# 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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# Disclosures

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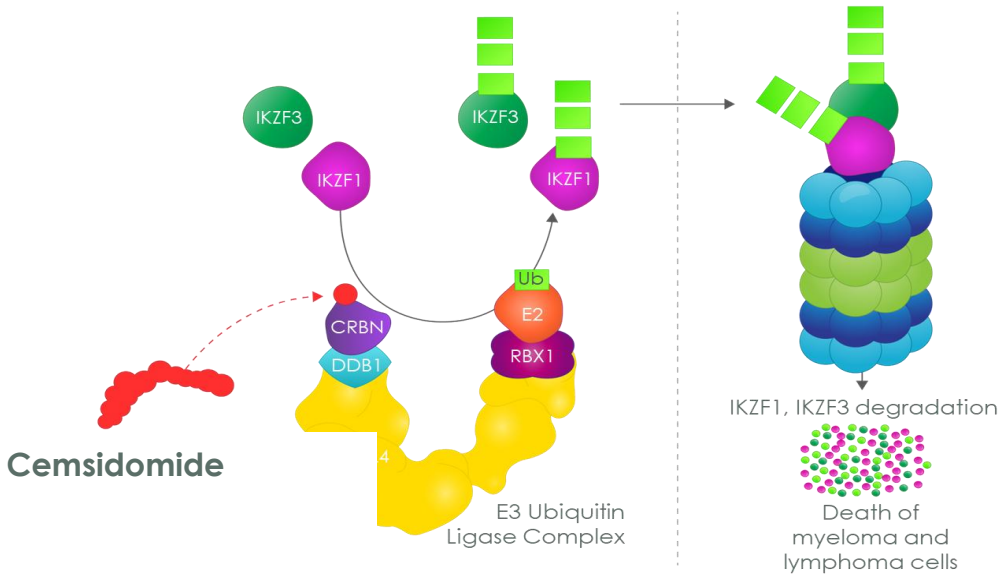
# Cemsidomide (CFT7455) Background

- 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

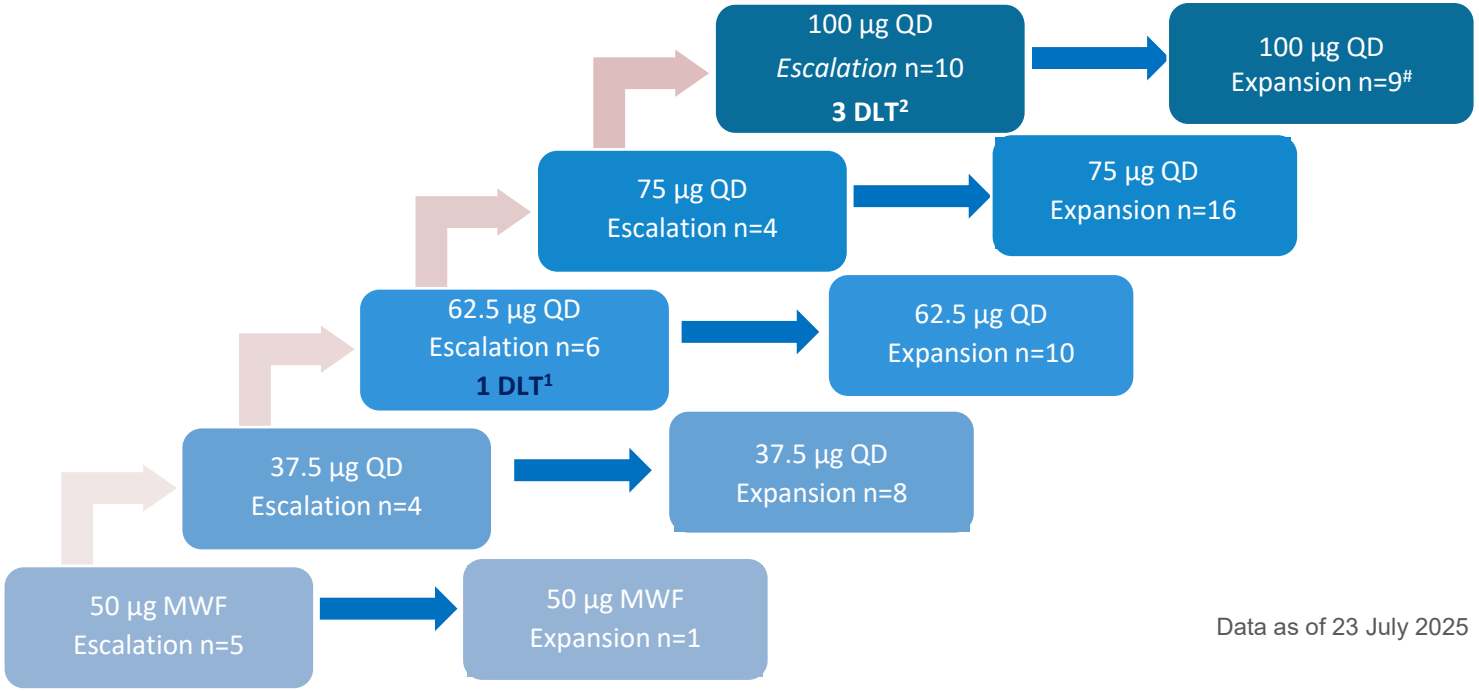
## KEY INCLUSION CRITERIA

- 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

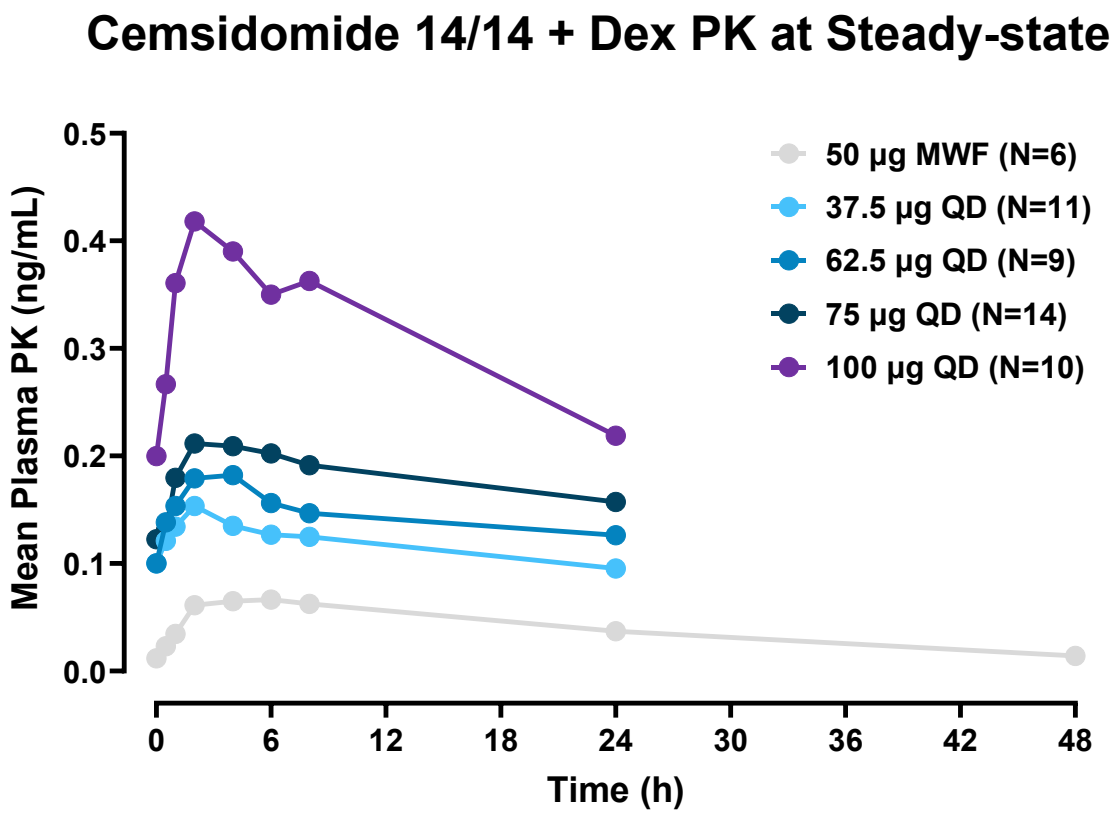
| Common (>20% All Grades) TEAEs and Events of Interest, n (%) | All Grades (N=72) | Grade 3 (N=72) | Grade 4 (N=72) | Grade 5 (N=72) |
|---|---|---|---|---|
| **Neutropenia** | 44 (61) | 17 (24) | 24 (33) | 0 |
| **Infections** | 42 (58) | 17 (24) | 0 | 1 (1) |
| Pneumonia | 10 (14) | 9 (13) | 0 | 0 |
| 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

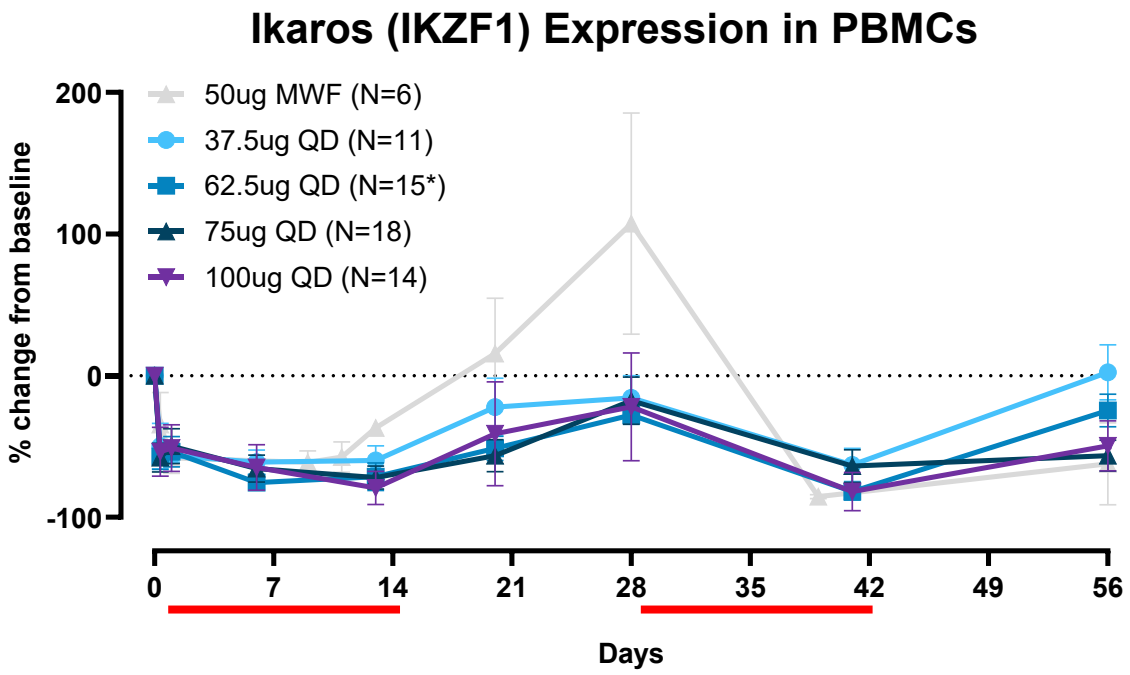


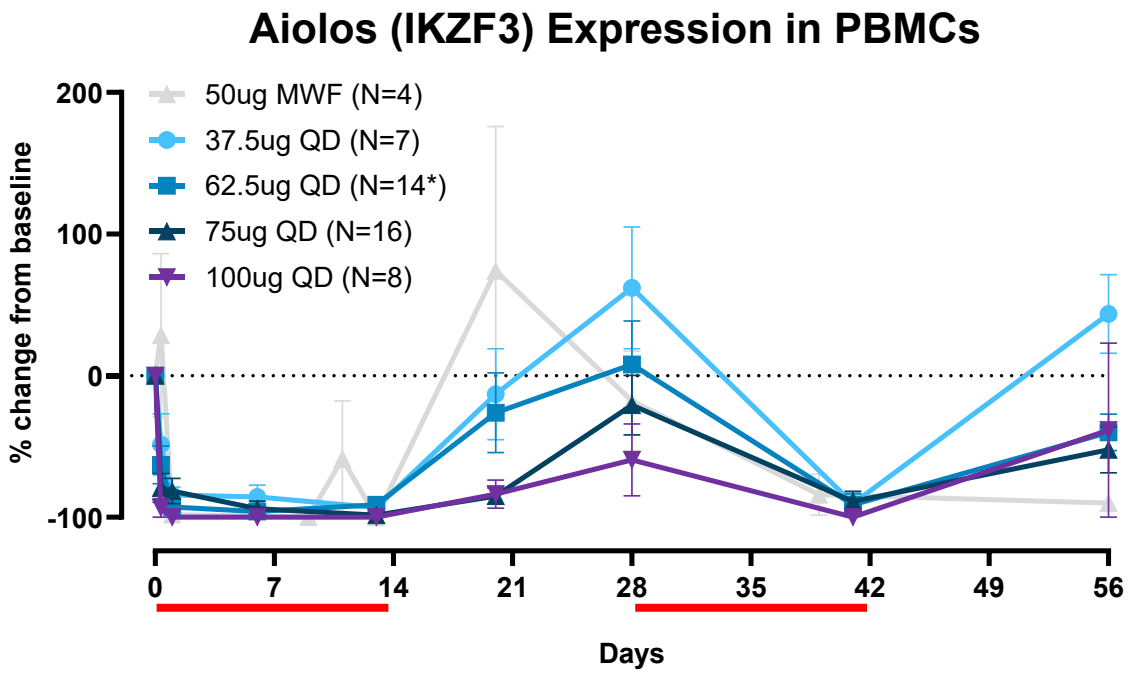

- Cemsidomide 14/14 exposure was dose-proportional when combined with Dex
- The overall geometric mean half-life estimate is approximately 2 days

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



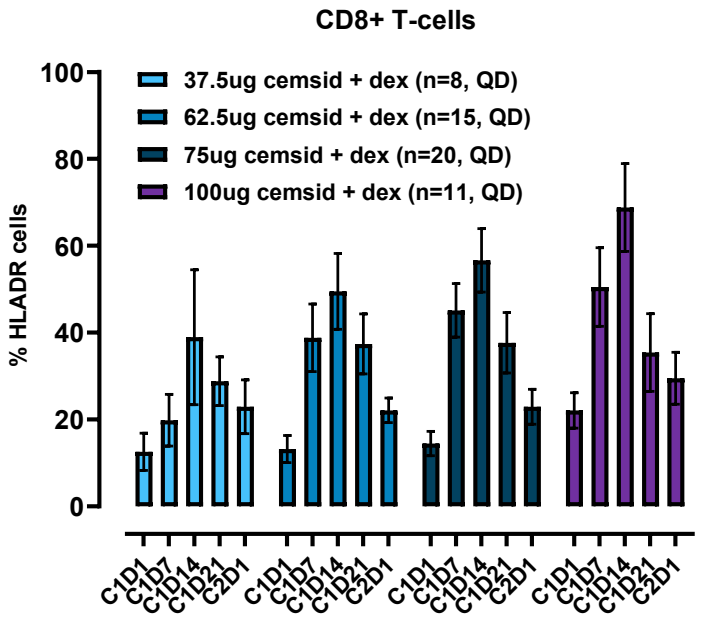

- Cemsidomide 14/14 + Dex achieves >50% degradation of IKZF1 and >80% degradation of IKZF3, as assessed by mass spectrometry in human PBMCs
- Sustained IKZF3 degradation up to day 20 observed at the two highest doses of cemsidomide (75µg and 100µg)

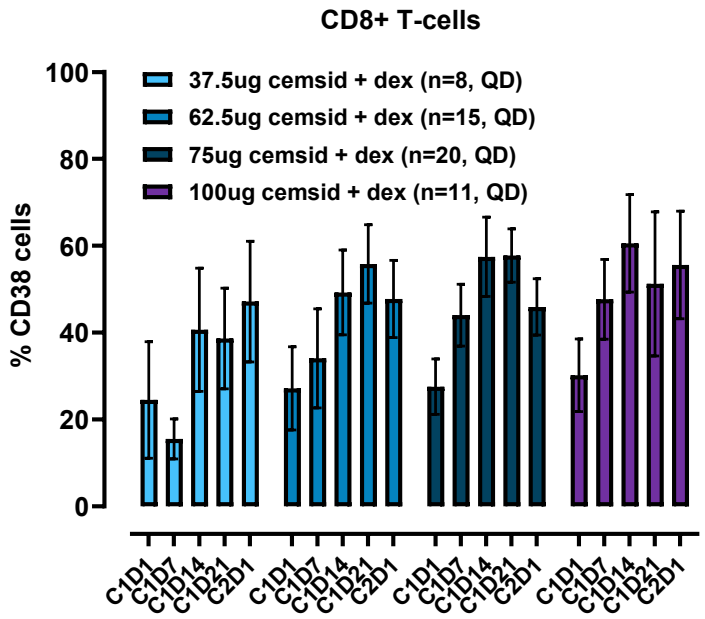
Red bar indicates the 14-day periods of cemsidomide dosing; *1 patient censored due to abnormal mass spectrometry values. Data as of 23 July 2025

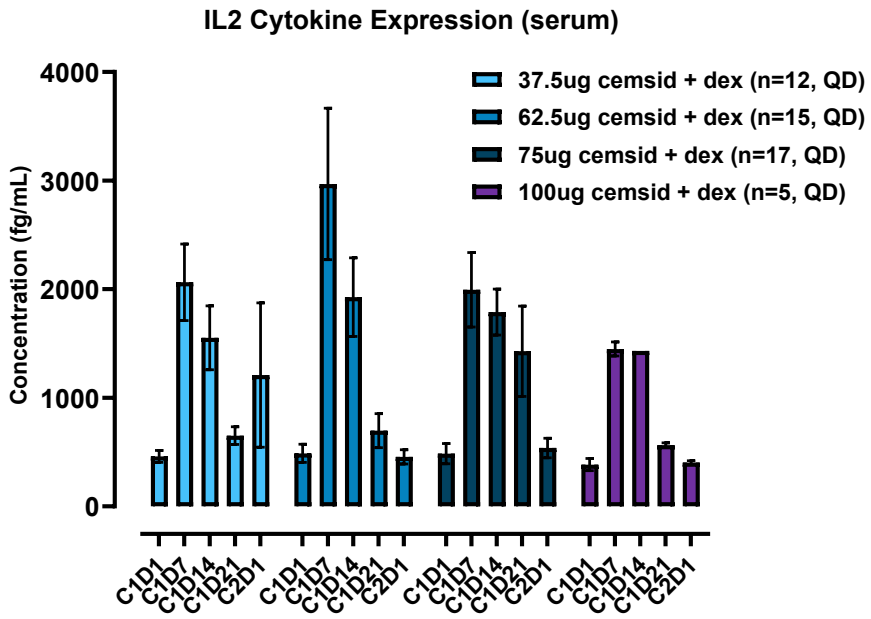
Dex, dexamethasone; IKZF1/3, Ikaros zinc finger protein 1/3 ; MWF, Monday Wednesday Friday; PBMC, peripheral blood mononuclear cell; QD, once daily

# Pharmacodynamics of Cemsidomide 14/14 + Dex

## CD8+ T-cell Activation Observed at All Dose Levels



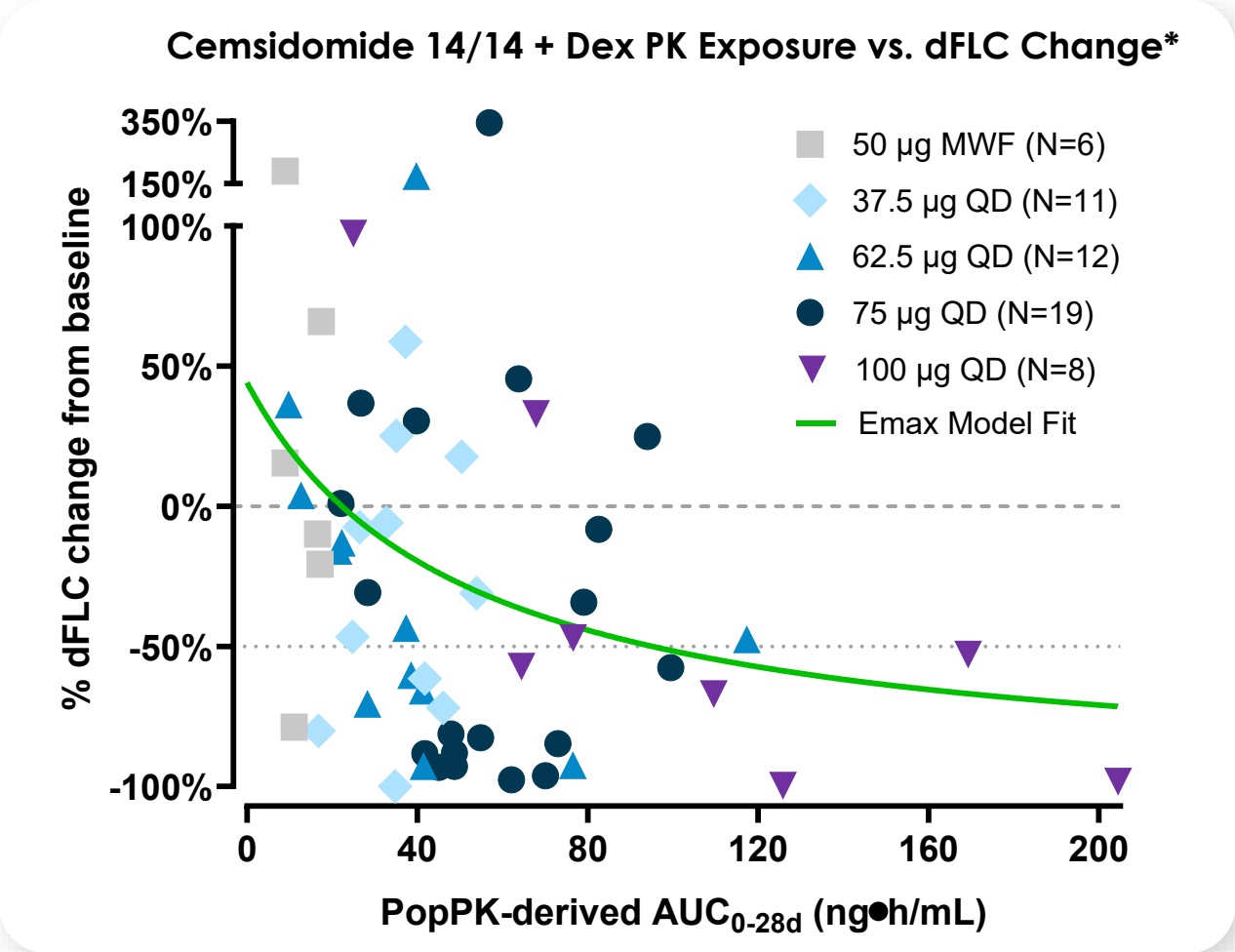




- Significant elevation of CD8+ T-cells harboring HLA-DR and CD38 markers after 7 and 14 days of dosing
- Activated T-cells continued to be observed until Cycle 1 Day 21
- CD8+ T-cell activation translates to increased serum IL2 cytokine expression

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%** |

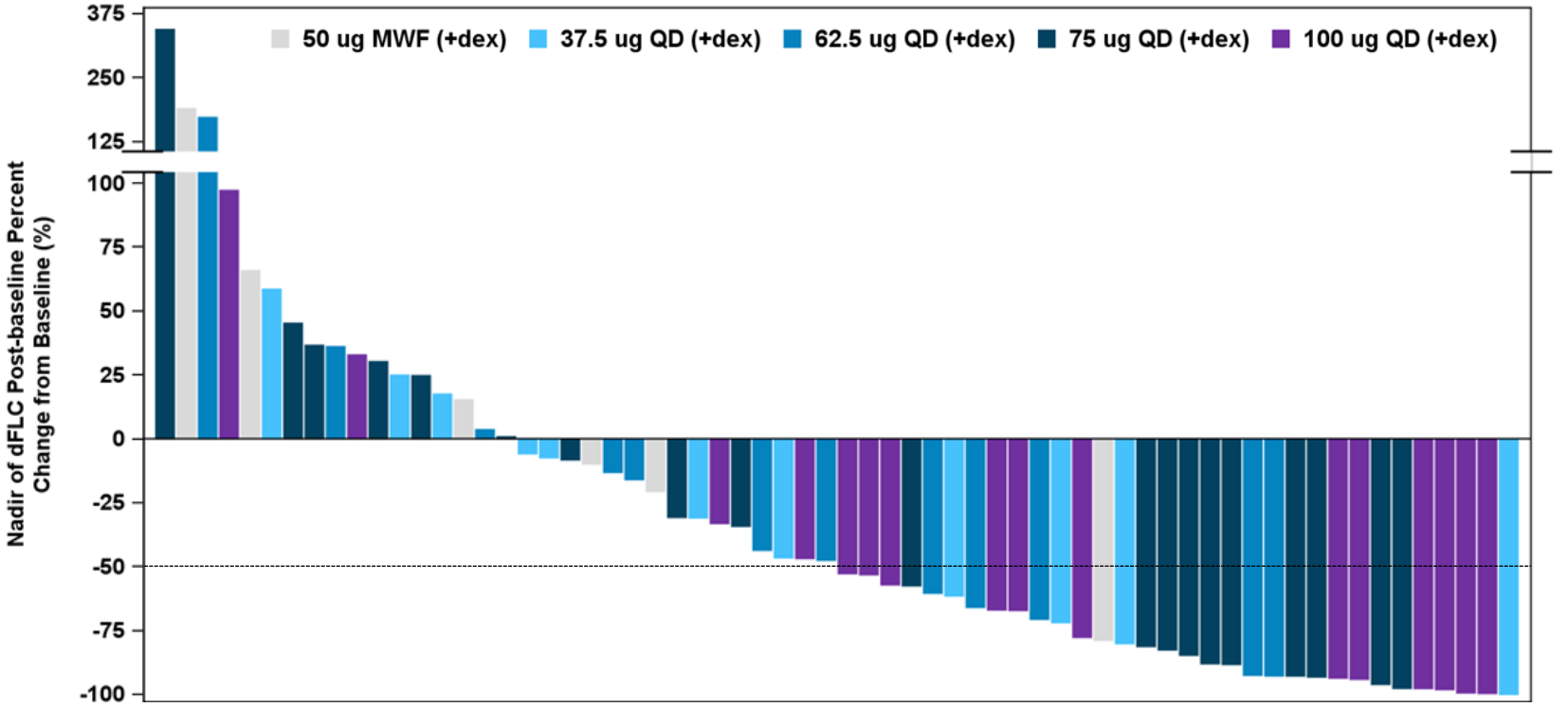
*Includes 56 patients with abnormal baseline sFLC defined as (A) kappa FLC >19.4 mg/L or lambda FLC >26.3 mg/L and (B) kappa-to-lambda FLC ratio >4 or <0.5.
AUC, area under the curve; Dex, dexamethasone; dFLC, difference in involved and uninvolved free light chain; Emax, maximum response; MWF, Monday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



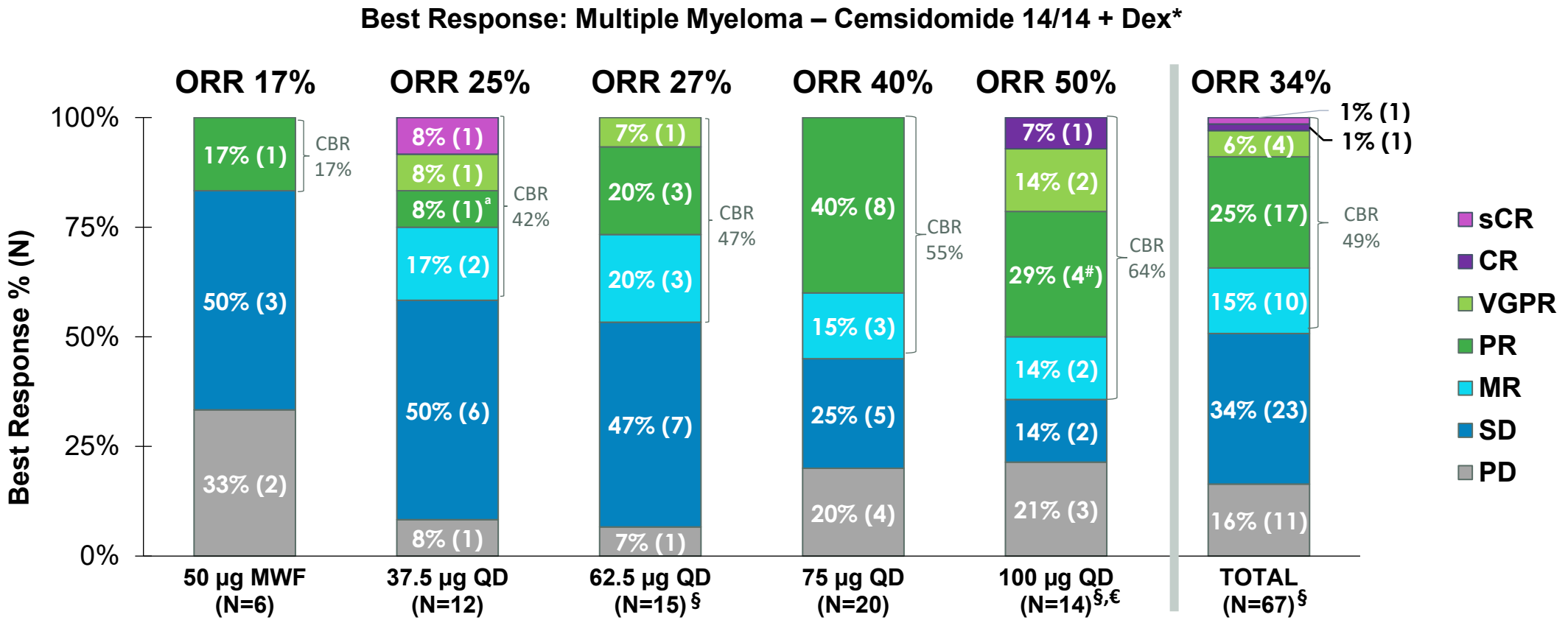

*Only includes treated subjects who meet both criterion (A) and (B): (A) baseline kappa free light chain value >19.4 mg/L or baseline lambda free light chain value >26.3 mg/L; (B) ratio of baseline free light chain kappa over baseline free light chain value lambda >4:1 or <1:2.

- 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)

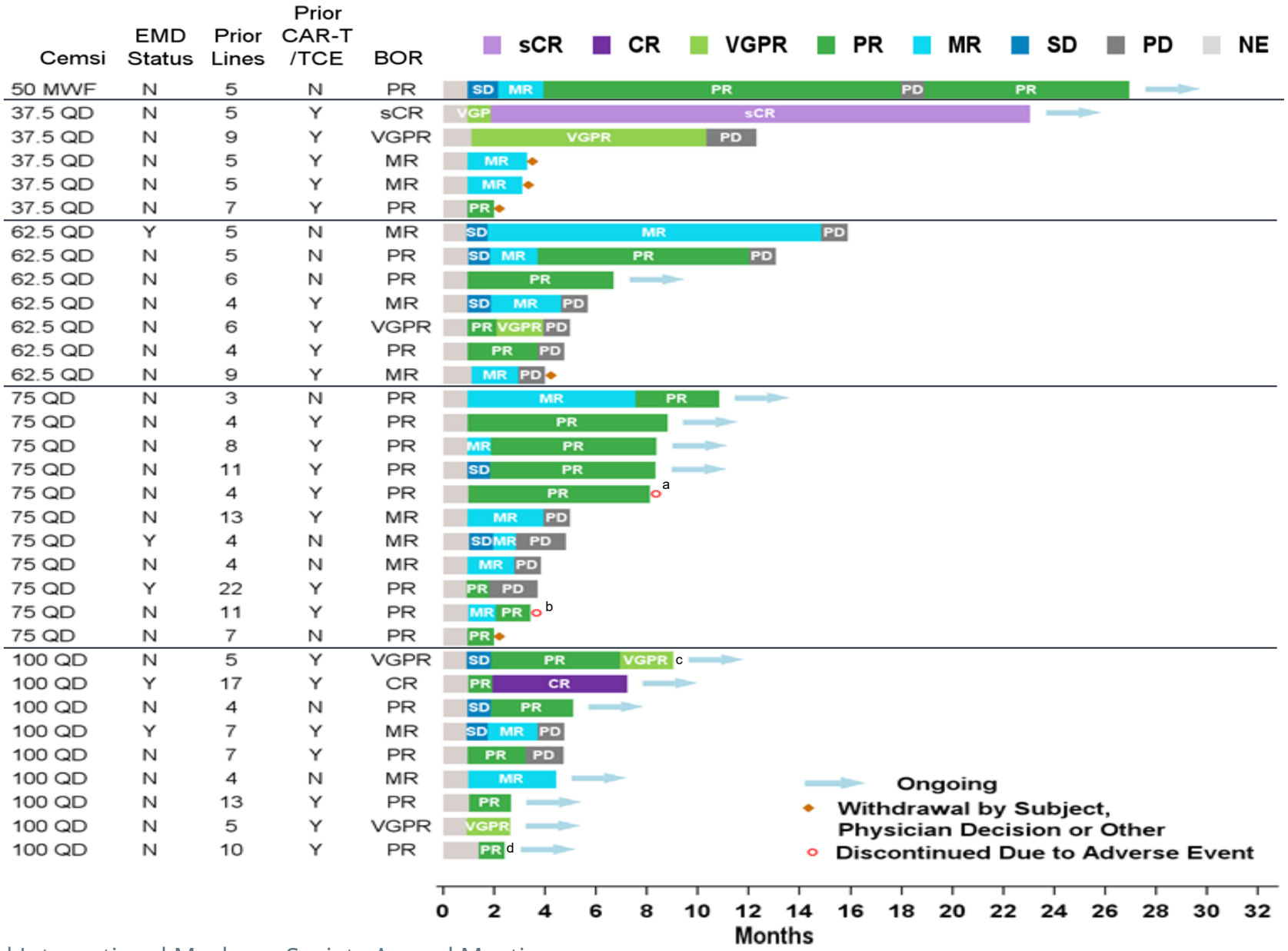
*Investigator assessed response; Data as of 23 July 2025.

§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