C4 Therapeutics

Educational KOL Webinar on the Evolving Multiple Myeloma Treatment Landscape, Role of IKZF1/3 Degradation, and Cemsidomide's Profile

June 18, 2026

Forward-looking Statements and Intellectual Property

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Cemsidomide Educational Webinar Agenda

1. **Introductions & Opening Remarks**
   Andrew Hirsch, President & CEO
2. **Multiple Myeloma & Treatment Landscape**
   Nisha Joseph, M.D.
3. **IKZF1/3 Degradation is Foundational Biology in MM**
   Nisha Joseph, M.D.
4. **Cemsidomide's Potential Best-in-Class Profile and Development Strategy**
   Len Reyno, M.D.
5. **Conclusion & Q&A**
   Andrew Hirsch; Len Reyno, M.D.; Nisha Joseph, M.D.

Andrew Hirsch
President, Chief Executive Officer

Nisha Joseph, M.D.
Associate Professor in the Department of Hematology and Medical Oncology at Emory University School of Medicine

Len Reyno, M.D.
Chief Medical Officer

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Opening Remarks

Andrew Hirsch

President and Chief Executive Officer

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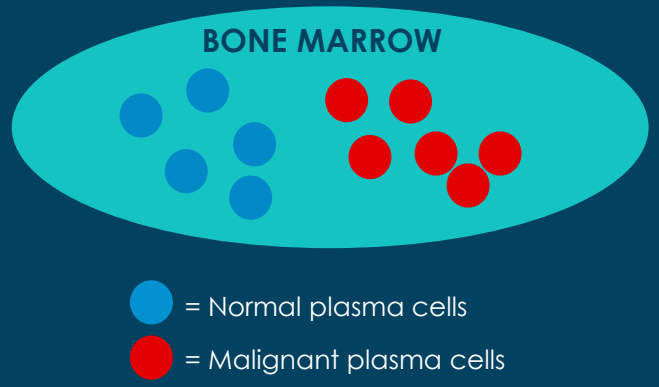
Setting the Stage: Multiple Myeloma and the Evolving Treatment Landscape

Nisha Joseph, M.D.
Associate Professor in the Department of Hematology and Medical Oncology at Emory University School of Medicine

Multiple Myeloma is a Complex Disease with Significant Unmet Need

MULTIPLE MYELOMA (MM)



- A blood cancer formed by malignant plasma cells originating in the bone marrow
  - Abnormal plasma cells crowd out normal blood cell production resulting in **anemia, immune suppression and bleeding risk**
- Characterized by repeated cycles of relapse

~35K+

New U.S. cases of MM each year[1]

2nd

Most common blood cancer[2]

~11K

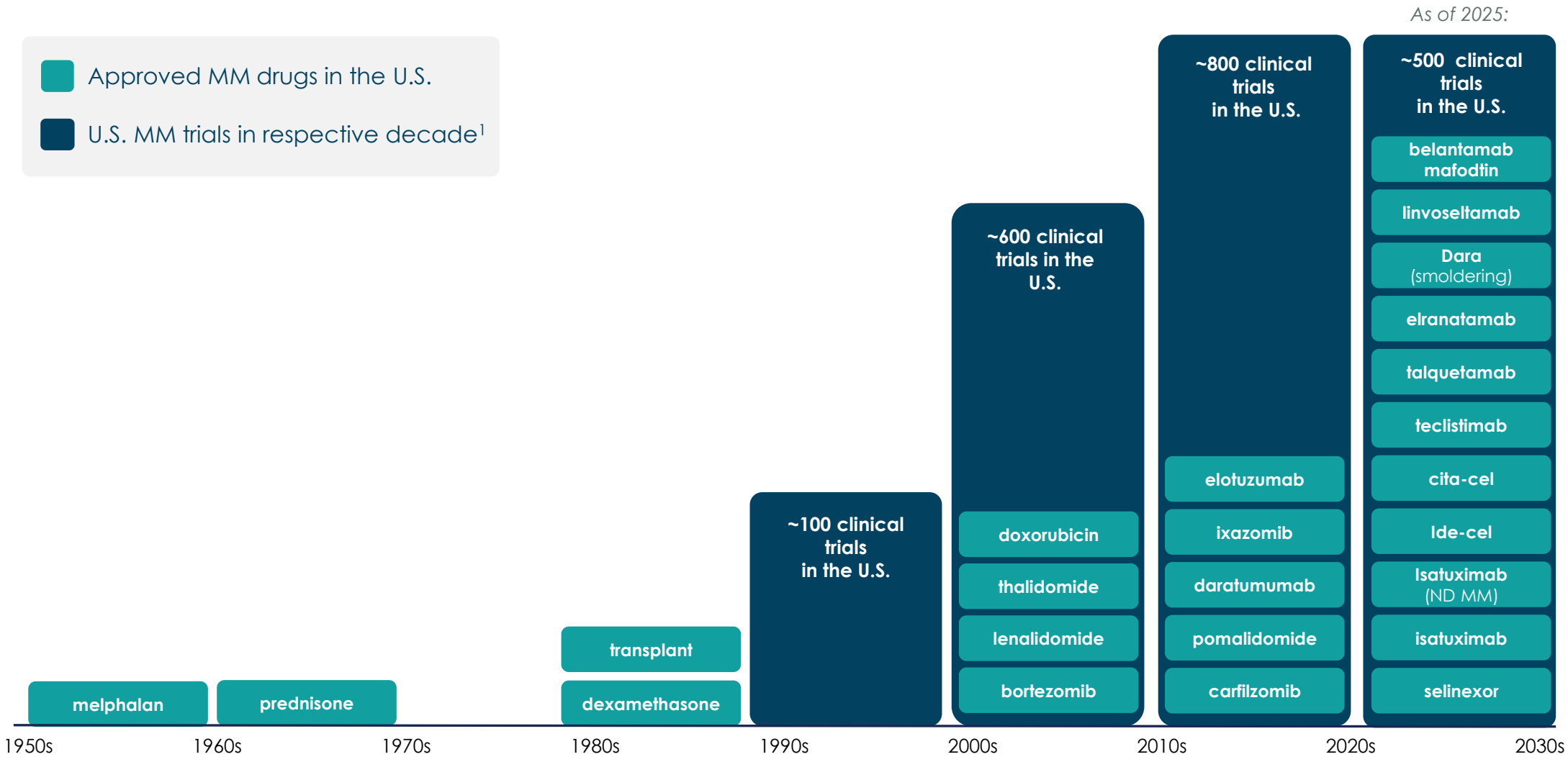
MM patient deaths expected in the U.S. in 2026[1]

~40%

of MM patients are not surviving beyond five years, despite recent treatment advances[3]

[1] Key Statistics for Multiple Myeloma | American Cancer Society (accessed 5/26/2026); [2] Multiple Myeloma - Cancer Research Institute (accessed 5/26/2026); [3] Myeloma — Cancer Stat Facts

Treatment Landscape for Multiple Myeloma is Rapidly Evolving Due to Significant Number of Approvals in Last Decade



[1] Clinical trials.gov
Multiple Myeloma (MM); Newly Diagnosed (ND)

IKZF1/3 Degraders Positioned Across Every Stage of Multiple Myeloma Patient Journey

Newly Diagnosed

- **First-generation IKZF1/3 degraders (IMiDs®)**
- Proteasome inhibitors
- Anti-CD38
- Autologous stem cell transplant

Relapsed/Refractory

- **First-generation IKZF1/3 degraders (IMiDs)**
- Proteasome inhibitors
- Anti-CD38
- Immune-based regimens (T-cell engagers, CAR-Ts)
- XPO1 inhibitor
- Anti-SLAMF7
- Anti-BCMA ADC

Emerging

- **Next-generation IKZF1/3 degraders (CELMoDs®; Cemsidomide)**
- P300/CBP inhibition
- Allogenic CAR-T
- Novel target bi-specifics
- Tri-specific t-cell engagers
- *In-vivo* CAR-T

Leverages Multiple MOAs in Combination Regimens

NCCN Guidelines; Antibody Drug Conjugate (ADC)
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Foundational Biology:
Why IKZF1/3 Degradation Matters

Nisha Joseph, M.D.
Associate Professor in the Department of Hematology and Medical Oncology at Emory University School of Medicine

IKZF1/3 are Transcription Factors That are Central Drivers of Multiple Myeloma Development and Progression

IMiDs (Pomalyst (pomalidomide) capsules, Revlimid (lenalidomide) capsules 2.5 · 5 · 10 · 15 · 20 · 25 mg), CELMoDs (*iberdomide, mezigdomide*), and cemsidomide all degrade IKZF1/3 to drive anti-myeloma activity

Key Roles of IKZF1/3

Physiological Functions:

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

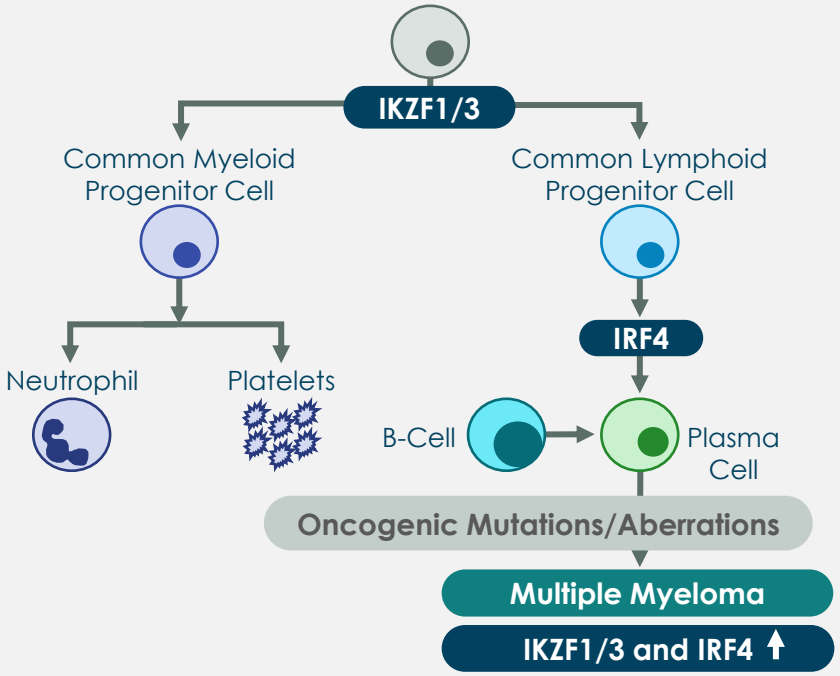
Oncogenic Functions:

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

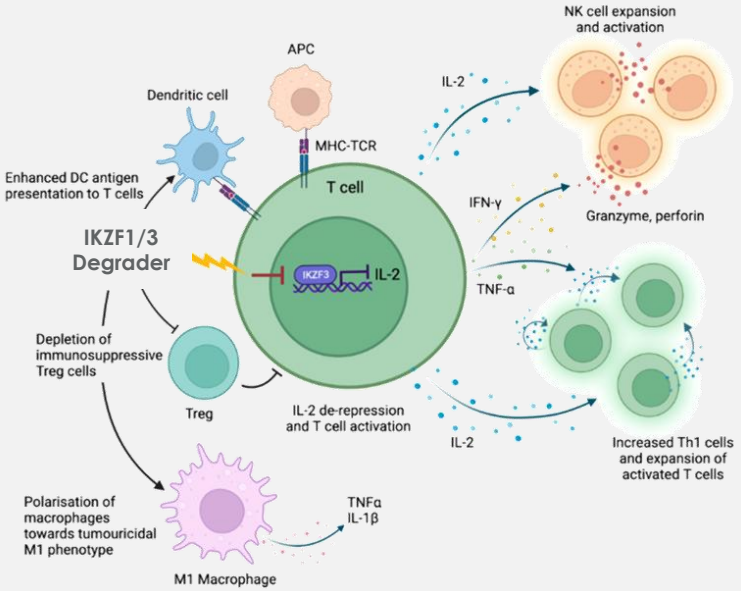
IKZF1/3 Degradation Leads to:

- Downregulation of IRF4 drives myeloma cell death and blocks proliferation
- T-cell activation
- On-target neutropenia

Hematopoietic Stem Cell



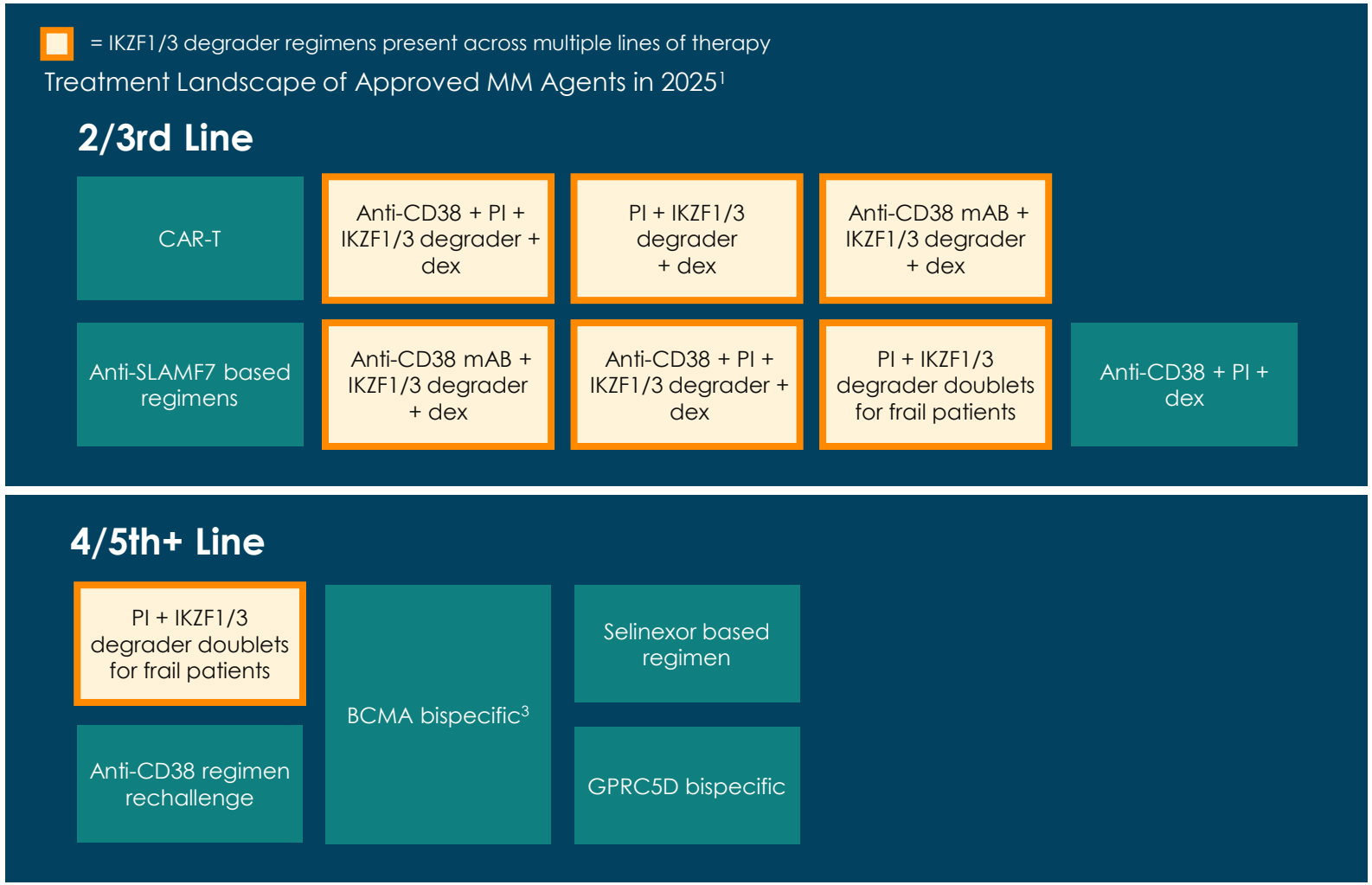
T-cell Activation



Adapted from Chen and Gooding, 2022

MOA of IKZF1/3 Degraders Supports Use Across Lines of Therapy and in Combination Regimens Across the Current Treatment Landscape

- IKZF1/3 degraders **remain relevant across multiple lines of therapy**
- IKZF1/3 degraders are an **important combination partner**



[1]NCCN guidelines, accessed in 2025 [3.] Linovesltamab is only approved in 5L
Multiple myeloma (MM); dexamethasone (dex)

Future Multiple Myeloma Treatment Landscape Supports Continued Role of IKZF1/3 Degraders as Foundational Therapy

Landscape Emerging Trends:

- Unmet need in the late-line setting for an all-oral regimen that is safe and efficacious for patients who have exhausted all options
- Emphasis on using the most potent drug for each MOA in earlier lines
- Immune-based regimens moving into earlier lines of therapy
- Late-line opportunity expected to grow as treatments are approved in earlier lines
- High CAR-T response rates create a need for simple maintenance to sustain response

IKZF1/3 Degraders Will Remain Relevant:

ABILITY TO COMBINE WITH OTHER MOAS GIVEN OVERALL PROFILE

NEXT-GENERATION IKZF1/3 DEGRADERS DEVELOPED TO ADDRESS POTENCY AND SELECTIVITY

CLINICALLY VALIDATED PATHWAY THAT WILL REMAIN RELEVANT
HAS BEEN RELEVANT FOR 20+ YEARS

USED ACROSS MULTIPLE LINES

- IKZF1/3 degraders will be an **important combination partner** in earlier lines due to **ability to drive anti-myeloma activity and activate T-cells**
  - T-cell exhaustion limits the depth and durability of immune-based regimens

Mechanism of action (MOA)

Cemsidomide: A Potential Best-in-Class IZKF1/3 Degrader in Multiple Myeloma

Len Reyno, M.D.

Chief Medical Officer

C4 Therapeutics

Next-generation IKZF1/3 Degraders Optimized for Greater Potency, Deeper Anti-myeloma Activity, and Better Combinability

Foundation
2003 – 2013

- Lenalidomide & pomalidomide developed as IMiDs
- Lenalidomide approved for MM (2006)
- CRBN identified as substrate receptor of CRL4^{c}CRBN E3 ubiquitin ligase (2010)
- Pomalidomide approved for RRMM (2013)

MOA unclear at approval

Mechanism Revealed
2013 – 2015

- Scientific papers confirm lenalidomide and pomalidomide degrade IKZF1/3 via CRBN
- Discovered targeting IKZF1/3 drives MM cell death and prevents proliferation
- Lenalidomide and pomalidomide not optimized for potency[1]
- Molecular glue mechanism discovered: IKZF1/3 recruited to CRL4^{c}CRBN complex

Limited Potency Only Prevents Proliferation, Resulting in Rise of Resistance Mechanisms

Next-gen IKZF1/3 Degrader Development
2015 – 2020s

- Next-generation IKZF1/3 degraders (CELMoDs and cemsidomide) designed to be more selective and potent vs. IMiDs
- CELMoDs (mezigdomide & iberdomide) developed using chemistry based on IMiDs
- Cemsidomide developed using novel CRBN-binder chemistry

Increased Potency Drives Cell Death AND Blocks Proliferation

Cemsidomide and CELMoDs® Advance
2020s – Present

- Cemsidomide demonstrated potential best-in-class profile in a Phase 1 trial in heavily pre-treated RRMM patients
- Cemsidomide advancing in Phase 2 MOMENTUM trial in 4L+ & Phase 1b combo w/ elranatamab[1]
- CELMoDs in late-stage trials: SUCCESSOR-1; SUCCESSOR-2; EXCALIBER trials in RRMM
- T-cell activation data emerging; Synergistic MOA with immune-based regimens

Addresses limitations of IMiDs and remains a foundational MOA

Cereblon (CRBN); Relapsed refractory multiple myeloma (MM); Mechanism of action (MOA)

[1] CELMoDs May Represent Next Wave of Immunomodulation Approaches in Multiple Myeloma | OncLive

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Cemsidomide is a Potentially Best-in-Class IKZF1/3 Degrader in Multiple Myeloma

Clinical Pharmacology

Highly potent & selective
IKZF1/3 degrader

High target specificity
Does not degrade off-target neosubstrates[1], including CK1α and GSPT1

No renal clearance
Relevant for ~50% of patients with renal impairment[2]

Low protein binding
Maximizes free drug availability

Design Elements

~2 day half life

Slower clearance sustains free drug at therapeutic concentrations, while **maintaining efficacy** and **allowing neutrophils to recover**

Results in an effective and convenient **14 days on / 14 days off dosing schedule**

Dosing Schedule + Safety Profile + Sustained Efficacy = Ideal Backbone for Combination Regimens

Development Strategy

Initial **differentiated label-enabling strategy** from other IKZF1/3 degraders focused on evolving landscape

Goal is to establish cemsidomide as a **foundational combination of choice across multiple lines of MM therapy**

IMiDs® and CELMoDs® are registered trademarks of BMS
[1] Source: C4T data on file; [2] Rana 2020 Blood Advances

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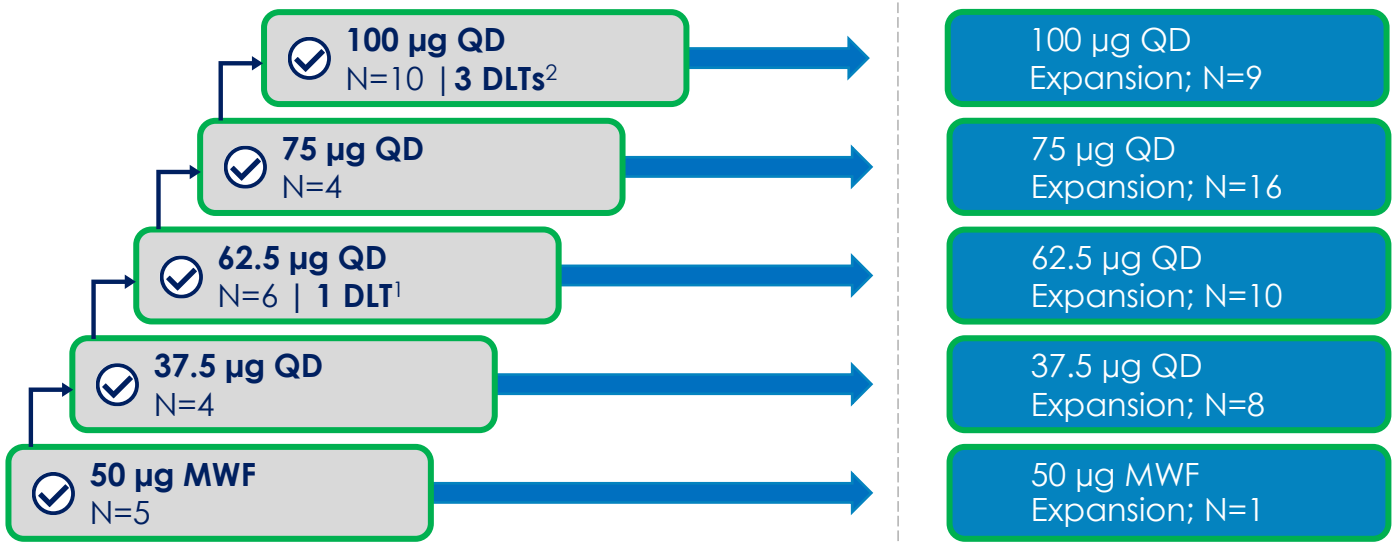
Phase 1 Trial of Cemsidomide + Dexamethasone for Multiple Myeloma Completed Enrollment in September 2025; 100 µg Selected as RP2D

DOSE ESCALATION
CEMSIDOMIDE 14/14 + DEX[#]

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



Heavily Pre-treated Patient Population

Cemsidomide's patient population is representative of current multi-refractory patients

Characteristics	Safety Population (N=73)
Prior therapies, median (range)	7 (3-22)
Prior CAR-T therapy, n (%)	37 (51)
Prior T-cell engager therapy, n (%)	40 (55)
Prior CAR T or T-cell engager therapy, n (%)	55 (75)
Prior CAR T and T-cell engager therapy, n (%)	22 (30)
Prior BCMA therapy, n (%)	55 (75)
Triple-class exposed*, n (%)	73 (100)
Penta-drug exposed†, n (%)	59 (81)

[#]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]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)
*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
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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Cemsidomide Phase 1 data cutoff as of 2/27/2026; Source: C4T data on file. Poster presentation at EHA 2026 (https://ir.c4therapeutics.com/static-files/0081f021-bc0d-4e7f-bdb9-9a01e95ed6eb)

Cemsidomide's Well-tolerated Safety Profile Is Ideal for Combinations

No discontinuations related to cemsidomide and minimal dose reductions

- ✔ TEAEs leading to dose reductions: **5/73 (7%)**[1]
- ✔ **3 TEAEs** leading to discontinuation, unrelated to cemsidomide[2]

Well-tolerated safety profile with manageable neutropenia

- ✔ Across all dose levels, Grade 3/4 neutropenia was **22%** and Grade 4 neutropenia was **36%**
- ✔ Low rates of febrile neutropenia across all dose levels, with only **4%** at Grade 3 and **1%** at Grade 4
- ✔ Limited grade 3/4 non-hematology side effects

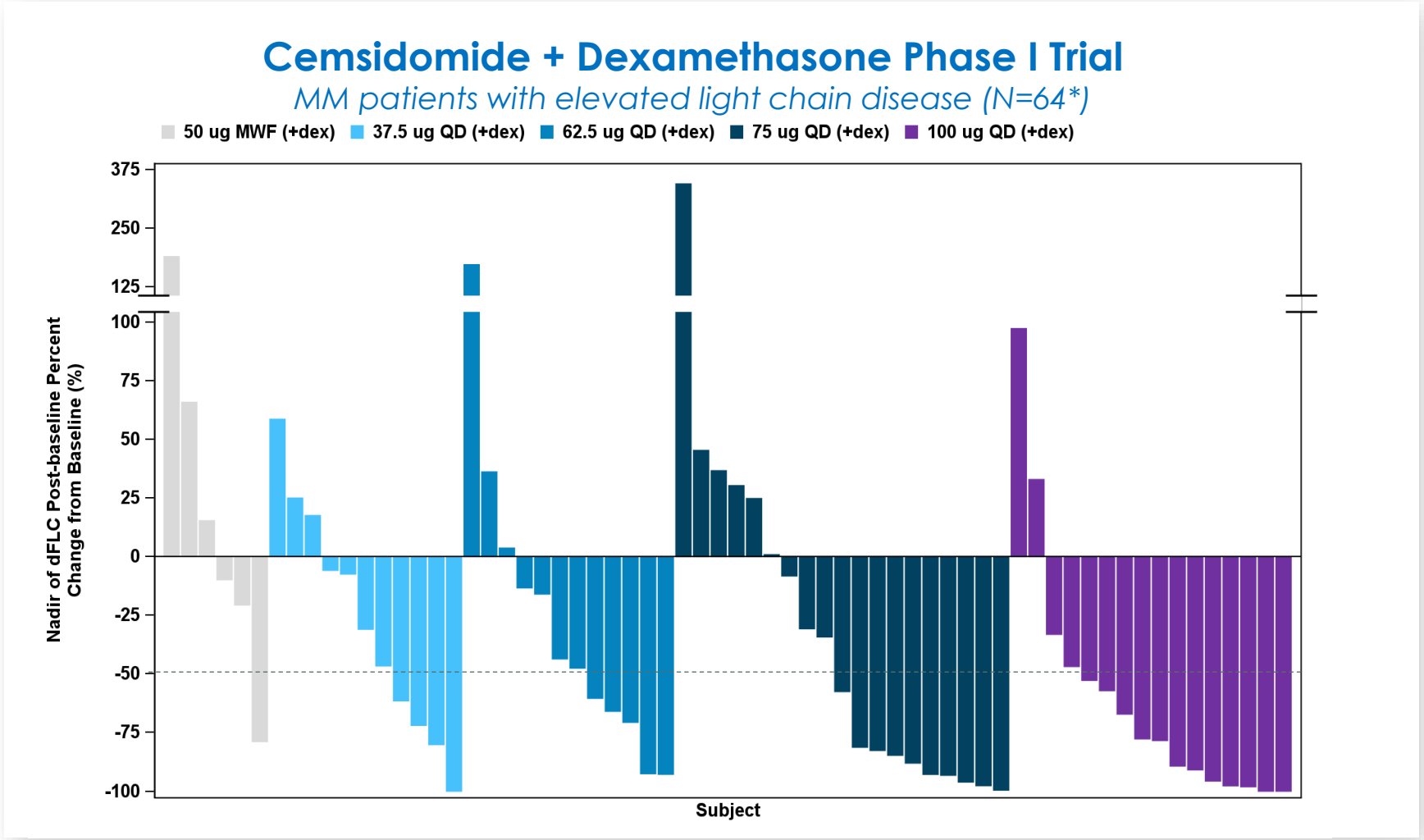
Risk of neutropenia does not increase over time; limited G-CSF use highlights minimal impact of neutropenia on patient experience

- ✔ Only **45% (33/73)** of patients received G-CSF across all doses
- ✔ **Few neutropenic events** occurred in later cycles coupled with low rates of G-CSF observed

[1]Dose Reductions: 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; Another patient at 100 µg had grade 3 neutropenia, both AEs possibly related to cemsidomide resulting in dose reduction; a patient in the 100 µg cohort had a dose reductions after an AE of arthralgia, deemed possibly related to cemsidomide; a patient in the 100 µg cohort had two dose reductions after two events of pseudomonal bacteremia, deemed unrelated to cemsidomide. [2] 3 patients discontinued due to a grade 5 AE of septic shock, grade 5 AE of T cell lymphoma, grade 5 AE of partial seizures, all deemed unrelated to cemsidomide
Treatment emergent adverse events (TEAEs); Granulocyte colony-stimulating factor (G-CSF)

Cemsidomide Phase 1 data cutoff as of 2/27/2026; Source: C4T data on file. Poster presentation at EHA 2026 (https://ir.c4therapeutics.com/static-files/0081f021-bc0d-4e7f-bdb9-9a01e95ed6eb)

Cemsidomide + Dexamethasone Demonstrated Deep and Consistent Reductions in sFLC Levels, Especially at the Highest Two Dose Levels



*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.
Serum free light chains (sFLC); Difference in free light chains (dFLC)

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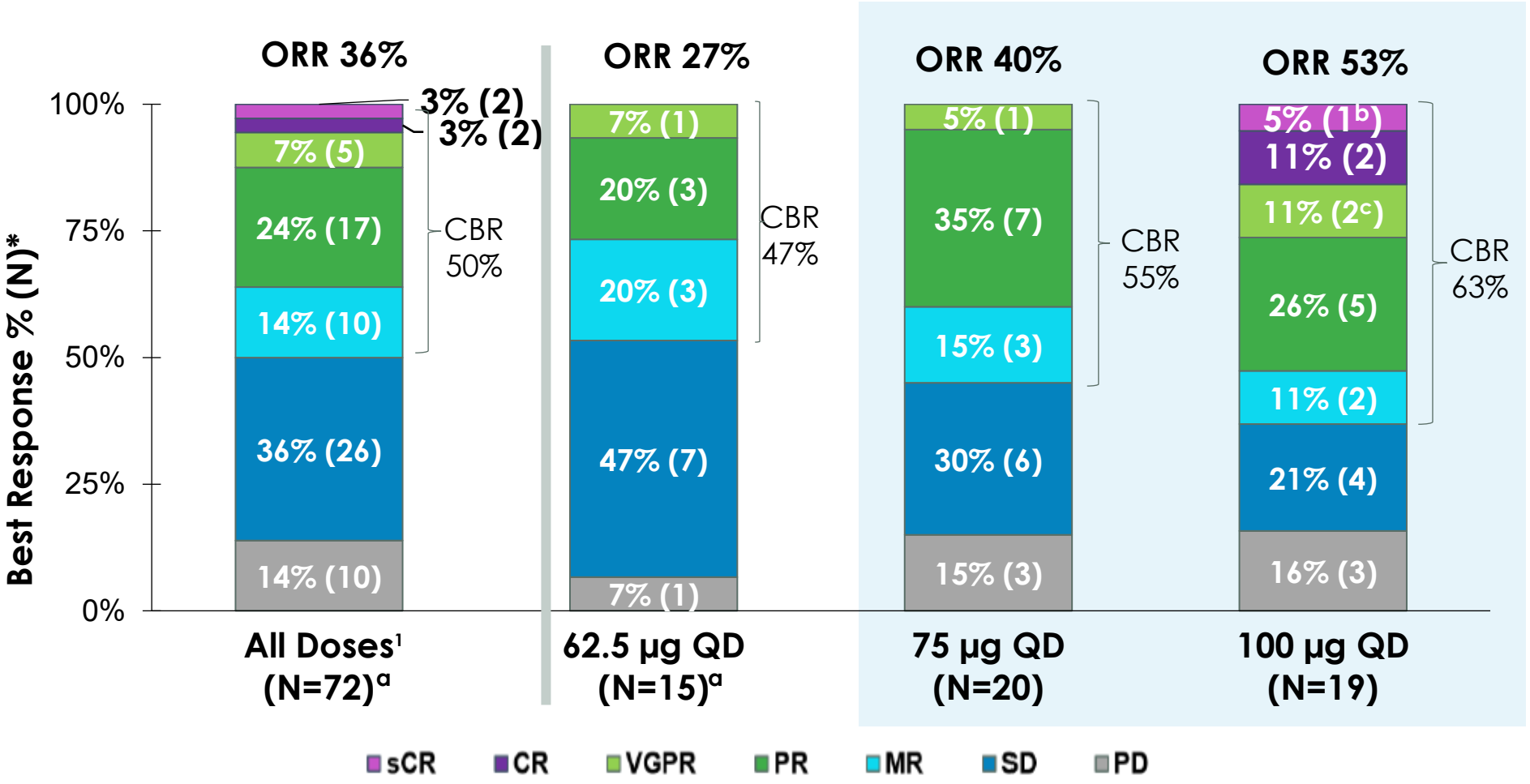
Cemsidomide Phase 1 data cutoff as of 2/27/2026; Source: C4T data on file. Poster presentation at EHA 2026 (https://ir.c4therapeutics.com/static-files/0081f021-bc0d-4e7f-bdb9-9a01e95ed6eb)

Cemsidomide + Dexamethasone Demonstrated Deep and Durable Responses Across the Highest Two Dose Levels



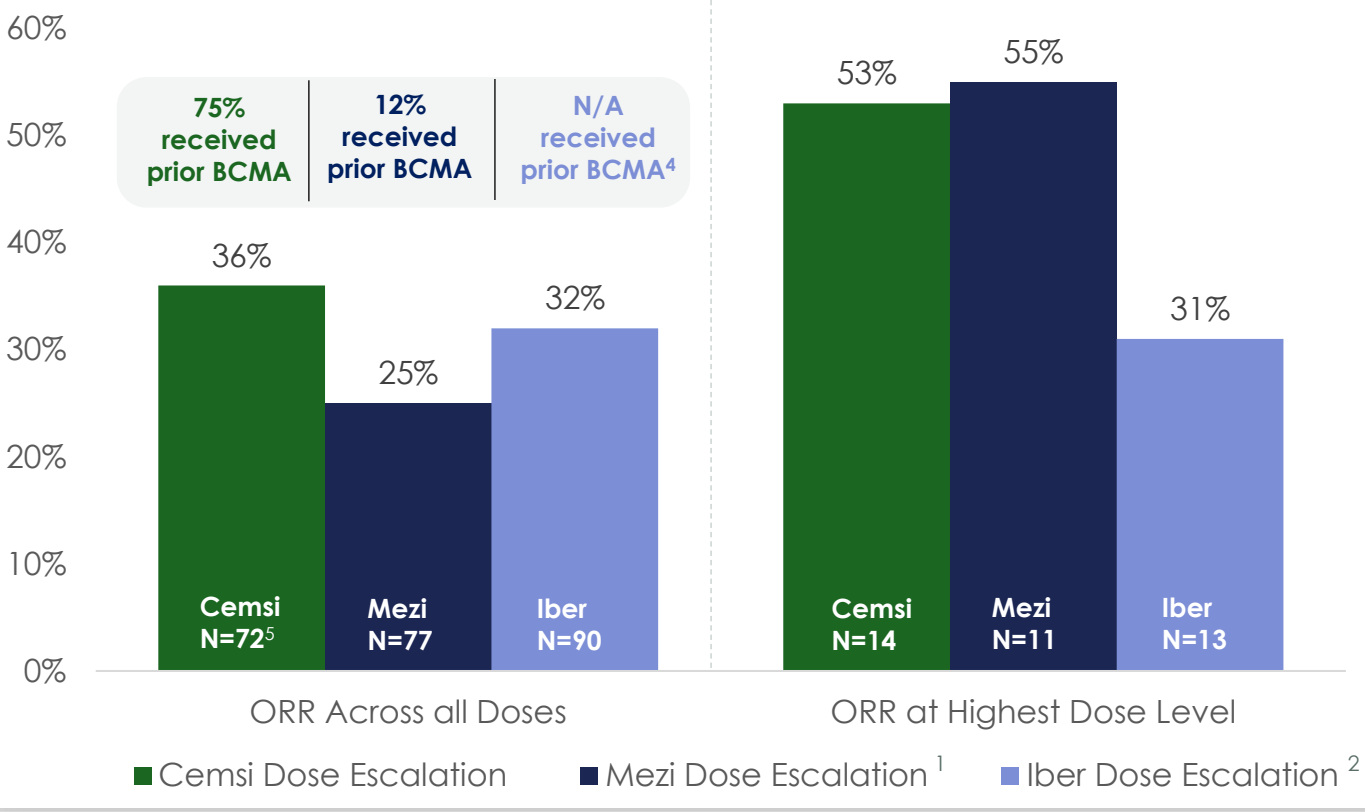
- At 100 µg: **Two patients** who achieved a sCR and CR also **achieved MRD negativity**
- **mPFS across all doses:** 3.9 months (95% CI, 3.2 – 5.6)
- **mDOR across all doses:** 7.9 months (95% CI, 3.0 - NE)

*Investigator assessed response; [1]In the Phase 1 cemsidomide + dexamethasone trial evaluated doses of 50 µg MWF, 37.5 µg MWF, 62.5 µg QD, 75 µg QD, 100µg QD; [a]1 patient in the 62.5 µg cohort did not have a post-baseline assessment; [#]2 patients in the 100 µg cohort had an unconfirmed PR in the October 2025 dataset ; [b] After the 2/27/26 data cutoff one patient went from VGPR to sCR; [c] After the 2/27/26 data cutoff one patient went from PR to VPGR; *Investigator accessed response rate
Clinical benefit rate (CBR); Dexamethasone (dex); Minimal response (MR); Minimal residual disease (MRD); 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); Confidence Interval (CI)

Cemsidomide Phase 1 data cutoff as of 2/27/2026; Source: C4T data on file. Poster presentation at EHA 2026 (https://ir.c4therapeutics.com/static-files/0081f021-bc0d-4e7f-bdb9-9a01e95ed6eb)

Cemsidomide + Dexamethasone Demonstrated Compelling Anti-myeloma Activity and mDOR vs. Other Next-gen IKZF1/3 Degraders in a More Heavily Pre-treated Population

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*	**7.9 (3.0 - 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 Hematology); [3] As of the February 26, 2026 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; 5. 1 patient in the 62.5 ug Cemsidomide Phase 1 dose escalation trial did not have post baseline assessment
Cemsidomide (Cemsi); Mezigdomide (Mezi); Iberdomide (Iber); Overall response rates (ORR); Not estimable (NE)

Cemsidomide Phase 1 data cutoff as of 2/27/2026; Source: C4T data on file. Poster presentation at EHA 2026 (https://ir.c4therapeutics.com/static-files/0081f021-bc0d-4e7f-bdb9-9a01e95ed6eb)

Cemsidomide Has the Potential to Be a Foundational Treatment Across Multiple Lines of Multiple Myeloma

3 strategic paths to capture multi-billion dollar opportunities

Late-line Opportunity
Combination with dexamethasone

RATIONALE

- Only next-generation IKZF1/3 degrader with a label-enabling development strategy for the 4L+
- Unmet need for an all-oral treatment regimen that is both well-tolerated and efficacious for patients who have exhausted all options
- Near-term value

STATUS

✓ **Enrolling Phase 2 MOMENTUM Trial**
- Cemsidomide + dexamethasone

- Data from the Phase 1 trial of cemsidomide + dexamethasone demonstrated a potential best-in-class profile[5]

Novel Combination
Combination with BCMAxCD3 Bispecific

RATIONALE

- For use in earlier lines
- Goal is to establish cemsidomide as an IKZF1/3 degrader of choice for novel combinations
- Complementary MOA via T-cell activation with potential to drive potent anti-myeloma effect

STATUS

✓ **Enrolling Phase 1b Trial**
- Cemsidomide + dexamethasone + elranatamab[3]

- Data from MagnetisMM-30 trial[1] demonstrates proof-of-concept for combination with opportunity to improve depth of response

IMiD Replacement Across Lines
Combination with a PI or CD38 antibody

RATIONALE

- Opportunity to improve upon first-generation IKZF1/3 degraders
- Establish dose of cemsidomide for potential standard of care combination approaches

STATUS

○ **Initiation of Phase 1b Trial w/ Two Arms Expected in 1H 2027**
- Cemsidomide + dexamethasone + PI
- Cemsidomide + dexamethasone + CD38 antibody

- Upcoming data from the EXCALIBER RRMM trial[2] and SUCCESSOR-1 trial[4]

GOAL: Develop a potential best-in-class IKZF1/3 degrader to become partner of choice for MM treatment

[1]Clinical trial evaluating elranatamab in combination with iberdomide in RRMM; [2].EXCALIBER RRMM trial is a Phase 3 trial comparing iberdomide, daratumumab and dexamethasone versus daratumumab, bortezomib, and dexamethasone [3]. Pfizer supplying elranatamab (ELREXFIO®), a B-cell maturation antigen CD3 targeted bispecific antibody, to C4T for the Phase 1b trial. [4]. SUCCESSOR-1 is a Phase 3 trial evaluating mezigdomide, bortezomib, dexamethasone versus pomalyst, bortezomib, dexamethasone IMiDs® are registered trademarks of BMS; [5].Cemsidomide Phase 1 data cutoff as of 2/27/2026; Source: C4T data on file. Poster presentation at EHA 2026 (https://ir.c4therapeutics.com/static-files/0081f021-bc0d-4e7f-bdb9-9a01e95ed6eb)

Cemsidomide is Positioned for Success

Continued Relevance

Despite recent approvals for immune-based therapies in the MM landscape, **IKZF1/3 are central drivers of MM development and progression, thus IKZF1/3 degraders** will **remain relevant across multiple lines and in combinations**

Generational Improvement

Next-generation IKZF1/3 degraders are designed to **overcome** the **limitations** of **first-generation IKZF1/3 degraders** (IMiDs)

Potential best-in-class profile

Cemsidomide has a **potential best-in-class profile** among other IKZF1/3 degraders, including CELMoDs, with a **clinically de-risked MOA**

Q&A

Nisha Joseph, M.D.
Associate Professor in the Department of Hematology and Medical Oncology at Emory University School of Medicine

Len Reyno, M.D.
Chief Medical Officer

Andrew Hirsch
President & CEO