MOMENTUM: A Phase 2, Open-Label, Single-Arm, Multicenter Study to Evaluate the Efficacy of Cemsidomide + Dexamethasone in Subjects With Relapsed/Refractory Multiple Myeloma

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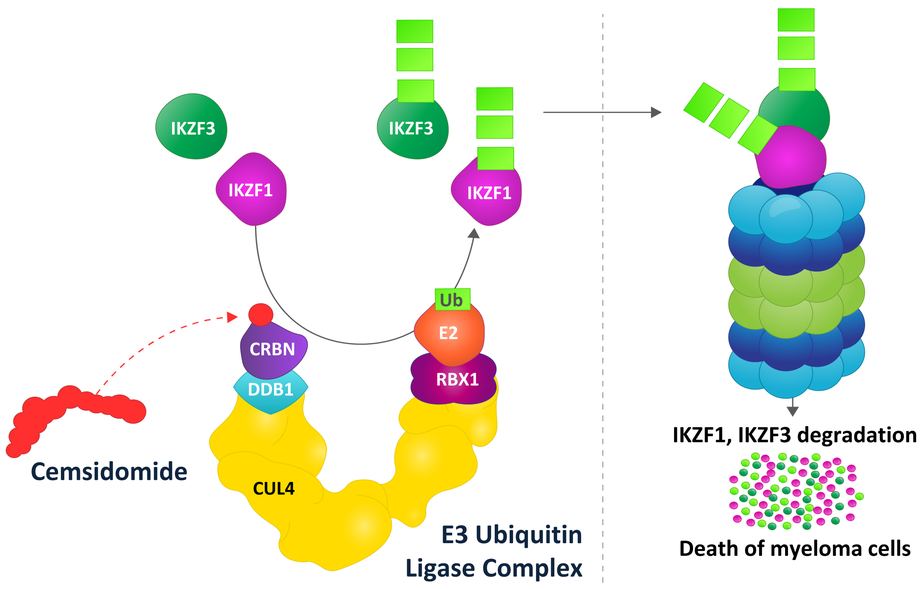
BACKGROUND

- Cemsidomide is a novel, highly potent, cereblon-based, IKZF1/3 MonoDAC® degrader, having a similar mechanism of action as BMS's IMiD® or CELMoD® degraders for MM
- Cemsidomide displays catalytic activity enabling rapid and deep target degradation with high binding affinity to overcome resistance due to low cereblon levels
- Cemsidomide binds to cereblon to facilitate the recruitment and ubiquitination of IKZF1/3 leading to the proteasomal degradation of both proteins (Figure 1)
- IKZF1/3 degradation induces multiple myeloma cell death, activation of fully differentiated T-cells which prevents T-cell exhaustion and promotes secretion of key immune stimulating cytokines[1]
- In a Phase 1 study, cemsidomide, given orally QD over 14 days with a 14 day "off" period (14/14) in combination with weekly dexamethasone in a heavily pre-treated patient population (7 median prior lines), was well tolerated and demonstrated durable anti-myeloma activity at increasing dose levels
  - A 53% ORR was observed as the highest dose of 100 µg QD 14/14, with a 36% ORR observed across all dose levels[1,2]

Figure 1: Mechanism of Action of Cemsidomide[3]

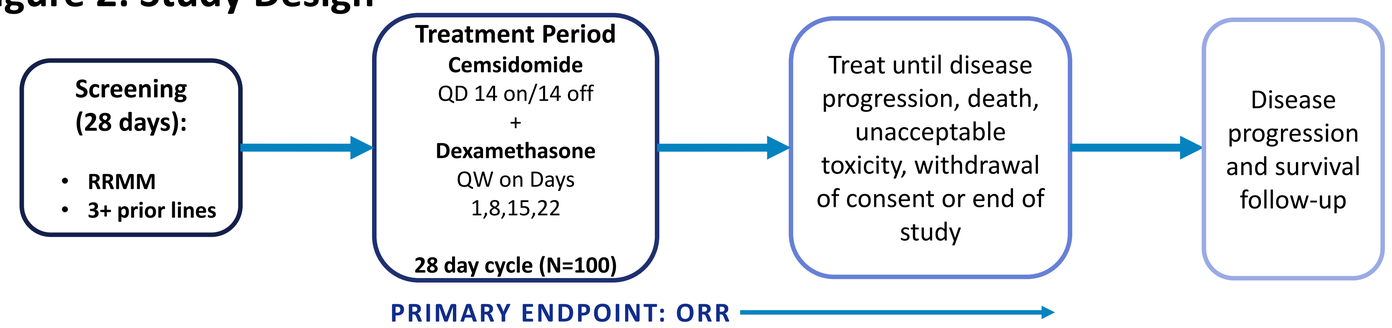


Objective

- To evaluate the antimyeloma activity and further characterize the safety, tolerability, PK, and PD of cemsidomide in combination with dexamethasone in subjects with relapsed/refractory multiple myeloma

METHODS/STUDY DESIGN

Figure 2: Study Design



KEY ELIGIBILITY CRITERIA

KEY INCLUSION CRITERIA

- ≥18 years of age at time of informed consent
- Subjects must have a documented diagnosis of MM and measurable disease
- Subjects must have received ≥3 prior anti-myeloma regimens including ≥2 consecutive cycles of:
  - Immunomodulatory drug (i.e., IKZF1/3 degrader)
  - Proteasome inhibitor
  - Anti-CD38 antibody
  - TCE or CAR-T therapy (unless not indicated and/or patient refusal)
- Refractory to or had documented disease progression within 60 days from the last dose of their prior MM treatment

KEY EXCLUSION CRITERIA

- Presence of myeloma in the CNS
- Treatment with mezigdomide or iberdomide during the subjects most recent line of therapy
- Nonsecretory or oligosecretory MM

STUDY ENDPOINTS

PRIMARY ENDPOINTS

- ORR per IMWG response criteria by IRC

SECONDARY ENDPOINTS

- DoR (IRC assessed)
- CR rate (include MRD status via local testing; IRC assessed)
- Time to response (IRC assessed)
- PFS (IRC assessed)
- OS
- Safety and tolerability of cemsidomide in combination with dexamethasone
- Plasma concentrations of cemsidomide

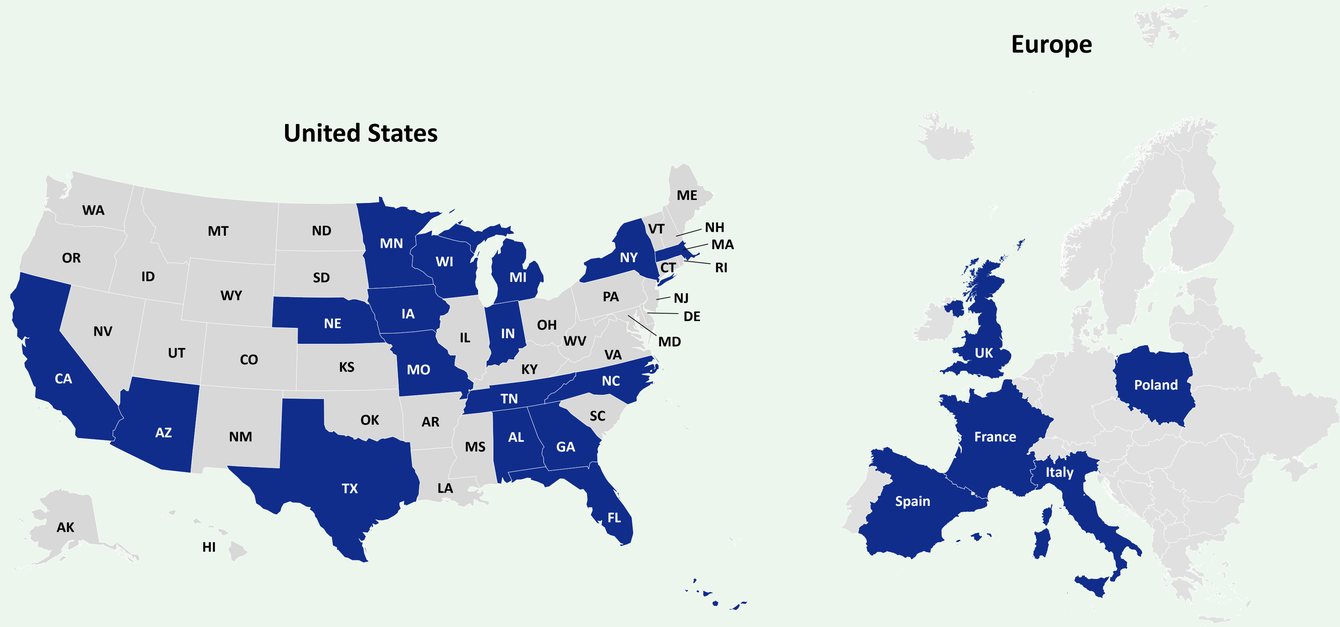
EXPLORATORY ENDPOINTS

- ORR (investigator assessed)
- DOR (investigator assessed)
- CR rate (including MRD status via local testing; investigator assessed)
- Time to response (investigator assessed)
- PFS (investigator assessed)
- Degradation of IKZF1/3 in PBMCs
- Change in EORTC QLQ-MY20 Disease Symptoms
- Change in EORTC QLQ-MY20 Treatment Side Effects
- Change in EORTC QLQ-C30 score

STUDY STATUS/ENROLLMENT[4]

The study enrolled its first patient in February 2026 and will be recruiting ~N=100 subjects from 60 sites* in the US and Europe

- Trial registration: NCT07284758[4]
- Contact information: *clinicaltrials@C4therapeutics.com*



*Blue-colored US states and EU countries indicate selected clinical trial sites.

Abbreviations

BMS, Bristol Myers Squibb; **CNS**, Central Nervous System; **CR**, Complete Response; **CRBN**, Cereblon; **DoR**, Duration of Response; **EROTC**, European Organisation for Research and Treatment of Cancer; **IKZF1/3**, Ikaros Family Zinc Finger 1 and 3; **IMWG**, International Myeloma Working Group; **IRC**, Independent Review Committee; **MM**, Multiple Myeloma; **MRD**, Minimal Residual Disease; **ORR**, Overall Response Rate; **OS**, Overall Survival; **PBMCs**, Peripheral Blood Mononuclear Cells; **PD**, Pharmacodynamics; **PFS**, Progression-Free Survival; **PK**, Pharmacokinetics; **QD**, Once daily; **QLQ**, Quality of Life Questionnaire; **QW**, Once weekly; **RRMM**, Relapsed/Refractory Multiple Myeloma; **TCE**, T-Cell Engager; **US**, United States

Disclosures

BD: consulting or advisory role: BMS, Janssen, Arcellx, Sanofi, GSK, Menarini, Genentech, Karyopharm, Pfizer, Kite, AstraZeneca; research funding: BMS, Janssen, Arcellx, Carsgen, Sanofi, Caribou, Gracell, Menarini, C4 Therapeutics; honoraria: Karyopharm, BMS, Janssen. **KR**: consulting or advisory role: Janssen, Adaptive Biotech, Amgen, Recordati, Takeda, AbbVie, Oncopeptides, Celgene – Bristol Myers Squibb, Pfizer, Menarini Stemline, Thermofisher (Binding site), GSK; research funding: Sanofi, Pfizer, GSK, Celgene – Bristol Myers Squibb; honoraria: Janssen, Adaptive Biotech, Amgen, Takeda, Abbvie, Oncopeptides, Celgene – Bristol Myers Squibb, Pfizer, Menarini stemline, Recordati, GSS; travel, accommodations, expenses: BMS, Amgen, Takeda, Recordati. **AA**: employed by and equity holder in C4 Therapeutics. **LL**: employed by and equity holder in C4 Therapeutics. **UC**: employed by and equity holder in C4 Therapeutics. **RL**: employed by and equity holder in C4 Therapeutics. **EH**: employed by and equity holder in C4 Therapeutics. **LR**: employed by and equity holder in C4 Therapeutics. **MK**: consulting or advisory role: AbbVie, Adaptive, BMS/Celgene, Johnson and Johnson, GSK, Karyopharm, Kite, Pfizer, Poolbeg, Regeneron, Roche, Sanofi, Takeda; research funding: BMS/Celgene; honoraria: AbbVie, Adaptive, BMS/Celgene, Johnson and Johnson, GSK, Sanofi, Takeda; travel, accommodations, expenses: BMS/Celgene, Johnson and Johnson, Takeda.

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References

1. Dhakal B, et al. *Clinical Lymphoma, Myeloma & Leukemia*, Vol. 25, No. S2, S35, 2025
2. C4 Therapeutics data on file.
3. Henderson J, et al. *Cancer Res* (2022) 82 (12_Supplement): ND13
4. NCT07284758. www.clinicaltrials.gov. Accessed April 30, 2026.

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