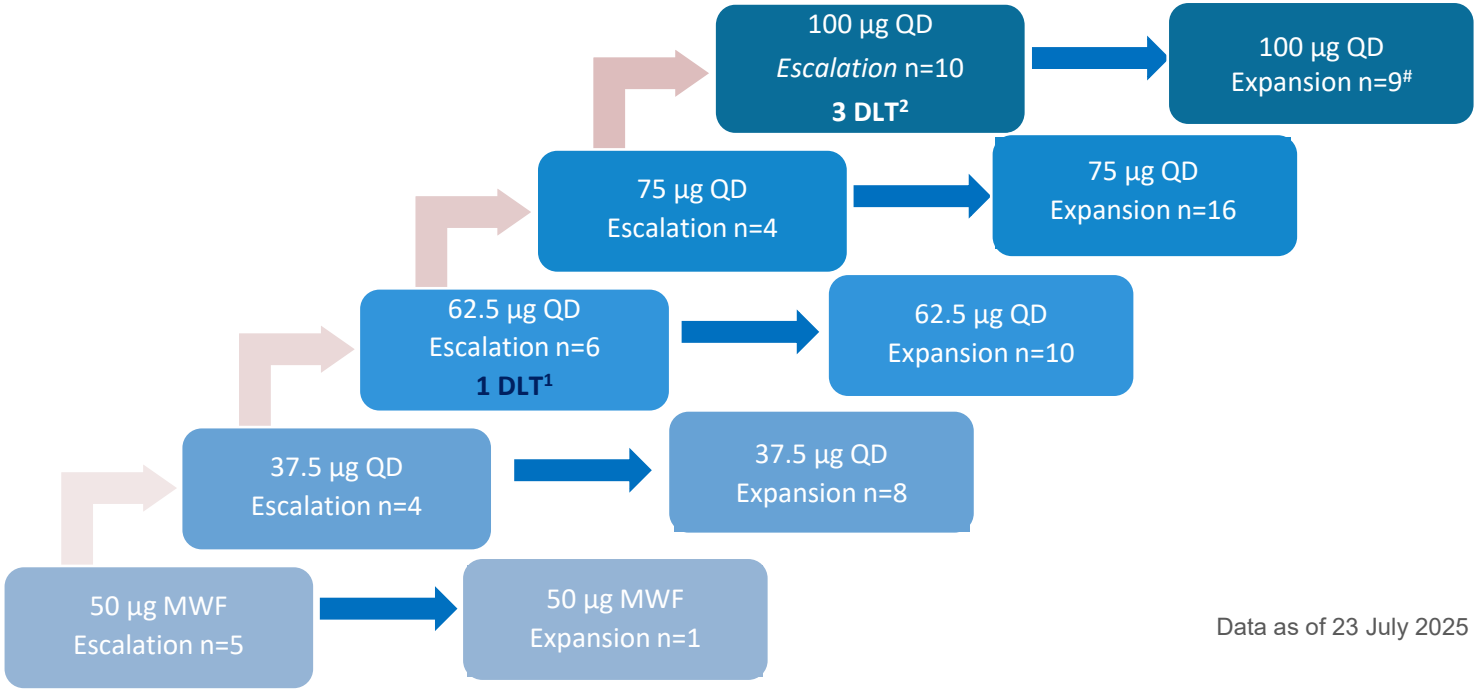
KEY INCLUSION CRITERIA

- Adults with MM, R/R to at least 3 prior lines of therapy that have included lenalidomide, pomalidomide, a proteasome inhibitor, a glucocorticoid, and an anti-CD38 monoclonal antibody
- Nonresponsive to or progressed within 60 days of prior therapy
- Creatinine clearance ≥40 mL/min
- ECOG ≤2

Phase 1 Study Endpoints

- **Primary: assess safety, tolerability and define the RP2D/MTD**
- **Secondary: assess PK, PD, and preliminary anti-tumor activity**

Phase 1 Dose Escalation Cemsidomide 14/14 + Dex*



Data as of 23 July 2025

*Cemsidomide administered as 14 days on/14 days off in a 28-day cycle; Dex was dosed on days 1, 8, 15, and 22 at doses of 40 mg orally for patients ≤75 years old and 20 mg orally for patients >75 years old;
#1 patient in the 100 µg QD expansion did not complete C1 as of data cut-off and is not included in the safety analysis set
[1]DLT in the 62.5 µg QD was due to grade 4 neutropenia lasting >7 days; [2] Three patients in the 100 µg QD escalation had 5 DLT events (G4 neutropenia, G3 pneumonia in 2 subjects, G3 ALT increase, G3 febrile neutropenia)

Dex, dexamethasone; ECOG, Eastern Cooperative Oncology Group; G-CSF, granulocyte colony stimulating factor; MM, multiple myeloma; MTD, maximum tolerated dose; MWF, Monday Wednesday Friday; PD, pharmacodynamics; PK, pharmacokinetics; QD, once daily; RP2D, recommended phase 2 dose; R/R, relapsed/refractory; SRC, safety review committee; 14/14, 14 days on/14 days off.

Baseline Characteristics and Prior Therapies

Heavily Pretreated RRMM Patient Population

Characteristics	Safety Population (N=72)
Age, median (range)	67 (39-90 years)
Male, n (%)	43 (60)
Time since initial diagnosis, median (range)	7 (2-22 years)
ECOG performance status, n (%)	
0	17 (24)
1	52 (72)
2	3 (4)
Asian	1 (1)
Black or African American, n (%)	14 (19)
White, n (%)	50 (69)
Other, n (%)	7 (10)
Revised ISS at screening, n (%)	
Stage 1	24 (33)
Stage 2	29 (40)
Stage 3	9 (13)
Missing	10 (14)
Presence of EMD, n (%)	23 (32)

Characteristics	Safety Population (N=72)
Prior therapies, median (range)	7 (3-22)
3L, n (%)	3 (4)
4L, n (%)	11 (15)
≥ 5L, n (%)	58 (81)
Prior stem cell transplant, n (%)	43 (60)
Prior lenalidomide, n (%)	72 (100)
Prior pomalidomide, n (%)	71 (99)
Prior anti-CD38 mAb, n (%)	72 (100)
Prior CAR-T therapy, n (%)	36 (50)
Prior T-cell engager therapy, n (%)	39 (54)
Prior CAR T or T-cell engager therapy, n (%)	54 (75)
Prior CAR T and T-cell engager therapy, n (%)	21 (29)
Prior BCMA therapy, n (%)	54 (75)
Prior GPRC5D therapy, n (%)	34 (47)
Triple-class exposed*, n (%)	72 (100)
Penta-class exposed†, n (%)	57 (79)

*Defined as exposed to ≥1 immunomodulatory agent, ≥ 1 proteasome inhibitor, and 1 anti-CD38 monoclonal antibody; †Defined as exposed to ≥2 immunomodulatory agents, ≥ 2 proteasome inhibitors, and 1 anti-CD38 monoclonal antibody. Data as of 23 July 2025.

BCMA, B cell maturation antigen; CAR-T, chimeric antigen receptor T cell; ECOG, Eastern Cooperative Oncology Group; EMD, extramedullary disease; mAb, monoclonal antibody; GPRC5D, G protein-coupled receptor class C group 5 member D; RRMM, relapsed/refractory multiple myeloma.

Patient Disposition

Majority of Discontinuations Were Due to Progressive Disease

Patient Disposition, n (%)	Safety Population (N=72)
Ongoing	20 (28)
Discontinued	52 (72)
Progressive disease	39 (54)
Withdrawal of consent	8 (11)
Adverse event	1 (1)*
Death	1 (1)#
Physician Decision	1 (1)
Other	1 (1)†

- At the time of data cutoff, treatment was ongoing for 20 patients (28%)
- The primary reason for discontinuation was progressive disease for 39 patients (54%)

*A patient in the 75 µg cohort had end of treatment reason updated from discontinued due to adverse event to disease progression after data cut off
#Death in a patient in the 62.5 µg cohort was due to subdural hematoma (related to a fall), unrelated to cemsidomide
†A patient in the 50 µg MWF cohort was transferred to hospice, did not meet IMWG definition of progressive disease
Data as of 23 July 2025

Overview of AEs Across Dose Levels

Cemsidomide 14/14 + Dex Was Well Tolerated Over the Range of Doses Tested

Adverse Events, n (%)	50 µg MWF (N=6)	37.5 µg QD (N=12)	62.5 µg QD (N=16)	75 µg QD (N=20)	100 µg QD (N=18)	Total (N=72)
TEAEs	6 (100)	12 (100)	16 (100)	20 (100)	18 (100)	72 (100)
TEAEs possibly related to cemsidomide	3 (50)	11 (92)	12 (75)	14 (70)	14 (78)	54 (75)
TESAEs	3 (50)	6 (50)	6 (38)	7 (35)	8 (44)	30 (42)
TESAEs possibly related to cemsidomide	0	4 (33)	3 (19)	5 (25)	4 (22)	16 (22)
Any grade ≥3 TEAEs	5 (83)	8 (67)	11 (69)	18 (90)	14 (78)	56 (78)
Any grade ≥3 TEAEs possibly related to cemsidomide	3 (50)	8 (67)	8 (50)	12 (60)	11 (61)	42 (58)
TEAEs leading to discontinuation	0	0	0	1 (5)*	0	1 (1)
TEAEs leading to reduction	0	0	0	1 (5)[#]	3 (17)[§]	4 (6)

- 4 DLTs: 1 patient at 62.5 µg had grade 4 neutropenia >7 days; 3 patients at 100 µg had 5 DLT events (grade 4 neutropenia >7 days, grade 3 ALT increase, grade 3 febrile neutropenia, grade 3 pneumonia in 2 subjects)

*A patient in the 75 µg cohort discontinued due to grade 5 AE of septic shock, deemed unrelated to cemsidomide; [#]A patient in the 75 µg cohort had grade 4 thrombocytopenia possibly related to cemsidomide resulting in dose reduction; [§]A patient in the 100 µg cohort had grade 3 pneumonia and another patient at 100µg had grade 3 neutropenia, both AEs possibly related to cemsidomide resulting in dose reduction, a patient in the 100 µg cohort had two dose reductions after two events of pseudomonal bacteremia, deemed unrelated to cemsidomide. Data as of 23 July 2025

AEs, adverse events; ALT, alanine aminotransferase; Dex, dexamethasone; DLT, dose limiting toxicities; MWF, Monday Wednesday Friday; QD, once daily; TEAEs, treatment emergent adverse events; TESAEs, treatment emergent serious adverse events

Most Common TEAEs and AEs of Interest

Majority of Grade 3/4 TEAEs Were Hematologic

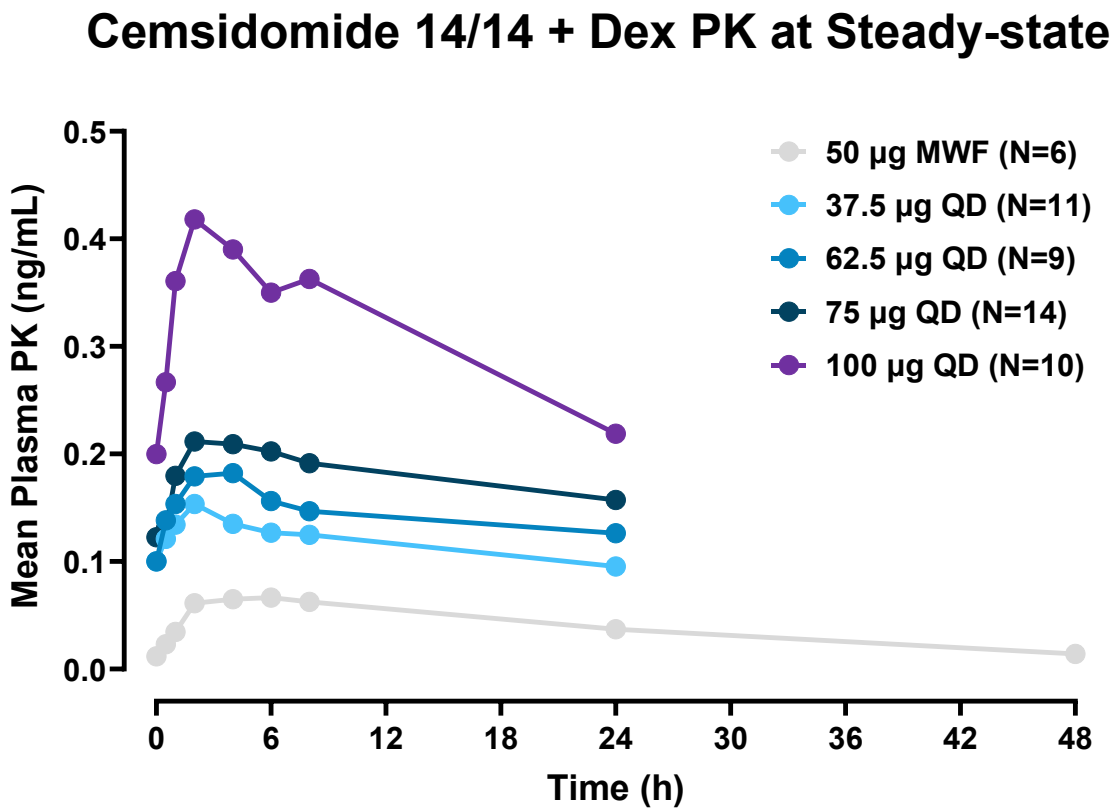
Common (>20% All Grades) TEAEs and Events of Interest, n (%)	All Grades (N=72)	Grade 3 (N=72)	Grade 4 (N=72)	Grade 5 (N=72)
Neutropenia	44 (61)	17 (24)	24 (33)	0
Infections	42 (58)	17 (24)	0	1 (1)
Pneumonia	10 (14)	9 (13)	0	0
Upper Respiratory Tract Infection	10 (14)	2 (3)	0	0
Septic Shock	1 (1)	0	0	1 (1)
Sepsis	2 (3)	2 (3)	0	0
Anemia	27 (38)	16 (22)	1 (1)	0
Fatigue	26 (36)	0	0	0
Diarrhea	26 (36)	1 (1)	0	0
Leukopenia	21 (29)	9 (13)	8 (11)	0
Thrombocytopenia	14 (19)	5 (7)	3 (4)	0
Lymphopenia	13 (18)	6 (8)	2 (3)	0
Febrile Neutropenia	4 (6)	3 (4)	1 (1)	0

- 2 patients experienced grade 5 AEs (septic shock and subdural hematoma), both deemed unrelated to cemsidomide
- G-CSF support was not allowed during cycle 1 for patients in dose escalation cohorts
- 41/72 (57%) of patients experienced grade 3/4 neutropenia, an anticipated on-target effect of IKZF1/3 degradation
  - Neutropenia was manageable with treatment interruptions and G-CSF use when permitted
  - Across all doses, 40% (29/72) of patients received G-CSF

AEs, adverse events; G-CSF, granulocyte colony stimulating factor; IKZF 1/3, Ikaros zinc finger protein 1/3; TEAEs, treatment emergent adverse events. Data as of 23 July 2025

Pharmacokinetics of Cemsidomide 14/14 + Dex

PK Was Dose-Proportional With an ~2-day Half-life

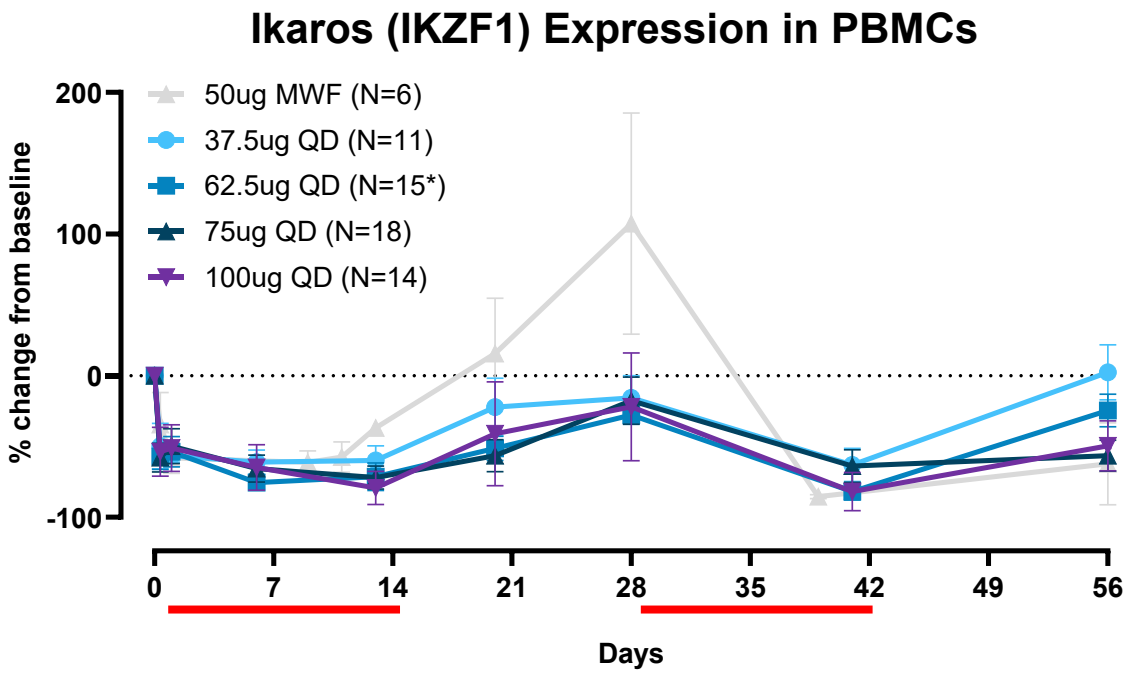


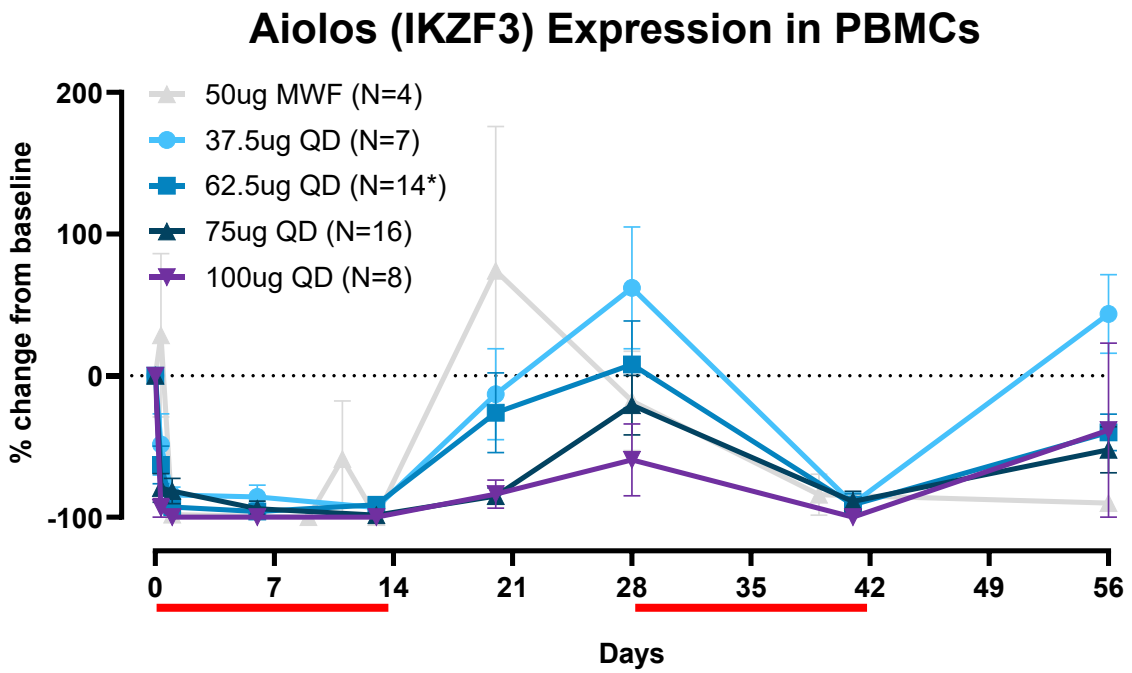
- Cemsidomide 14/14 exposure was dose-proportional when combined with Dex
- The overall geometric mean half-life estimate is approximately 2 days

Dex, dexamethasone; MWF, Monday Wednesday Friday; PK, pharmacokinetics; QD, once daily. Data as of 23 July 2025

Pharmacodynamics of Cemsidomide 14/14 + Dex

Optimal Degradation of IKZF1/3 Observed at 100µg Dose Level





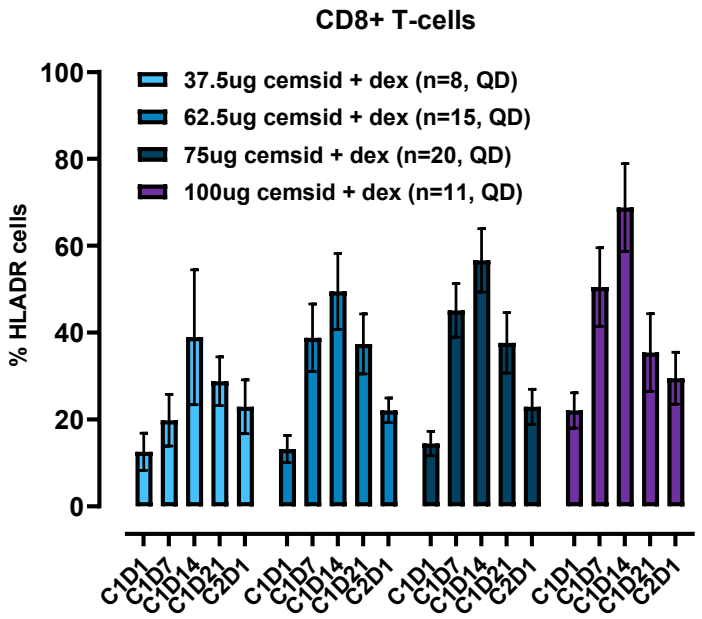
- Cemsidomide 14/14 + Dex achieves >50% degradation of IKZF1 and >80% degradation of IKZF3, as assessed by mass spectrometry in human PBMCs
- Sustained IKZF3 degradation up to day 20 observed at the two highest doses of cemsidomide (75µg and 100µg)

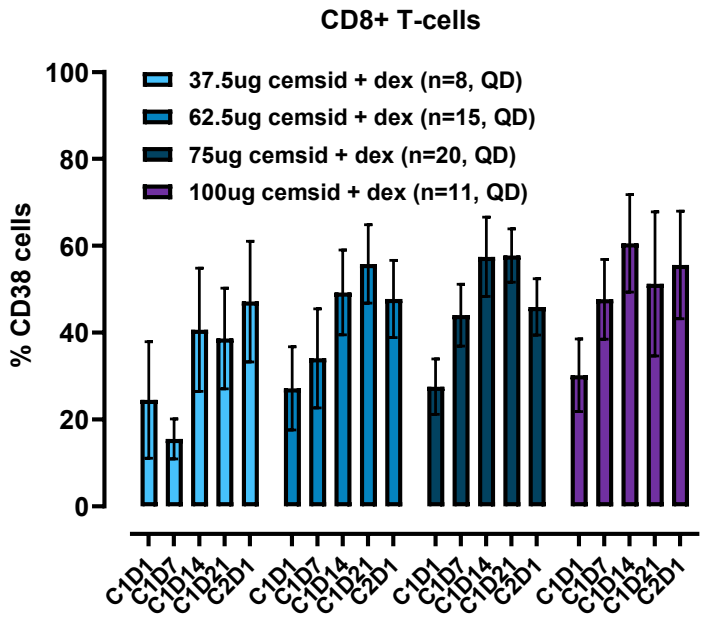
Red bar indicates the 14-day periods of cemsidomide dosing; *1 patient censored due to abnormal mass spectrometry values. Data as of 23 July 2025

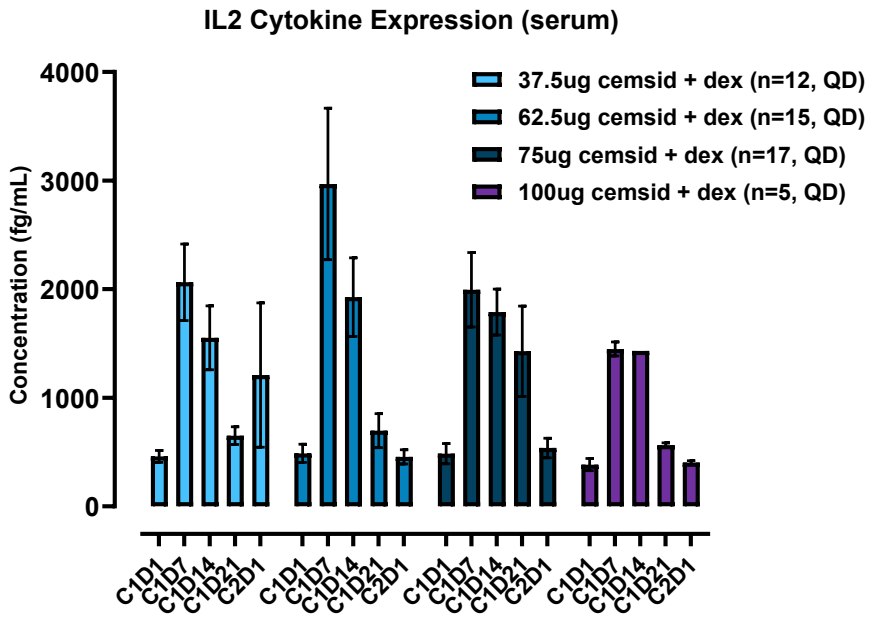
Dex, dexamethasone; IKZF1/3, Ikaros zinc finger protein 1/3 ; MWF, Monday Wednesday Friday; PBMC, peripheral blood mononuclear cell; QD, once daily

Pharmacodynamics of Cemsidomide 14/14 + Dex

CD8+ T-cell Activation Observed at All Dose Levels





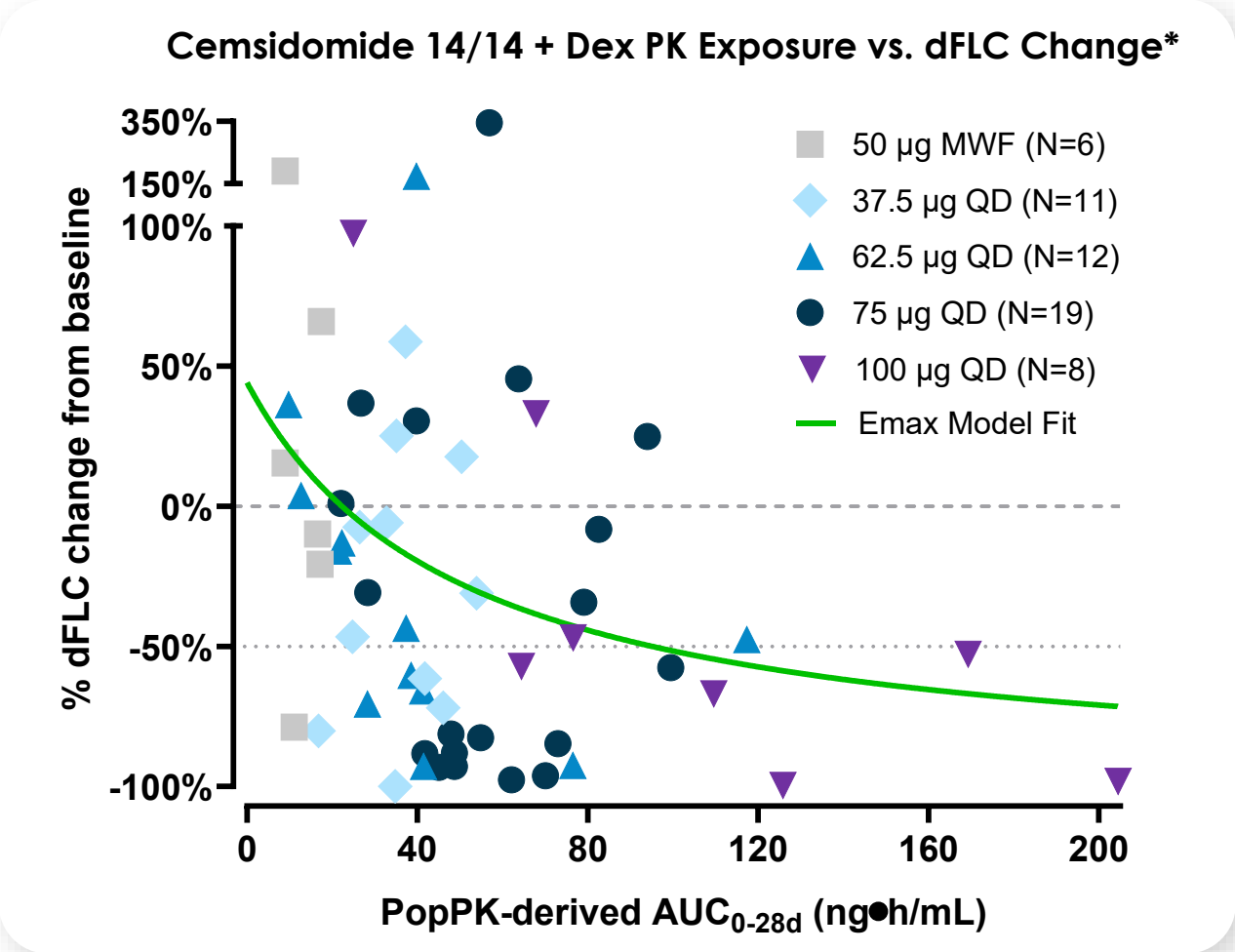


- Significant elevation of CD8+ T-cells harboring HLA-DR and CD38 markers after 7 and 14 days of dosing
- Activated T-cells continued to be observed until Cycle 1 Day 21
- CD8+ T-cell activation translates to increased serum IL2 cytokine expression

Dex, dexamethasone; HLA-DR, human leukocyte antigen-DR isotype; IL2, interleukin 2, QD, once daily. Data as of 23 July 2025.

Cemsidomide 14/14 + Dex PK Exposure vs dFLC Change

100µg QD Drives Sufficient Exposure With Meaningful Reductions in FLC



Exposure (AUC) Quartiles

	<Q1 (N=14)	Q1-Q2 (N=14)	Q2-Q3 (N=14)	>Q3 (N=14)
Mean $AUC_{0\text{-}28d}$ (ng*h/mL)	16.8	34.9	51.9	**103.3**
Mean Change in dFLC from Baseline	+10%	-11%	-31%	**-52%**

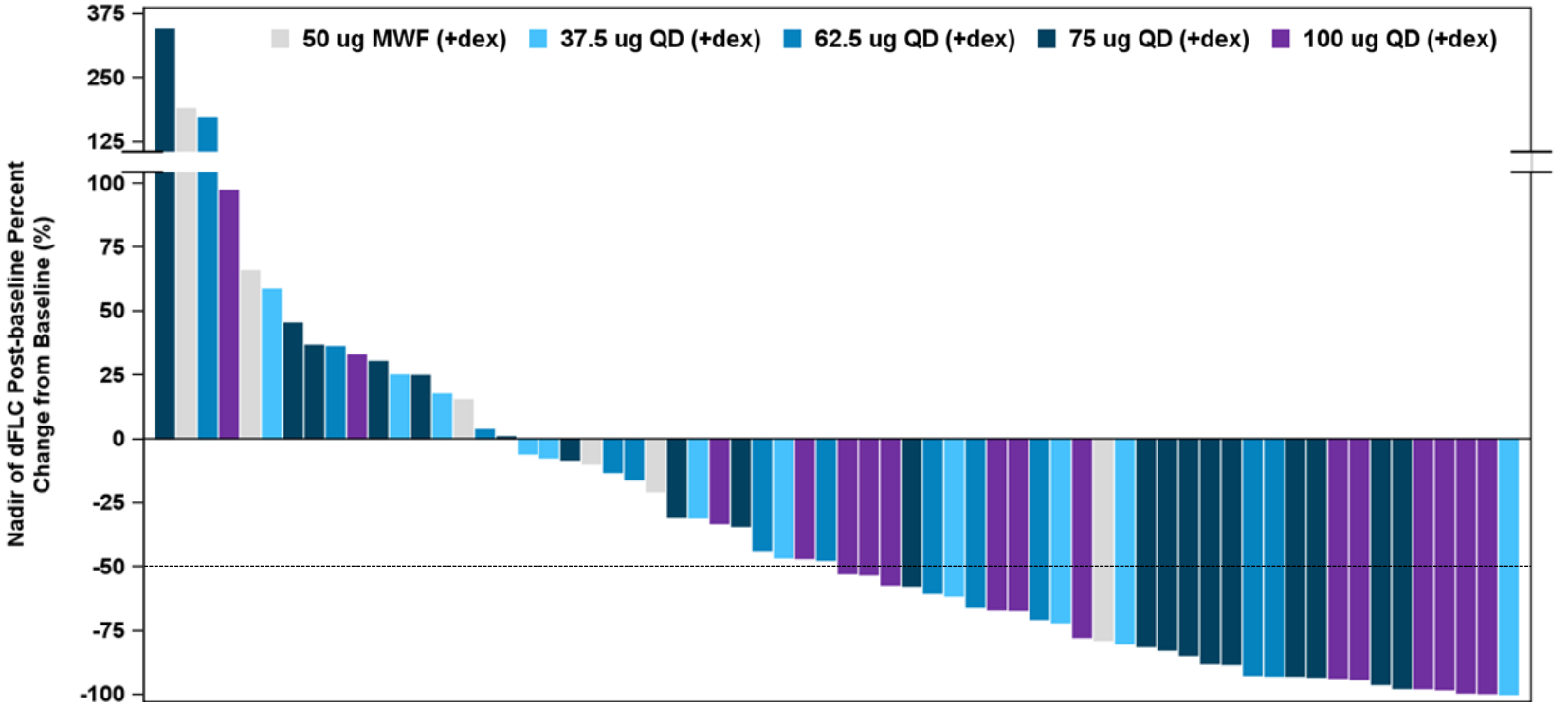
*Includes 56 patients with abnormal baseline sFLC defined as (A) kappa FLC >19.4 mg/L or lambda FLC >26.3 mg/L and (B) kappa-to-lambda FLC ratio >4 or <0.5.
AUC, area under the curve; Dex, dexamethasone; dFLC, difference in involved and uninvolved free light chain; Emax, maximum response; MWF, Monday Wednesday Friday; QD, once daily; popPK, population pharmacokinetics; PK, pharmacokinetic

Best Change in dFLC from Baseline

50% of Patients With Elevated Light Chains Achieved ≥ 50% Decrease in dFLC

Best Change in dFLC from Baseline (*Cemsidomide 14/14 + Dex)*

*Multiple Myeloma Patients w/ Elevated Light Chain Disease (N=64)**



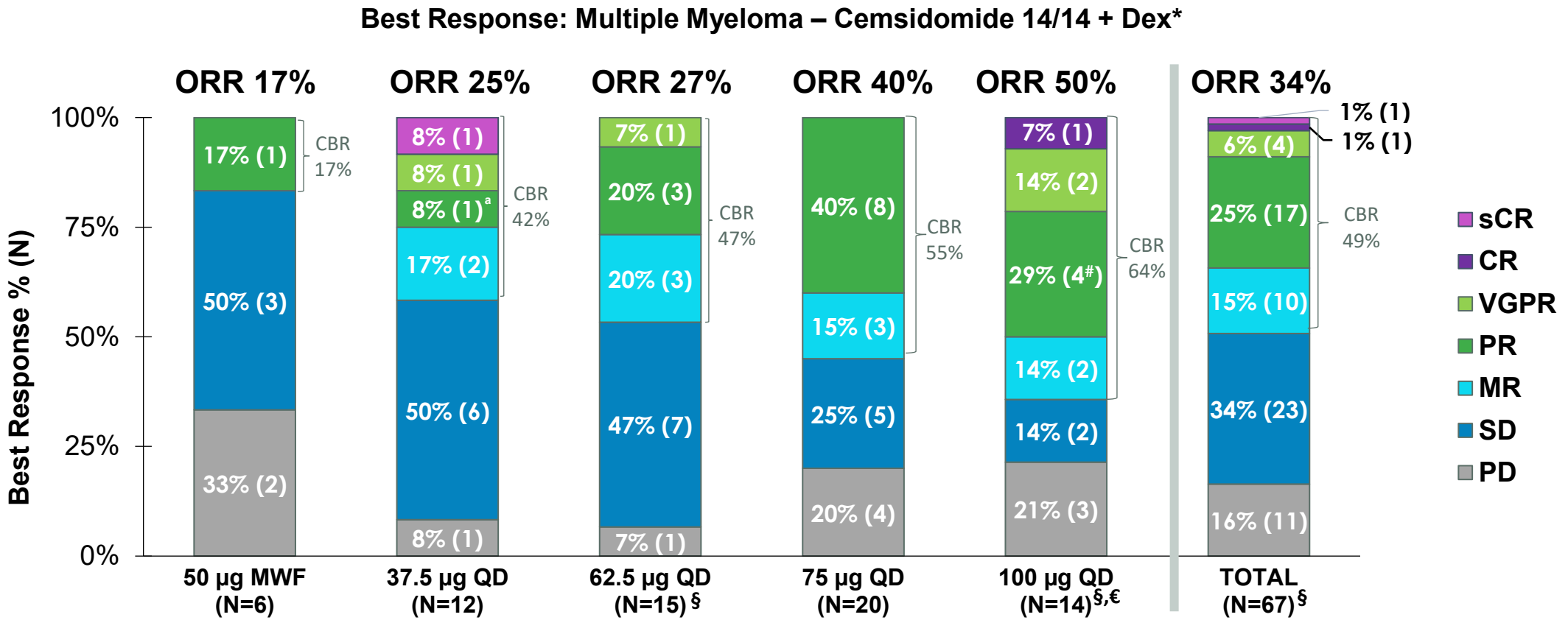
*Only includes treated subjects who meet both criterion (A) and (B): (A) baseline kappa free light chain value >19.4 mg/L or baseline lambda free light chain value >26.3 mg/L; (B) ratio of baseline free light chain kappa over baseline free light chain value lambda >4:1 or <1:2.

- Cemsidomide 14/14 + Dex induced dFLC decrease in 73% (47/64) of patients, with 50% of patients having a reduction of ≥ 50%
- Cemsidomide 14/14 + Dex demonstrated anti-myeloma activity across a broad range of doses

Dex, dexamethasone; dFLC, difference in involved and uninvolved free light chain; MWF, Monday Wednesday Friday; QD, once daily. Data as of 23 July 2025.

Best Response of Cemsidomide 14/14 + Dex

Response Rate of 50% Achieved at 100µg in Heavily Pretreated RRMM population



- ORR (≥ PR) of 34% (23/67) was achieved across all dose levels with a clinical benefit rate (≥ MR) of 49%
- ORR at the highest dose level of cemsidomide 100µg was 50% with a clinical benefit rate of 64%
- MRD negativity achieved in 1 patient with a CR at the highest dose level of cemsidomide (100µg)

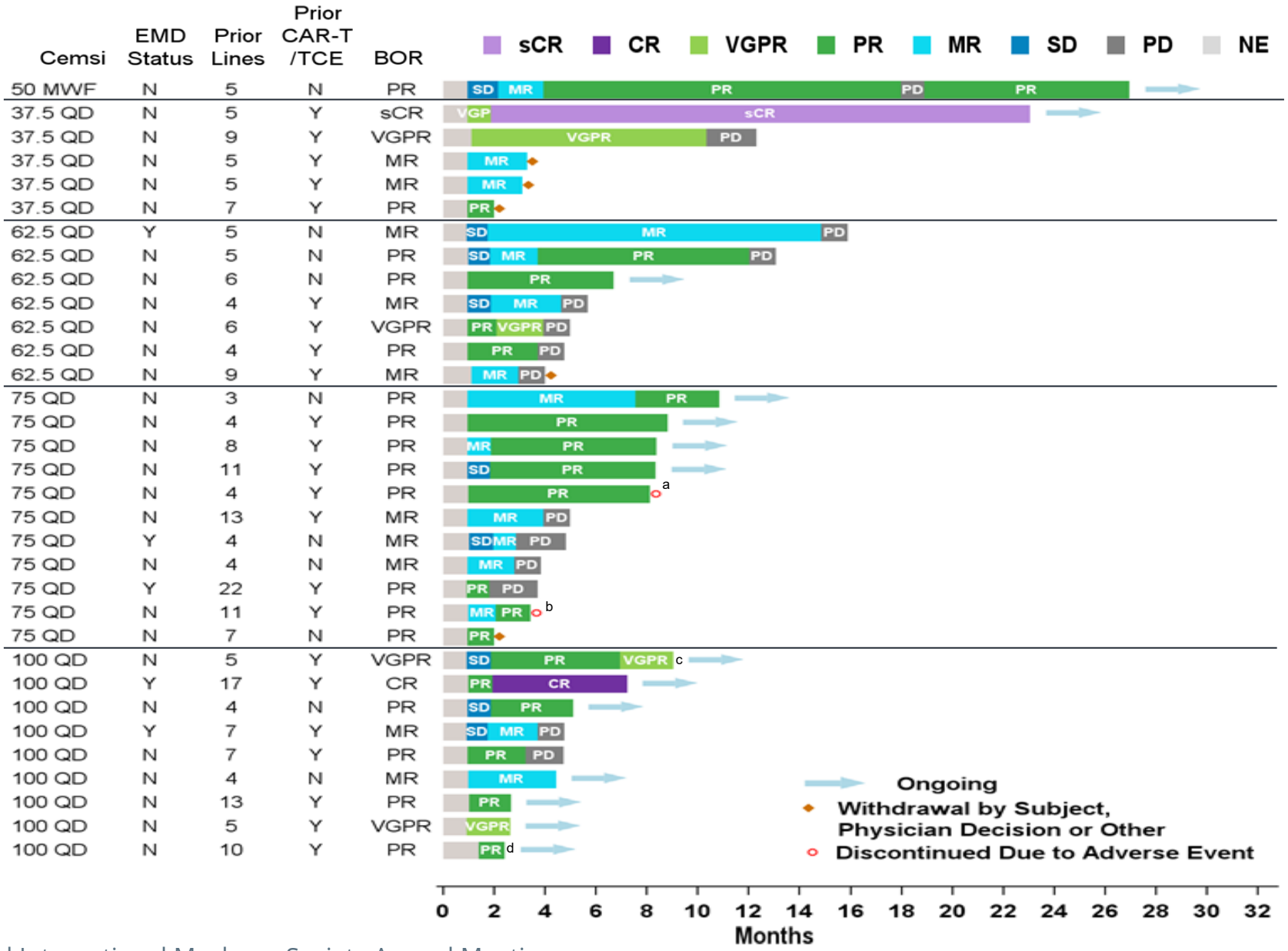
*Investigator assessed response; Data as of 23 July 2025.

§1patient in the 62.5µg cohort did not have a post-baseline assessment and 4 patients in 100µg cohort did not have a post-baseline assessment performed at the time of data cutoff, #1 patient in the 100µg cohort had a PR confirmed after data cut off date, [a]1 patient in the 37.5µg cohort achieved a PR based on light chains, no follow up M protein available. €After the data cut off date, one patient in the 100µg cohort depicted as VGPR in the figure converted to a CR and one additional patient in the 100µg cohort who was not efficacy evaluable previously achieved a PR

CBR, clinical benefit rate; Dex, dexamethasone; MR, minimal response; MRD, minimal residual disease; MWF, Monday Wednesday Friday; ORR, objective response rate; PD, progressive disease; PR, partial response; QD, once daily; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; SD, stable disease; VGPR, very good partial response

Exposure and Clinical Responses (MR or Better)*

Durable Responses Across a Broad Range of Doses in a Heavily Pre-Treated Patient Population



All doses (N=72)	Months (95% CI)
Median PFS	3.7 (2.9-5.6)
Median DOR	9.3 (2.8-NE)

Data as of 23 July 2025. *Investigator assessed response; swimmer plot only includes patients that achieved an MR or better (33/72 patients)

[a]Patient at 75µg had EOT reason updated from discontinued due to AE to disease progression after data cut off, [b]Patient at 75µg discontinued due to grade 5 AE of septic shock, deemed unrelated to cemsidomide. [c]After the data cut off date, patient at 100µg cohort depicted as VGPR in the figure converted to a CR, [d]Patient in 100µg had PR confirmed after data cut off date

AE, adverse event; BOR, best overall response; CAR-T, chimeric antigen receptor-t cell; CI, confidence interval; DOR, duration of response; EMD, extramedullary disease; EOT, end of treatment; MR, minimal response; NE, not estimable; PFS, progression-free survival; PD, progressive disease; PR, partial response; QD, once daily; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; SD, stable disease; TCE, t-cell engager; VGPR, very good partial response

Conclusions

- Cemsidomide 14/14 plus Dex was well tolerated and demonstrated durable anti-myeloma activity at increasing dose levels
  - A 50% ORR was observed at the highest dose of 100µg QD, with a 34% ORR observed across all dose levels
  - TEAEs were manageable with minimal treatment discontinuations or reductions
- Cemsidomide 14/14 plus Dex has an ~2-day half-life, induces potent IKZF1/3 degradation and promotes CD8 T-cell activation
- Cemsidomide is well suited for further development across multiple lines of treatment and in combination with other anti-myeloma agents, including proteasome inhibitors, monoclonal antibodies, antibody-drug conjugates, and T-cell engagers
- Based on these results, cemsidomide 14/14 plus Dex will be further assessed in a Phase 2 study in the 4L+ patient population and in a Phase 1b study in combination with a BCMA-BiTE

BCMA-BiTE, B cell maturation antigen targeted bispecific T-cell engager; Dex, dexamethasone; IKZF 1/3, Ikaros zinc finger protein 1/3; ORR, objective response rate; QD, once daily

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- All authors contributed to and approved the presentation