UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 9, 2024 (December 8, 2024)

C4 THERAPEUTICS, INC.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-39567**	**47-5617627**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
490 Arsenal Way, Suite 120 Watertown, MA		**02472**
(Address of Principal Executive Offices)		**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (617) 231-0700

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	CCCC	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On December 8, 2024, C4 Therapeutics, Inc. (the "Company") presented a clinical update at the American Society of Hematology Annual Meeting ("ASH Annual Meeting"). A copy of the slides, which has been published to the "Events & Presentations" section of the Company's website, is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

On December 8, 2024, the Company also issued a Press Release reporting clinical data from the ongoing Phase 1/2 trial of cemsidomide in multiple myeloma and non-Hodgkin's lymphoma as presented in the ASH Annual Meeting. A copy of the Press Release is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

On December 9, 2024, the Company posted a corporate presentation that includes data from the ongoing Phase 1/2 trial of cemsidomide on its website at *https://ir.c4therapeutics.com/events-presentations*. A copy of the corporate presentation is filed as Exhibit 99.3 to this Current Report on Form 8-K and is incorporated herein by reference

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits. The exhibits shall be deemed to be filed or furnished, depending on the relevant item requiring such exhibit, in accordance with the provisions of Item 601 of Regulation S-K (17 CFR 229.601) and Instruction B.2 to this form.

Exhibit Number	Description
99.1	Slides from C4 Therapeutics, Inc.'s ASH Annual Meeting Presentation, dated December 8, 2024
99.2	Press release issued December 8, 2024
99.3	Corporate presentation of the Company dated December 2024
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

C4 Therapeutics, Inc.

Date: December 9, 2024

By: /s/ Jolie M. Siegel

Jolie M. Siegel

Chief Legal Officer

C4 Therapeutics

Updated Data in Multiple Myeloma and First Data in Non-Hodgkin's Lymphoma from the Ongoing Cemsidomide Phase 1/2 Trial

American Hematology Annual Meeting (ASH)

December 8, 2024

Forward-looking Statements and Intellectual Property

FORWARD-LOOKING STATEMENTS

The following presentation contains forward-looking statements. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "look forward to," "may," "plan," "potential," "predict," "project," "should," "will," "would" and similar expressions. These forward-looking statements include, but are not limited to, statements regarding the therapeutic potential of C4 Therapeutics, Inc.'s technology and products. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. Among the factors that could cause actual results to differ materially from those described or projected herein include uncertainties associated generally with research and development, clinical trials and related regulatory reviews and approvals, as well as the fact that the product candidates that we are developing or may develop may not demonstrate success in clinical trials. Prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. The forward-looking statements included in this presentation are subject to a variety of risks and uncertainties, including those set forth in our most recent and future filings with the Securities and Exchange Commission. Our actual results could vary significantly from those anticipated in this presentation, and our financial condition and results of operations could be materially adversely affected. C4 Therapeutics, Inc. undertakes no obligation to update or revise the information contained in this presentation, whether as a result of new information, future events or circumstances or otherwise.

INTELLECTUAL PROPERTY

C4 Therapeutics, Inc. owns various registered and unregistered trademarks and service marks in the U.S. and internationally, including, without limitation, C4 THERAPEUTICS, our housemark logo, the name of our TORPEDO platform, and the names of our BIDAC and MONODAC degrader products. All trademarks, service marks, or trade names referred to in this presentation that we do not own are the property of their respective owners. Solely for convenience, the trademarks, service marks, and trade names in this presentation are referred to without the symbols ®, SM and ™, but those references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights to.

Today's Agenda

Introductions	Courtney Solberg, Senior Manager of IR
Opening Remarks	Andrew Hirsch, President and CEO
Cemsidomide Phase 1 MM & NHL 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

C4 Therapeutics

Opening Remarks

Andrew Hirsch
President and Chief Executive Officer

C4 Therapeutics

C4T Has Delivered a Steady Flow of Clinical Updates and Innovative Collaborations Over the Past 12 Months…

Significant Progress Across Clinical Programs

Cemsidomide

- ✓ Compelling activity in both multiple myeloma and non-Hodgkin's lymphoma
- ✓ Modest and manageable neutropenia
- ✓ Emerging data demonstrate positive exposure-response relationship
- ✓ Evidence of immunomodulatory effects, consistent with the class

CFT1946

- ✓ Monotherapy anti-tumor activity, including tumor reductions across various V600 mutation types
- ✓ Dose-dependent bioavailability
- ✓ Well-tolerated; no Grade ≥ 3 cutaneous adverse events commonly seen with BRAF inhibitors
- ✓ Preclinical data demonstrate ability to cross blood-brain barrier

CFT8919

- ✓ Clinical trial initiated in Greater China in partnership with Betta Pharmaceuticals

Collaborations Have Further Validated TORPEDO Platform

Biogen

- ✓ Delivered two development candidates for non-oncology targets

MERCK

- ✓ Established partnership to discover and develop degrader antibody conjugates

Merck KGaA
Darmstadt, Germany

- ✓ Announced collaboration to discover targeted protein degraders against critical oncogenic proteins

…Which Set the Stage to Unlock Value

VALUE DRIVERS	KEY CATALYSTS
Cemsidomide IKZF1/3	Further development in multiple myeloma and non-Hodgkin's lymphoma positions cemsidomide to potentially be best-in-class IKZF1/3 degrader
CFT1946 BRAF V600 Mutant	Phase 1 data updates to further validate initial anti-tumor activity and safety profile in melanoma and colorectal cancer
CFT8919 EGFR L858R	Phase 1 data from Greater China clinical trial to inform US and rest-of-world development plans
TORPEDO Platform	Develop orally bioavailable degraders in oncology and non-oncology targets through internal research and collaborations

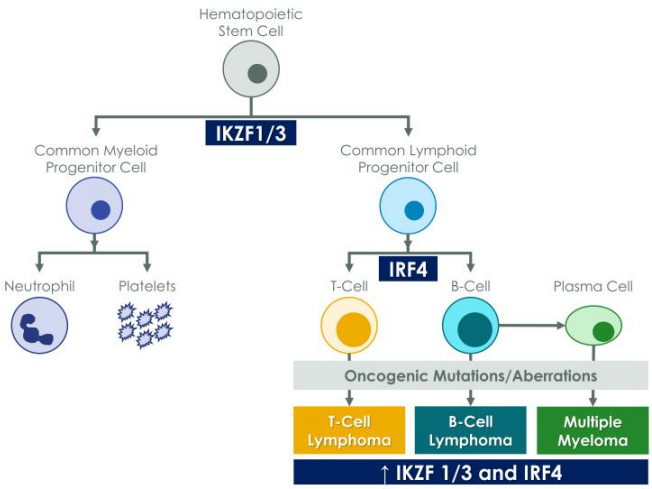
C4T is positioned to become a **fully integrated biotechnology** company focused on **orally bioavailable degraders**

Cemsidomide First-in-Human Clinical Program

Relapsed Refractory Multiple Myeloma and Non-Hodgkin's Lymphoma

C4 Therapeutics

IKZF1/3 Are Key Promoters of Myeloma and Lymphoma Cell Survival and Will Remain Important Therapeutic Targets in MM and NHL



Key Roles of IKZF1/3

Physiological Functions:

- **IKZF1/3** are key transcriptional regulators of hematopoietic stem cell differentiation
- **IKZF1/3** directly regulate the activity of **IRF4**, another transcription factor that regulates downstream immune cell differentiation

Oncogenic Functions:

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

IKZF1/3 Degradation Leads to:

- Downregulation of **IRF4**, promoting the death of myeloma and lymphoma cells
- On-target neutropenia

Multiple myeloma (MM); non-Hodgkin's lymphoma (NHL)

C4 Therapeutics

Cemsidomide First-in-Human Phase 1 Trial Continues to Progress

Data to date reinforce potential of drug to become best-in-class IKZF1/3 degrader used as a backbone therapy of choice

PHASE 1 DOSE ESCALATION TRIAL

2022	2023	ASH 2024	ASH 2024
R/R MM Monotherapy **Dosing:** QD 21 days on/ 7 days off N=5 **Status:** Complete	**R/R MM** Monotherapy **Dosing:** MWF & QD 14 days on/ 14 days off N=22 **Status:** Complete	**R/R MM** Dex Combo **Dosing:** MWF & QD 14 days on/ 14 days off N=~40 **Status:** Enrolling	**R/R NHL** Monotherapy **Dosing:** MWF & QD 14 days on/ 14 days off N=~25 **Status:** Enrolling
	• 14 days on/14 days off established as an effective dosing schedule • Demonstrated monotherapy anti-myeloma and immunomodulatory effects supporting combination with other anti-myeloma agents	• Well-tolerated with manageable neutropenia and low rates of infections and febrile neutropenia • Wide therapeutic index with anti-myeloma activity across a broad range of doses	• Well-tolerated with additional dose finding ongoing • Compelling anti-lymphoma activity across a broad range of doses in PTCL

Monday, Wednesday, Friday dosing (MWF); once daily (QD); peripheral T-cell lymphoma (PTCL); relapsed refractory multiple myeloma (R/R MM); relapsed refractory non-Hodgkin's lymphoma (R/R NHL)

Multiple Myeloma

Cemsidomide + Dexamethasone

C4 Therapeutics

With a Potentially Best-in-Class Profile, Cemsidomide Is Positioned to Be an IKZF1/3 Degrader of Choice Across Various Combinations

EVOLVING MULTIPLE MYELOMA TREATMENT LANDSCAPE

U.S. Addressable Patients (2024)	~33,000[1]	~29,000	~25,000	~20,000	≤12,000
Treatment Line	1L	2L	3L	4L	5L+

CEMSIDOMIDE OPPORTUNITY

- IKZF1/3 degraders are currently used across lines of therapy, from post-transplant maintenance to 5L+ doublets, and will remain backbone therapies in various combination approaches
- **Cemsidomide has the potential to become the IKZF1/3 degrader of choice** in numerous regimens across lines of therapy given its potent anti-myeloma activity, differentiated safety profile, and immunomodulatory effects

[1] Approximately 30% of multiple myeloma patients undergo a hematopoietic stem cell transplant and receive post-transplant maintenance therapy.
[2] Other MOAs approved in MM include anti-SLAMF7 mAbs and XPO1 inhibitors and potential future treatment options include FcRH5 bispecific T-cell engagers, BCL-2 inhibitors, and others.
Sources: NCI SEER, NCCN guidelines, consulting engagements with Health Advances and Clearview.
B-cell maturation antigen (BCMA); G protein-coupled receptor, class C, group 5, member D (GPRC5D); monoclonal antibodies (mAbs); mechanism of action (MOA)

Cemsidomide + Dexamethasone Dose Escalation Trial in MM Continues to Progress; Have Not Exceeded the Maximum Tolerated Dose

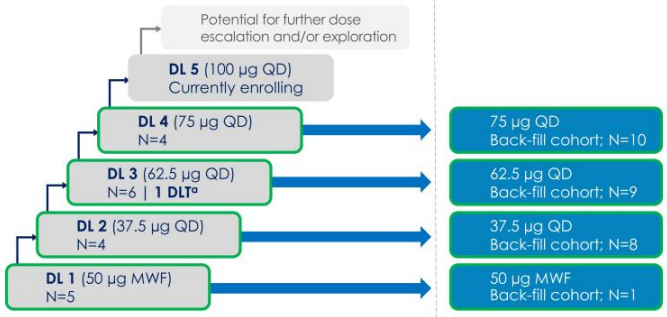
KEY INCLUSION CRITERIA

- 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; 2 patients at 100 µg are excluded as they had not completed Cycle 1 as of the data cut off date.
[a]DLT at 62.5 µg QD was due to Grade 4 neutropenia lasting >7 days.
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)

C4 Therapeutics

Data cutoff: 10/11/24

Heavily Pre-Treated Patient Population With Majority Having Received Prior CAR-T, BCMA, or T-Cell Engager Therapy

Baseline Characteristics

Characteristics	Safety Population (N=47)
Age, median (range)	67 (39-82 years)
Male, n (%)	25 (53)
Years since initial diagnosis, median (range)	7 (2-18)
ECOG performance status, n (%) 0 1 2	 10 (21) 34 (72) 3 (7)
Black or African American, n (%) **White, n (%)** **Other, n (%)**	9 (19) 33 (70) 5 (11)
Revised ISS at screening, n (%) Stage 1 Stage 2 Stage 3 Missing	 21 (45) 15 (32) 5 (11) 6 (13)
Presence of EMD, n (%)	14 (30)

Prior Therapies

Characteristics	Safety Population (N=47)
Prior therapies, median (range)	6 (3-22)
Prior lenalidomide, n (%)	47 (100)
Prior pomalidomide, n (%)	46 (98)
Prior anti-CD38 mAb, n (%)	47 (100)
Prior CAR-T therapy, n (%)	19 (40)
Prior TCE therapy, n (%)	21 (45)
Prior CAR-T or TCE therapy, n (%)	31 (66)
Prior CAR-T and TCE therapy, n (%)	9 (19)
Prior BCMA therapy, n (%)	33 (70)
Triple-class exposed*, n (%)	47 (100)
Penta-class exposed†, n (%)	40 (85)

*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); Eastern Cooperative Oncology Group (ECOG); extramedullary disease (EMD); International Staging System (ISS); monoclonal antibody (mAb); T-cell engager (TCE)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Was Well-Tolerated With Manageable Neutropenia and No Treatment Emergent Adverse Events Lead to Dose Reductions

- **1 DLT** (Grade 4 neutropenia lasting >7 days at the 62.5 µg dose level)
- **No TEAEs lead to dose reductions**
- **TEAEs leading to dose interruption: 32%** (15/47)
- **TEAEs leading to discontinuation[1]: 4%** (2/47)

Common (>20% All Grades) TEAEs and Events of Interest, n (%)	All Grades (N=47)	Grade 3 (N=47)	Grade 4 (N= 47)	Grade 5 (N=47)
Neutropenia	22 (47)	6 (13)	12 (26)	0
Infections	18 (38)	7 (15)	0	1(2)
Pneumonia	5 (11)	5 (11)	0	0
Upper respiratory tract infection	7 (15)	1 (2)	0	0
Septic shock	1 (2)	0	0	1(2)
Anemia	17 (36)	10 (21)	0	0
Fatigue	14 (30)	0	0	0
Thrombocytopenia	10 (21)	3 (6)	2 (4)	0
Diarrhea	10 (21)	0	0	0
Lymphopenia	9 (19)	6 (13)	0	0
Febrile neutropenia	3 (6)	3 (6)	0	0

2 patients experienced Grade 5 AEs (septic shock and subdural hematoma), both deemed unrelated to cemsidomide

[1]Primary reason of discontinuation of patient at 37.5 µg was due to withdrawal of consent; primary reason of discontinuation of patient at 75 µg was due to death unrelated to cemsidomide.
Adverse events (AEs); dose limiting toxicity (DLT); treatment emergent adverse events (TEAEs)

C4 Therapeutics

Data cutoff: 10/11/24

Grade ≥3 Neutropenia, Febrile Neutropenia and Infections Were Infrequent and Rates Did Not Increase With Higher Cemsidomide Doses

Common Hematologic and Infection Grade ≥3 TEAEs, n (%)	50 µg MWF (N=6)	37.5 µg QD (N=12)	62.5 µg QD (N=15)	75 µg QD (N=14)	Total (N=47)
Neutropenia	2 (33)	6 (50)	6 (40)	4 (29)	18 (38)
Anemia	1 (17)	3 (25)	3 (20)	3 (21)	10 (21)
Infections	0	4 (33)	1 (7)	3 (21)	8 (17)
Upper respiratory tract infection	0	0	0	1 (7)	1 (2)
Pneumonia	0	3 (25)	1 (7)	1 (7)	5 (11)
Septic shock	0	0	0	1 (7)	1 (2)
Thrombocytopenia	2 (33)	1 (8)	1 (7)	1 (7)	5 (11)
Lymphopenia	0	4 (33)	2 (13)	0	6 (13)
Febrile neutropenia	1 (17)	2 (17)	0	0	3 (6)

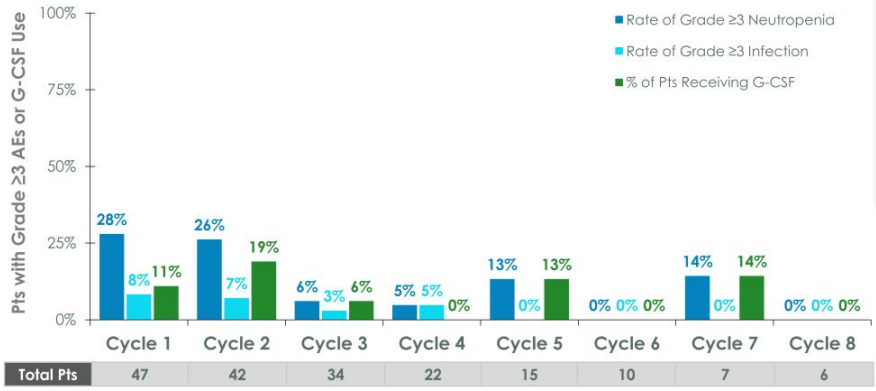
Once daily (QD); Monday Wednesday Friday (MWF); treatment emergent adverse events (TEAEs)

C4 Therapeutics

Data cutoff: 10/11/24

Compelling Cemsidomide Safety Profile With Low Rates of Neutropenia and Infections With Limited G-CSF Use

Rates of Neutropenia, Infections, and G-CSF Use by Cycle



- **Only 26% (12/47) of pts received G-CSF** across the study
- **Only one patient experienced Grade ≥3 neutropenia for the first time after completing cycle 2**

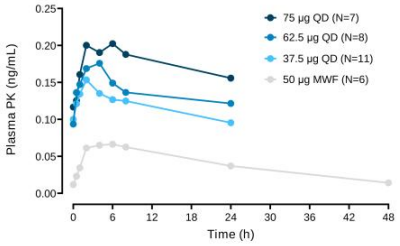
Notes: No cases of Grade ≥3 neutropenia were recorded after Cycle 7. One patient experienced a Grade ≥3 infection in a Cycle >8. G-CSF use was not permitted during Cycle 1 in escalation cohorts. One patient in the 50 µg MWF cohort came off study during Cycle 1 and received G-CSF after treatment was discontinued. No patients received G-CSF after Cycle 7.
The same patients that experienced neutropenia at Cycle 5 and Cycle 7, also received G-CSF.
Adverse events (AEs); granulocyte colony-stimulating factor (G-CSF); patients (Pts)

C4 Therapeutics

Data cutoff: 10/11/24

Across Doses, 40% (14/35) of Multiple Myeloma Patients With Elevated Light Chains Demonstrated at Least a 50% Decrease in dFLC

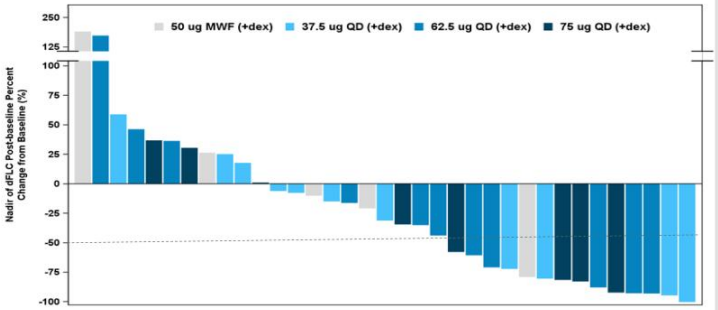
Dose Proportional Exposure



- Overall geometric mean half-life estimate is approximately 2 days

Best Change in dFLC from Baseline (Cemsidomide + Dex)

*Multiple Myeloma Patients w/ Elevated Light Chain Disease (N=35)**



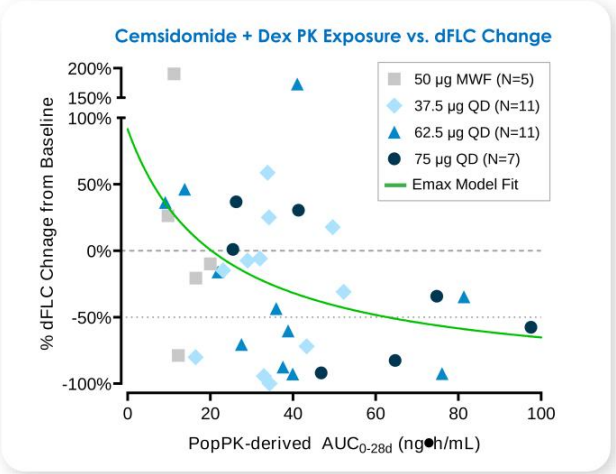
- **69% (24/35)** of patients with elevated light chain disease demonstrated a **decrease in dFLC**

*Only included treated patients 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.
Difference in involved and uninvolved free light chain (dFLC); once daily (QD); Monday Wednesday Friday (MWF); multiple myeloma (MM); pharmacokinetic (PK)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide 75 µg Dose Level or Greater Drives Sufficient Exposure Resulting in Meaningful Reductions in Light Chains



Exposure (AUC) Quartiles

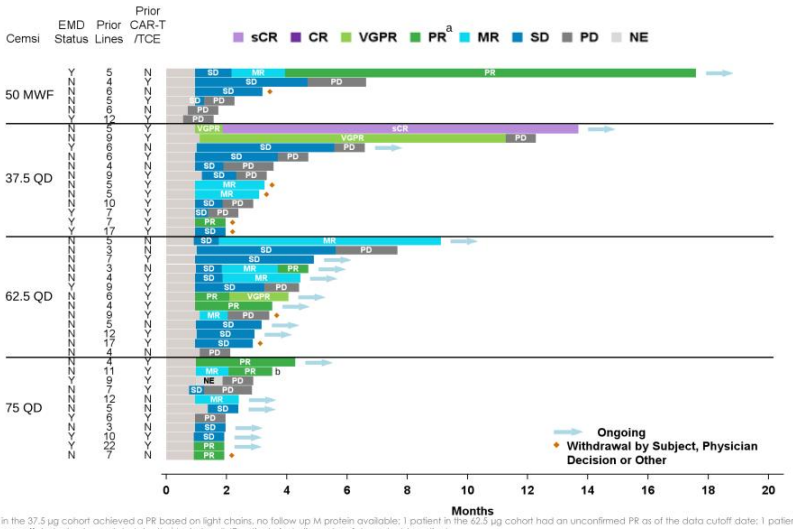
	<Q1 (N=9)	Q1-Q2 (N=8)	Q2-Q3 (N=8)	>Q3 (N=9)
Mean $AUC_{0\text{-}28d}$ (ng*h/mL)	14.6	28.8	37.9	**65.2**
Mean Change in dFLC from Baseline	+10%	-12%	-20%	**-53%**
Cemsidomide + Dex Dose	~17 µg QD	~35 µg QD	~45 µg QD	**~78 µg QD**

N=34 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.
Cemsidomide dose was back-calculated based on the population PK model.
Area under the curve (AUC); difference in involved and uninvolved free light chain (dFLC); maximum response (Emax); Monday Wednesday Friday (MWF); once daily (QD); population pharmacokinetics (popPK); pharmacokinetic (PK)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Demonstrated Anti-Myeloma Activity Across Dose Levels



As of the data cutoff:

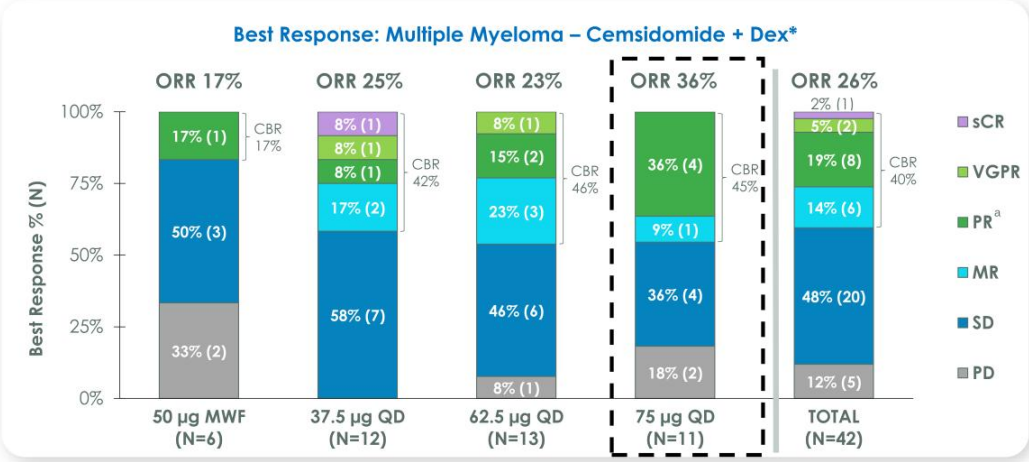
- **26% ORR** and **40% clinical benefit rate across all dose levels** evaluated
- At the two highest dose levels evaluated to date (62.5 µg and 75 µg), **62% of all patients remain on treatment**[1]

[a]1 patient in the 37.5 µg cohort achieved a PR based on light chains, no follow up M protein available; 1 patient in the 62.5 µg cohort had an unconfirmed PR as of the data cutoff date; 1 patient in the 75 µg cohort had an unconfirmed PR as of the data cutoff date. [b]Patient came off study due to unrelated death. [1] Includes all 47 patients, including only safety evaluable patients.
Complete response (CR); minimal response (MR); Monday Wednesday Friday (MWF); non-evaluable (NE); once daily (QD); partial response (PR); progressive disease (PD); stable disease (SD); stringent complete response (sCR); T-cell-engaging antibodies (TCE); very good partial response (VGPR); Clinical Benefit Rate (≥ MR) (CBR)

C4 Therapeutics

Data cutoff: 10/11/24

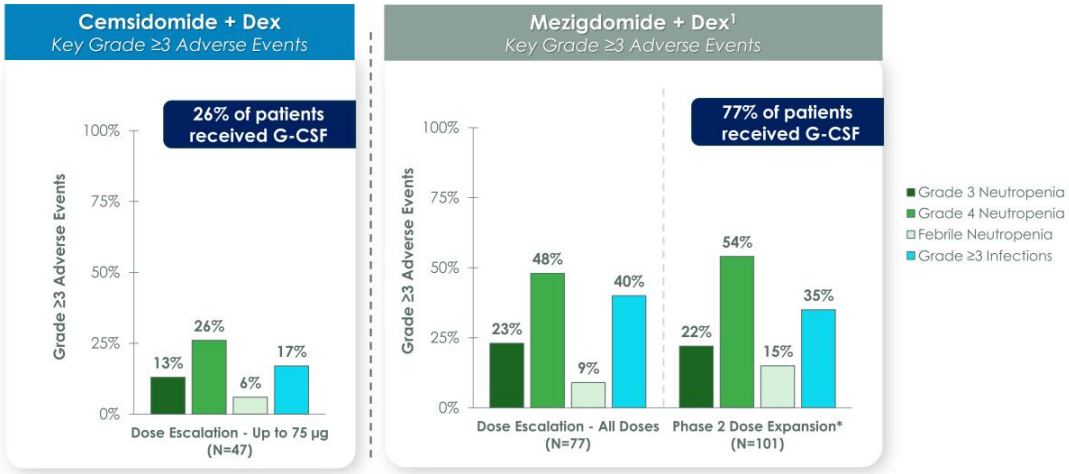
75 µg Cemsidomide Dose Level Resulted in Compelling Anti-Myeloma Activity With a 36% ORR and 45% CBR



*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; 1 patient in the 62.5 µg cohort had an unconfirmed PR as of the data cutoff date; 1 patient in the 75 µg cohort had an unconfirmed PR as of the data cutoff date.
Minimal response (MR); Monday Wednesday Friday (MWF); once daily (QD); partial response (PR); progressive disease (PD); stable disease (SD); stringent complete response (sCR); very good partial response (VGPR)
Overall Response Rate (≥ PR) (ORR); Clinical Benefit Rate (≥ MR) (CBR)

C4 Therapeutics
Data cutoff: 10/11/24

Cemsidomide's Differentiated Safety Profile Is Well Suited for Combination Studies, Potentially Resulting in Fewer Disruptive Adverse Events



Cross trial comparisons only to be used as benchmarks for relative comparison

[1]Richardson 2023 NEJM.
*Mezigdomide recommended Phase 2 dose expansion dose was 1.0 mg daily dosing (QD) 21 days on/7 days off.
Note: All cases of febrile neutropenia in the cemsidomide trial were Grade 3. In the mezigdomide dose escalation and expansion cohorts, febrile neutropenia splits between Grade 3/4 were 5%/4% and 13%/2% ,respectively.

C4 Therapeutics
Data cutoff: 10/11/24

Cemsidomide Has the Potential to Be a Backbone Therapy of Choice Where IKZF1/3 Degradation Is Warranted

Cemsidomide + dex demonstrated compelling anti-myeloma activity across a broad range of doses, highlighting a wide therapeutic range

- 36% ORR at the highest dose level evaluated to date (75 µg QD)
- 26% ORR across all dose levels

Cemsidomide + dex was well-tolerated with a compelling safety profile

- 38% of patients experienced Grade 3/4 neutropenia, which was manageable, and no cases resulted in cemsidomide discontinuation

75 µg is a target dose for various + dex regimens with potential for higher doses to also be considered for development as dose escalation continues

- For immune-based combination strategies, doses lower than 75 µg are optimal based on anti-myeloma activity and immune activation observed in the monotherapy data set[1]

Cemsidomide is well suited for further development across treatment lines and in combination with other anti-myeloma agents

[1]Monotherapy cemsidomide dataset in multiple myeloma was presented in December 2023
Once daily (QD); overall response rate (ORR)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide's Profile Supports Development Across Multiple Lines of Treatment in MM, Estimated to Be ~$42B Market Opportunity by 2030[1]

INITIAL COMBINATION TRIALS:

Prior Lines of Therapy	*Trial Design*
1 – 3	**Cemsidomide + BCMA bispecific[2]** - Safety dose escalation followed by Phase 2 expansion
2 – 4 (Post anti-BCMA therapy)	**Cemsidomide + anti-CD38[3] + dex** - Safety dose escalation followed by Phase 2 expansion

Additional Combinations
(not exhaustive):

- **Proteasome inhibitors** (bortezomib, carfilzomib, ixazomib)
- **GPRC5D bispecifics** (talquetamab, RG6234)
- **BCMA ADC** (bela-maf)
- **FcRH5 bispecific** (cevostamab)
- **Anti-SLAMF7** (elotuzumab)
- **XPO1 inhibitor** (selinexor)
- **CAR-T maintenance**

NEXT STEPS:

- **Complete Phase 1 dose escalation trial** in multiple myeloma to establish go forward doses
- **Initiate initial combination trials**
- **Engage regulatory authorities** on registrational path

[1]Source: Evaluate Pharma - Multiple myeloma market opportunity
[2]Could choose from approved BCMA bispecifics teclistamab or elitranatamab. Also other BCMA bispecifics in development (e.g., linvoseltamab).
[3]Could choose from approved anti-CD38 antibodies daratumumab or isatuximab.
Antibody-drug conjugates (ADC); B-cell maturation antigen (BCMA); maximum tolerated dose (MTD); multiple myeloma (MM)

Non-Hodgkin's Lymphoma (NHL)

Monotherapy Cemsidomide

C4 Therapeutics

Cemsidomide Has the Potential to Be Developed Across NHL Subtypes and Lines of Treatment

	B-Cell Lymphomas				T-Cell Lymphomas
	DLBCL Diffuse Large B-Cell Lymphoma	**FL** Follicular Lymphoma	**MZL** Marginal Zone Lymphoma	**MCL** Mantle Cell Lymphoma	**PTCL Subtypes** Peripheral T-Cell Lymphoma
U.S. Annual Incidence (2023)[1]	~26,000	~15,000	~5,000	~4,000	~5,000
Lenalidomide FDA Approved[2]	✓	✓	✓	✓	
Lenalidomide in NCCN Guidelines	✓	✓	✓	✓	✓

Cemsidomide Opportunity

- IKZF1/3 degraders (e.g., lenalidomide) are widely used across NHL subtypes
- Cemsidomide has the potential to be developed as a **monotherapy in the R/R setting** and in **combination with frontline standard of care regimens**

[1]SEER, American Cancer Society, Lymphoma Research Foundation.
[2]FL, MZL, and MCL FDA approved in the Revlimid (lenalidomide) label and DLBCL approved in the Monjuvi (tafasitamab) label.
U.S. Food and Drug Administration (FDA); National Comprehensive Cancer Network (NCCN); non-Hodgkin's lymphoma (NHL); relapsed refractory (R/R)

Dose Exploration Continues for the Cemsidomide Monotherapy Dose Escalation Trial in R/R NHL

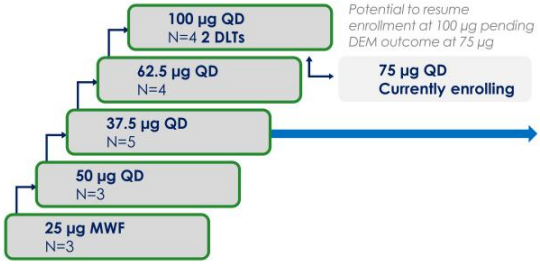
KEY INCLUSION CRITERIA

- Adults with NHL, R/R to prior therapy
  - PTCL patients must have received at least 1 prior alkylator-based chemotherapy
  - ALCL patients must have also received a CD-30 mAb
- 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
Utilizing a Bayesian logistic regression model until determination of the MTD and/or RP2D



BACK-FILL COHORT(S)

37.5 µg QD
Back-fill cohort; N=4

PHASE 2

Phase 2 Expansion

Anaplastic large cell lymphoma (ALCL); dose escalation meeting (DEM); dose limiting toxicities (DLT); Eastern Cooperative Oncology Group (ECOG); monoclonal antibody (mAb); maximum tolerated dose (MTD); Monday Wednesday Friday (MWF); non-Hodgkin's lymphoma (NHL); once daily (QD); pharmacodynamic (PD); pharmacokinetic (PK); peripheral T-cell lymphoma (PTCL); recommended Phase 2 dose (RP2D); relapsed refractory (R/R)

C4 Therapeutics
Data cutoff date: 10/11/2024

Heavily Pre-Treated Population Where Majority of Patients Were Diagnosed With PTCL, Reflecting High Unmet Need

Characteristics	Safety Population (N=23)
Age, median (range)	68 (28-85 years)
Male, n (%)	14 (61)
Years since initial diagnosis, median (range)	2 (0.4-21)
ECOG performance status, n (%)	
0	11 (48)
1	9 (39)
2	2 (9)
Missing	1 (4)
Black or African American, n (%)	6 (26)
White, n (%)	13 (57)
Other, n (%)	4 (17)
IPI at screening, n (%)	
1	2 (9)
2	6 (26)
3	7 (30)
4	3 (13)
Missing	5 (22)

Characteristics	Safety Population (N=23)
Prior therapies, median (range)	3 (1-14)
1	2 (9)
2	7 (30)
3	3 (13)
≥4	11 (48)
PTCL, n (%)	17 (74)
PTCL-NOS	5 (22)
AITL	4 (17)
ALCL	3 (13)
ATLL	5 (22)
B-cell lymphoma, n (%)	6 (26)
DLBCL	4 (17)
MCL	1 (4)
MZL/MALT	1 (4)
Prior CAR-T therapy, n (%)	4 (17)
Prior HCT, n (%)	4 (17)
Autologous	3 (13)
Allogenic	1(4)

Angioimmunoblastic T-cell lymphoma (AITL); anaplastic large cell lymphoma (ALCL); adult T-cell leukemia/lymphoma (ATLL); diffuse large B-Cell lymphoma (DLBCL); Eastern cooperative oncology group (ECOG); hematopoietic cell transplantation (HCT); International Prognostic Index (IPI); mantle cell lymphoma (MCL); marginal zone lymphoma/mucosa-assisted lymphoid tissue (MZL/MALT); peripheral T-cell lymphoma (PTCL); PTCL-not otherwise specified (PTCL-NOS)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Was Well-tolerated With Manageable Incidents of On-target Neutropenia

- **2 DLTs occurred at 100 µg QD** (Grade 4 thrombocytopenia and Grade 3 febrile neutropenia)
- **TEAEs leading to discontinuation: 9%** (2/23)
- **39% (9/23) of patients received G-CSF**
  - 3 of 9 patients received G-CSF in Cycle 1

Common (>20% All Grades) TEAEs and Events of Interest*, n (%)	All Grade (N=23)	Grade 3 (N=23)	Grade 4 (N=23)
Infections	15 (65)	4 (17)	2 (9)
Upper respiratory tract infection	4 (17)	0	0
Sepsis	1(4)	0	1 (4)
Bacteremia	1(4)	0	1 (4)
Pneumonia	2 (9)	2 (9)	0
Neutropenia	11 (48)	4 (17)	7 (30)
Fatigue	11 (48)	1 (4)	0
Cough	7 (30)	0	0
Anemia	6 (26)	4 (17)	0
Peripheral edema	5 (22)	0	0
Febrile neutropenia*	4 (17)	4 (17)	0
Thrombocytopenia*	4 (17)	1 (4)	2 (9)
Maculopapular rash*	3 (13)	2 (9)	0

One patient experienced a Grade 5 AE (hip fracture resulting in transfer to hospice)

*Events of Interest
Adverse event (AE); dose limiting toxicities (DLTs); granulocyte colony-stimulating factor (G-CSF); once daily (QD); treatment emergent adverse events (TEAEs)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Monotherapy Adverse Events by Dose Level

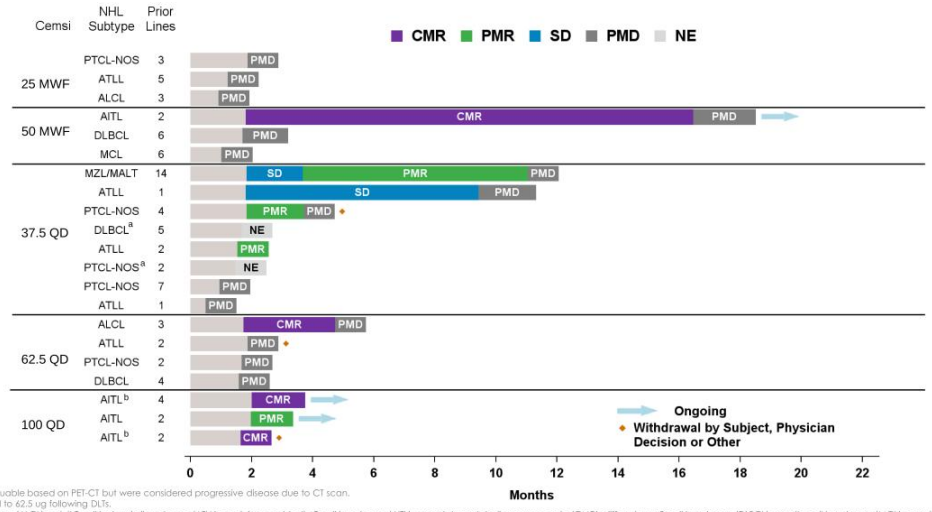
Common Grade ≥3 TEAEs, n (%)	25 µg MWF (N=3)	50 µg MWF (N=3)	37.5 µg QD (N=9)	62.5 µg QD (N=4)	100 µg QD (N=4)	Total (N=23)
Neutropenia	0	0	5 (56)	4 (100)	2 (50)	11 (48)
Infections	0	0	3 (33)	0	3 (75)	6 (26)
Pneumonia	0	0	1 (11)	0	1 (25)	2 (9)
Sepsis	0	0	1 (11)	0	0	1 (4)
Urinary tract infection	0	0	1 (11)	0	0	1 (4)
Bacteremia	0	0	0	0	1 (25)	1 (4)
Skin infection	0	0	0	0	1 (25)	1 (4)
Anemia	0	0	3 (33)	0	1 (25)	4 (17)
Febrile neutropenia	0	0	1 (11)	1 (25)	2 (50)	4 (17)
Thrombocytopenia	0	0	1 (11)	0	2 (50)	3 (13)
Maculopapular rash	0	0	1 (11)	1 (25)	0	2 (9)

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

C4 Therapeutics

Data cutoff: 10/11/24

Clinical Responses Were Observed Across a Broad Range of Doses

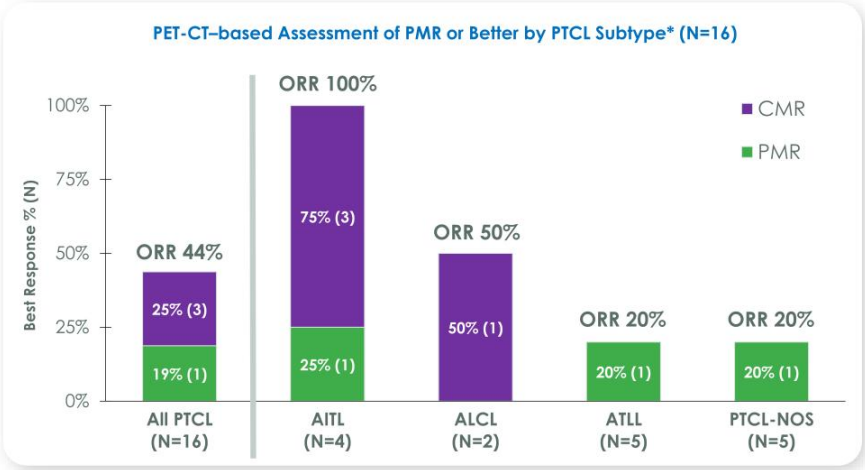


[a] Both patients were not evaluable based on PET-CT but were considered progressive disease due to CT scan.
[b] Both patients dose reduced to 62.5 ug following DLTs.
Anaplastic large cell lymphoma (ALCL); adult T-cell leukemia/lymphoma (ATLL); angioimmunoblastic T-cell lymphoma (AITL); complete metabolic response rate (CMR); diffuse large B-cell lymphoma (DLBCL); mantle cell lymphoma (MCL); marginal zone lymphoma/mucosa-assisted lymphoid tissue (MZL/MALT); Monday Wednesday Friday (MWF); non-evaluable (NE); once daily (QD); overall response rate (ORR); partial metabolic response (PMR); peripheral T-cell lymphoma (PTCL); PTCL-not otherwise specified (PTCL-NOS); progressive metabolic disease (PMD); stable disease (SD)

C4 Therapeutics

Data cutoff: 10/11/24

Compelling and Deep Responses Achieved Across PTCL Subtypes



- Cemsidomide monotherapy **produced responses in all four PTCL subtypes**
- **All AITL patients (4/4)** experienced **a metabolic response**

*Investigator assessed response; 2 patients were evaluated based on CT scan and were PD but not evaluable based on PET-CT, both patients are included as PMD for PET-CT based assessment; 2 additional subjects that came off study prior to follow up scans were not considered efficacy evaluable.
Angioimmunoblastic T-cell lymphoma (AITL); anaplastic large cell lymphoma (ALCL); adult T-cell lymphoma (ATLL); complete metabolic response (CMR); overall response rate (ORR); partial metabolic response (PMR); peripheral T-cell lymphoma (PTCL); peripheral T-cell lymphoma not-otherwise specified (PTCL-NOS)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Is Well-suited for Further Development in Earlier Lines of Treatment and in Combination

Cemsidomide as a single agent demonstrated compelling anti-lymphoma activity across a broad range of doses in PTCL patients, suggesting a wide therapeutic index

- 44% ORR was observed in PTCL with a 25% CMR rate

Cemsidomide was well-tolerated with additional dose finding ongoing

- 2 DLTs at 100 µg (Grade 4 thrombocytopenia) with enrollment at 75 µg currently ongoing
  - Per BLRM, maximum tolerated dose not yet exceeded
- Grade 3/4 neutropenia cases were manageable with no cases resulting in discontinuation

Profile supports cemsidomide's development as a monotherapy in relapsed refractory settings and potentially in combination in NHL subtypes across treatment lines

Bayesian logistic regression model (BLRM); complete metabolic response (CMR); dose limiting toxicities (DLTs); overall response rate (ORR); peripheral t-cell lymphoma (PTCL)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Profile Supports Development Across Multiple Lines of Treatment in NHL, Estimated to Be ~$30B Market Opportunity by 2030[1]

NEXT STEPS:

- **Complete Phase 1 dose escalation trial in NHL** and identify go forward dose
- **Initiate expansion cohort** for PTCL
- **Engage regulatory authorities** on registrational path

[1]Source: Evaluate Pharma – NHL Market Opportunity: Non-Hodgkin's lymphoma (NHL): peripheral T-cell lymphoma (PTCL)

Cemsidomide Is Positioned to Potentially Be a Best-in-Class Therapy in Two Distinct Indications with Opportunities Across Multiple Lines of Therapy

IKZF1/3 is a fundamental target for MM and NHL and data supports cemsidomide as a potential backbone therapy within the evolving treatment landscape

- Well-tolerated with a compelling safety profile
- Compelling anti-tumor activity across a range of dose levels

MM Market Opportunity

Estimated **~$42B** by 2030[1]

NHL Market Opportunity

Estimated **~$30B** by 2030[1]

[1]Source: Evaluate Pharma
Multiple myeloma (MM); non-Hodgkin's lymphoma (NHL)

C4 Therapeutics

Q&A

C4 Therapeutics

Exhibit 99.2

C4 Therapeutics Presents Cemsidomide Phase 1 Data at the American Society for Hematology (ASH) Annual Meeting that Demonstrated Potential to Become Best-in-Class IKZF1/3 Degrader

In Multiple Myeloma, Cemsidomide in Combination with Dexamethasone at Highest Dose Level Explored to Date Achieved 36 Percent Overall Response Rate (ORR) and 45 Percent Clinical Benefit Rate (CBR); Responses Seen Across All Dose Levels

Multiple Myeloma Arm Demonstrated Well-Tolerated Safety Profile; On-Target Neutropenia Was Manageable With Low Rates of Febrile Neutropenia and Infections; No Treatment Emergent Adverse Events Leading to Dose Reduction

In Non-Hodgkin's Lymphoma, Cemsidomide Monotherapy Demonstrated a 38 Percent ORR and 19 Percent Complete Metabolic Response (CMR) Rate Across All Subtypes; In Peripheral T-Cell Lymphoma (PTCL), Cemsidomide Achieved a 44 Percent ORR and 25 Percent CMR Rate

Cemsidomide is Well Positioned for Future Development in Multiple Myeloma Combination Regimens and Various Non-Hodgkin's Lymphoma Subtypes and Therapeutic Regimens to Unlock Potential in Growing Markets

C4T To Host Webcast Today at 5 pm EST; Webcast Link Available Here

WATERTOWN, Mass., December 8, 2024 (GLOBE NEWSWIRE) -- C4 Therapeutics, Inc. (C4T) (Nasdaq: CCCC), a clinical-stage biopharmaceutical company dedicated to advancing targeted protein degradation science, today presented clinical data from the ongoing Phase 1 trial of cemsidomide, an orally bioavailable small molecule degrader of IKZF1/3, at the ASH Annual Meeting. Presentations included a poster highlighting results for cemsidomide in combination with dexamethasone in multiple myeloma, and an oral presentation delivering initial results for cemsidomide as a monotherapy for non-Hodgkin's lymphoma. These presentations reinforce the potential of cemsidomide to become a backbone therapy of choice in both multiple myeloma and non-Hodgkin's lymphoma where IKZF1/3 degradation is warranted.

C4T designed cemsidomide to be a more potent and selective degrader of IKZF1/3 with unique pharmacokinetic properties, with the goal to improve the therapeutic index to treat multiple myeloma and non-Hodgkin's lymphoma—both alone and in combination with other therapeutic agents in these therapeutic areas.

"Cemsidomide continues to deliver clinical data demonstrating its potential to be used in both multi-refractory patients and as part of combination therapies across all lines of treatment for a significant number of patients with multiple myeloma or non-Hodgkin's lymphoma," said Len Reyno, M.D., chief medical officer of C4 Therapeutics. "We look forward to leveraging today's data to inform clinical development strategies in both multiple myeloma and non-Hodgkin's lymphoma that has the potential to unlock the value of cemsidomide for patients in need of innovative therapies across treatment lines."

Multiple Myeloma (MM)

At the ASH Annual Meeting, C4T presented safety and anti-myeloma data demonstrating cemsidomide has the potential to become a best-in-class IKZF1/3 degrader used as a backbone therapy of choice for

patients with multiple myeloma where IKZF1/3 degradation is warranted. These data support the future development of cemsidomide across treatment lines in combination with other anti-myeloma agents.

As of the data cutoff date of October 11, 2024, a total of 47 patients received cemsidomide in combination with dexamethasone across four dose levels (50 µg dosed Monday, Wednesday, Friday (MWF); 37.5 µg dosed once daily (QD); 62.5 µg QD; 75 µg QD). Patients were heavily pretreated, receiving a median of six prior therapies. All patients (100 percent) were triple-class exposed, defined as exposure to one or more immunomodulatory agents, one or more proteasome inhibitors, and one anti-CD38 antibody. Thirty-three patients (70 percent) received prior BCMA directed therapy. Thirty-one patients (66 percent) received prior CAR-T or T-cell engager therapy.

Safety: Cemsidomide in combination with dexamethasone was well tolerated.

- As of the data cutoff date, 47 patients were evaluable for safety.
- The most common adverse events (AEs) Grade 3 or above were neutropenia (n=18), anemia (n=10) and infections (n=8). No patients discontinued therapy due to neutropenia.
- No patients experienced a treatment emergent adverse event that led to dose reduction.
- The maximum tolerated dose has not yet been identified. Enrollment is currently ongoing at the 100 µg QD dose level.

Anti-myeloma activity: Cemsidomide in combination with dexamethasone demonstrated anti-myeloma activity across a broad range of doses, highlighting a wide therapeutic range.

- As of the data cutoff, 42 patients were evaluable for anti-myeloma activity.
- Across all dose levels, cemsidomide in combination with dexamethasone achieved a 26 percent ORR and a 40 percent clinical benefit rate (CBR).
- At the highest dose level explored to date (75 µg QD), cemsidomide achieved a 36 percent ORR and a 45 percent CBR.
- At the two highest dose levels evaluated to date (62.5 µg QD and 75 µg QD), 62 percent of patients remained on therapy as of the data cutoff date.

Binod Dhakal, M.D., M.S., associate professor of medicine, Medical College of Wisconsin, Division of Hematology, presented a poster highlighting the MM results. He commented: “The data presented at the ASH Annual Meeting demonstrate cemsidomide in combination with dexamethasone is active and well-tolerated over a range of doses in a heavily pretreated, relapsed/refractory multiple myeloma patient population—including a majority of patients who have received T-cell directed therapies who are challenging to treat. I look forward to cemsidomide’s continued development as a potential new treatment option for patients in the evolving myeloma landscape.”

C4T has identified 75 µg QD as a target dose for various dexamethasone combination regimens; as dose escalation continues, higher doses may also be considered. For immune-based combination strategies, C4T believes doses lower than 75 µg QD will be optimal based on anti-myeloma activity and immune activation observed in the previously disclosed monotherapy data set.

C4T has identified the following next steps in cemsidomide MM development:

- Complete Phase 1 dose escalation trial in MM to establish go forward doses
- Initiate initial combination trials
- Engage regulatory authorities on registrational path

Non-Hodgkin's Lymphoma (NHL)

At the ASH Annual Meeting, C4T also presented safety and anti-lymphoma data that reinforce C4T's belief that IKZF1/3 degradation remains relevant in lymphoma. Based on the emerging anti-lymphoma signal demonstrated in patients with PTCL, C4T believes cemsidomide could be further developed in areas of high unmet need.

As of the data cutoff date of October 11, 2024, a total of 23 patients received cemsidomide monotherapy across five dose levels (25 µg MWF; 50 µg MWF QD; 37.5 µg QD; 62.5 µg QD; 100 µg QD). Patients were heavily pretreated, receiving a median of three prior therapies. Seventeen patients had refractory progressive PTCL and six patients had refractory progressive B-cell lymphoma.

Safety: Cemsidomide monotherapy was well tolerated and additional dose finding is ongoing.

- As of the data cutoff, 23 patients were evaluable for safety.
- The most common AEs Grade 3 or above were neutropenia (n=11), infections (n=6), febrile neutropenia (n=4) and anemia (n=4). No patients discontinued therapy due to neutropenia.
- At this time, the maximum tolerated dose has not been defined. Two dose-limiting toxicities occurred at the 100 µg QD dose level. As a result, a 75 µg QD cohort was opened to refine the understanding of dose and safety in the NHL population; this cohort is currently enrolling patients. Escalation above 75 µg QD may be explored pending the outcome of the cohort.

Anti-lymphoma activity: Cemsidomide monotherapy demonstrated anti-lymphoma activity across a broad range of doses.

- As of the data cutoff, 21 patients were evaluable for efficacy, 16 of which had PTCL.
- Cemsidomide displays a differentiated pharmacokinetic profile with an approximate two-day half-life and an ability to induce rapid and potent degradation of IKZF1/3.
- Across all dose levels explored, cemsidomide achieved a 38 percent ORR and 19 percent CMR rate.
- In patients with PTCL, cemsidomide achieved a 44 percent ORR and 25 percent CMR rate.

Steve Horwitz, M.D., lymphoma specialist and cellular therapist, Memorial Sloan Kettering Cancer Center, delivered an oral presentation highlighting the NHL results at the ASH Annual Meeting. He commented: "I am pleased to share the first clinical data on monotherapy cemsidomide in non-Hodgkin's lymphoma, which demonstrated its well-tolerated safety profile and compelling anti-lymphoma activity. These initial data are encouraging, particularly in PTCL where relapsed/refractory patients lack effective targeted therapies. We believe these Phase 1 monotherapy data demonstrate that cemsidomide is well suited for further development in earlier lines of treatment and in combination with other anti-lymphoma agents."

C4T has identified the following next steps in cemsidomide NHL development:

- Complete Phase 1 dose escalation trial and identify go forward dose
- Initiate expansion cohort for PTCL
- Engage regulatory authorities on registrational path

C4T Webcast for Analysts and Investors C4T will host an investor webcast today December 8, 2024, at 5 pm EST. To join the webcast, please visit this link or the "Events & Presentations" page of the Investors section on the company's website at www.c4therapeutics.com. A replay of the webcast will be archived and available following the event.

About Cemsidomide

Cemsidomide is an investigational, orally bioavailable small-molecule degrader designed to be a more potent and selective degrader of IKZF1/3, transcription factors that drive multiple myeloma (MM) and non-Hodgkin's lymphomas (NHL), with unique pharmacokinetic properties. Clinical data has shown that cemsidomide is well-tolerated. In MM, cemsidomide displays evidence of anti-myeloma activity and immunomodulatory effects. In NHL, cemsidomide displays evidence of anti-lymphoma activity. More information may be accessed at www.clinicaltrials.gov (identifier: NCT04756726).

About IKZF1/3

IKZF1 (Ikaros) and IKZF3 (Aiolos) are transcription factors that directly regulate the activity of IRF4, a transcription factor that regulates downstream immune cell differentiation. Aberrant IRF4 is associated with both lymphoma and multiple myeloma proliferative T, B and plasma cell populations. Down regulation of IRF4 promotes the death of both myeloma and lymphoma cells.

About Multiple Myeloma

Multiple myeloma (MM) is a rare blood cancer affecting plasma cells. Approximately 36,000 people in the United States are diagnosed with MM each year. Despite advances in treatment, multiple myeloma remains incurable. Treatment combinations include IKZF1/3 degraders, which are established backbone therapies, across lines of therapy.

About non-Hodgkin's Lymphoma

Non-Hodgkin's lymphoma (NHL) is one of the most common cancers in the United States. NHL forms in cells of the immune system called lymphocytes. In the United States, approximately 80,000 people are diagnosed with NHL each year. IKZF1/3 degraders are used across NHL subtypes.

About C4 Therapeutics

C4 Therapeutics (C4T) (Nasdaq: CCCC) is a clinical-stage biopharmaceutical company dedicated to delivering on the promise of targeted protein degradation science to create a new generation of medicines that transforms patients' lives. C4T is progressing targeted oncology programs through clinical studies and leveraging its TORPEDO® platform to efficiently design and optimize small-molecule medicines to address difficult-to-treat diseases. C4T's degrader medicines are designed to harness the body's natural protein recycling system to rapidly degrade disease-causing proteins, offering the potential to overcome drug resistance, drug undruggable targets and improve patient outcomes. For more information, please visit www.c4therapeutics.com.

Forward Looking Statements

This press release contains "forward-looking statements" of C4 Therapeutics, Inc. within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements may include, but may not be limited to, express or implied statements regarding our ability to develop potential therapies for patients; the design and potential efficacy of our therapeutic approaches; the predictive capability of our TORPEDO® platform in the development of novel, selective, orally bioavailable BiDAC™ and MonoDAC™ degraders; the potential timing, design and advancement of our preclinical studies and clinical trials, including the potential timing for and receipt of regulatory authorization related to clinical trials and other clinical development activities including clinical trial commencement or cohort initiation; our ability and the potential to successfully manufacture and supply our product candidates for clinical trials; our ability to replicate results achieved in our preclinical studies or clinical trials in any future studies or trials; our ability to replicate interim or early-stage results from our clinical trials in the results

obtained when those clinical trials are completed or when those therapies complete later-stage clinical trials; regulatory developments in the United States and foreign countries; the potential timing for updates on our clinical and research programs; and our ability to fund our future operations. Any forward-looking statements in this press release are based on management's current expectations and beliefs of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: uncertainties related to the initiation, timing, advancement and conduct of preclinical and clinical studies and other development requirements for our product candidates; the risk that any one or more of our product candidates will cost more to develop or may not be successfully developed and commercialized; and the risk that the results of preclinical studies and/or clinical trials will or will not be predictive of results in connection with future studies or trials. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in C4 Therapeutics' most recent Annual Report on Form 10-K and/or Quarterly Report on Form 10-Q, as filed with the Securities and Exchange Commission. All information in this press release is as of the date of the release and C4 Therapeutics undertakes no duty to update this information unless required by law.

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C4 Therapeutics

Protein degraded.
Disease targeted.
Lives transformed.

December 2024

Forward-looking Statements and Intellectual Property

Forward-looking Statements

The following presentation contains forward-looking statements. All statements other than statements of historical fact are forward-looking statements, which are often indicated by terms such as "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "look forward to," "may," "plan," "potential," "predict," "project," "should," "will," "would" and similar expressions. These forward-looking statements include, but are not limited to, statements regarding the therapeutic potential of C4 Therapeutics, Inc.'s technology and products. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. Among the factors that could cause actual results to differ materially from those described or projected herein include uncertainties associated generally with research and development, clinical trials and related regulatory reviews and approvals, as well as the fact that the product candidates that we are developing or may develop may not demonstrate success in clinical trials. Prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. The forward-looking statements included in this presentation are subject to a variety of risks and uncertainties, including those set forth in our most recent and future filings with the Securities and Exchange Commission. Our actual results could vary significantly from those anticipated in this presentation, and our financial condition and results of operations could be materially adversely affected. C4 Therapeutics, Inc. undertakes no obligation to update or revise the information contained in this presentation, whether as a result of new information, future events or circumstances or otherwise.

This presentation also contains estimates, projections and other information concerning the markets for C4 Therapeutics, Inc.'s product candidates, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions and patient use of medicines. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events, and circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, the Company obtained this industry, business, market and other data from reports, research surveys, clinical trials studies and similar data prepared by market research firms and other third parties, from industry, medical and general publications, from other publicly available information, and from government data and similar sources.

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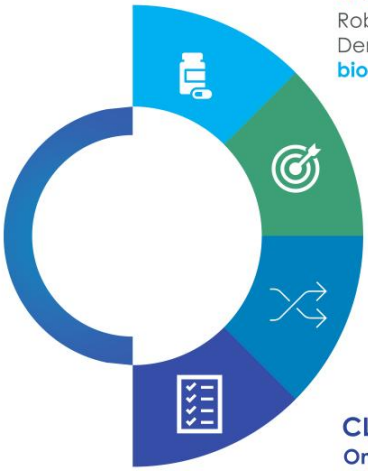
C4T Is a Recognized Leader in Delivering on the Promise of Targeted Protein Degradation

Our Mission

To deliver on the promise of targeted protein degradation science to create a new generation of medicines that transform patients' lives



WORLD-CLASS DEGRADER PLATFORM

Robust patent portfolio of novel cereblon binders; Demonstrated ability to design **orally bioavailable, catalytically efficient degraders**

RIGOROUS TARGET SELECTION

Focus on targets with a **clear degrader rationale**

BROAD DEGRADER APPROACH

MonoDAC and **BiDAC** degraders, as well as **degrader-antibody conjugates**

CLINICAL PIPELINE

Oncology degraders against targets of high unmet need

Advancing a Broad Pipeline to Deliver Near-Term Value

Program	Target	Indications	Discovery	Preclinical	Early Phase Development	Late Phase Development	Rights
Cemsidomide	**IKZF1/3**	Multiple Myeloma & Non-Hodgkin's Lymphoma					
CFT1946	**BRAF V600 Mutant**	V600 Mutant Cancers					
CFT8919[1]	**EGFR L858R**	Non-Small Cell Lung Cancer					
Discovery Stage Programs		Various Cancers					
Collaboration Programs		Autoimmune & Cancer		2 targets			Roche
		Cancer		2 targets			Merck KGaA Darmstadt, Germany
		Cancer		1 target			MERCK
		Autoimmune & Neurological			2 targets		Biogen[2]

[1]License and collaboration agreement with Betta Pharmaceuticals for development and commercialization in Greater China; [2]Delivered development candidates to Biogen in Q1 2024 and Q3 2024

C4T Has Delivered a Steady Flow of Clinical Updates and Innovative Collaborations Over the Past 12 Months…

Significant Progress Across Clinical Programs

Cemsidomide

- ✓ Compelling activity in both multiple myeloma and non-Hodgkin's lymphoma
- ✓ Modest and manageable neutropenia
- ✓ Emerging data demonstrate positive exposure-response relationship
- ✓ Evidence of immunomodulatory effects, consistent with the class

CFT1946

- ✓ Monotherapy anti-tumor activity, including tumor reductions across various V600 mutation types
- ✓ Dose-dependent bioavailability
- ✓ Well-tolerated; no Grade ≥ 3 cutaneous adverse events commonly seen with BRAF inhibitors
- ✓ Preclinical data demonstrate ability to cross blood-brain barrier

CFT8919

- ✓ Clinical trial initiated in Greater China in partnership with Betta Pharmaceuticals

Collaborations Have Further Validated TORPEDO Platform

Biogen
- ✓ Delivered two development candidates for non-oncology targets

MERCK
- ✓ Established partnership to discover and develop degrader antibody conjugates

Merck KGaA
Darmstadt, Germany
- ✓ Announced collaboration to discover targeted protein degraders against critical oncogenic proteins

…Which Set the Stage to Unlock Value

VALUE DRIVERS	KEY CATALYSTS
Cemsidomide IKZF1/3	Further development in multiple myeloma and non-Hodgkin's lymphoma positions cemsidomide to potentially be best-in-class IKZF1/3 degrader
CFT1946 BRAF V600 Mutant	Phase 1 data updates to further validate initial anti-tumor activity and safety profile in melanoma and colorectal cancer
CFT8919 EGFR L858R	Phase 1 data from Greater China clinical trial to inform US and rest-of-world development plans
TORPEDO Platform	Develop orally bioavailable degraders in oncology and non-oncology targets through internal research and collaborations

C4T is positioned to become a **fully integrated biotechnology** company focused on **orally bioavailable degraders**

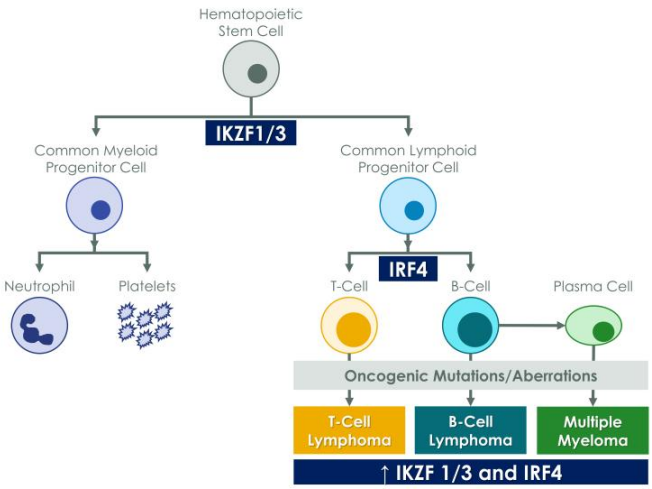
Cemsidomide

Targeting IKZF1/3

Multiple Myeloma (MM)
& Non-Hodgkin's Lymphoma (NHL)

C4 Therapeutics

IKZF1/3 Are Key Promoters of Myeloma and Lymphoma Cell Survival and Will Remain Important Therapeutic Targets in MM and NHL



Key Roles of IKZF1/3

Physiological Functions:

- **IKZF1/3** are key transcriptional regulators of hematopoietic stem cell differentiation
- **IKZF1/3** directly regulate the activity of **IRF4**, another transcription factor that regulates downstream immune cell differentiation

Oncogenic Functions:

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

IKZF1/3 Degradation Leads to:

- Downregulation of **IRF4**, promoting the death of myeloma and lymphoma cells
- On-target neutropenia

Multiple myeloma (MM); non-Hodgkin's lymphoma (NHL)

C4 Therapeutics

Cemsidomide First-in-Human Phase 1 Trial Continues to Progress

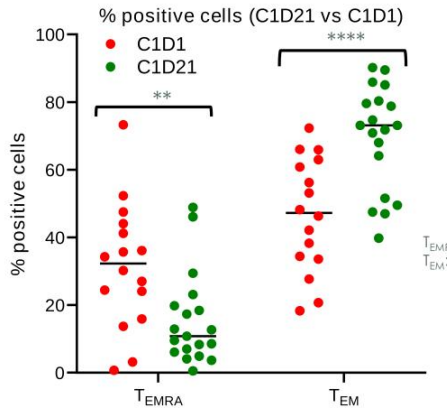
Data to date reinforce potential of drug to become best-in-class IKZF1/3 degrader used as a backbone therapy of choice

PHASE 1 DOSE ESCALATION TRIAL

2022	2023	ASH 2024	
R/R MM Monotherapy **Dosing:** QD 21 days on/ 7 days off N=5 **Status:** Complete	**R/R MM** Monotherapy **Dosing:** MWF & QD 14 days on/ 14 days off N=22 **Status:** Complete	**R/R MM** Dex Combo **Dosing:** MWF & QD 14 days on/ 14 days off N=~40 **Status:** Enrolling	**R/R NHL** Monotherapy **Dosing:** MWF & QD 14 days on/ 14 days off N=~25 **Status:** Enrolling
	• 14 days on/14 days off established as an effective dosing schedule • Demonstrated monotherapy anti-myeloma and immunomodulatory effects supporting combination with other anti-myeloma agents	• Well-tolerated with manageable neutropenia and low rates of infections and febrile neutropenia • Wide therapeutic index with anti-myeloma activity across a broad range of doses	• Well-tolerated with additional dose finding ongoing • Compelling anti-lymphoma activity across a broad range of doses in PTCL

Monday, Wednesday, Friday dosing (MWF); once daily (QD); peripheral T-cell lymphoma (PTCL); relapsed refractory multiple myeloma (R/R MM); relapsed refractory non-Hodgkin's lymphoma (R/R NHL)

Clinical Evidence of Immune T-cell Activation With Cemsidomide Monotherapy



T_{EMRA}: Terminally differentiated T-cells
T_{EM}: Effector memory T-cells

- 19 patient samples (PBMCs) analyzed by flow cytometry
- Aggregate data of 25 µg, 50 µg, and 75 µg MWF and QD

Supports potential of cemsidomide as a maintenance therapy option and in combination with novel MM agents to improve efficacy:

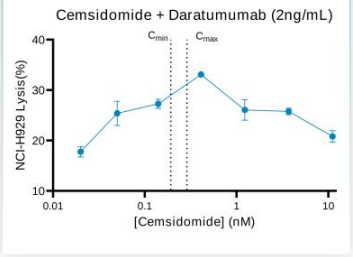
- ✓ Cemsidomide induces CD8+ T-cell activation by increasing effector memory T-cell subset
- ✓ T-cell activation is observed at well-tolerated monotherapy clinical doses
- ✓ Clinical data consistent with the preclinical *in vitro* data reported for cemsidomide

Peripheral Blood Mononuclear Cells (PBMCs); Daily dosing (QD); Monday, Wednesday, Friday Dosing Schedule (MWF); Multiple Myeloma (MM)
Source: C4T data on file as of 11/28/2023

Cemsidomide Combined With Novel MM Agents Demonstrated Enhanced Immune Cell Lysis in Non-clinical Translational Models

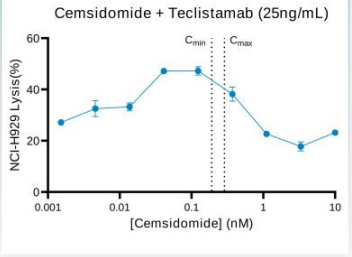
DARZALEX® (daratumumab)

Cemsidomide + Daratumumab (Anti-CD38)



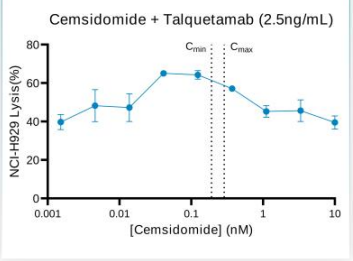
TECVAYLI™ (teclistamab)

Cemsidomide + Teclistamab (BCMA Bispecific)



TALVEY® (talquetamab-tgvs)

Cemsidomide + Talquetamab (GPRC5D Bispecific)



Notes: Daratumumab combos performed using an Antibody-Dependent Cell-Mediated Cytotoxicity Assay (ADCC) and the teclistamab and talquetamab combos used a T-cell Dependent Cellular Cytotoxicity Assay (TDCC). CD8+ T-cells were isolated from PBMCs and pretreated with cemsidomide ex vivo at various concentrations for 6 days and then co-cultured with myeloma cells. C_{min} and C_{max} represent human plasma concentrations for a 50 µg dose of Cemsidomide.

Cemsidomide + Dexamethasone Dose Escalation Trial in MM Continues to Progress; Have Not Exceeded the Maximum Tolerated Dose

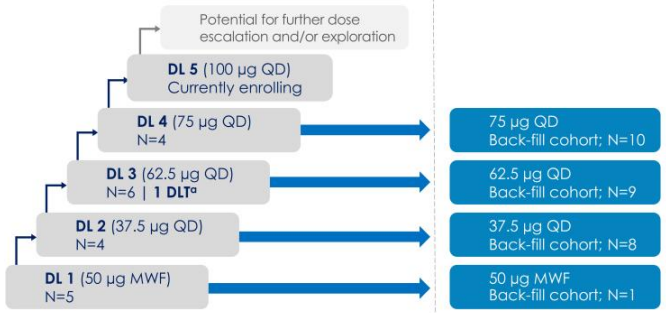
KEY INCLUSION CRITERIA

- 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; 2 patients at 100 µg are excluded as they had not completed Cycle 1 as of the data cut off date.
[a]DLT at 62.5 µg QD was due to Grade 4 neutropenia lasting >7 days.
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)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Is Well-Tolerated With Manageable Neutropenia and No Treatment Emergent Adverse Events Lead to Dose Reductions

- **1 DLT** (Grade 4 neutropenia lasting >7 days at the 62.5 µg dose level)
- **No TEAEs lead to dose reductions**
- **TEAEs leading to dose interruption: 32%** (15/47)
- **TEAEs leading to discontinuation[1]: 4%** (2/47)

Common (>20% All Grades) TEAEs and Events of Interest, n (%)	All Grades (N=47)	Grade 3 (N=47)	Grade 4 (N= 47)	Grade 5 (N=47)
Neutropenia	22 (47)	6 (13)	12 (26)	0
Infections	18 (38)	7 (15)	0	1(2)
Pneumonia	5 (11)	5 (11)	0	0
Upper respiratory tract infection	7 (15)	1 (2)	0	0
Septic shock	1 (2)	0	0	1(2)
Anemia	17 (36)	10 (21)	0	0
Fatigue	14 (30)	0	0	0
Thrombocytopenia	10 (21)	3 (6)	2 (4)	0
Diarrhea	10 (21)	0	0	0
Lymphopenia	9 (19)	6 (13)	0	0
Febrile neutropenia	3 (6)	3 (6)	0	0

2 patients experienced Grade 5 AEs (septic shock and subdural hematoma), both deemed unrelated to cemsidomide

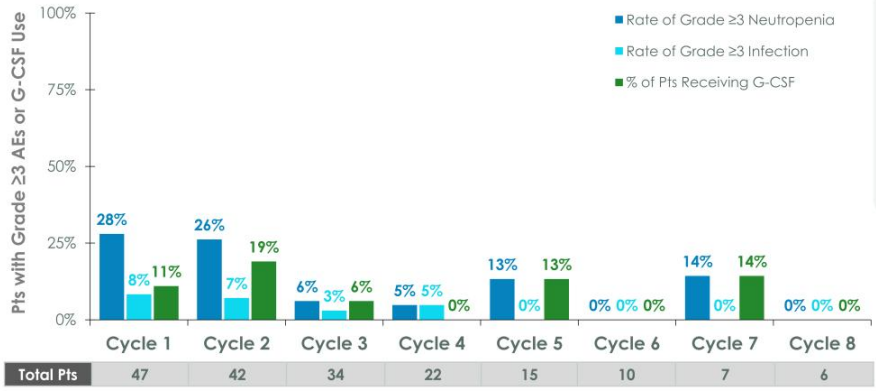
[1]Primary reason of discontinuation of patient at 37.5 µg was due to withdrawal of consent; primary reason of discontinuation of patient at 75 µg was due to death unrelated to cemsidomide.
Adverse events (AEs); dose limiting toxicity (DLT); treatment emergent adverse events (TEAEs)

C4 Therapeutics

Data cutoff: 10/11/24

Compelling Safety Profile With Low Rates of Neutropenia and Infections With Limited G-CSF Use

Rates of Neutropenia, Infections, and G-CSF Use by Cycle



- **Only 26% (12/47) of pts received G-CSF** across the study
- **Only one patient experienced Grade ≥3 neutropenia for the first time after completing cycle 2**

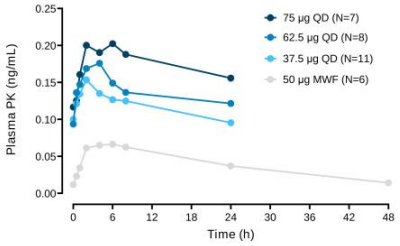
Notes: No cases of Grade ≥3 neutropenia were recorded after Cycle 7. One patient experienced a Grade ≥3 infection in a Cycle >8. G-CSF use was not permitted during Cycle 1 in escalation cohorts. One patient in the 50 µg MWF cohort came off study during Cycle 1 and received G-CSF after treatment was discontinued. No patients received G-CSF after Cycle 7.
The same patients that experienced neutropenia at Cycle 5 and Cycle 7, also received G-CSF.
Adverse events (AEs); granulocyte colony-stimulating factor (G-CSF); patients (Pts)

C4 Therapeutics

Data cutoff: 10/11/24

Across Doses, 40% (14/35) of Multiple Myeloma Patients With Elevated Light Chains Demonstrated at Least a 50% Decrease in dFLC

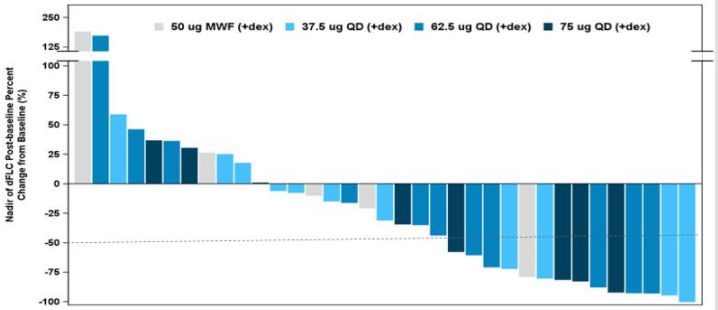
Dose Proportional Exposure



- Overall geometric mean half-life estimate is approximately 2 days

Best Change in dFLC from Baseline (Cemsidomide + Dex)

*Multiple Myeloma Patients w/ Elevated Light Chain Disease (N=35)**



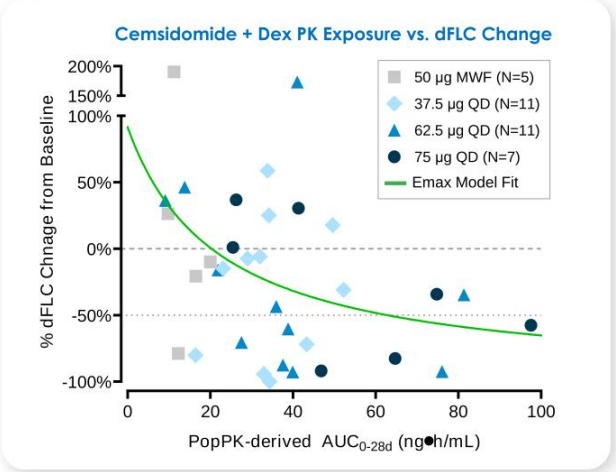
- **69% (24/35)** of patients with elevated light chain disease demonstrated a **decrease in dFLC**

*Only included treated patients 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.
Difference in involved and uninvolved free light chain (dFLC); once daily (QD); Monday Wednesday Friday (MWF); multiple myeloma (MM); pharmacokinetic (PK)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide 75 µg Dose Level or Greater Drives Sufficient Exposure Resulting in Meaningful Reductions in Light Chains



Exposure (AUC) Quartiles

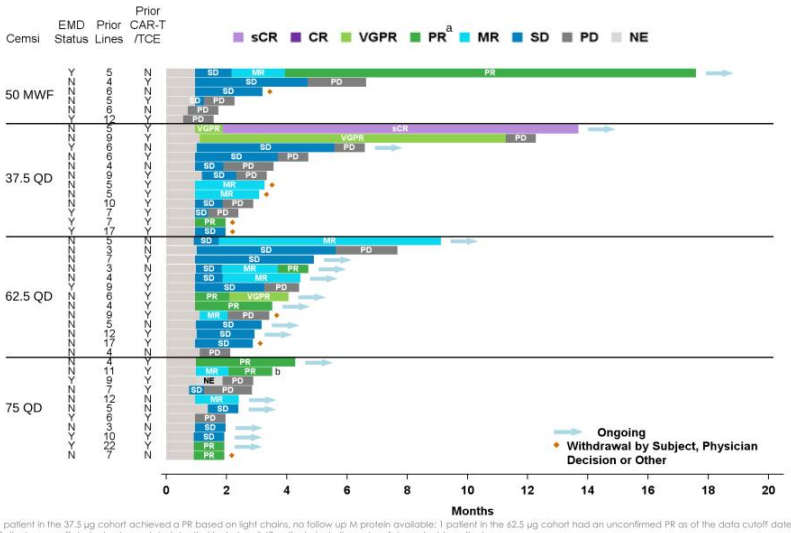
	<Q1 (N=9)	Q1-Q2 (N=8)	Q2-Q3 (N=8)	>Q3 (N=9)
Mean $AUC_{0\text{-}28d}$ (ng*h/mL)	14.6	28.8	37.9	**65.2**
Mean Change in dFLC from Baseline	+10%	-12%	-20%	**-53%**
Cemsidomide + Dex Dose	~17 µg QD	~35 µg QD	~45 µg QD	**~78 µg QD**

N=34 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.
Cemsidomide dose was back-calculated based on the population PK model.
Area under the curve (AUC); difference in involved and uninvolved free light chain (dFLC); maximum response (Emax); Monday Wednesday Friday (MWF); once daily (QD); population pharmacokinetics (popPK); pharmacokinetic (PK)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Demonstrated Anti-Myeloma Activity Across Dose Levels



As of the data cutoff:

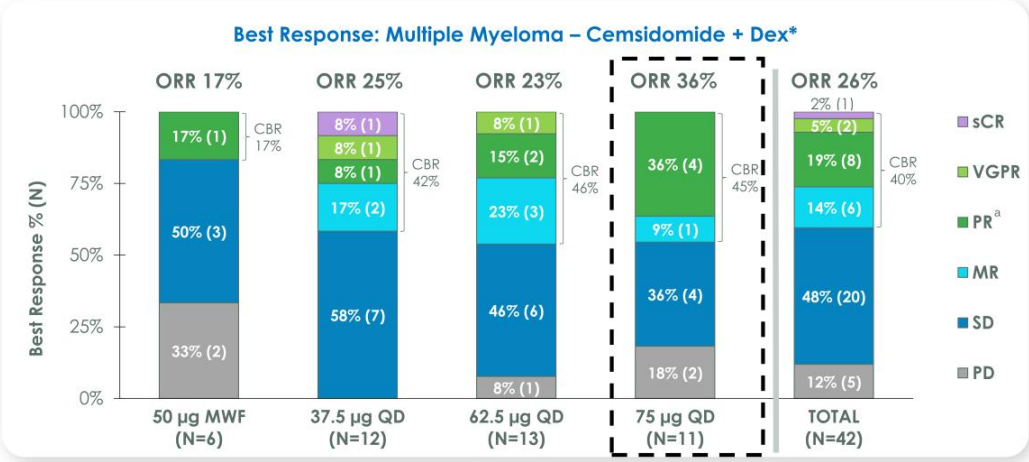
- **26% ORR** and **40% clinical benefit rate across all dose levels** evaluated
- At the two highest dose levels evaluated to date (62.5 µg and 75 µg), **62% of all patients remain on treatment**[1]

[a]1 patient in the 37.5 µg cohort achieved a PR based on light chains, no follow up M protein available; 1 patient in the 62.5 µg cohort had an unconfirmed PR as of the data cutoff date; 1 patient in the 75 µg cohort had an unconfirmed PR as of the data cutoff date.
[b] Patient came off study due to unrelated death. [1] Includes all 47 patients, including only safety evaluable patients.
Complete response (CR); minimal response (MR); Monday Wednesday Friday (MWF); non-evaluable (NE); once daily (QD); partial response (PR); progressive disease (PD); stable disease (SD); stringent complete response (sCR); T-cell-engaging antibodies (TCE); very good partial response (VGPR); Clinical Benefit Rate (≥ MR) (CBR)

C4 Therapeutics

Data cutoff: 10/11/24

75 µg Cemsidomide Dose Level Resulted in Compelling Anti-Myeloma Activity With a 36% ORR and 45% CBR



*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; 1 patient in the 62.5 µg cohort had an unconfirmed PR as of the data cutoff date; 1 patient in the 75 µg cohort had an unconfirmed PR as of the data cutoff date.
Minimal response (MR); Monday Wednesday Friday (MWF); once daily (QD); partial response (PR); progressive disease (PD); stable disease (SD); stringent complete response (sCR); very good partial response (VGPR)
Overall Response Rate (≥ PR) (ORR); Clinical Benefit Rate (≥ MR) (CBR)

C4 Therapeutics
Data cutoff: 10/11/24

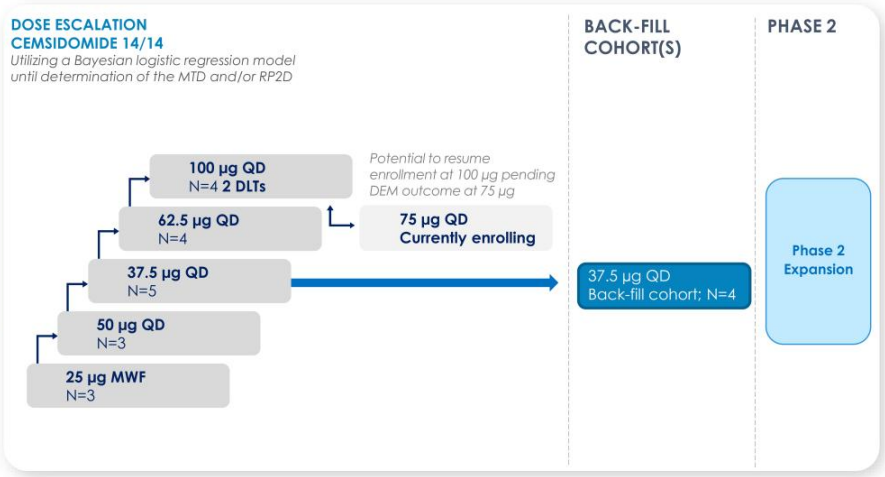
Dose Exploration Continues for the Cemsidomide Monotherapy Dose Escalation Trial in R/R NHL

KEY INCLUSION CRITERIA

- Adults with NHL, R/R to prior therapy
  - PTCL patients must have received at least 1 prior alkylator-based chemotherapy
  - ALCL patients must have also received a CD-30 mAb
- 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



Anaplastic large cell lymphoma (ALCL); dose escalation meeting (DEM); dose limiting toxicities (DLT); Eastern Cooperative Oncology Group (ECOG); monoclonal antibody (mAb); maximum tolerated dose (MTD); Monday Wednesday Friday (MWF); non-Hodgkin's lymphoma (NHL); once daily (QD); pharmacodynamic (PD); pharmacokinetic (PK); peripheral T-cell lymphoma (PTCL); recommended Phase 2 dose (RP2D); relapsed refractory (R/R)

C4 Therapeutics

Data cutoff date: 10/11/2024

Heavily Pre-Treated Population Where Majority of Patients Were Diagnosed With PTCL, Reflecting High Unmet Need

Characteristics	Safety Population (N=23)
Age, median (range)	68 (28-85 years)
Male, n (%)	14 (61)
Years since initial diagnosis, median (range)	2 (0.4-21)
ECOG performance status, n (%)	
0	11 (48)
1	9 (39)
2	2 (9)
Missing	1 (4)
Black or African American, n (%)	6 (26)
White, n (%)	13 (57)
Other, n (%)	4 (17)
IPI at screening, n (%)	
1	2 (9)
2	6 (26)
3	7 (30)
4	3 (13)
Missing	5 (22)

Characteristics	Safety Population (N=23)
Prior therapies, median (range)	3 (1-14)
1	2 (9)
2	7 (30)
3	3 (13)
≥4	11 (48)
PTCL, n (%)	17 (74)
PTCL-NOS	5 (22)
AITL	4 (17)
ALCL	3 (13)
ATLL	5 (22)
B-cell lymphoma, n (%)	6 (26)
DLBCL	4 (17)
MCL	1 (4)
MZL/MALT	1 (4)
Prior CAR-T therapy, n (%)	4 (17)
Prior HCT, n (%)	4 (17)
Autologous	3 (13)
Allogenic	1(4)

Angioimmunoblastic T-cell lymphoma (AITL); anaplastic large cell lymphoma (ALCL); adult T-cell leukemia/lymphoma (ATLL); diffuse large B-Cell lymphoma (DLBCL); Eastern cooperative oncology group (ECOG); hematopoietic cell transplantation (HCT); International Prognostic Index (IPI); mantle cell lymphoma (MCL); marginal zone lymphoma/mucosa-assisted lymphoid tissue (MZL/MALT); peripheral T-cell lymphoma (PTCL); PTCL-not otherwise specified (PTCL-NOS)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Is Well-tolerated With Manageable Incidents of On-target Neutropenia

- **2 DLTs occurred at 100 µg QD** (Grade 4 thrombocytopenia and Grade 3 febrile neutropenia)
- **TEAEs leading to discontinuation: 9%** (2/23)
- **39% (9/23) of patients received G-CSF**
  - 3 of 9 patients received G-CSF in Cycle 1

Common (>20% All Grades) TEAEs and Events of Interest*, n (%)	All Grade (N=23)	Grade 3 (N=23)	Grade 4 (N=23)
Infections	15 (65)	4 (17)	2 (9)
Upper respiratory tract infection	4 (17)	0	0
Sepsis	1(4)	0	1 (4)
Bacteremia	1(4)	0	1 (4)
Pneumonia	2 (9)	2 (9)	0
Neutropenia	11 (48)	4 (17)	7 (30)
Fatigue	11 (48)	1 (4)	0
Cough	7 (30)	0	0
Anemia	6 (26)	4 (17)	0
Peripheral edema	5 (22)	0	0
Febrile neutropenia*	4 (17)	4 (17)	0
Thrombocytopenia*	4 (17)	1 (4)	2 (9)
Maculopapular rash*	3 (13)	2 (9)	0

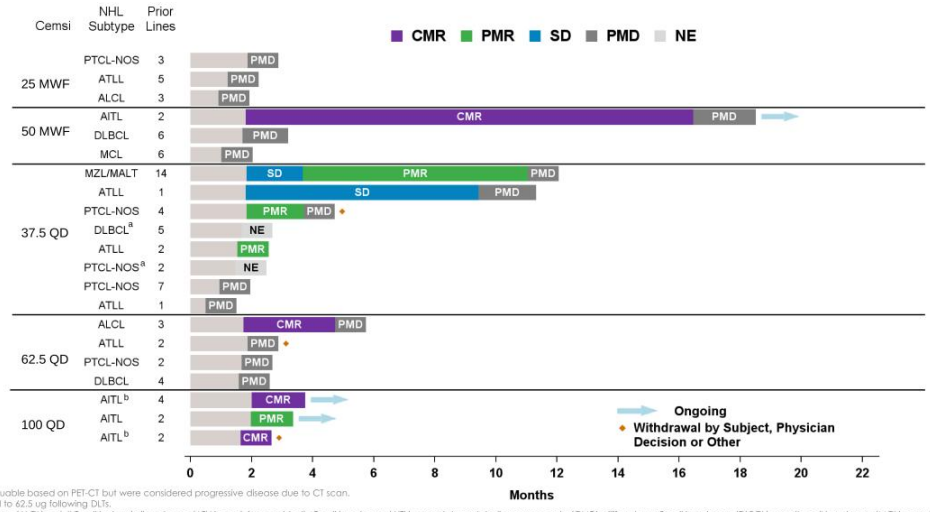
One patient experienced a Grade 5 AE (hip fracture resulting in transfer to hospice)

*Events of Interest
Adverse event (AE); dose limiting toxicities (DLTs); granulocyte colony-stimulating factor (G-CSF); once daily (QD); treatment emergent adverse events (TEAEs)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Clinical Responses Were Observed Across a Broad Range of Doses

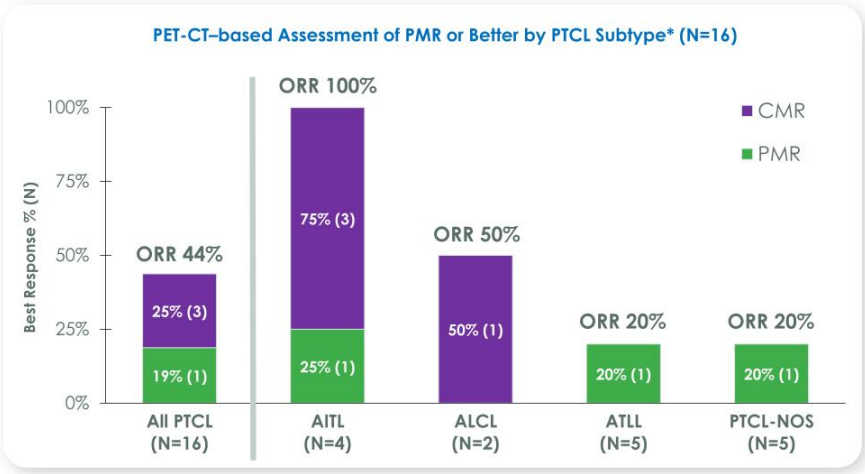


[a] Both patients were not evaluable based on PET-CT but were considered progressive disease due to CT scan.
[b] Both patients dose reduced to 62.5 ug following DLTs.
Anaplastic large cell lymphoma (ALCL); adult T-cell leukemia/lymphoma (ATLL); angioimmunoblastic T-cell lymphoma (AITL); complete metabolic response rate (CMR); diffuse large B-cell lymphoma (DLBCL); mantle cell lymphoma (MCL); marginal zone lymphoma/mucosa-assisted lymphoid tissue (MZL/MALT); Monday Wednesday Friday (MWF); non-evaluable (NE); once daily (QD); overall response rate (ORR); partial metabolic response (PMR); peripheral T-cell lymphoma (PTCL); PTCL-not otherwise specified (PTCL-NOS); progressive metabolic disease (PMD); stable disease (SD)

C4 Therapeutics

Data cutoff: 10/11/24

Compelling and Deep Responses Achieved Across PTCL Subtypes



- Cemsidomide monotherapy **produced responses in all four PTCL subtypes**
- **All AITL patients (4/4)** experienced **a metabolic response**

*Investigator assessed response; 2 patients were evaluated based on CT scan and were PD but not evaluable based on PET-CT, both patients are included as PMD for PET-CT based assessment; 2 additional subjects that came off study prior to follow up scans were not considered efficacy evaluable.
Angioimmunoblastic T-cell lymphoma (AITL); anaplastic large cell lymphoma (ALCL); adult T-cell lymphoma (ATLL); complete metabolic response (CMR); overall response rate (ORR); partial metabolic response (PMR); peripheral T-cell lymphoma (PTCL); peripheral T-cell lymphoma not-otherwise specified (PTCL-NOS)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Is Positioned to Potentially Be a Best-in-Class Therapy in Two Distinct Indications With Opportunities Across Multiple Lines of Therapy

IKZF1/3 is a fundamental target for MM and NHL and data supports cemsidomide as a potential backbone therapy within the evolving treatment landscape

- Well-tolerated with a compelling safety profile
- Compelling anti-tumor activity across a range of dose levels

MM Market Opportunity

Estimated ~$42B by 2030[1]

NHL Market Opportunity

Estimated ~$30B by 2030[1]

[1]Souce: Evaluate Pharma.
Multiple myeloma (MM); non-Hodgkin's lymphoma (NHL)

C4 Therapeutics

CFT1946

Targeting BRAF V600 Mutant

Melanoma, Colorectal (CRC)
& Non-Small Cell Lung Cancer (NSCLC)

C4 Therapeutics

CFT1946 Has the Potential to Overcome Several Shortcomings Seen With Inhibitors for BRAF V600X Cancers

Key Limitations of Approved BRAF Inhibitors:

- **Durable and deep responses are often not seen** in melanoma, NSCLC and CRC patients, due to **MAPK pathway resistance**
- **Poor tolerability**, such as high-rates of cutaneous adverse events
- Often **combined with a MEK inhibitor** to **enhance both efficacy and minimize side effects resulting from paradoxical activation** by BRAF inhibitors
- **Limited approved treatment options** for BRAF V600 **patients who do not have a BRAF V600E or V600K mutation**

Despite limitations, current BRAF inhibitor market is **~$2B**[2]

BRAF inhibitor market is estimated to grow to **~$3B by 2028**[2]

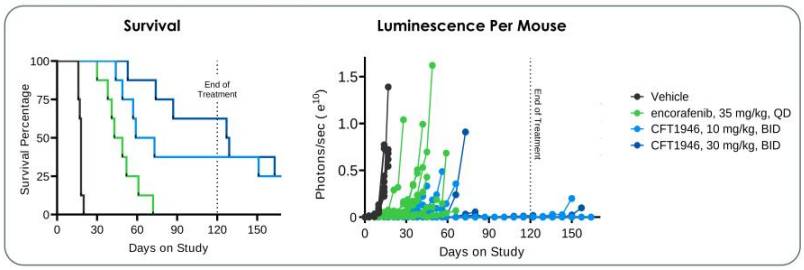
Potential Advantages of CFT1946, a Novel, Oral, BRAF V600 Mutant BiDAC degrader:

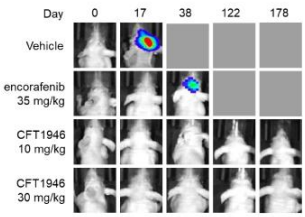
- ✓ Prevents BRAF V600 mutant **mono/heterodimer formation**[1]
- ✓ **Avoids paradoxical activation** seen with approved inhibitors[1]
- ✓ **Addresses MAPK pathway alterations** resulting from BRAF inhibitor resistance (e.g., BRAF splice variants, BRAF amplification)[1]
- ✓ **Specifically targets BRAF V600 mutations**, which includes BRAF V600 mutations beyond BRAF V600E
- ✓ Spares wild-type BRAF[1], likely **avoiding AEs associated with inhibition of wild-type BRAF**
- ✓ Enables deep elimination of mutant BRAF signaling to **create potential durable responses** through degrader molecule recycling and catalytic effect

[1]Kreger B et al. Abstract 1658. AACR 2024; [2]Evaluate Pharma 2023
Adverse event (AE); Mitogen-activated protein kinase (MAPK)

$Kp_{U,U}$ Results Demonstrate CFT1946's Ability to Cross the Blood-Brain Barrier and Support Activity in Preclinical Intercranial Metastatic Models

A375 BRAF V600E-Luc Intracranial Model





$Kp_{U,U}$ values for CFT1946 were experimentally measured using independent methods in two different species

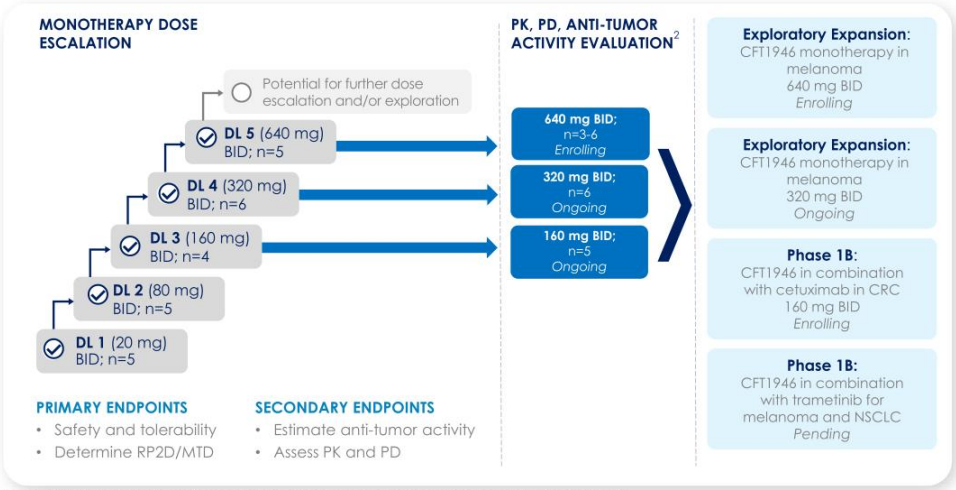
The CFT1946 values of $Kp_{U,U}$ range from 0.34 – 0.88

These results demonstrate the ability of CFT1946 to cross the blood-brain barrier and highlight the potential for drug delivery to CNS tumors

CFT1946 Phase 1/2 Dose Escalation Trial Continues to Progress Across BRAF V600 Mutant Driven Solid Tumors

KEY INCLUSION CRITERIA[1]

- Evidence of BRAF V600 mutation obtained from tumor tissue or liquid biopsy
- BRAF V600 mutant measurable solid tumors with ≥1 prior line of SoC therapy for unresectable locally advanced or metastatic disease
- Melanoma patients must have received prior BRAF inhibitor therapy
- CRC, ATC, NSCLC or other non-CNS solid tumors: prior BRAF inhibitor therapy unless not available per SoC
- No patient with CNS involvement (primary tumor or metastatic disease), except if clinically stable



[1]NCT05668585. www.clinicaltrials.gov. Accessed 01/09/2024; [2]Evaluating additional patients for pharmacodynamic assessment pre- and post-drug exposure biopsies
Colorectal cancer (CRC); Anaplastic thyroid cancer (ATC); Non-small cell lung cancer (NSCLC); Central nervous system (CNS); Standard of care (SoC); Dose Level (DL); Twice daily (BID); Recommended Phase 2 dose (RP2D); Maximum tolerated dose (MTD); Pharmacokinetic (PK); Pharmacodynamic (PD)

CFT1946 Monotherapy Phase 1 Data Demonstrated Proof of Mechanism and Provided Early Evidence of Proof of Degrader Concept

Proof of Mechanism

- **Well tolerated** and **selective degrader**, resulted in **no Grade ≥ 3 cutaneous adverse events**, which are commonly seen with wild-type BRAF inhibition
- **Increased drug exposure** observed with dose escalation
- **Degraded BRAF V600E** protein in all available post-treatment biopsies collected to date

Proof of Degrader Concept

- Early evidence of monotherapy **anti-tumor activity** in patients who progressed after treatment with BRAF inhibitors
- Anti-tumor activity seen **across multiple BRAF V600 mutants**
- Degradation of mutant BRAF protein overcame resistance mechanisms and resulted in potentially **deeper** and more **durable responses than BRAF inhibitors**

CFT1946 has the potential to **disrupt the treatment landscape** and become an **important option for patients** with **BRAF V600 mutant driven solid tumors**

Well-Tolerated Monotherapy Safety Profile, Consistent With BRAF V600 Mutant Selectivity Design of CFT1946

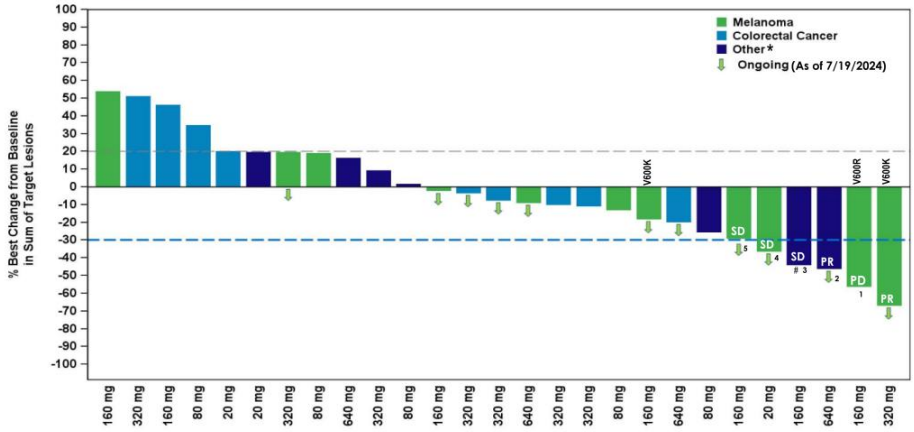
- No DLTs
- Majority of TEAEs observed were mild to moderate
- No treatment-related SAEs
- No Grade ≥ 3 treatment-related cutaneous adverse events
- No new primary malignancies

Summary of TEAEs ≥ 10% of 36 patients treated with CFT1946

Preferred Term	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	Total (n=36) n (%)
Patients with any TEAEs^	3 (8)	14 (39)	11 (31)	2 (6)	1 (3)#	31 (86)
Anemia	1 (3)	4 (11)	2 (6)	0	0	7 (19)
Abdominal pain	4 (11)	1 (3)	2 (6)	0	0	7 (19)
Peripheral edema	5 (14)	1 (3)	0	0	0	6 (17)
Pyrexia	4 (11)	2 (6)	0	0	0	6 (17)
Fatigue	1 (3)	4 (11)	0	0	0	5 (14)
Lipase increased	3 (8)	2 (6)	0	0	0	5 (14)
Back pain	1 (3)	2 (6)	1 (3)	0	0	4 (11)
Hypophosphatemia	1 (3)	3 (8)	0	0	0	4 (11)
Constipation	1(3)	2 (6)	0	0	0	4 (11)*

^A patient is only counted once with the highest severity and preferred term
#Patient had a fatal cerebrovascular accident not related to CFT1946
CTCAE v5.0 grading criteria; *Grade missing for 1 patient with TEAE
Serious adverse events (SAEs); Dose limiting toxicities (DLTs); Treatment-emergent adverse events (TEAEs)
Source: ESMO Congress 2024; C4T data as of 7/19/2024

Early Signs of CFT1946 Anti-tumor Activity: 59% of Patients Demonstrated Target Lesion Tumor Reductions



*Other tumor types include cholangiocarcinoma, non-small cell lung cancer, pancreatic carcinoma, and small intestine cancer; BRAF V600 mutation is V600E unless otherwise specified; #This patient did not receive prior BRAF inhibitor therapy, all other patients received prior BRAF inhibitor therapy. Dotted lines represent partial response (-30%, blue line) and progressive disease (20%, gray line) per RECIST v1.1.
[1] Patient on 160 mg BID had 56.2% reduction on target lesion, progression on non-target lesion and a new lesion, hence assessed as PD for overall response; [2] Patient on 640 mg BID had PR confirmed after data cut off, and as of ESMO Congress (9/13/2024); [3] Patient on 160 mg BID had PD following first PR (-43.9%), hence assessed as SD for overall response; [4] Patient on 20 mg BID had unconfirmed PR, hence assessed as SD for overall response; [5] Patient on 160 mg BID had -29% reduction on target lesion, hence assessed as SD

Source: ESMO Congress 2024; C4T data on file as of 7/19/2024

CFT1946 Has the Potential to Address Multiple Tumor Types With BRAF V600X Mutations Where BRAF Inhibitors Are Insufficient

	BRAF V600X Mutation Rate	2023 U.S. Incidence of BRAF V600X Patients[4]	Approved BRAF Inhibitors	BRAF Inhibitor Regimen mPFS[5]
Melanoma	~35%[1]	~35,000	• Dabrafenib • Encorafenib • Vemurafenib *All used in combination with MEK inhibitors*	**11.4 months** (dabrafenib + trametinib in 1L+)
Colorectal Cancer	5-10%[2]	~11,000	• Encorafenib *Used in combination with cetuximab (anti-EGFR)*	**4.2 months** (encorafenib + cetuximab in 2L+)
Non-Small Cell Lung Cancer	1-2%[3]	~3,000	• Dabrafenib • Encorafenib *Both used in combination with MEK inhibitors*	**15.2 months** (dabrafenib + trametinib in 2L+)

[1] Owsley 2021 Exp Biol Med. [2] Paik 2011 J Clin Oncol. [3] Bylsma 2020 Cancer Med. [4] NCI SEER; consulting work done by Health Advances. [5] FDA labels

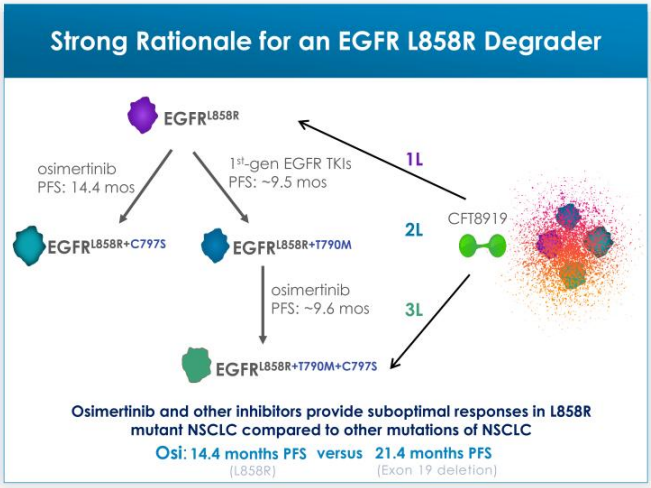
CFT8919

Targeting EGFR L858R

Non-Small Cell Lung Cancer (NSCLC)

C4 Therapeutics

Potential for CFT8919 to Improve Outcomes for NSCLC Patients With EGFR L858R Mutations



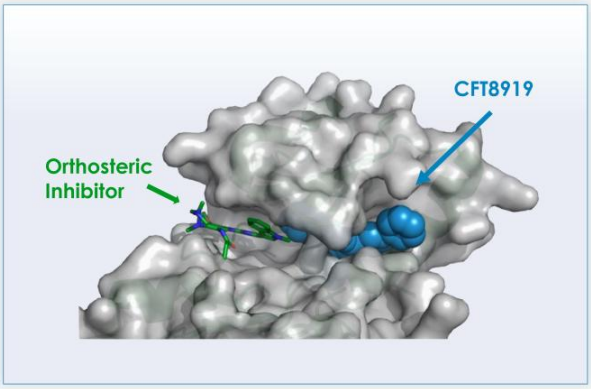
CFT8919 Key Properties
- Orally bioavailable
- Potent and selective against L858R, regardless of secondary mutations
- Allosteric binding

Market Size
- ~$6B approved EGFR inhibitor market[1]

Progress to Date
- Achieved FDA clearance of U.S. IND
- Betta received CTA clearance from China's NMPA

Non-small cell lung cancer (NSCLC); Tyrosine Kinase Inhibitor (TKI); Osimertinib (Osi); Investigational New Drug (IND); Clinical Trial Application (CTA)
Sources: Soria, J.C. et al. NEJM 378, 113–125 (2018); Sher, T. et al. Mayo Clin. Proc. 83, 355-367 (2008); 1. 2023 market size from EvaluatePharma.

CFT8919 is a Potent, Oral, Allosteric, Mutant-selective Degrader of EGFR L858R

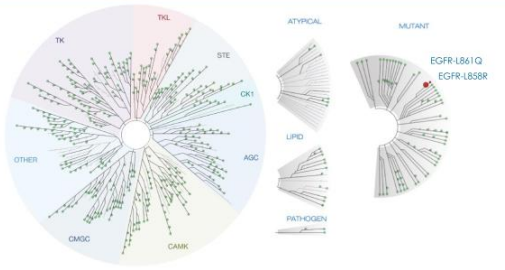


- CFT8919 exploits **allosteric binding site**, close to L858R activating mutation
- Allosteric binding site avoids known resistance-causing mutations in **orthosteric binding site**
- Allosteric binders do not require covalent binding through C797S and do not compete with orthosteric binding

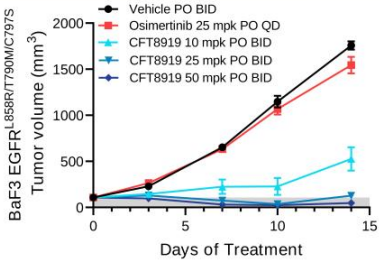
Allosteric binding avoids resistance mutations, wild-type activity, and is combinable with orthosteric inhibitors

CFT8919 is Selective for EGFR L858R and Active in a Setting of Osimertinib Resistance in Preclinical Models

Specific for EGFR Exon 21 Mutants



Active in setting of EGFR C797S



Source: C4T data on file; Keystone Symposium 2021 Investigational New Drug Application (IND)

C4T Is Progressing Multiple Clinical and Preclinical Programs

Cemsidomide IKZF1/3	**ASH 2024 (Dec.):** Presented updated data from Phase 1 dose escalation +dex trial in R/R MM **ASH 2024 (Dec.):** Presented data from Phase 1 dose escalation monotherapy trial in R/R NHL
CFT1946 BRAF V600 Mutant	**2Q 2024:** Presented preclinical data demonstrating differentiated activity in BRAF V600 mutant driven melanoma, CRC, NSCLC, and brain metastasis models at AACR **ESMO Congress 2024:** Presented monotherapy data from Phase 1 dose escalation trial in melanoma, CRC, NSCLC and other BRAF V600 mutant driven cancers
CFT8919 EGFR L858R	**2024:** Supported trial start-up activities related to Betta's Phase 1 dose escalation trial in China
Discovery	**1Q 2024:** Launched collaboration with Merck KGaA, Darmstadt, Germany to discover two targeted protein degraders against critical oncogenic proteins **2024:** Delivered development candidate to collaboration partner

Expected Runway Into 2027[1], Beyond Value Inflection Milestones

Relapsed or refractory multiple myeloma (R/R MM); Relapsed or refractory non-Hodgkin lymphoma (R/R NHL); Colorectal cancer (CRC); Non-small cell lung cancer (NSCLC)
[1] As of December 9, 2024