C4 Therapeutics

Updated Data From Phase 1 Trial of Cemsidomide in Multiple Myeloma & Next Steps

International Myeloma Society (IMS) Annual Meeting

September 2025

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Today's Agenda

Introductions	Courtney Solberg, Associate Director of IR
Opening Remarks	Andrew Hirsch, President and CEO
Cemsidomide Phase 1 MM Data & Next Steps	Len Reyno, M.D., CMO
Concluding Remarks & Q&A Session	Andrew Hirsch, President and CEO Len Reyno, M.D., CMO Kendra Adams, CFO Binod Dhakal, M.D., M.S

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Opening Remarks

Andrew Hirsch
President and Chief Executive Officer

C4 Therapeutics

C4T Is Positioned to Unlock Value Across the Portfolio

Unlocking the clinical potential of a **class-leading IKZF1/3 degrader** and quickly delivering on an optimized portfolio of degraders against **novel targets to address sizeable indications** of unmet need

Deliver value from high-potential clinical programs

- Advance cemsidomide to realize its potential as an IKZF1/3 degrader with class-leading efficacy and a differentiated safety & tolerability profile with potential $2.5B-$4B[1] peak revenue for label opportunities
- Utilize CFT8919 Phase 1 data to determine next steps

Build upon ~10 years of experience developing degraders against multiple target classes

- Advance a new portfolio of novel targets in non-oncology and oncology indications with the potential for multiple development candidates

Roche

Merck KGaA
Darmstadt, Germany

MERCK

Continue to advance our established collaborations in oncology and non-oncology

- Expand application of targeted protein degradation through high-value collaborations

Source: [1] Health Advances (2022), ClearView (2023), and C4T analysis, opportunity across two market segments – 2L+ with BCMA BiTE and 4L+ with dexamethasone

Cemsidomide Has the Potential to Be Best-in-Class IKZF1/3 Degrader in a Large and Growing Relapsed/Refractory Multiple Myeloma Market

Highly Competitive Profile

Potential to be best-in-class;
MOA is relevant across multiple lines of MM treatment

Class-leading anti-myeloma activity with **50% ORR** achieved at highest dose level

Median DOR of 9.3 months across all dose levels and **not yet reached at two highest dose levels**

Differentiated safety & tolerability profile

Efficient Path Forward

Clear and distinct paths to market

Phase 1 data **de-risks upcoming clinical trials**

Differentiated label-enabling strategy

Two distinct opportunities for accelerated approval

Phase 3 trial has potential to **unlock full approval**

Large Market Opportunity

Potential to be clear leader in 2L+ or 4L+ in combo w/ a BCMA BiTE and dex, respectively

MM market projected to be **$46B by 2030**[1]

Potential **$2.5B-$4B**[2] peak revenue opportunity across two market segments: **2L+ with a BCMA BiTE** and **4L+ with dex**

Captures 2L+ treatment landscape, **where IKZF1/3 degraders are widely used**

Sources: [1]Evaluate Pharma (8/14/2025) [2]Health Advances (2022), ClearView (2023), and C4T analysis

Overall Response Rate (ORR); Duration of Response (DOR); Mechanism of Action (MOA); Dexamethasone (dex); Second line or later (2L+); Fourth line or later (4L+); Multiple myeloma (MM)

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Source: C4T data on file as of 7/23/2025

Cemsidomide First-in-Human Clinical Program

Relapsed Refractory Multiple Myeloma

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Degrading IKZF1/3 Leads to Myeloma Cell Death and T-Cell Activation, Supporting This Target's Important Role in Treating MM

Multiple myeloma (MM) is a cancer of plasma cells, which are part of the immune system

Key Roles of IKZF1/3

Physiological Functions:

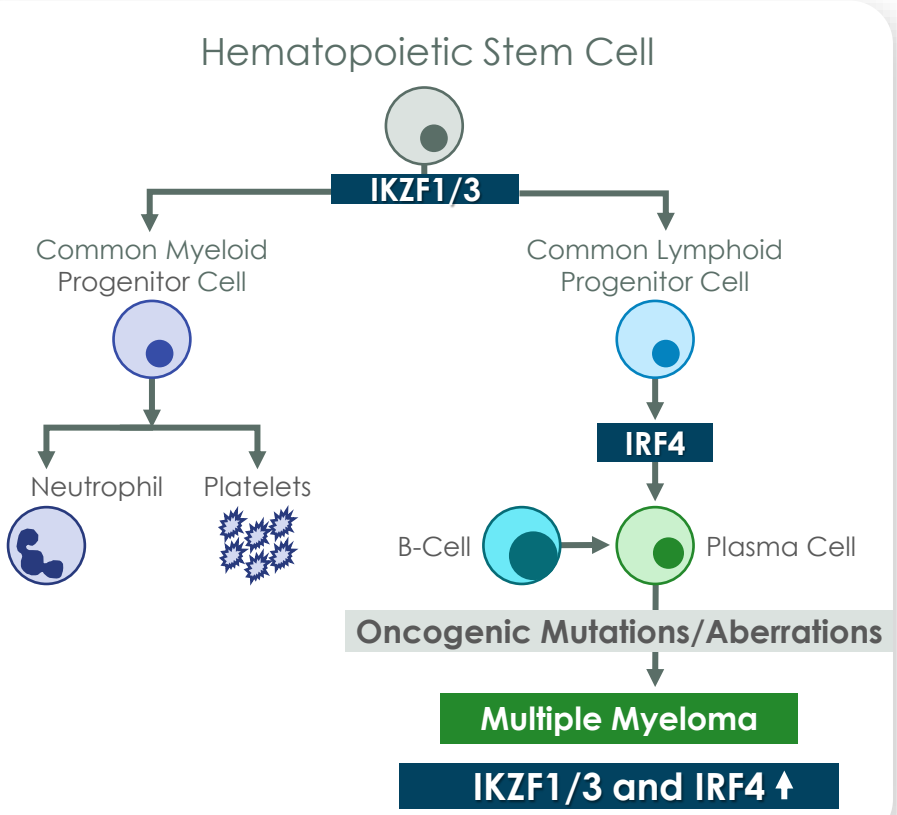
- **IKZF1/3** directly regulate the activity of **IRF4**, another transcription factor that regulates downstream immune cell differentiation

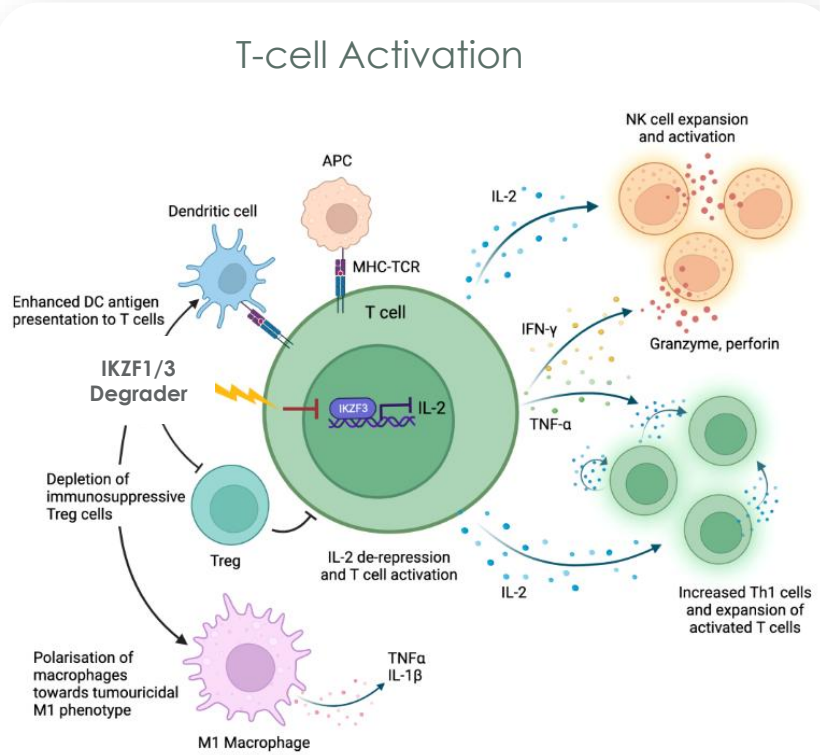
Oncogenic Functions:

- Multiple myeloma cells rely on **IKZF1/3** and **IRF4** for survival

IKZF1/3 Degradation Leads to:

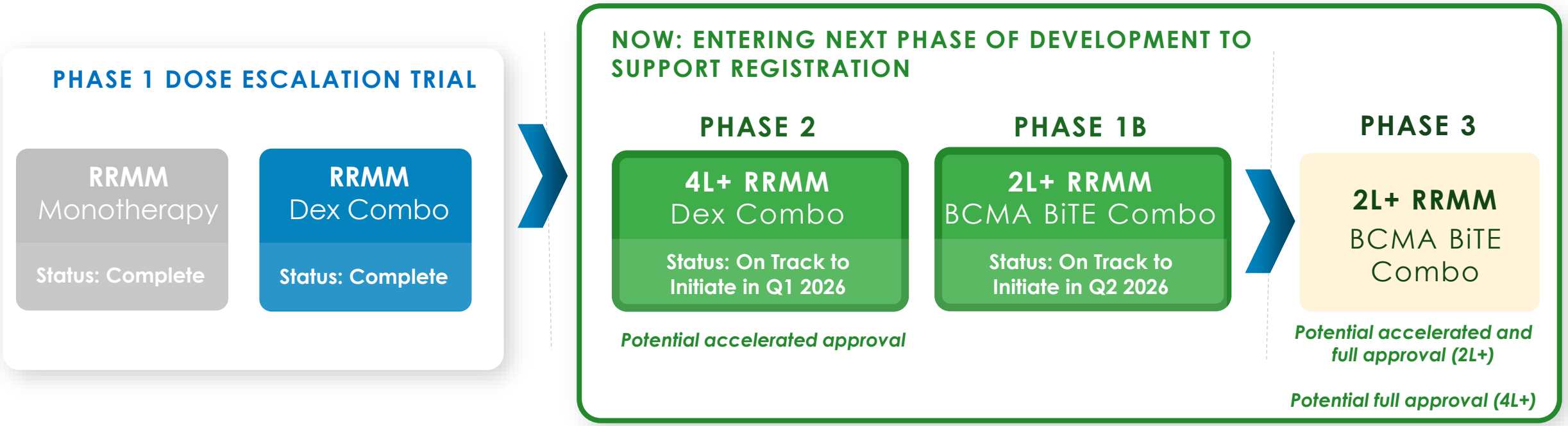
- Downregulation of **IRF4** promoting the death of myeloma cells
- T-cell activation
- On-target neutropenia





Adapted from Chen and Gooding, 2022

Phase 1 Dose Escalation Trial Enabled Advancement to Next Phase of Development with Two Opportunities for Accelerated Approvals in RRMM



Phase 1 data reinforces potential best-in-class profile with compelling anti-myeloma activity, enhanced immunomodulatory effects, and a differentiated safety & tolerability profile, de-risking next clinical trials

Monday, Wednesday, Friday dosing (MWF); Once daily (QD); Dexamethasone (dex); Relapsed refractory multiple myeloma (RRMM); Bispecific T-cell engager (BCMA BiTE); Cemsidomide (cemsi)

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Cemsidomide + Dexamethasone Phase 1 MM Dose Escalation Is Complete; 100 µg Is the Maximum Administered Dose

KEY INCLUSION CRITERIA

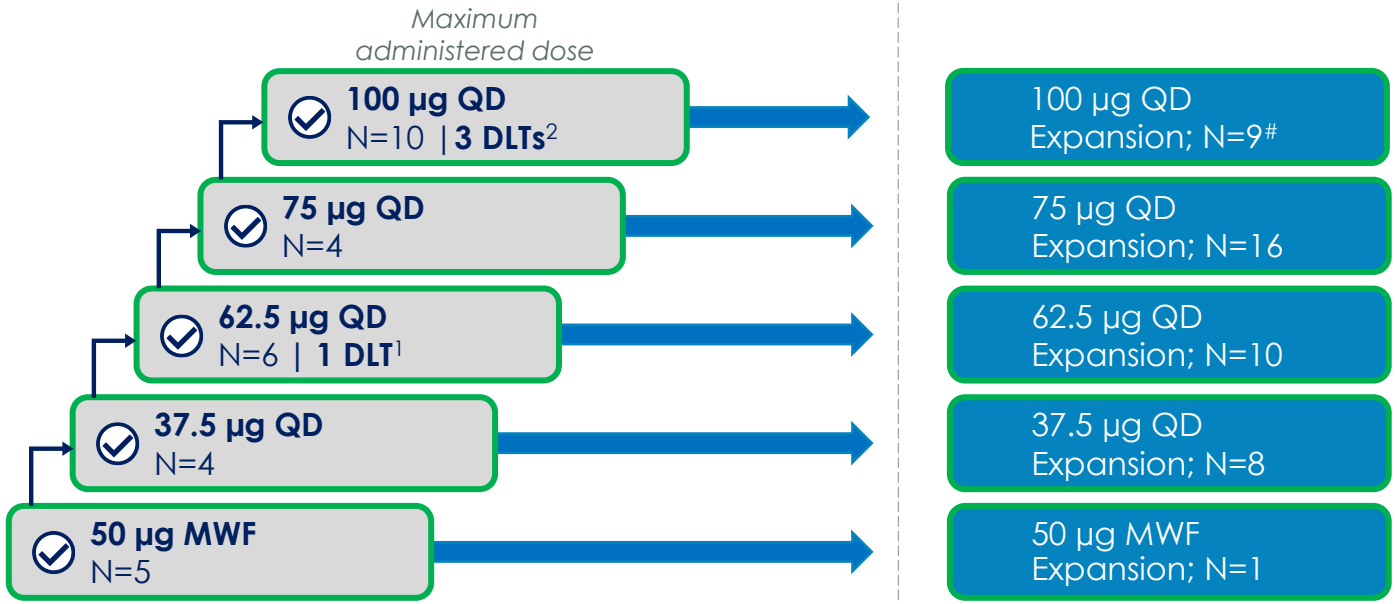
- Adults with MM, R/R to at least 3 prior lines of therapy that have included lenalidomide, pomalidomide, a proteasome inhibitor, a glucocorticoid, and an anti-CD38 monoclonal antibody
- Nonresponsive to or progressed within 60 days of prior therapy
- Creatinine clearance ≥40 mL/min
- ECOG ≤2

Phase 1 Study Endpoints

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

DOSE ESCALATION CEMSIDOMIDE 14/14 + DEX*

Utilizing a Bayesian logistic regression model until determination of the MTD and/or RP2D



*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 at 100 µg QD expansion did not complete C1 as of data cut-off and is not included in the safety analysis set

[1]DLT at 62.5 µg QD was due to Grade 4 neutropenia lasting >7 days; [2]Three patients at 100 µg QD had 5 DLT events (G4 neutropenia, G3 pneumonia in 2 patients, G3 ALT increase, G3 febrile neutropenia)

Eastern Cooperative Oncology Group (ECOG); Maximum tolerated dose (MTD); Monday Wednesday Friday (MWF); Multiple myeloma (MM); Once daily (QD); Pharmacodynamics (PD); Pharmacokinetic (PK); Recommended Phase 2 dose (RP2D); relapsed refractory (R/R); Dexamethasone (dex); Dose limiting toxicity (DLT)

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Source: C4T data on file as of 7/23/2025

Enrolled a Heavily Pre-Treated MM Patient Population, 75% of Whom Received Prior BCMA Therapy

Baseline Characteristics

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 1 2	 17 (24) 52 (72) 3 (4)
Asian **Black or African American, n (%)** **White, n (%)** **Other, n (%)**	1 (1) 14 (19) 50 (69) 7 (10)
Revised ISS at screening, n (%) Stage 1 Stage 2 Stage 3 Missing	 24 (33) 29 (40) 9 (13) 10 (14)
Presence of EMD, n (%)	23 (32)

Prior Therapies

Characteristics	Safety Population (N=72)
Prior therapies, median (range) 3L, n (%) 4L, n (%) ≥ 5L, n (%)	7 (3-22) 3 (4) 11 (15) 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.

B-cell maturation antigen (BCMA); extramedullary disease (EMD); International Staging System (ISS); Monoclonal antibody (mAb); Chimeric Antigen Receptor T-cell Therapy (CAR-T); Eastern Cooperative Oncology Group (ECOG); Multiple myeloma (MM)

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Source: C4T data on file as of 7/23/2025

Safety & Tolerability Profile

Cemsidomide + Dexamethasone

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Cemsidomide's Differentiated Safety & Tolerability Profile Is Ideal for Combinations

No discontinuations related to cemsidomide and minimal dose reductions

- ✔ TEAEs leading to dose reductions: **4/72 (6%)**
- ✔ **1 TEAE** leading to discontinuation, unrelated to cemsidomide

Differentiated safety profile with manageable neutropenia

- ✔ Across all dose levels, Grade 3 neutropenia was **24%** and Grade 4 neutropenia was **33%**
- ✔ Low rates of febrile neutropenia across all dose levels, with only **4%** at Grade 3 and **1%** at Grade 4

Risk of neutropenia does not increase over time; limited G-CSF use highlights minimal impact of neutropenia on patient experience

- ✔ **Few neutropenic events** occurred in later cycles coupled with low rates of G-CSF observed

Treatment emergent adverse events (TEAEs); Granulocyte colony-stimulating factor (G-CSF)

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Source: C4T data on file as of 7/23/2025

Cemsidomide Demonstrated a Differentiated Tolerability Profile With Minimal Dose Reductions and Discontinuations

Minimal Dose Reductions

- TEAEs leading to dose reductions: 4/72 (6%)[1]

No Discontinuations Related to Cemsidomide

- 1 TEAE led to discontinuation, unrelated to cemsidomide[2]

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

[1] Dose Reductions: 1 patient at 75 µg had grade 4 thrombocytopenia possibly related to cemsidomide resulting in dose reduction; A patient at 100 µg had grade 3 pneumonia and another patient at 100 µg had grade 3 neutropenia, both possibly related to cemsidomide and resulting in dose reduction; a patient at 100 µg had two dose reductions after two events of pseudomonal bacteremia, deemed unrelated to cemsidomide [2] Patient at 75 µg discontinued due to grade 5 AE of septic shock, deemed unrelated to cemsidomide *2 patients experienced grade 5 AEs (septic shock and subdural hematoma), both deemed unrelated to cemsidomide

Treatment emergent adverse events (TEAEs)

Source: C4T data on file as of 7/23/2025

Neutropenia Was Manageable and Relatively Consistent Across All Dose Levels With Low Rates of Febrile Neutropenia

Common Hematologic and Infections Grade ≥3 TEAEs, 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)
Neutropenia[1]	3 (50)	7 (58)	7 (44)	14 (70)	10 (56)	41 (57)
Anemia	1 (17)	3 (25)	3 (19)	5 (25)	5 (28)	17 (24)
Infections	0	4 (33)	4 (25)	5 (25)	5 (28)	18 (25)
Upper respiratory tract infection	0	0	1 (6)	1 (5)	0	2 (3)
Pneumonia	0	3 (25)	2 (13)	1 (5)	3 (17)	9 (13)
Septic shock	0	0	0	1 (5)	0	1 (1)
Sepsis	0	1 (8)	1 (6)	0	0	2 (3)
Thrombocytopenia	2 (33)	1 (8)	1 (6)	2 (10)	2 (11)	8 (11)
Lymphopenia	0	3 (25)	2 (13)	0	3 (17)	8 (11)
Febrile neutropenia	1 (17)	1 (8)	0	1 (5)	1 (6)	4 (6)

- [1]95% of patients at the 75 µg dose level received prior stem cell transplants, the highest percentage of patients at any of the dose levels studied. Across other dose levels, the rate of prior stem cell transplant ranged from 33% - 56%
- Patients who have received prior stem cell transplant are highly susceptible to neutropenia

Treatment Emergent Adverse Events (TEAEs); Once daily (QD); Monday, Wednesday, Friday dosing (MWF)

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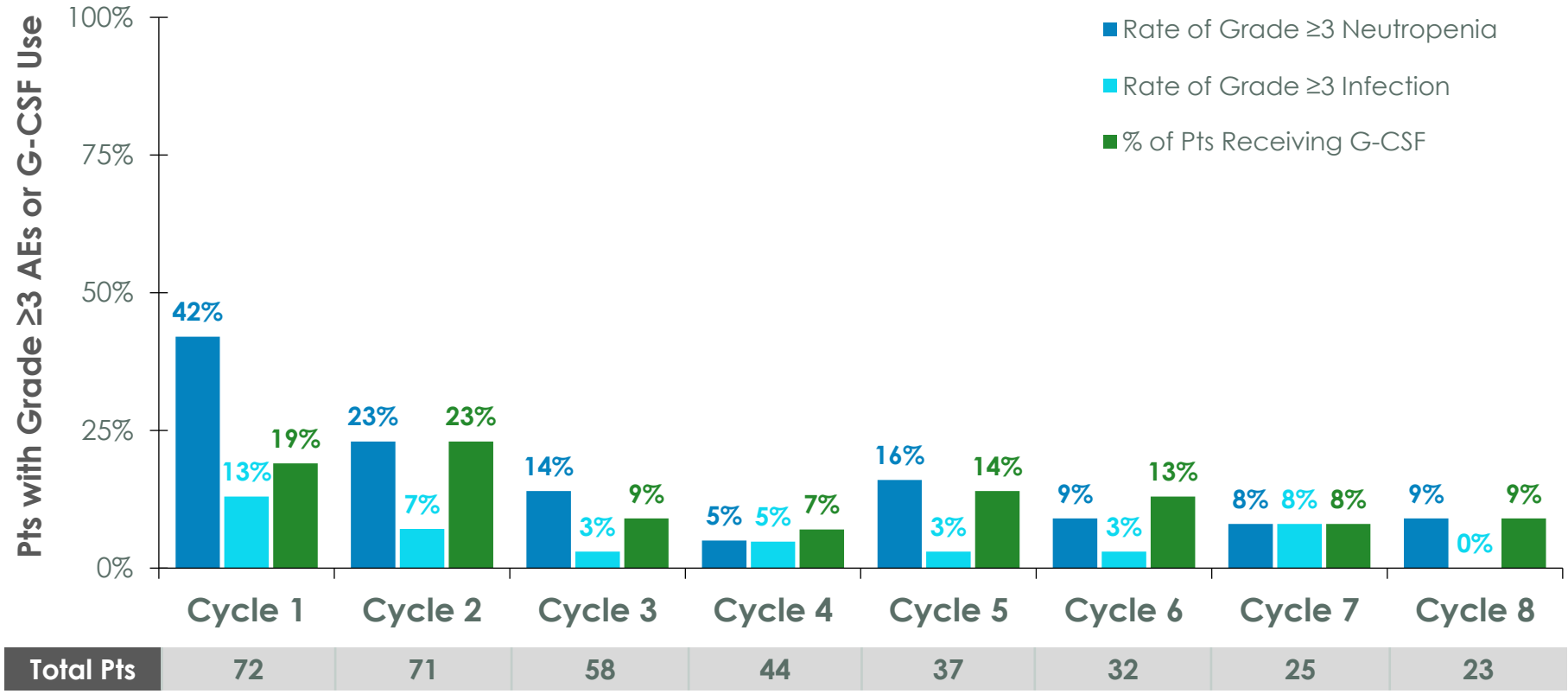
Source: C4T data on file as of 7/23/2025

Majority of Neutropenic Events Occurred in Earlier Cycles and Resulted in Low Rates of G-CSF Usage and Limited Clinical Consequences

Rates of Neutropenia, Infections, and G-CSF Use by Cycle
(All doses)



Total Pts	72	71	58	44	37	32	25	23

Risk of neutropenia does not increase over time:

- **29/72 (40%)** of patients **received G-CSF** across the study
- **Only 4/72 (6%) of patients** experienced **Grade ≥3 neutropenia for the first time after completing cycle 2**

Granulocyte – Colony Stimulating Factor (G-CSF); Patients (Pts)

Source: C4T data on file as of 7/23/2025

Anti-myeloma Activity Profile

Cemsidomide + Dexamethasone

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Cemsidomide Phase 1 Data Has Demonstrated Class-leading Anti-myeloma Activity

Patients who responded experienced durable benefit, supporting cemsidomide's differentiated profile in a heavily pre-treated patient population

- ✔ As of data cutoff, median duration of response was **9.3 months** across all doses and median duration of response not yet reached at two highest dose levels
- ✔ **67%** of efficacy evaluable patients who achieved a PR or better at the 75 µg and 100 µg dose levels remain on treatment

Compelling anti-myeloma activity achieved at the two highest dose levels

- ✔ Achieved **40% ORR** at the 75 µg dose level and **50% ORR** at the 100 µg dose level
  - ✔ MRD negativity achieved in 1 patient with a CR at the 100 µg dose level

Higher exposure with cemsidomide is correlated with greater reductions in dFLC

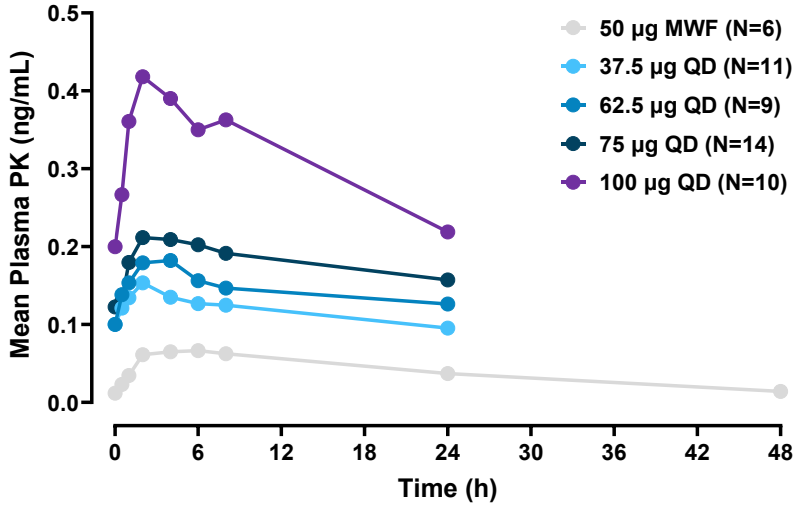
- ✔ Across all doses, **50%** of multiple myeloma patients with elevated light chains achieved at least a **50% decrease in dFLC**

Difference in involved and uninvolved free light chain (dFLC); Complete response (CR); Overall response rate (ORR)

Source: C4T data on file as of 7/23/2025

Pharmacokinetics Were Dose Proportional and Demonstrated Optimal Degradation of IKZF1/3 at 100 µg Dose Level

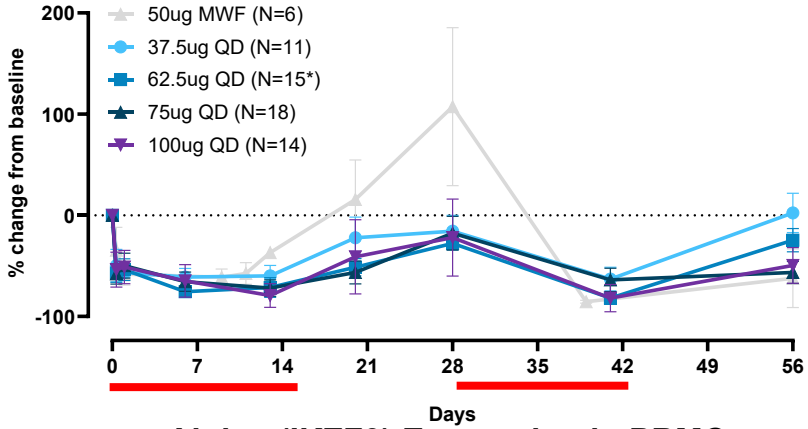
Dose Proportional Exposure



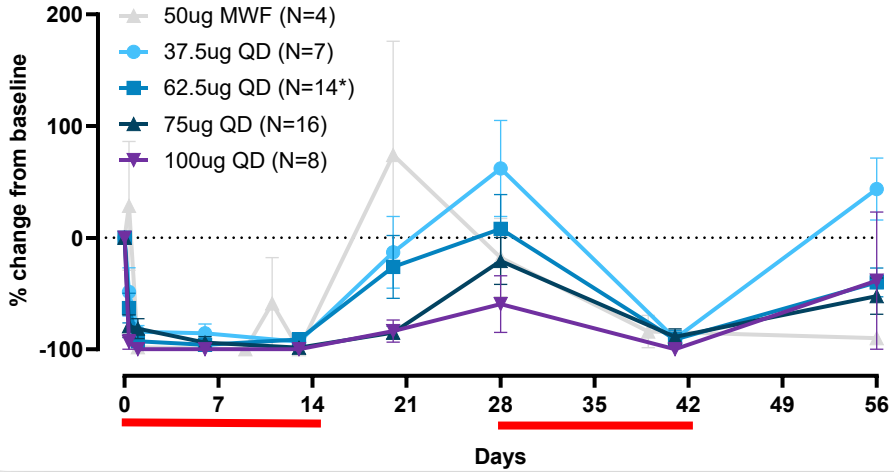
- Cemsidomide 14/14 exposure was dose-proportional when combined with dex
- The overall geometric mean half-life estimate is approximately 2 days

Pharmacodynamics

Ikaros (IKZF1) Expression in PBMCs



Aiolos (IKZF3) Expression in PBMCs



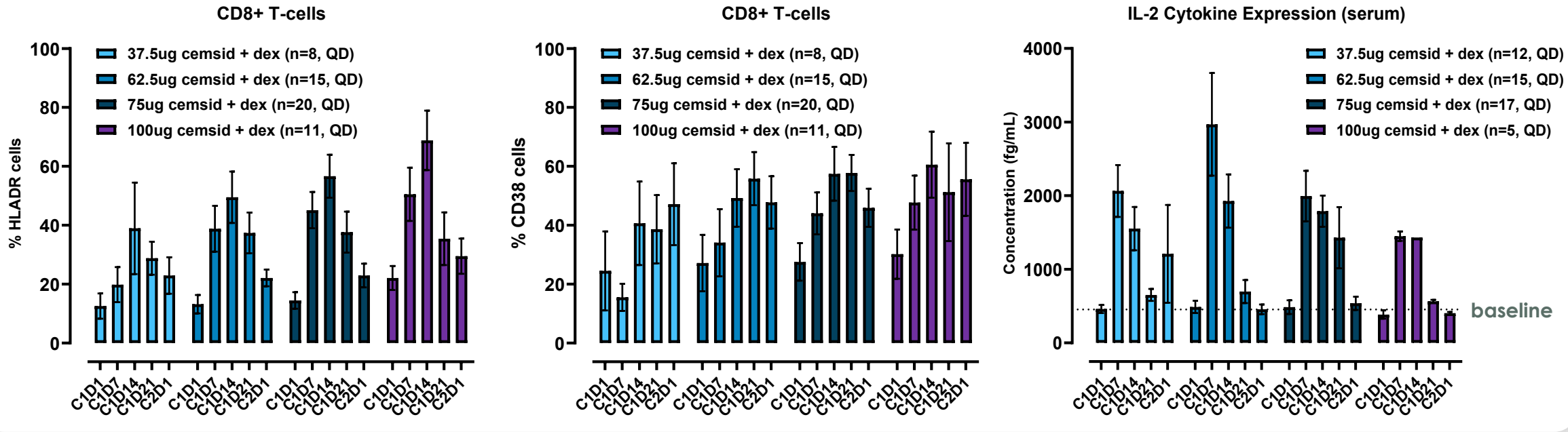
- Cemsidomide 14/14 + dex achieves >50% degradation of IKZF1 and >80% degradation of IKZF3, as assessed by mass spectrometry in human PBMCs
- Sustained IKZF3 degradation up to day 20 observed at the two highest doses of cemsidomide (75 µg and 100 µg)

Red bar indicates the 14-day periods of cemsidomide dosing

*1 patient censored due to abnormal mass spectrometry values
Note: PD data were not available for all patients at all time points
Ikaros zinc finger protein 1/3 (IKZF1/3); Monday Wednesday Friday (MWF); Peripheral blood mononuclear cell (PBMC); Once daily (QD); Difference in involved and uninvolved free light chain (dFLC); Dexamethasone (dex); Once daily (QD); Monday, Wednesday, Friday dosing (MWF)

Source: C4T data on file as of 7/23/2025

T-cell Activation Is Observed Across All Dose Levels With Cemsidomide + Dex



Cemsidomide + Dexamethasone:

- 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 IL-2 cytokine expression compared to baseline

Cemsidomide Monotherapy:

- Data shared previously demonstrated clinical evidence of T-cell activation with monotherapy[1]

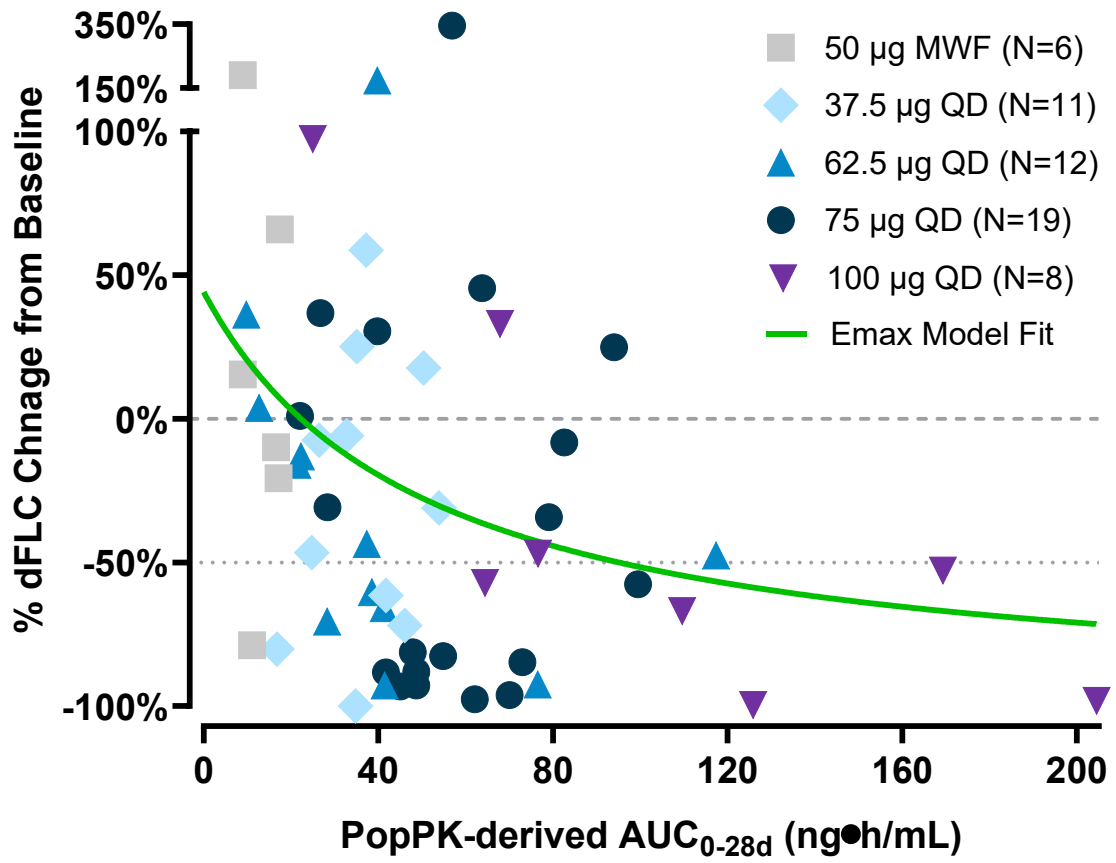
Source: [1]C4T data on file as of 11/28/2023 presented in December 2023 (https://ir.c4therapeutics.com/static-files/ec59b02e-3074-484d-ad88-e81831bf37ed)

Dexamethasone (dex); Human leukocyte antigen-DR isotype (HLA-DR); Interleukin 2 (IL2); Once daily (QD)

Source: C4T data on file as of 7/23/2025

Cemsidomide 100 µg Dose Level Drives Sufficient Exposure, Resulting in Meaningful Reductions in Light Chains

Cemsidomide + dex PK Exposure vs. dFLC Change*



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.

Area under the curve (AUC); Dexamethasone (dex); Difference in involved and uninvolved free light chain (dFLC,); Maximum response (Emax); Monday Wednesday Friday dosing (MWF); Once daily (QD); Population pharmacokinetics (popPK); Pharmacokinetic (PK)

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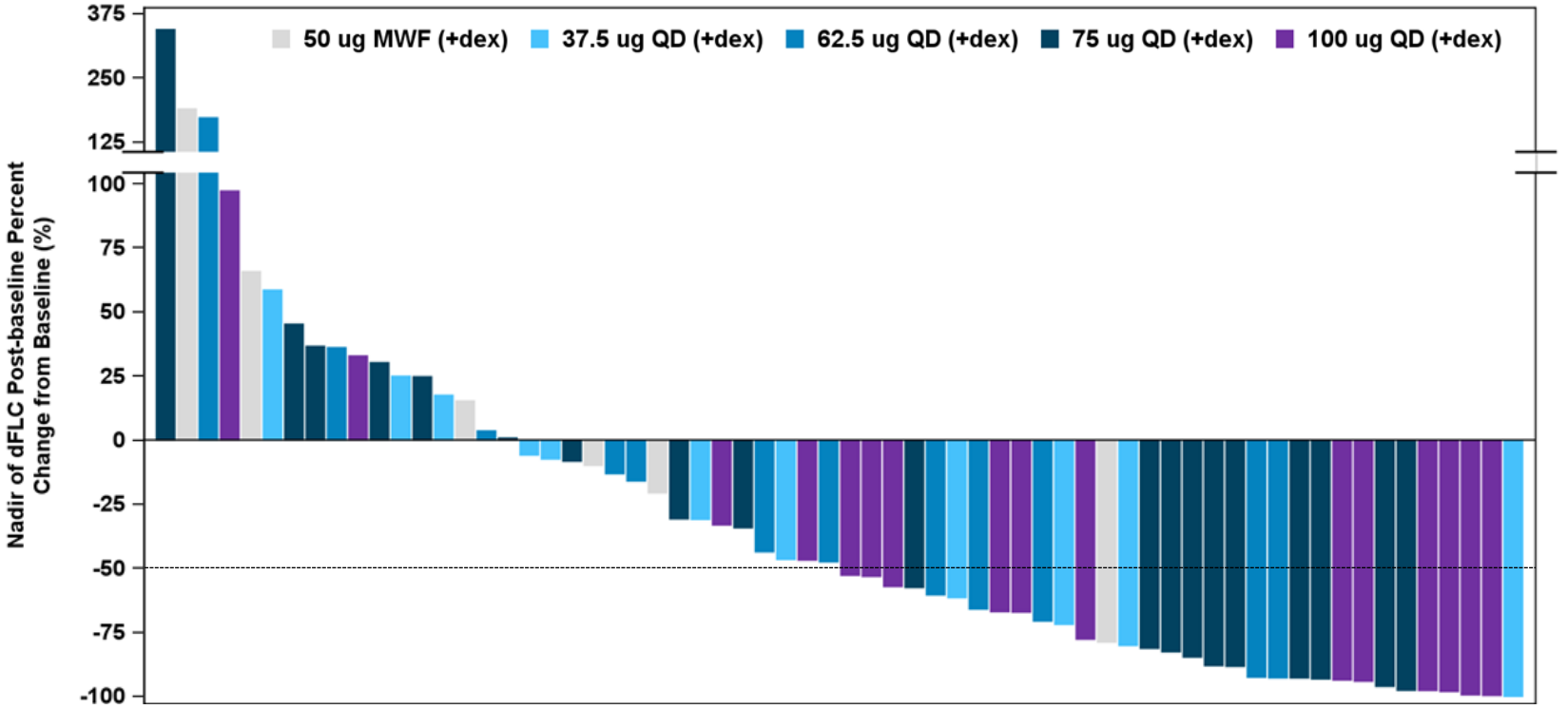
Source: C4T data on file as of 7/23/2025

Across All Doses, 50% of Multiple Myeloma Patients With Elevated Light Chains Achieved at Least a 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

Dexamethasone (dex); Difference in involved and uninvolved free light chain (dFLC); Monday Wednesday Friday (MWF); Once daily (QD)

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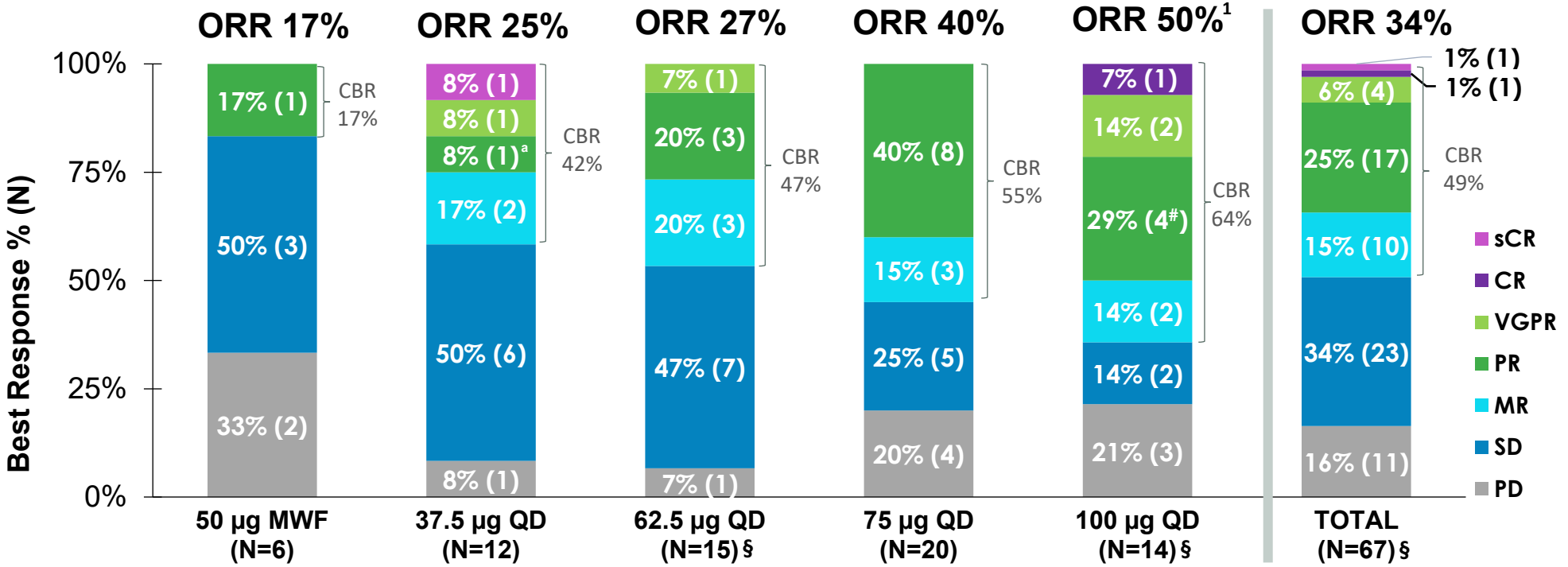
Source: C4T data on file as of 7/23/2025

Class-leading Anti-myeloma Activity With a 40% and 50% ORR at the Two Highest Dose Levels

Best Response: Multiple Myeloma – Cemsidomide 14/14 + Dex*



- 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 (100 µg) 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 (100 µg)**

[1]As of September 5, 2025 at the 100 µg dose level:

- One patient (not reflected in the graph) **became efficacy evaluable and achieved a PR**
- One patient who was included in the table **as a VGPR converted to a CR**

*Investigator assessed response

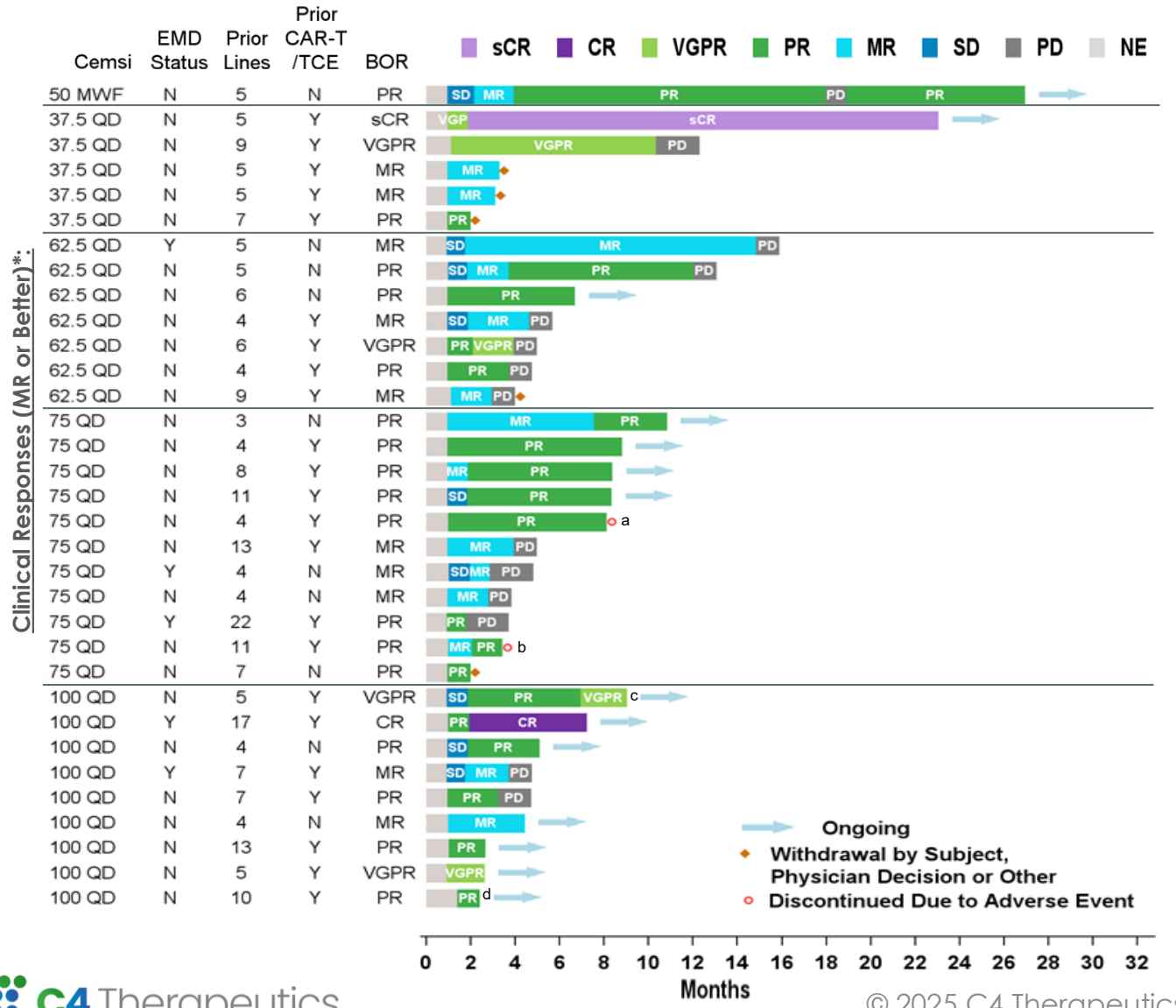
[a]1 patient in the 37.5 µg cohort achieved a PR based on light chains, no follow up M protein available; §1patient at 62.5 µg did not have a post-baseline assessment and 4 patients in 100 µg did not have a post-baseline assessment performed at the time of data cutoff; [#]1 patient in 100 µg had a PR confirmed after data cut off date, which is reflected in the graph above

Clinical benefit rate (CBR); Dexamethasone (dex); Minimal response (MR); Monday Wednesday Friday (MWF); Objective response rate (ORR); Progressive disease (PD); Partial response (PR); Once daily (QD); Relapsed/refractory multiple myeloma (RRMM); Stringent complete response (sCR); Stable disease (SD); Very good partial response (VGPR); Minimal residual disease MRD); Complete response (CR)

C4 Therapeutics

Source: C4T data on file as of 7/23/2025

In a Heavily Pre-treated Population, Patients Who Responded Remained on Therapy for Clinically Meaningful Duration



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

67% (10/15) of efficacy evaluable patients who achieved a PR or better remain on treatment
at two highest dose levels evaluated
(75 µg and 100 µg)

*Investigator assessed response and swimmer plot only includes patients that achieved and MR or better (33/72) patients

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

Adverse event (AE); Duration of response (DOR); End of treatment (EOT); Extramedullary disease (EMD); Minimal response (MR); Progression-free survival (PFS); Progressive disease (PD); Partial response (PR); Once daily (QD); Relapsed/refractory multiple myeloma (RRMM); Stringent complete response (sCR); Stable disease (SD); Very good partial response (VGPR); Complete response (CR); stable disease (SD); Best overall response (BOR); Progression free survival (PFS); Confidence interval (CI); Not estimable (NE)

C4 Therapeutics

Source: C4T data on file as of 7/23/2025

Cemsidomide Phase 1 Patient Population Was More Heavily Pre-treated Than Other IKZF1/3 Degraders in Development, Representative of Current Multi-Refractory Patients

Prior Therapies

	Cemsidomide Dose Escalation N=72	Mezigdomide Dose Escalation[1] N=77	Iberdomide Dose Escalation[2] N=90
Prior lines of therapy, median (range)	7 (3-22)	6 (2-13)	5 (4-8)
Prior BCMA therapy	75%	12%	N/A[3]
Prior anti-CD38 mAb[4]	100%	78%	76%
Triple-class exposed[5]	100%	56%	59%

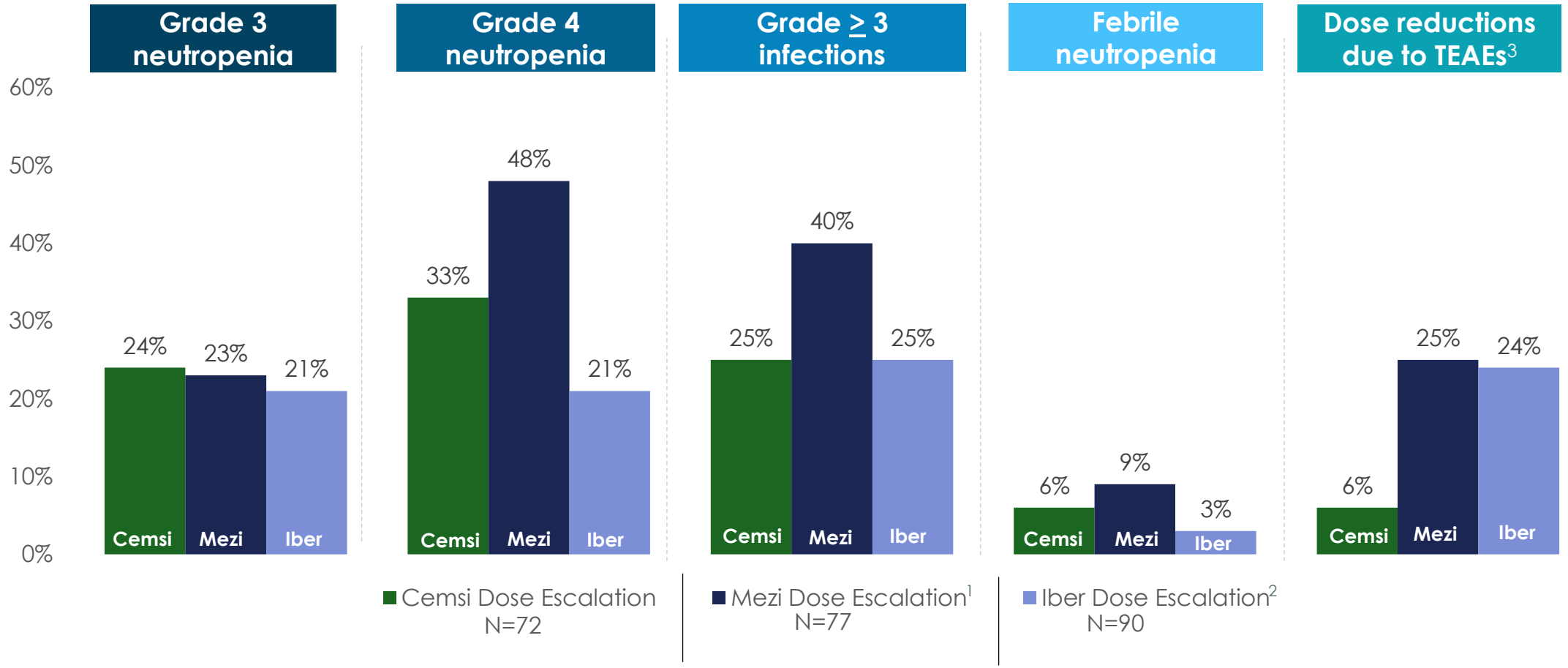
Sources: [1]Richardson 2023 NEJM. [2]Phase I dose escalation (Lonial 2022 Lancet Haematology); [3]Dose escalation trial was conducted from 2016 – 2020 and BCMA therapies were not approved until 2021 [4]Anti-CD38 mAB is also known as Anti-CD38 antibody [5]Triple-class exposed is defined as refractory to at least one immunomodulatory drug, at least one proteasome inhibitor, and at least one CD38 monoclonal antibody.

Monoclonal antibody (mAb)

C4 Therapeutics

Source: C4T data on file as of 7/23/2025

Cemsidomide Demonstrated Minimal Treatment Disruptive Adverse Events, Differentiated From Other IKZF1/3 Degraders in Development



Cross-trial comparisons should be used with caution and only as benchmarks for relative comparison; no head-to-head studies have been conducted

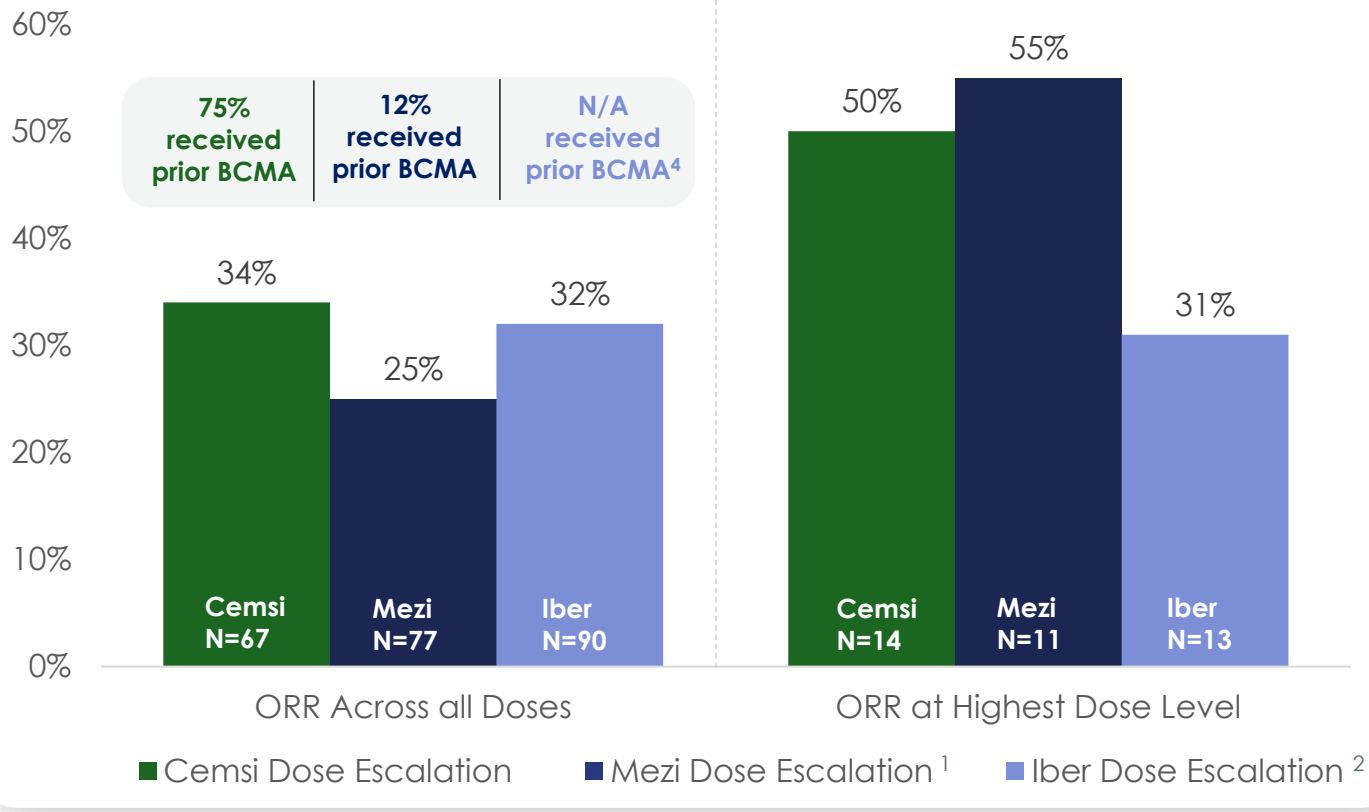
Sources: [1]Richardson 2023 NEJM. [2]Phase I dose escalation (Lonial 2022 Lancet Haematology) [3]Cemsidomide and Iber reported reductions due to TEAEs, while Mezi reported reductions due to AEs
Cemsidomide (Cemsi); Mezigdomide (Mezi); Iberdomide (Iber); Treatment Emergent Adverse Events (TEAEs); Adverse events (AEs); B-cell maturation antigen (BCMA)

C4 Therapeutics

Source: C4T data on file as of 7/23/2025

Cemsidomide Demonstrates Compelling Anti-Myeloma Activity and Median Duration of Response

Cemsi and Mezi Have Similar Response Rate In Respective Phase 1 Dose Escalation Trials



Cemsi-treated Patients Have Compelling Duration of Response

Patients treated with cemsi **are in a more contemporaneous and relevant late-line setting and 75% were pre-treated with BCMA therapies**

	Median Duration of Response Months (95% CI)
Cemsi *Dose Escalation*	**9.3 (2.8-NE)**[3]
Mezi[1] *Dose Escalation*	**6.0 (1.9-11.1)**
Iber[2] *Dose Escalation*	**10.4 (4.6-15.7)**

Cross-trial comparisons should be used with caution and only as benchmarks for relative comparison; no head-to-head studies have been conducted

Sources: [1]Richardson 2023 NEJM. [2] Phase I dose escalation (Lonial 2022 Lancet Haematology); [3] As of the July 23, 2025 data cutoff, the upper duration of response has not been achieved as patients continue on the study; [4] Dose escalation trial was conducted from 2016 – 2020 and BCMA therapies were not approved until 2021

Cemsidomide (Cemsi); Mezigdomide (Mezi); Iberdomide (Iber); Overall response rates (ORR); Not estimable (NE)

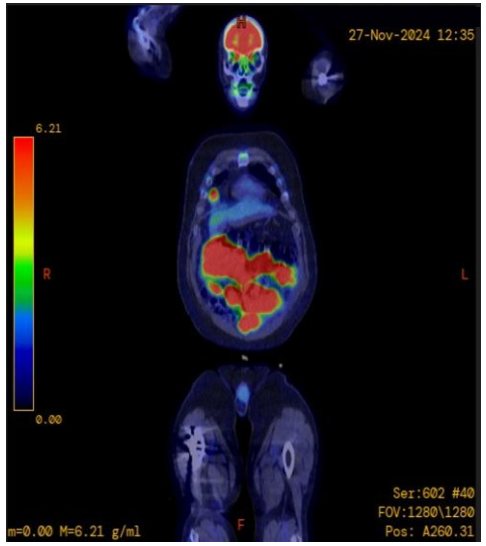
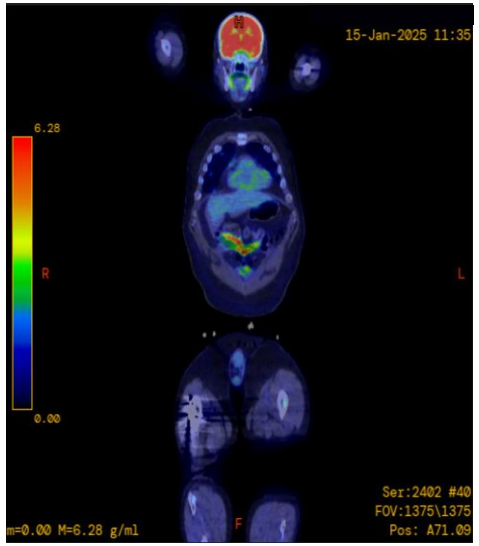
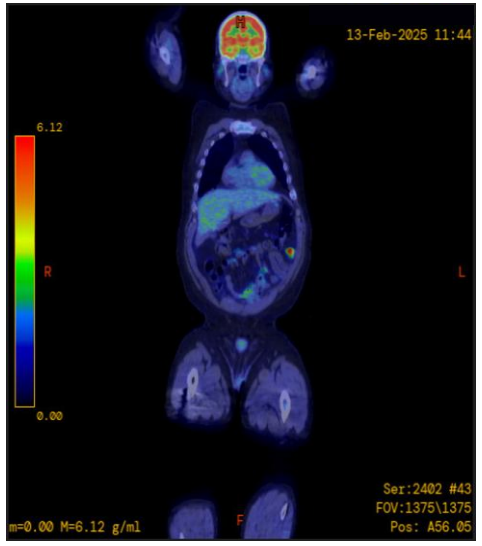
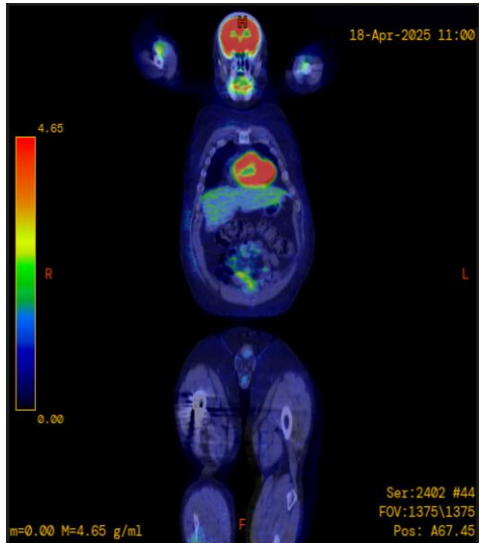
C4 Therapeutics

Source: C4T data on file as of 7/23/2025

Patient Vignette: Penta-class Refractory Patient With EMD Who Progressed on Prior T-Cell Engager Therapy Achieved MRD Negative CR, With Treatment Ongoing

- 42-year-old male, enrolled at the 100 µg dose level of cemsidomide in December 2024
- Stage 2 MM diagnosed in June 2020
- Patient with EMD received 17 prior therapies; last treatment prior to study start was talquetamab (GPRC5D – T-cell engager) where the best overall response was progressive disease
- As of data cutoff, patient remained on cemsidomide treatment at cycle 8

Per IMWG response criteria, patient achieved MRD negative complete response

Baseline	C2D1	C3D1	C5D1
			
SPD: 9290 mm^2	SPD: 1372 mm^2 (-85%)	SPD: None	SPD: None

Multiple myeloma (MM); International Myeloma Working Group (IMWG); Extramedullary disease (EMD); Sum of products of the maximal perpendicular diameters of measured lesions (SPD); Minimal Residual Disease (MRD)

Source: C4T data on file as of 7/23/2025

Patient Vignette: 90-Year-Old Patient Who Progressed on Prior IKZF1/3 Degraders Achieved a Very Good Partial Response With Cemsidomide

- 90-year-old female enrolled at the 100 µg dose level of cemsidomide in May 2025
- Stage 3 MM diagnosed in August 2020
- Patient received 5 prior therapies; last treatment prior to study start was teclistamab
  - Did not receive prior CAR-T therapy
- As of data cutoff, patient remained on cemsidomide treatment at cycle 4

Time	IgG Levels (mg/dL)	Serum M Protein (g/dL)	Urine M Protein mg/24 hr	Kappa (mg/L)	Lambda (mg/L)	BOR: Cemsi + dex
Baseline	758	Undetectable	124	**426**	**1.3**	
C2D1	811	Undetectable	Not done	**35 (-93.5%)**	**1.3**	**VGPR**
C2D14	546	Undetectable	Not done	**13.2 (-97.7%)**	**1.3**	
C2D22			Undetectable (IFE + Kappa)			
C3D1	685	Undetectable	Not done	**33.4 (-94%)**	**1.3**	**VGPR**

Multiple myeloma (MM); Chimeric antigen receptor t-cell therapy (CAR-T); Pomalidomide (pom); Very good partial response (VGPR)

Source: C4T data on file as of 7/23/2025

Cemsidomide's Potential Best-in-Class Profile Supports Opportunity to be the IKZF1/3 Degrader of Choice Across the MM Landscape

Class-leading anti-myeloma activity in heavily pre-treated patient population, a majority of whom received a prior BCMA BiTE or T-cell engager, highlighting that IKZF1/3 degradation is a critical MOA regardless of prior treatment

- ✓ **75%** of patients received prior BCMA therapy
- ✓ **40% ORR** at the 75 µg dose level and **50% ORR** at 100 µg dose level
  - ✓ 1 patient at 100 µg dose level achieved MRD negativity

Patients who responded experienced durable benefit, supporting cemsidomide's differentiated profile

- ✓ Median duration of response is **9.3 months** across all doses; median duration of response not yet reached at two highest dose levels
- ✓ **67%** of efficacy evaluable patients who achieved a PR or better at the 75 µg and 100 µg dose levels remain on treatment

Differentiated safety & tolerability profile with no discontinuations related to cemsidomide safety and minimal dose reductions

- ✓ Well-tolerated profile, including at the two highest dose levels evaluated
- ✓ Manageable neutropenia supported by low G-CSF use and patients remaining on treatment

Cemsidomide, as a monotherapy and in combination with dex, activates T-cells, providing a strong rationale for a BCMA BiTE combination

Mechanism of Action (MOA); Overall response rate (ORR); Granulocyte colony stimulatory factor (G-CSF); Bispecific T-cell engager (BCMA BiTE); Minimal response (MR); Minimal residual disease (MRD); Chimeric antigen receptor t-cell therapy (CAR-T)

C4 Therapeutics

Source: C4T data on file as of 7/23/2025

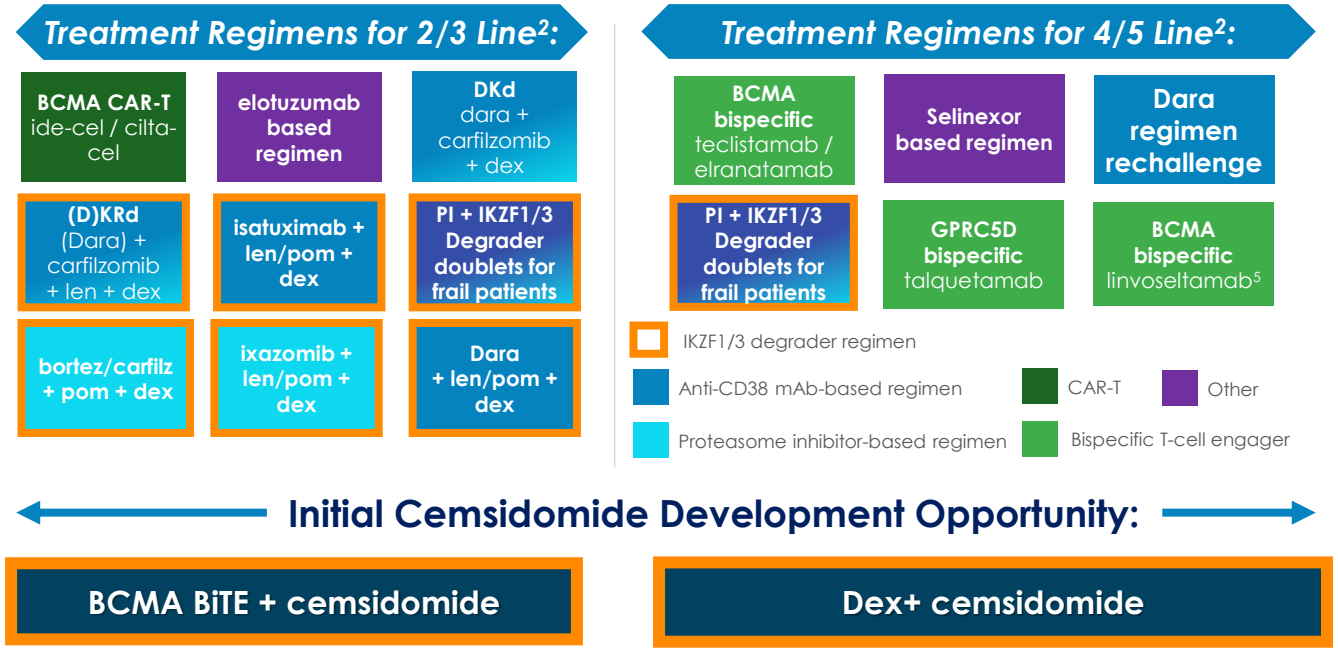
Market Opportunity & Path Forward for Cemsidomide

C4 Therapeutics

Cemsidomide Is Well-Positioned to Compete in the RRMM Treatment Paradigm and Be Incorporated as a 2L+ Treatment Option

U.S. + EU4 + UK Addressable Patients (2024)[4]	~65,000	~56,000	~49,000	~42,000	≥23,000
Treatment Line	1L	2L	3L	4L	5L+

$2.5 to $4B[1] peak revenue potential, if labels are achieved in combinations with a BCMA BiTE and dex



TOTAL GLOBAL PROJECTED MM MARKET IS $46B BY 2030[3]

Sources: [1]Health Advances (2022), ClearView (2023), and C4T analysis [2]NCCN guidelines [3] Evaluate Pharma (8/14/2025) [4] EvaluatePharma (accessed 8/28/25) [5] Linovesltamab is only approved in 5L
Relapsed refractory multiple myeloma (RRMM); Dexamethasone (dex); Bispecifc T-cell engager (BCMA BiTE)

C4 Therapeutics

Multiple Myeloma Is a Growing Patient Population With Persistent Unmet Need as Patients Continue to Progress

MM Represents a Large and Growing Population With Tremendous Unmet Need

In the US, UK, and EU4, the addressable patient population in 2024 for:

2L = ~56,000[2]

4L = ~42,000[2]

Majority of Patients Continue to Progress Despite Novel Treatment Options:

- Many patients experience relapse after receiving a BCMA therapy
  - Despite high initial response rates, **2/3 of CARVYKTI-treated patients relapse before 5 years[3]**
- Later lines are expected to grow as patients live longer on newer treatments but ultimately progress
  - **Range of median OS for patients treated with BiTEs: 22 – 34 months[4]**

Survival outcomes with current options are low[1]:

Median OS in RRMM (penta-refractory)	~5.6 months
Median OS (triple/quad refractory)	~9.2 months

Sources: [1] Mammoth Study (275 patients evaluated across the study) Podar, K., & Leleu, X. (2021). Relapsed/Refractory Multiple Myeloma in 2020/2021 and Beyond. Cancers, 13(20), 5154 https://pmc.ncbi.nlm.nih.gov/articles/PMC6820050/ [2] EvaluatePharma (accessed 8/28/25) [3] Legend Biotech Press Release June 3, 2025 (https://investors.legendbiotech.com/news-releases/news-release-details/legend-biotech-unveils-groundbreaking-5-year-survival-data)
[4] https://www.jnjmedicalconnect.com/media/attestation/congresses/oncology/2024/ims/longterm-followup-from-the-phase-12-majestec1-trial-of-teclistamab-in-patients-with-relapsedrefracto.pdf; https://www.pfizer.com/news/press-release/press-release-detail/elrexfiotm-shows-median-overall-survival-more-two-years ; https://www.jnjmedicalconnect.com/products/talvey/medical-content/talvey-monumental1-mmy1001-study

Overall Survival (OS); Germany, Italy, France, and Spain (EU4)

C4 Therapeutics

Combination With BCMA-BiTE Has Potential to Capture Growing Market by Being a More Convenient Regimen Option With Potentially Similar Efficacy to CAR-Ts

Challenge:
CAR-T Has Better ORR Than BiTEs[1]

	ORR Range
CAR-T	~85%
VS	
BCMA BiTEs	~58% - 70%

Opportunity:
By activating T-cells with a potential best-in-class profile, cemsidomide could increase BCMA BiTE efficacy to be in line with CAR-Ts while offering a more attractive overall profile, thereby potentially taking market share from CAR-Ts

Validated Biology

THE LANCET Haematology

Mechanism of resistance against t-cell engaging bispecific antibodies in multiple myeloma: implications for novel treatment strategies

Prof Niels W C J van de Donk, MD [a,b] · Prof Ajai Chari, MD [c] · Prof Maria Victoria Mateos, MD [d]

*"**Long-term exposure to bispecific antibodies** with chronic T-cell stimulation further **aggravates T-cell dysfunction**, which could contribute to **failure of disease control**"*

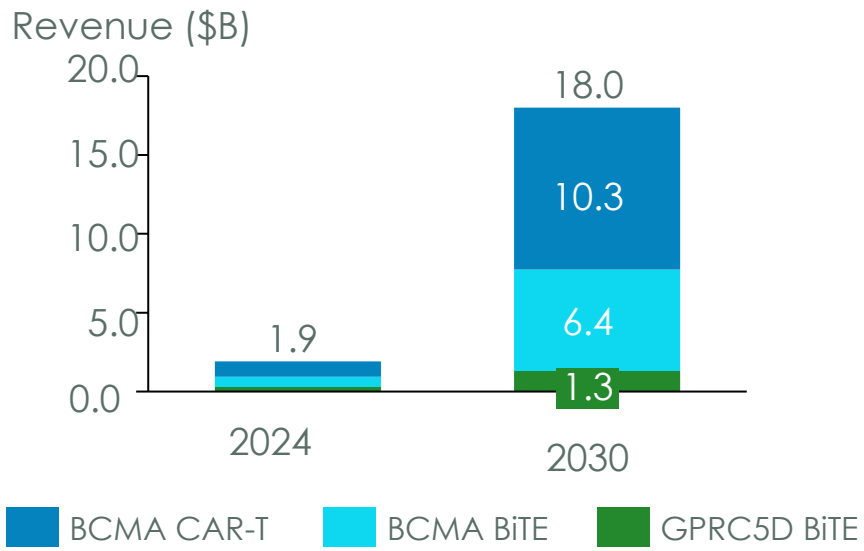
MOLECULAR CANCER THERAPEUTICS | LARGE MOLECULE THERAPEUTICS

IMiDs Augment CD3-Bispecific Antibody–Induced CD8$^+$ T-Cell Cytotoxicity and Expansion by Enhancing IL2 Production

Ji Li, Dionysos Slaga, Jennifer Johnston, and Teemu T. Junttila

Mezigdomide Reverses T-Cell Exhaustion Through Degradation of Aiolos/Ikaros and Reinvigoration of Cytokine Production Pathways

CAR-T and BCMA-BiTE Market Predicted to Grow at ~50% CAGR[2]

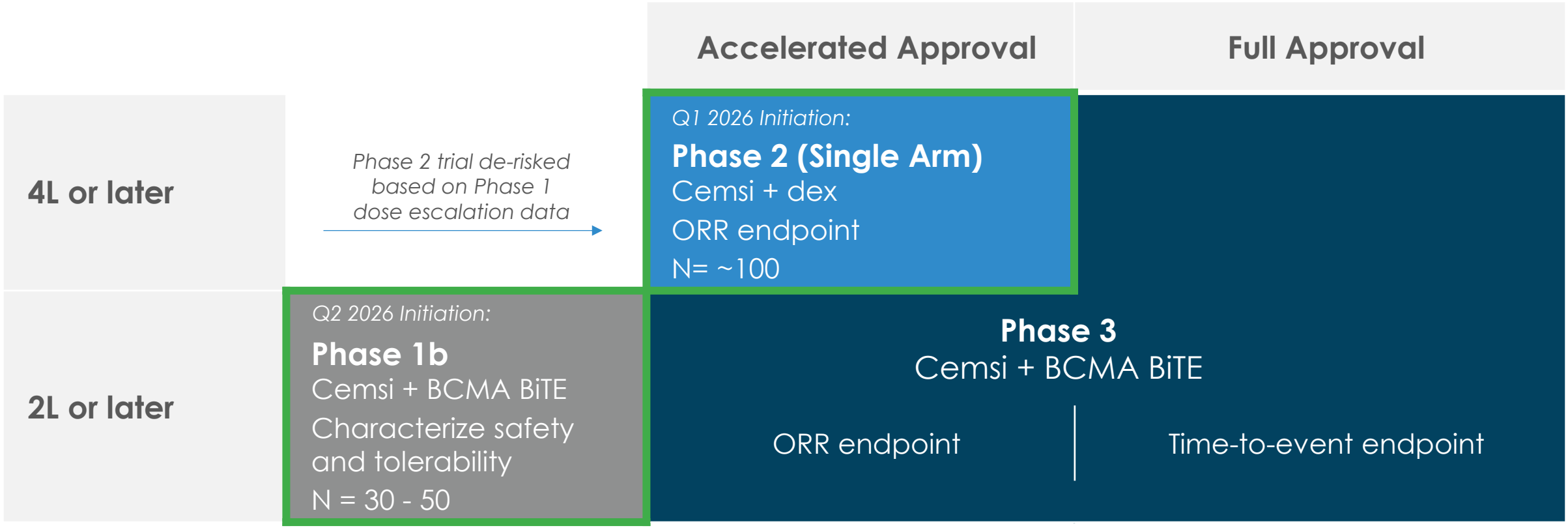


Sources: [1] Packaging Insert for each product (carvykti, tecvayli; elrexflo; lynozyfic) accessed 8/26/25 – the data is not a head-to-head trial . [2] Evaluate Pharma; C4T Analysis (accessed 8/15/2025)
Compound Annual Growth Rate (CAGR)

C4 Therapeutics

Cemsidomide Development Plan Provides Efficient Path to Registration and Addresses a Growing Patient Population

2 trials pave way for 2 distinct potential accelerated approvals based on ORR endpoint



A single, randomized controlled Phase 3 study would be used to support accelerated approval in 2L+ and full approval in 2L+ and 4L+ based on a time-to-event endpoint

C4 Therapeutics = next trial initiations

Overall response rate (ORR); Dexamethasone (dex)

Phase 2 Initial ORR Data of Cemsidomide + Dex in 4L+ Expected in 2H 2027

Q1 2026 EXPECTED TRIAL INITIATION

Phase 2 Trial
Cemsidomide + dex (single arm)
4L+
N = ~100
Formally select RP2D by year-end

Potential for accelerated approval

Phase 2 initial ORR data expected in 2H 2027

PHASE 2 TRIAL DESIGN:

- **Endpoints:** ORR per IMWG response criteria assessed by independent review committee
  - 100 patients will provide ~94% power to detect a 20% absolute improvement with a 1-sided alpha of 0.025
- **Objective:** ORR in RRMM
- **RP2D:** Expect to formally align with FDA by year-end on an RP2D
- **Schedule:** QD 14/14

Dexamethasone (dex); Overall response rate (ORR); Bispecific t cell engager (BCMA BiTE); Second line (2L); Fourth line (4L); Recommended Phase 2 dose (RP2D); Overall response (ORR); International Myeloma Working Group (IMWG); Once daily (QD)

C4 Therapeutics

Phase 1b Trial Will Evaluate Optimal Dose for Safety and T-Cell Activation in Combination With a BCMA BiTE, With Data Expected by Mid-2027

Q2 2026 EXPECTED TRIAL INITIATION

Phase 1b
Cemsi + BCMA BiTE
2L+
N = 30 - 50
Evaluation of three cemsidomide doses:
• 50 µg QD • 75 µg QD • 100 µg QD

Potential to expand at each dose level

Phase 1b data expected by mid-2027

PHASE 1b TRIAL DESIGN:

Primary Objectives:

- Characterize the safety and tolerability of cemsidomide in combination with a BCMA BiTE

Dosing Regimen:

- Cemsidomide: QD 14/14
- Dexamethasone: QW through cycle 4
- BCMA BiTE: Per label

Dexamethasone (dex); Bispecific t cell engager (BCMA BiTE); Once daily (QD); Once weekly (QW); Cemsidomide (cemsi)

C4 Therapeutics

Cemsidomide Has the Potential to Be Best-in-Class For Use Across Multiple Lines of Therapy in Multiple Myeloma

Potential best-in-class profile	• Differentiated safety & tolerability profile with class-leading anti-myeloma activity
Clear and distinct regulatory path	• De-risked development plan with two distinct opportunities for accelerated approval
Large addressable market opportunity	• Potential $2.5 - $4B[1] peak revenue in combination with a BCMA BiTE in the 2L+ and with dexamethasone in 4L+
Next steps	• Formally align with the FDA on a recommended Phase 2 dose by year-end • Initiate Phase 2 trial of cemsidomide + dex in Q1 2026 • Initiate Phase 1b of cemsidomide + BCMA BiTE in Q2 2026

Source: [1]Health Advances (2022), ClearView (2023), and C4T analysis
Bispecific T cell engagers (BCMA BiTE); Dexamethasone (dex); Multiple myeloma (MM)

C4 Therapeutics

Q&A

C4 Therapeutics