C4 Therapeutics

Protein degraded.
Disease targeted.
Lives transformed.

August 2023

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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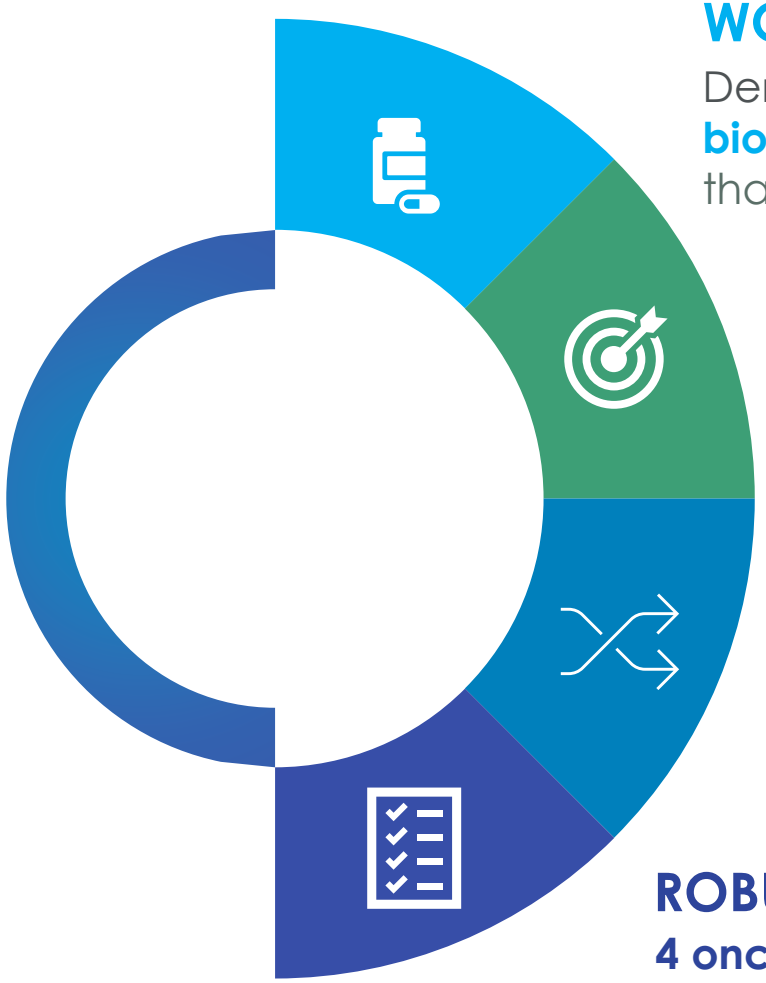
C4 Therapeutics, Inc. owns various registered and unregistered trademarks and service marks in the U.S. and internationally, including, without limitation, C4 THERAPEUTICS, our housemark logo, the name of our TORPEDO platform, and the names of our BIDAC and MONODAC degrader products. All trademarks, service marks, or trade names referred to in this presentation that we do not own are the property of their respective owners. Solely for convenience, the trademarks, service marks, and trade names in this presentation are referred to without the symbols ®, SM and ™, but those references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights to.

C4T is a 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

Demonstrated ability to design **orally bioavailable, catalytically efficient degraders** that maximize the benefits of degradation

RIGOROUS TARGET SELECTION

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

BROAD DEGRADER APPROACH

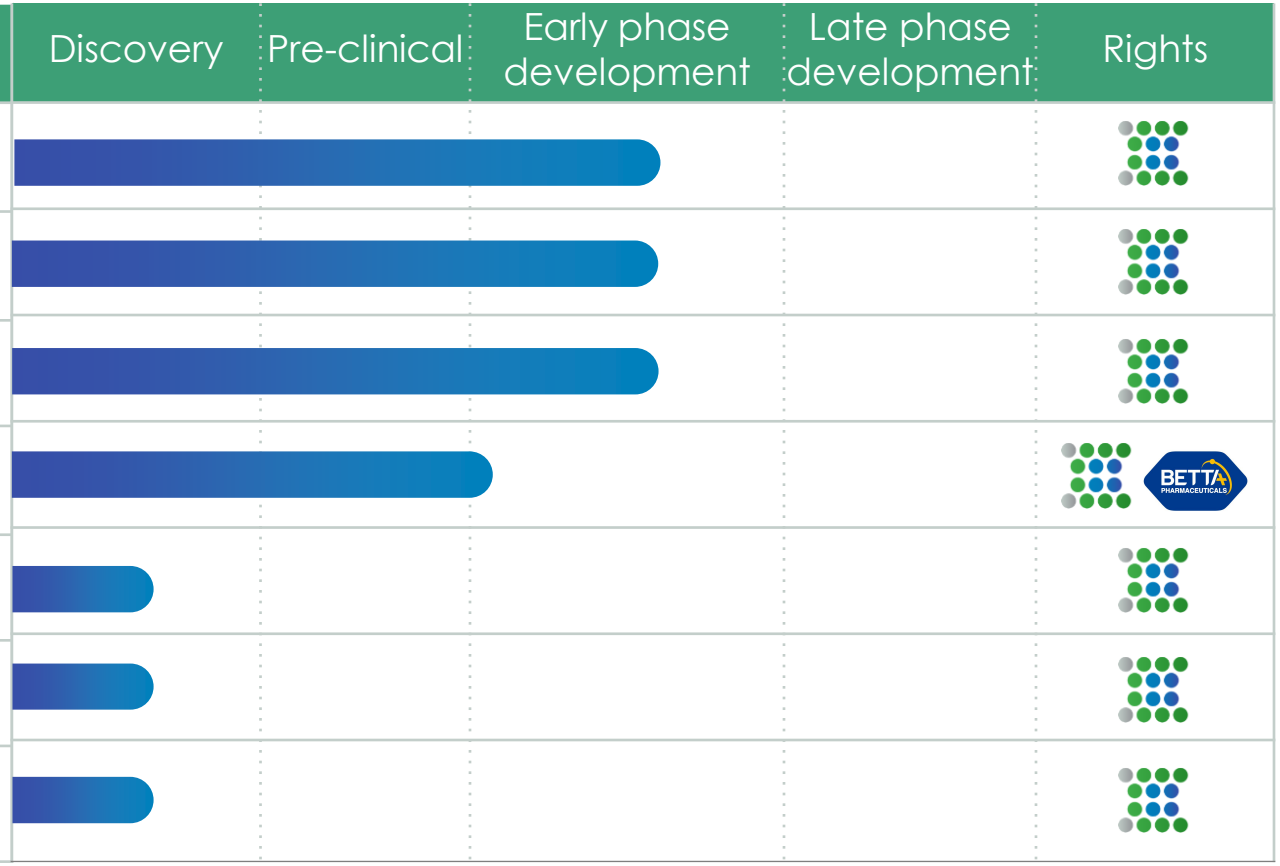
Only company with both **MonoDAC and BiDAC degraders** in the clinic

ROBUST CLINICAL PIPELINE

4 oncology degraders against targets of high unmet need

Robust Pipeline of Degrader Medicines Pursuing Multiple Targets in Oncology

Program	Target	Indications
CFT7455	**IKZF1/3**	Multiple Myeloma & Non-Hodgkin's Lymphoma
CFT8634	**BRD9**	Synovial Sarcoma & SMARCB1-null Cancers
CFT1946	**BRAF-V600**	V600 Mutant Cancers
CFT8919[1]	**EGFR L858R**	Non-Small Cell Lung Cancer
Chromatin Regulating Targets		Various Cancers
Oncogenic Signaling Targets		Various Cancers
Transcription Factor Targets		Various Cancers



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1. Exclusive Licensing Agreement with Betta Pharmaceuticals for the development and commercialization in Greater China

Two Clinical Readouts On Track by Year-End

CFT7455 IKZF1/3	• Present Phase 1 dose escalation data from the Phase 1/2 trial **2H**
CFT8634 BRD9	• Present Phase 1 dose escalation data from the Phase 1/2 trial **2H**
CFT1946 BRAF V600	✓ First patient dosed in the Phase 1/2 trial ✓ Present new preclinical data
CFT8919 EGFR L858R	✓ Secure China Partnership ✓ Achieved FDA clearance of IND

Cash Runway into 2H 2025[1]

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1. Cash runway as of June 30, 2023, along with the anticipated equity investments from Betta

CFT7455

Targeting IKZF1/3

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

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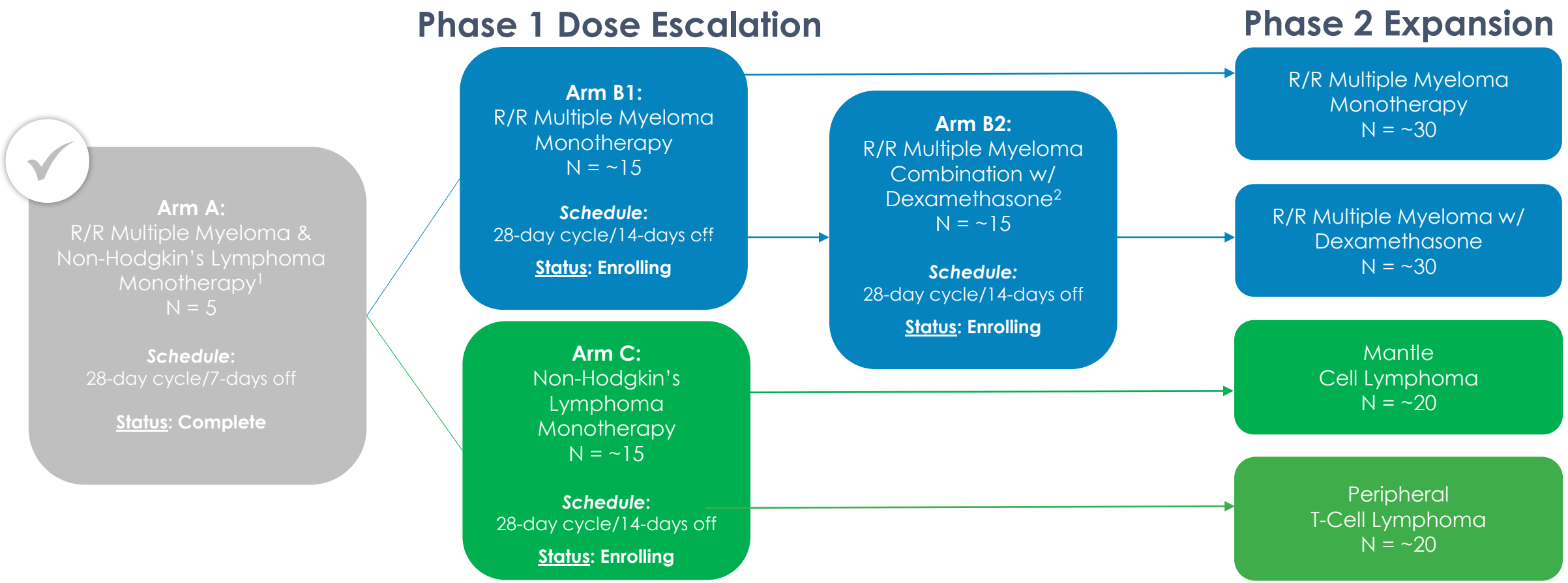
CFT7455 Phase 1/2 Trial Progressing through Dose Escalation

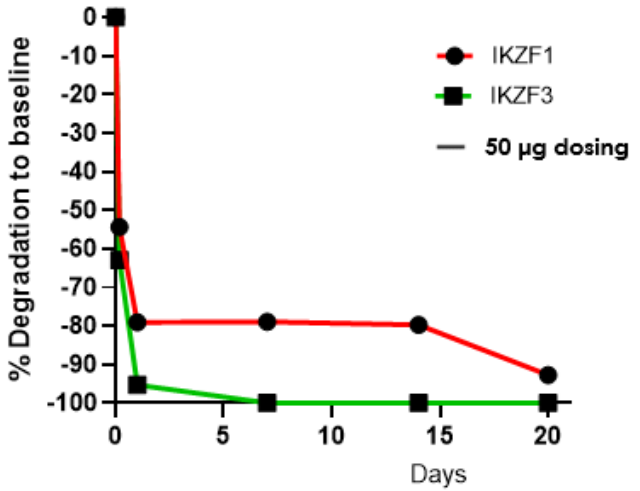


1. 28-day cycle /7 days off dose limiting toxicity (DLT) window
2. Combination therapy arms will open once the selected CFT7455 dose level has been cleared for safety

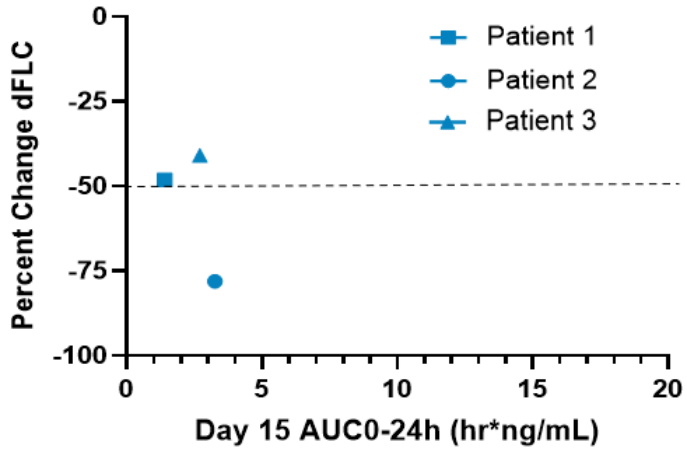
6–12 patient food effect enrichment arm also included during escalation, not pictured in schema

Single Agent CFT7455 Arm A Data Demonstrated Potent On Target Degradation; Dosing Schedule Modified to Improve Therapeutic Index

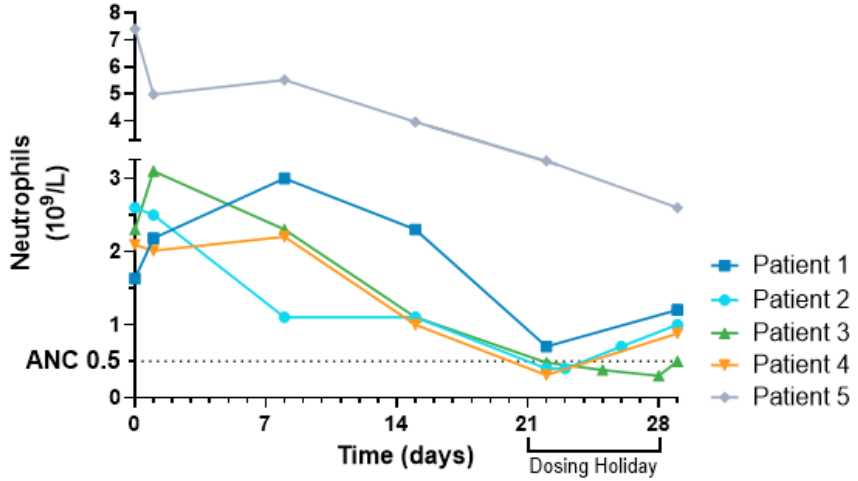
Deep Degradation of IKZF1/3



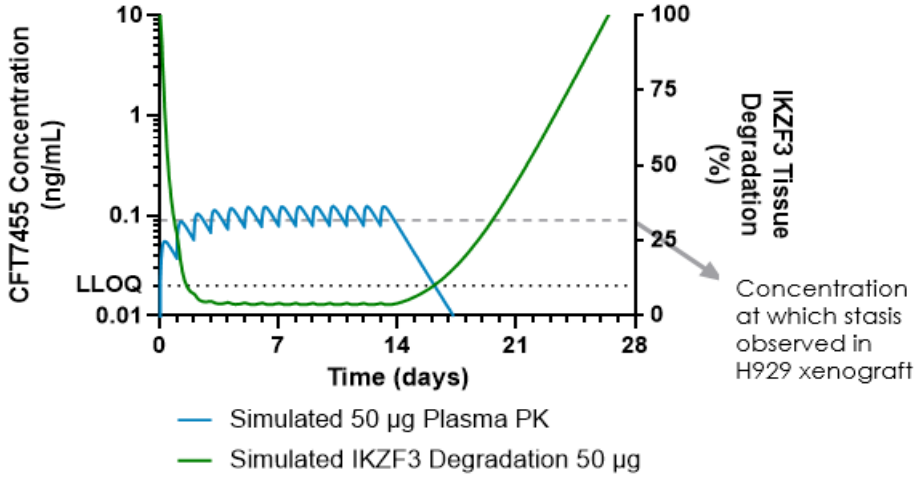
Meaningful Reductions in dFLC



Grade 4 Neutropenia



Modified Dosing Schedule with 14 Days Off

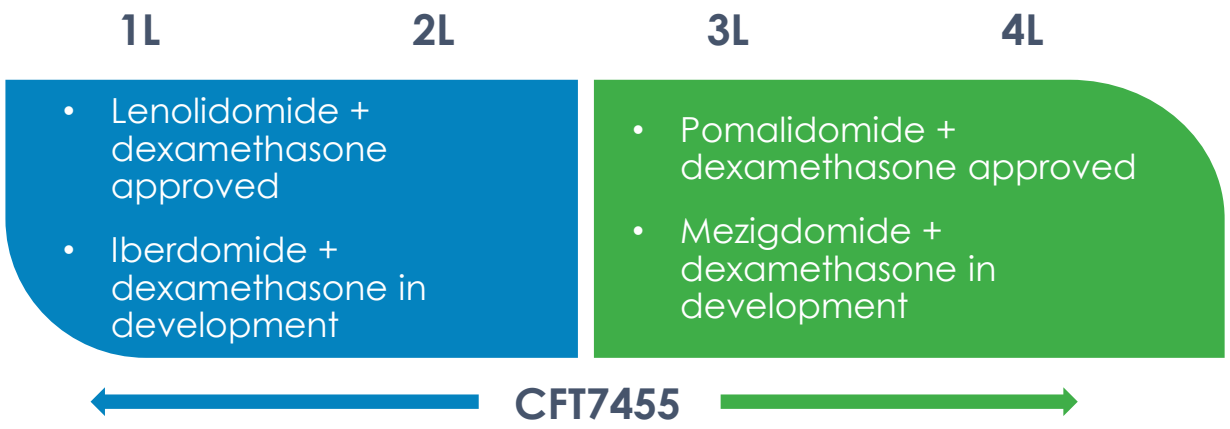


Source: C4T data on file; AACR 2022
Difference of serum free light chain (dFLC)

Multiple Paths to Success for CFT7455 across Evolving Multiple Myeloma Landscape

Potential for CFT7455 to replace other IKFZ1/3 degraders and become a backbone therapy

IKZF1/3 degrader competitive landscape



CFT7455, as one molecule, has the potential to be utilized across all lines of therapy with or without dexamethasone

Potential to combine CFT7455 with next-generation therapies

Bi-specific T-Cell Engagers	CAR T-Cell Therapies
Antibody-Drug Conjugates	BCMA-CD38
Monoclonal Antibodies	Small Molecule Inhibitors/ Modulators

CFT8634

Targeting BRD9

Synovial Sarcoma & SMARCB1-Null Solid Tumors

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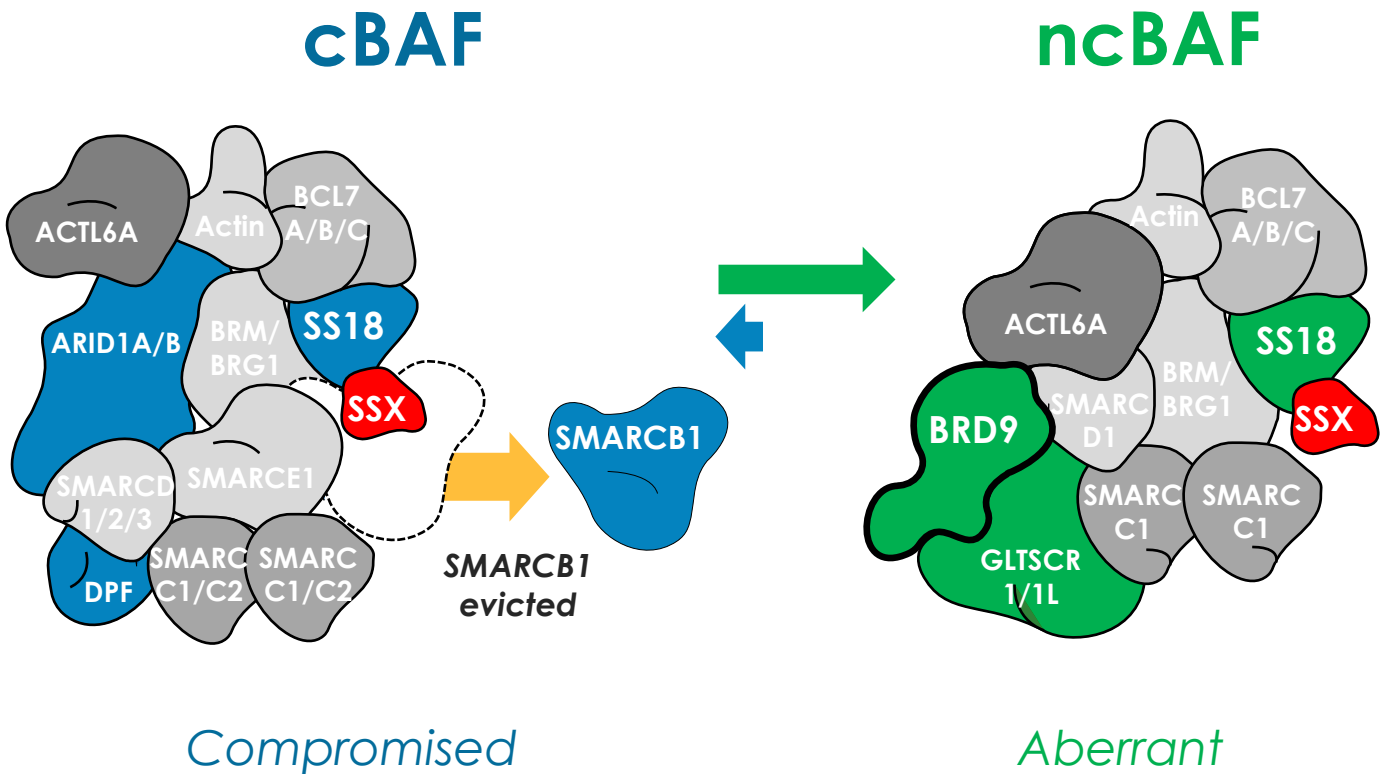
Oncogenic SS18-SSX Fusion Leads to BRD9 Dependency in Synovial Sarcoma



cBAF, canonical BAF; ncBAF, noncanonical BAF; pBAF, polybromoBAF.

1. Incorporation of SS18-SSX fusion results in eviction of SMARCB1
   - cBAF complex compromised
   - Oncogenic state
2. Inactivation of SMARCB1 leads to dependency on ncBAF complex
   - BRD9 is uniquely present in ncBAF
   - ***Synthetic lethal dependency on BRD9*** in synovial sarcoma and other SMARCB1-deficient cancers

CFT8634 Phase 1/2 Trial Progressing through Dose Escalation

Phase 1 Dose Escalation

CFT8634 Monotherapy
Synovial Sarcoma and SMARCB1-null Solid Tumors
N = ~20

Status: Enrolling

Enrichment Cohort for Synovial Sarcoma and SMARCB1-null Solid Tumors
N= ~10

Status: Enrolling

RP2D

Phase 2 Expansion

CFT8634 Monotherapy

Synovial Sarcoma
N = ~30

CFT8634 Monotherapy

SMARCB1-null Solid Tumors
N = ~20

BRD9 Previously Considered an Undruggable Target where Inhibitors are Ineffective for Synovial Sarcoma

Unmet Need

No approved therapies specifically for synovial sarcoma

Current treatment options offer limited benefit:

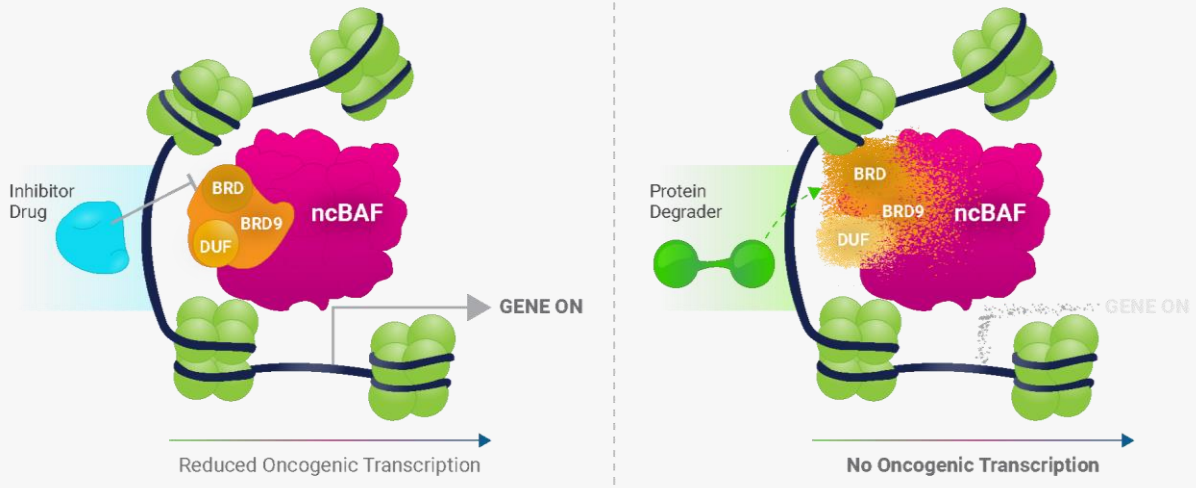
- **PFS of ~7 months**[1] in the front-line setting
- **PFS ~5 months**[2] in the relapsed refractory setting

Key Properties of CFT8634

- Orally bioavailable
- Potent
- Selective

Degrader Rationale

Oncogenicity of BRD9 depends on protein function not addressed by traditional inhibitors



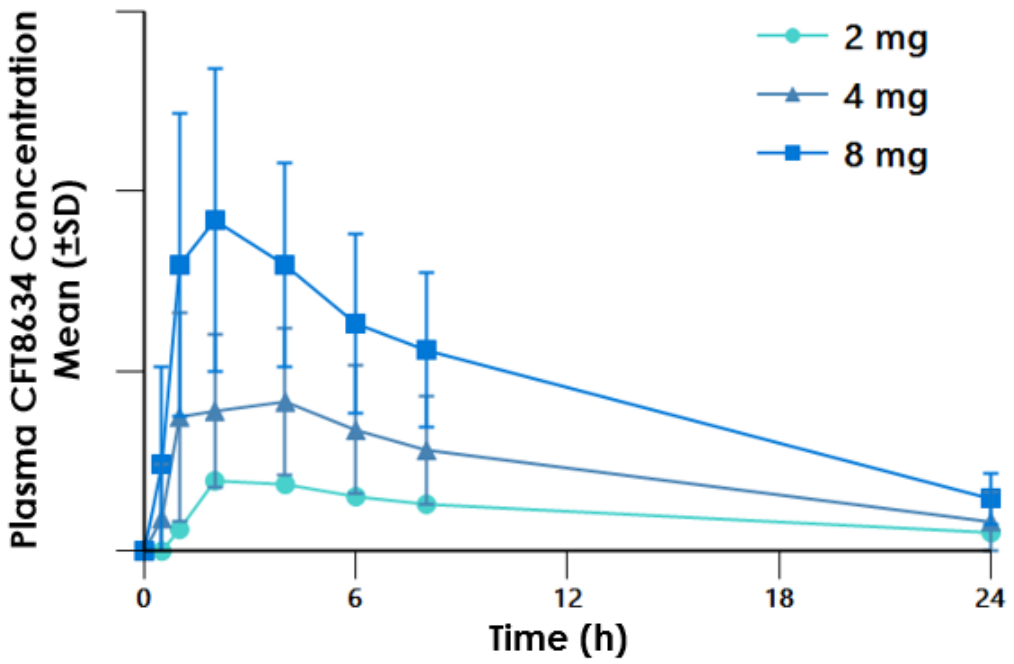
Sources:

1. Wang BC, et al. *Front Oncol.* 2021;11:76228.
2. Sleijfer S, et al. J Clin Oncol. 2009;27(19):3126-3132.

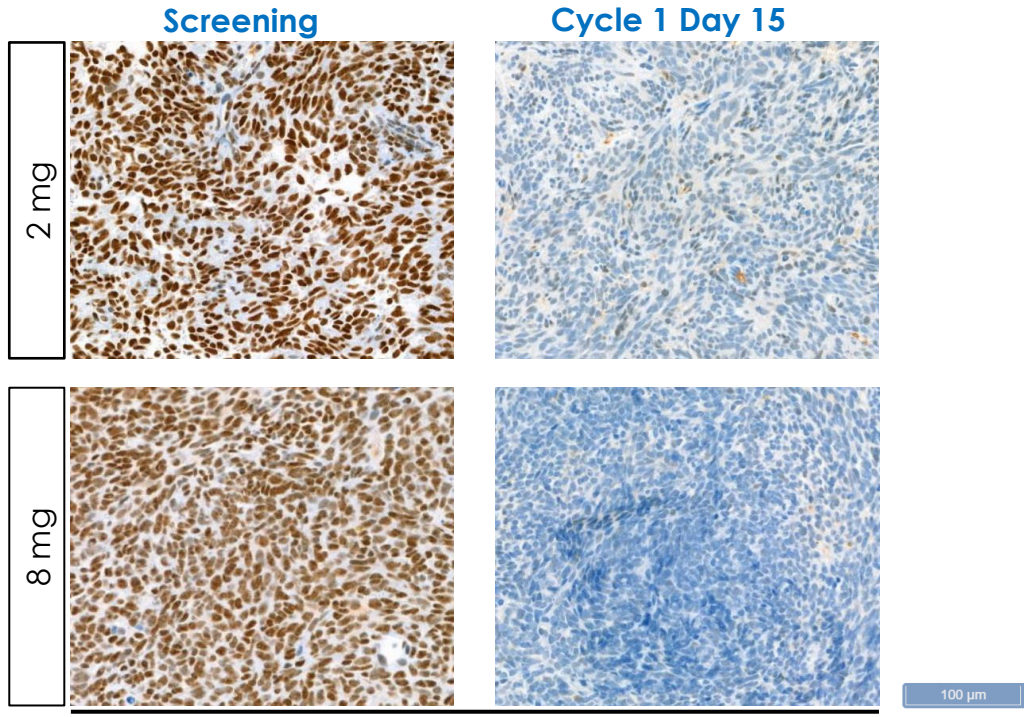
Progression Free Survival (PFS)

CFT8634 Pharmacokinetic and Pharmacodynamic Data Supportive of Proof of Mechanism

Dose-proportional Exposure with Strong Oral Bioavailability



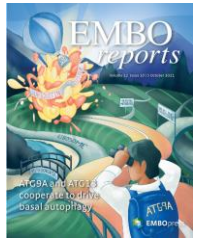
Robust BRD9 Degradation in Tumor Samples



α–BRD9 immunohistochemistry

Effective Degradation of a Previously Undruggable Target

Recent Publications Support Potential Additional Indications for BRD9



Interferonopathies

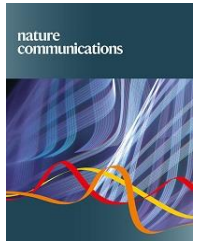
BRD9 is a druggable component of interferon-stimulated gene expression and antiviral activity

EMBOpress

Interferonopathies

BRD9 regulates interferon-stimulated genes during macrophage activation via cooperation with BET protein BRD4

PNAS



Ovarian Cancer

The bromodomain containing protein BRD-9 orchestrates RAD51–RAD54 complex formation and regulates homologous recombination-mediated repair

Nature Communications

Clear Cell Renal Cell Carcinoma

Aberrant activation of m6A demethylase FTO renders HIF2a$^{low/-}$ clear cell renal cell carcinoma sensitive to BRD9 inhibitors

Science Translational Medicine

Prostate Cancer

BRD9 Is a Critical Regulator of Androgen Receptor Signaling and Prostate Cancer Progression

AACR Journals

Multiple Myeloma

BRD9 Is Essential for Ribosome Biogenesis and the Survival of Multiple Myeloma Cells

ASH Annual Meeting 2022

Currently Evaluating Opportunities for Indication Expansion

CFT1946

Targeting BRAF V600

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

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Current Standard of Care BRAF Inhibitors Lead to Resistance

Unmet Need

Resistance to approved BRAF inhibitors results **in a median PFS of less than 15 months**[2]

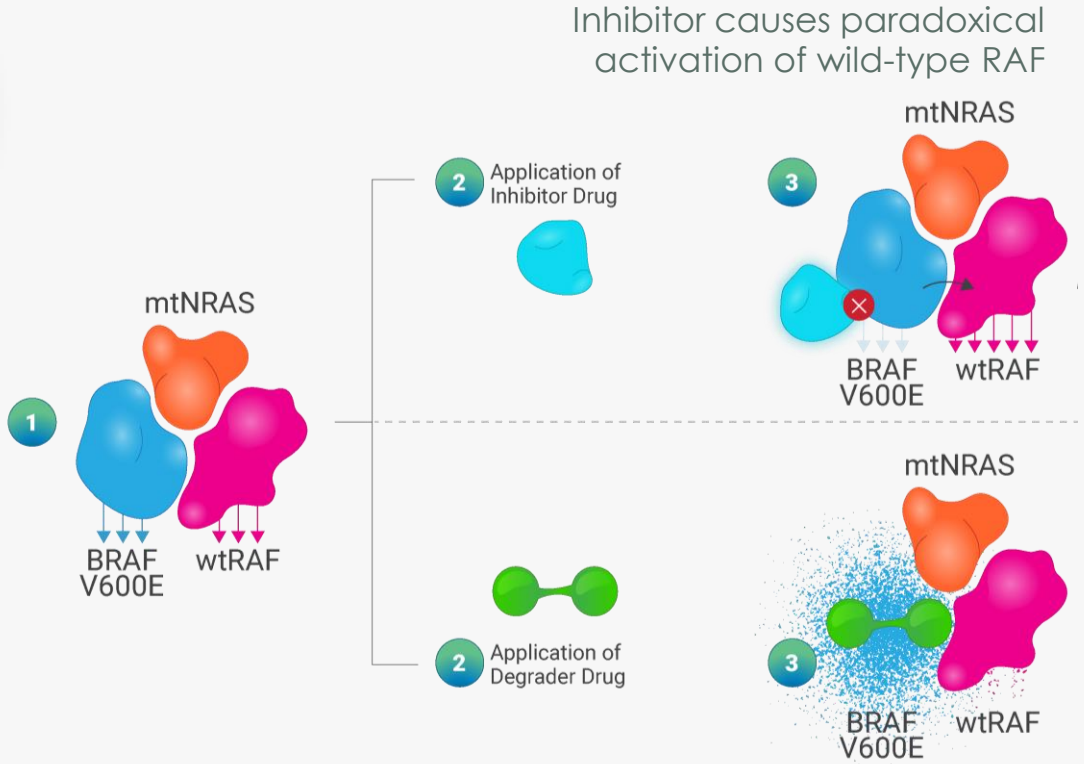
Toxicity associated with inhibiting wild-type BRAF

~$2B approved BRAF inhibitor market[1]

Key Properties of CFT1946

- Orally bioavailable
- Potent and selective against BRAF V600 mutant targets while sparing wild-type activity
- Preclinical activity in setting of resistance to BRAF inhibitors

Degrader Rationale



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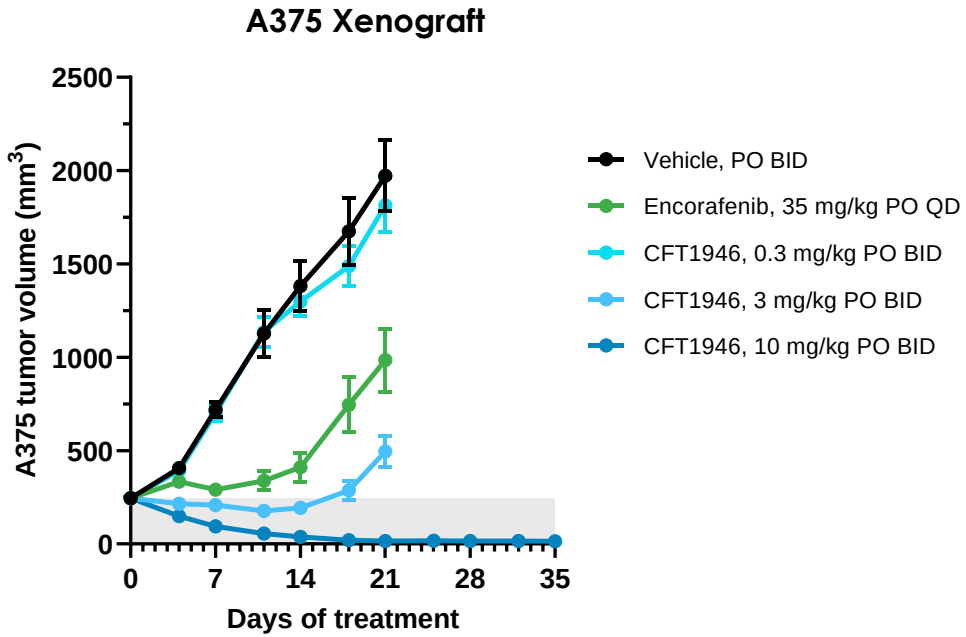
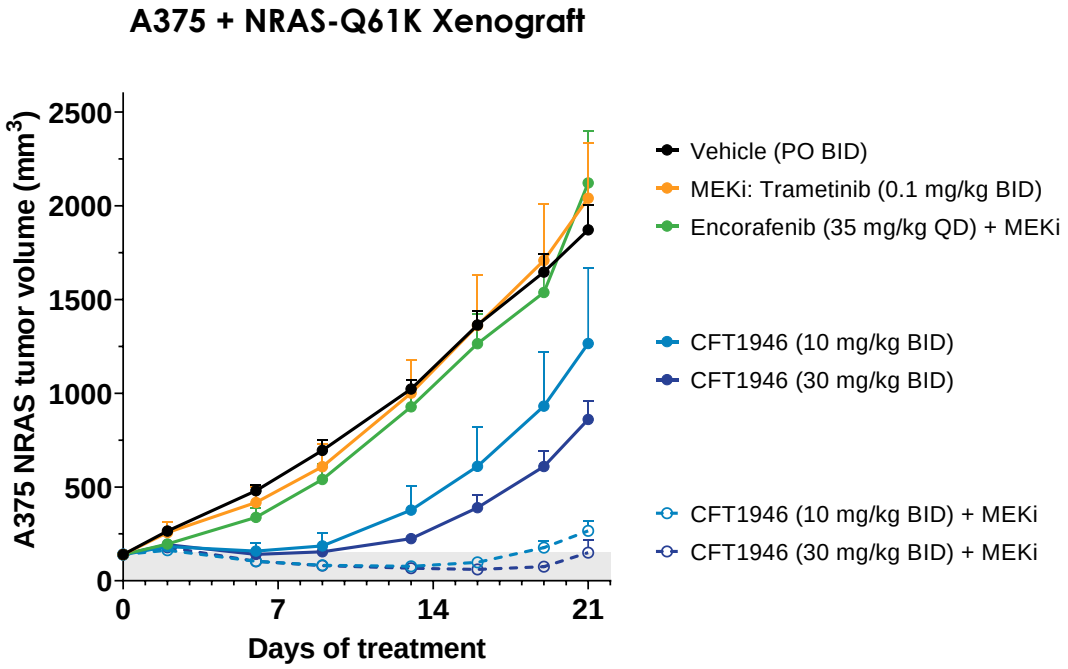
Sources:
1. 2022 Market size from EvaluatePharma.
2. NIH SEER Database, Primary Literature Consensus. https://www.ncbi.nlm.nih.gov/pmc/articles/MC5931274/, https://pubmed.ncbi.nlm.nih.gov/26980021/

CFT1946 Shows Superior Efficacy Compared to Approved BRAF Inhibitor in Preclinical Models

CFT1946 Shows More Durable Efficacy than Encorafenib



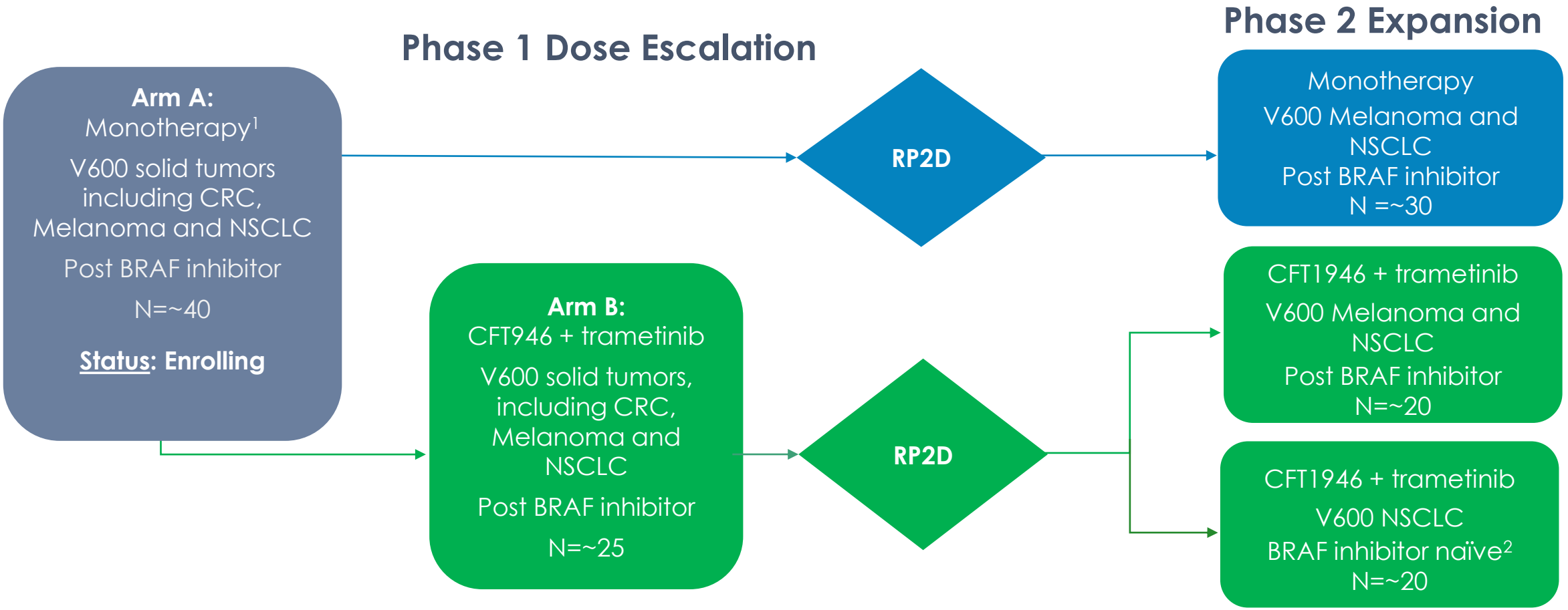
Combination Treatment of BRAFi Resistant Xenograft Model with CFT1946 and MEKi Shows Tumor Growth Inhibition/Regression



Source: C4T data on file; AACR 2022

BRAF inhibitor (BRAFi); MEK inhibitor (MEKi); By mouth (PO); Pharmacokinetics/pharmacodynamics (PK/PD); Once daily (QD); Twice daily (BID

CFT1946 is the First Clinical BRAF V600 Degrader



1. 28-day cycle/ dose limiting toxicity (DLT) window
2. BRAF inhibitor naïve expansion arm to be aligned across global health authorities

Colorectal cancer (CRC); Recommended Phase 2 dose (RP2D); Non-Small Cell Lung Cancer (NSCLC)

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19

CFT1946 Has the Potential to Address Multiple Tumor Types with BRAF V600 Mutations

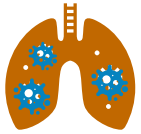
1.9M Cancer Diagnoses Each Year in the United States[1]

BRAF Mutations Occur in ~5% of All Cancers[2]

~100K annual incidence of BRAF mutated cancers[1]

~70-90% of BRAF mutations are V600

35% Late-stage Melanoma[2]



1-2% Non-Small Cell Lung Cancer[3]

5-10% Colorectal Cancer[4]

Sources:
1. ACS Figures & Facts 2022: https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2022.html
2. Owsley J, et al. *Experimental Biology and Medicine*. 2021;246(1):31-39
3. Paik, P. K.,, et al. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2011; 29(15), 2046–2051.
4. Bylsma, L. C., et al. *Cancer medicine*.2020;9(3), 1044–1057.

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CFT8919

Targeting EGFR L858R

EGFR L858R + Non-Small Cell Lung Cancer (NSCLC)

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

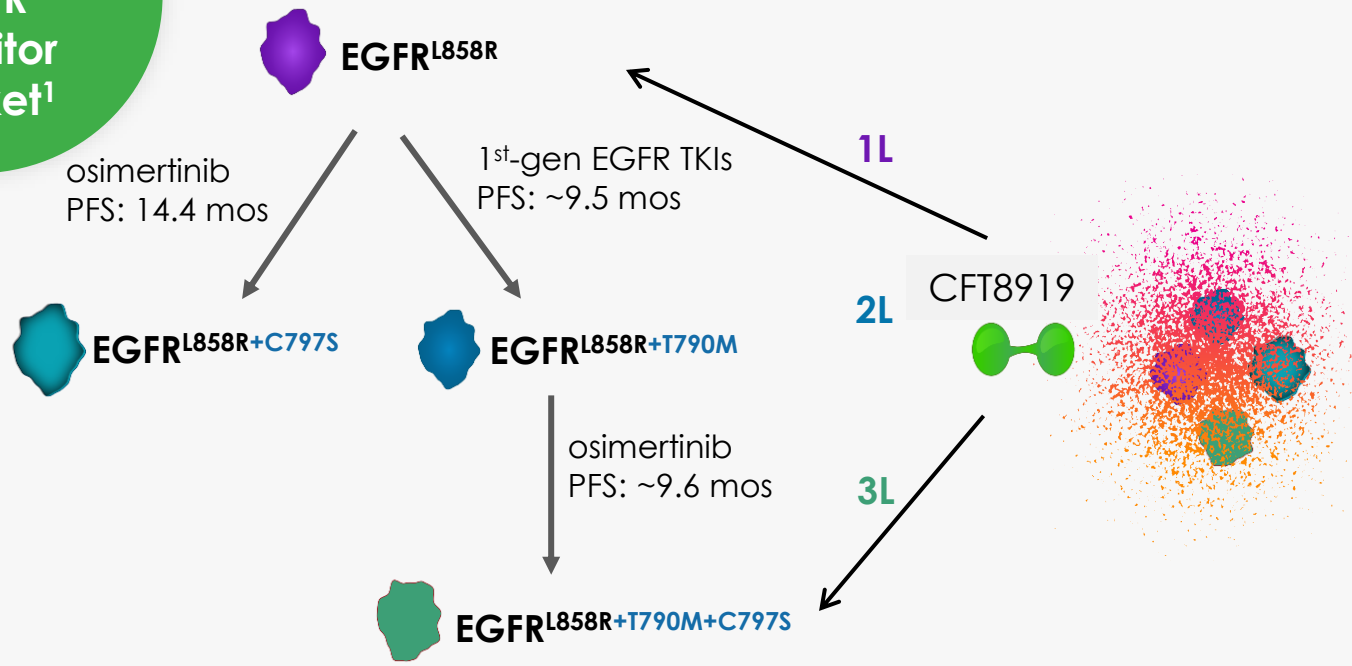
Osimertinib and other inhibitors provide suboptimal response for NSCLC patients with L858R mutation

OSI **14.4 months PFS** (L858R)

OSI **21.4 months PFS** (Exon 19 deletion)

~$6B approved EGFR inhibitor market[1]

Degrader Rationale



Key Properties of CFT8919

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

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Sources:
- Soria, J.-C. et al. NEJM 378, 113–125 (2018),
- Sher, T. et al, *Mayo Clin. Proc.* 83, 355-367 (2008),

1. 2022 market size from EvaluatePharma.

Mutant EGFR (mEGFR); Non-small cell lung cancer (NSCLC); Tryosine Kinase Inhibitor (TKI)

Strategic Partnership with Betta Pharmaceuticals in Greater China

Expert Partner in Greater China

- Betta has a proven track record of developing NSCLC medicines including EGFR inhibitors

Expedite Development

- High prevalence of EGFR L858R driven NSCLC in Greater China allows for faster clinical development in target population

Expected Next Steps:

- Betta to file a CTA with the NMPA
- Phase 1 dose escalation to begin in Greater China

Deal Terms:

- **$10 million upfront** and **$25 million equity investment**
- C4T eligible to **receive up to $357 million** in potential milestones and **low to mid-double-digit percent royalties** on net sales in the licensed territories

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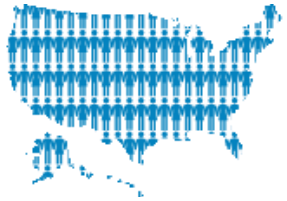
Investigational New Drug (IND); Food and Drug Administration (FDA); CTA (Clinical Trial Application); National Medical Products Administration (NMPA)

EGFR L858R Driven NSCLC has Higher Prevalence in Asia

Non-Small Cell Lung Cancer (NSCLC)



~200K
Patients in the US diagnosed in 2022

~693K
Patients in Asia diagnosed in 2020

~10 – 15% of NSCLC patients have mutant EGFR (mEGFR) in the **U.S.** population

~40% of NSCLC patients have mEGFR in the **Asian** population

~40% of mEGFR NSCLC patients have the L858R activating mutation

Sources:
- Recondo 2018 Nature Rev Clin Oncol https://www.nature.com/articles/s41571-018-0081-4
- Globacan 2020
- American Cancer Society. Facts & Figures 2023. American Cancer Society.
- SEER Cancer Stat Facts: Lung and bronchus cancer. National Cancer Institute, https://seer.cancer.gov/statfacts/html/lungb.html.
- Mao 2021 Pathol Oncol Res (https://pubmed.ncbi.nlm.nih.gov/34257561/)
- Melosky 2021 Mol Diagnosis Ther (https://link.springer.com/article/10.1007/s40291-021-00563-1)

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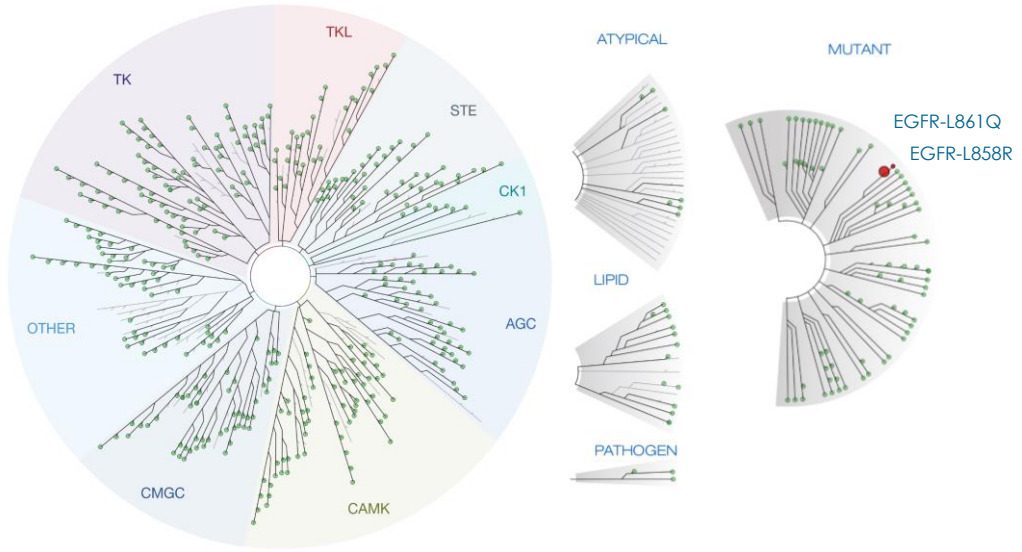
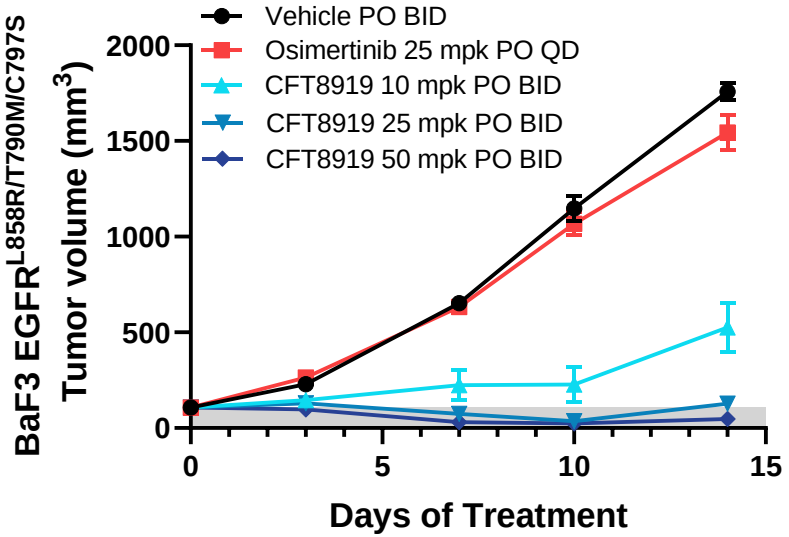
CFT8919 is Selective for EGFR L858R and Active in a Setting of Osimertinib Resistance in Preclinical Models

Specific for EGFR Exon 21 Mutants



Active in setting of EGFR C797S



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

Thank You!

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