UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 26, 2021

C4 THERAPEUTICS, INC.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-39567**	**47-5617627**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
490 Arsenal Way, Suite 200 **Watertown, MA** **(Address of Principal Executive Offices)**		**02472** **(Zip Code)**

Registrant's Telephone Number, Including Area Code: (617) 231-0700

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	CCCC	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure

On May 26, 2021, C4 Therapeutics, Inc. (the "Company") issued a press release entitled "C4 Therapeutics to Advance CFT8919, A Selective Degrader of EGFR L858R, Into IND-enabling Studies." The Company also posted a corporate presentation on its website at https://ir.c4therapeutics.com/events-presentations. A copy of the press release and the investor presentation are attached as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K.

The information in this Current Report on Form 8-K, including Exhibits 99.1 and 99.2 attached hereto, is being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, nor shall it be deemed subject to the requirements of amended Item 10 of Regulation S-K, nor shall it be deemed incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing. The furnishing of this information hereby shall not be deemed an admission as to the materiality of any such information.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits. The exhibits shall be deemed to be filed or furnished, depending on the relevant item requiring such exhibit, in accordance with the provisions of Item 601 of Regulation S-K (17 CFR 229.601) and Instruction B.2 to this form.

Exhibit Number	Description
99.1	Press Released dated May 26, 2021 (furnished herewith)
99.2	Corporate Presentation of the Company dated May 26, 2021 (furnished herewith)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

C4 Therapeutics, Inc.

Date: May 26, 2021

By: /s/ Jolie M. Siegel
Jolie M. Siegel
Chief Legel Officer

C4 Therapeutics to Advance CFT8919, A Selective Degrader of EGFR L858R, Into IND-enabling Studies

– *IND Submission for CFT8919 Anticipated mid-2022; Phase 1/2 Trial Initiation Expected by YE 2022* –

– *CFT8919 is Potent and Mutant-Selective BiDAC™ Degrader of EGFR L858R for the Treatment of Non-Small Cell Lung Cancer* –

– *CFT8919 Pre-clinical Data on EGFR L858R-driven NSCLC to be Presented at Keystone Symposium on Targeted Protein Degradation* –

– *Conference Call and Webcast Scheduled for June 7, 2021 at 8:00 am ET* –

WATERTOWN, Mass., May 26, 2021 (GLOBE NEWSWIRE) – C4 Therapeutics, Inc. (C4T) (Nasdaq: CCCC), a biopharmaceutical company pioneering a new class of small-molecule medicines that selectively destroy disease-causing proteins through degradation, today announced that it has decided to advance CFT8919, a novel degrader of epidermal growth factor receptor (EGFR) in non-small cell lung cancer (NSCLC), into investigational new drug (IND)-enabling studies and anticipates filing an IND for this program by mid-2022, with the goal to initiate a Phase 1/2 clinical trial by year-end 2022.

“The ongoing progress we have made across our portfolio reflects our goal of transforming patient care through the development of novel protein degraders,” said Andrew Hirsch, chief executive officer of C4 Therapeutics. “We are excited to announce that we recently determined we will advance CFT8919, a BiDAC degrader targeting EGFR in NSCLC, into IND-enabling studies and now expect to submit an IND for this program in mid-2022 to enable the initiation of a clinical trial by year-end 2022. We are also looking forward to sharing the first preclinical data for CFT8919 at the upcoming Keystone Symposium for Targeted Protein Degradation in early June. These efforts are part of our ongoing efforts to advance treatments for patients through targeted protein degradation and, with the advancement of this program, we remain on track to achieve our goal to have four product candidates in the clinic by year-end 2022.”

CFT8919, a Potent and Mutant-Selective BiDAC Degrader of EGFR L858R

The preclinical data C4T will present at the upcoming Keystone Symposium establish CFT8919 as a potent and selective degrader of EGFR L858R that is based on an allosteric EGFR binding motif. As a single agent, CFT8919 is active in both *in vitro* and *in vivo* models of EGFR L858R-driven NSCLC without resistance-causing secondary mutations in EGFR, as well as in similar models that harbor secondary resistance mutations such as EGFR T790M and C797S. Additionally, CFT8919 demonstrates intracranial activity, indicating that it has the potential to treat brain metastases. Together, these data suggest CFT8919 may be active, as single agent, in patients with resistance to EGFR L858R-driven tumors due to secondary mutations in EGFR, including T790M and C797S, as well as in the front-line setting with the potential to avoid the emergence of resistance-causing secondary EGFR mutations seen with currently approved EGFR inhibitors.

Progress to 2021 Key Milestones:

- **Initiate patient dosing for CFT7455 in 1H 2021.** The Company’s first-in-human Phase 1/2 clinical trial of CFT7455 is open for enrollment and clinical sites have begun to screen patients. The program remains on track to begin dosing patients in 1H 2021. The Phase 1/2 clinical trial is an open-label, two-part, dose-escalation and expansion study evaluating CFT7455 across multiple hematologic malignancies, including multiple myeloma and various non-Hodgkin’s lymphomas,

including peripheral T cell lymphoma and mantle cell lymphoma. More information about this trial may be accessed at www.clinicaltrials.gov (identifier: NCT04756726).

- **Submit an IND application for CFT8634 in 2H 2021.** CFT8634 is an orally bioavailable BiDAC degrader targeting BRD9 for the treatment of synovial sarcoma and SMARCB1-deleted solid tumors.
- **Advance the BRAF program into IND-enabling studies in 2021.** The objective of the BRAF program is to develop an orally bioavailable BiDAC degrader targeting BRAF V600E mutations for the treatment of genetically defined solid tumors, including locally advanced or metastatic melanoma and non-small cell lung cancer (NSCLC). The BRAF program is partnered with Roche.
- **Continue lead optimization activities for the RET program through 2021.** The objective of the RET program is to develop an orally bioavailable BiDAC degrader targeting genetically altered RET for the treatment of solid tumors, including relapsed or refractory NSCLC and sporadic medullary thyroid cancers that are resistant to RET inhibitors.

Upcoming Events

- May 26, 2021 – C4T will participate in a Fireside Chat at 8:00 am ET at the UBS Global Healthcare Conference. Details of this event are available on the Investors section of the C4T website, under Events & Presentations.
- June 1, 2021 – C4T will participate in a Fireside Chat at 10:30 am ET at the Jefferies Global Healthcare Conference. Details of this event are available on the Investors section of the C4T website, under Events & Presentations.
- June 6-9, 2021 – C4T will present preclinical data from CFT8919 in a virtual poster presentation at the Keystone Symposium, Targeted Protein Degradation: From Small Molecules to Complex Organelles.
- June 7, 2021 – C4T will host a live webcast at 8:00 a.m. E.T. to discuss the CFT8919 preclinical data presented at the Keystone Symposium. Details of this event are included below.
- June 18-22, 2021 – C4T will present preclinical data on CFT7455 in non-Hodgkin's lymphoma (NHL) at the 16th Annual ICML meeting. CFT7455 is a novel, IKZF1/3 MonoDAC™ degrader that has demonstrated potent tumor regression in a spectrum of NHL xenograft models.

Investor Event and Webcast Information

C4T will host a live webcast on Monday, June 7, 2021 at 8:00 a.m. E.T. to discuss the CFT8919 data presented at the Keystone Symposium. The webcast can be accessed through the Events and Presentations page on the Investors section of C4T's website at www.c4therapeutics.com. A replay of the webcast will be available on C4T's website for 30 days following the event.

About C4 Therapeutics

C4 Therapeutics (C4T) is a biopharmaceutical company focused on harnessing the body's natural regulation of protein levels to develop novel therapeutic candidates to target and destroy disease-causing proteins for the treatment of cancer and other diseases. This targeted protein degradation approach offers advantages over traditional therapies, including the potential to treat a wider range of diseases, reduce drug resistance, achieve higher potency, and decrease side effects through greater selectivity. To learn more about C4 Therapeutics, visit www.C4Therapeutics.com.

Forward-Looking Statements

This press release contains "forward-looking statements" of C4 Therapeutics, Inc. within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements may include, but

may not be limited to, express or implied statements regarding our ability to develop potential therapies for patients; the design and potential efficacy of our therapeutic approaches; the predictive capability of our TORPEDO™ platform in the development of novel, selective, orally bioavailable degraders; the potential timing, design and advancement of our preclinical studies and clinical trials, including the potential timing for regulatory submissions and authorization related to clinical trials; our ability and the potential to successfully manufacture and supply our product candidates for clinical trials; our ability to replicate results achieved in our preclinical studies or clinical trials in any future studies or trials; our current resources and cash runway; regulatory developments or approvals in the United States and foreign countries; and upcoming events that C4T will participate in. Any forward-looking statements in this press release are based on management's current expectations and beliefs of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: uncertainties related to the initiation, timing, advancement and conduct of preclinical and clinical studies and other development requirements for our product candidates; the risk that any one or more of our product candidates will cost more to develop or may not be successfully developed and commercialized; and the risk that the results of preclinical studies and/or clinical trials will or will not be predictive of future results in connection with future studies or trials. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in C4 Therapeutics' most recent Annual Report on Form 10-K and/or Quarterly Report on Form 10-Q, as filed with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and C4 Therapeutics undertakes no duty to update this information unless required by law.

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Media Contact:
Loraine Spreen
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LSpreen@c4therapeutics.com

Exhibit 99.2

C4 Therapeutics

Corporate Presentation

May 2021

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. 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.

Intellectual Property

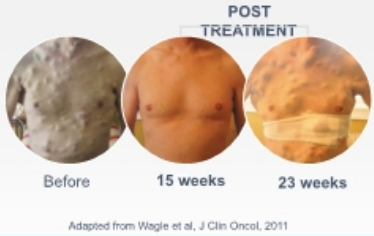
C4 Therapeutics, Inc. owns various registered and unregistered trademarks in the U.S. and internationally, including, without limitation, C4 THERAPEUTICS, our housemark logo, the name of our TORPEDO platform, and the names of our BIDAC and MONODAC degrader products. All trademarks or trade names referred to in this presentation that we do not own are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the symbols ® 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 thereto.

Targeted Protein Degradation Has the Potential to Transform Treatment of Disease

<15%

Of Human Proteome Addressable by Small Molecule Inhibitors

Substantial opportunity to develop treatments for targets previously considered undruggable



Adapted from Wagle et al, J Clin Oncol, 2011

Cancers become resistant to standard therapies and treatment options are then limited

$63B

2018 Global Revenue

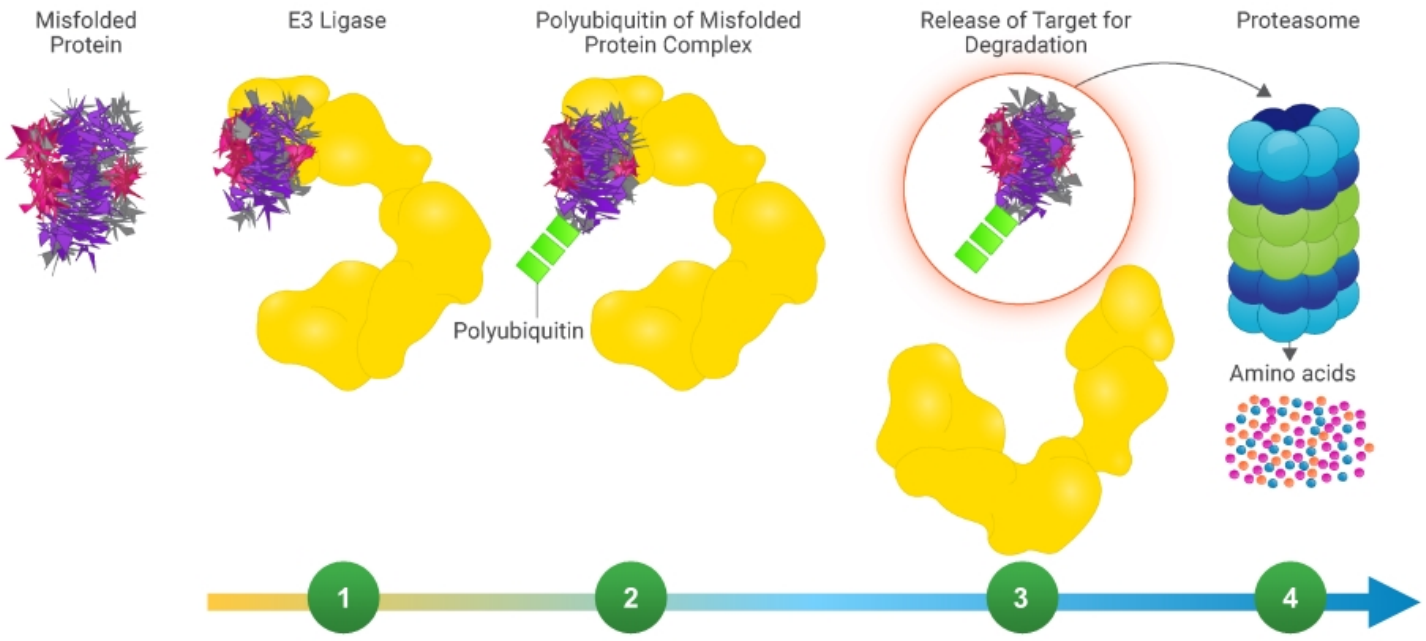
Oncology small molecule therapies generate significant revenue despite known limitations

Targeted Protein Degradation Has Potential to Drug the Remaining ~85% of the Human Proteome and Overcome Resistance to Existing Inhibitor Medicines

Sources: Hopkins, A., Groom, C. The druggable genome. Nat Rev Drug Discov 1, 727–730 (2002). https://doi.org/10.1038/nrd892; "A view on drug resistance in cancer" Nature | Vol 575 | 14 November 2019; Fact.MR: https://www.factmr.com/report/3747/oncology-small-molecule-drugs-market

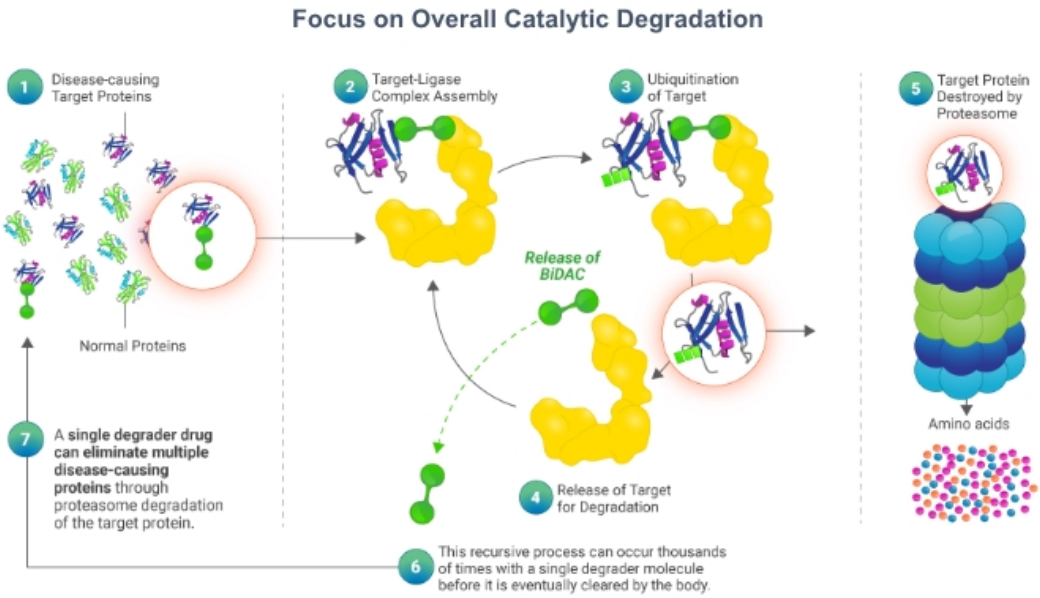
C4T is Well Positioned to Develop Targeted Protein Degradation Medicines to Transform Patient Care

The Human Body Has A Natural Process to Destroy Unwanted Proteins



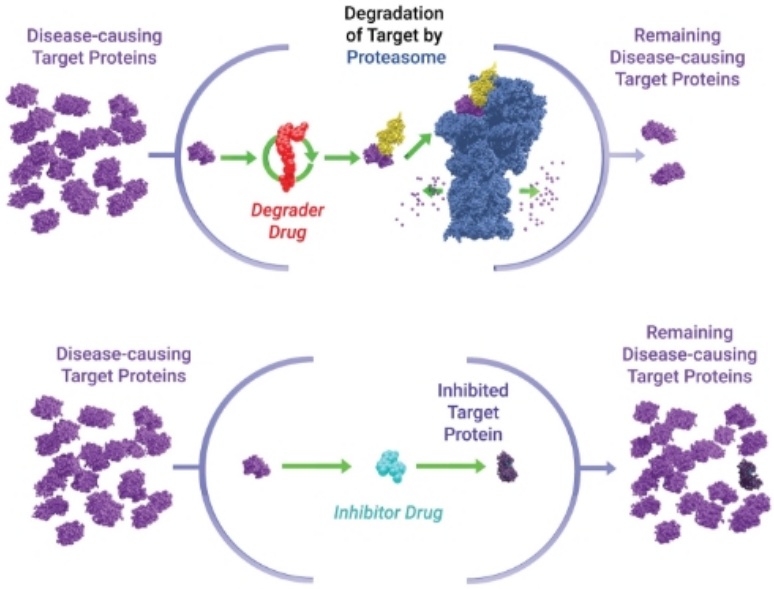
C4 Therapeutics

Targeted Protein Degradation Leverages the Body's Natural Process to Destroy Disease-Causing Proteins



Targeted Protein Degradation Offers Fundamental Advantages Over Protein Inhibition

1. **Improved Potency**
2. **Fast Response**
3. **High Selectivity**
4. **Expansive Target Landscape**



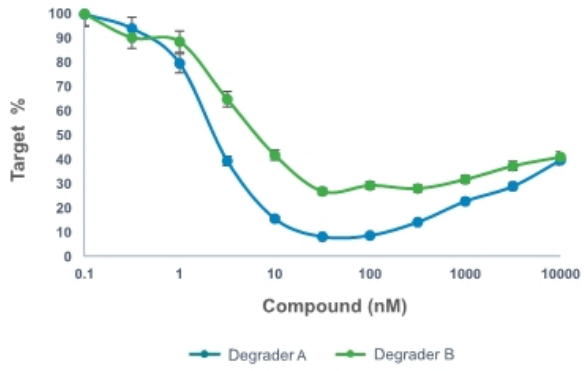
TORPEDO (Target ORiented ProtEin Degrader Optimizer) Platform

Our TORPEDO Platform Has Potential to Efficiently Design Highly Potent Targeted Protein Degrader Medicines

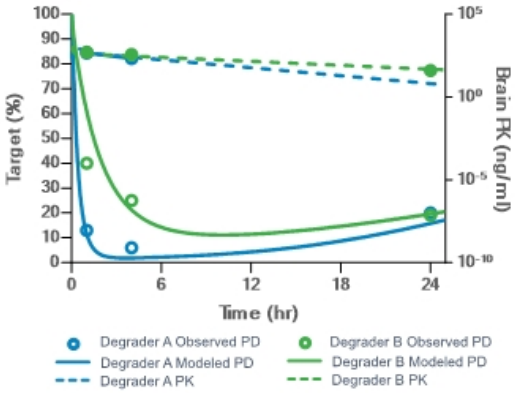
Elements	Benefits
Focus on Catalytic Efficiency	Optimization of overall degradation process results in maximal efficacy
Ability to Design, Analyze & Predict Degrader Performance	Rapid delivery of potent drug candidates through informed and efficient drug discovery
Investment in Cereblon as E3 Ligase	Cereblon is expressed in all tissues and cellular compartments, thereby providing the largest target selection opportunity
Ability to Develop Both MonoDAC & BiDAC Degraders	Flexibility to address different targets with tailored approach

Enhanced Catalytic Activity Drives Efficacy

Improved Catalytic Activity of Degrader A…



…Drives Significant Improvement in Target Knockdown



Source: C4T data on file

TORPEDO Platform: Robust Drug Discovery Process Enabling Higher Confidence in *In Vivo* Efficacy

Design

Computational method incorporates experimental data to identify top models

Atomic-level degrader design utilized to improve selectivity and potency

Analyze

Cellular degradation data fitted using an enzymology framework

Key parameters describe intrinsic degradation activity

Predict

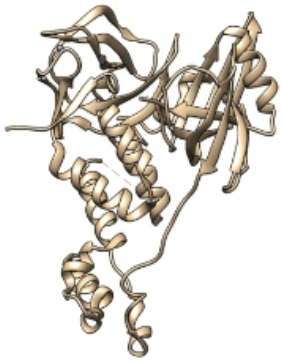
Universal modeling framework merges degradation activity with degrader exposure

Robust predictions of depth and duration of *in vivo* target degradation at any dose

Rapid Delivery of Potent Drug Candidates Through Informed and Efficient Drug Discovery

TORPEDO is Based on a Deep Focus on Cereblon, Providing the Largest Target Selection Opportunity

Cereblon E3 Ligase

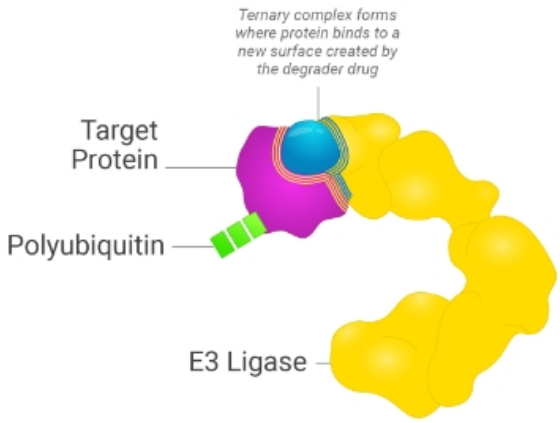


- Cereblon, harnessed by IMiDs, is the only clinically validated ligase for targeted protein degradation
- Cereblon is expressed in all tissues and in all cellular compartments
- Investment in rich toolkit of intellectual property with more than 15 structurally distinct Cereblon binders
- C4T's binders enable drug discovery with enhanced oral bioavailability, solubility, permeability & stability

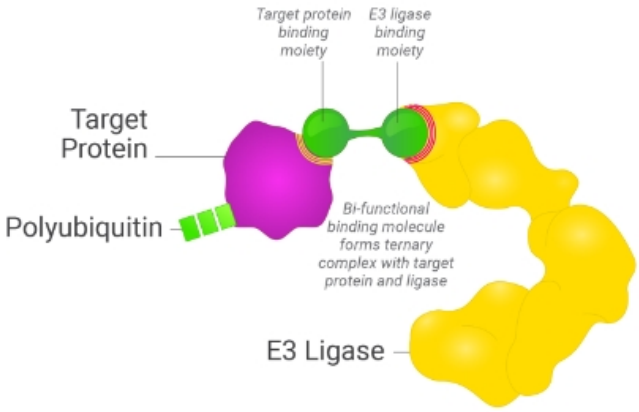
Programs Benefit from Desirable Properties of C4T's Cereblon Binders

TORPEDO Platform Offers Flexibility to Design MonoDAC and BiDAC Degraders

MonoDAC Degrader



BiDAC Degrader



Flexibility to Address Different Targets with Tailored Approach

TORPEDO Platform Has Delivered a Robust Degrader Pipeline; Four Clinical Programs Expected by End of 2022

Target	Indication(s)	Discovery	Preclinical	Clinical	Ownership
IKZF1/3 (CFT7455)	Multiple Myeloma & Lymphoma			●	C4 Therapeutics
BRD9 (CFT8634)	Synovial Sarcoma & SMARCB1 Deleted Tumors			●	C4 Therapeutics
EGFR (CFT8919)	Drug-Resistant EGFR+ NSCLC		●		C4 Therapeutics
BRAF V600E	Drug-Resistant BRAF mutant Tumors		●		C4 Therapeutics, Roche
RET	Drug-Resistant RET-Altered Tumors		●		C4 Therapeutics
Transcriptional Control	Undisclosed Solid Tumors	●			C4 Therapeutics
Cancer Signaling	Undisclosed Cancers	●			C4 Therapeutics
Transcriptional Control	Undisclosed Liquid Tumors	●			C4 Therapeutics
Cancer Signaling	Undisclosed Solid Tumors	●			C4 Therapeutics

Nine Additional Undisclosed Collaborator Programs in Discovery

Three Strategic Target Platform Collaborations Expand Platform Potential

IKZF1/3 CFT7455

IKZF1/3: Maximal Catalytic Activity Leads to Improved Efficacy

Strong Rationale for Degrader Approach

- Multiple myeloma (MM) and Non-Hodgkin's lymphomas (NHLs) are dependent on IKZF1/3
- Existing IKZF1/3 degraders have limited potency

Clear Unmet Need

- Patients progress on approved IMiD therapies
- Approved IMiDs have limited activity in NHLs

Defined Patient Populations

- MM: ~32K cases/year; median 5-year overall survival (OS): 52%
- NHL: ~77K cases/year
- PTCL: ~4% of all NHLs; median 5-year OS: 20-32%
- MCL: ~7% of all NHLs; median OS: 4-5 years

Compelling Development Opportunity

- Potential for accelerated approval in select indications
- Opportunity to expand into earlier lines of MM therapy

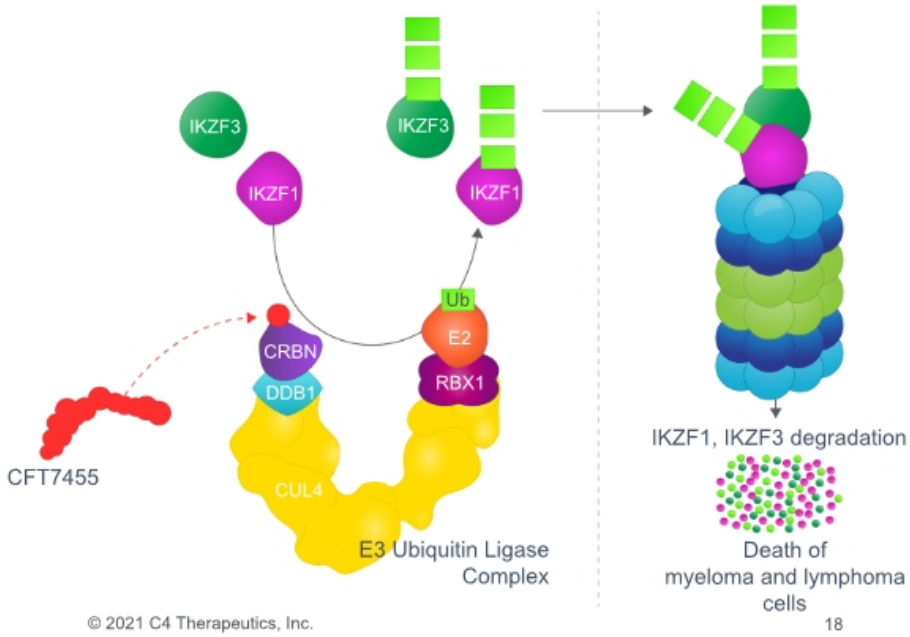
Source: NIH SEER Database, Primary Literature Consensus

Patient figures represent estimated U.S. annual incidence
PTCL = peripheral T-cell lymphoma; MCL = mantle cell lymphoma

CFT7455: Potent Small Molecule IKZF1/3 Degrader Optimized for Catalytic & Pharmacologic Properties

Goal: Develop an IKZF1/3 Monofunctional Degradation Activating Compound (MonoDAC) with these properties:

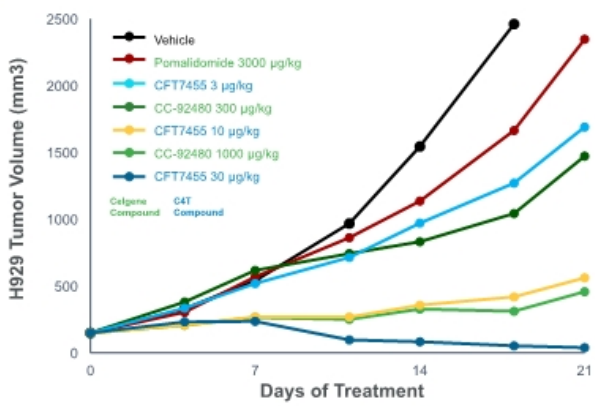
- Class-leading catalytic activity to enable potent, rapid, and deep target degradation
- High binding affinity to overcome IMiD resistance
- Selective to reduce off-target liabilities
- Optimized pharmacologic profile to enable sustained IKZF1/3 degradation



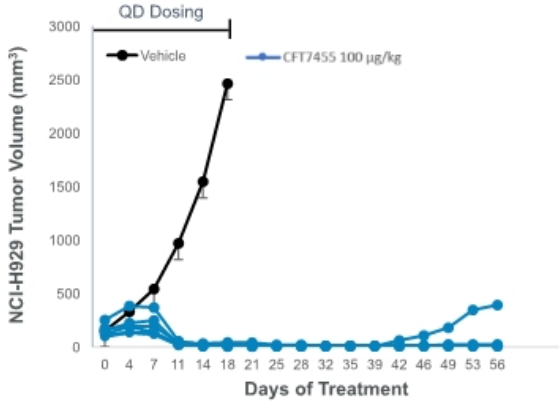
C4 Therapeutics

CFT7455 Demonstrates Improved Efficacy Compared to Both Approved and Most Advanced Development-stage IKZF1/3 Degraders

CFT7455 *In Vivo* Efficacy – Complete Regression in MM Model



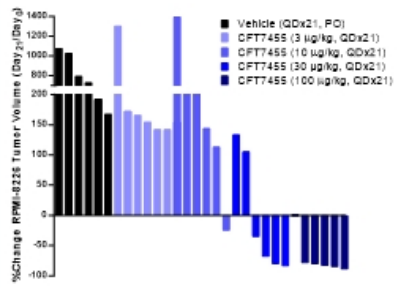
CFT7455 *In Vivo* Efficacy Durable After End of Dosing Period



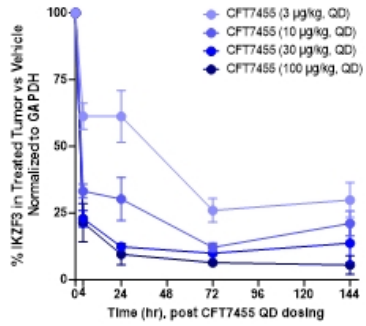
Source: C4T data on file

Depth and Duration of IKZF3 Degradation Associated with CFT7455 Efficacy

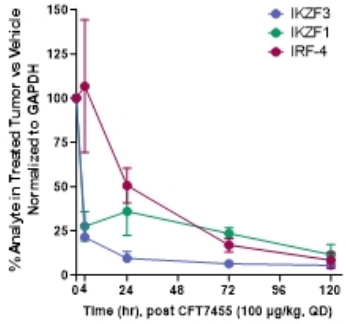
Dose Dependent Efficacy



Dose-Dependent IKZF3 Degradation



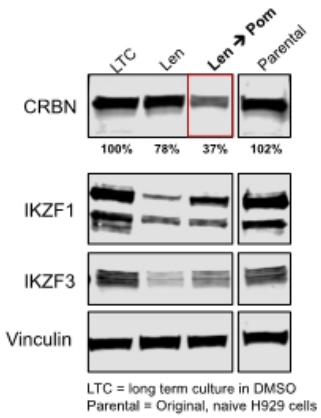
Loss of IRF-4 via IKZF1/3 Degradation



Source: C4T data on file

CFT7455 Demonstrates Tumor Regression in Multiple Myeloma Xenograft Insensitive to Pomalidomide

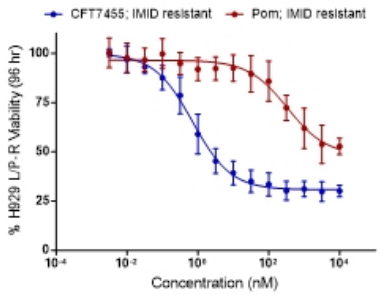
Reduction in CRBN Expression with Chronic IMiD Dosing



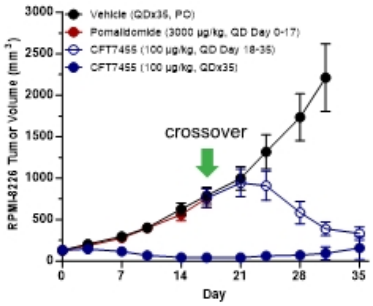
LTC = long term culture in DMSO
Parental = Original, naive H929 cells

Len, lenalidomide; L/P-R, Len/Pom-Resistant

CFT7455 Retains Activity in Len- & Pom-Resistant MM Cells

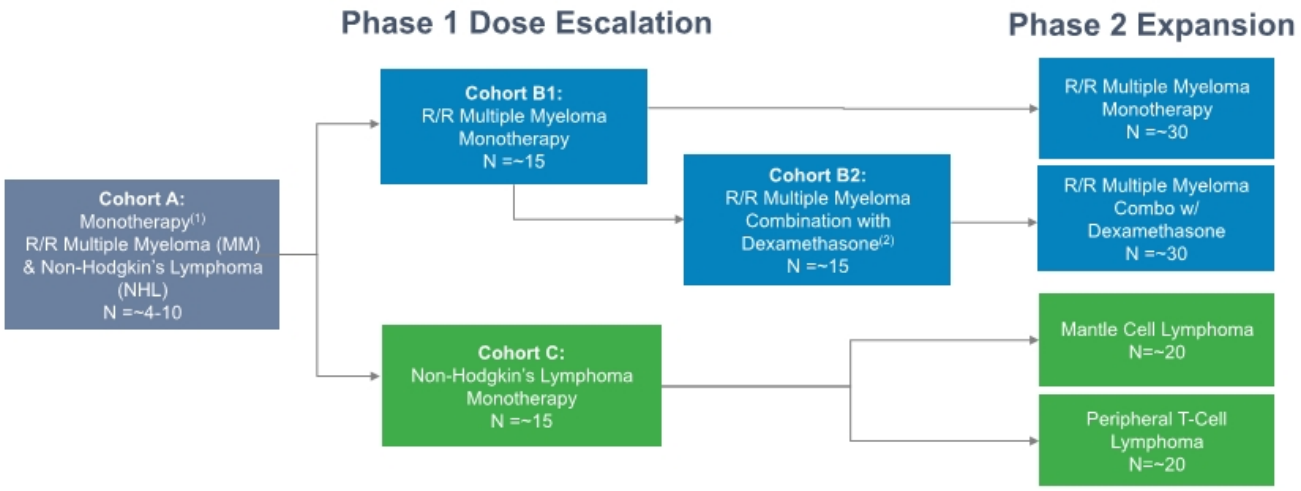


CFT7455 Promotes Regression in Tumors Insensitive to Pomalidomide



Source: C4T data on file

CFT7455 Phase 1/2 Trial Design Offers Potential for Accelerated Approval Across Three Indications



Trial Open for Enrollment, First Clinical Data Expected in 2022

(1) 28-day cycle / dose limiting toxicity (DLT) window; (2) Combination therapy cohorts will open once the selected CFT7455 dose level has been cleared for safety
6-12 patient food effect enrichment cohort also included during escalation, not pictured in the schema

BRD9
CFT8634

BRD9: Drugging the Undruggable with a Degrader Approach

Strong Rationale for Degrader Approach

- Synovial sarcoma (SS) is dependent on BRD9, which is caused by the oncogenic SS18-SSX translocation
- Oncogenicity of BRD9 depends on sub-domains not addressed by traditional inhibitors

Clear Unmet Need

- Very limited benefit of treatments for metastatic or advanced SS – median survival ~18 months

Defined Patient Populations

- SS: ~900 cases/year
- ~10% of all soft tissue sarcomas

Compelling Development Opportunity

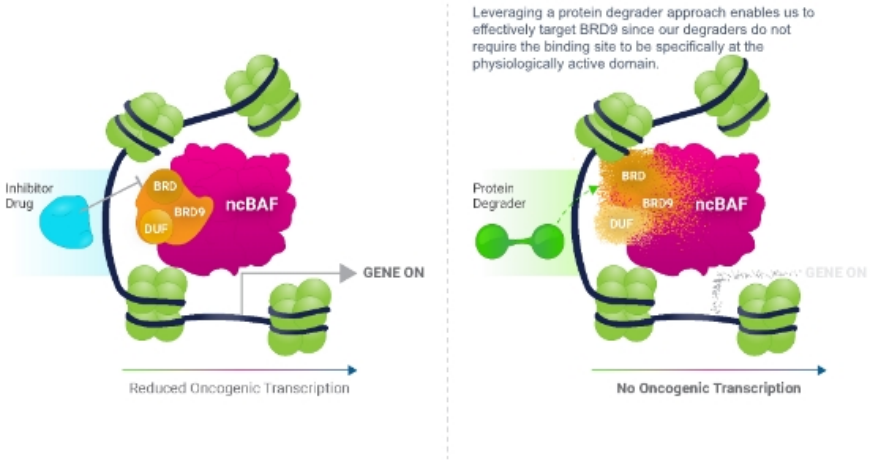
- Well defined path to registration in SS and metastatic population already under management at academic centers
- Precedent for approval with a single-arm study in second-line setting

Source: NIH SEER Database, Primary Literature Consensus

Patient figures represent estimated U.S. annual incidence

BRD9 Dependency in Synovial Sarcoma

Mechanistic Rationale

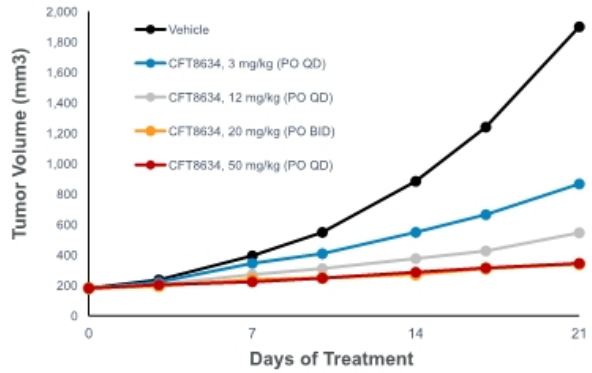


Advantages of BRD9 degradation

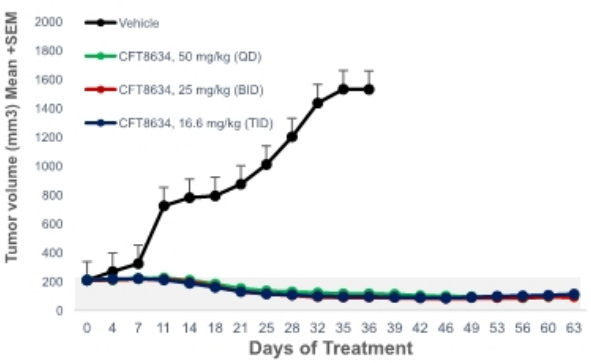
- Specifically degrades BRD9 and spares BRD4 and BRD7, avoiding potential off-target toxicities
- Oncogenicity of BRD9 depends on sub-domains not addressed by traditional inhibitors

Robust Responses of CFT8634 Seen in Preclinical Synovial Sarcoma Models

Dose Response Activity
Yamato Xenograft Model

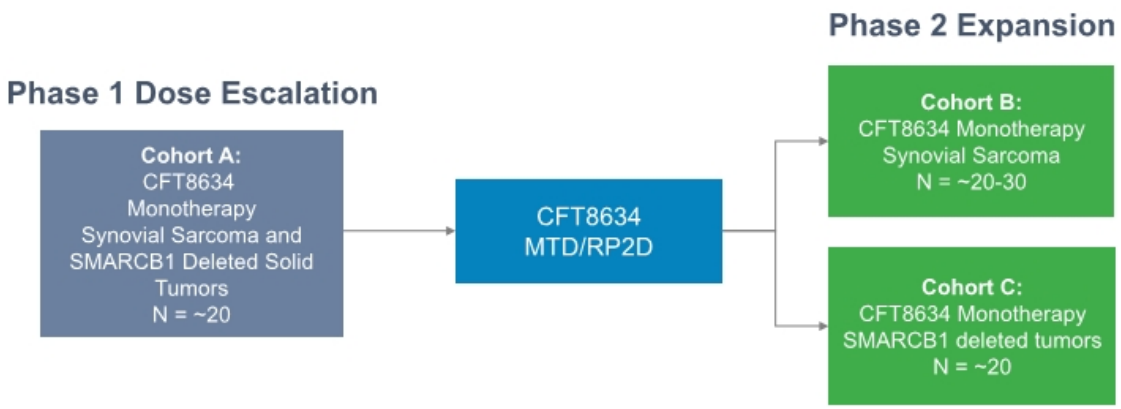


Dose Response Activity
Patient Derived Xenograft Model



Source: C4T data on file

CFT8634 First-in-Human Protocol Concept Schema



IND Submission for CFT8634 Expected in 2H 2021

MTD = Maximum Tolerated Dose; RP2D = Recommended Phase 2 Dose

EGFR
CFT8919

EGFR: Utilizing a Degrader Approach to Overcome Resistance to Approved EGFR Inhibitors and Address a Wider Range of Mutations

Strong Rationale for Degrader Approach

- Overcome resistance to approved EGFR inhibitors
- Ability to address wide range of EGFR resistance mutations
- Potential to effect deeper and more durable response due to advantages of degraders

Clear Unmet Need

- Patients whose tumors harbor EGFR L858R do less well on approved EGFR inhibitors
- Osimertinib 1st line PFS:
  - L858R: 14.4 mo
  - Ex19del: 21.4 mo
- Current therapies all bind at the same site and resistance can occur by genetic changes that block inhibitor binding

Defined Patient Populations

- NSCLC comprises ~85% of all US lung cancer cases, ~195K patients diagnosed in 2020
- EGFR is the most common receptor tyrosine kinase (RTK) driver in NSCLC
- 25-40% of mEGFR NSCLC driven by L858R activating mutation

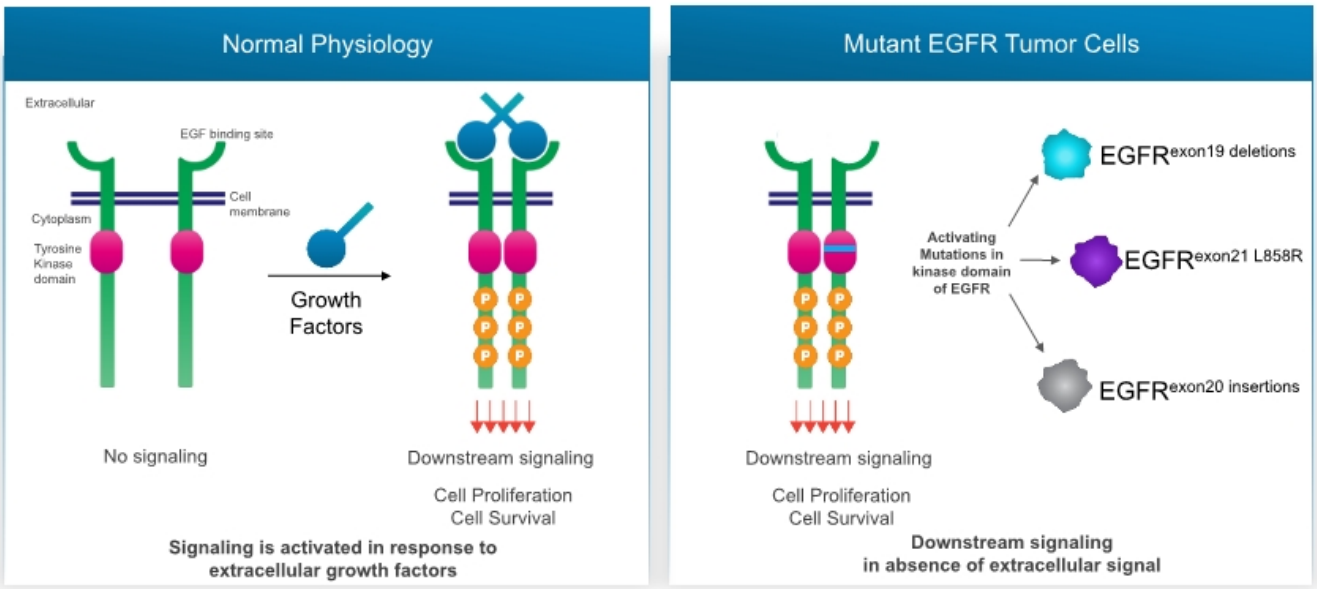
Compelling Development Opportunity

- Target Population: patients who have progressed on approved EGFR inhibitors and potential for frontline opportunity

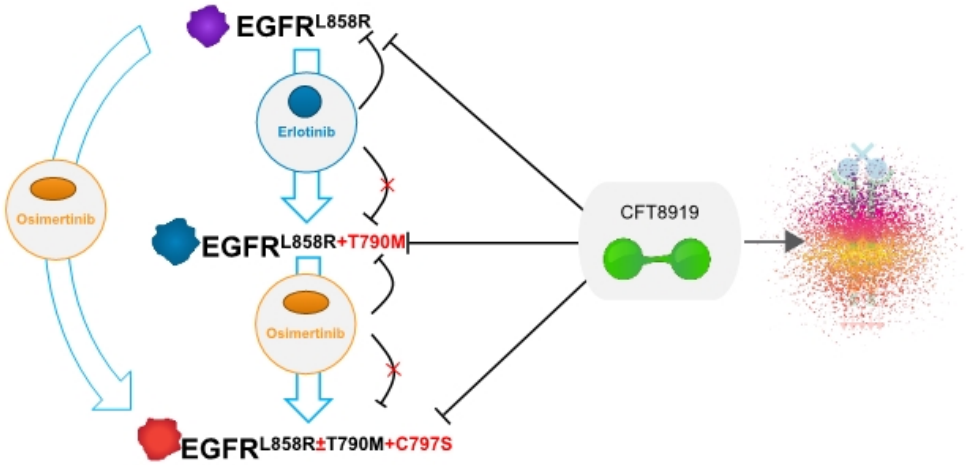
Source: https://www.nejm.org/doi/10.1056/NEJMoa1713137, NIH SEER Database, Primary Literature Consensus

Patient figures represent estimated U.S. annual incidence

EGFR Activating Mutations Drive NSCLC Cancer Growth



CFT8919 May Overcome Resistance to Approved EGFR Inhibitors and Address a Wide Range of Acquired EGFR Resistance Mutations



CFT8919 Compelling Profile

- Orally bioavailable, selective, allosteric degrader of EGFR L858R
- Active *in vitro* and *in vivo* in models with secondary mutations
- Demonstrates intracranial activity
- Potential to be active as single agent in the frontline setting

IND Submission Expected mid-2022 with Potential Phase 1/2 Trial Initiation by YE 2022

Sources: Yang, J. C.-H. et al., J. Clin Oncol. 35, 1288-1296 (2017); Soria, J.-C. *et al. New Engl J Medicine* 378, 113–125 (2018)

BRAF

BRAF: Utilizing a Degrader Approach to Overcome Resistance Mutations

Strong Rationale for Degrader Approach

- Approved BRAF inhibitors cause paradoxical RAF activation, which may result in diminished efficacy
- Potential for degraders to effect deeper elimination of mutant BRAF signaling and create more durable response

Clear Unmet Need

- BRAF mutations occur in ~15% of all cancers
- ~70% - 90% of BRAF mutations are V600E
- Resistance to three approved BRAF inhibitors emerges through multiple paths, resulting in a median PFS of <15 months

Defined Patient Populations

- >70K annual incidence across melanoma, NSCLC, colorectal cancer (CRC) and other malignancies
- 50% of late-stage melanoma
- 1-2% of NSCLC
- 10-20% of CRC
- 50% of papillary thyroid cancer
- 100% of hairy cell leukemia
- >50% of Langerhans cell histiocytosis (LCH)

Compelling Development Opportunity

- Large patient population defined by failure of available BRAF inhibitors
- Target Population: V600E melanoma and/or NSCLC after failure of MEK inhibitor + BRAF inhibitor with indication specific expansion opportunities

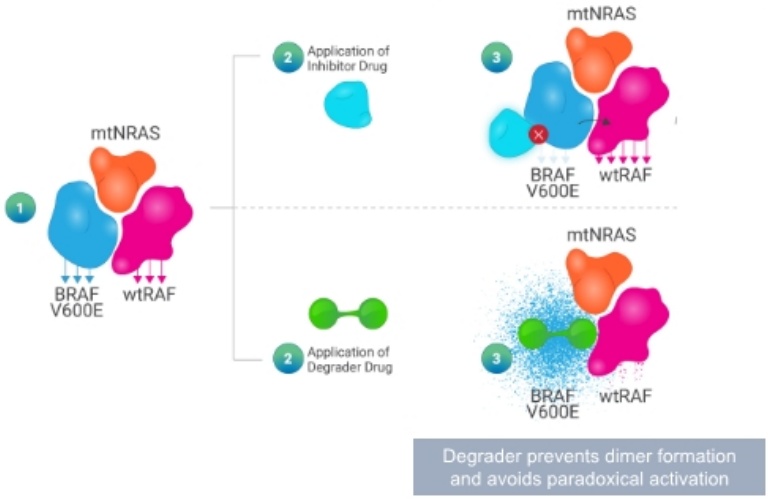
Source: NIH SEER Database, Primary Literature Consensus

Patient figures represent estimated U.S. annual incidence

BRAF program is partnered with Roche

BRAF Degrader to Overcome Limitations of Approved BRAF Inhibitors

Mechanistic Rationale



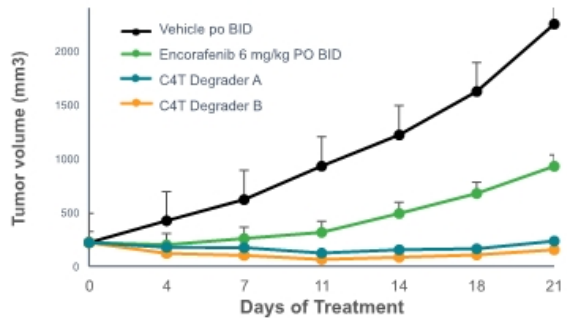
Advantages of BRAF V600E Degradation

- Specifically target mutant BRAF over wildtype BRAF
- Prevent mutant BRAF incorporation into RAF dimers
- Avoid paradoxical activation and associated failure of therapy due to resistance mechanisms dependent on BRAF inhibitor mediated paradoxical activation

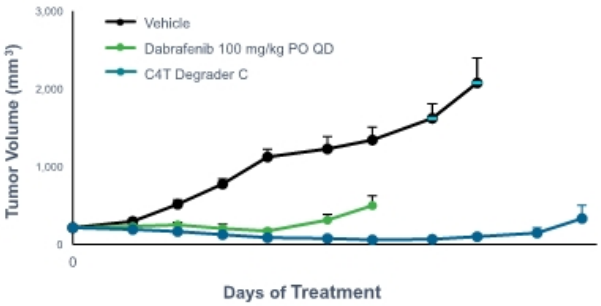
BRAF program is partnered with Roche

BRAF Degraders Show Superior Efficacy Compared to Approved BRAF Inhibitors

C4T BRAF Degrader Shows More Durable Efficacy Than Encorafenib



C4T BRAF Degrader Shows More Durable Efficacy Than Dabrafenib



IND Enabling Studies Planned for 2021

Source: C4T data on file

BRAF program is partnered with Roche

RET

RET Degradation: Opportunity to Overcome Resistance Mutations

Strong Rationale for Degrader Approach

- RET is a receptor tyrosine kinase (RTK) that plays a role in normal development but can cause cancer when mutated
- Resistance develops to approved RET inhibitors due to mechanisms including new RET mutations, which make inhibitors inactive

Clear Unmet Need

- No effective targeted therapy after failure of approved first-line RET inhibitors

Defined Patient Populations

- ~10K annual incidence of RET-driven disease across lung, thyroid, and other cancers
- 1-2% of NSCLC
- 60% of sporadic medullary thyroid cancer

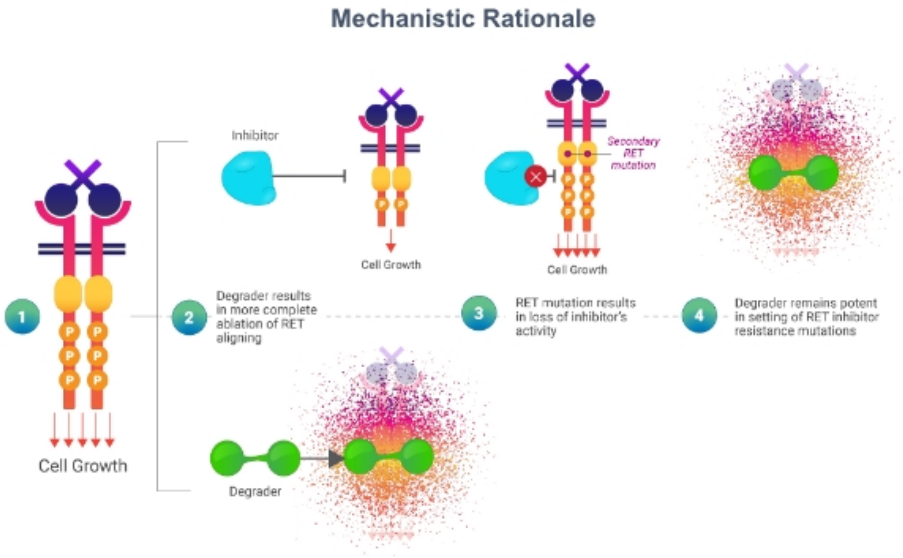
Compelling Development Opportunity

- Well defined registration path in existing, genetically defined patient population with no effective treatment option after RET tyrosine kinase inhibition (TKI)
- Target Population: second line RET-altered cancers; potential for front-line opportunity

Sources: NIH SEER Database, https://pubmed.ncbi.nlm.nih.gov/29284153/, Primary Literature Consensus

Patient figures represent estimated U.S. annual incidence

RET Degradation May Have Improved Activity Compared to Best-In-Class RET Inhibitors



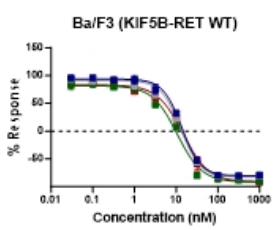
Advantages of RET Degradation

- RET degrader is active against key secondary mutations that cause resistance, including both the gatekeeper and solvent front mutations
- Against RET without secondary mutation, as in the front-line setting, degradation may offer deeper and more durable response than inhibition

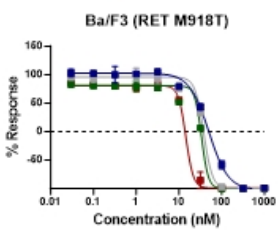
RET Degrader Has an Excellent Cell Growth Inhibition Profile In RET Fusions and Common Resistance Mutations

Drug Naïve, Driver Translocation/Mutation

KIF5B-RET Fusion

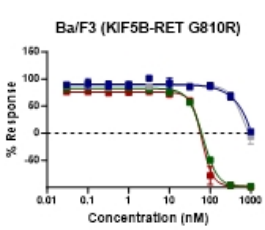


Activating Mutation

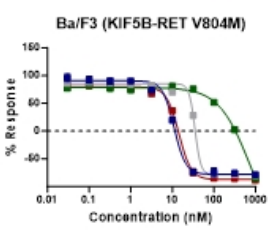


RET Inhibitor Acquired-Resistance Mutants

Solvent Front Mutation



Gatekeeper Mutation



Pralsetinib Selpercatinib 2nd Gen RET TKI CFT RET Degrader

Continue Lead Optimization Activities in 2021

Source: C4T data on file

2021 Milestones Support Progress Toward Goal of Four Clinical-Stage Programs by Year-End 2022

	2021	2021
IKZF1/3 (CFT7455)	❑ Phase 1/2 Initiation	❑ Phase 1 Top-line Safety & Efficacy ❑ Proof of Mechanism
BRD9 (CFT8634)	❑ IND Submission	❑ Phase 1 Initiation
EGFR (CFT8919)	❑ IND Enabling Studies	❑ IND Submission ❑ Phase 1 Initiation
BRAF	❑ IND Enabling Studies	❑ IND Submission ❑ Phase 1 Initiation
RET	❑ Lead Optimization	

C4T is Well Positioned to Develop Targeted Protein Degradation Medicines to Transform Patient Care

C4 Therapeutics

Thank You