C4 Therapeutics

Protein degraded.
Disease targeted.
Lives transformed.

December 2024

Forward-looking Statements and Intellectual Property

Forward-looking Statements

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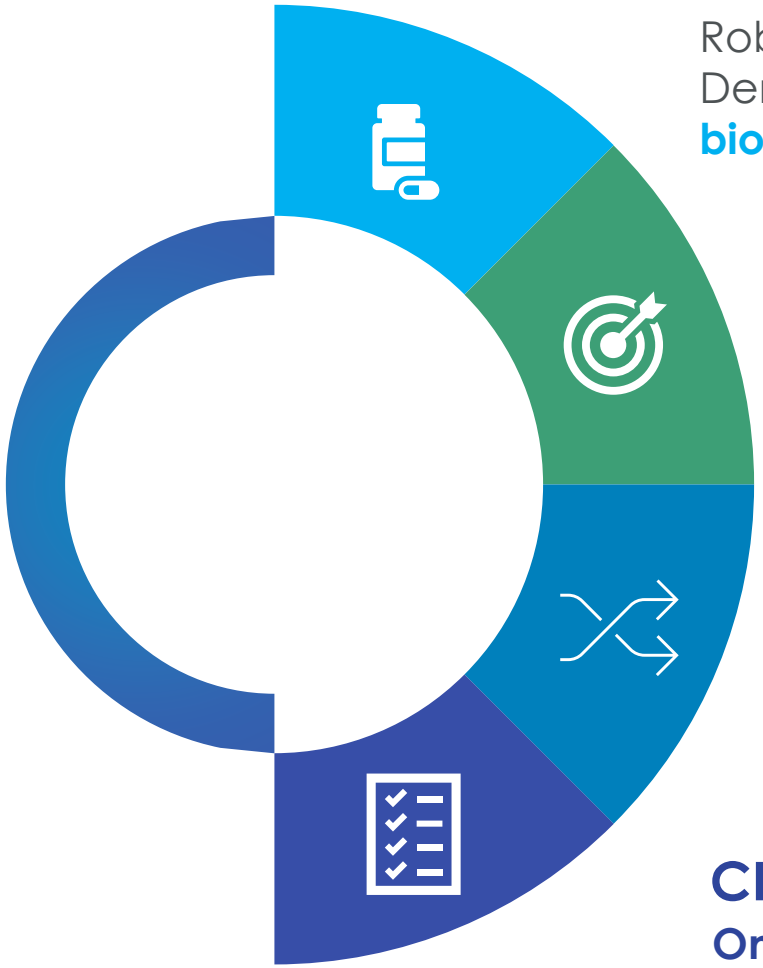
C4T Is a Recognized Leader in Delivering on the Promise of Targeted Protein Degradation

Our Mission

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



WORLD-CLASS DEGRADER PLATFORM

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

RIGOROUS TARGET SELECTION

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

BROAD DEGRADER APPROACH

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

CLINICAL PIPELINE

Oncology degraders against targets of high unmet need

Advancing a Broad Pipeline to Deliver Near-Term Value

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

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

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

Significant Progress Across Clinical Programs

Cemsidomide

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

CFT1946

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

CFT8919

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

Collaborations Have Further Validated TORPEDO Platform

Biogen

- ✓ Delivered two development candidates for non-oncology targets

MERCK

- ✓ Established partnership to discover and develop degrader antibody conjugates

Merck KGaA
Darmstadt, Germany

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

…Which Set the Stage to Unlock Value

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

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

C4 Therapeutics

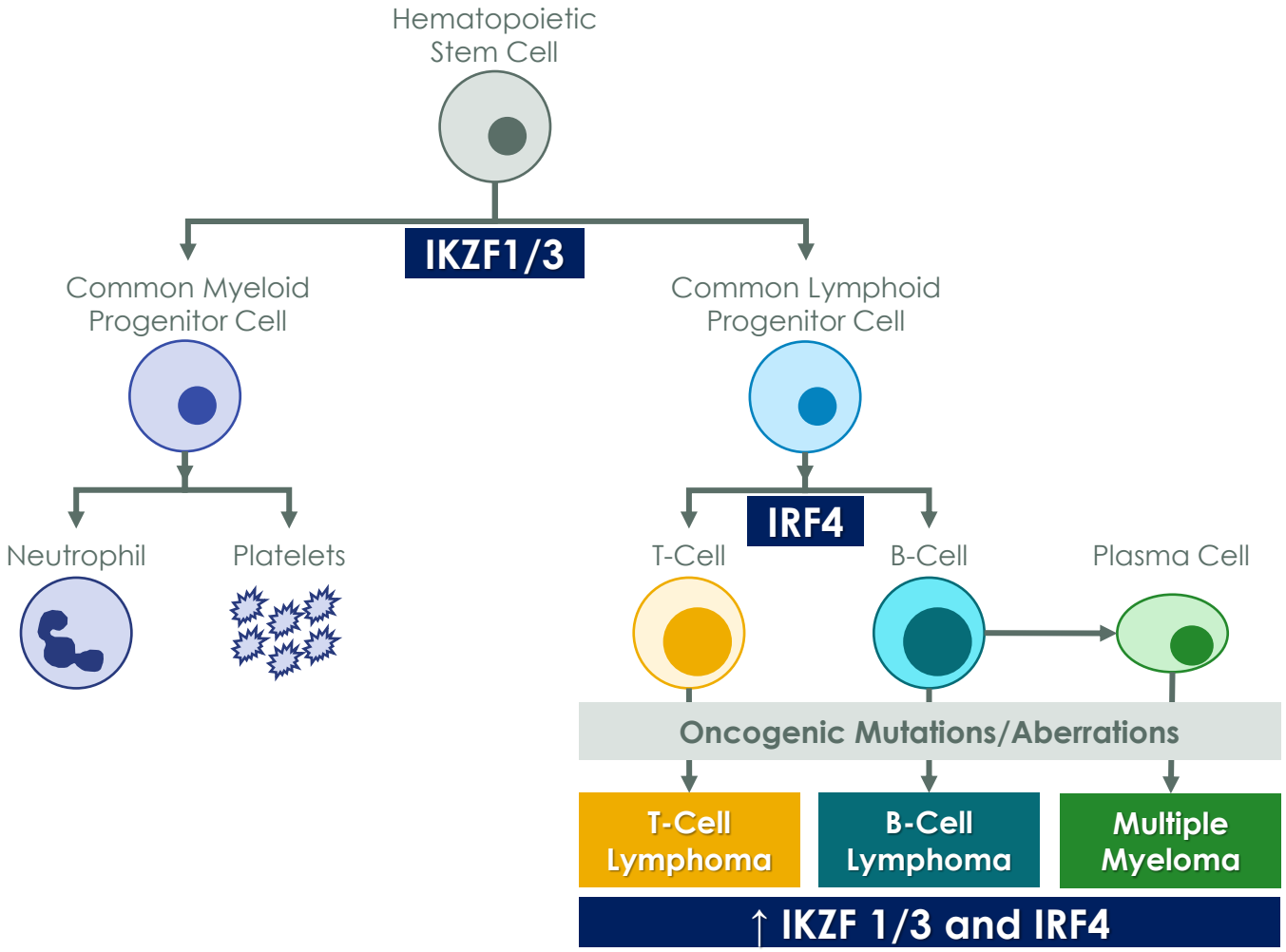
Cemsidomide

Targeting IKZF1/3

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

C4 Therapeutics

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



Key Roles of IKZF1/3

Physiological Functions:

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

Oncogenic Functions:

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

IKZF1/3 Degradation Leads to:

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

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

C4 Therapeutics

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

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

PHASE 1 DOSE ESCALATION TRIAL

2022

R/R MM
Monotherapy

Dosing: QD

21 days on/
7 days off

N=5

Status: Complete

2023

R/R MM
Monotherapy

Dosing: MWF & QD

14 days on/
14 days off

N=22

Status: Complete

- 14 days on/14 days off established as an effective dosing schedule
- Demonstrated monotherapy anti-myeloma and immunomodulatory effects supporting combination with other anti-myeloma agents

ASH 2024

R/R MM
Dex Combo

Dosing: MWF & QD

14 days on/
14 days off

N=~40

Status: Enrolling

- Well-tolerated with manageable neutropenia and low rates of infections and febrile neutropenia
- Wide therapeutic index with anti-myeloma activity across a broad range of doses

R/R NHL
Monotherapy

Dosing: MWF & QD

14 days on/
14 days off

N=~25

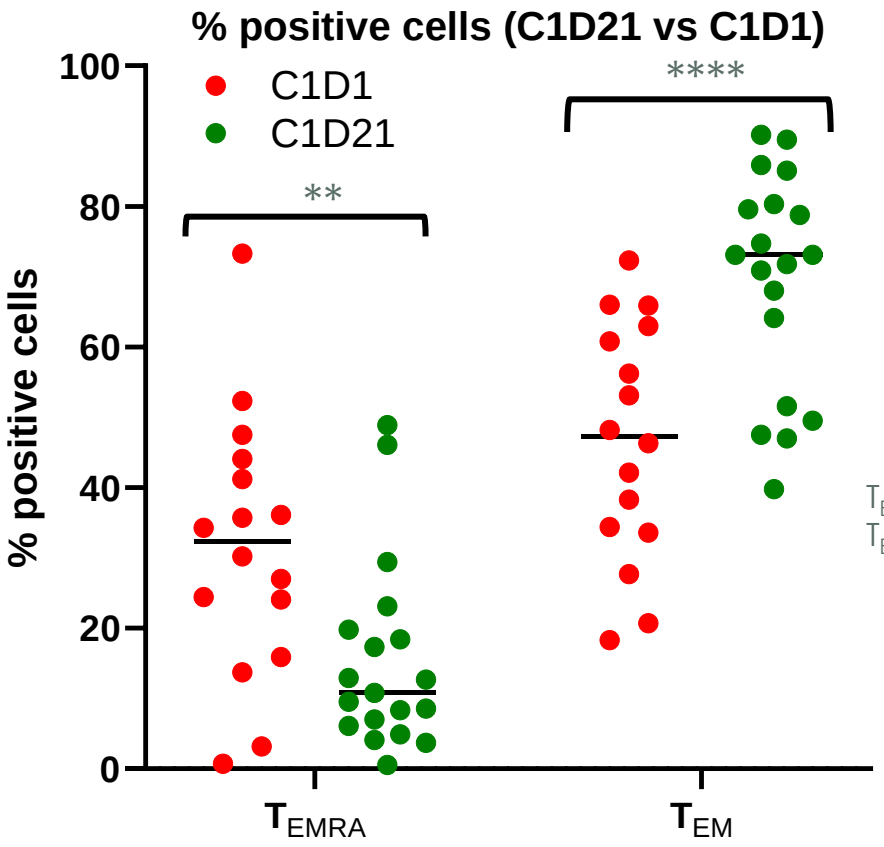
Status: Enrolling

- Well-tolerated with additional dose finding ongoing
- Compelling anti-lymphoma activity across a broad range of doses in PTCL

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

C4 Therapeutics

Clinical Evidence of Immune T-cell Activation With Cemsidomide Monotherapy



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

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

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

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

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

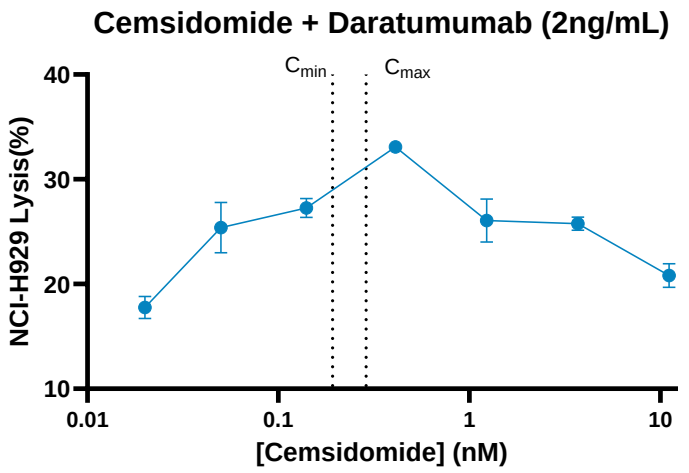
Cemsidomide Combined With Novel MM Agents Demonstrated Enhanced Immune Cell Lysis in Non-clinical Translational Models

DARZALEX® (daratumumab)

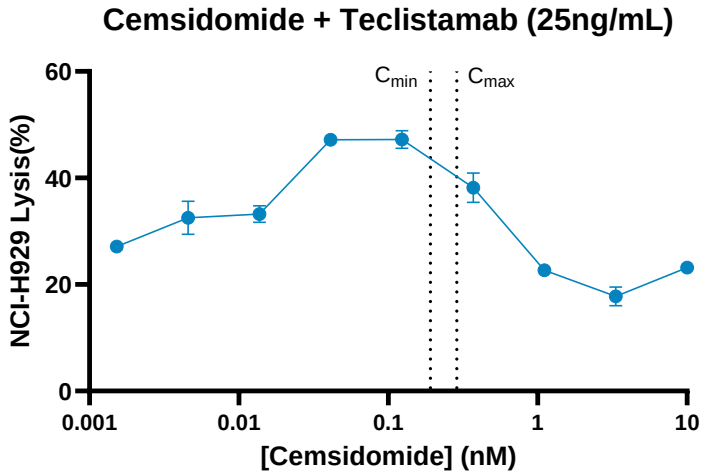
TECVAYLI™ (teclistamab)

TALVEY® (talquetamab-tgvs)

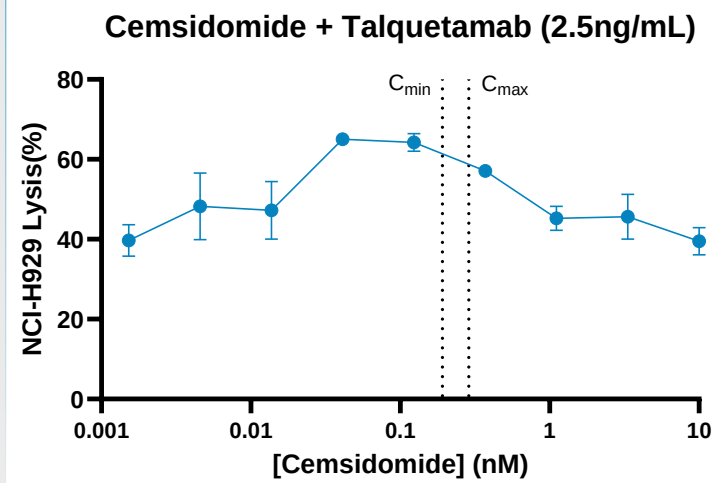
Cemsidomide + Daratumumab (Anti-CD38)



Cemsidomide + Teclistamab (BCMA Bispecific)



Cemsidomide + Talquetamab (GPRC5D Bispecific)



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

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

KEY INCLUSION CRITERIA

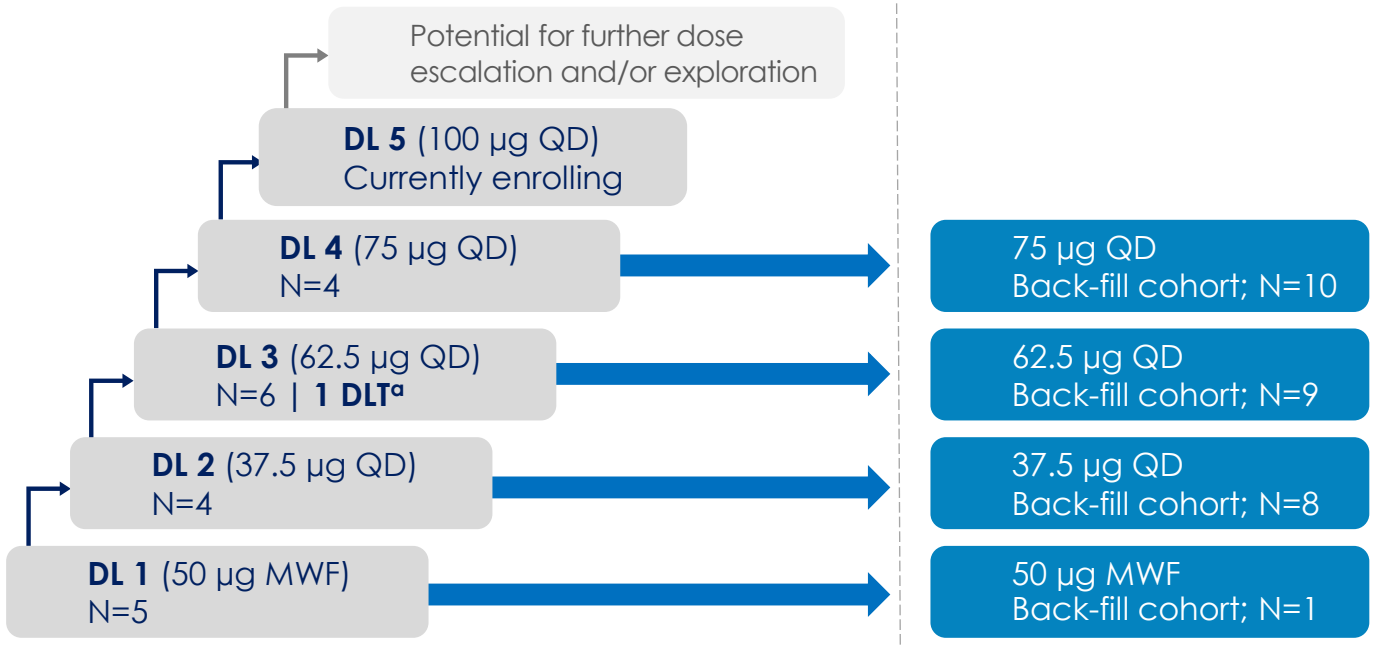
- Adults with MM, R/R to at least 3 prior lines of therapy that have included lenalidomide, pomalidomide, a proteasome inhibitor, a glucocorticoid, and an anti-CD38 monoclonal antibody
- Nonresponsive to or progressed within 60 days of prior therapy
- Creatinine clearance ≥40 mL/min
- ECOG ≤2

Phase 1 Study Endpoints

- **Primary:** assess safety, tolerability and define the RP2D/MTD
- **Secondary:** assess PK, PD, and preliminary anti-tumor activity

DOSE ESCALATION
CEMSIDOMIDE 14/14 + DEX*

Utilizing a Bayesian logistic regression model until determination of the MTD and/or RP2D



*Cemsidomide administered as 14 days on/14 days off in a 28-day cycle; Dex was dosed on days 1, 8, 15, and 22 at doses of 40 mg orally for patients ≤75 years old and 20 mg orally for patients >75 years old; 2 patients at 100 µg are excluded as they had not completed Cycle 1 as of the data cut off date.

[a]DLT at 62.5 µg QD was due to Grade 4 neutropenia lasting >7 days.

Eastern Cooperative Oncology Group (ECOG); maximum tolerated dose (MTD); Monday Wednesday Friday (MWF); multiple myeloma (MM); once daily (QD); pharmacodynamics (PD); pharmacokinetic (PK); recommended Phase 2 dose (RP2D); relapsed refractory (R/R)

C4 Therapeutics

Data cutoff: 10/11/24

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

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

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

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

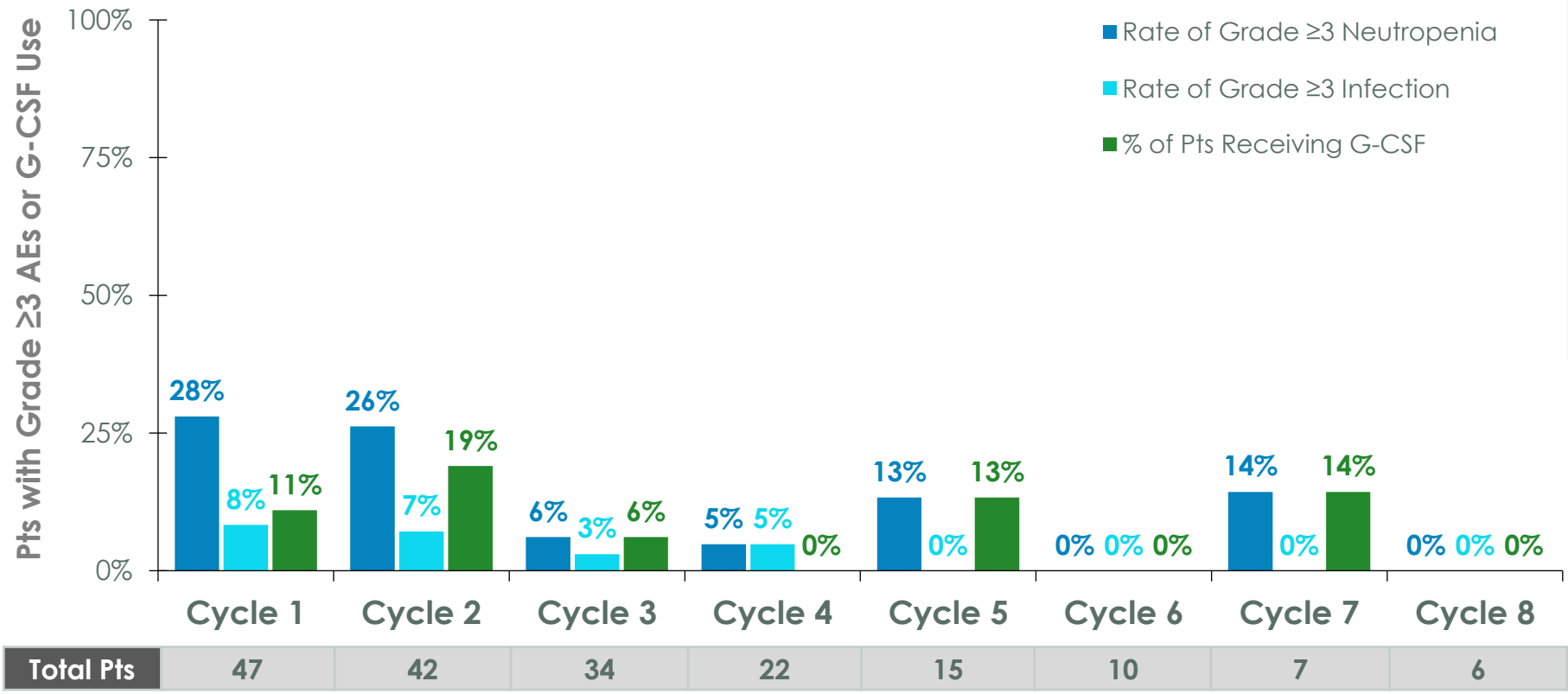
[1]Primary reason of discontinuation of patient at 37.5 µg was due to withdrawal of consent; primary reason of discontinuation of patient at 75 µg was due to death unrelated to cemsidomide.
Adverse events (AEs); dose limiting toxicity (DLT); treatment emergent adverse events (TEAEs)

C4 Therapeutics

Data cutoff: 10/11/24

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

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



Total Pts	47	42	34	22	15	10	7	6

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

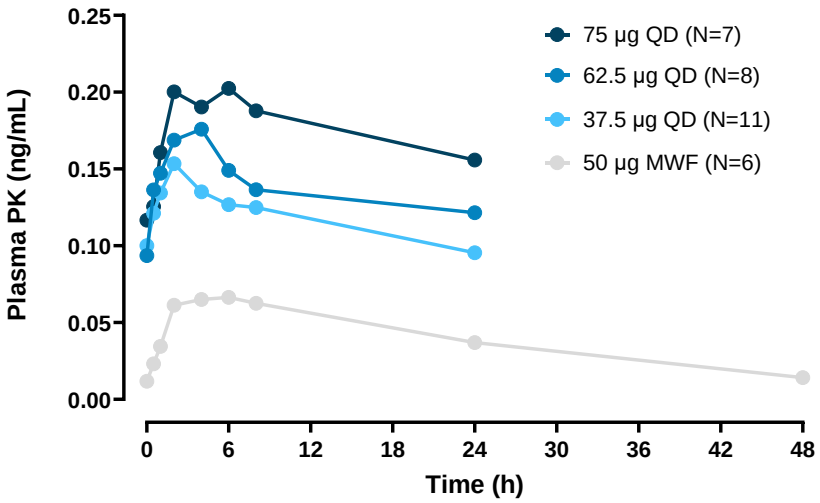
Notes: No cases of Grade ≥3 neutropenia were recorded after Cycle 7. One patient experienced a Grade ≥3 infection in a Cycle >8. G-CSF use was not permitted during Cycle 1 in escalation cohorts. One patient in the 50 µg MWF cohort came off study during Cycle 1 and received G-CSF after treatment was discontinued.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

C4 Therapeutics

Data cutoff: 10/11/24

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

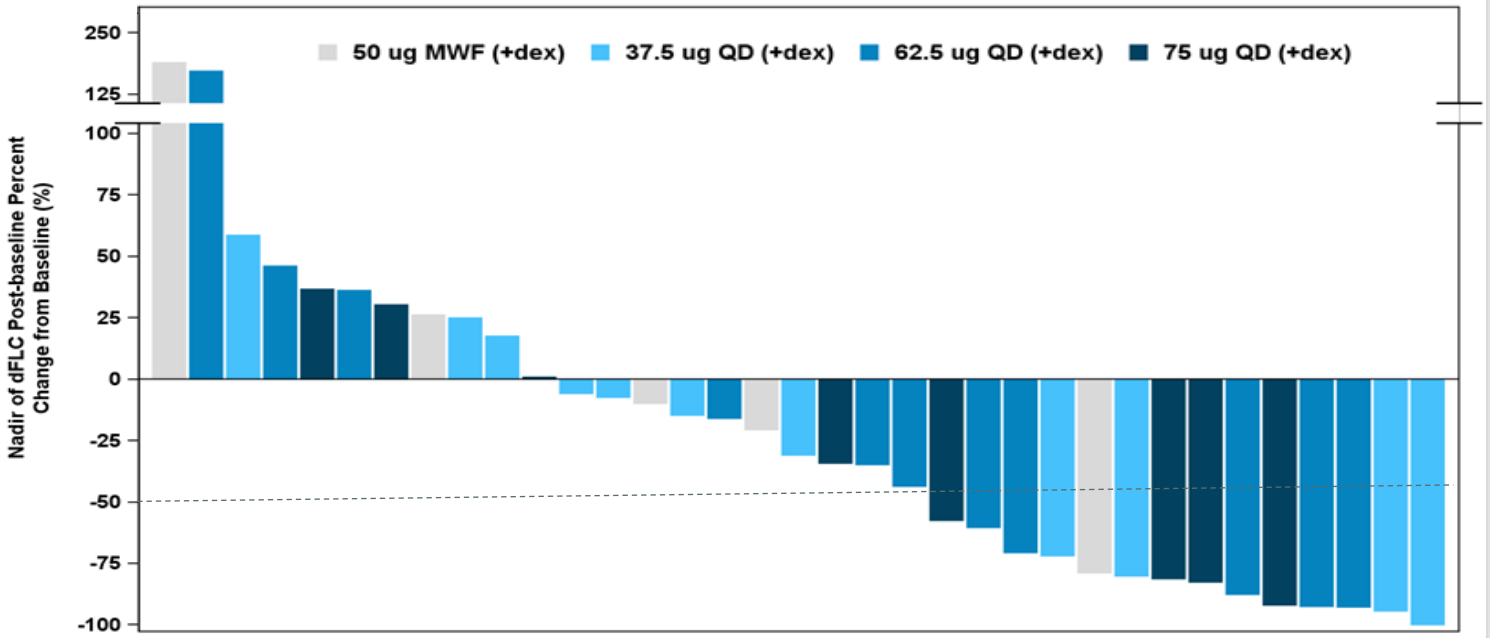
Dose Proportional Exposure



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

Best Change in dFLC from Baseline (Cemsidomide + Dex)

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



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

*Only included treated patients who meet both criterion (A) and (B). (A) baseline kappa free light chain value >19.4 mg/L or baseline lambda free light chain value >26.3 mg/L. (B) ratio of baseline free light chain kappa over baseline free light chain value lambda >4:1 or <1:2.

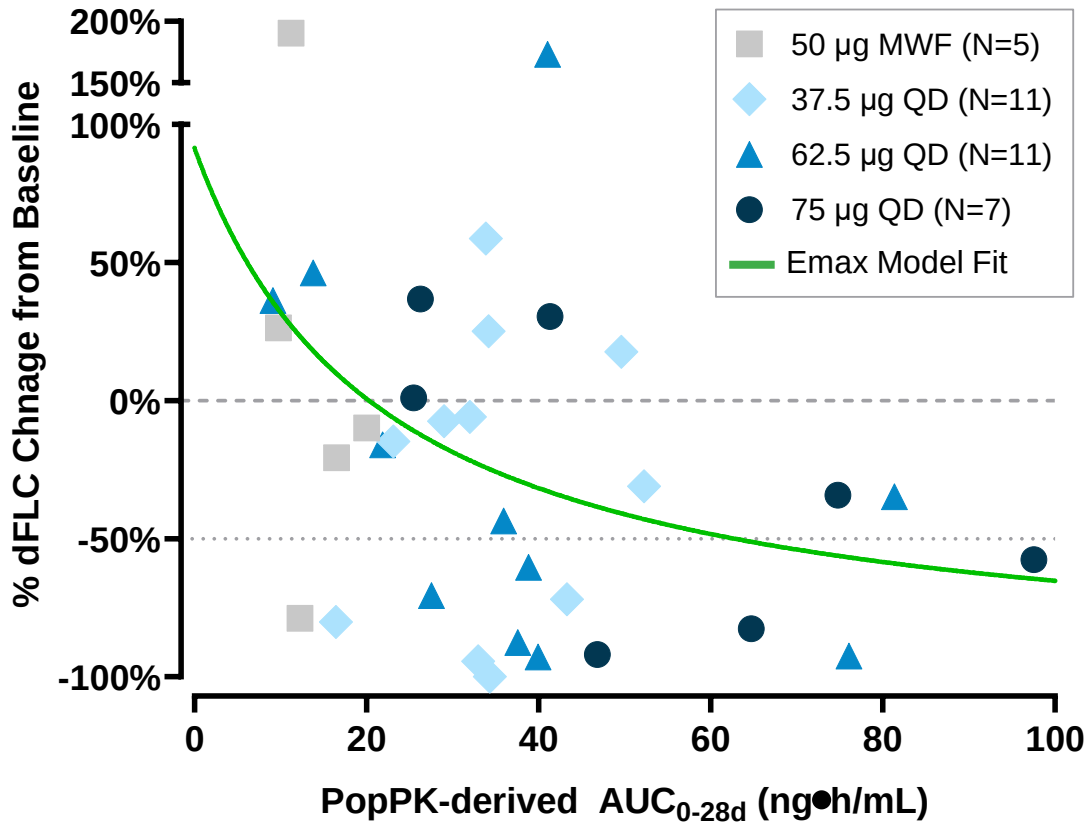
Difference in involved and uninvolved free light chain (dFLC); once daily (QD); Monday Wednesday Friday (MWF); multiple myeloma (MM); pharmacokinetic (PK)

C4 Therapeutics

Data cutoff: 10/11/24

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

Cemsidomide + Dex PK Exposure vs. dFLC Change



Exposure (AUC) Quartiles

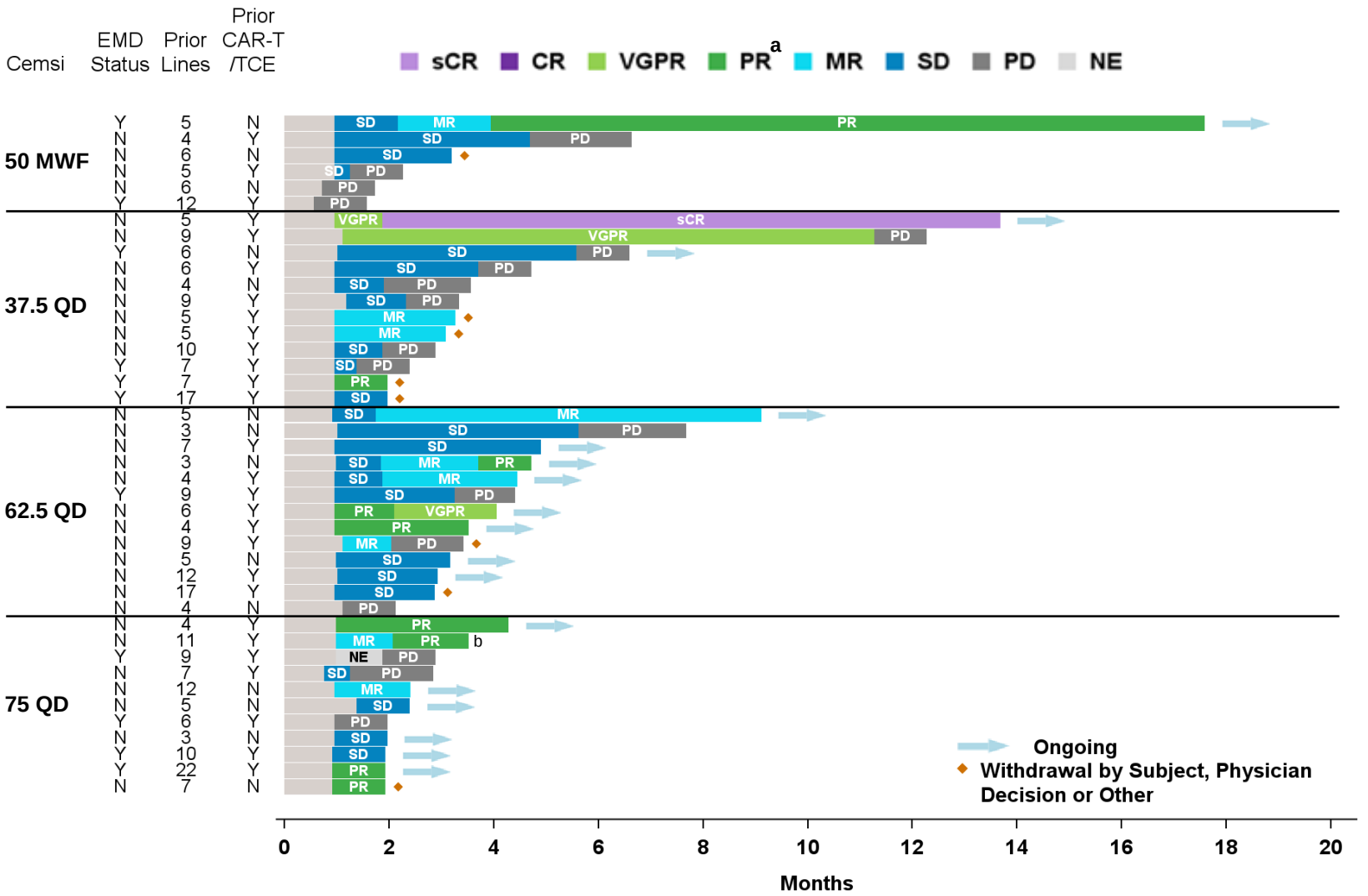
	<Q1 (N=9)	Q1-Q2 (N=8)	Q2-Q3 (N=8)	>Q3 (N=9)
Mean $AUC_{0\text{-}28d}$ (ng*h/mL)	14.6	28.8	37.9	**65.2**
Mean Change in dFLC from Baseline	+10%	-12%	-20%	**-53%**
Cemsidomide + Dex Dose	**~17 µg** QD	**~35 µg** QD	**~45 µg** QD	**~78 µg** QD

N=34 with abnormal baseline sFLC defined as (A) kappa FLC >19.4 mg/L or lambda FLC >26.3 mg/L and (B) kappa-to-lambda FLC ratio >4 or <0.5.
Cemsidomide dose was back-calculated based on the population PK model.
Area under the curve (AUC); difference in involved and uninvolved free light chain (dFLC); maximum response (Emax); Monday Wednesday Friday (MWF); once daily (QD); population pharmacokinetics (popPK); pharmacokinetic (PK)

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Demonstrated Anti-Myeloma Activity Across Dose Levels



As of the data cutoff:

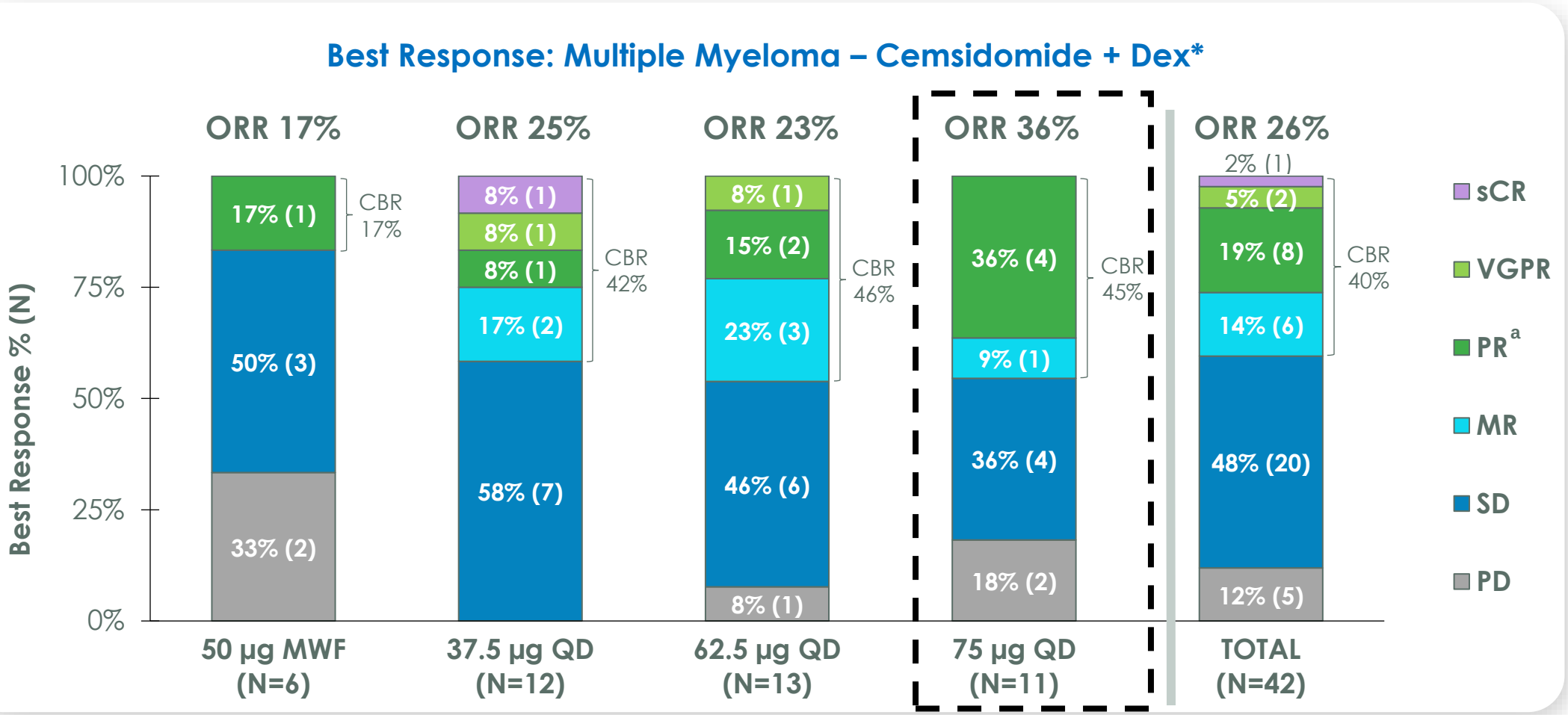
- **26% ORR** and **40% clinical benefit rate across all dose levels** evaluated
- At the two highest dose levels evaluated to date (62.5 µg and 75 µg), **62% of all patients remain on treatment**[1]

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

C4 Therapeutics

Data cutoff: 10/11/24

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



*Investigator assessed response

[a]1 patient in the 37.5 µg cohort achieved a PR based on light chains, no follow up M protein available; 1 patient in the 62.5 µg cohort had an unconfirmed PR as of the data cutoff date; 1 patient in the 75 µg cohort had an unconfirmed PR as of the data cutoff date.

Minimal response (MR); Monday Wednesday Friday (MWF); once daily (QD); partial response (PR); progressive disease (PD); stable disease (SD); stringent complete response (sCR); very good partial response (VGPR)

Overall Response Rate (≥ PR) (ORR); Clinical Benefit Rate (≥ MR) (CBR)

C4 Therapeutics

Data cutoff: 10/11/24

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

KEY INCLUSION CRITERIA

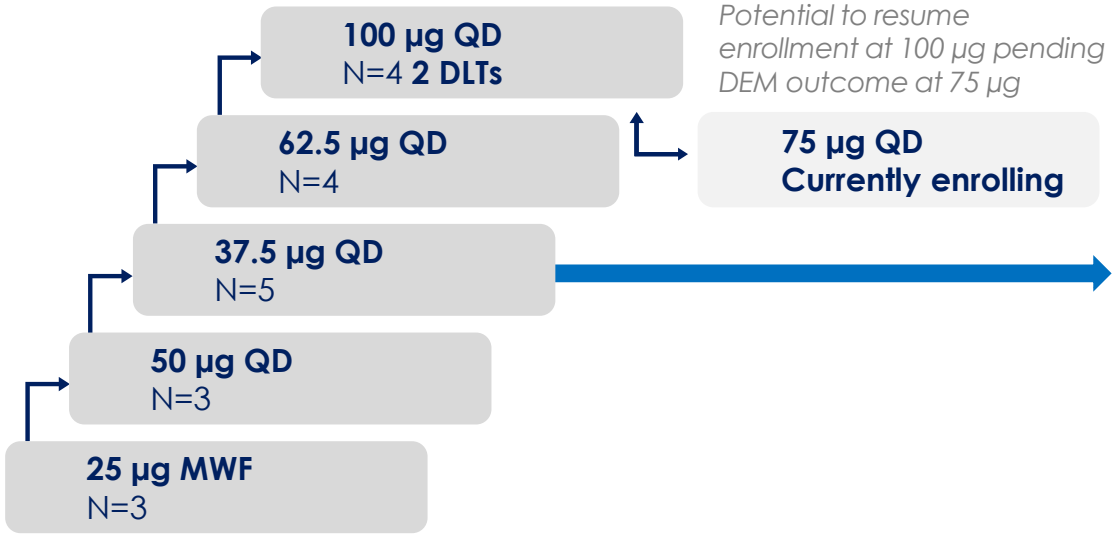
- Adults with NHL, R/R to prior therapy
  - PTCL patients must have received at least 1 prior alkylator-based chemotherapy
  - ALCL patients must have also received a CD-30 mAb
- Nonresponsive to or progressed within 60 days of prior therapy
- Creatinine clearance ≥40 mL/min
- ECOG ≤2

Phase 1 Study Endpoints

- **Primary:** assess safety, tolerability and define the RP2D/MTD
- **Secondary**: assess PK, PD, and preliminary anti-tumor activity

DOSE ESCALATION CEMSIDOMIDE 14/14

Utilizing a Bayesian logistic regression model until determination of the MTD and/or RP2D



BACK-FILL COHORT(S)

37.5 µg QD
Back-fill cohort; N=4

PHASE 2

Phase 2 Expansion

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

C4 Therapeutics

Data cutoff date: 10/11/2024

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

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

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

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

Data cutoff: 10/11/24

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

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

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

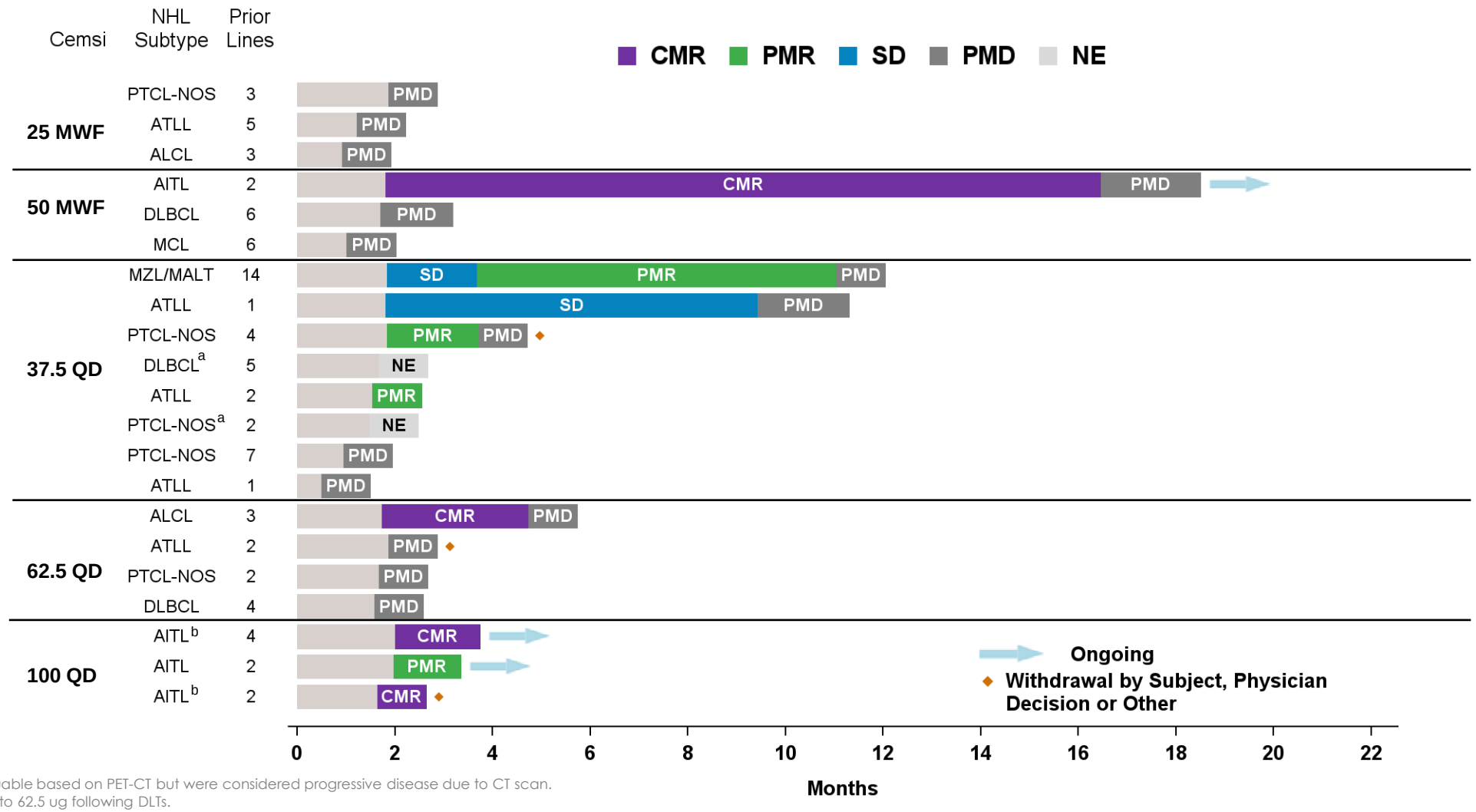
One patient experienced a Grade 5 AE (hip fracture resulting in transfer to hospice)

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

C4 Therapeutics

Data cutoff: 10/11/24

Cemsidomide Clinical Responses Were Observed Across a Broad Range of Doses

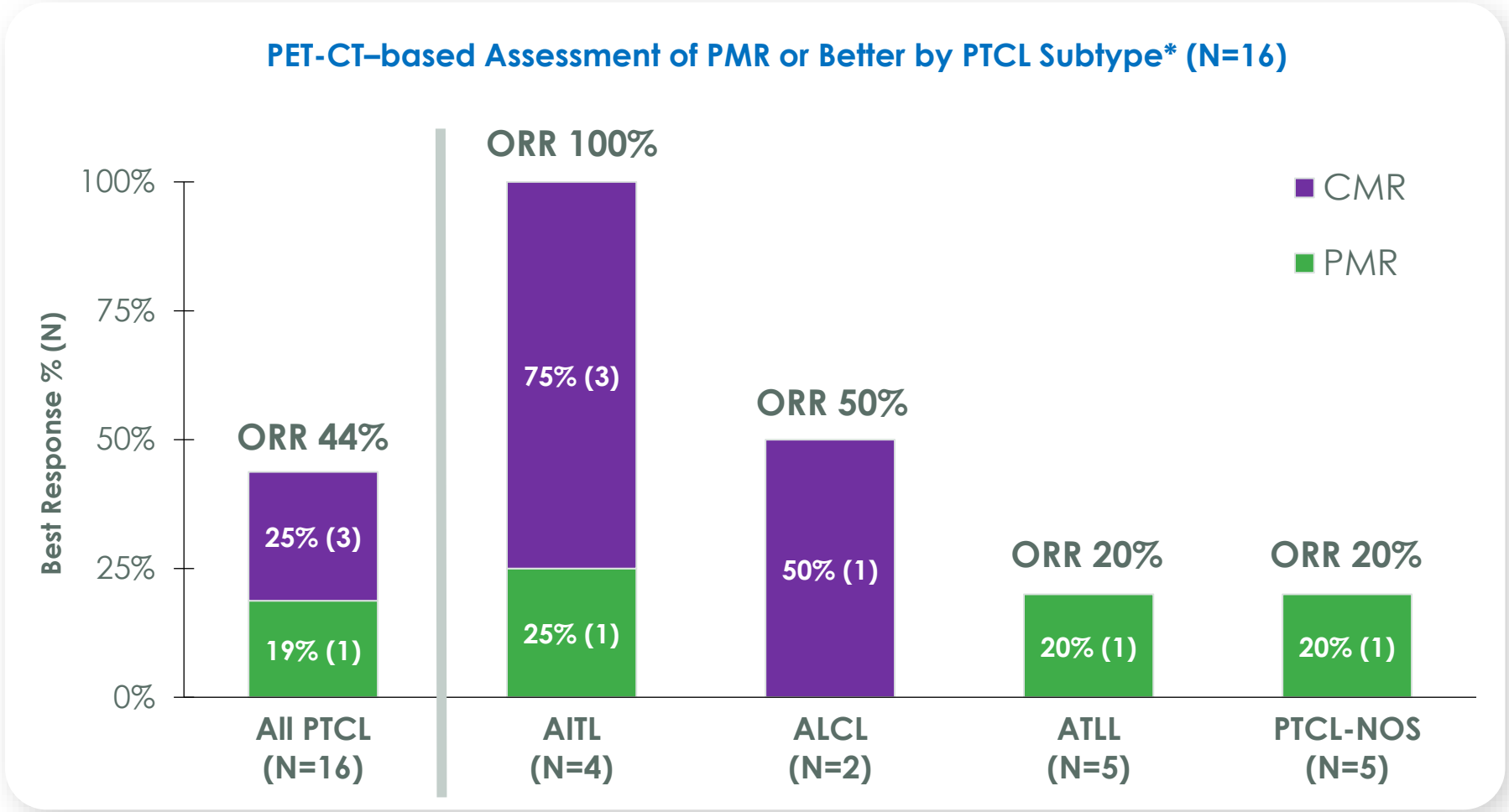


[a] Both patients were not evaluable based on PET-CT but were considered progressive disease due to CT scan.
[b] Both patients dose reduced to 62.5 ug following DLTs.
Anaplastic large cell lymphoma (ALCL); adult T-cell leukemia/lymphoma (ATLL); angioimmunoblastic T-cell lymphoma (AITL); complete metabolic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

C4 Therapeutics

Data cutoff: 10/11/24

Compelling and Deep Responses Achieved Across PTCL Subtypes



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

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

C4 Therapeutics

Data cutoff: 10/11/24

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

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

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

MM Market Opportunity

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

NHL Market Opportunity

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

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

C4 Therapeutics

CFT1946

Targeting BRAF V600 Mutant

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

C4 Therapeutics

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

Key Limitations of Approved BRAF Inhibitors:

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

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

BRAF inhibitor market is estimated to grow to

~$3B by 2028[2]

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

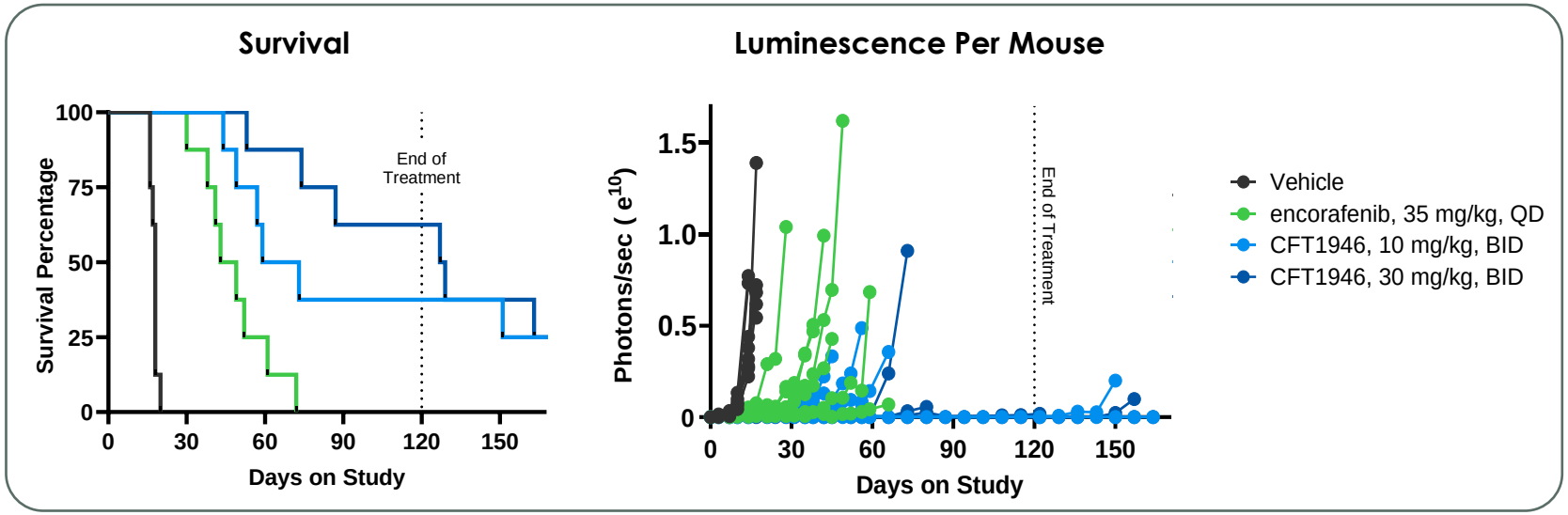
- ✓ Prevents BRAF V600 mutant **mono/heterodimer formation**[1]
- ✓ **Avoids paradoxical activation** seen with approved inhibitors[1]
- ✓ **Addresses MAPK pathway alterations** resulting from BRAF inhibitor resistance (e.g., BRAF splice variants, BRAF amplification)[1]
- ✓ **Specifically targets BRAF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

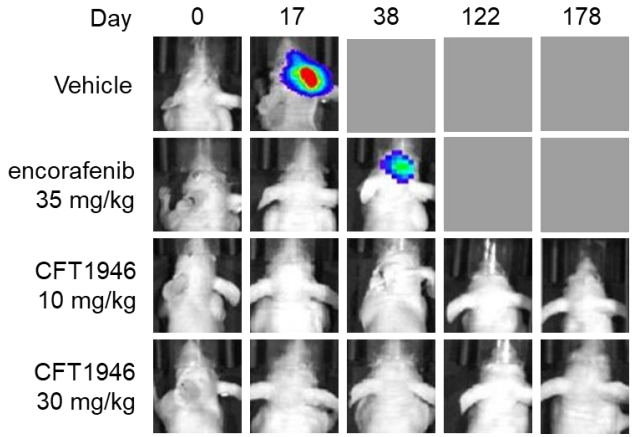
[1]Kreger B et al. Abstract 1658, AACR 2024; [2]Evaluate Pharma 2023
Adverse event (AE); Mitogen-activated protein kinase (MAPK)

C4 Therapeutics

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

A375 BRAF V600E-Luc Intracranial Model





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

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

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

Central nervous system (CNS)

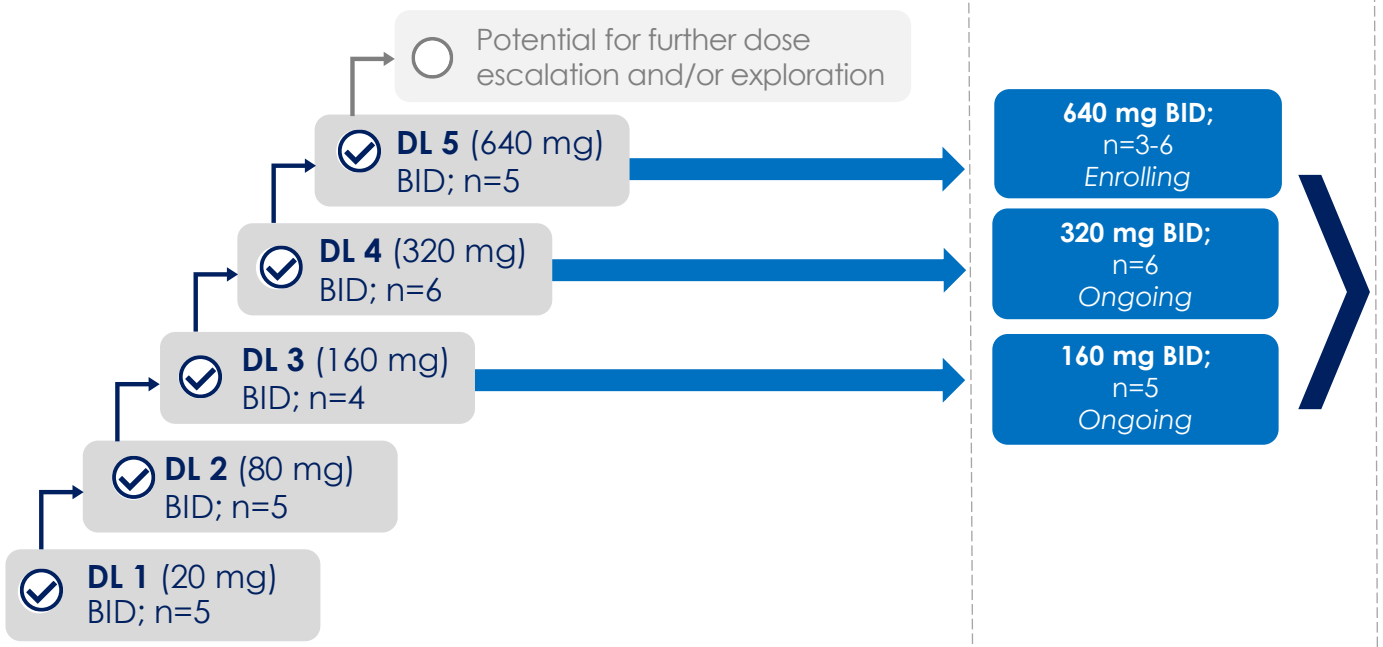
C4 Therapeutics

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

KEY INCLUSION CRITERIA[1]

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

MONOTHERAPY DOSE ESCALATION



PK, PD, ANTI-TUMOR ACTIVITY EVALUATION[2]

640 mg BID; n=3-6 *Enrolling*

320 mg BID; n=6 *Ongoing*

160 mg BID; n=5 *Ongoing*

Exploratory Expansion: CFT1946 monotherapy in melanoma 640 mg BID *Enrolling*

Exploratory Expansion: CFT1946 monotherapy in melanoma 320 mg BID *Ongoing*

Phase 1B: CFT1946 in combination with cetuximab in CRC 160 mg BID *Enrolling*

Phase 1B: CFT1946 in combination with trametinib for melanoma and NSCLC *Pending*

PRIMARY ENDPOINTS

- Safety and tolerability
- Determine RP2D/MTD

SECONDARY ENDPOINTS

- Estimate anti-tumor activity
- Assess PK and PD

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

C4 Therapeutics

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

Proof of Mechanism

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

Proof of Degrader Concept

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

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

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

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

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

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

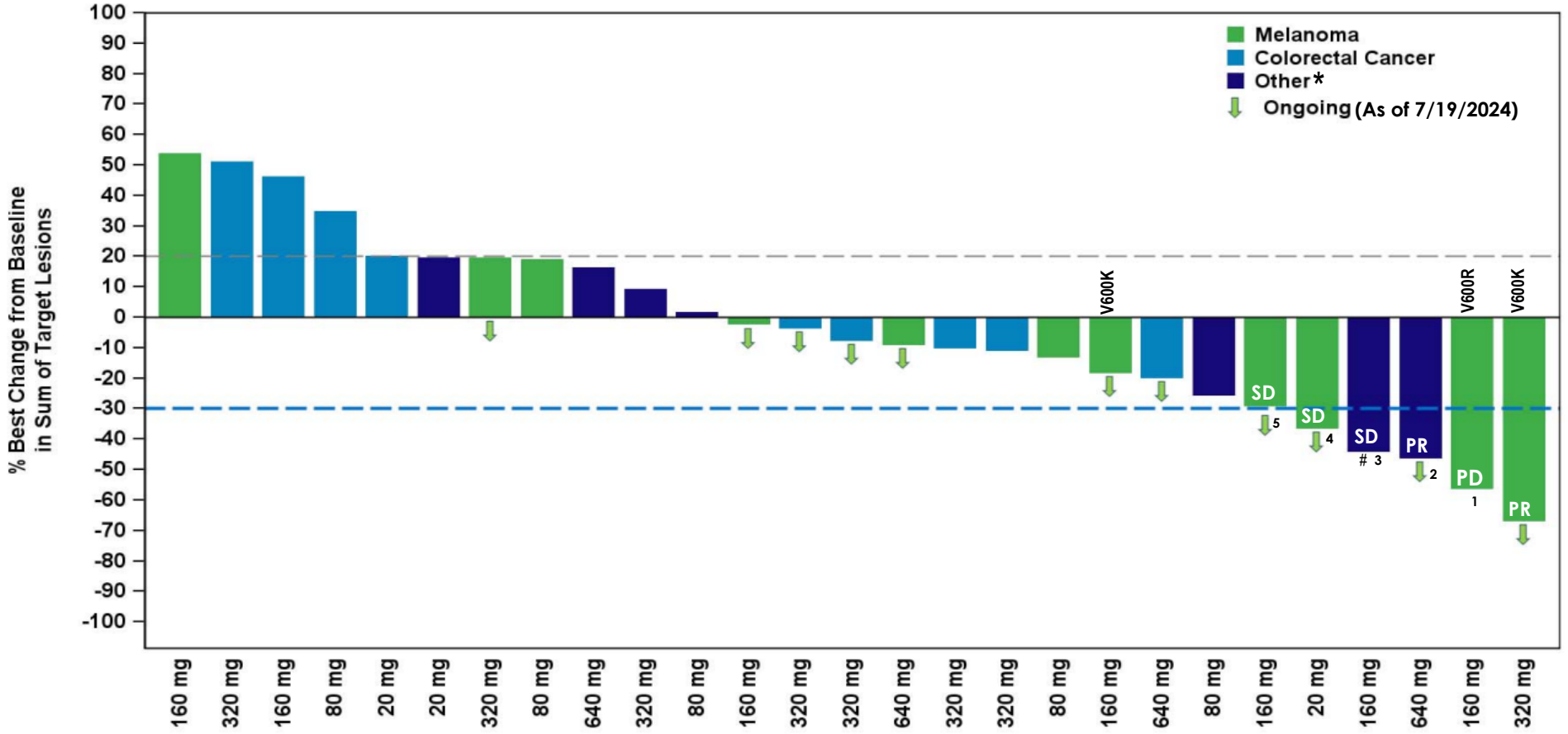
^A patient is only counted once with the highest severity and preferred term
#Patient had a fatal cerebrovascular accident not related to CFT1946
CTCAE v5.0 grading criteria; *Grade missing for 1 patient with TEAE

Serious adverse events (SAEs); Dose limiting toxicities (DLTs); Treatment-emergent adverse events (TEAEs)

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

C4 Therapeutics

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



*Other tumor types include cholangiocarcinoma, non-small cell lung cancer, pancreatic carcinoma, and small intestine cancer; BRAF V600 mutation is V600E unless otherwise specified; #This patient did not receive prior BRAF inhibitor therapy, all other patients received prior BRAF inhibitor therapy. Dotted lines represent partial response (-30%, blue line) and progressive disease (20%, gray line) per RECIST v1.1.

[1] Patient on 160 mg BID had 56.2% reduction on target lesion, progression on non-target lesion and a new lesion, hence assessed as PD for overall response; [2] Patient on 640 mg BID had PR confirmed after data cut off, and as of ESMO Congress (9/13/2024); [3] Patient on 160 mg BID had PD following first PR (-43.9%), hence assessed as SD for overall response; [4] Patient on 20 mg BID had unconfirmed PR, hence assessed as SD for overall response; [5] Patient on 160 mg BID had -29% reduction on target lesion, hence assessed as SD

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

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

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

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

C4 Therapeutics

CFT8919

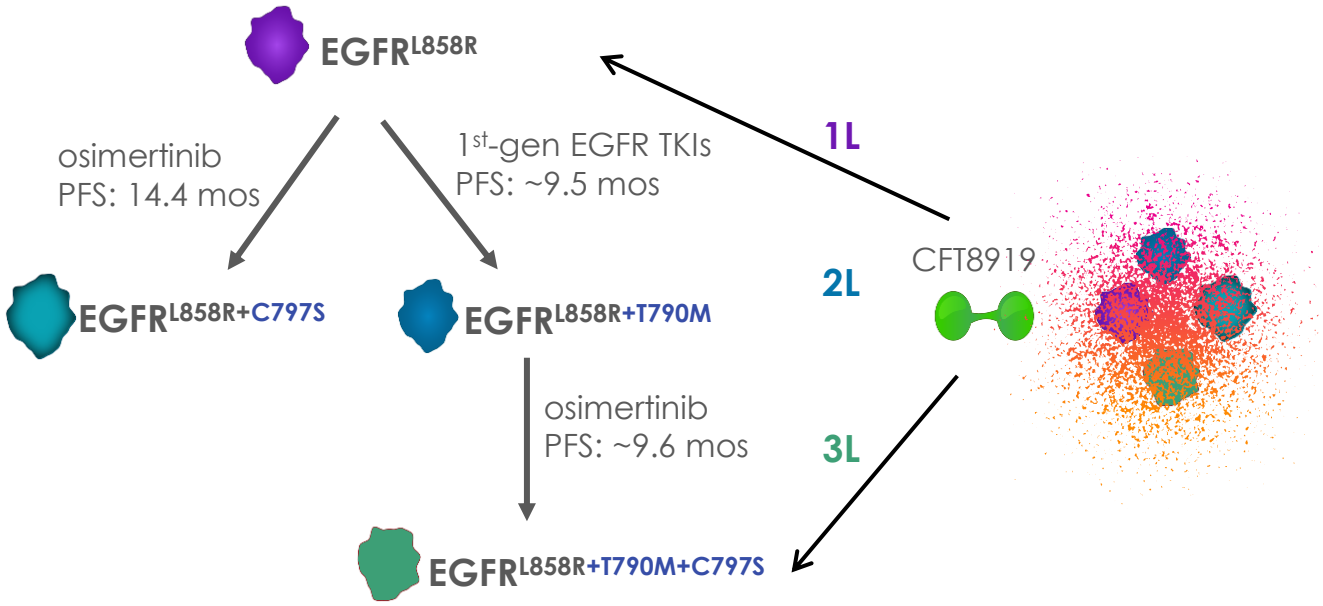
Targeting EGFR L858R

Non-Small Cell Lung Cancer (NSCLC)

C4 Therapeutics

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

Strong Rationale for an EGFR L858R Degrader



Osimertinib and other inhibitors provide suboptimal responses in L858R mutant NSCLC compared to other mutations of NSCLC

Osi: 14.4 months PFS versus 21.4 months PFS
(L858R) (Exon 19 deletion)

CFT8919 Key Properties

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

Market Size

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

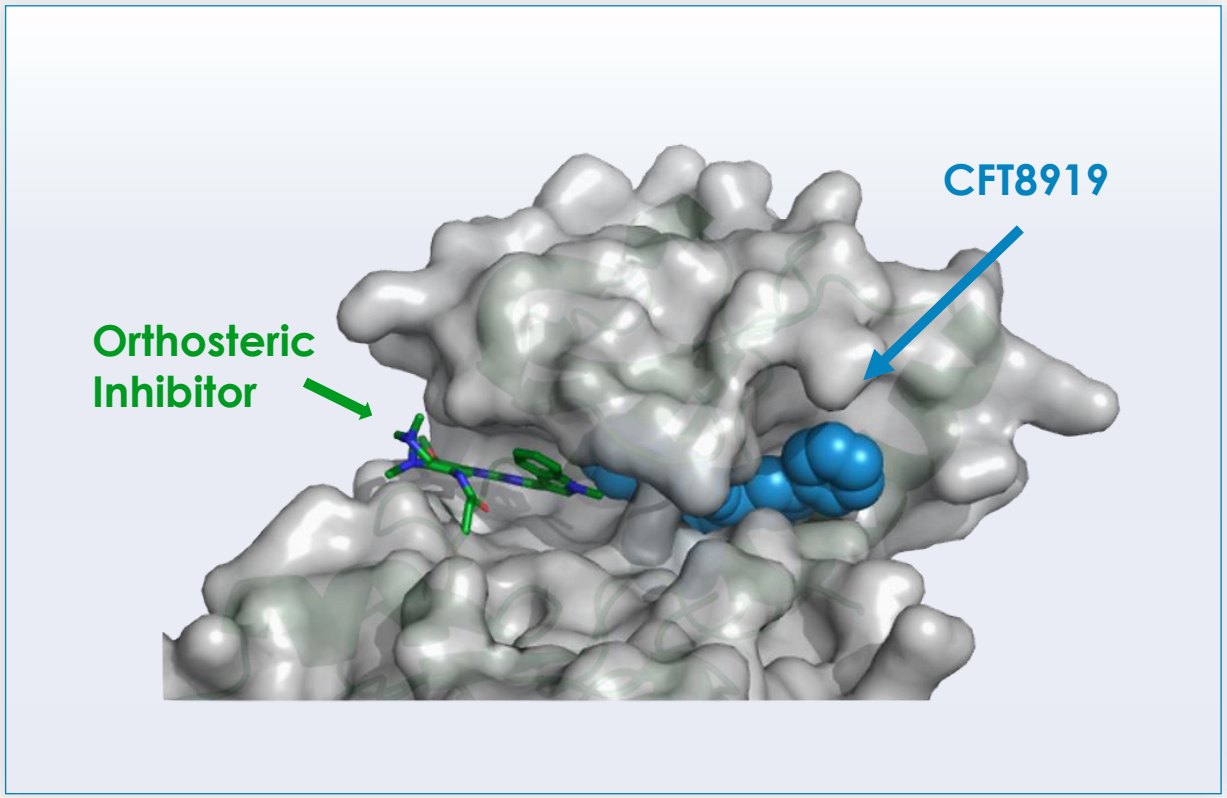
Progress to Date

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

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

C4 Therapeutics

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

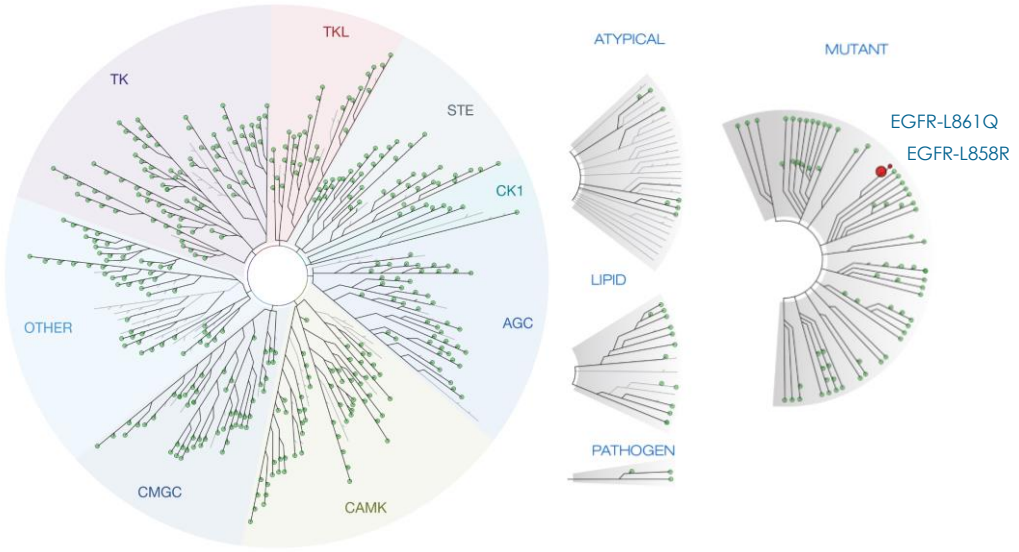


- CFT8919 exploits **allosteric binding site**, close to L858R activating mutation
- Allosteric binding site avoids known resistance-causing mutations in **orthosteric binding site**
- Allosteric binders do not require covalent binding through C797S and do not compete with orthosteric binding

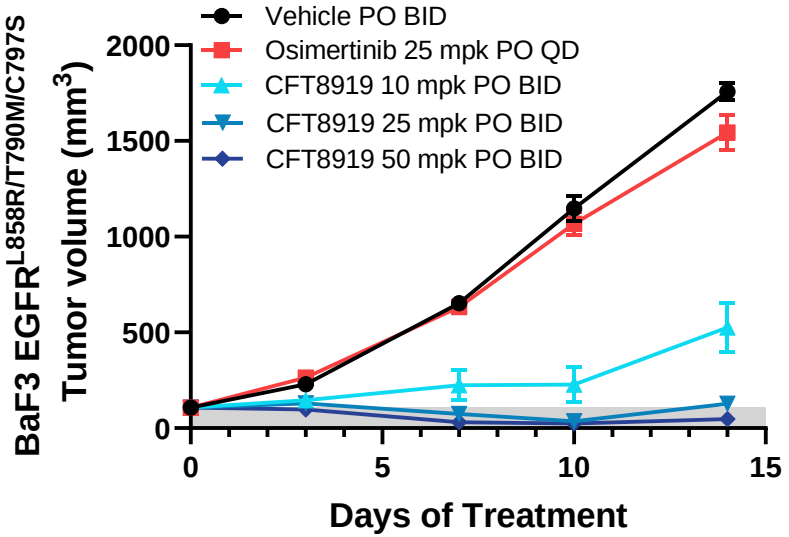
Allosteric binding avoids resistance mutations, wild-type activity, and is combinable with orthosteric inhibitors

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

Specific for EGFR Exon 21 Mutants



Active in setting of EGFR C797S



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

C4 Therapeutics

C4T Is Progressing Multiple Clinical and Preclinical Programs

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

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

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