C4 Therapeutics

Protein degraded.
Disease targeted.
Lives transformed.

September 2024

Forward-looking Statements and Intellectual Property

Forward-looking Statements

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

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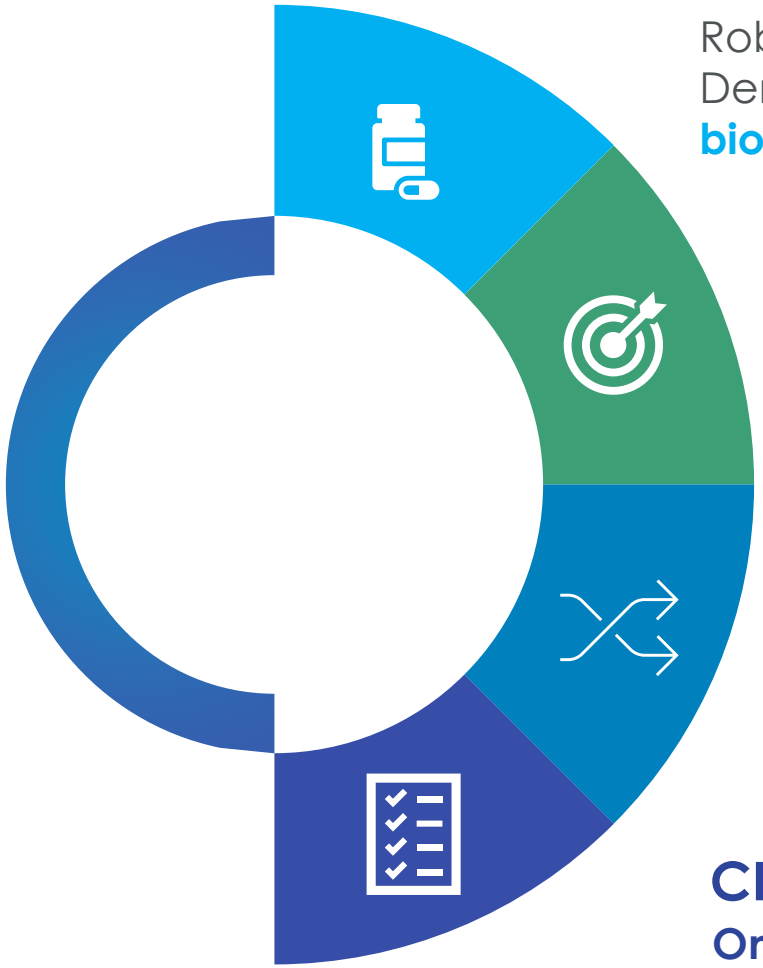
C4T is a Recognized Leader in Delivering on the Promise of Targeted Protein Degradation

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**

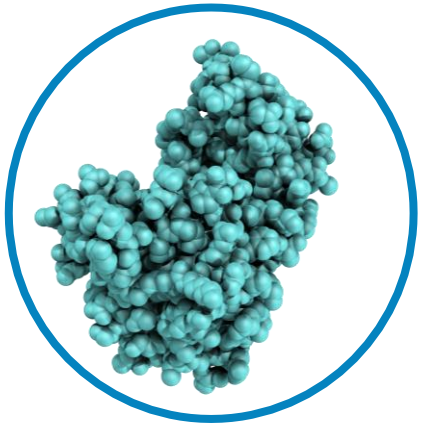
BROAD DEGRADER APPROACH

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

CLINICAL PIPELINE

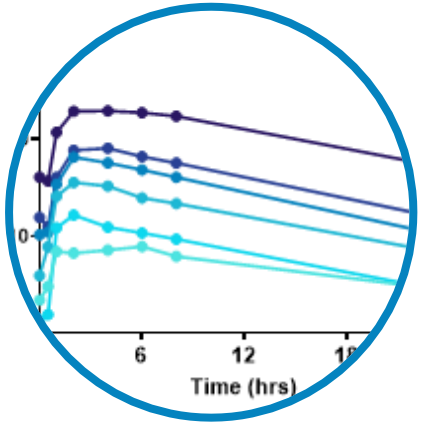
Oncology degraders against targets of high unmet need

We Have Designed and Advanced Degraders into the Clinic Across a Range of Target Classes, Resulting in Robust Target Degradation

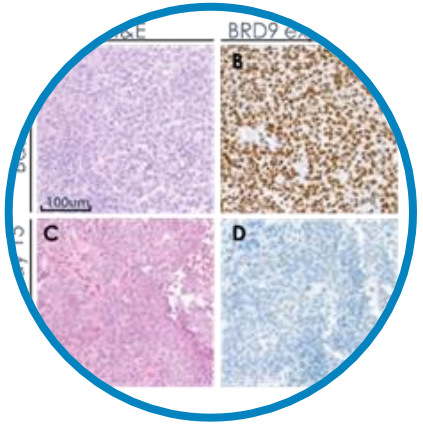


Interrogated Diverse Target Classes

Attained IND Clearance



Achieved Desirable Drug-like Properties



Degraded Target as Predicted

Discovered degraders and advanced **4 INDs** against a transcription factor, a chromatin modifier, and two kinases

To date, we have evaluated **3 programs** in the clinic[1], with each demonstrating robust target degradation in patients

1. Evaluated three programs in the clinic as of 6/30/2024
Investigational New Drug Application (IND)

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Advancing 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 V600X**	V600X Mutant Cancers					
CFT8919[1]	**EGFR L858R**	Non-Small Cell Lung Cancers					BETTA PHARMACEUTICALS
Discovery Stage Programs		Various Cancers					
Collaboration Programs		Autoimmune & Cancer	*2 targets*				Roche
		Autoimmune & Neurological	*2 targets*				Biogen
		Cancer	*1 target*				MERCK
		Cancer	*2 targets*				Merck KGaA Darmstadt, Germany

1. License and Collaboration Agreement with Betta Pharmaceuticals for development and commercialization in Greater China

2024 Milestones: Advancing High-potential Programs

Multiple Value Inflection Points over Next 12 Months with Sufficient Runway (into 2027[1]) Beyond These Milestones

Cemsidomide IKZF1/3	• **4Q 2024:** Present updated data from Phase 1 dose escalation +dex trial in R/R MM • **4Q 2024:** Present data from Phase 1 dose escalation monotherapy trial in R/R NHL • **By YE 2024:** Complete Phase 1 dose exploration in R/R MM and R/R NHL
CFT1946 BRAF V600X	✓ **2Q 2024:** Present preclinical data demonstrating differentiated activity in BRAF V600X melanoma, CRC, NSCLC, and brain metastasis models at AACR • **ESMO Congress 2024 (September 13):** Present monotherapy data from Phase 1 dose escalation trial in melanoma, CRC, NSCLC, and other BRAF V600X cancers
CFT8919 EGFR L858R	• **2024:** Support trial start-up activities related to Betta's Phase 1 dose escalation trial in China
Discovery	✓ **1Q 2024:** Collaboration with Merck KGaA, Darmstadt, Germany to discover two targeted protein degraders against critical oncogenic proteins ✓ **2024:** Deliver development candidate to collaboration partner

1. Cash, cash equivalents and marketable securities as of June 30, 2024 were $295.7 million

Dexamethasone (dex); Colorectal cancer (CRC); Non-small cell lung cancer (NSCLC); Year-end (YE)

Cemsidomide

Targeting IKZF1/3

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

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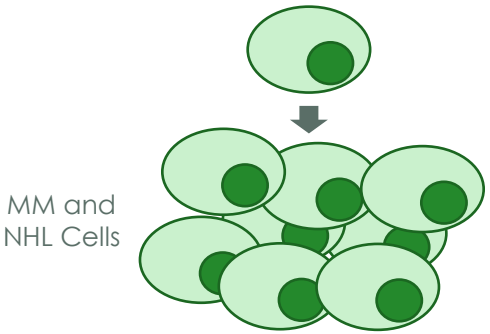
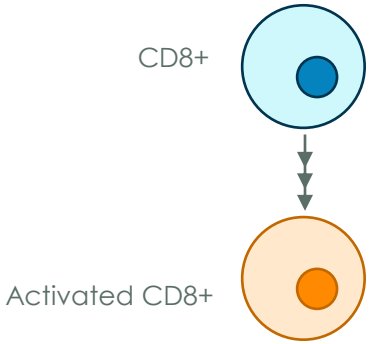
IKZF1/3 Degradation Drives Three Distinct Areas of Hematopoietic Biology; Degrading IKZF1/3 is a Validated Therapeutic Strategy in MM and NHL

IKZF1 / IKZF3 Transcription Factors

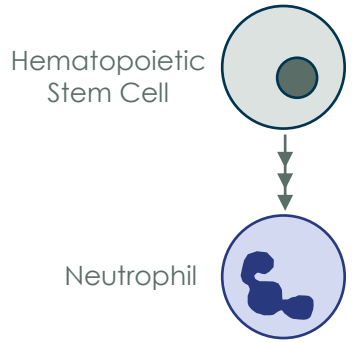
Drive MM and NHL Cell Growth and Survival



Activate Fully Differentiated T-cells



Regulate Hematopoietic Stem Cell Differentiation



Consequences of IKZF1/3 Degradation:

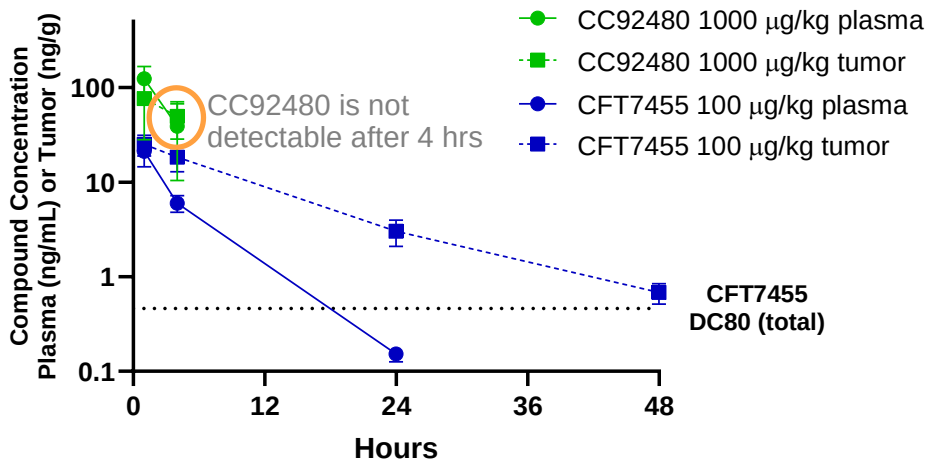
- **MM and NHL Cell Death**
- **T-cell Activation**
- **On-target Neutropenia**

Ikaros Family Zinc Finger proteins 1 and 3 (IKZF1/3); Multiple Myeloma (MM); Non-Hodgkin's Lymphoma (NHL)

Differentiated PK and Class-leading Catalytic Activity of Cemsidomide Leads to Sustained Degradation Compared to Other Agents in this Class

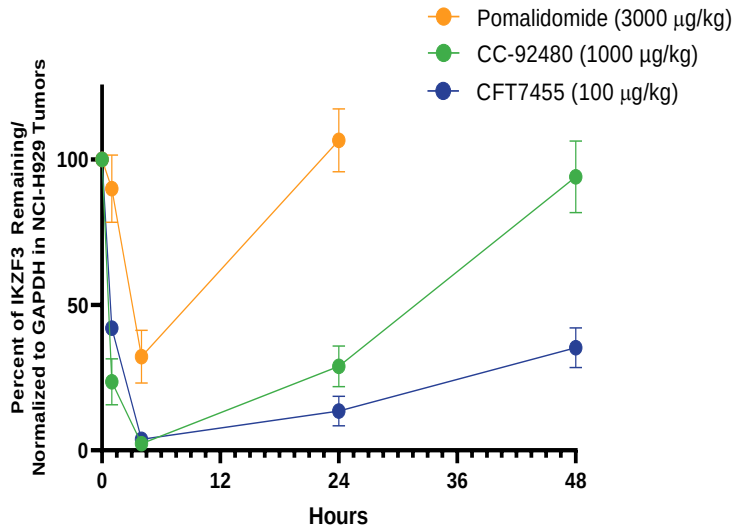
Extended Plasma and Tumor Exposure

In Vivo Tumor PK



Leads to Optimized Degradation Kinetics

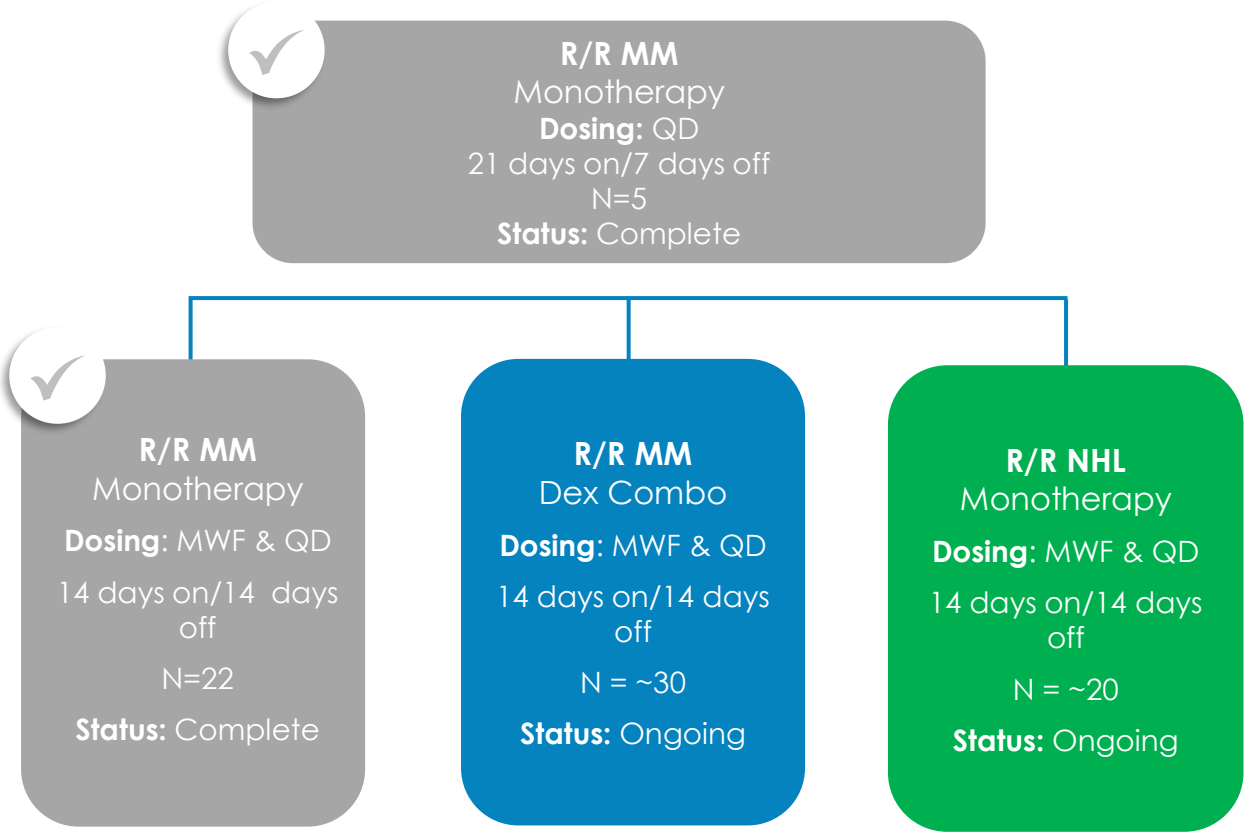
In Vivo Degradation Kinetics (48 hrs.)



mezigdomide (CC-92480); Ikaros family zinc finger protein (IKZF3); multiple myeloma (MM); pharmacodynamics (PD); pharmacokinetics (PK); once daily (QD)
Source: AACR 2022 presentation

Cemsidomide Phase 1 Dose Escalation Trial's Goal is to Define the Safety Profile and Identify Signs of Anti-Tumor Activity in R/R MM and R/R NHL

Phase 1 Dose Escalation Trial



Endpoints

Primary:

- Safety and tolerability
- Determine the maximum tolerated doses

Secondary:

- Estimate anti-tumor activity
- Assess PK

Exploratory:

- Characterize target engagement
- Assess kinetics, depth, recovery and consistency of target engagement
- Assess immunomodulation

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

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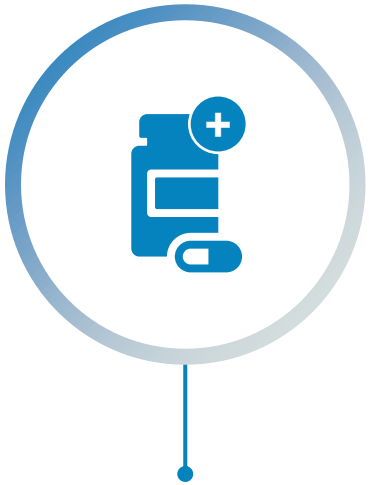
Schedule Adjustment Yielding Expected Results for Cemsidomide as a Potential MM Therapy

Established Safety Profile and Dosing Schedule

- Cemsidomide is well tolerated with no DLTs resulting in treatment discontinuations
- The 14 days on/14 days off schedule is optimal



Demonstrated Monotherapy Activity

- Anti-myeloma activity and immunomodulatory effects observed at well tolerated doses
- Opportunity in combination with novel MM agents for early-line patients and as a maintenance therapy option

Promising Responses with Cemsidomide + Dexamethasone

- Multiple patients achieved IMWG responses at low doses with best responses in patients refractory to BCMA therapies
- Opportunity in combination with dexamethasone for multi-refractory patients

Cemsidomide is a **potential treatment for multi-refractory MM patients** with the ability **to move into earlier lines** with numerous combination opportunities

Dose Limiting Toxicities (DLTs); Multiple myeloma (MM); B cell maturation antigen (BCMA); International Myeloma Working Group (IMWG)
Source: C4T data on file as 11/28/2023

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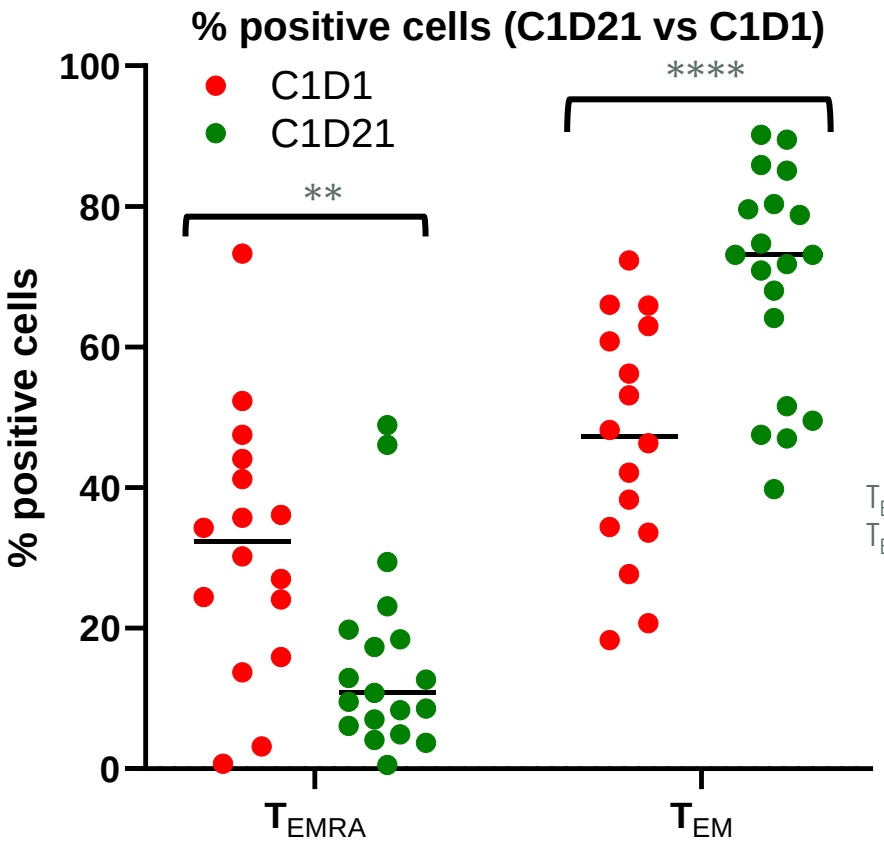
Clinical Evidence of Immune T-cell Activation with Cemsidomide Monotherapy



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:

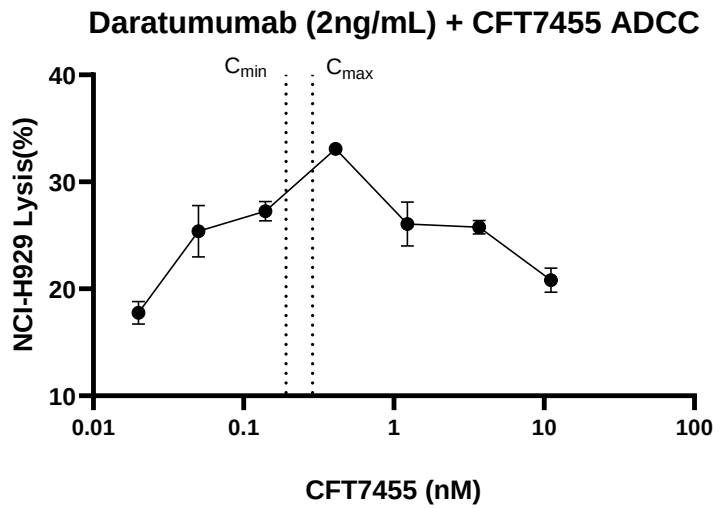
- ✓ Cemsidomide induces CD8+ T-cell activation by increasing effector memory T-cell subset
- ✓ T-cell activation is observed at well tolerated monotherapy clinical doses
- ✓ The clinical data consistent with the preclinical *in vitro* data reported for cemsidomide

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

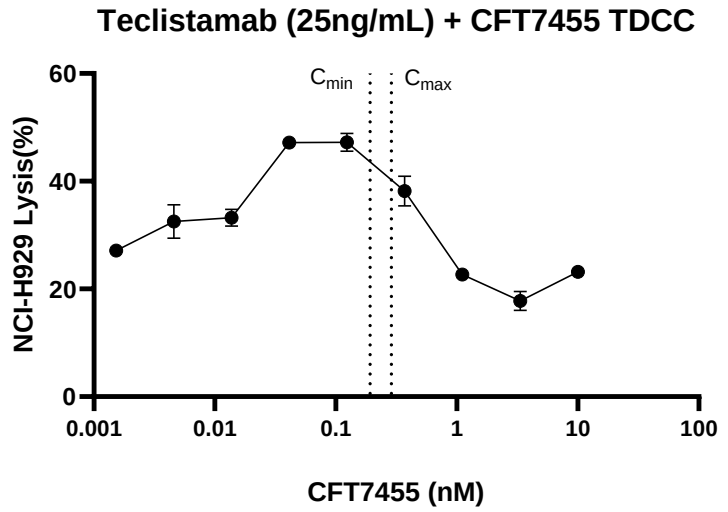
Daratumumab (Anti-CD38) Combo

Antibody-Dependent Cell-Mediated Cytotoxicity Assay (ADCC)



Teclistamab (BCMA BiTE) Combo

T-cell Dependent Cellular Cytotoxicity Assay (TDCC)



C_{min} and C_{max} represent human plasma concentrations for a 50 µg dose of cemsidomide

Bispecific T-Cell Engager (BiTE)
Source: C4T data on file as of 11/28/2023

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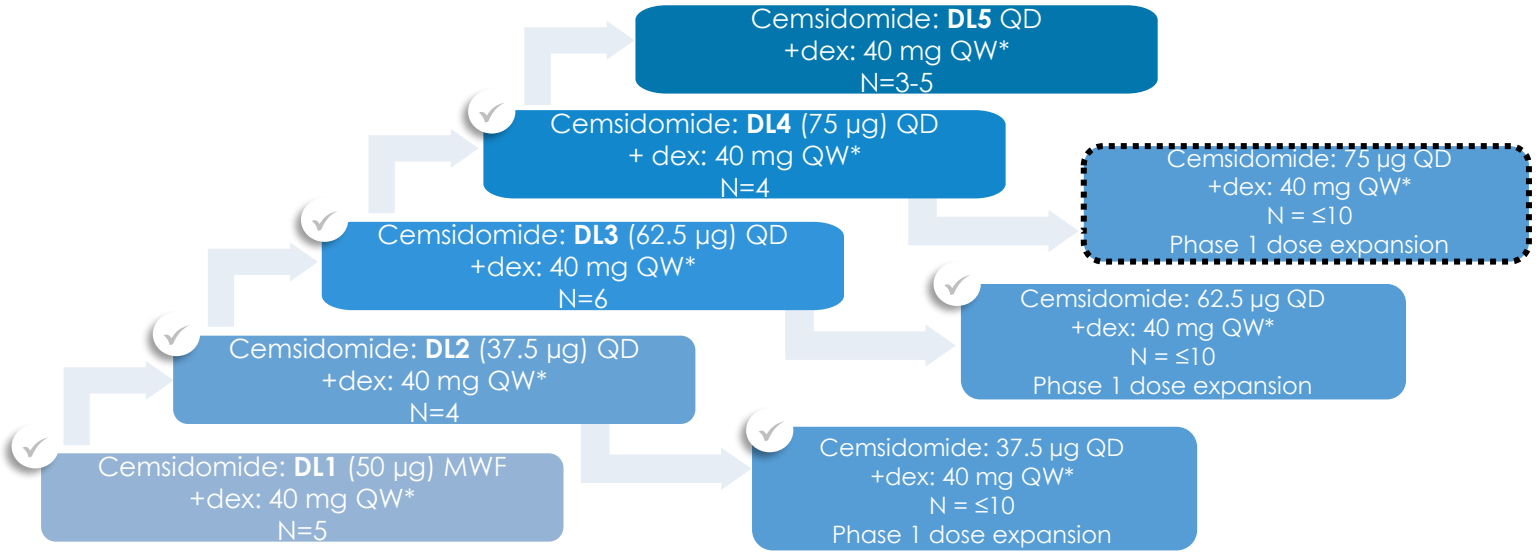
Cemsidomide + Dexamethasone Dose Escalation in R/R MM Continues to Progress

KEY INCLUSION CRITERIA

- Adults with R/R MM, at least 3 prior lines 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
- Measurable disease
- Adequate bone marrow function (ANC ≥1000, Hgb ≥8.0, platelets ≥75,000)
- Creatinine clearance ≥40 mL/min
- ECOG ≤2

Phase 1: Dose Escalation + Dexamethasone 14 Days On/14 Days Off



- 75 µg dose has been declared safe
- Additional patients are enrolling at the 75 µg expansion cohort
- Dose escalation continues as maximum tolerated dose has not yet been reached

Phase 2

Cohort Expansion N=~30

Eastern Cooperative Oncology Group (ECOG); Monday, Wednesday, Friday dosing (MWF); Daily Dosing (QD); Relapsed/Refractory multiple myeloma (R/R MM); Absolute neutrophil count (ANC); Hemoglobin (Hgb); Dexamethasone (Dex); Dose level (DL)
*+Dex is dosed on days 1, 8,15, and 22 and dose is reduced for older patients.

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Cemsidomide + Dexamethasone is Well Tolerated and Best Responses in Patients Refractory to BCMA Therapies

Anti-myeloma Activity:

Dosing Schedule	Dose Level	EMD Status	Prior CAR-T or TCE	# of Prior Lines	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycle 7	Cycle 8	Cycle 9	Cycle 10	Cycle 11
14 days on/ 14 days off	Cemsidomide 50 µg MWF +dex: 40 mg QW	No	No	6		PD									
		No	Yes	4		SD				PD					
		No	No	5		SD	MR		PR	→					
		Yes	Yes	12		PD									
		No	No	6		SD			■						
	Cemsidomide 37.5 µg QD +dex: 40 mg QW	No	Yes	5		VGPR	sCR		→						
		No	Yes	9		PR		→							
		Yes	No	7		SD	■								
		Yes	Yes	7		NE	→								

- Stringent Complete Response (sCR)
- Very good partial response (VGPR)
- Partial Response (PR)
- Minimal Response (MR)
- Stable Disease (SD)
- Progressive Disease (PD)
- Not Evaluable (NE)
- → Ongoing
- ■ Withdrawal of consent or physician decision

Safety:

- Cemsidomide + dexamethasone is well tolerated
- Consistent with the monotherapy safety signal
- No AEs have led to dose reductions, discontinuations or DLTs

Extramedullary Disease (EMD); T-Cell Engager (TCE); Daily Dosing (QD); One Weekly (QW); Monday, Wednesday, Friday Dosing (MWF); Dose Limiting Toxicity (DLTs); Dexamethasone (dex); B cell maturation antigen (BCMA); Adverse events (AEs)
Source: C4T data on file as of 11/28/2023

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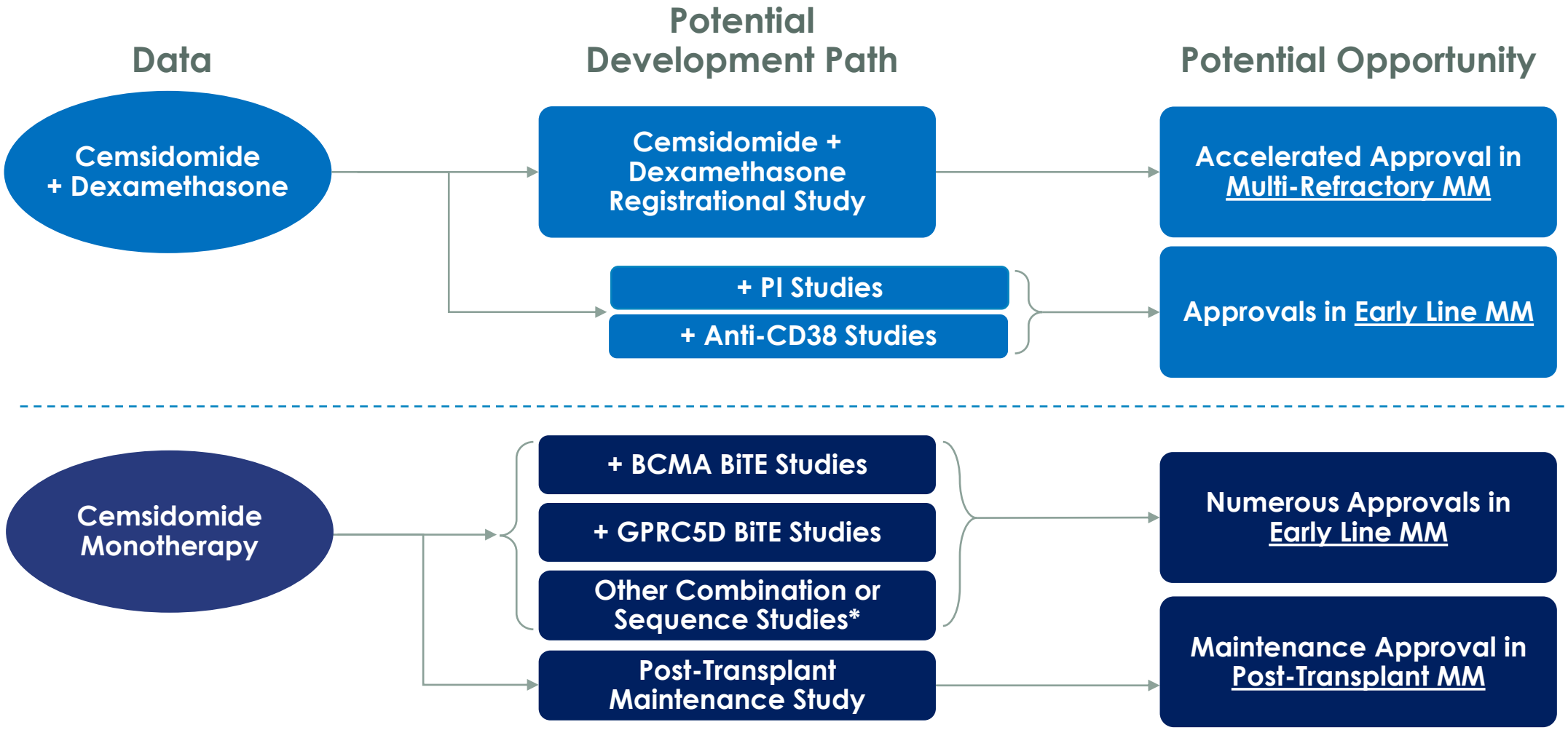
Cemsidomide Profile Supports Multiple Opportunities across MM Landscape



* Other combination opportunities may include CAR-T, anti-SLAMF7, XPO1 inhibitors, FcRH5 BiTE, among others.
Bi-specific T-cell Engager (BiTE); Proteasome Inhibitors (PI); Multiple myeloma (MM); B cell maturation antigen (BCMA); G protein–coupled receptor, class C, group 5, member D (GPRC5D)

CFT1946

Targeting BRAF V600X

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

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Strong Rationale for Advancing CFT1946, a Selective BRAF V600X Degrader

- **BRAF V600X is a clinically validated target, but resistance mechanisms limit benefit of inhibition**

- **Strong degrader rationale for overcoming limitations and resistance mechanisms of inhibitors**

- **~100K annual incidence of BRAF mutated cancers in the U.S.[1]**

Source:1. ACS Figures & Facts 2022: https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2022.html

CFT1946 has the Potential to Overcome Several Shortcomings Seen with Inhibitors for BRAF V600X Cancers

Key Liabilities of BRAF V600X Inhibitors

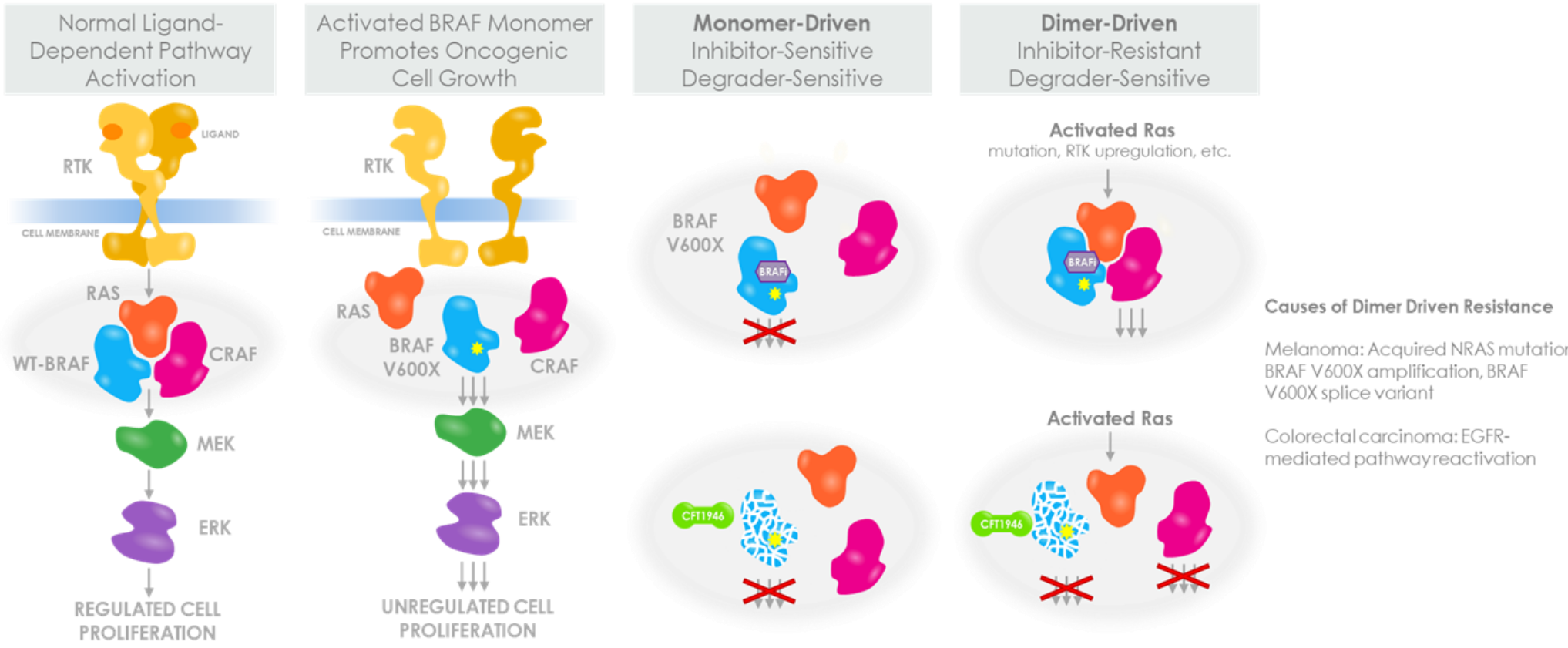
- Promote **dimer resistance** and **paradoxical activation occurs**
- **Limited treatment options** for BRAF V600 **patients who do not have a BRAF V600E mutation**
- Hits wild-type, **resulting in wild-type toxicities** which include **skin rash, alopecia, and arthralgia**
- **Durable and deep responses are often not seen** in melanoma and CRC patients

Potential Advantages of BRAF V600X Degradation

- ✓ Degrader **prevents dimer formation** and **avoids paradoxical activation**
- ✓ **Addresses MAPK pathway alterations** resulting from BRAF inhibitor resistance (e.g., BRAF splice variants, BRAF amplification)
- ✓ **Specifically targets all BRAF V600X mutations**, which includes BRAF V600 mutations beyond BRAF V600E
- ✓ Spares wild-type BRAF, likely **avoiding wild-type toxicities**
- ✓ Enables deep elimination of mutant BRAF signaling to **create potential durable responses** through degrader molecule recycling and catalytic effect

BRAF V600X Degrader Advantages Vary by Indication and Treatment Paradigms May Require Combination

The Degrader Benefit in BRAF V600X Monomer and Dimer-Dependent Diseases



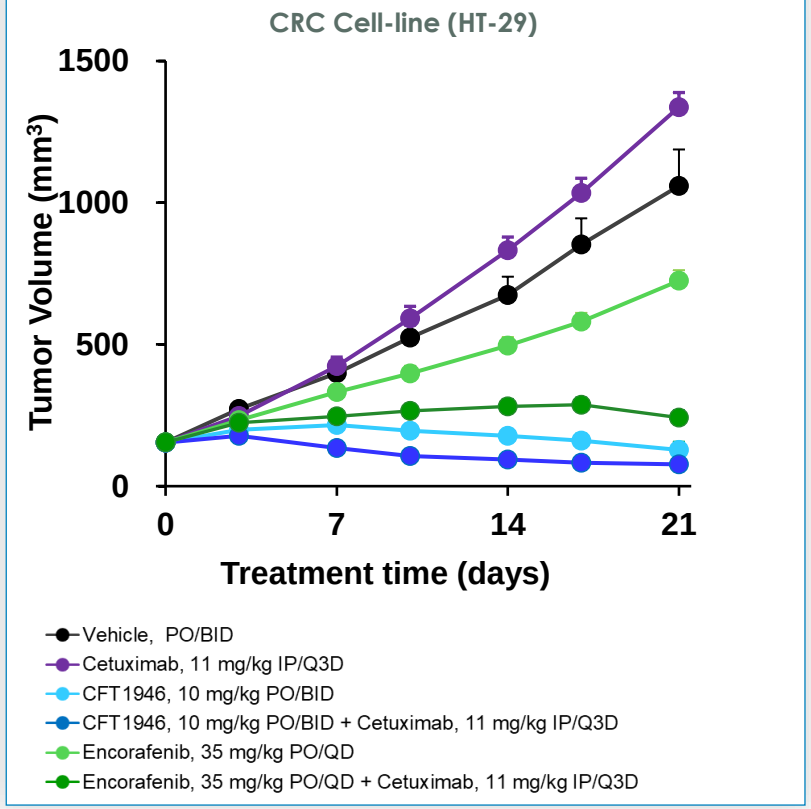
CFT1946 has the Potential to Address Multiple Tumor Types with BRAF V600X Mutations Where BRAF Inhibitors are Insufficient

	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+)

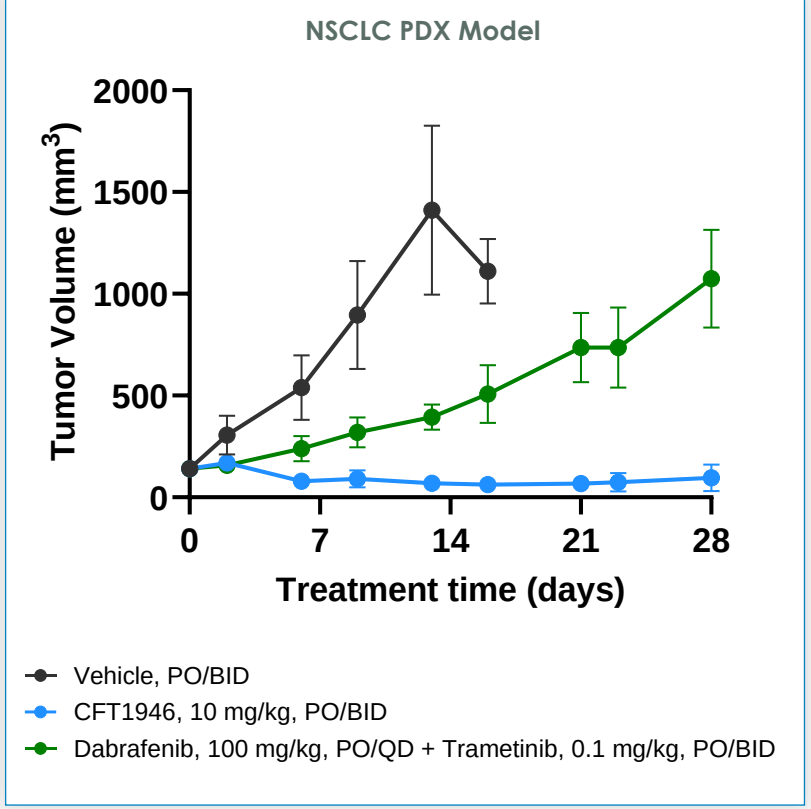
Sources: 1. Owsley 2021 Exp Biol Med. 2. Paik 2011 J Clin Oncol. 3. Bylsma 2020 Cancer Med. 4. NCI SEER, consulting work done by Health Advances. 5. FDA Labels

CFT1946 is More Efficacious than SOC in CRC & NSCLC BRAF V600X Xenograft Models and in a Melanoma PDX BRAF Inhibitor Resistance Model

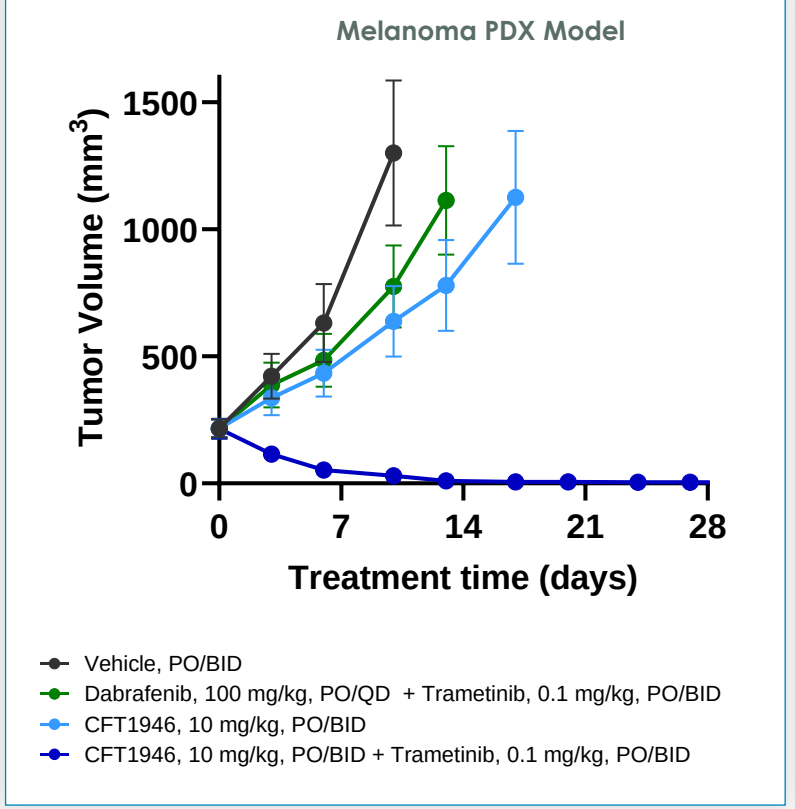
CRC
CFT1946 as a monotherapy and + cetuximab shows enhanced responses



NSCLC
CFT1946 as a monotherapy shows enhanced responses to dabrafenib + trametinib



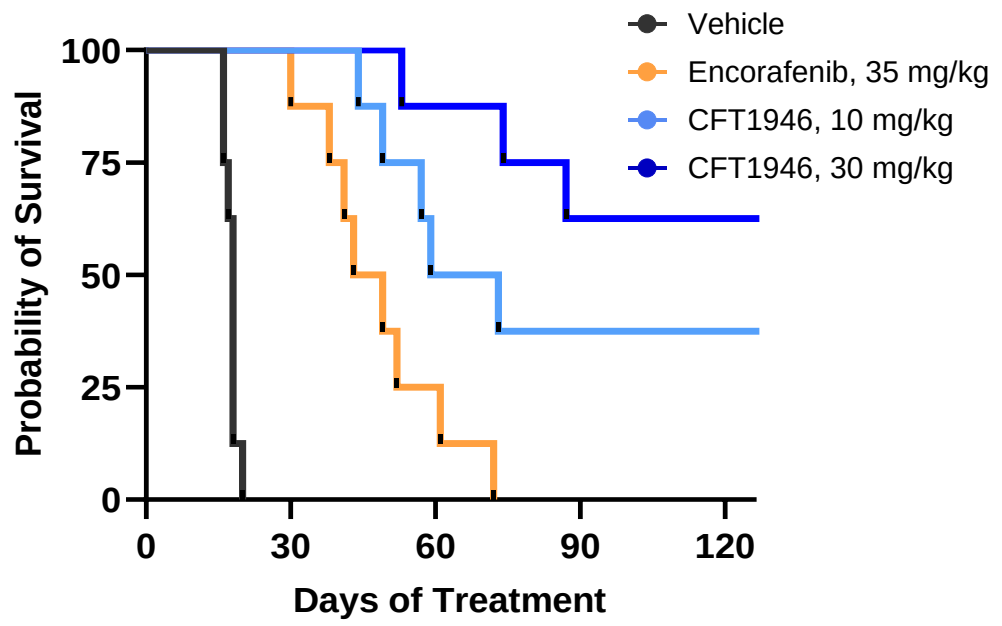
MELANOMA
CFT1946 + trametinib shows deep tumor regression



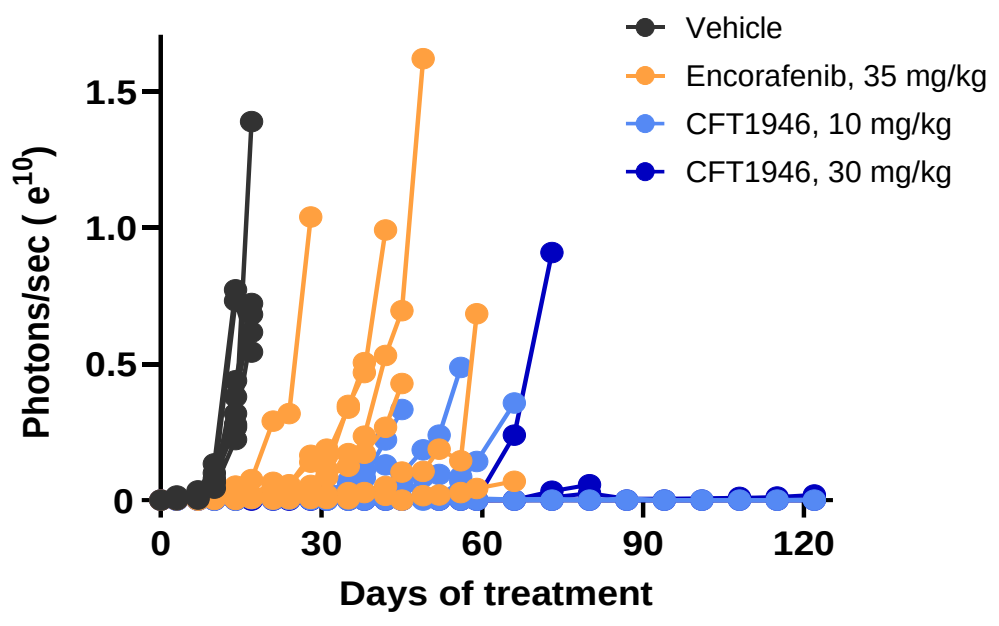
Oral administration (PO); Twice a day dosing (BID); Intraperitoneal injections (IP); Standard of Care (SOC)
Source: C4T data on file as of 12/31/23

CFT1946 is Active in Preclinical Metastatic Melanoma CNS Models

CFT1946 Prolongs Survival Compared to Encorafenib (BRAF inhibitor) in CDX Model



CFT1946 Reduces CNS Tumor Burden in Metastatic Melanoma CNS Model



8 mice per group tracked individually

Cell Derived Xenograft (CDX)
Source: C4T data on file as of 12/26/2023

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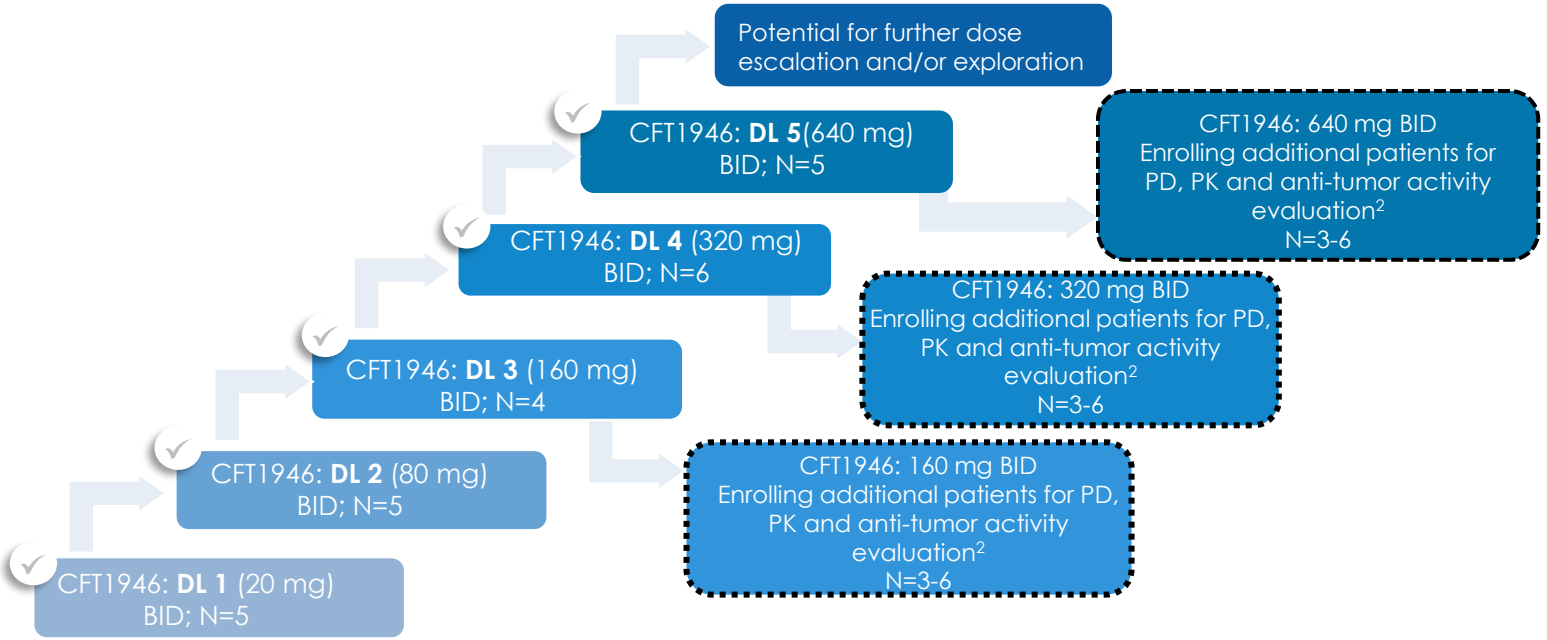
CFT1946 Phase 1/2 Dose Escalation Trial Continues to Progress

KEY INCLUSION CRITERIA[1]

- ≥18 years of age
- Evidence of a BRAF V600X mutation obtained from tumor tissue or liquid biopsy
- Received ≥1 prior line of SoC therapy for unresectable locally advanced or metastatic disease, NSCLC, CRC, Melanoma, ATC or other BRAF V600X mutation-positive tumors
- No patient with CNS involvement (primary tumor or metastatic disease), except if clinically stable
- No patient with known malignancy other than trial indication that is progressing or has required treatment within the past 3 years, except for conditions that have undergone potentially curative therapy

Phase 1: Dose Escalation for V600X Solid Tumors including CRC, Melanoma and NSCLC (Post BRAF Inhibitor)



Exploratory Expansion:
✓ CFT1946 monotherapy in melanoma now enrolling (320 mg) BID

Phase 1B:
✓ CFT1946 in combination with cetuximab in CRC now enrolling (160 mg BID)

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

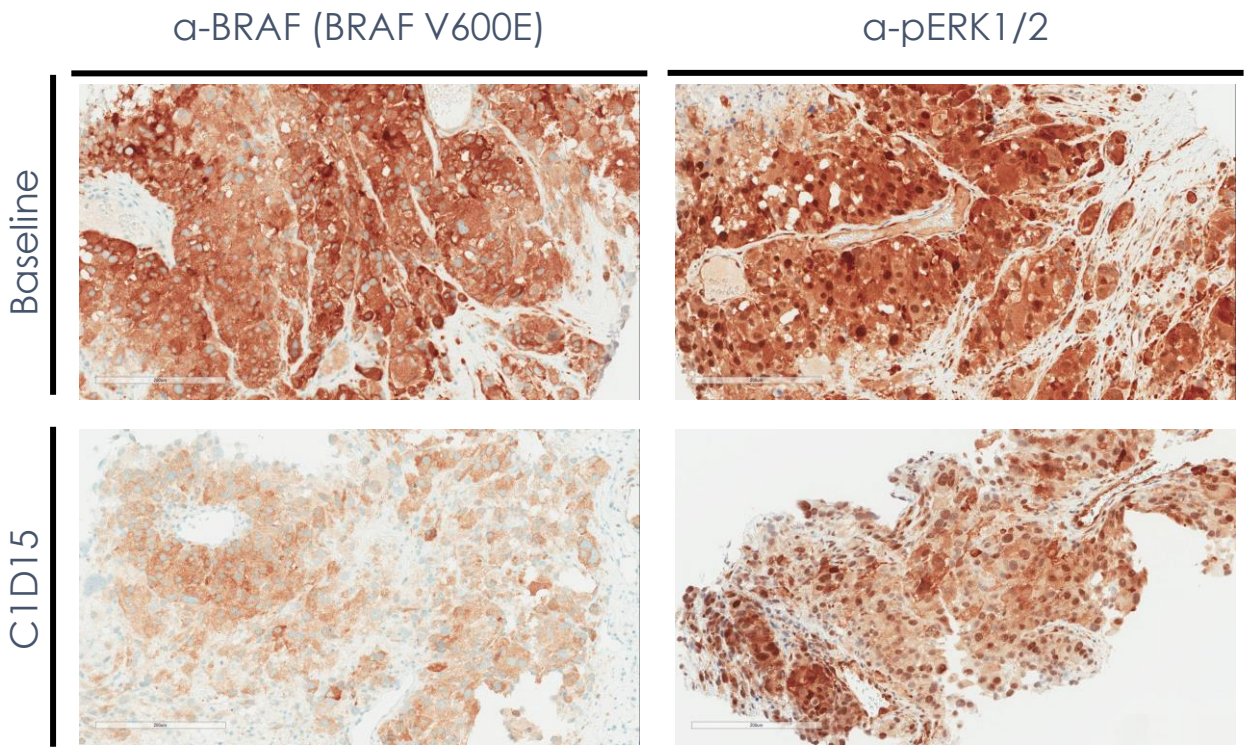
- Dose level 5 (640 mg BID) has completed enrollment
- Currently enrolling patients in a monotherapy exploratory expansion cohort in melanoma at the 320 mg BID dose level
- Phase 1b portion is enrolling CRC patients evaluating CFT1946 in combination with cetuximab at the 160 mg BID dose level

Twice a day (BID); standard of care (SoC); Non-small cell lung cancer (NSCLC); Colorectal Cancer (CRC); Anaplastic thyroid cancer (ATC); Central nervous system (CNS); Dose Level (DL)
1. NCT05668585. www.clinicaltrials.gov. Accessed January 9, 2024. 2. Evaluating additional patients for pharmacodynamic evaluation pre- and post-drug exposure biopsies

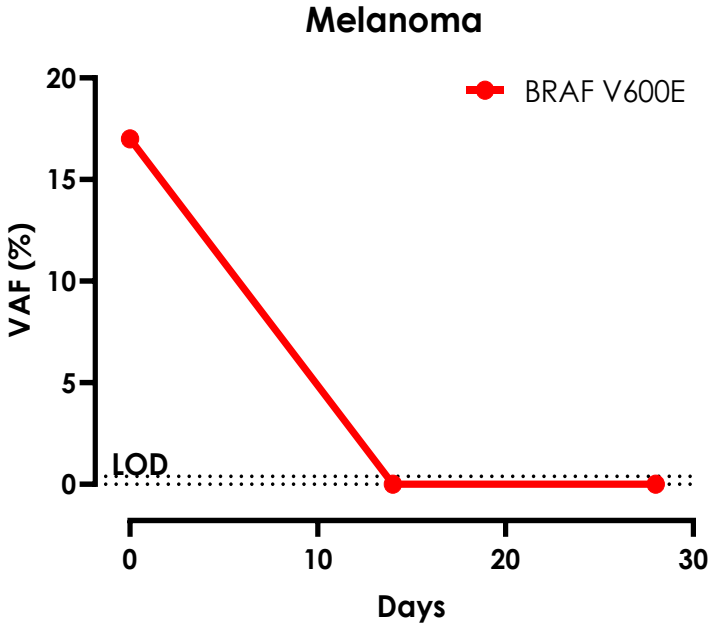
C4 Therapeutics

At 80 mg, CFT1946 Degrades BRAF V600E in Melanoma Tissue and Demonstrates Rapid Decrease of BRAF V600E VAF in ctDNA

Patient 1: At 80 mg, CFT1946 Degrades BRAF V600E in Melanoma Tissue and Results in Reduced ERK Signaling



Patient 2: Rapid Decrease of BRAF V600E VAF at 15 Days of CFT1946 Treatment at 80 mg



Patient also demonstrated 7% decrease in tumor volume in correlation with the ctDNA data

Limit of Detection (LOD); Variant Allele Frequency (VAF); Circulating tumor DNA (ctDNA)
Source: C4T data on file as of 11/14/2023

CFT8919

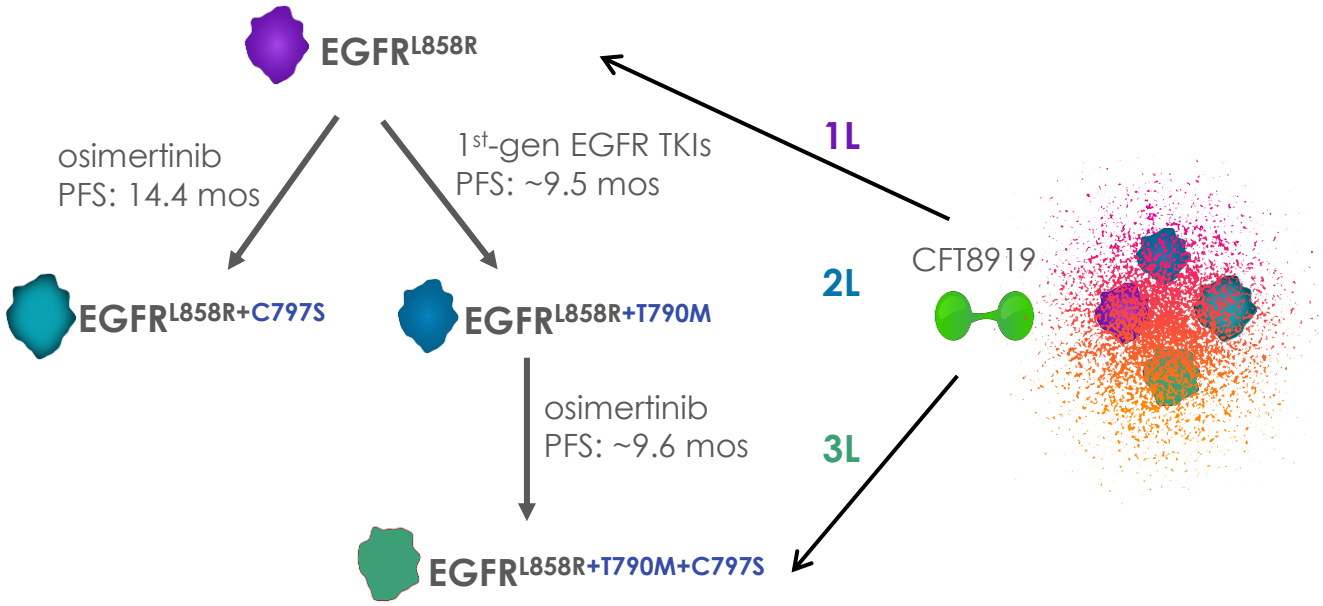
Targeting EGFR L858R

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]

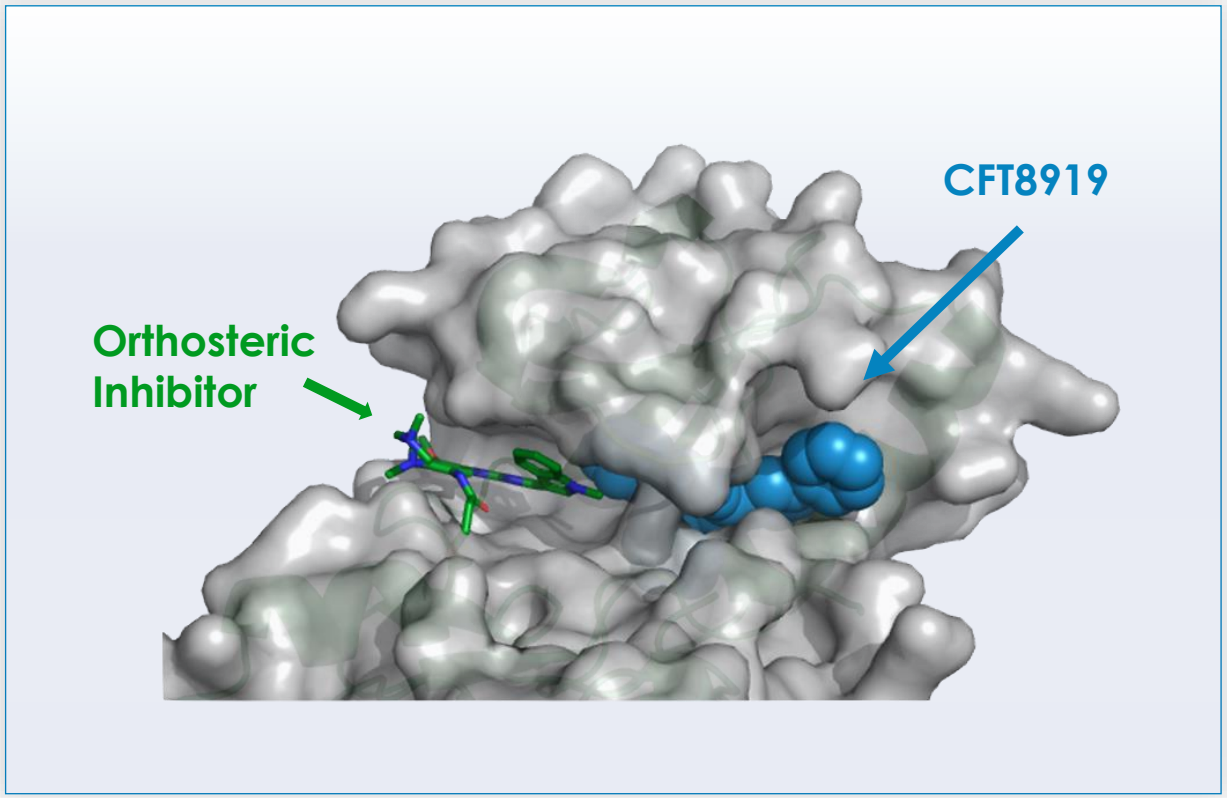
Progress to Date

- 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

2024 Milestones: Advancing High-potential Programs

Multiple Value Inflection Points over Next 12 Months with Sufficient Runway (into 2027[1]) Beyond These Milestones

Cemsidomide IKZF1/3	• **4Q 2024:** Present updated data from Phase 1 dose escalation +dex trial in R/R MM • **4Q 2024:** Present data from Phase 1 dose escalation monotherapy trial in R/R NHL • **By YE 2024:** Complete Phase 1 dose exploration in R/R MM and R/R NHL
CFT1946 BRAF V600X	✓ **2Q 2024:** Present preclinical data demonstrating differentiated activity in BRAF V600X melanoma, CRC, NSCLC, and brain metastasis models at AACR • **ESMO Congress 2024 (September 13):** Present monotherapy data from Phase 1 dose escalation trial in melanoma, CRC, NSCLC, and other BRAF V600X cancers
CFT8919 EGFR L858R	• **2024:** Support trial start-up activities related to Betta's Phase 1 dose escalation trial in China
Discovery	✓ **1Q 2024:** Collaboration with Merck KGaA, Darmstadt, Germany to discover two targeted protein degraders against critical oncogenic proteins ✓ **2024:** Deliver development candidate to collaboration partner

1. Cash, cash equivalents and marketable securities as of June 30, 2024 were $295.7 million

Dexamethasone (dex); Colorectal cancer (CRC); Non-small cell lung cancer (NSCLC); Year-end (YE)