

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): November 18, 2020

C4 THERAPEUTICS, INC.

(Exact name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction
of Incorporation)

490 Arsenal Way, Suite 200
Watertown, MA
(Address of Principal Executive Offices)

001-39567
(Commission File Number)

47-5617627
(IRS Employer
Identification No.)

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 November 18, 2020, C4 Therapeutics, Inc. (the “Company”) posted an investor presentation to its website at <https://ir.c4therapeutics.com/events-presentations>. A copy of the investor presentation is attached as Exhibit 99.1 to this Current Report on Form 8-K.

The information in this Current Report on Form 8-K, including Exhibit 99.1 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.

<u>Exhibit Number</u>	<u>Description</u>
99.1	<u>Investor Presentation of the Company dated November 2020 (furnished herewith).</u>

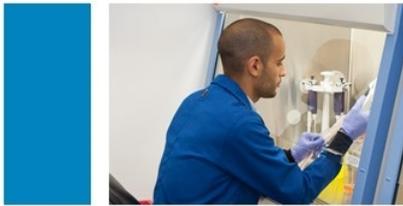
SIGNATURES

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: November 19, 2020

By: /s/ Andrew J. Hirsch
Andrew J. Hirsch
President and Chief Executive Officer



C4 Therapeutics

Destroying
INHIBITING DISEASE-CAUSING
PROTEINS TO DELIVER HOPE

Corporate Presentation

November 2020



© 2020 C4 Therapeutics, Inc.

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 overseas, including, without limitation, C4 THERAPEUTICS, TORPEDO, BIDAC and MONODAC. 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.



Pioneering protein degradation as a new class of medicine by:

- Harnessing the body's natural cellular quality control mechanisms to target and destroy disease-causing proteins
- Perfecting a novel discovery and validation platform to rapidly and cost-effectively bring transformative medicines to patients

Investment Highlights

Novel and Transformative Modality

- Degraders **control protein levels** by leveraging the cell's natural "**quality control**" system
- Label harmful or disease-causing proteins for **destruction rather than merely inhibiting their function**

Differentiated and Proprietary Technology Platform

- Enables **quick and efficient advancement** of programs from target identification to candidate development stage
- Proprietary tools to design, assess and **predict degrader activity**
- Degraders optimized for **speed and potency**
- Deep investment in **Cereblon**

Robust Pipeline

- **Four programs expected to be in the clinic by the end of 2022**
- MonoDACs and BiDACs
- **Lead targets selected to min dev risk:**
 - Clinically validated targets
 - Expectation of **tolerability**
 - Opportunity for **accelerated approval**

Anchored by Lead Program Addressing Unmet Need

- **Lead product candidate (CFT7455) exhibited complete regression** of tumor in preclinical multiple myeloma mouse model
- **Potency and speed** of lead molecule results in **cell death at very low doses**
- IND filing for lead program expected by **end of 2020**

High-Value Partnerships

- Have received **\$150M+ in non-dilutive capital**, with **\$2B+ in unrealized potential milestones**, plus additional potential royalties

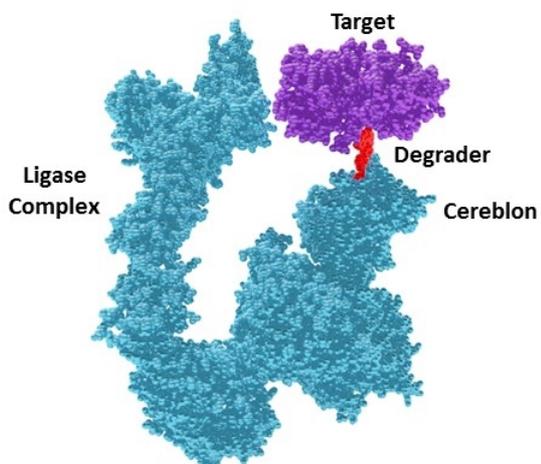
 Biogen Calico

 Roche

Degradation Leverages Natural Cellular Machinery to Target Diseases

Protein degraders harness the body's **natural protein degradation machinery** to **target and destroy** selected disease-causing proteins

C4 Therapeutics' Degraders: The Match Makers that Let the Body Do the Heavy Lifting



C4T's Technology

1. "The Match Maker" – C4T's Degraders

C4T's degraders direct Cereblon (a clinically validated E3 ligase) to label a specific disease-causing target protein for degradation, allowing the body's natural protein degradation process to destroy the protein and control the disease

Natural Machinery

2. "The Quality Control Inspector" – Cereblon

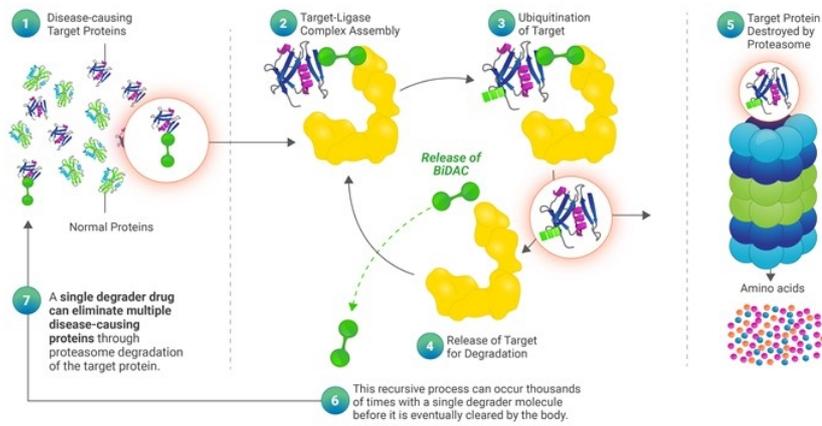
Applies a "destroy me" label on the target proteins recruited by the C4T degrader

3. "The Destroyer" – The Proteasome

Labelled proteins are destroyed by the cell's "recycling plant," the proteasome

Targeted Protein Degradation: An Integrated Approach for a Novel Modality

C4 Therapeutics maintains a broad focus on **overall catalytic degradation** rather than a specific part of the degradation cycle, **providing opportunities to drug the undruggable**

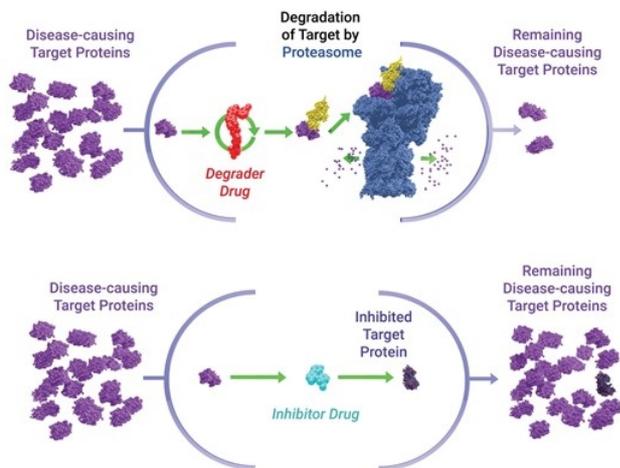


Overview of Targeted Protein Degraders

- **Degraders control protein levels** by leveraging the cell's natural "quality control" or "protein recycling" system through a process called **ubiquitination**
- Degraders induce **targeted destruction of harmful or disease-causing proteins** by tagging them for ubiquitination
- **Tagged proteins** are subsequently **degraded by the proteasome**
- **A single degrader molecule** participates in **multiple rounds** of targeted protein target degradation, maximizing both **potency and efficiency**

Protein Degradation is Fundamentally Different than Protein Inhibition

Protein degraders allow for a **more potent and durable pharmacological response** at lower overall exposure levels than inhibitors



Key Advantages of Efficient Catalysis

1. Improved Potency

Degraders are recycled and can engage multiple target proteins, resulting in improved activity against resistant proteins, greater depth of effect, and more durable outcomes

2. Fast Response

Rapid degradation of target leads to strong and prolonged biological response

3. High Selectivity

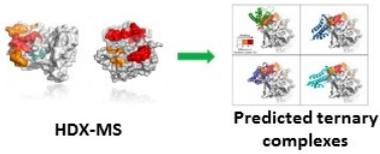
Degraders can leverage multiple layers of selectivity in cellular machinery

4. Expansive Target Landscape

Degraders can be designed to bind to any part of the protein and are not limited to the active site, like most small molecule inhibitors, which means that previously undruggable targets may be degraded

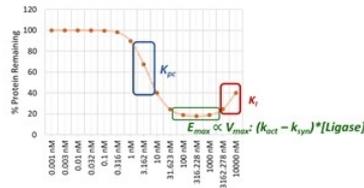
TORPEDO Platform: Robust Drug Discovery and Higher Confidence in Clinical Outcomes

Design



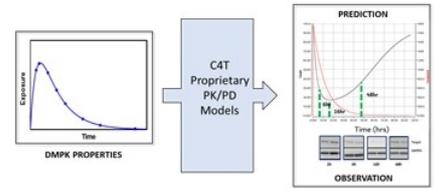
- Computational method incorporates experimental data to identify top models
- Atomic-level degrader design utilized to improve selectivity and potency

Analyze



- Cellular degradation data fitted using an enzymology framework
- Key parameters describe intrinsic degradation activity

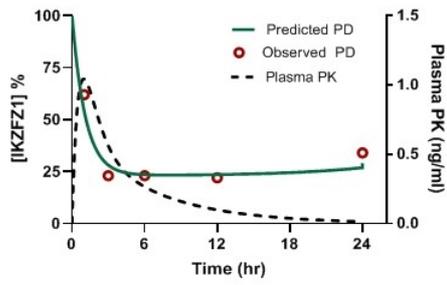
Predict



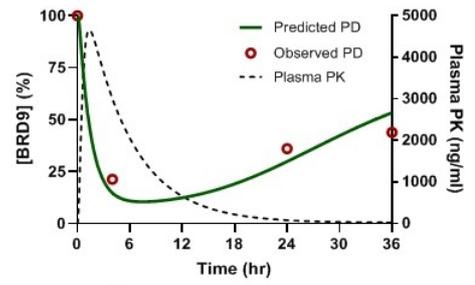
- Universal modeling framework merges degradation activity with degrader exposure
- Robust predictions of depth and duration of *in vivo* target degradation at any dose

Rapid delivery of potent drug candidates through informed and efficient drug discovery

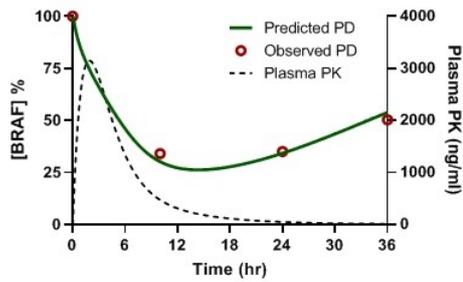
PK/PD Models Provide Robust Predictions Across the Lead Programs



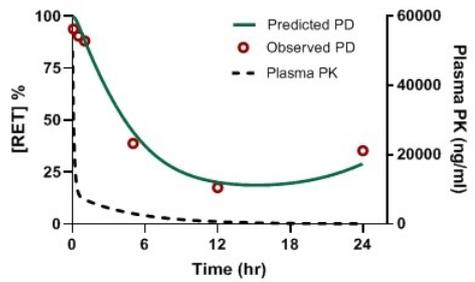
CFT7455, 1 mg/kg dose po, KI-KJ ALCL model



CFT7503, 10 mg/kg dose po, Yamato Synovial Sarcoma model



CFT-17977, 30 mg/kg dose po, A375 model



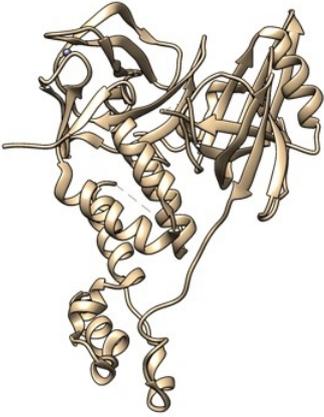
CFT-12521, 30 mg/kg dose iv, KIF-5B:RET Fusion model



TORPEDO is Based on a Deep Focus on Cereblon, Rather than the Entire Set of Available Ligases

Our TORPEDO platform has a **diverse and rich toolkit of novel, structurally distinct Cereblon binders** – small molecules that are suitable for clinical targeted protein degradation

Cereblon E3 Ligase



Cereblon, harnessed by lenalidomide, or IMiDs, is the **only clinically validated ligase** for targeted protein degradation



Cereblon is **expressed in all tissues** and in **all cellular compartments**



Invested heavily in rich toolkit of intellectual property with **14 structurally distinct Cereblon binders**, giving C4T a **competitive advantage**



C4T's binders enable drug discovery with enhanced **oral bioavailability, solubility, permeability and stability**



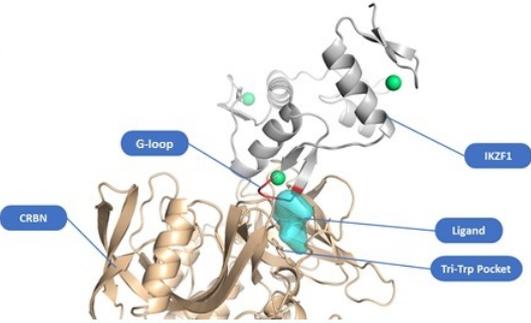
All projects benefit from desirable properties offered by C4T's Cereblon binders

Robust Pipeline With Four Clinical Programs Anticipated By End of 2022

Target/Product Designation	Indication(s)	Degradation Type	Route of Administration	Phase of Development					Ownership
				Discovery	Pre-Clinical	Phase 1	Phase 2	Phase 3	
IKZF1/3 CFT7455	Hematologic malignancies	MonoDAC	Oral	[Progress bar: Discovery to Pre-Clinical]					C4 Therapeutics
BRD9 CFT8634	Sarcoma	BiDAC	Oral	[Progress bar: Discovery to Pre-Clinical]					C4 Therapeutics
BRAF V600E	Genetically defined resistant solid tumors	BiDAC	Oral	[Progress bar: Discovery]					C4 Therapeutics
RET	Genetically defined resistant solid tumors	BiDAC	Oral	[Progress bar: Discovery]					C4 Therapeutics

Target selection emphasizes **target validated, mitigated tolerability risks and opportunity for accelerated approval**

CFT7455: Clear Unmet Need Combined with Compelling Development Opportunity

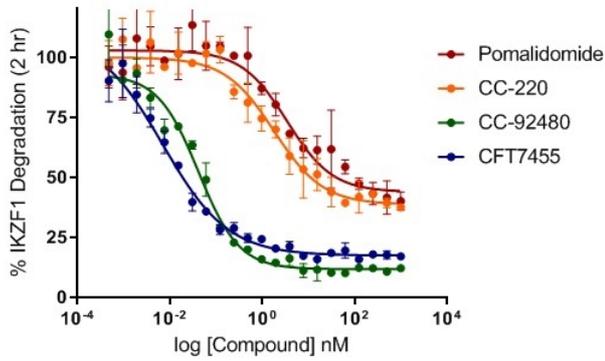
IKZF1/3 Mutations		<p>IKZF1 and IKZF3 are central to lymphoid cell differentiation and maintenance</p> 
Strong Mechanistic Rationale	<ul style="list-style-type: none"> Multiple myeloma (MM) and Non-Hodgkin lymphomas (NHLs) are dependent on IKZF1/3 	
Clear Unmet Need	<ul style="list-style-type: none"> IKZF1/3 degraders are the backbone of MM treatment Relapsed / refractory MM remains an unmet medical need Approved IMiDs have limited activity in NHL, including mantle cell lymphoma (MCL) and peripheral T-cell lymphoma (PTCL) 	
Defined Patient Population	<ul style="list-style-type: none"> MM: ~32,270 cases/year (US); median 5-year overall survival (OS): 53.9% NHL: ~77,240 cases/year (US) <ul style="list-style-type: none"> - PTCL: ~4% of all NHLs (US); median 5-year OS: 20-32% - MCL: ~7% of all NHLs (US); median OS of 4-5 years 	
Compelling Development Opportunity	<ul style="list-style-type: none"> Opportunity to expand into early lines of MM therapy 	
		<p>Potential Clinical Indications</p> <ul style="list-style-type: none"> Multiple myeloma Other B-cell lymphomas – MCL, diffuse large B-cell lymphoma (DLBCL), and follicular lymphoma PTCL represents unrealized path for development Additional indication line extension potential

Source: NIH SEER Database, Primary Literature Consensus

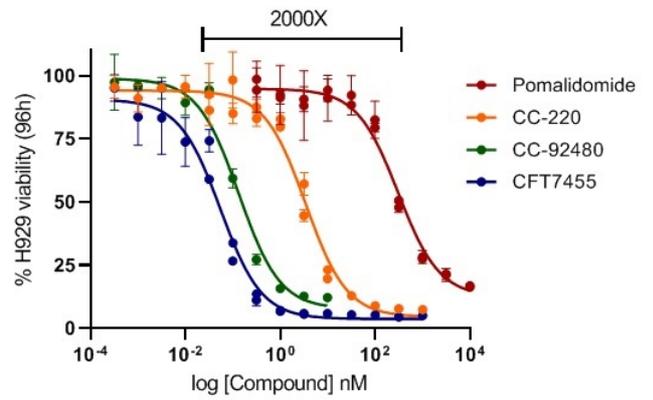


CFT7455 Is a Potent IKZF1/3 MonoDAC, as Demonstrated in Preclinical Studies

CFT7455 Degradation Potency

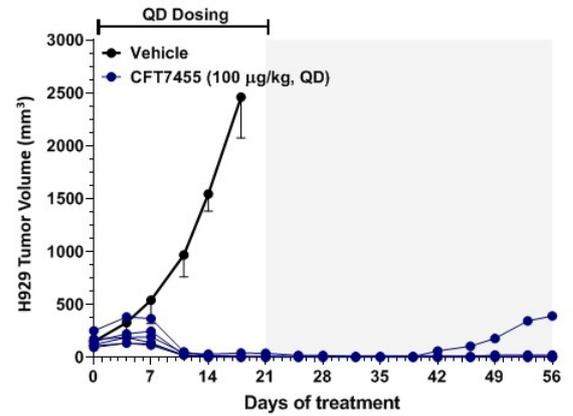
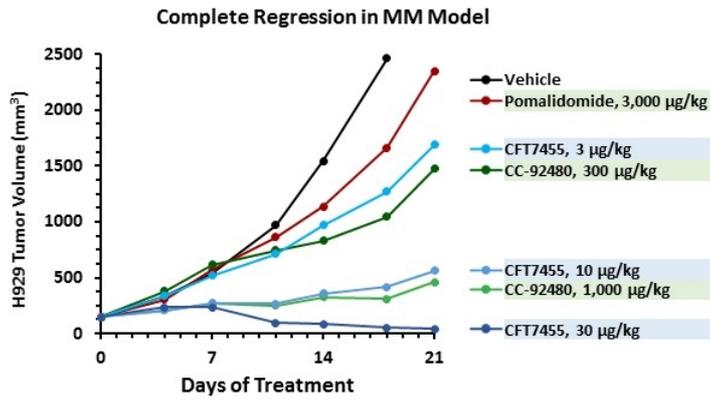


CFT7455 Viability Profile



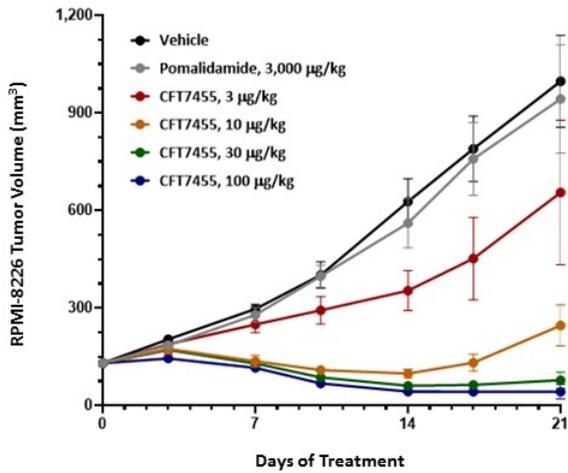
Catalytic activity results in potent degradation and activity

CFT7455: Potent Efficacy, *In Vivo*, with Complete Regressions as Single Agent in MM

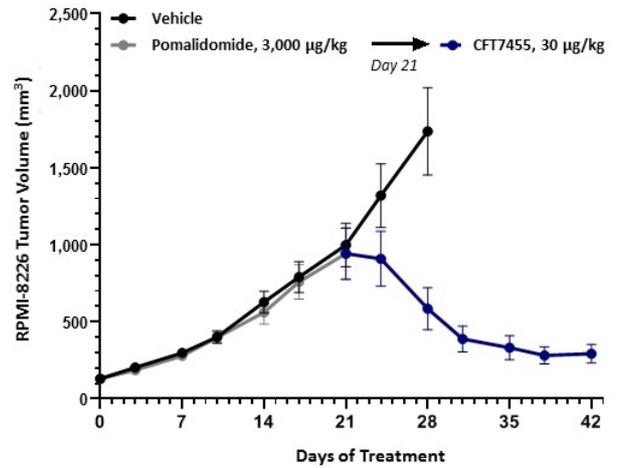


- **Potency and speed** of CFT7455 translates into better **cell killing** with **lower doses** achieving the **same endpoint**
 - Improvement in **oral bioavailability** (i.e., half dose provides same exposure)
 - Pharmacologic properties translate into **100x lower dose** *in vivo* to get to same efficacy
- Differentiated pharmacologic profile may also **enable intermittent daily dosing**
- Deep and durable responses observed as single agent
- Comparable efficacy seen in models of **PTCL, MCL** and **DLBCL**

Multiple Myeloma Xenograft Insensitive to Pomalidomide Responds to CFT7455

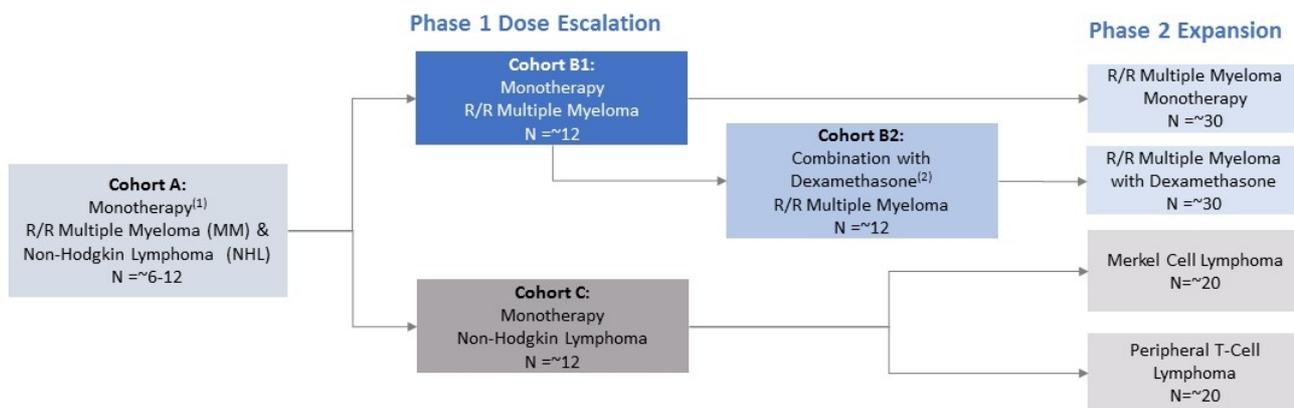


- CFT7455 is active in RPMI-8226, relative to pomalidomide



- CFT7455 is active in RPMI-8226 after the tumor has progressed on pomalidomide treatment

Proposed CFT7455 First-In-Human Trial Design Offers Potential for Accelerated Approval



- Primary objectives are to **characterize safety and tolerability** and **estimate anti-tumor activity**, with key secondary objective to **assess pharmacokinetics**
- Trial design allows for **three potential indications**, each with **opportunity for accelerated approval if expansion portions are successful**
- Expansion stage **doses will be at maximum tolerable dose (MTD) / recommended Phase 2 dose (RP2D)** with different dosing strategy for MM vs. NHL due to historical lower tolerability for NHL and need for combination with dexamethasone in MM

(1) 28-day cycle / dose limiting toxicity (DLT) window

(2) Combination therapy cohorts will open once each CFT7455 dose level has been cleared for safety

BRD9 Degradation: Clear Clinical Opportunity

BRD9/BAF Complex Alterations Summary	
Strong Mechanistic Rationale	<ul style="list-style-type: none"> • Bromodomain containing protein 9 (BRD9) is a BAF complex component and is non-essential in normal cells • Synovial sarcoma is dependent on BRD9, which is caused by the oncogenic SS18-SSX translocation
Clear Unmet Need	<ul style="list-style-type: none"> • Very limited benefit of treatments for metastatic synovial sarcoma or advanced synovial sarcoma – median survival ~18 months
Defined Patient Population	<ul style="list-style-type: none"> • ~900 US yearly incidence of synovial sarcoma cases • ~10% of all soft tissue sarcoma
Compelling Development Opportunity	<ul style="list-style-type: none"> • Initial Target Population: Synovial Sarcoma, after 1L therapy failure • Well defined path to registration in synovial sarcoma and metastatic population already under management at academic treatment centers • Precedent for approval in uncontrolled study in second-line setting

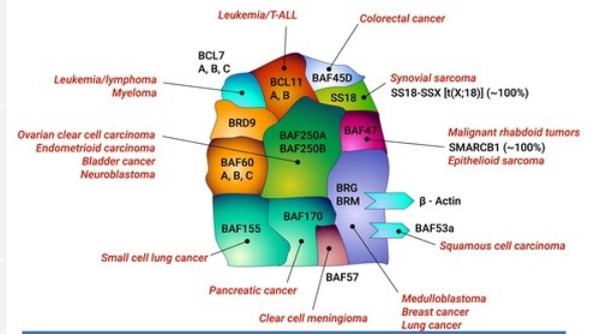
Source: NIH SEER Database, Primary Literature Consensus



© 2020 C4 THERAPEUTICS, INC.

17

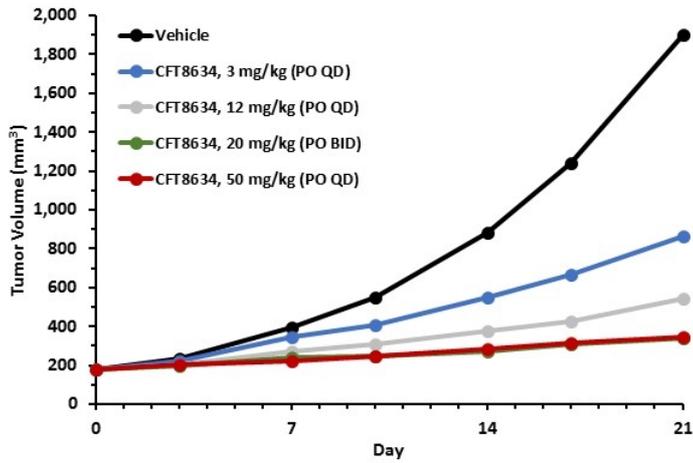
BAF subunit mutations are present in >20% of cancers



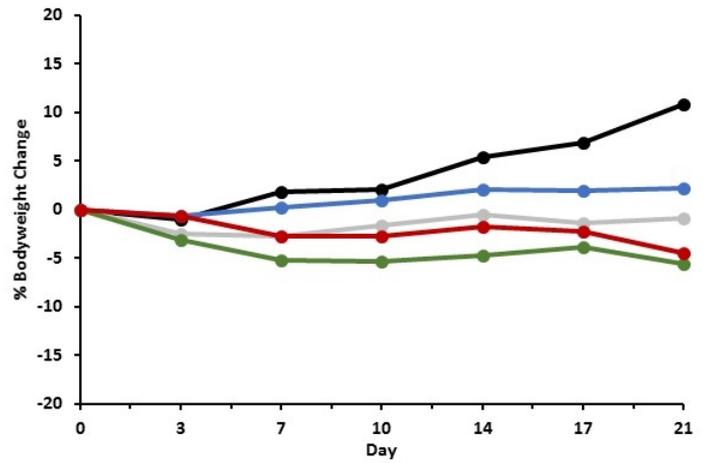
Potential Clinical Indications

- 100% of synovial sarcoma
- 100% of malignant rhabdoid tumors
- Potential in other emerging indications (e.g., acute myeloid lymphoma)

Robust, Dose-Dependent Response in Yamato Xenograft Model Achieved with CFT8634* at Tolerable Dose Levels



Dose responsive activity



Tolerated at all doses

* CFT8634 is the purified enantiomer of CFT7503 (a racemic mixture) and is the drug candidate moving into clinical development

CFT8634 First-in-Human Protocol Concept Schema

Phase 1 Dose Escalation

Cohort A:
CFT8634
Monotherapy
Synovial Sarcoma and
SMARCB1 deleted solid tumors
N = ~18

CFT8634
MTD/RP2D

Phase 2 Expansion

Cohort B:
CFT8634 Monotherapy
Synovial Sarcoma
N = 20

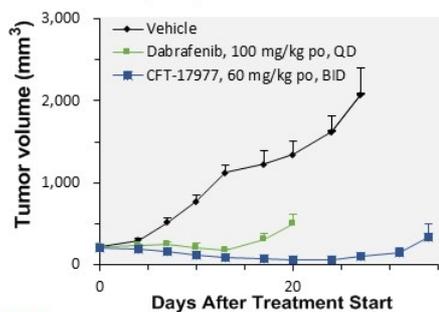
Cohort C:
CFT8634 Monotherapy
SMARCB1 deleted tumors
N = TBD

BRAF Degradator to Overcome Liability of Approved BRAF Inhibitors

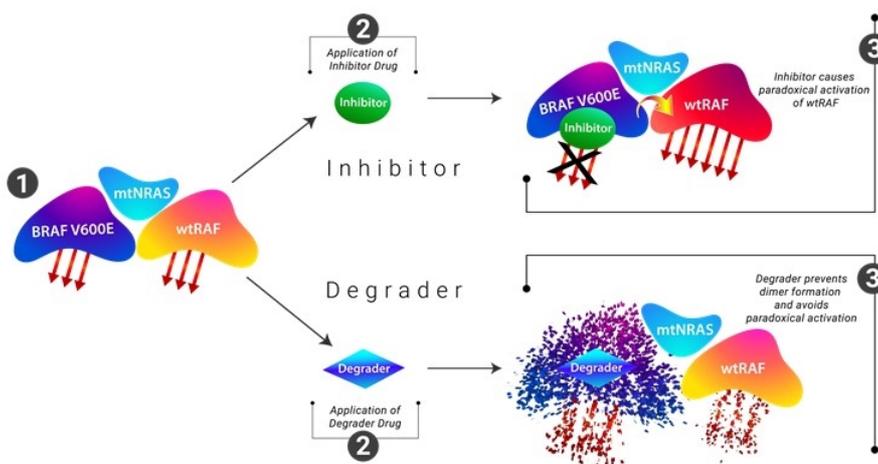
Potential advantages of BRAF V600E Degradation

- Specifically target **mutant BRAF over wildtype**
- Prevents mutant BRAF incorporation into RAF dimers, **avoiding paradoxical RAF activation and activation-associated toxicity**
- **Overcome resistance** to current standard of care
- Effect **deeper and more durable responses**

C4T degrader shows a more durable efficacy response than BRAF inhibition



Mechanistic Rationale

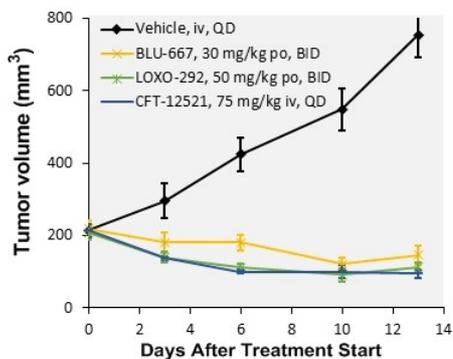


RET Degradation May Significantly Improve Activity of Best-In-Class RET Inhibitors

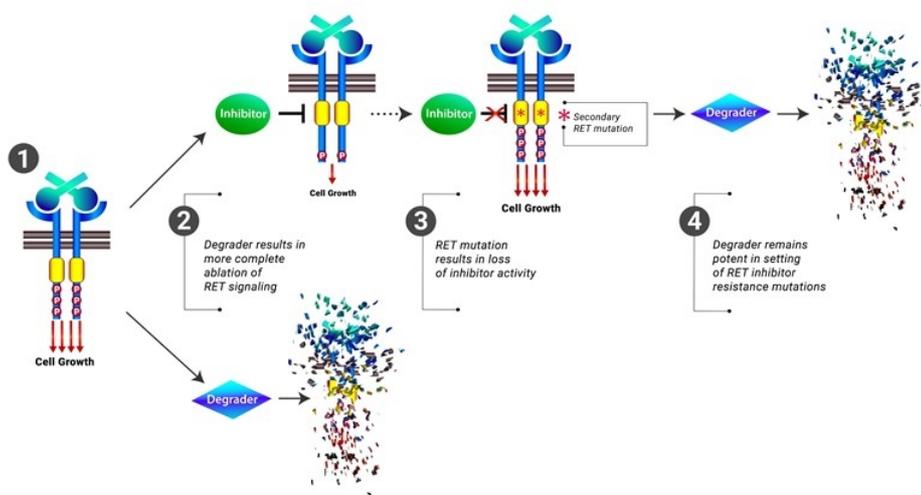
Potential advantages of RET Degradation

- **Overcome resistance** to standard of care RET inhibitors
- Potential to effect **deeper and more durable response** due to advantages of degraders

C4T RET degrader is as effective as approved RET inhibitors

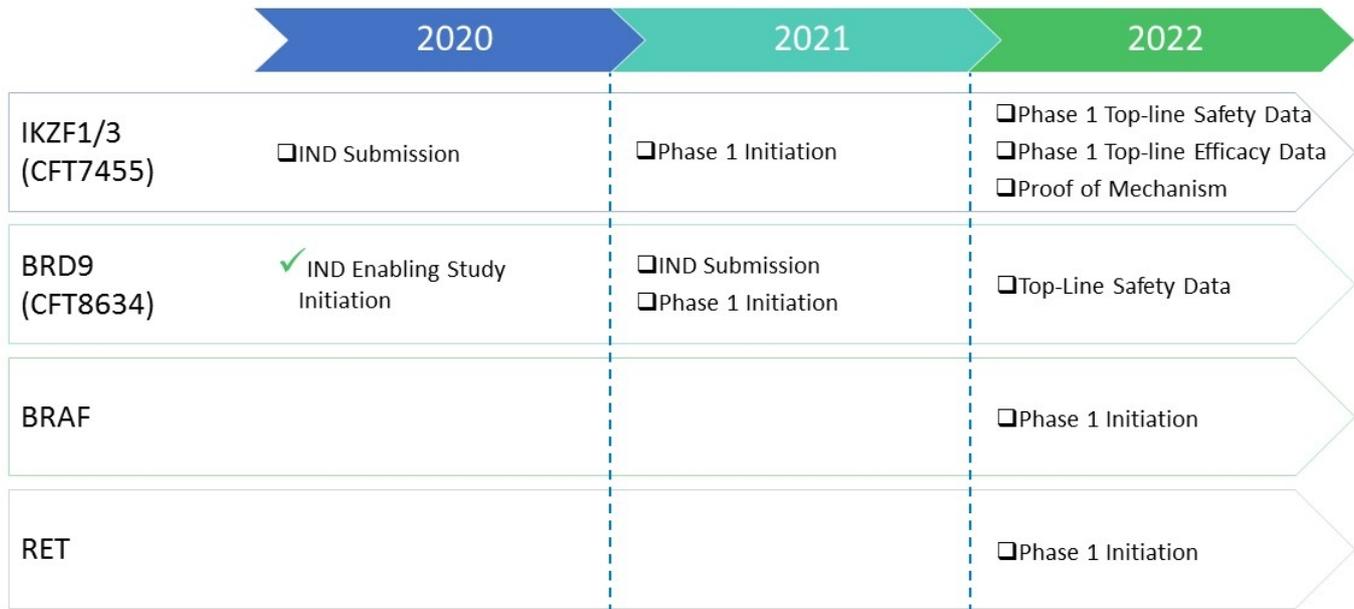


Mechanistic Rationale

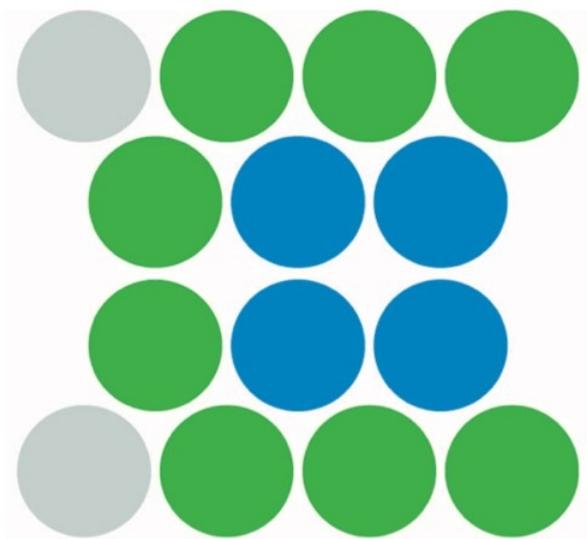


Potential for Multiple Near-term Milestones Across Lead Programs

Pro-Forma cash balance of \$390M as of 9/30/20 provides runway into H2 2023



Note: Other undisclosed targets have potential milestones during this time frame; cash runway guidance as of 11/12/2020



C4 Therapeutics

