C4 Therapeutics

Protein degraded.
Disease targeted.
Lives transformed.

May 2025

Forward-looking Statements and Intellectual Property

FORWARD-LOOKING STATEMENTS

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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[1]

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

CFT8919

targeting EGFR L858R for non-small cell lung cancer

Internal Discovery Pipeline

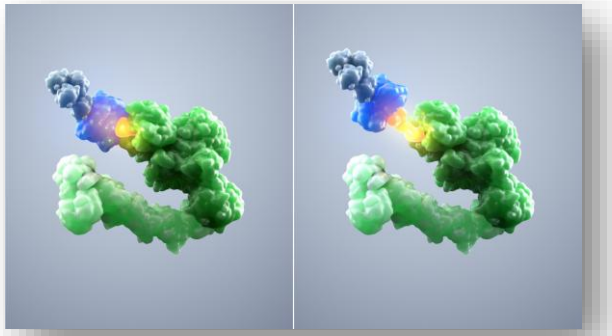
targets in therapeutic areas in and beyond oncology with a strong degrader rationale and genetic link to disease

[1]CFT1946 Phase 1 trial is ongoing. C4T will not advance CFT1946 beyond the Phase 1 trial

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



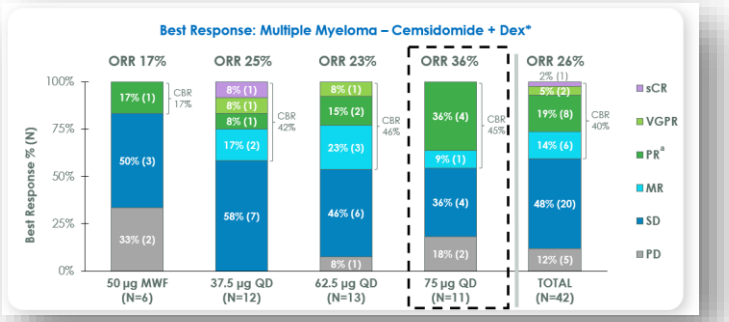
Built TORPEDO platform to design highly catalytic, orally bioavailable degraders

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



MM cemsidomide data presented in December 2024 at ASH

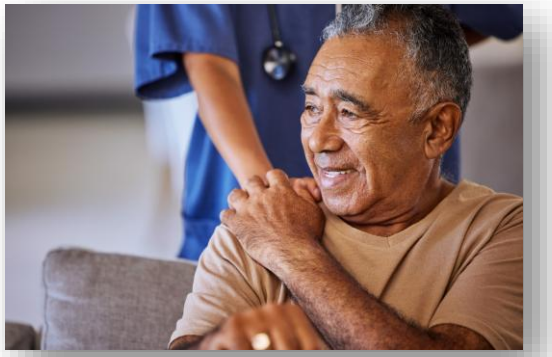
Progressed four development candidates into the clinic with three clinical trials ongoing

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

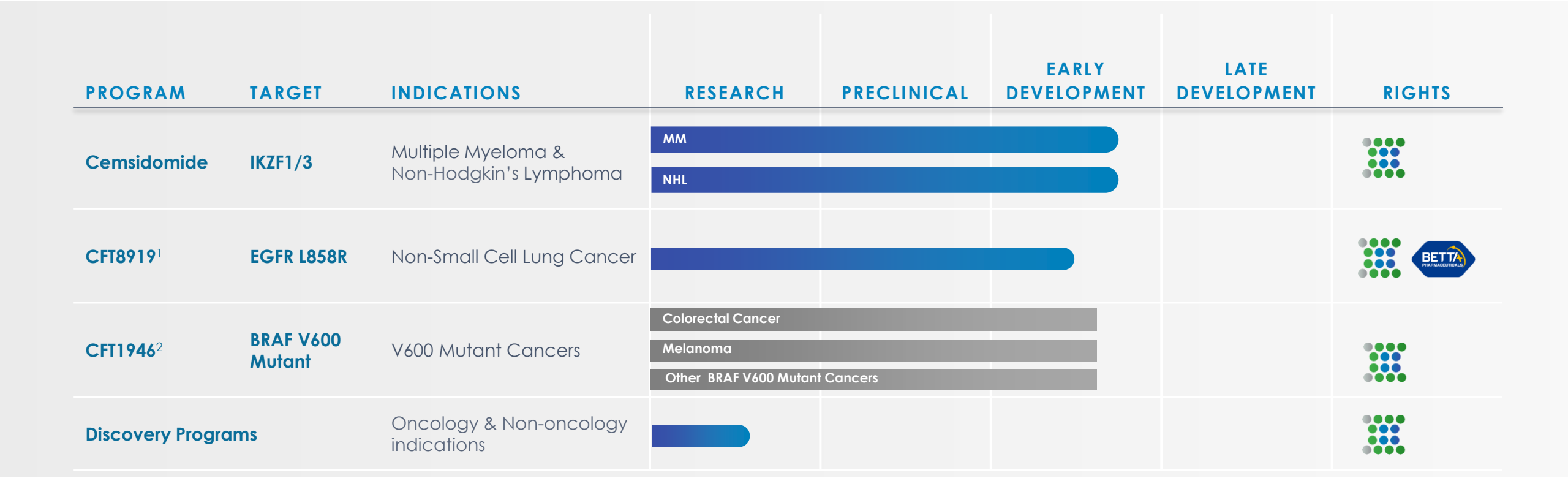


Advancing clinical programs to approval for patients with high unmet needs

Leveraging TORPEDO platform to develop a sustainable pipeline against targets with a strong degrader rationale and genetic link to disease in therapeutic areas in and beyond oncology

Expanding application of targeted protein degradation through high-value collaborations

Focused Pipeline to Advance a Portfolio of Degrader Medicines Targeting Areas of High Unmet Need



[1] License and collaboration agreement with Betta Pharmaceuticals for development and commercialization in Greater China
[2] In May 2025, C4T announced CFT1946 will not advance beyond Phase 1 and that the company will seek partnership for the BRAF program

Prioritized Portfolio with Multiple 2025 Milestones

Cemsidomide *IKZF1/3*	✓ **2Q 2025:** Completed Phase 1 dose escalation in MM **3Q 2025:** Present data from completed Phase 1 dose escalation in MM **4Q 2025:** Complete Phase 1 dose escalation in NHL and present data **2H 2025:** Open expansion cohort(s) in PTCL in the ongoing Phase 1/2 trial **2025:** Enable initiation of the next phase of clinical development for cemsidomide with new studies expected to initiate in early 2026
CFT8919 *EGFR L858R*	**Year-end 2025:** Utilize data from Phase 1 dose escalation trial in Greater China to inform ex-China clinical development
CFT1946 *BRAF V600 Mutant*	✓ **2Q 2025:** Complete monotherapy Phase 1 dose escalation trial in BRAF V600 mutant solid tumors ✓ **2Q 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
Discovery	✓ **2Q 2025:** Advanced two programs to preclinical milestones through the Roche collaboration **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 Oncology and Non-oncology Discovery Programs with Collaboration Partners

Roche	Merck KGaA Darmstadt, Germany	MERCK	Biogen
Evaluating targets in autoimmune diseases & oncology Advanced two programs to preclinical milestones	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

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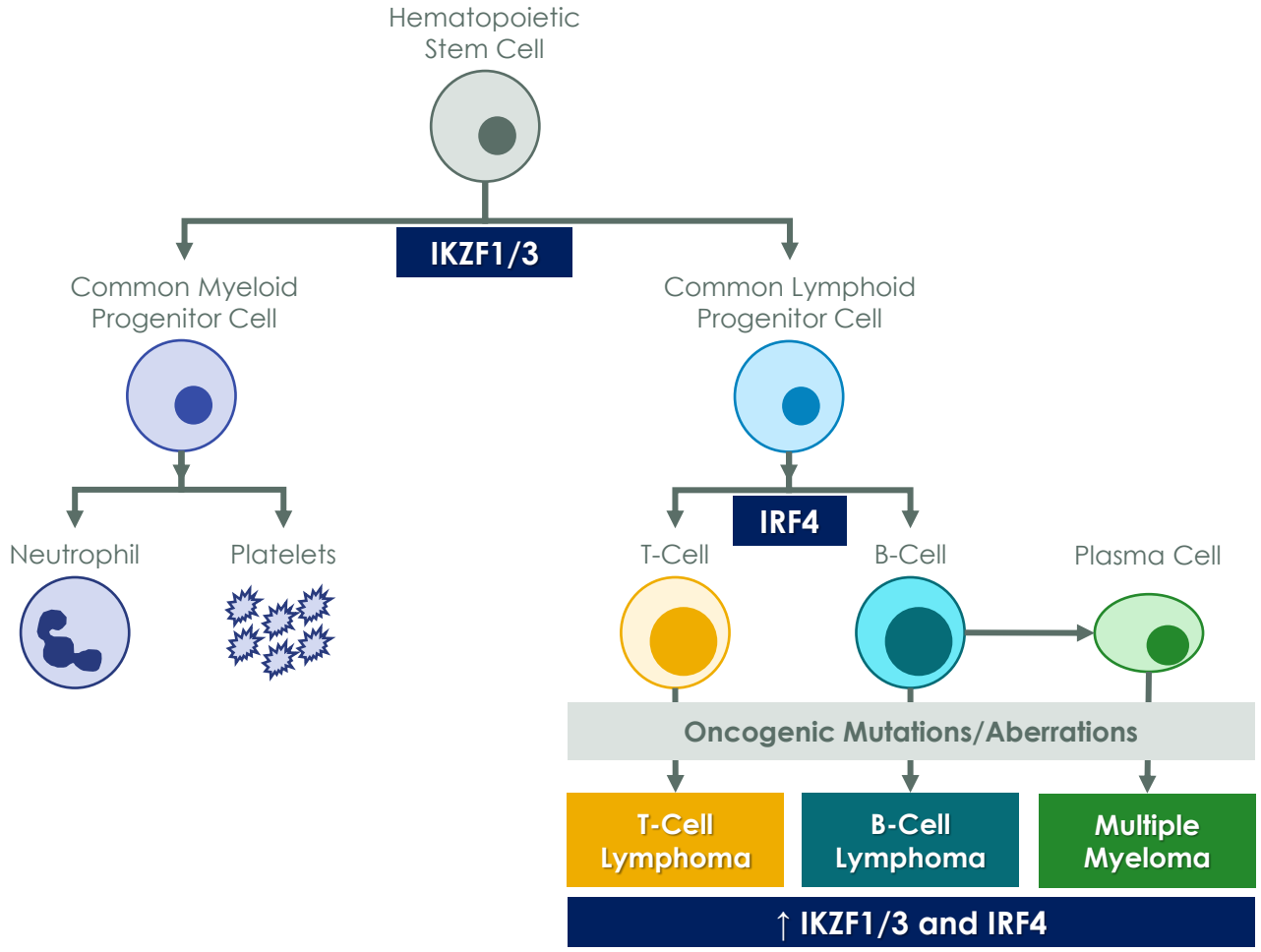
IKZF1/3 Are Key Promoters of Myeloma and Lymphoma Cell Survival and Will Remain Important Therapeutic Targets for These Indications



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**

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)

Cemsidomide Dose Escalation Is Complete With 100 µg QD Dose Level Declared Safe; Patients Enrolling in the Expansion Cohort at this Dose Level

KEY INCLUSION CRITERIA

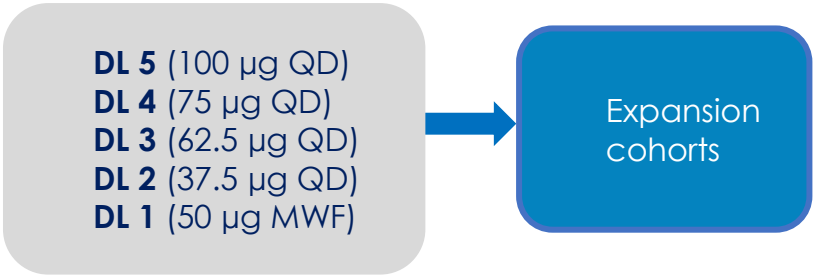
- Adults with MM, R/R to at least 3 prior lines of therapy that have included lenalidomide, pomalidomide, a proteasome inhibitor, a glucocorticoid, and an anti-CD38 monoclonal antibody
- Nonresponsive to or progressed within 60 days of prior therapy
- Creatinine clearance ≥40 mL/min
- ECOG ≤2

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

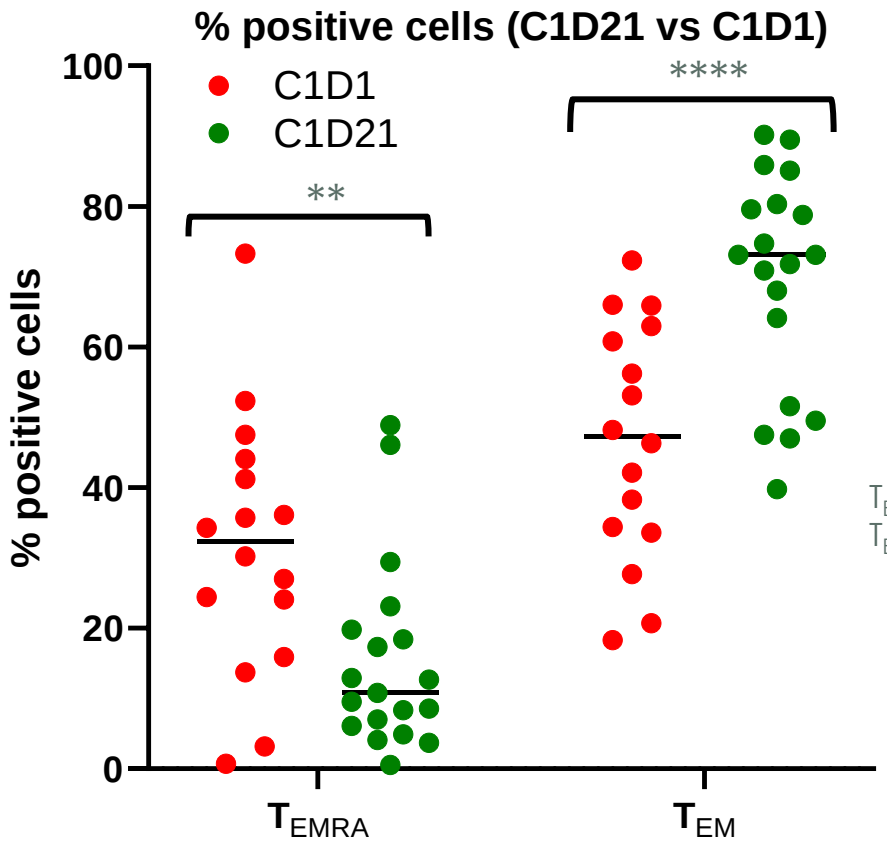


- 10 additional patients will enroll in the 100 µg QD expansion cohort to further characterize cemsidomide's profile

*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)

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

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)

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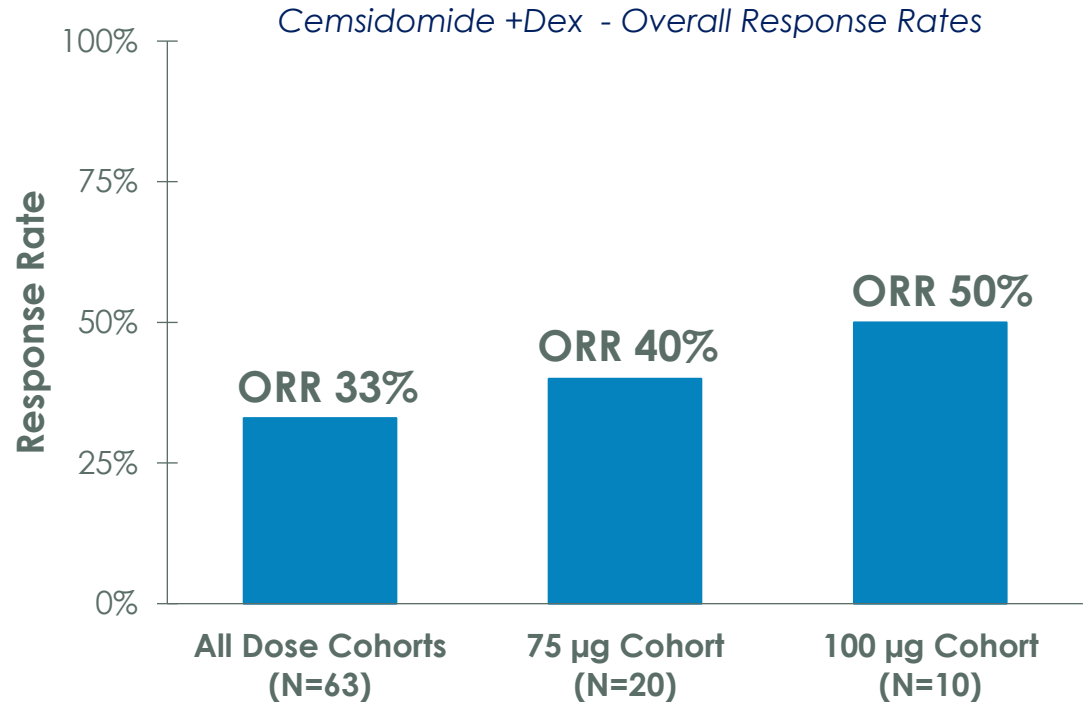
Updated Cemsidomide Multiple Myeloma Data Further Demonstrate its Potential to Have a Best-in-Class Profile

Cemsidomide continued to be well-tolerated with manageable neutropenia[1]

Compelling anti-myeloma activity observed across multiple doses[1]



At the 100 µg dose level:

- One patient achieved an MRD negative CR
- Eight patients (80%) received prior CAR-T or T-cell engager therapy

1. Data cut-off date as of April 30,2025; C4T data on file
Data presented at ASH with data cutoff date as of 10/11/24, can be found here: https://ir.c4therapeutics.com/static-files/32ae4fdb-d4d9-4a17-a77d-83289c66e91f
Overall Response Rate (ORR); minimal residual disease (MRD); complete response (CR); once daily (QD)

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Cemsidomide Has the Potential to Become a Treatment Option Across Lines of Therapy and Address a Growing Relapsed Refractory 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)

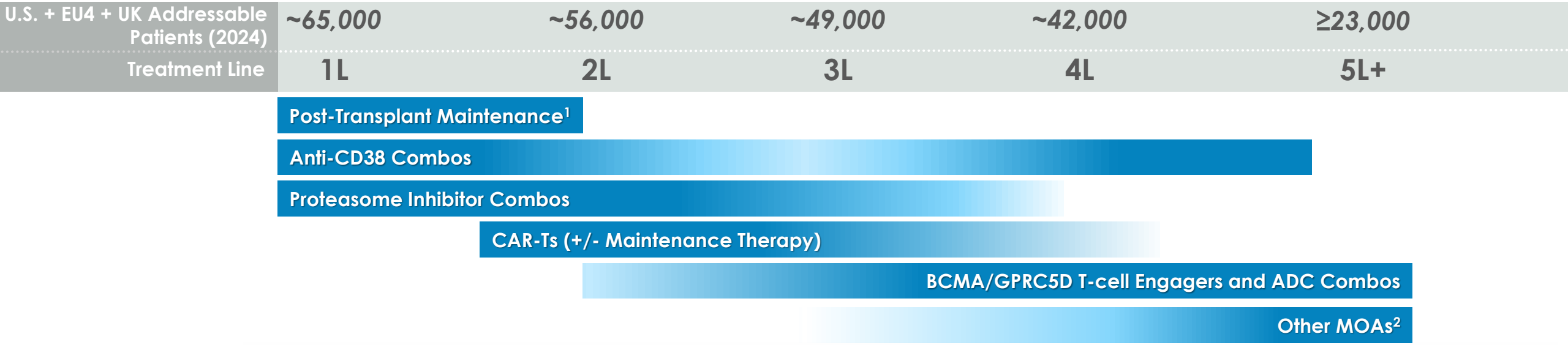
Randomized Phase 3
Cemsidomide/Dex + Anti-CD38
(2-4 prior lines; post anti-BCMA)

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. Germany, Italy, France, and Spain (EU4).
B-cell maturation antigen (BCMA); dexamethasone (Dex); T-Cell engager (TCE); multiple myeloma (MM)

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

EVOLVING MULTIPLE MYELOMA TREATMENT LANDSCAPE



CEMSIDOMIDE OPPORTUNITY

- **Potential to address a growing patient population** as current 5L+ treatment options start to be used in earlier lines
- **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
- Cemsidomide has the potential to achieve peak annual revenues of **~$1B as a 5L+ treatment option +dex and over $6B** if labels in combination with a BCMA bispecific and in combination with dex + an anti-CD38 are achieved

[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); dexamethasone (dex); G protein-coupled receptor, class C, group 5, member D (GPRC5D); monoclonal antibodies (mAbs); mechanism of action (MOA); Germany, Italy, France, and Spain (EU4)

Cemsidomide Phase 1 Dose Escalation Trial in NHL Continues to Progress

KEY INCLUSION CRITERIA

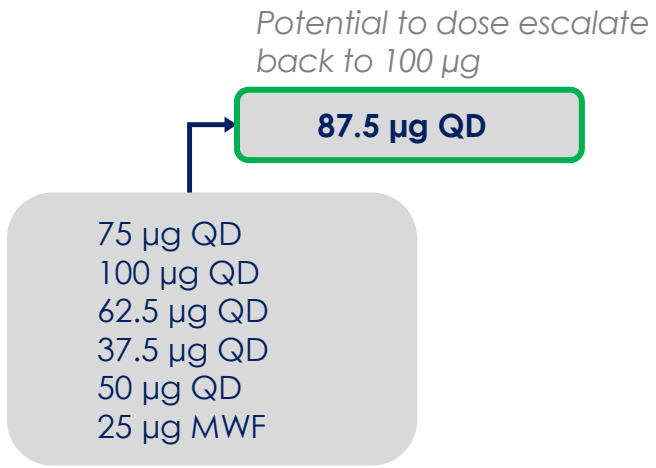
- Adults with NHL, R/R to prior therapy
  - PTCL patients must have received at least 1 prior alkylator-based chemotherapy
  - ALCL patients must have also received a CD-30 mAb
- Nonresponsive to or progressed within 60 days of prior therapy
- Creatinine clearance ≥40 mL/min
- ECOG ≤2

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

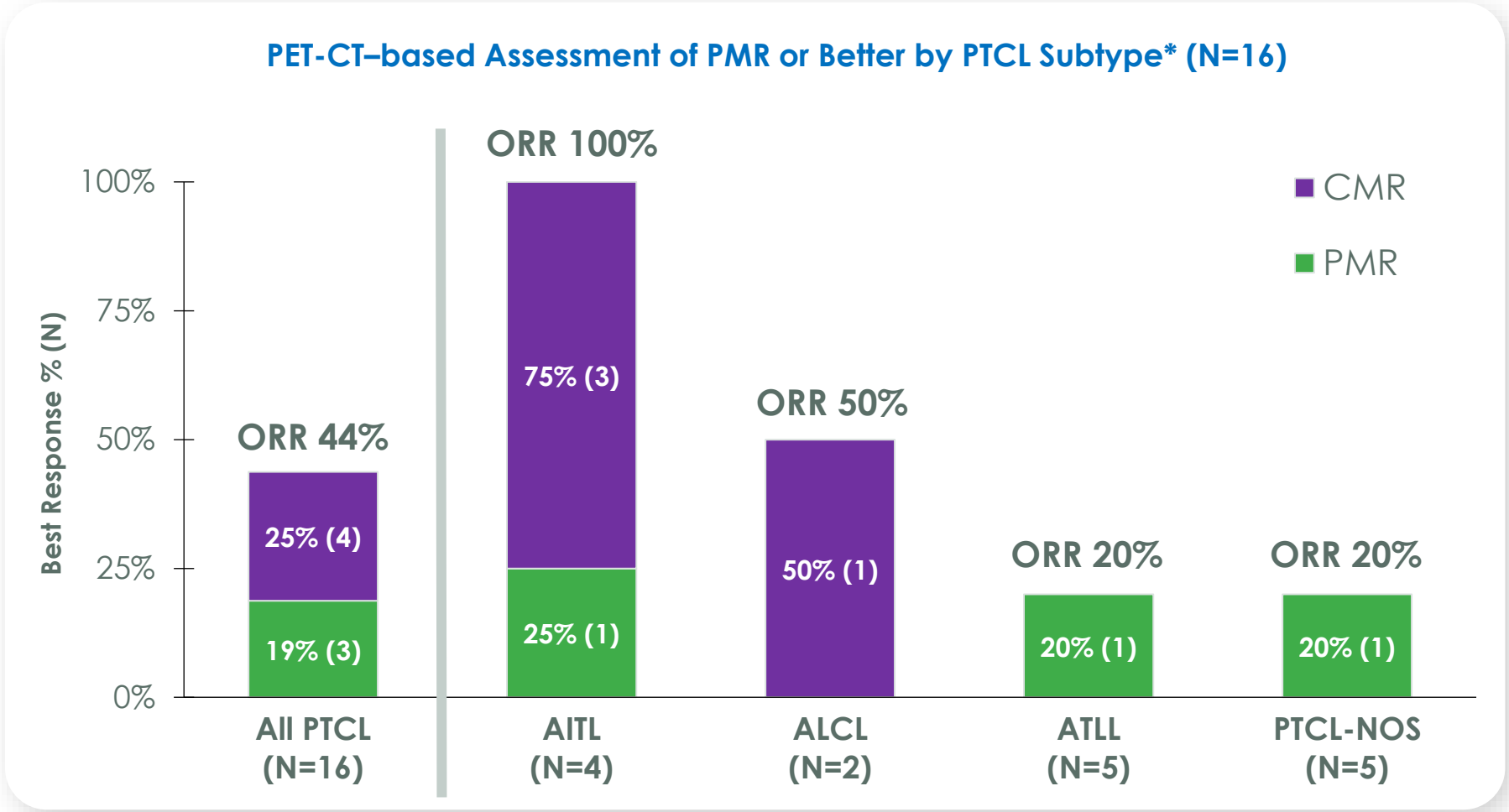
- **2 DLTs occurred at 100 µg QD** (Grade 4 thrombocytopenia and Grade 3 febrile neutropenia)
- **TEAEs leading to discontinuation: 9%** (2/23)
- **39% (9/23) of patients received G-CSF**
  - 3 of 9 patients received G-CSF in Cycle 1

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-83289c66e91f)

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)

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

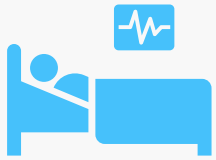
INITIAL CEMSIDOMIDE DEVELOPMENT PATH IN PTCL

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

1



- Highest unmet patient need opportunities in a growing population
- Fastest path to label

Dex combination in late-line MM

Monotherapy in 2L+ PTCL

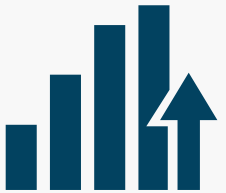
2

- Combination strategies with other MM agents to expand to 2L+ MM
- Combine with standard of care in front-line NHLs

In combination with MM agents in 2/3L

Expand to 1L PTCL in combination with SOC

3



- Maximize broad applicability
- Drive revenue growth

Establish as backbone treatment across MM (1L+)

Establish as backbone treatment across NHL

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

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CFT8919

EGFR L858R Degrader

Non-Small Cell Lung Cancer

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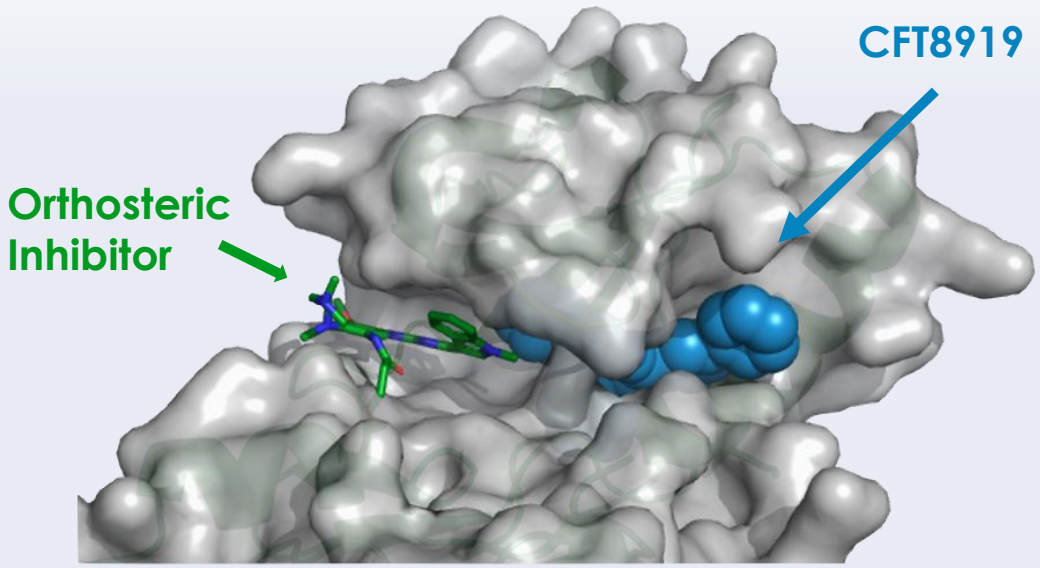
CFT8919 Is a Potent, Oral, Allosteric, Mutant-selective Degrader of EGFR L858R With Potential to Improve Outcomes for NSCLC Patients



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)

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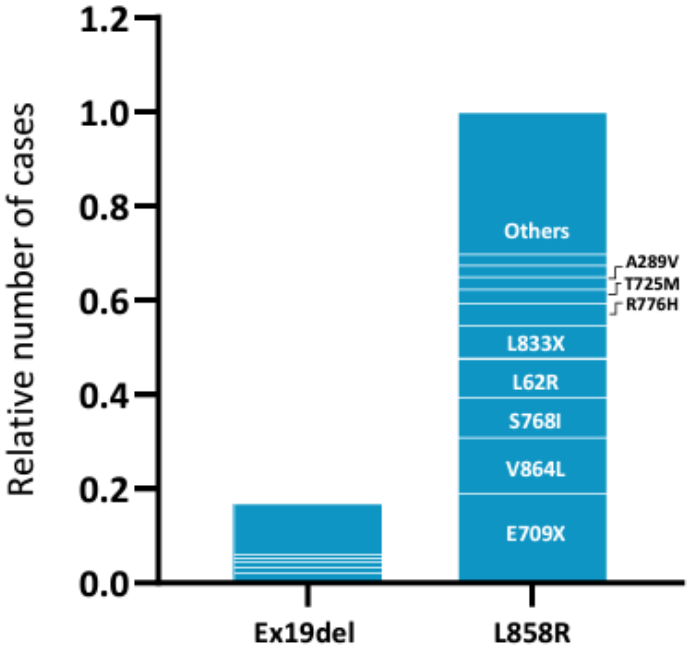
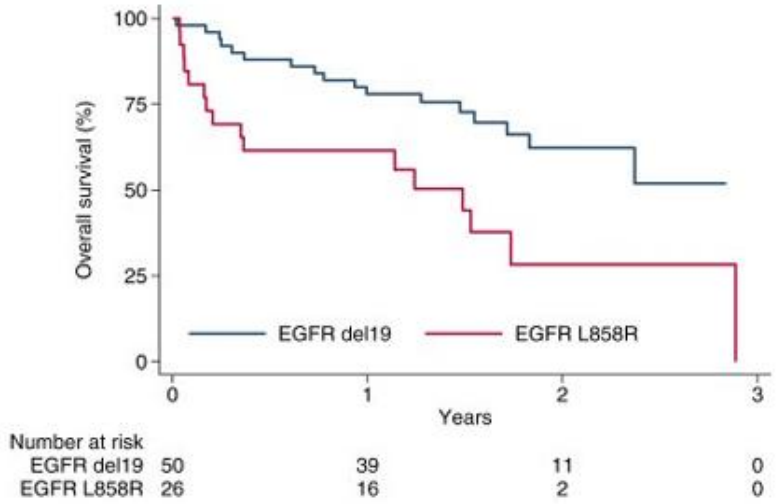
CFT8919 Binds to Allosteric Site, Avoiding Impact of L858R Non-classical Co-mutations in the Orthosteric Binding Pocket

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



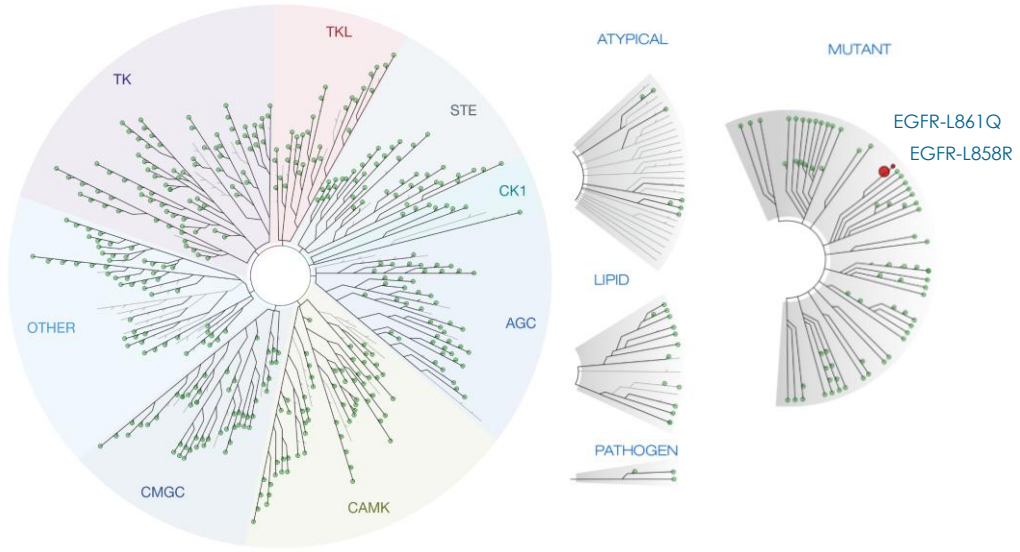
Overall survival by type of mutation in patients with Stage IV EGFR mutated NSCLC and brain metastasis who received first-line treatment with osimertinib

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

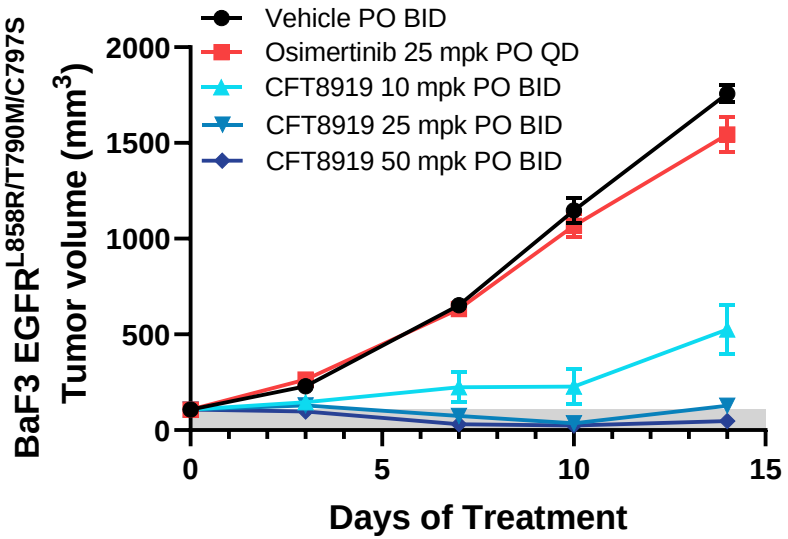
Sources: 1. From Black Diamond's analyses of 94,939 sequencing reports from treatment naive NSCLC (Guardant Health) presented at AACR 2024 (https://blackdiamondtherapeutics.com/assets/files/AACR_2024__BDTX-1535_FINAL_Presentation_20240405.pdf) 2. Gitenbeek, et al. 2023 Progression free survival (PFS)

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

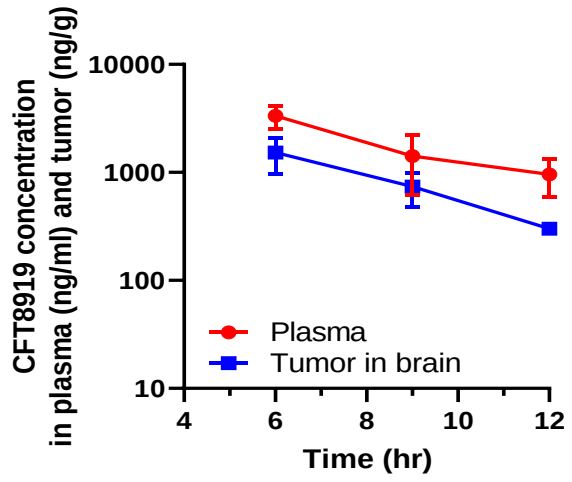


Source: C4T data on file; Presented at Keystone Symposium 2021 (https://c4therapeutics.com/wp-content/uploads/Preclinical-Evaluation-of-CFT8919-as-a-Mutant-Selective-Degrader-of-EGFR-with-L858R-Activating-Mutations-for-the-Treatment-of-Non-Small-Cell-Lung-Can.pdf)
Investigational new drug application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

C4 Therapeutics

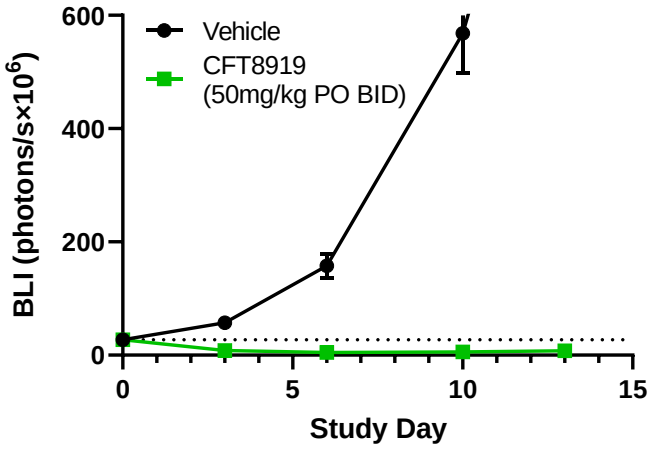
CFT8919 Demonstrates Activity in Brain Metastasis Model

Mean Plasma & Tumor Concentration

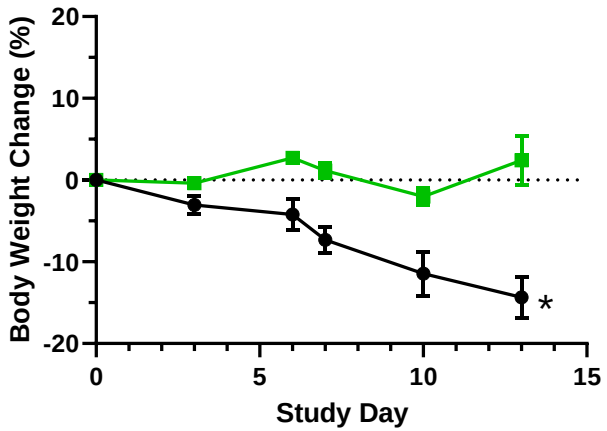


Plasma clearance $t_{1/2}$ = 3.1 hrs
50 mg/kg single dose PO

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)

C4 Therapeutics

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+

Development Rationale:

- Fast path to market
- Lack of therapies after patients relapse with secondary mutation (i.e., C797S)

Front-line

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)

Prioritized Portfolio with Multiple 2025 Milestones

Cemsidomide *IKZF1/3*	✓ **2Q 2025:** Completed Phase 1 dose escalation in MM **3Q 2025:** Present data from completed Phase 1 dose escalation in MM **4Q 2025:** Complete Phase 1 dose escalation in NHL and present data **2H 2025:** Open expansion cohort(s) in PTCL in the ongoing Phase 1/2 trial **2025:** Enable initiation of the next phase of clinical development for cemsidomide with new studies expected to initiate in early 2026
CFT8919 *EGFR L858R*	**Year-end 2025:** Utilize data from Phase 1 dose escalation trial in Greater China to inform ex-China clinical development
CFT1946 *BRAF V600 Mutant*	✓ **2Q 2025:** Complete monotherapy Phase 1 dose escalation trial in BRAF V600 mutant solid tumors ✓ **2Q 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
Discovery	✓ **2Q 2025:** Advanced two programs to preclinical milestones through the Roche collaboration **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