C4 Therapeutics

Protein degraded.
Disease targeted.
Lives transformed.

43rd Annual J.P. Morgan Healthcare Conference

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.

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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

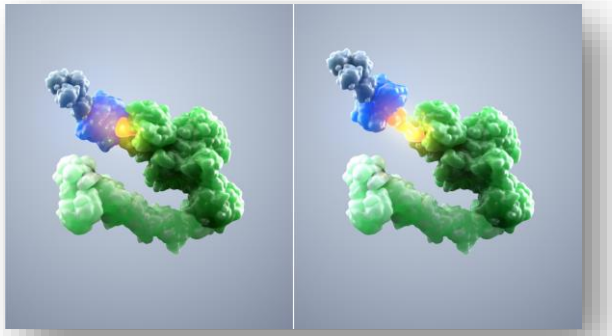
Internal Discovery Pipeline

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



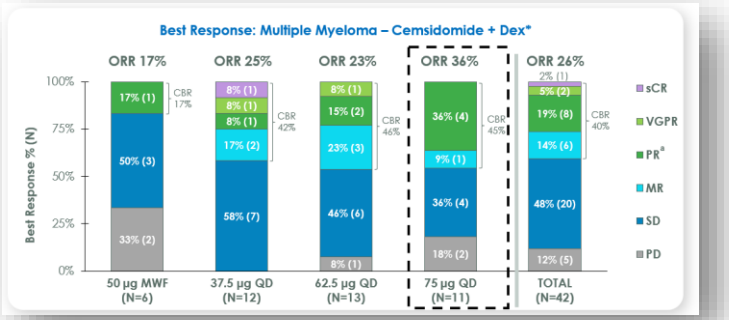
Built TORPEDO platform to design highly catalytic, orally bioavailable degraders

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)

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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

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Cemsidomide

IKZF1/3 Degrader

Multiple Myeloma & Non-Hodgkin's Lymphoma

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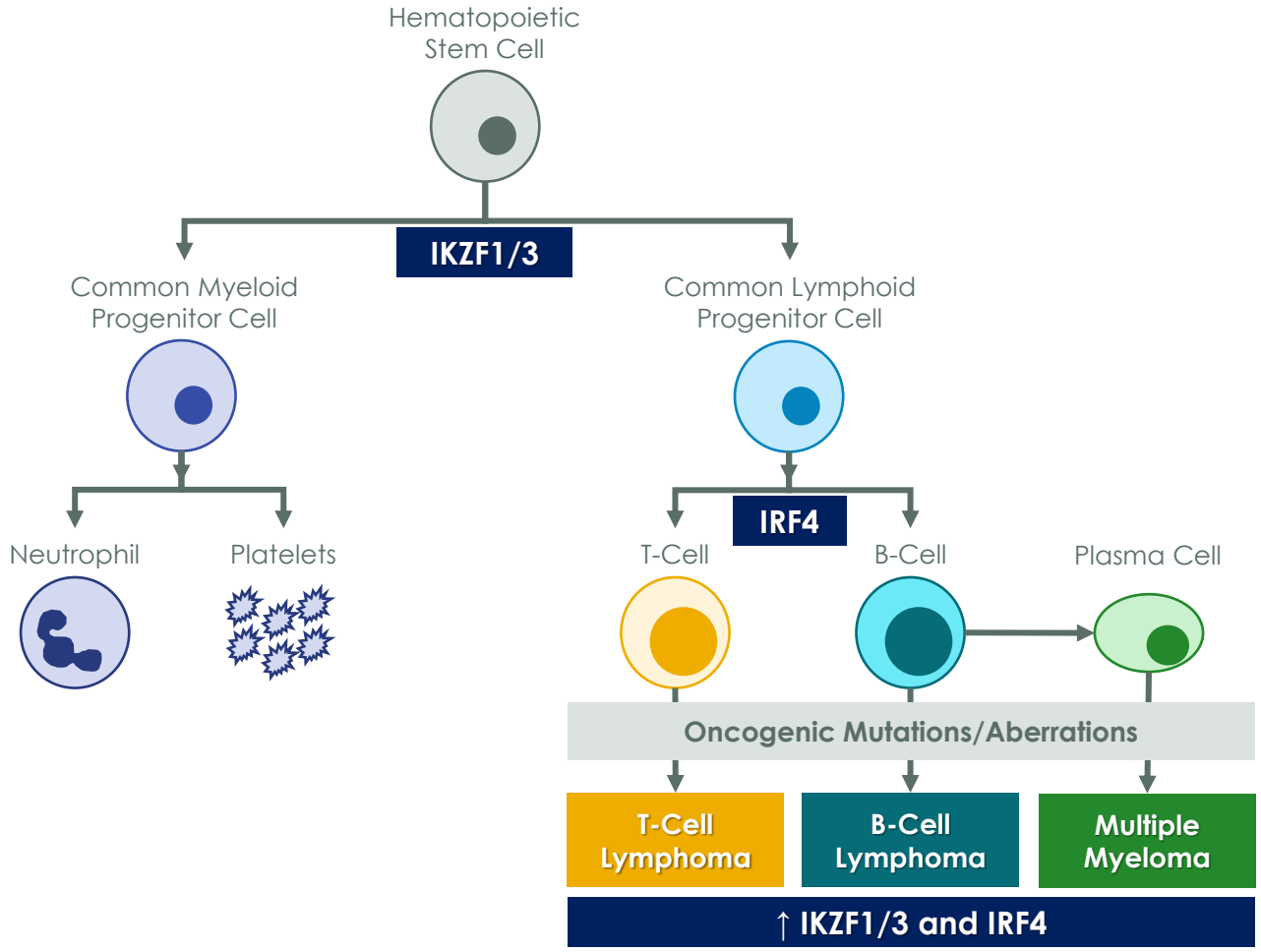
IKZF1/3 Are Key Promoters of Myeloma and Lymphoma Cell Survival and Will Remain Important Therapeutic Targets for These Indications



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**

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)

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Cemsidomide Phase 1 Dose Escalation Trial in MM and NHL Continues to Progress

PHASE 1 DOSE ESCALATION TRIAL

R/R MM
Monotherapy
Dosing: QD
21 days on/
7 days off

Status: Complete

- Different dosing schedule required due to longer than anticipated half-life

R/R MM
Monotherapy
Dosing: MWF & QD
14 days on/
14 days off

Status: Complete

- Confirmed 14 days on/14 days off schedule
- Clinical evidence of anti-myeloma activity and immune T-cell activation

R/R MM
Dex Combo
Dosing: MWF & QD
14 days on/
14 days off

Status: Ongoing

- Currently enrolling at 100 µg QD
- Have not exceeded maximum tolerated dose

R/R NHL
Monotherapy
Dosing: MWF & QD
14 days on/
14 days off

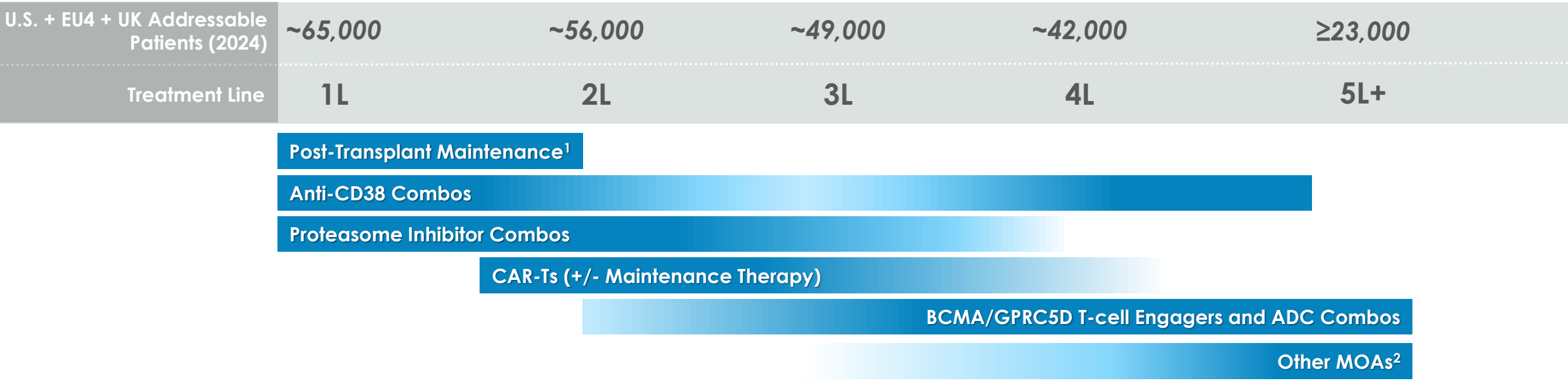
Status: Ongoing

- Currently enrolling at 75 µg QD
- Additional dose finding ongoing

Monday, Wednesday, Friday dosing (MWF); once daily (QD); relapsed refractory multiple myeloma (R/R MM); relapsed refractory non-Hodgkin's lymphoma (R/R NHL)

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

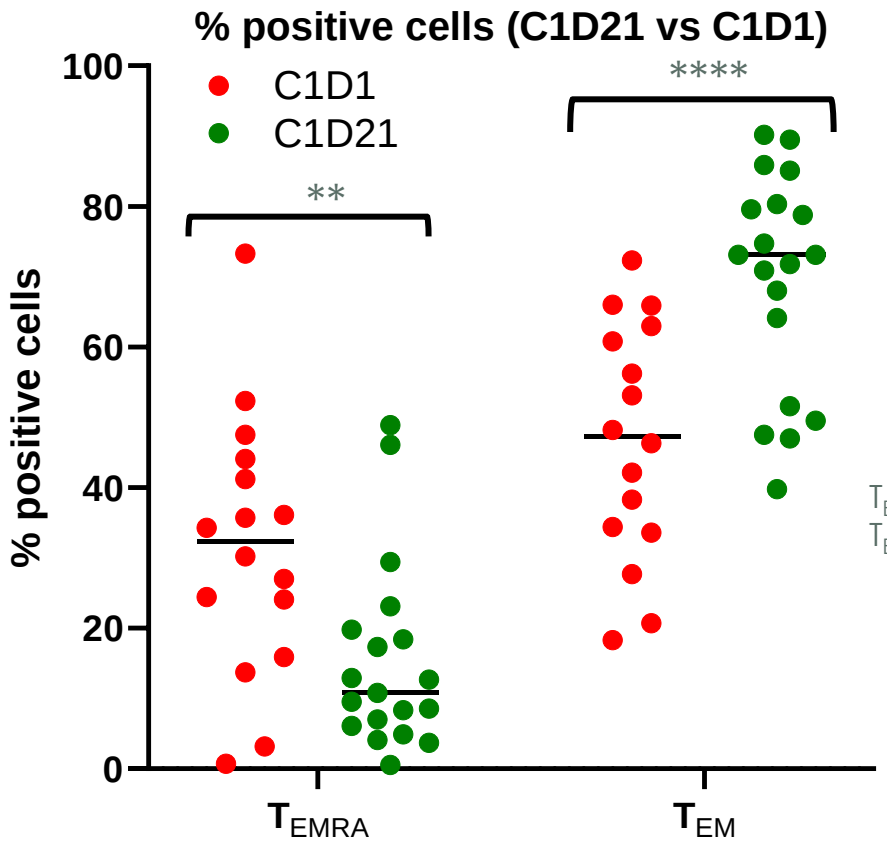


CEMSIDOMIDE OPPORTUNITY

- 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



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

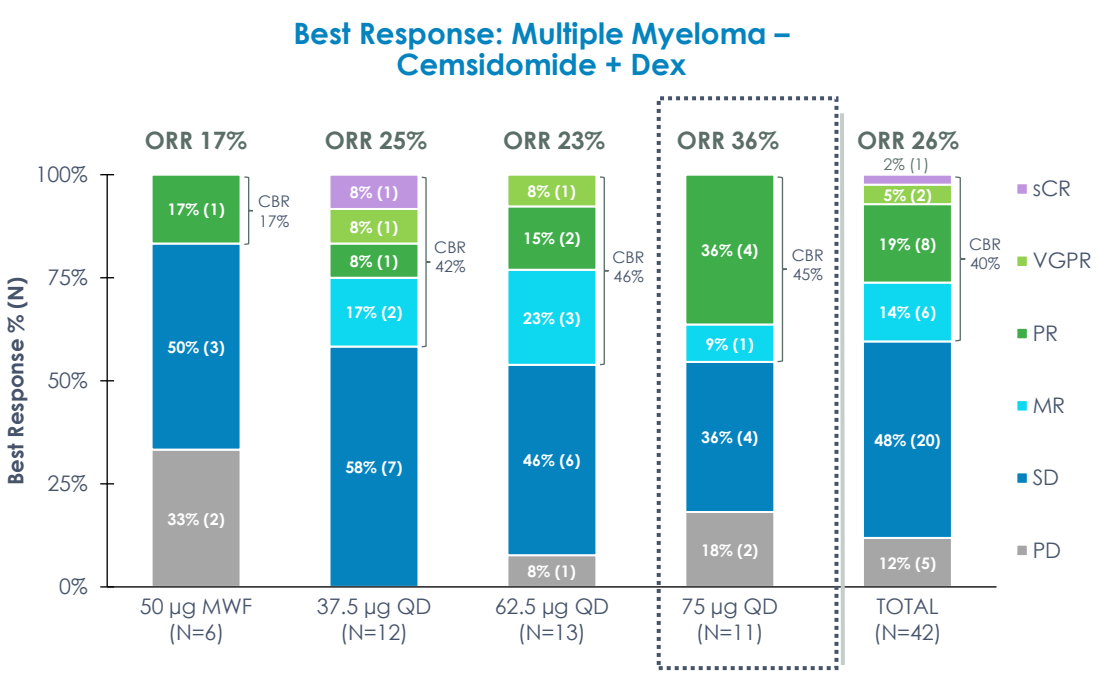
Supports potential of cemsidomide as a maintenance therapy option and in combination with other MM agents to improve efficacy:

- ✓ 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

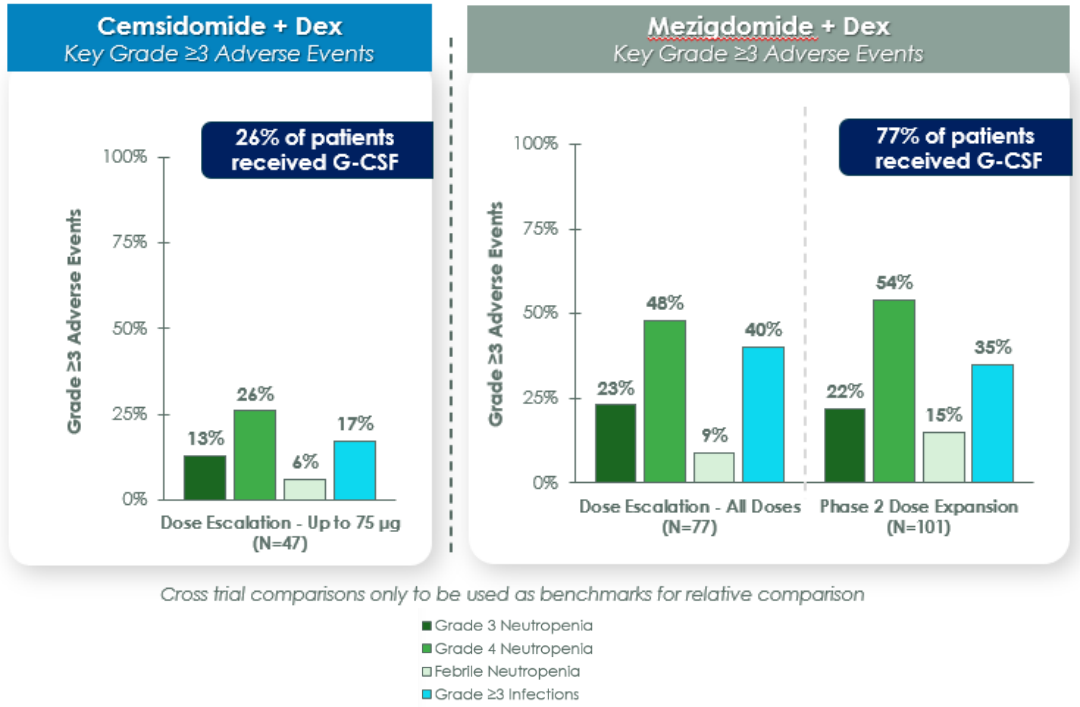
Peripheral blood mononuclear cells (PBMCs); daily dosing (QD); Monday, Wednesday, Friday dosing (MWF); multiple myeloma (MM)
Source: C4T data on file as of 11/28/2023 (https://ir.c4therapeutics.com/static-files/ec59b02e-3074-484d-ad88-e81831bf37ed)

Cemsidomide + Dex Data Demonstrated a Potential Best-in-Class Profile

75 µg Cemsidomide Dose Level Resulted in a 36% ORR and 45% CBR



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



Profile supports cemsidomide's development in combination with dexamethasone in the late-line setting and in combination with other MM agents in earlier lines of the treatment paradigm

Source: ASH 2024; C4T data as of 10/11/2024 (https://ir.c4therapeutics.com/static-files/32ae4fdb-d4d9-4a17-a77d-83289c66e91f): see slide 20 of the ASH presentation for complete footnotes for the left panel; see slide 21 of the ASH presentation for complete footnotes for the right panel
Dexamethasone (Dex); once daily (QD)

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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)

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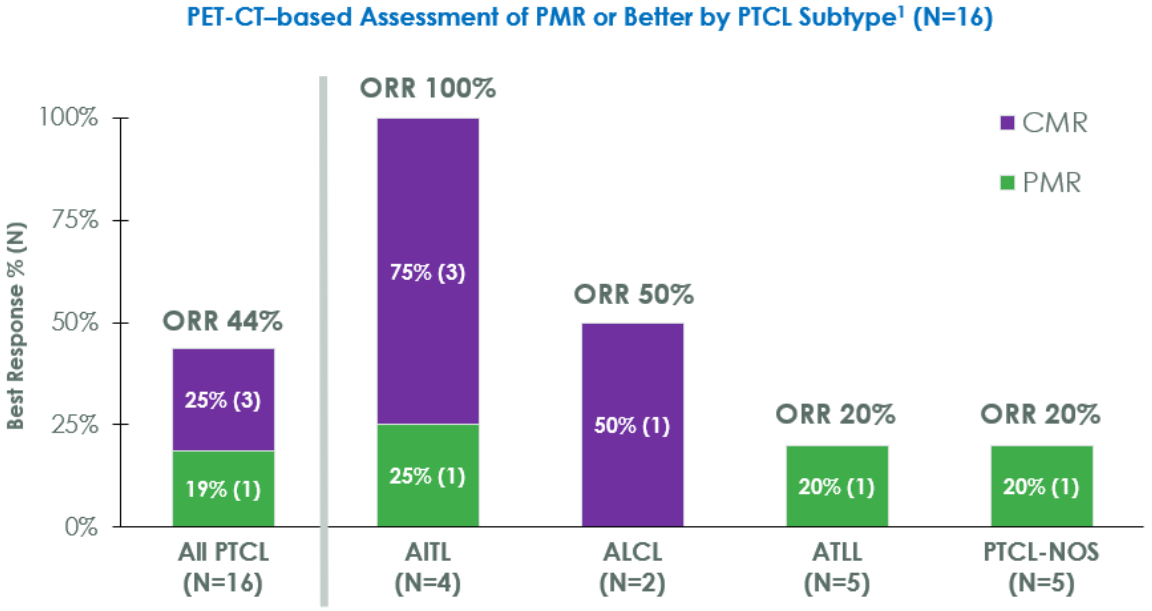
Cemsidomide Data at ASH Demonstrated a Well-tolerated Profile, as Well as Compelling and Deep Responses in PTCL Patients

Compelling & Deep Responses Achieved Across PTCL Subtypes



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)

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

[1] 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. *Events of Interest

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); 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)

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

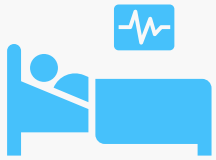
INITIAL CEMSIDOMIDE DEVELOPMENT PATH IN PTCL

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
- Fastest path to label

Dex combination in late-line MM

Monotherapy in 2L+ PTCL

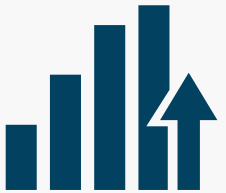
2

- 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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CFT1946

BRAF Mutant V600 Degrader

Colorectal Cancer, Melanoma &
Other BRAF Mutant Solid Tumors

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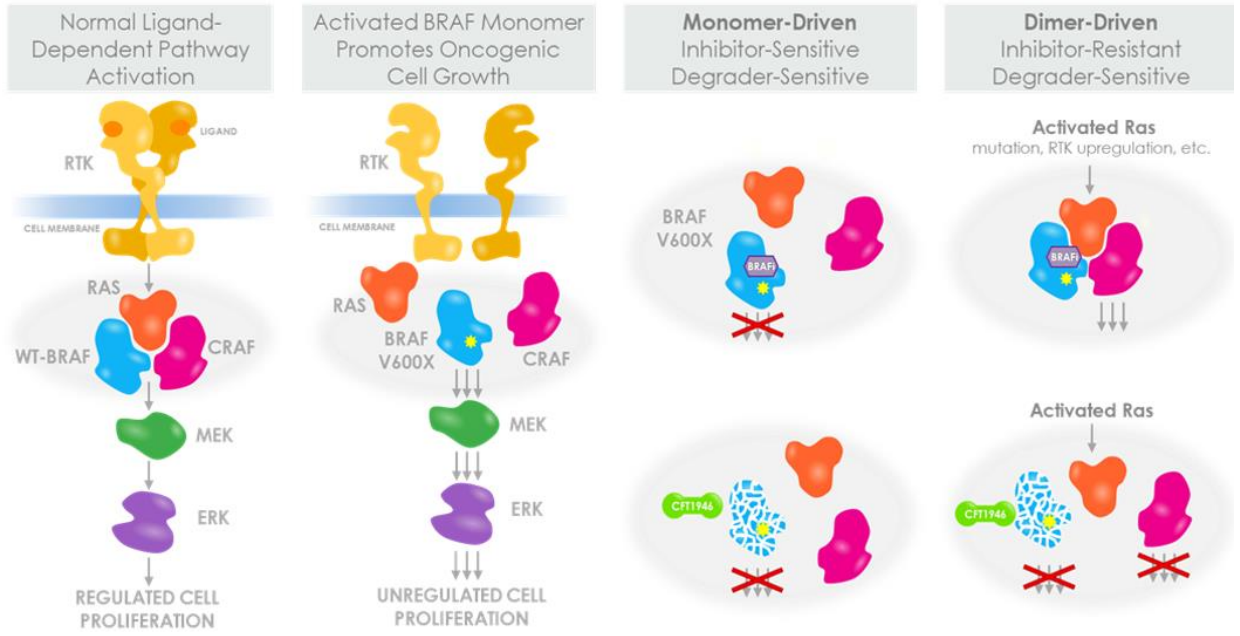
CFT1946 Is an Oral, Potent Degrader of BRAF V600 Mutants With Potential to Improve Outcomes for Patients

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:

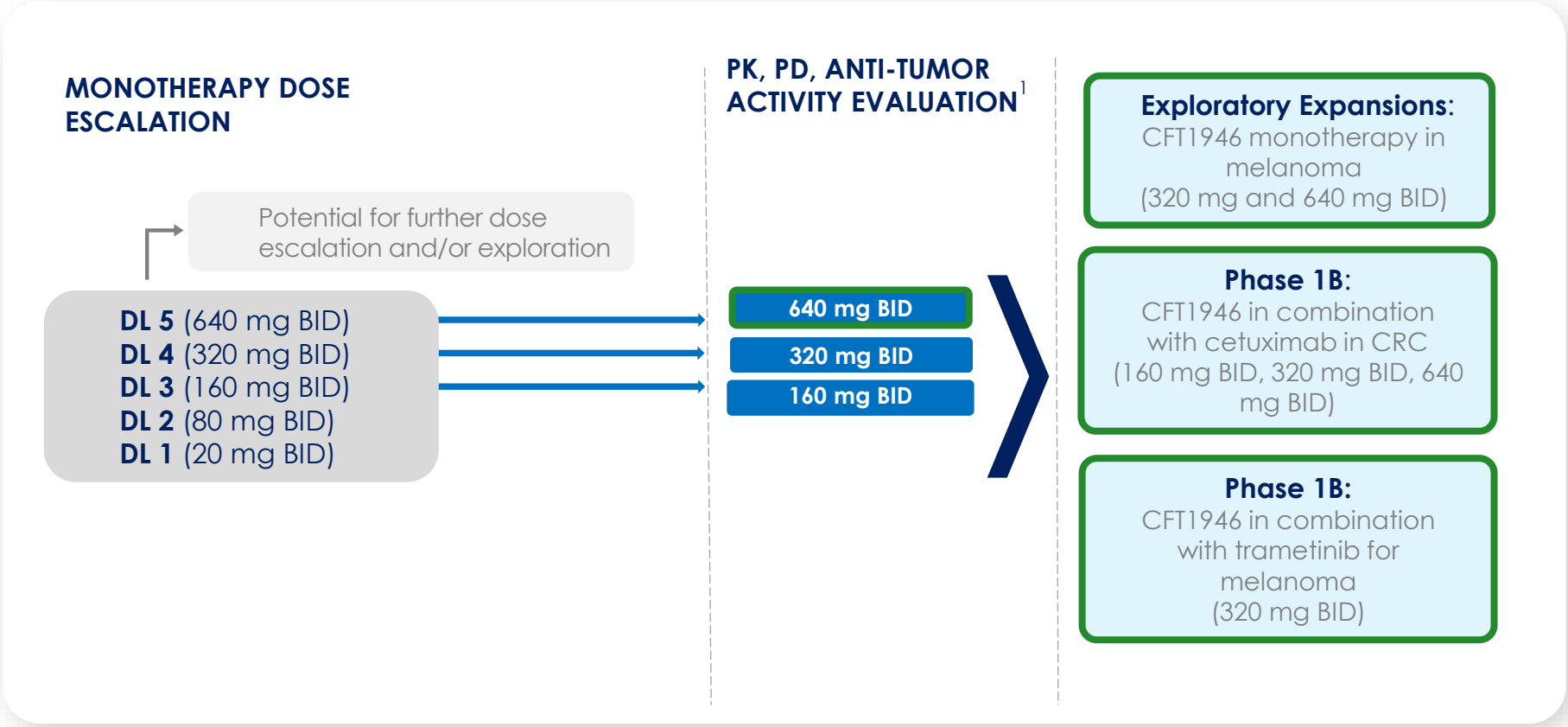
- Resistance mechanisms lead to **limited duration of response**
- Toxicities associated with inhibition of wild-type BRAF **limit tolerability**

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)

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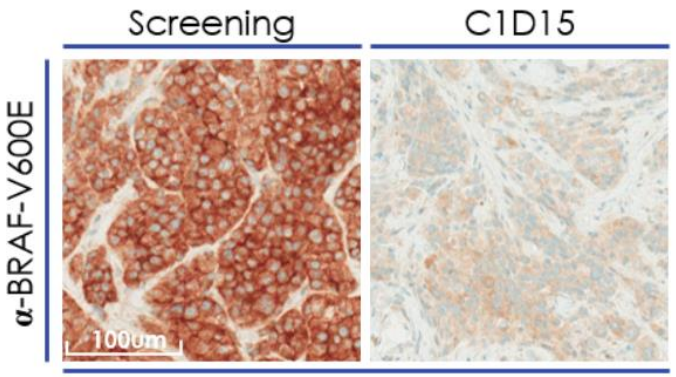
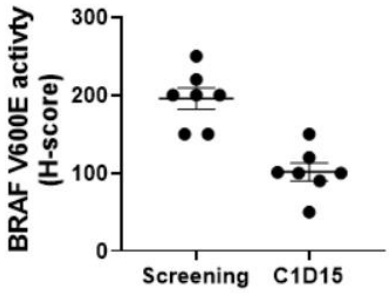
CFT1946 Monotherapy Phase 1 Data Presented at ESMO Demonstrate Proof of Mechanism and Provide Early Evidence of Proof of Degrader Concept

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

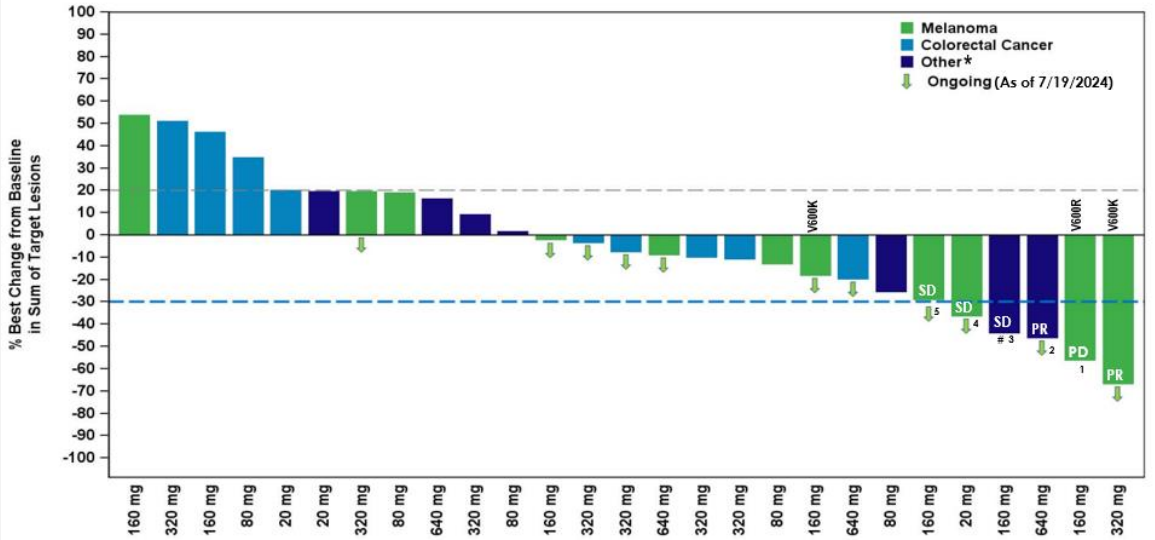


BRAF V600E degradation in paired biopsies at different dose levels (n=1, 80 mg; n=3,160 mg; n=3, 320 mg)

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

Early Evidence of Monotherapy Anti-tumor Activity in Patients who Progressed After Treatment with BRAF inhibitors



*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

Multiple data readouts expected in 2H 2025 to define and enable next phase of development

Serious adverse events (SAEs); dose limiting toxicities (DLTs); treatment-related adverse events (TRAES); 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)

C4 Therapeutics

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).

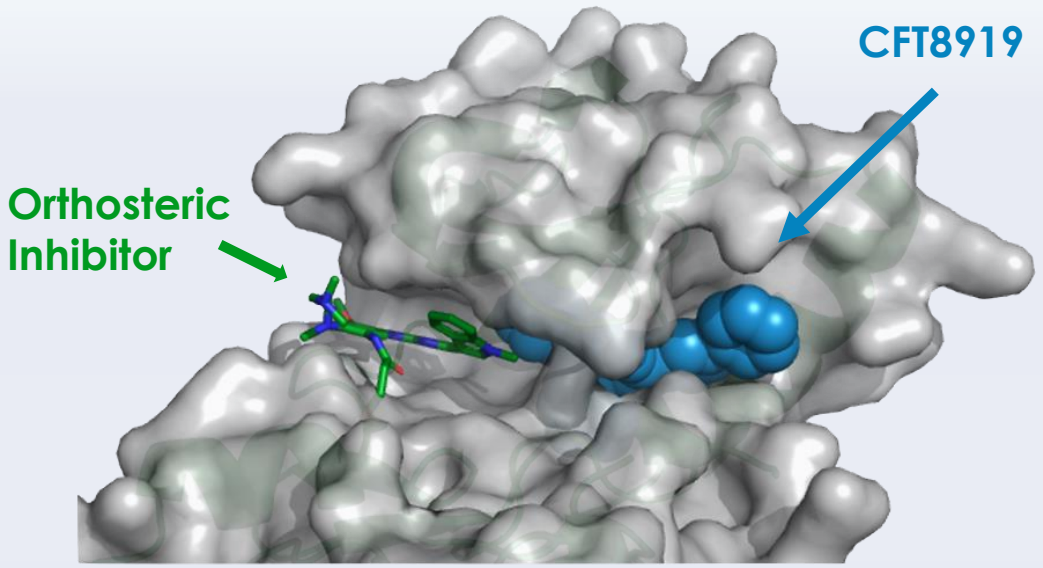
CFT8919

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:

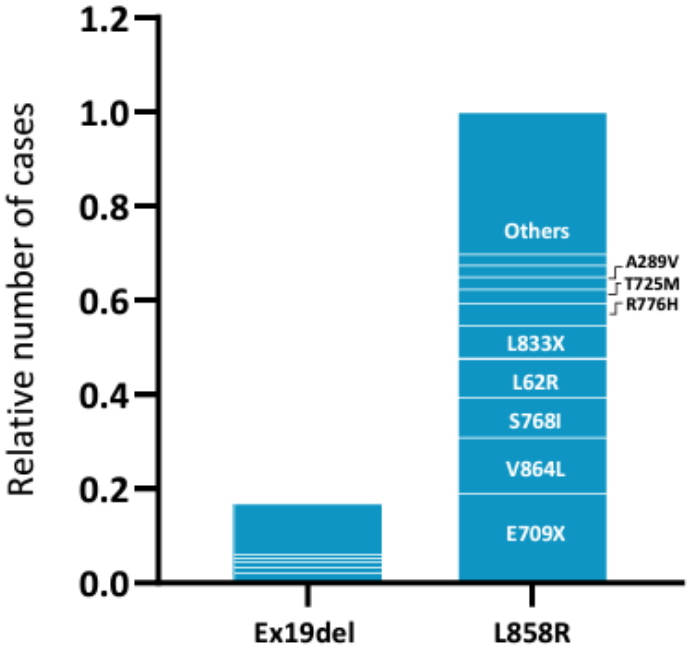
- CFT8919 exploits an allosteric binding site created by the L858R mutation, thereby avoiding resistance mutations to the orthosteric site
- Potent and selective against L858R regardless of secondary mutations with potential for more durable activity in this setting
- Does not hit wild-type, potentially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

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

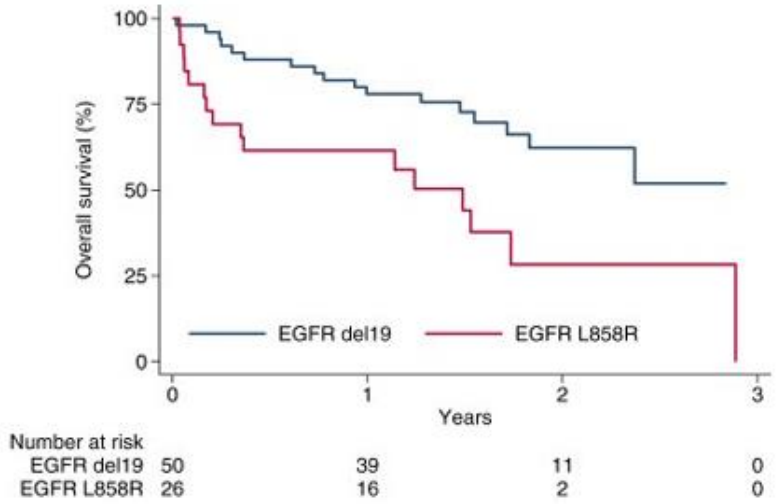
C4 Therapeutics

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



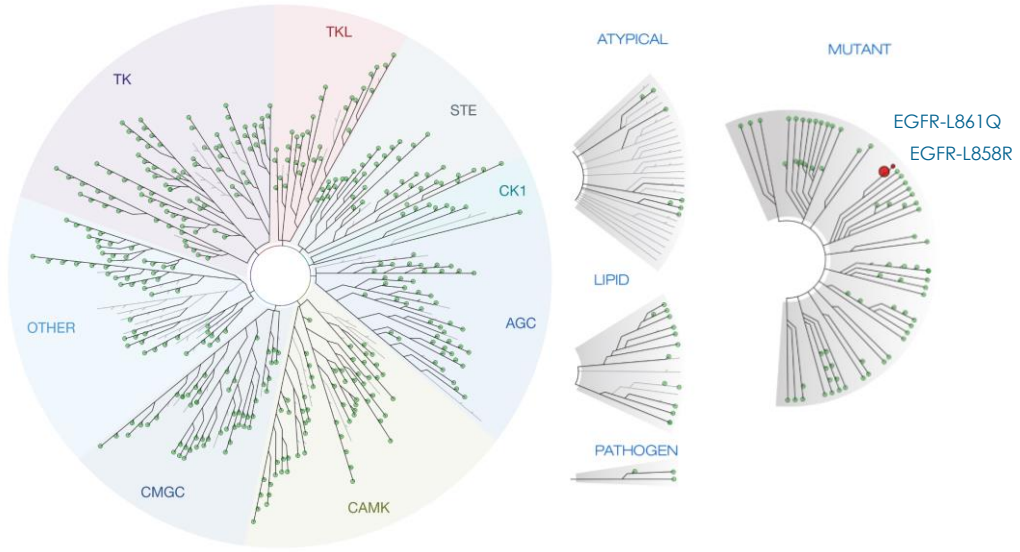
Overall survival by type of mutation in patients with Stage IV EGFR mutated NSCLC and brain metastasis who received first-line treatment with osimertinib

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

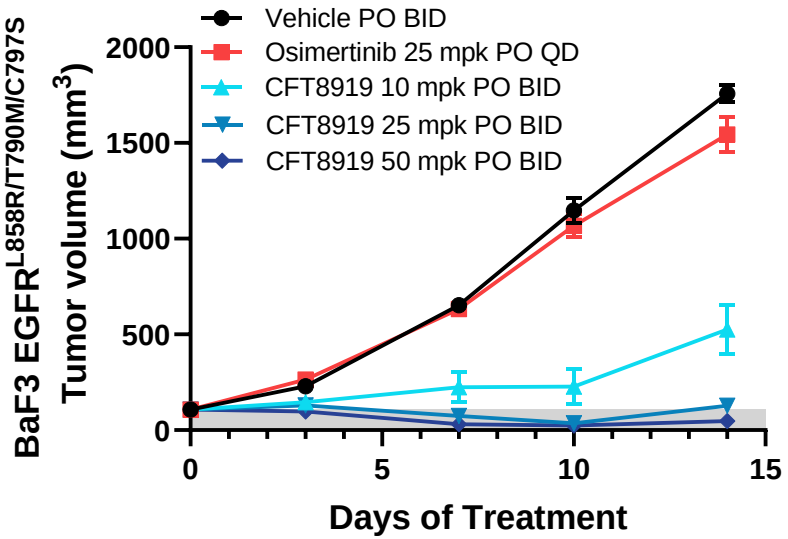
Sources: 1. From Black Diamond's analyses of 94,939 sequencing reports from treatment naive NSCLC (Guardant Health) presented at AACR 2024 (https://blackdiamondtherapeutics.com/assets/files/AACR_2024__BDTX-1535_FINAL_Presentation_20240405.pdf) 2. Gitenbeek, et al. 2023 Progression free survival (PFS)

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)

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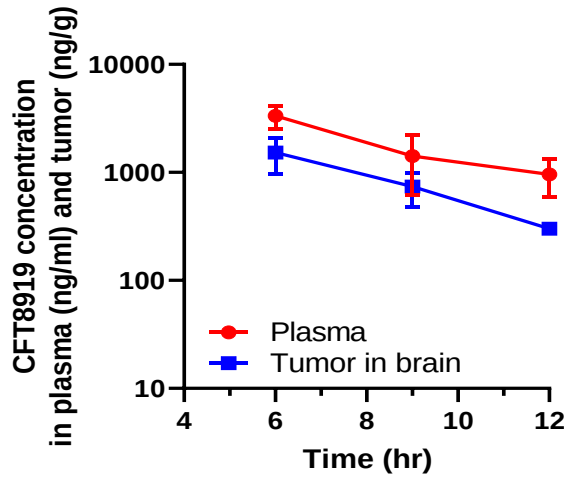
CFT8919 Demonstrates Activity in Brain Metastasis Model

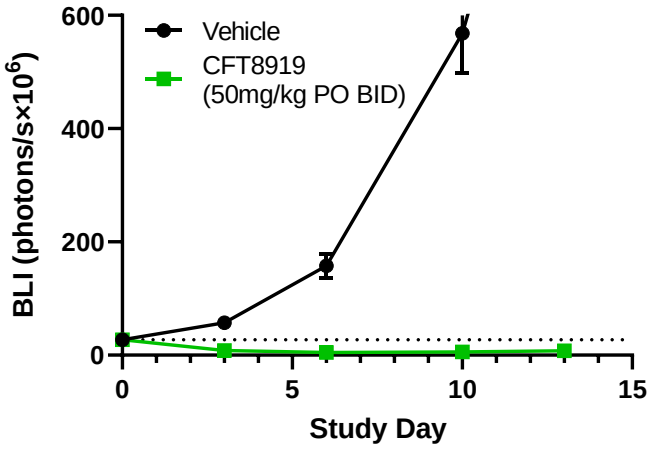
Mean Plasma & Tumor Concentration



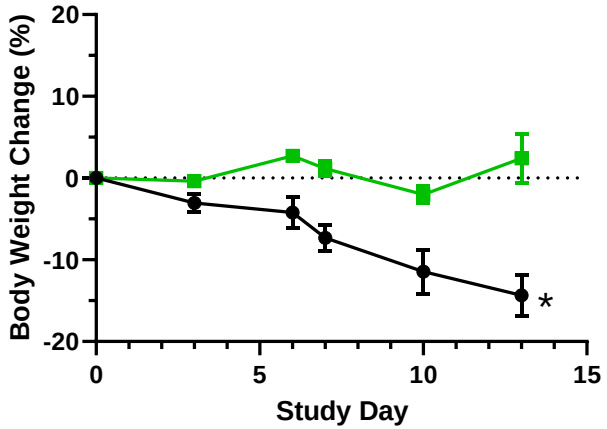
Plasma clearance $t_{1/2}$ = 3.1 hrs

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)

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**