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): January 14, 2025

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 2.02 Results of Operations and Financial Condition.

On January 14, 2025, C4 Therapeutics, Inc. (the "**Company**") disclosed that its unaudited cash, cash equivalents, and marketable securities as of December 31, 2024, will enable the Company to fund its operating plan into 2027.

The information contained in Item 2.02 of this Form 8-K is unaudited and preliminary and does not present all information necessary for an understanding of the Company's financial condition as of December 31, 2024 and its results of operations for the three months and year ended December 31, 2024. The audit of the Company's consolidated financial statements for the year ended December 31, 2024 is ongoing and could result in changes to the information set forth above.

The information contained in Item 2.02 of this Current Report on Form 8-K is being furnished and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), or otherwise subject to the liabilities of that section and shall not be incorporated by reference in any filing under the Securities Act of 1933, as amended (the "**Securities Act**"), or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 7.01 Regulation FD Disclosure.

On January 14, 2025, the Company issued a press release announcing its key milestones anticipated for 2025 and also that it will present at the 43rd Annual J.P. Morgan Healthcare Conference on Wednesday, January 15, 2025 at 2:15 pm PST (5:15 pm EST), with a live webcast that will be available for viewing under "Events & Presentations" on the Investors page of the Company's website at www.c4therapeutics.com. A replay of the webcast will be made available on the Company website for at least two weeks. A copy of the press release is furnished herewith as Exhibit 99.1 to this Current Report on Form 8-K.

On January 14, 2025, the Company also posted a corporate presentation on its website at https://ir.c4therapeutics.com/events-presentations. A copy of the presentation is furnished herewith as Exhibit 99.2 to this Current Report on Form 8-K.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.1 and 99.2 attached hereto, is being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that Section, nor shall it be deemed subject to the requirements of amended Item 10 of Regulation S-K, nor shall it be deemed incorporated by reference into any filing of the Company under the Securities Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing. The furnishing of this information hereby shall not be deemed an admission as to the materiality of any such information.

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	Press release issued January 14, 2025
99	Corporate presentation of the Company dated January 2025
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: January 14, 2025

By: /s/ Jolie M. Siegel

Jolie M. Siegel

Chief Legal Officer and Secretary

Exhibit 99.1

C4 Therapeutics Announces 2025 Milestones Across Clinical Portfolio of Degrader Medicines Pursuing Targets of High Unmet Need in Oncology

Cemsidomide Data Presented at American Society of Hematology (ASH) Annual Meeting Support Best-in-Class Profile; Program Advancing to Next Phase of Clinical Development in Multiple Myeloma and Non-Hodgkin's Lymphoma

CFT1946 Phase 1 Trial Continues to Progress in BRAF V600X Solid Tumors With Monotherapy Dose Escalation Expected to Complete in 1H 2025; Data in Melanoma and Colorectal Cancer Expected in Second Half of 2025

CFT8919 Progressing Through Phase 1 Dose Escalation in Greater China; Phase 1 Data Will Inform Future Development Plans Outside of China

Cash Runway Expected to Fund Operations Into 2027

WATERTOWN, Mass., January 14, 2025 (GLOBE NEWSWIRE) -- C4 Therapeutics, Inc. (C4T) (Nasdaq: CCCC), a clinical-stage biopharmaceutical company dedicated to advancing targeted protein degradation science, today announced its anticipated 2025 milestones as it continues its evolution into becoming a fully integrated biotechnology company focused on orally bioavailable degraders.

"Stellar execution in 2024 has set up 2025 to be a pivotal year for the company as we work to generate important data that will position us to advance programs and bring degrader medicines to patients searching for new therapeutic options," said Andrew Hirsch, president and chief executive officer of C4 Therapeutics. "The cemsidomide data presented at the ASH Annual Meeting in December support a potentially best-in-class profile and we are preparing for the next phase of development of this molecule. We continue to progress the CFT1946 Phase 1/2 study and will leverage data from the tumor specific cohorts to determine the development path for this program. In addition, we expect data from the CFT8919 Phase 1 dose escalation study run by our partner Betta Pharmaceuticals in China, which will define its potential for non-small cell lung cancer patients with the EGFR L858R mutation. We are excited about the degrader rationale for these programs, which we believe have the potential to deliver value for patients, caregivers, physicians and shareholders."

ANTICIPATED 2025 MILESTONES

Cemsidomide: Cemsidomide is an oral degrader of IKZF1/3 for the potential treatment of relapsed/refractory (R/R) multiple myeloma (MM) and R/R non-Hodgkin's lymphoma (NHL).

Multiple Myeloma

- Enable initiation of the next phase of clinical development to investigate cemsidomide in combination with dexamethasone in the late-line setting, and in combination with other MM agents for earlier lines of treatment. These new studies are expected to initiate in early 2026.
- Complete Phase 1 dose escalation and present data in the second half of 2025.

Non-Hodgkin's Lymphoma

- Complete Phase 1 dose escalation and present data in the second half of 2025.
- Open expansion cohort(s) of the current Phase 1/2 trial in patients with peripheral T-cell lymphoma (PTCL) in the second half of 2025.

- Enable initiation of the next phase of clinical development to investigate cemsidomide monotherapy in later lines of therapy in PTCL. This new study is expected to initiate in early 2026.

CFT1946: CFT1946 is an oral degrader targeting BRAF V600 mutations for the potential treatment of solid tumors including colorectal cancer (CRC), melanoma and other malignancies with V600 mutations.

- Complete monotherapy Phase 1 dose escalation in BRAF V600 mutant solid tumors in the first half of 2025.
- Generate data from the Phase 1 cohorts exploring monotherapy CFT1946 in melanoma, CFT1946 in combination with cetuximab in CRC and CFT1946 in combination with trametinib in melanoma. Data from these cohorts will define and enable the next phase of development.
- Present Phase 1 data in the second half of 2025. These presentations will include: (1) monotherapy in BRAF V600 mutant solid tumors, (2) monotherapy expansion cohorts in melanoma, and (3) in combination with cetuximab in CRC.

CFT8919: CFT8919 is an oral degrader targeting EGFR bearing an oncogenic L858R mutation for the potential treatment of non-small cell lung cancer (NSCLC).

- Evaluate data from the Phase 1 dose escalation study in Greater China, which is led by partner Betta Pharmaceuticals, in patients with locally or advanced metastatic NSCLC harboring an EGFR L858R mutation. These data will be used to determine the next phase of development.

Discovery: C4T will continue to utilize its TORPEDO® platform to develop orally bioavailable degraders for oncology and non-oncology targets for internal research and collaboration programs. To further highlight its deep expertise in drug discovery, C4T plans to:

- Present and publish preclinical work from its internal pipeline and TORPEDO® platform.
- Advance internal and collaboration programs to key milestones.

2024 ACCOMPLISHMENTS

Cemsidomide: C4T advanced the Phase 1/2 clinical trial and delivered data reinforcing the potential of cemsidomide to become a backbone therapy of choice in MM and NHL where IKZF1/3 degradation is warranted.

Multiple Myeloma

- At ASH, presented data on cemsidomide in combination with dexamethasone. As of the data cutoff date of October 11, 2024, the dose level exploring 75 µg once daily (QD) achieved an overall response rate (ORR) of 36 percent. Cemsidomide was well-tolerated across all dose levels.
- The maximum tolerated dose has not yet been reached. Patients are enrolling in the 100 µg QD cohort.

Non-Hodgkin's Lymphoma

- At ASH, presented data on cemsidomide monotherapy. As of the data cutoff date of October 11, 2024, cemsidomide demonstrated a 38 percent ORR across all subtypes and doses studied. In PTCL, cemsidomide achieved a 44 percent ORR and a 25 percent complete metabolic response rate.

- The maximum tolerated dose has not yet been reached. Patients are enrolling in the 75 µg QD cohort.

CFT1946: C4T advanced the Phase 1/2 clinical trial across multiple arms and delivered monotherapy data demonstrating proof of mechanism and early evidence of proof of concept.

- At the European Society of Medical Oncology (ESMO) Congress, presented monotherapy data demonstrating CFT1946 is well tolerated across all dose levels and demonstrates initial signs of anti-tumor activity across all dose levels.
- At the TPD Summit, presented new preclinical data demonstrating CFT1946 has the ability to cross the blood-brain barrier, with $Kp_{u,u}$ values in the range of 0.34 to 0.88.
- Progressed the Phase 1 monotherapy dose escalation study. Began enrolling patients across multiple exploratory cohorts: CFT1946 monotherapy in melanoma, CFT1946 in combination with trametinib in melanoma, and CFT1946 in combination with cetuximab in CRC.

CFT8919: Betta Pharmaceuticals, with C4T support, initiated the Phase 1 clinical trial of CFT8919 in Greater China.

Discovery: C4T further validated its TORPEDO® platform and advanced key research efforts.

- Delivered two development candidates for non-oncology targets to collaborator Biogen.
- Established a new collaboration with Merck KGaA, Darmstadt, Germany focused on two critical oncogenic proteins.
- Continued to progress its internal discovery portfolio of orally bioavailable degraders.

Corporate: C4T further strengthened its leadership across its management team and Board of Directors to supports its evolution into a fully integrated biotechnology company.

- Paige Mahaney, Ph.D., was appointed chief scientific officer. Dr. Mahaney is an experienced drug developer who has helped leading pharmaceutical companies build clinical portfolios across a wide range of disease indications and treatment modalities.
- C4T continued to evolve its governance by appointing three new members to its Board of Directors who bring deep experience across drug discovery, commercialization and lifecycle management.

Cash Guidance

C4T expects that its cash, cash equivalents and marketable securities as of December 31, 2024, together with anticipated collaboration expense reimbursements, but excluding any collaboration option or milestone payments, will enable the company to fund its operating plan into 2027.

JP Morgan Presentation

C4T will present at the 43rd Annual J.P. Morgan Healthcare Conference on Wednesday, January 15, 2025 at 2:15 pm PST (5:15 pm EST). A live webcast will be available under “Events & Presentations” in the Investors section of the company’s website at www.c4therapeutics.com. A replay of the webcast will be archived on the C4T website for at least two weeks following the presentation.

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.

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 CFT1946

CFT1946 is an investigational, orally bioavailable brain penetrant small molecule degrader of BRAF V600 mutations in solid tumors currently being evaluated in a Phase 1/2 global clinical trial in patients refractory to BRAF inhibitors. CFT1946 is designed to be potent and selective against the BRAF V600 mutant form. Initial clinical data from the Phase 1 trial demonstrate that CFT1946 has a well-tolerated safety profile, demonstrates dose-dependent bioavailability and degradation of BRAF V600E protein, and demonstrates evidence of monotherapy anti-tumor activity. CFT1946 is the only degrader of BRAF V600 mutant solid tumors in clinical trials. More information about this trial may be accessed at www.clinicaltrials.gov (identifier: NCT05668585).

About CFT8919

CFT8919 is an orally bioavailable allosteric degrader that is designed to be potent and selective against EGFR bearing an oncogenic L858R mutation. In preclinical studies, CFT8919 is active in *in vitro* and *in vivo* models of L858R driven non-small cell lung cancer. Importantly, CFT8919 retains full activity against additional EGFR mutations that confer resistance against approved EGFR inhibitors including L858R-C797S, L858R-T790M, and L858R-T790M-C797S.

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 anticipated timing and content of presentations of data from our clinical trials; 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 sufficient capital to fund our future operations will be available to us on acceptable terms or at the times required. 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.

Contacts:
Investors:
Courtney Solberg
Senior Manager, Investor Relations
CSolberg@c4therapeutics.com

Media:
Loraine Spreen
Senior Director, Corporate Communications & Patient Advocacy
LSpreen@c4therapeutics.com

C4 Therapeutics

Protein degraded.
Disease targeted.
Lives transformed.

January 2025

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.

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.

C4 Therapeutics

Our Mission

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

Our portfolio of degrader medicines pursues targets that may benefit from a degrader approach:

Cemsidomide
targeting IKZF1/3 for multiple myeloma and non-Hodgkin's lymphoma

CFT1946
targeting BRAF V600 mutant for solid tumors including melanoma & colorectal cancer

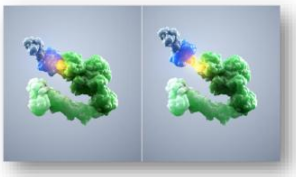
CFT8919
targeting EGFR L858R for non-small cell lung cancer

Internal Discovery Pipeline
targets with unmet need and strong degrader rationale

C4T Has Been at the Forefront of TPD Science and Is On the Path to Becoming a Fully Integrated Biotechnology Company

Leading the Way in Designing Orally Bioavailable Degraders

2015 – 2020



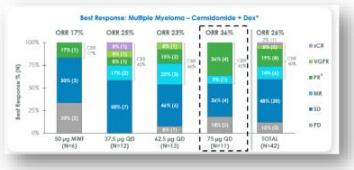
Built TORPEDO platform to design highly catalytic, orally bioavailable degraders

Established collaborations with leading global pharmaceutical companies, building expertise across a range of diseases and target classes

Assembled strong catalog of intellectual property

Demonstrating Proof of Concept

2020 – 2025



Progressed four development candidates into clinical trials, including three trials underway today

Delivered two development candidates to a collaborator for non-oncology targets

Achieved blood-brain barrier penetration in several development candidates

Delivering on the Promise of Targeted Protein Degradation

2025 and beyond

Advancing clinical programs to approval for patients with high unmet needs

Leveraging TORPEDO platform to develop a sustainable pipeline against targets of high unmet need with strong degrader rationale in large commercial markets

Expanding application of targeted protein degradation through high-value collaborations

C4T Is Advancing a Portfolio of Rationally Designed Degraders Against Targets of High Unmet Need in Oncology

	Cemsidomide Targeting IKZF1/3 *Transcription Factor*	**CFT1946** Targeting BRAF V600X *Scaffolding Kinase*	**CFT8919** Targeting EGFR L858R *Receptor Tyrosine Kinase*
Degrader Rationale	Approved IKZF1/3 degraders were not rationally designed and provide less than optimal potency and selectivity	Degradation has the potential to avoid resistance mechanisms and enable a longer duration of response	Degradation facilitates targeting an allosteric L858R-specific binding site distinct from current inhibitors leading to increased selectivity over wild-type, activity against inhibitor resistance mutations & an opportunity for use in conjunction with current SOC
Clinical Progress	**Data to date supports best-in-class profile:** ✓ Differentiated safety profile ✓ Competitive ORR in combination with dex at 75 µg in MM ✓ Immune activity demonstrated as monotherapy ✓ Encouraging ORR and CMR rate in PTCL	**Data to date demonstrates:** ✓ Proof of mechanism established ✓ Early signs of anti-tumor activity in Phase 1 dose escalation	✓ Clinical trial initiated in Greater China[1]
Potential Patient Population	**Across U.S., EU4 and UK:** • **MM:** ~65,000[2] • **PTCL:** ~16,000[2]	**Across U.S., EU4 and UK:** • **Melanoma:** ~66,000[3] • **Colorectal cancer:** ~33,000[3]	**Across U.S., EU4, UK and China:** • **EGFR L858R Mutated NSCLC:** ~219,000[4]
Commercial Rights			

TORPEDO platform has produced highly catalytic, brain penetrant, oral degraders across a broad range of target classes

[1]License and collaboration agreement with Betta Pharmaceuticals for development and commercialization in Greater China
[2] NCI SEER, consulting engagements with Health Advances and Clearview.
[3]2024 Evaluate Ltd. US + EU4 + UK population
[4] EvaluatePharma, consulting engagements with Health Advances and Clearview.
Complete metabolic response (CMR); dexamethasone (dex); multiple myeloma (MM); Overall response rate (ORR); peripheral T-cell lymphoma (PTCL); Germany, Italy, France, and Spain (EU4); Standard of care (SOC)

C4 Therapeutics

Multiple 2025 Data Based Inflection Points to Unlock Value Across Entire Portfolio

Cemsidomide *IKZF1/3*	**2025:** Enable initiation of the next phase of clinical development for MM and PTCL. These new studies are expected to initiate in early 2026 **2H 2025:** Complete Phase 1 dose escalation trial in MM and NHL and present data **2H 2025**: Open expansion cohort(s) in PTCL in the ongoing Phase 1/2 trial
CFT1946 *BRAF V600 Mutant*	**1H 2025:** Complete monotherapy Phase 1 dose escalation trial in BRAF V600 mutant solid tumors **2H 2025:** Generate data from Phase 1 cohorts evaluating CFT1946 as a monotherapy in melanoma, in combination with trametinib in melanoma, and in combination with cetuximab in CRC to define and enable next phase of development **2H 2025:** Present Phase 1 data: monotherapy in BRAF V600 mutant solid tumors; monotherapy expansion cohorts in melanoma; combination with cetuximab in colorectal cancer
CFT8919 *EGFR L858R*	**Year-end 2025**: Utilize data from Phase 1 dose escalation trial in Greater China to inform ex-China clinical development
Discovery	**2025:** Present and publish preclinical work from internal pipeline and TORPEDO platform **2025:** Advance internal and collaboration programs to key discovery milestones

Multiple myeloma (MM); peripheral T-cell lymphoma (PTCL), a subtype of NHL

Advancing a Portfolio of Degrader Medicines Targeting Areas of High Unmet Need

PROGRAM	TARGET	INDICATIONS	DISCOVERY	PRECLINICAL	EARLY DEVELOPMENT	LATE DEVELOPMENT	RIGHTS
Cemsidomide	IKZF1/3	Multiple Myeloma & Non-Hodgkin's Lymphoma	MM, NHL				
CFT1946	BRAF V600 Mutant	V600 Mutant Cancers	CRC, Melanoma, Other BRAF V600 Mutant Cancers				
CFT8919[1]	EGFR L858R	Non-Small Cell Lung Cancer					BETTA
Discovery Stage Programs		Various Cancers					

[1]License and collaboration agreement with Betta Pharmaceuticals for development and commercialization in Greater China

Advancing Multiple Oncology and Non-oncology Discovery Programs with Collaboration Partners

Roche	Merck KGaA Darmstadt, Germany	MERCK	Biogen
• Evaluating two targets in autoimmune diseases & cancer	• Discovering targeted protein degraders against critical oncogenic proteins	• Discovering and developing degrader antibody conjugates in oncology	• Delivered two development candidates for non-oncology targets[1]

[1]Delivered development candidates to Biogen in Q1 2024 and Q3 2024

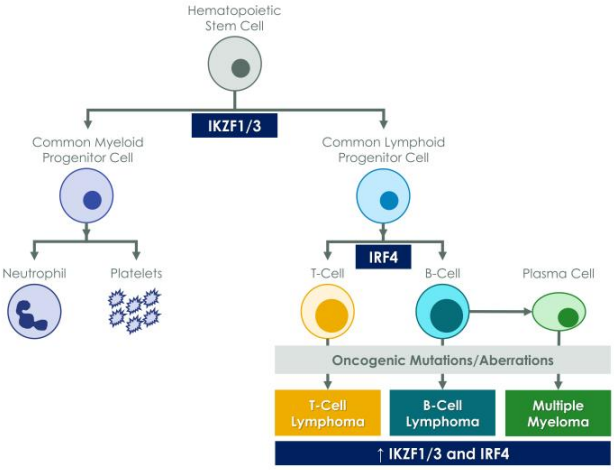
Cemsidomide

IKZF1/3 Degrader

Multiple Myeloma & Non-Hodgkin's Lymphoma

C4 Therapeutics

IKZF1/3 Are Key Promoters of Myeloma and Lymphoma Cell Survival and Will Remain Important Therapeutic Targets for These Indications



Key Roles of IKZF1/3:

- Multiple myeloma and lymphoma cells rely on **IKZF1/3** and **IRF4** for survival
- Degrading **IKZF1/3** leads to down regulation of **IRF4**, promoting myeloma and lymphoma cell death and on-target neutropenia
- **IKFZ1/3** degradation combined with MM immune-based regimens have potential to enhance activity through T-cell activation and cancer cell death by downregulation of **IRF4**

Degrader Advantages of Cemsidomide:

- ✓ Cemsidomide is more potent than approved and development stage IKZF1/3 degraders
- ✓ Increased selectivity for IKZF1/3 resulting in reduced off-target toxicity

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

C4 Therapeutics

Cemsidomide Phase 1 Dose Escalation Trial in MM Continues to Progress; Have Not Exceeded the Maximum Tolerated Dose

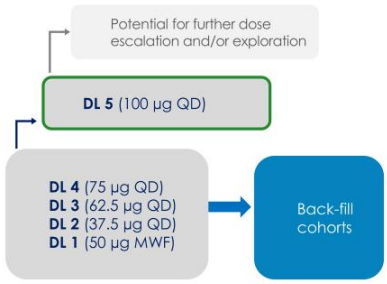
KEY INCLUSION CRITERIA

- 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.
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)

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

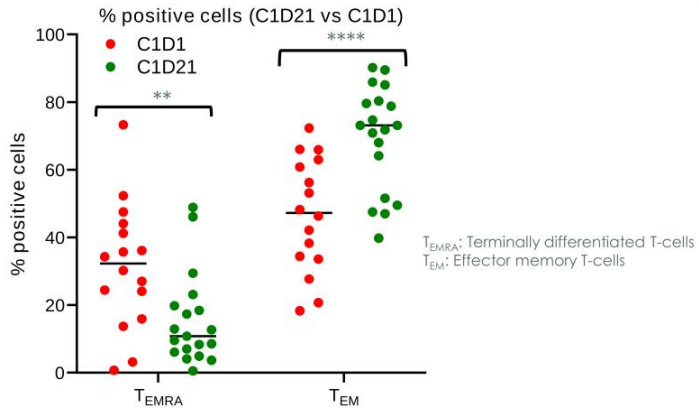
U.S. + EU4 + UK Addressable Patients (2024)	~65,000	~56,000	~49,000	~42,000	≥23,000
Treatment Line	1L	2L	3L	4L	5L+

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 dexamethasone combos, anti-SLAMF7 mAbs and XPO1 inhibitors. Potential future treatment options include FcRH5 bispecific T-cell engagers, BCL-2 inhibitors, and others.
Sources: EvaluatePharma (accessed 1/8/25), 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); Germany, Italy, France, and Spain (EU4)

Clinical Evidence of Immune T-cell Activation With Cemsidomide Monotherapy



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

Supports potential of cemsidomide as a maintenance therapy option and in combination with other 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 (MWF); multiple myeloma (MM)
Source: C4T data on file as of 11/28/2023 (https://ir.c4therapeutics.com/static-files/ec59b02e-3074-484d-ad88-e81831bf37ed)

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

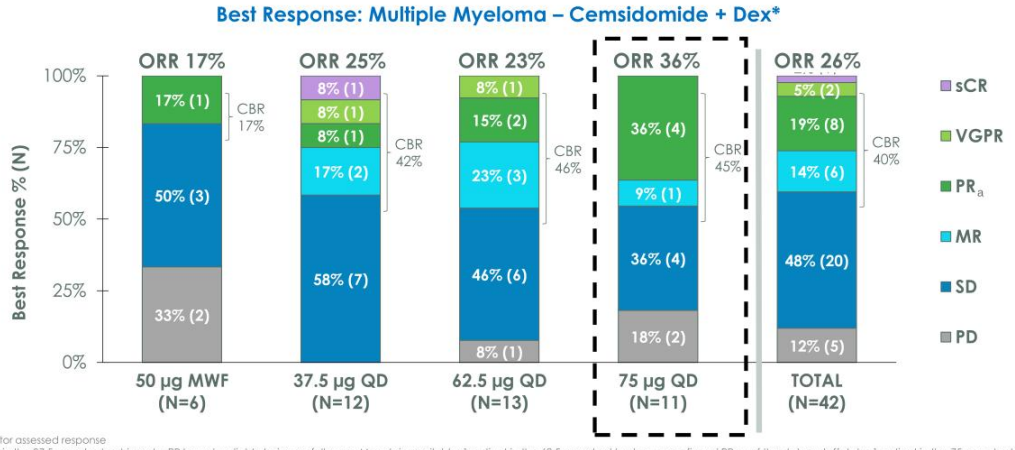
- **1 DLT** (Grade 4 neutropenia lasting >7 days at the 62.5 µg dose level)
- **No TEAEs lead to dose reductions**
- **TEAEs leading to dose interruption: 32%** (15/47)
- **TEAEs leading to discontinuation[1]: 4%** (2/47)

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

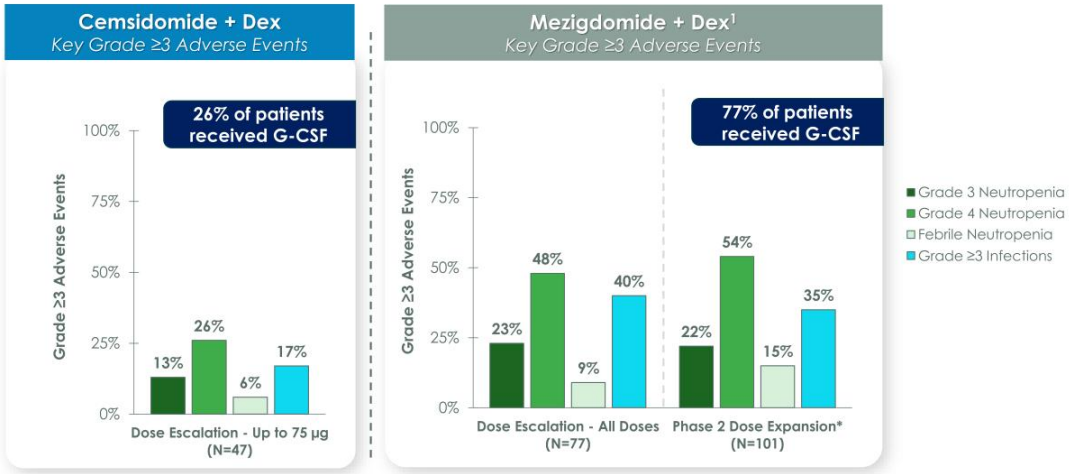
[1]Primary reason of discontinuation of patient at 37.5 µg was due to withdrawal of consent; primary reason of discontinuation of patient at 75 µg was due to death unrelated to cemsidomide.
Adverse events (AEs); dose limiting toxicity (DLT); treatment emergent adverse events (TEAEs)
Source: ASH 2024; C4T data as of 10/11/2024 (https://ir.c4therapeutics.com/static-files/32ae4fdb-d4d9-4a17-a77d-83289c66e911)

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)
Source: ASH 2024; C4T data as of 10/11/2024 (https://ir.c4therapeutics.com/static-files/32ae4fdb-d4d9-4a17-a77d-83289c66e911)

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
Source: ASH 2024; C4T data as of 10/11/2024.(https://ir.c4therapeutics.com/static-files/32ae4fdb-d4d9-4a17-a77d-83289c66e911)

Cemsidomide Has the Potential to Become a Treatment Option Across Lines of Therapy and Address a Growing Patient Population

INITIAL CEMSIDOMIDE DEVELOPMENT PATH IN MM

U.S. + EU4 + UK Addressable Patients (2024)[1]	~65,000	~56,000	~49,000	~42,000	≥23,000
Treatment Line	1L	2L	3L	4L	5L+
Studies Currently Being Enabled		**Phase 1/2 (Escalation/Expansion)** Cemsidomide/Dex + Anti-CD38 and Cemsidomide + BCMA Bispecific			**Phase 2 (Single Arm)** Cemsidomide + Dex (Post anti-BCMA) *Potential Accelerated Approval*
Studies for Registrational Intent		**Randomized Phase 3** Cemsidomide + BCMA Bispecific (1-3 prior lines)		**Randomized Phase 3** Cemsidomide/Dex + Anti-CD38 (2-4 prior lines; post anti-BCMA)	
Development Rationale		Potentially enhances response durability and treatment duration of BCMA bispecific by preventing T-cell exhaustion		Provides post anti-BCMA patients a potentially highly efficacious combo where there are limited proven options	Potential to provide highly refractory patients a treatment option that is tolerable and efficacious where there are limited options

[1] EvaluatePharma (accessed 1/8/25), consulting engagements with Health Advances and Clearview. EU4 = Germany, Italy, France, and Spain.
B-cell maturation antigen (BCMA); dexamethasone (Dex); T-Cell engager (TCE); multiple myeloma (MM)

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. + EU4 + UK Annual Incidence (2024)[1]	~54,000	~33,000	~12,000	~8,000	~16,000
Lenalidomide FDA Approved[2]	✓	✓	✓	✓	
Lenalidomide in NCCN Guidelines	✓	✓	✓	✓	✓

Cemsidomide Opportunity

- Lenalidomide is approved across NHL subtypes
- Cemsidomide has the potential to be developed as a **monotherapy in the R/R setting** and in **combination with front-line standard of care regimens**

[1] EvaluatePharma (accessed 1/8/25), American Cancer Society, Leukemia & Lymphoma Society. EU4 = Germany, Italy, France, and Spain.
[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)

Cemsidomide Phase 1 Dose Escalation Trial in NHL Continues to Progress

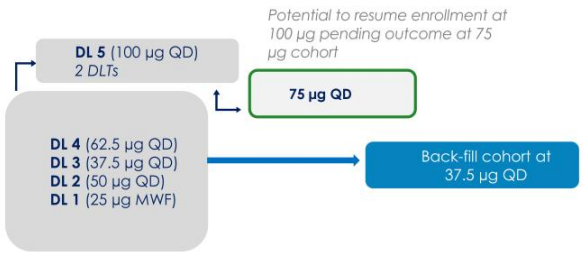
KEY INCLUSION CRITERIA

- 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



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)

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

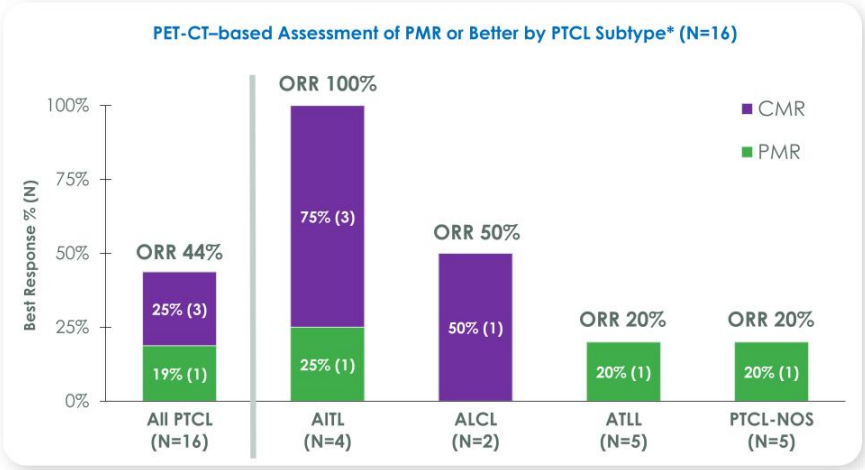
- **2 DLTs occurred at 100 µg QD** (Grade 4 thrombocytopenia and Grade 3 febrile neutropenia)
- **TEAEs leading to discontinuation: 9%** (2/23)
- **39% (9/23) of patients received G-CSF**
  - 3 of 9 patients received G-CSF in Cycle 1

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)
Source: ASH 2024; C4T data as of 10/11/2024.(https://ir.c4therapeutics.com/static-files/32ae4fdb-d4d9-4a17-a77d-83289c66e911)

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)
Source: ASH 2024; C4T data as of 10/11/2024.(https://ir.c4therapeutics.com/static-files/32ae4fdb-d4d9-4a17-a77d-83289c66e91f)

Cemsidomide NHL Data Supports Further Development in PTCL, Which Provides the Fastest Path to Market

INITIAL CEMSIDOMIDE DEVELOPMENT PATH IN PTCL

U.S. + EU4 + UK Addressable Patients (2024)[1]	~16,000	≤12,000
Treatment Line	1L	2L+
Study Currently Being Enabled		Phase 2 (Single Arm) Cemsidomide Monotherapy (2L+ R/R PTCL) *Potential Accelerated Approval*
Study for Registrational Intent	Randomized Phase 3 Cemsidomide + SOC[2] (treatment naïve)	
Development Rationale	Potentially enhance response durability and decrease chemotherapy use, thus providing a more tolerable and durable option	Potentially provides R/R patients a treatment option that is tolerable and efficacious where there are limited options

[1] EvaluatePharma, ACS, consulting engagements with Health Advances and Clearview.
[2] Standard of care (SOC) for 1L patients with CD30+ disease is brentuximab vedotin +/- chemotherapy and for CD30- patients it is the CHOP chemotherapy regimen (cyclophosphamide, doxorubicin, vincristine, prednisone) Germany, Italy, France, and Spain (EU4); peripheral t-cell lymphoma (PTCL); relapsed refractory (R/R); standard of care (SOC)

Cemsidomide Has a Strategic Path to Become a Potential Backbone Therapy for MM and NHL Across Various Lines of Treatment

Multiple myeloma (MM); non-Hodgkin's lymphoma (NHL); peripheral T-cell lymphoma (PTCL); standard of care (SOC)

CFT1946

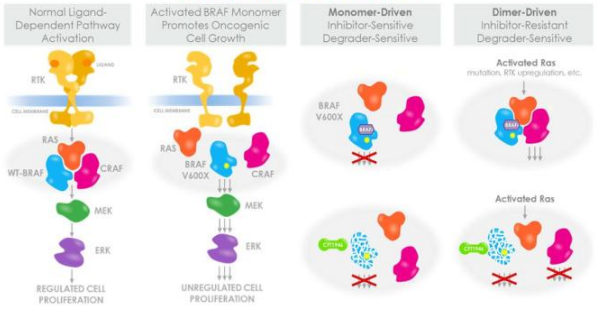
BRAF Mutant V600 Degrader

Colorectal Cancer, Melanoma &
Other BRAF Mutant Solid Tumors

C4 Therapeutics

CFT1946 Is an Oral, Potent Degrader of BRAF V600 Mutants With Potential to Improve Outcomes for Patients

Degrader Benefit in BRAF V600 Mutant Monomer and Dimer-dependent Diseases



Causes of Dimer-Driven Resistance

Melanoma: Acquired NRAS mutation, BRAF V600 mutant amplification, BRAF V600 mutant splice variant

CRC: EGFR-mediated pathway reactivation

Current Approved BRAF Inhibitors Have Limitations:

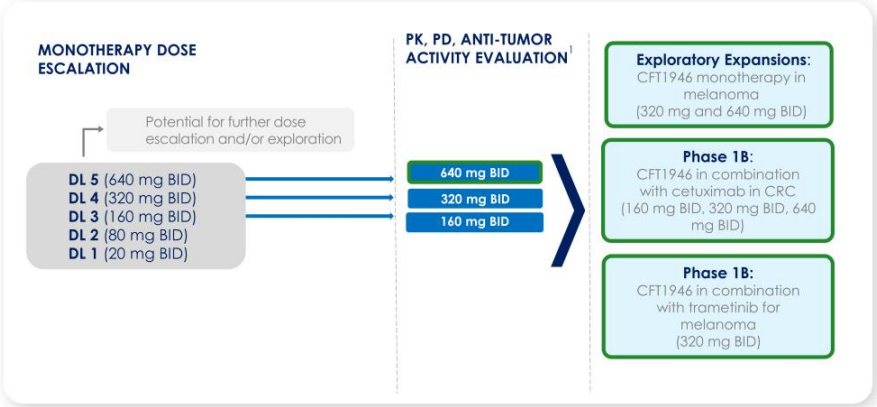
- Resistance mechanisms lead to **limited duration of response**
- Toxicities associated with inhibition of wild-type BRAF **limit tolerability**

Potential Degrader Advantages of CFT1946:

- Enables deep elimination of mutant BRAF signaling to avoid resistance mechanisms and enable a longer duration of response
- Spares wild-type BRAF[1], likely avoiding AEs associated with inhibition of wild-type BRAF
- Ability to cross the blood-brain barrier and highlight the potential for drug delivery to CNS tumors, with $Kp_{U,U}$ values ranging from 0.34 to 0.88

[1]Kreger B et al. Abstract 1658. AACR 2024 Adverse event (AE);); colorectal cancer (CRC); central nervous system (CNS); mitogen-activated protein kinase (MAPK);progression free survival (PFS); BRAF inhibitor (BRAFi).

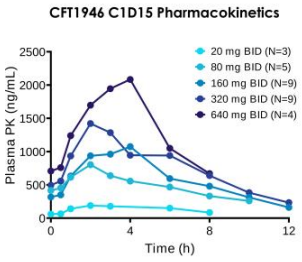
CFT1946 Phase 1/2 Trial Continues to Progress Across BRAF V600 Mutant Driven Solid Tumors



[1]Evaluating additional patients for pharmacodynamic assessment via pre- and post-drug exposure biopsies
Colorectal cancer (CRC); dose Level (DL); twice daily (BID; pharmacokinetic (PK); pharmacodynamic (PD)

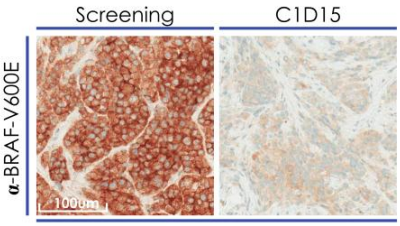
Initial CFT1946 Pharmacokinetic and Pharmacodynamic Data Support Proof of Mechanism

Exhibited dose-dependent bioavailability

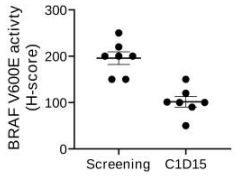


Mean plasma concentration shown for n > 2

BRAF V600E degradation determined by H-score of paired biopsies from different tumor types



IHC on paired biopsy of a melanoma patient dosed at 320 mg



BRAF V600E degradation in paired biopsies at different dose levels (n=1, 80 mg; n=3,160 mg; n=3, 320 mg)

H-Score Calculation:

- IHC staining is measured using BRAF VE1 (BRAF V600E) clone from Roche Laboratories
- H-scores (combining both proportion of cells and intensity of cell staining) are used as a surrogate for quantitative BRAF V600E levels

Immunohistochemistry (IHC); Twice Daily (BID, Cycle 1, Day 15 (C1D15); Pharmacokinetic (PK)
Source: ESMO Congress 2024; C4T data on file as of 7/19/2024 (https://ir.c4therapeutics.com/static-files/b648e3ae-c2db-4f5e-9d47-324b0c8a2b2b)

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

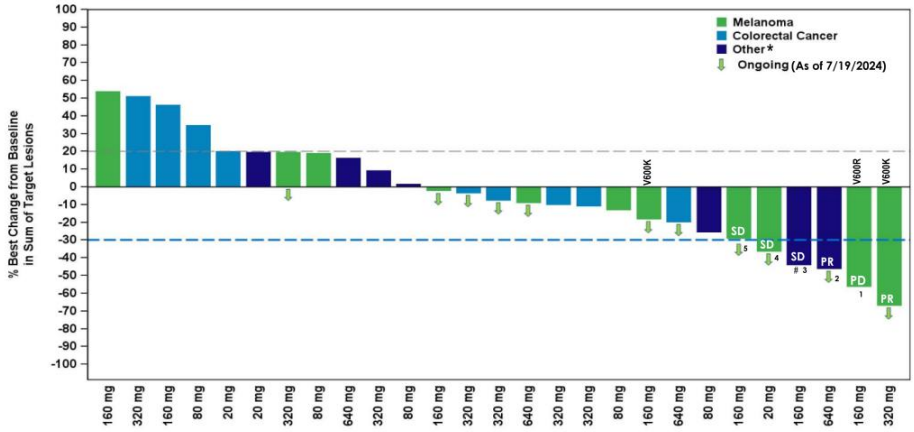
- No DLTs
- Majority of TEAEs observed were mild to moderate
- No treatment-related SAEs
- No Grade ≥ 3 treatment-related cutaneous adverse events
- No new primary malignancies

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 (https://ir.c4therapeutics.com/static-files/b648e3ae-c2db-4f5e-9d47-324b0c8a2b2b)

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 (https://ir.c4therapeutics.com/static-files/b648e3ae-c2db-4f5e-9d47-324b0c8a2b2b)

Potential for Multiple Paths to a Label for CFT1946 to Address High Unmet Needs in BRAF V600 Mutant Melanoma and CRC

Data-Driven Decisions to Inform Next Steps

Melanoma
(BRAF V600 Mutation Rate: ~35%[1])

CFT1946 +/- MEKi in BRAFi-exposed patients	CFT1946 + MEKi in BRAFi-naive patients	CFT1946 + immune checkpoint inhibitor in the front-line

Monotherapy melanoma data will inform fastest path to label

Development Rationale:

- Improvement on durability due to resistance mechanisms that emerge with BRAF inhibitors
- Large patient population **(~66,000 BRAF V600 mutant melanoma patients)**[3]

Colorectal Cancer
(BRAF V600 Mutation Rate: 5-10%[2])

+ cetuximab CRC data will inform fastest path to label:

CFT1946 in combination with an EGFR antibody in the front-line

Development Rationale:

- Limited efficacious and tolerable treatment options for a large patient population **(~33,000 patients BRAF V600 mutant CRC patients)**[3]
- Patients typically treated with chemotherapy

[1] Owsley 2021 Exp Biol Med. [2] Paik 2011 J Clin Oncol. [3]2024 EvaluatePharma (accessed 1/8/25); comprises the U.S. + EU4 + UK population. Germany, Italy, France, and Spain (EU4); Mek inhibitor (MEKi) BRAF inhibitor (BRAFi); colorectal cancer (CRC).

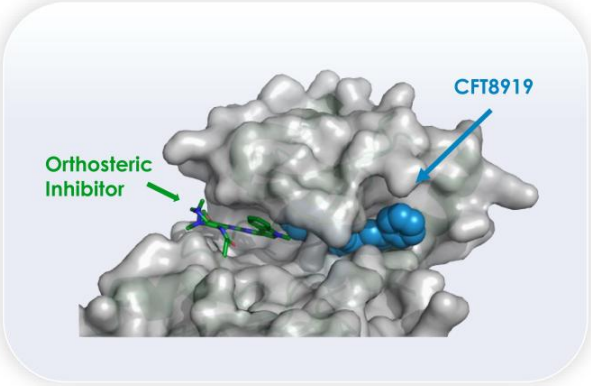
CFT8919

EGFR L858R Degrader

Non-Small Cell Lung Cancer

C4 Therapeutics

CFT8919 Is a Potent, Oral, Allosteric, Mutant-selective Degrader of EGFR L858R With Potential to Improve Outcomes for NSCLC Patients



Current Approved EGFR Inhibitors Have Limitations:

- Patients **become refractory due to secondary mutations**
- NSCLC patients with **L858R have inferior clinical outcomes**
- Toxicities associated with inhibition of wild-type EGFR **limit tolerability**

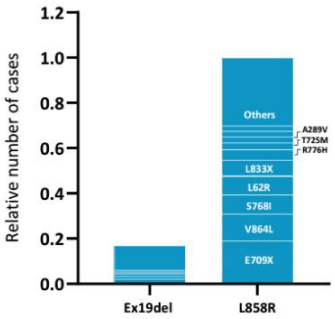
Potential Degrader Advantages of CFT8919:

- ✓ CFT8919 exploits an allosteric binding site created by the L858R mutation, thereby avoiding resistance mutations to the orthosteric site
- ✓ Potent and selective against L858R regardless of secondary mutations with potential for more durable activity in this setting
- ✓ Does not hit wild-type, potentially resulting in better tolerability

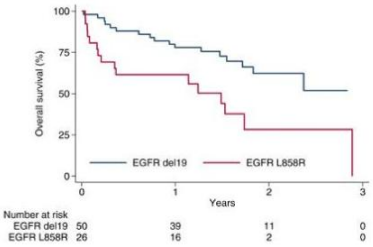
Non-small cell lung cancer (NSCLC); epidermal growth factor receptor (EGFR)

CFT8919 Binds to Allosteric Site, Avoiding Impact of L858R Non-classical Co-mutations in the Orthosteric Binding Pocket

EGFR-L858R Tumors More Frequently Co-express Non-classical EGFR Mutations Before Exposure to EGFR TKI[1]



Patients with L858R Do Less Well on Osimertinib Therapy vs Ex19del



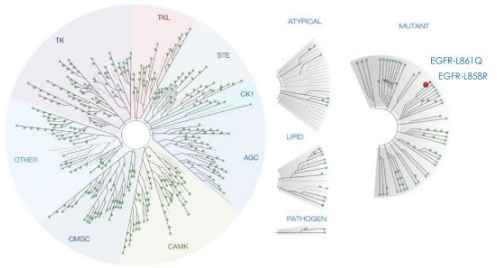
Overall survival by type of mutation in patients with Stage IV EGFR mutated NSCLC and brain metastasis who received first-line treatment with osimertinib

CFT8919 binds to the allosteric site, potentially avoiding the impact of non-classical co-mutations with L858R, where inhibitors demonstrate lower PFS in this patient population than those with EXON 19 deletion

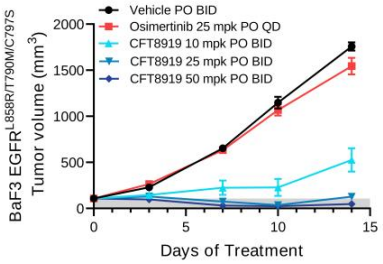
Sources: 1. From Black Diamond's analyses of 94,939 sequencing reports from treatment naive NSCLC (Guardant Health) presented at AACR 2024 (https://blackdiamondtherapeutics.com/assets/files/AACR_2024_-_BDTX-1535_FINAL_Presentation_20240405.pdf) 2. Gitenbeek, et al. 2023
Progression free survival (PFS)

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

Specific for EGFR Exon 21 Mutants



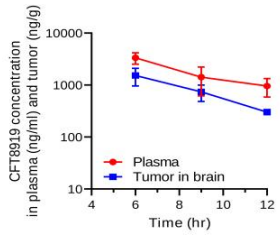
Active in Setting of EGFR C797S



Source: C4T data on file; Presented at Keystone Symposium 2021 (https://c4therapeutics.com/wp-content/uploads/Preclinical-Evaluation-of-CFT8919-as-a-Mutant-Selective-Degrader-of-EGFR-with-L858R-Activating-Mutations-for-the-Treatment-of-Non-Small-Cell-Lung-Can.pdf)
Investigational new drug application (IND)

CFT8919 Demonstrates Activity in Brain Metastasis Model

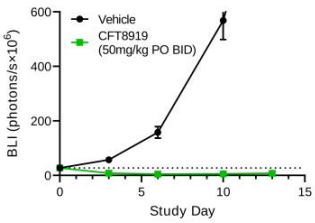
Mean Plasma & Tumor Concentration



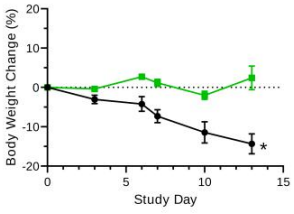
Plasma clearance $t_{1/2}$ = 3.1 hrs

50 mg/kg single dose PO

In vivo Efficacy



In vivo Body Weight Change



*Body weight loss due to tumor burden

Source: C4T data on file; presented at TPD Summit 2021 (https://c4therapeutics.com/wp-content/uploads/C4_CFT8919_TPD_Summit_Presentation.pdf)
By mouth (PO); twice daily (BID)

CFT8919 Has the Potential to Address Multiple Opportunities with High Unmet Needs

CFT8919's Fastest Path to Market Is in 2L+ With Potential to Expand Into Front-Line

2L+	Front-line
Development Rationale: • Fast path to market • Lack of therapies after patients relapse with secondary mutation (i.e., C797S)	**Development Rationale:** • Large patient opportunity • Potential to increase responses and durability in L858R patients

Dose escalation in Greater China is advancing; C4T to utilize data to inform ex-China clinical development

2024 Annual Incidence of EGFR L858R Mutated NSCLC[1]:

- **U.S.:** ~17,000
- **China:** ~189,000
- **EU4 + UK:** ~13,000

[1] EvaluatePharma (accessed on 1/10/25), consulting engagements with Health Advances and Clearview. Germany, Italy, France, and Spain (EU4)

Multiple 2025 Inflection Points to Unlock Value Across Entire Portfolio

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 U.S. and rest-of-world development plans
TORPEDO Platform	Develop orally bioavailable degraders in oncology and non-oncology targets for internal research and collaborations

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