C4 Therapeutics

Corporate Presentation

March 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.

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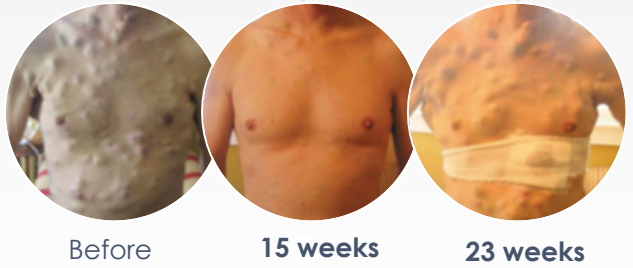
Targeted Protein Degradation Has the Potential to Transform Treatment of Disease

<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

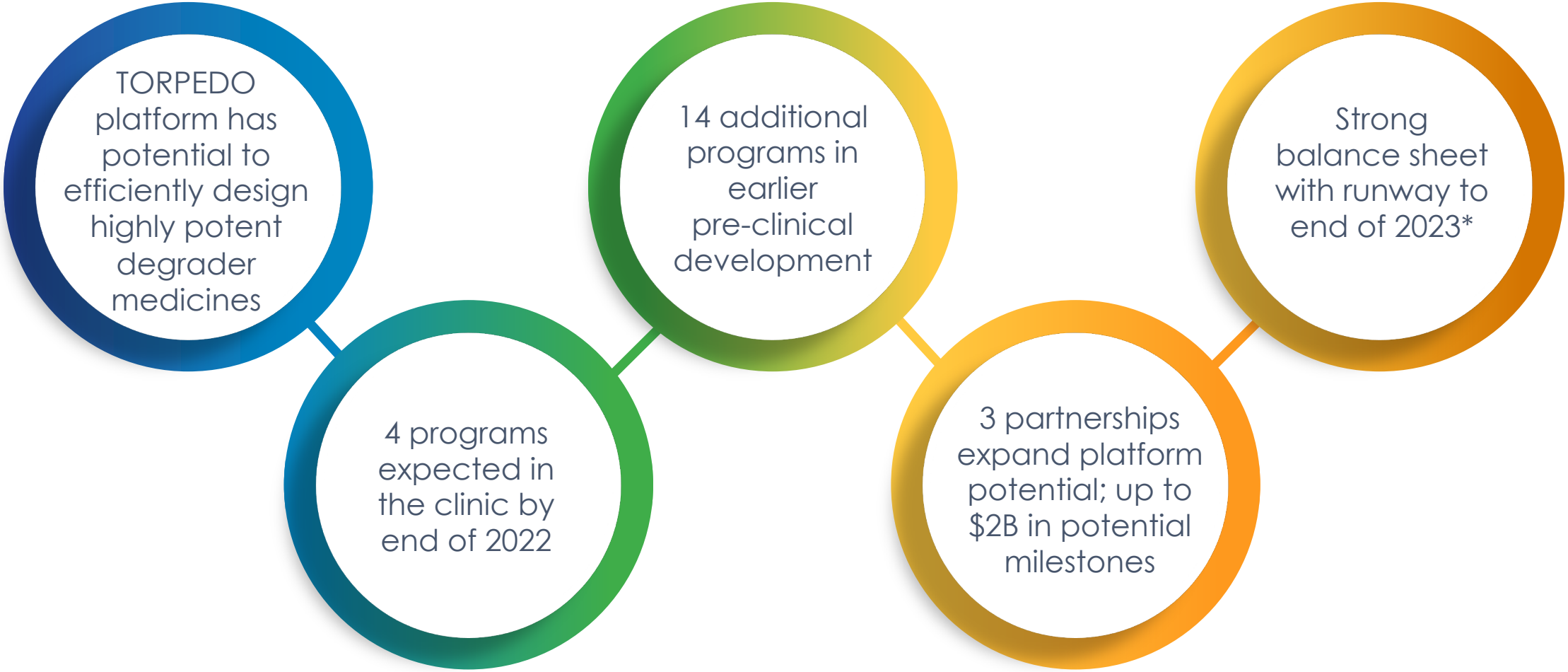
Oncology small molecule therapies generate significant revenue despite known limitations

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

C4 Therapeutics

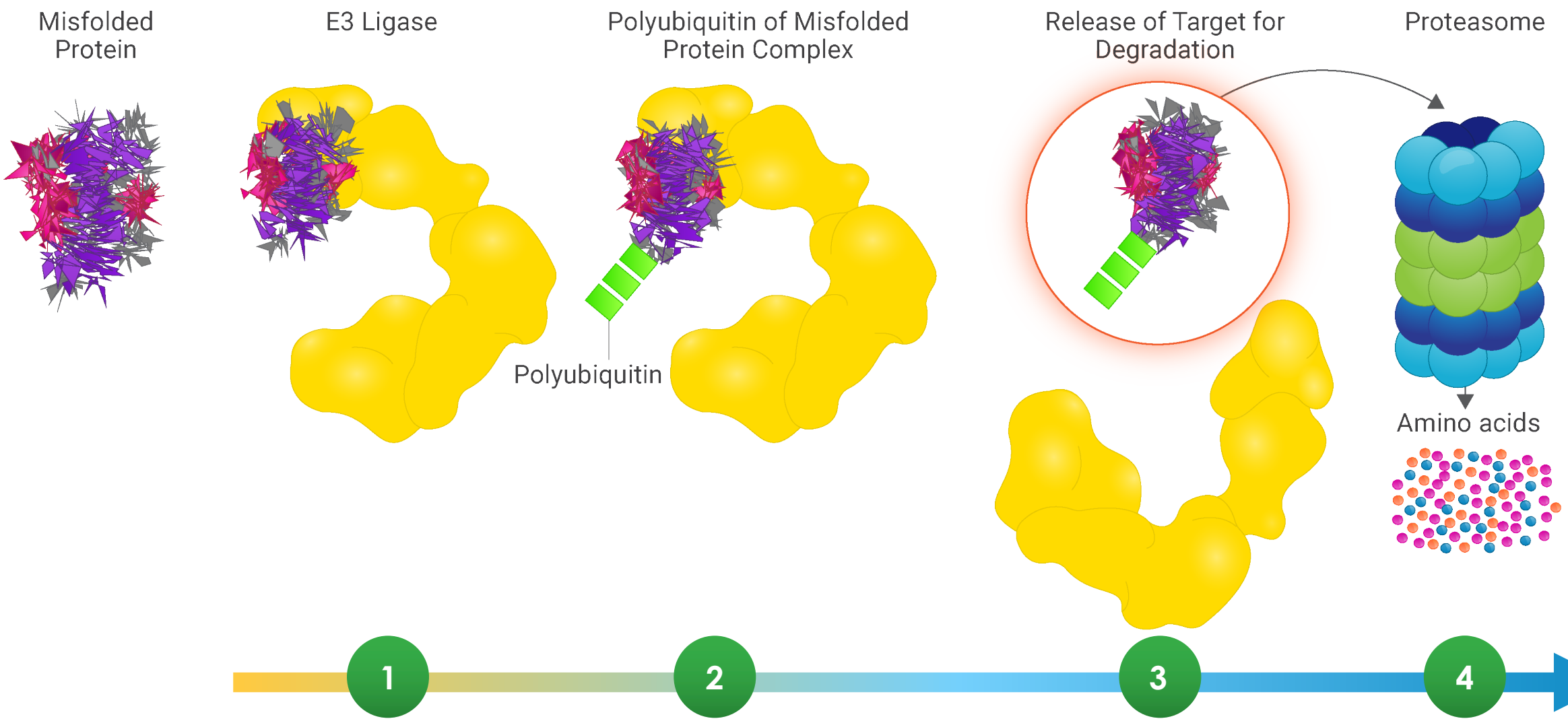
C4T is Well Positioned to Develop Targeted Protein Degradation Medicines to Transform Patient Care



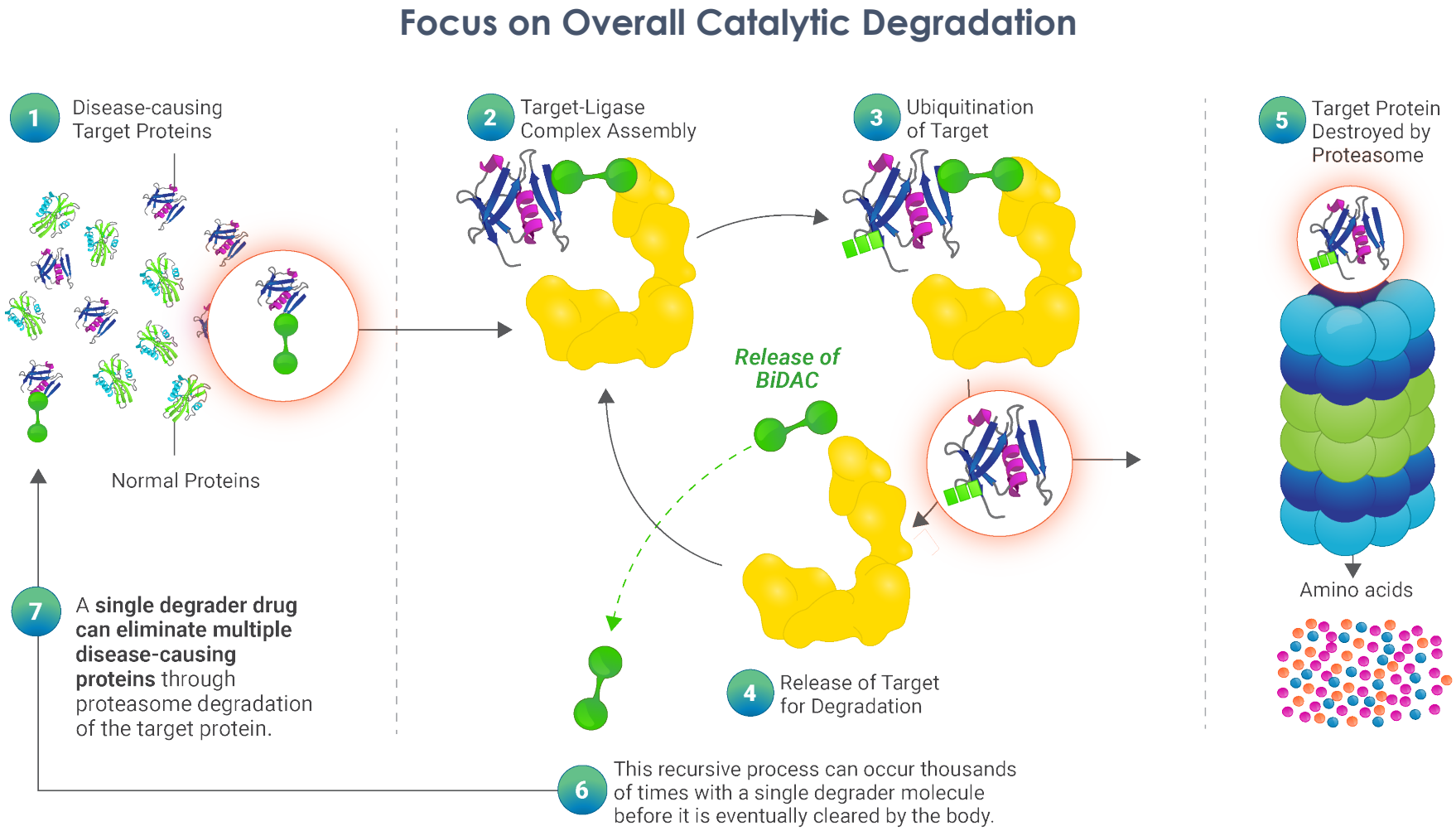
*12/31/20 unaudited cash balance of approximately $370M

C4 Therapeutics

The Human Body Has A Natural Process to Destroy Unwanted Proteins

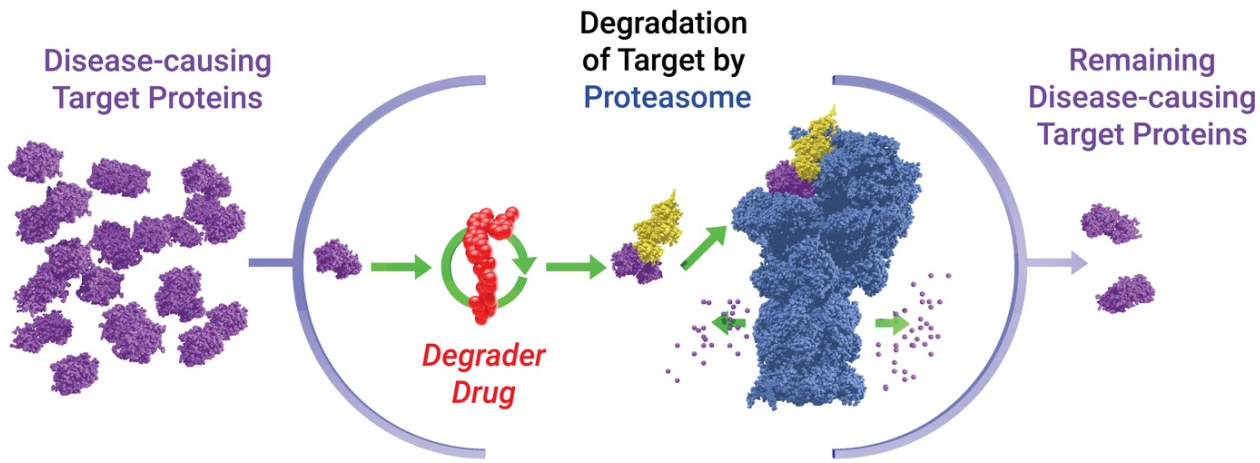


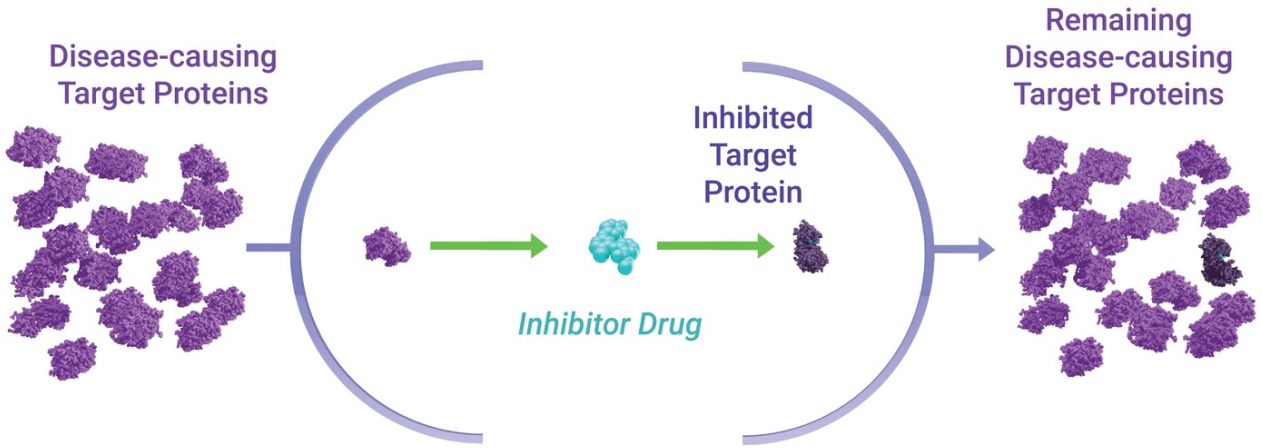
Targeted Protein Degradation Leverages the Body's Natural Process to Destroy Disease-Causing Proteins



Targeted Protein Degradation Offers Fundamental Advantages Over Protein Inhibition

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





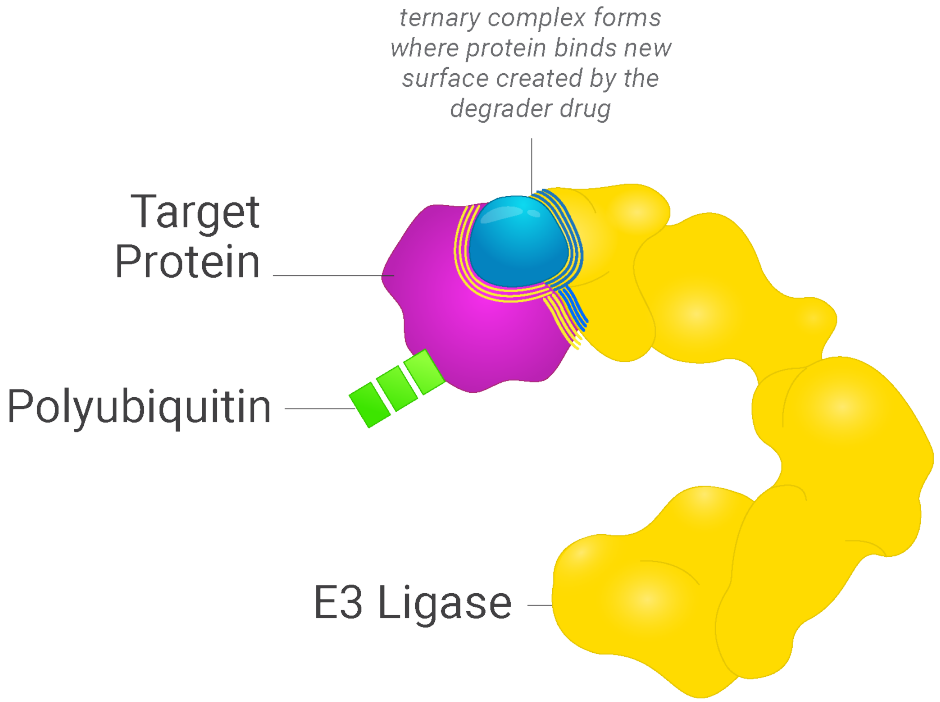
TORPEDO (Target ORiented ProtEin Degrader Optimizer) Platform

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

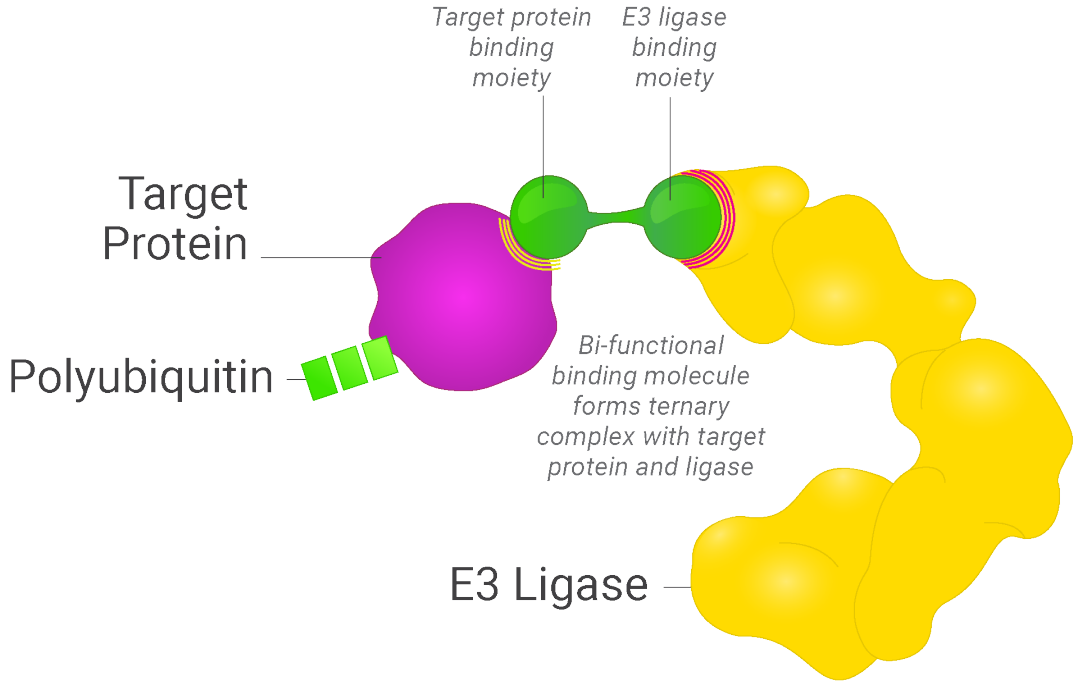
Elements	Benefits
Ability to Develop both MonoDAC & BiDAC Degraders	Flexibility to address different targets with tailored approach
Focus on Catalytic Efficiency	Optimization of overall degradation process results in maximal efficacy
Ability to Design, Analyze & Predict Degrader Performance	Rapid delivery 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

TORPEDO Platform Offers Flexibility to Design MonoDAC and BiDAC Degraders

MonoDAC



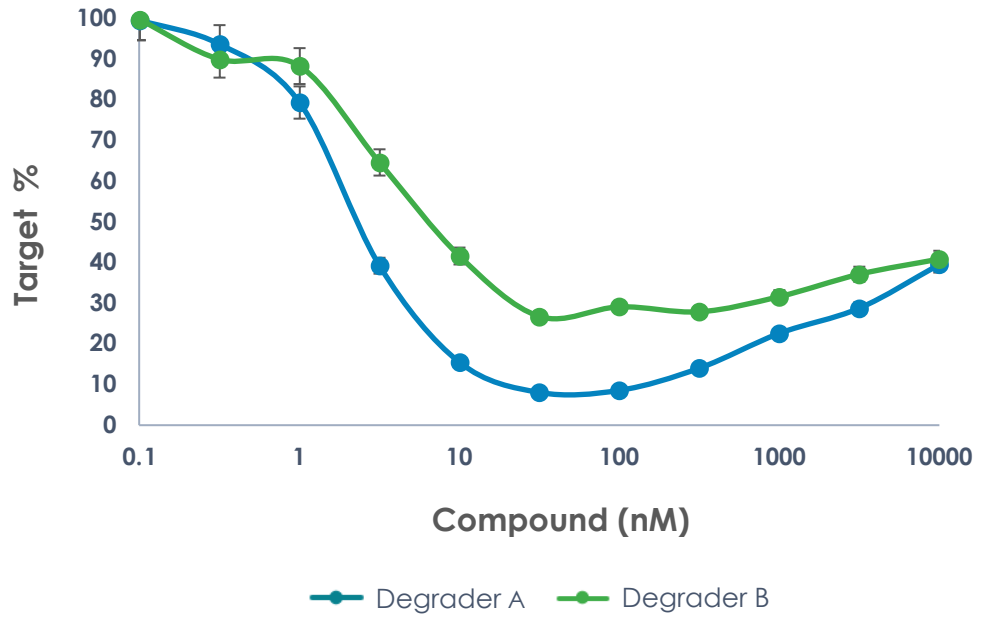
BiDAC



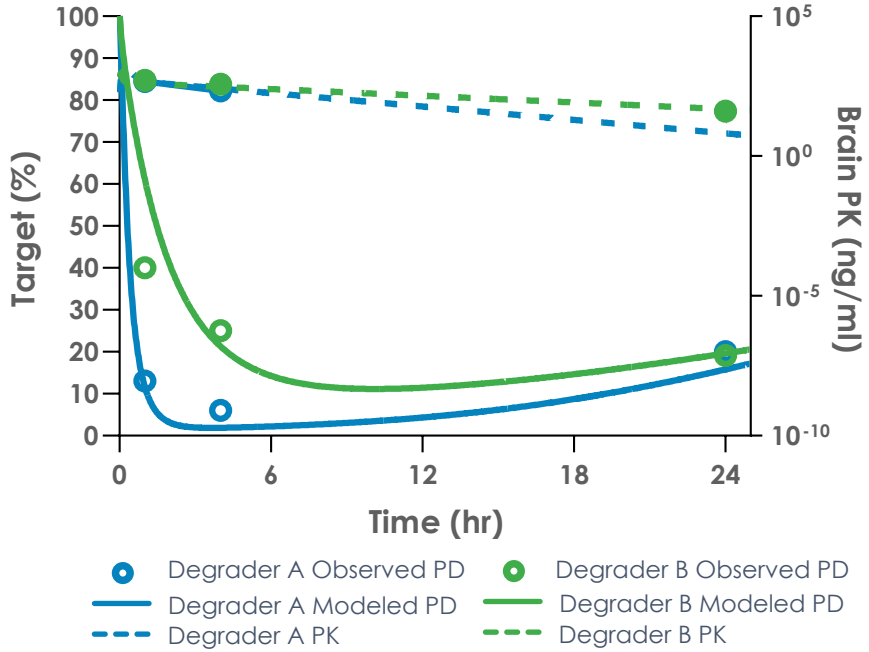
Flexibility to Address Different Targets with Tailored Approach

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

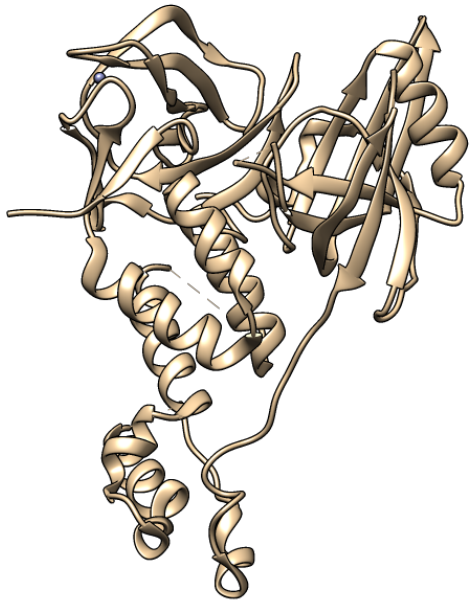
Robust predictions of depth and duration of *in vivo* target degradation at any dose

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

C4 Therapeutics

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 14 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 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
BRAF V600E	Drug-Resistant BRAF mutant Melanoma & NSCLC				C4 Therapeutics, Roche
RET	Drug-Resistant RET-Altered Tumors				C4 Therapeutics
EGFR	Drug-Resistant EGFR+ NSCLC				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

9 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

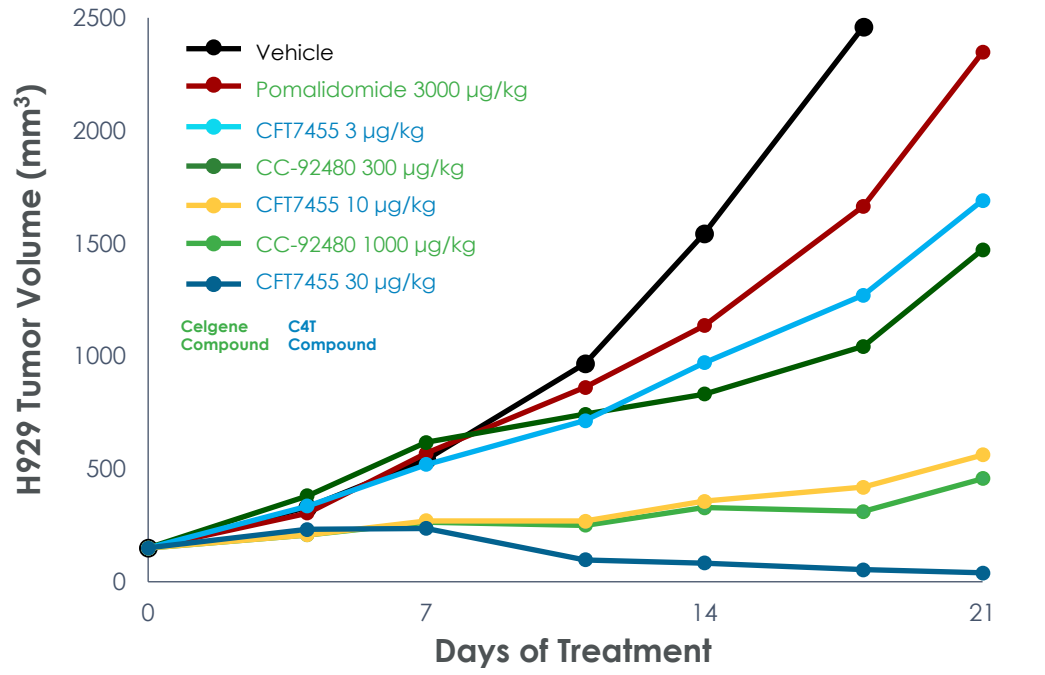
Source: NIH SEER Database, Primary Literature Consensus

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

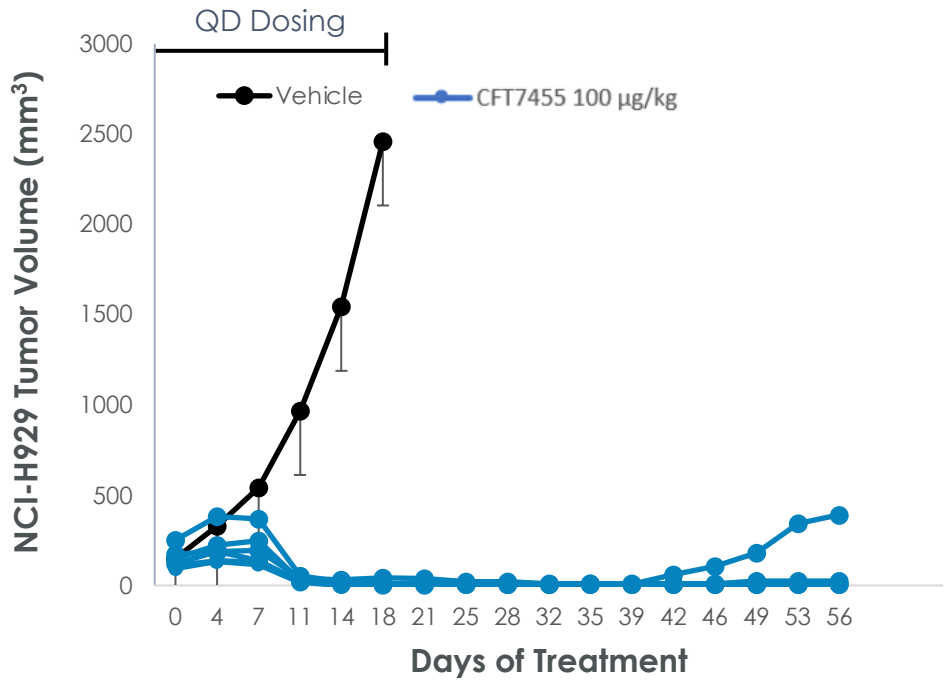
C4 Therapeutics

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



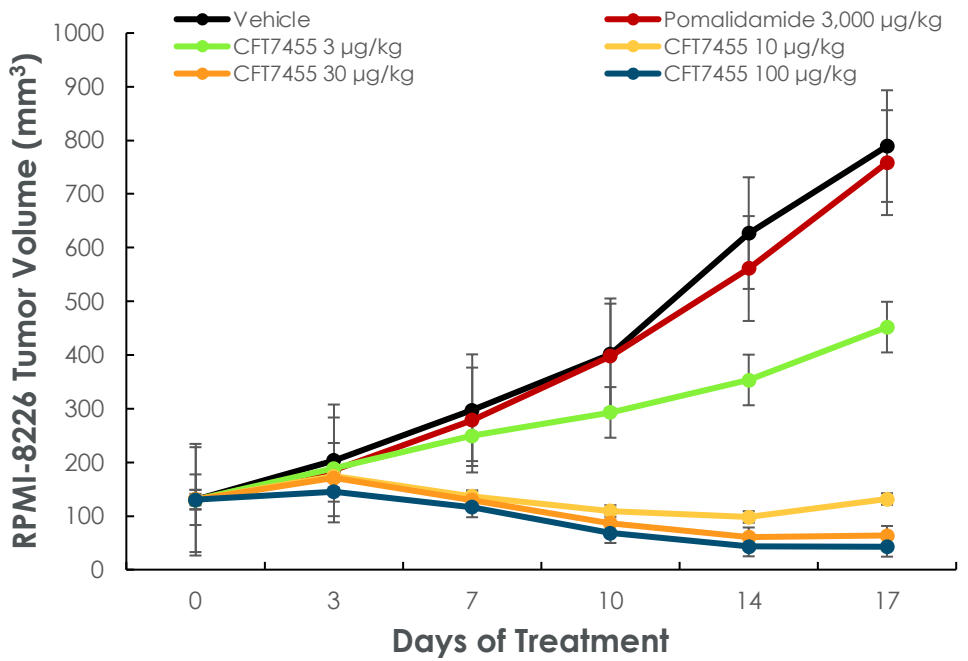
CFT7455 *In Vivo* Efficacy Durable After End of Dosing Period



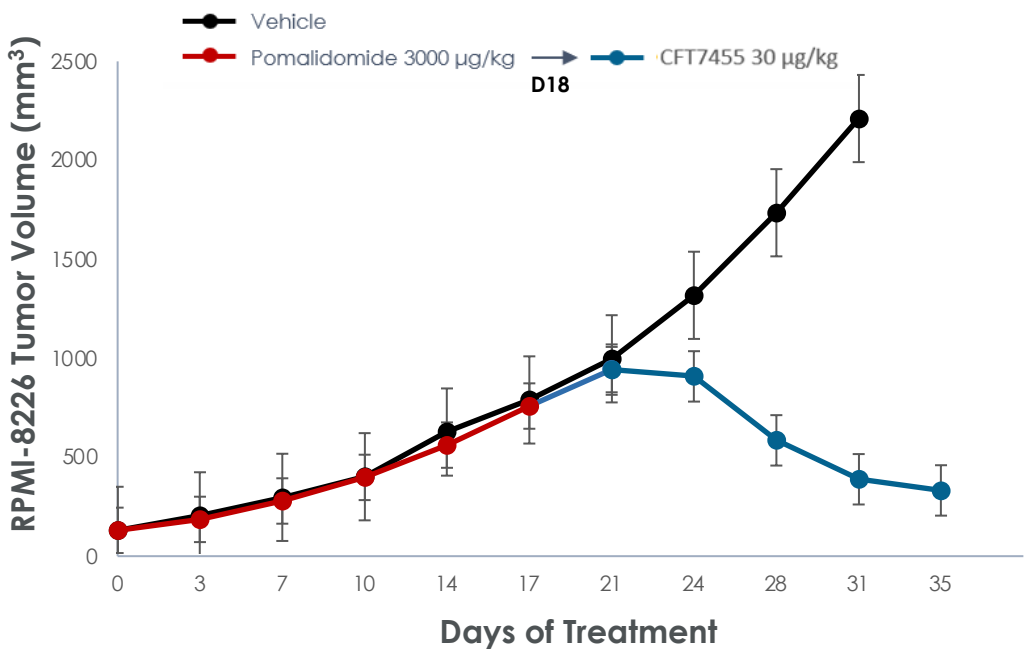
Source: C4T data on file

CFT7455 Demonstrates Tumor Regression in Multiple Myeloma Xenograft Insensitive to Pomalidomide

CFT7455 Active in RPMI-8226, Relative to Pomalidomide

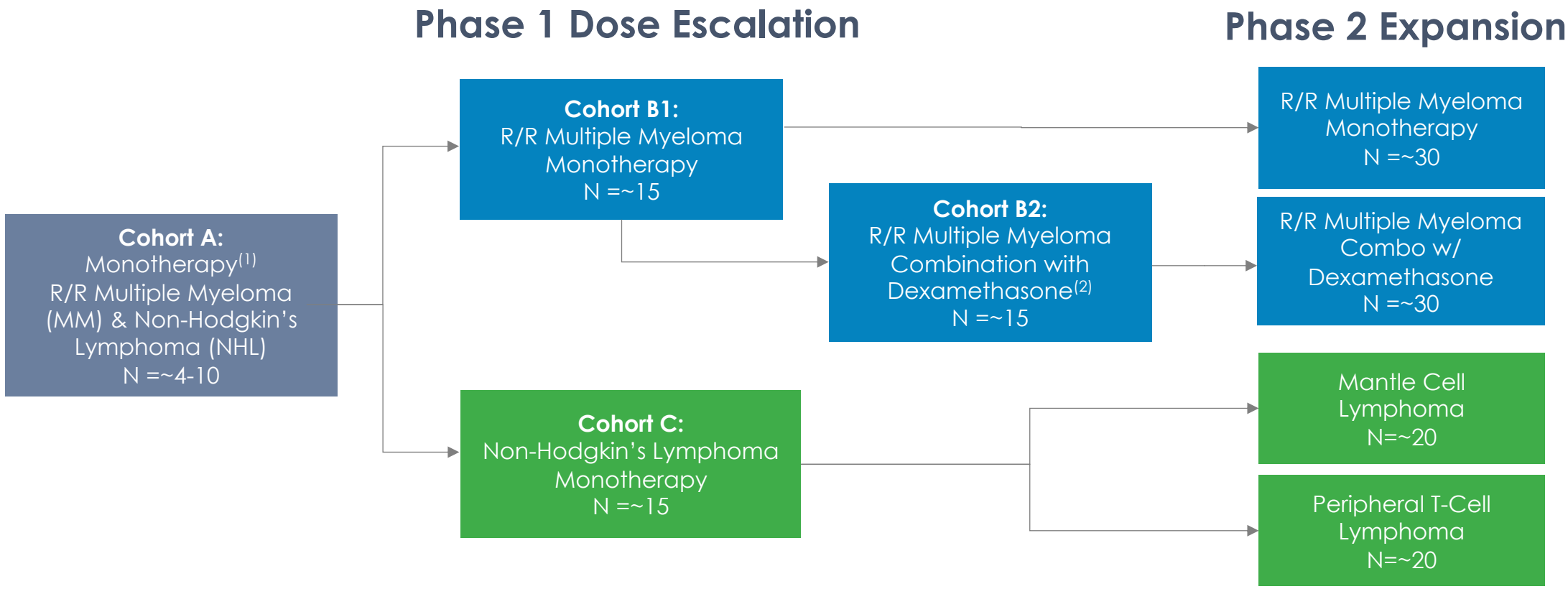


CFT7455 Active in RPMI-8226 After Tumor Progression on Pomalidomide Treatment



Source: C4T data on file

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



IND Clearance Achieved; Trial Expected to Initiate in 1H 2021

(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

C4 Therapeutics

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

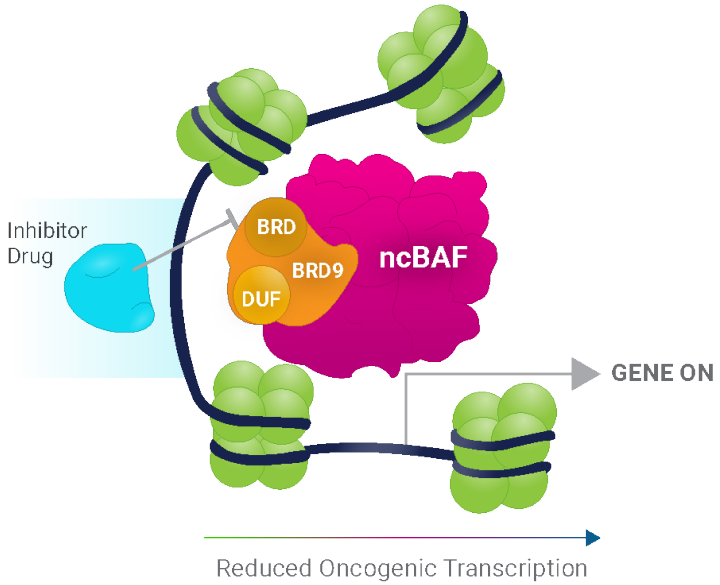
Source: NIH SEER Database, Primary Literature Consensus

Patient figures represent estimated U.S. annual incidence

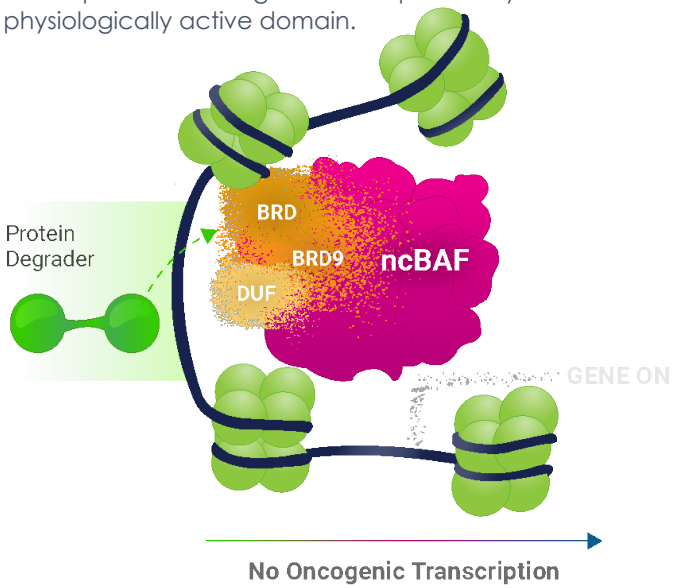
C4 Therapeutics

BRD9 Dependency in Synovial Sarcoma

Mechanistic Rationale



Leveraging a protein degrader approach enables us to effectively target BRD9 since our degraders do not require the binding site to be specifically at the physiologically active domain.

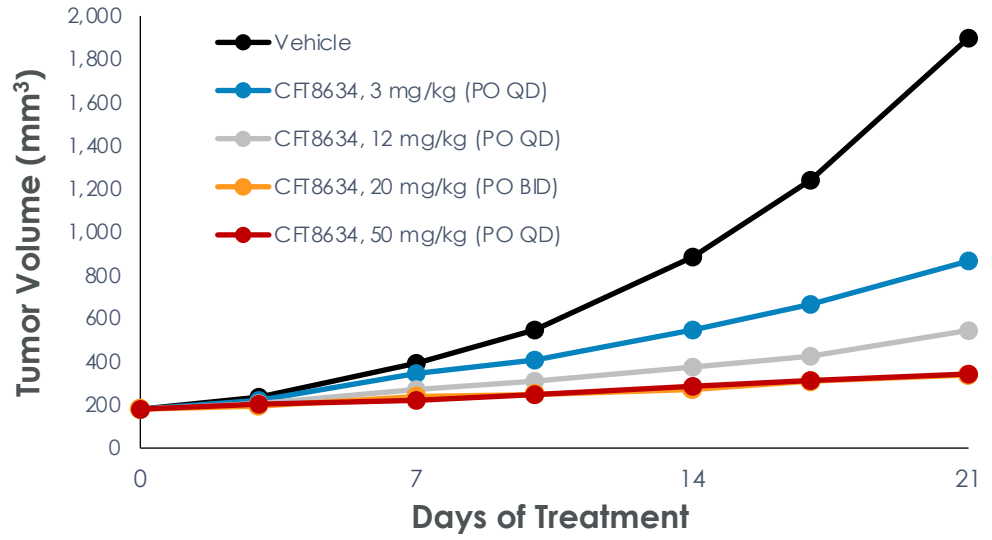


Advantages of BRD9 degradation

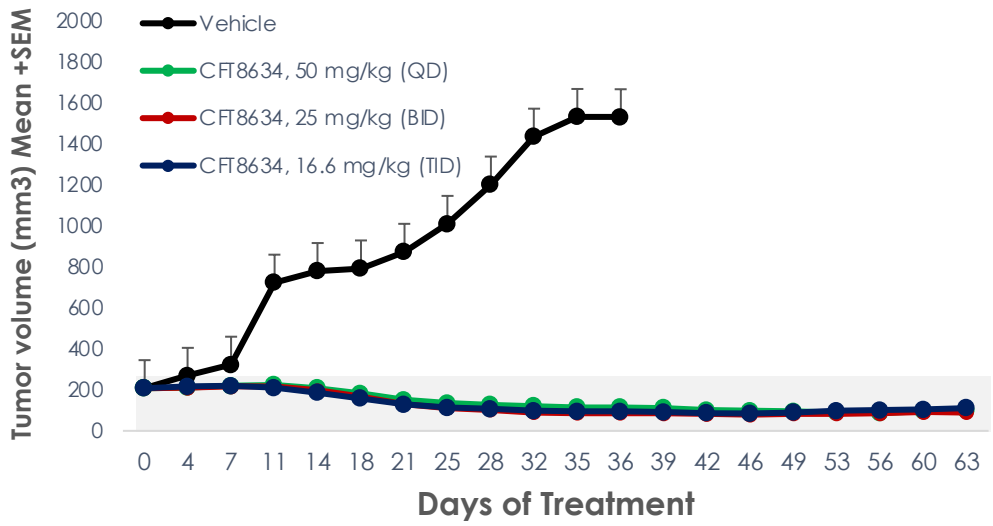
- Specifically degrades BRD9 and spares BRD4 and BRD7, avoiding potential off-target toxicities
- Oncogenicity of BRD9 depends on sub-domains not addressed by traditional inhibitors

Robust Responses of CFT8634 Seen in Preclinical Synovial Sarcoma Models

Dose Response Activity
Yamato Xenograft Model



Dose Response Activity
Patient Derived Xenograft Model



IND Submission for CFT8634 Expected in 2H 2021

Source: C4T data on file

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

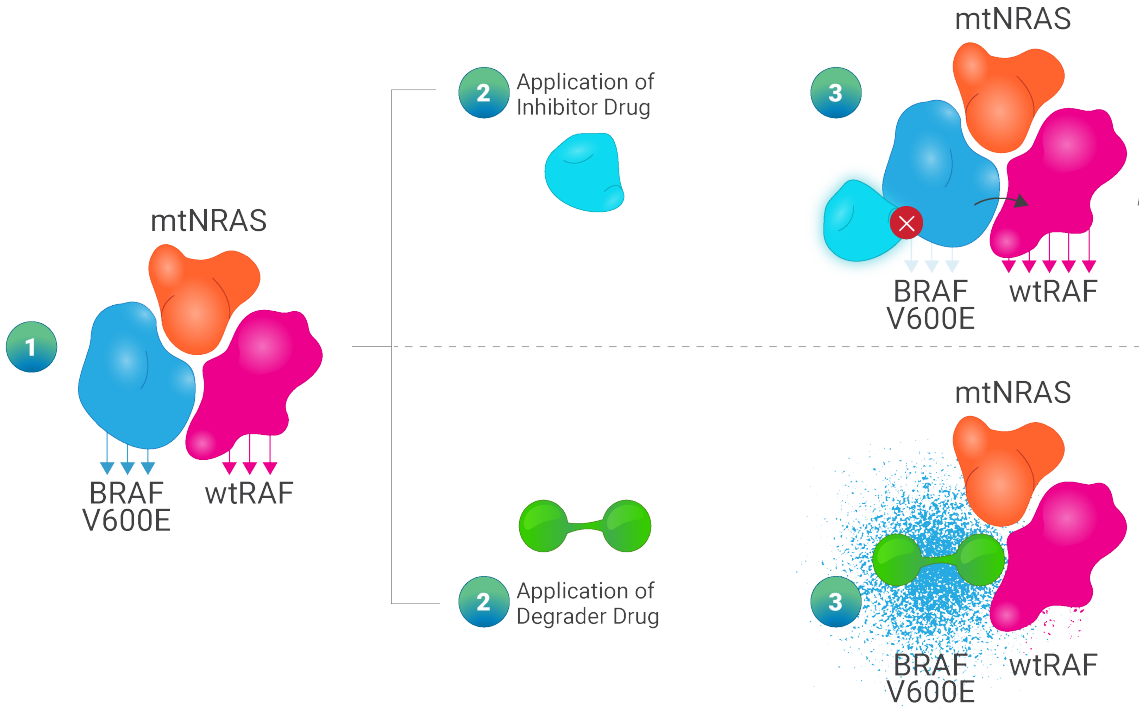
Patient figures represent estimated U.S. annual incidence

BRAF program is partnered with Roche

C4 Therapeutics

BRAF Degrader to Overcome Limitations of Approved BRAF Inhibitors

Mechanistic Rationale



Inhibitor causes paradoxical activation of wildtype RAF

Degrader prevents dimer formation and avoids paradoxical activation

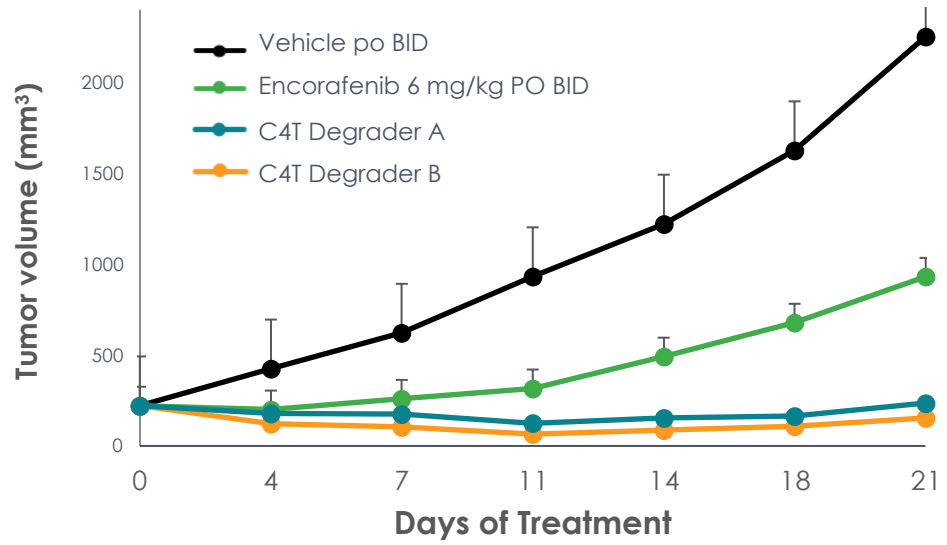
Advantages of BRAF V600E Degradation

- 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

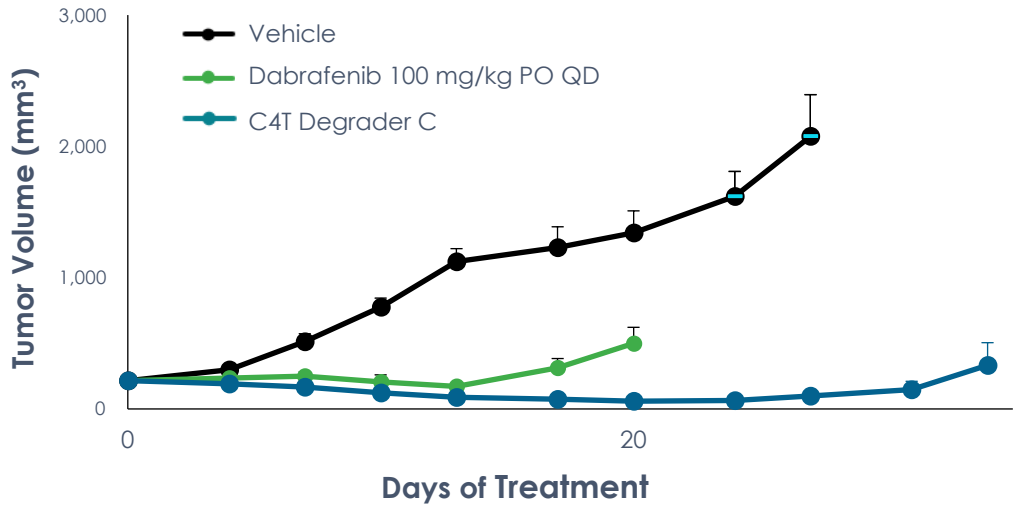
BRAF program is partnered with Roche

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

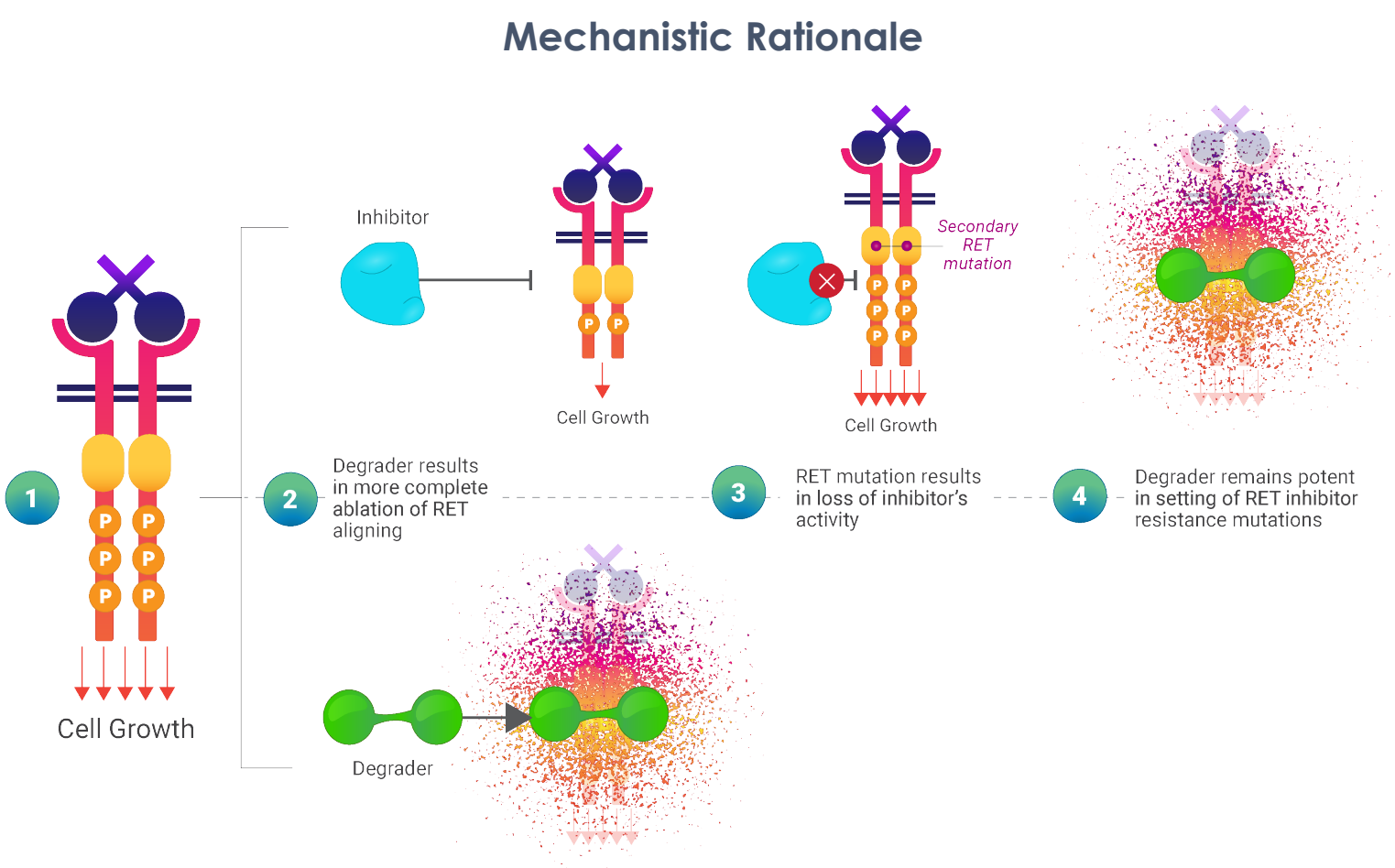
Compelling Development Opportunity

- 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



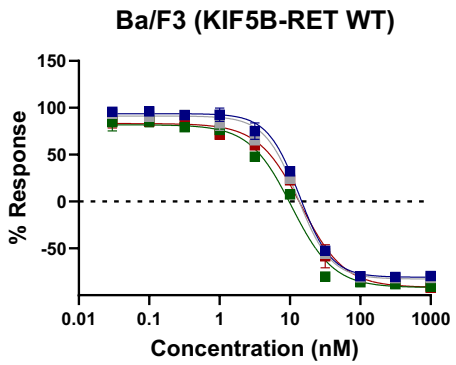
Advantages of RET Degradation

- 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

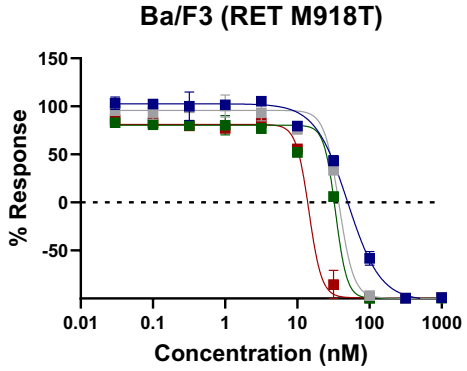
RET Degrader Has an Excellent Cell Growth Inhibition Profile In RET Fusions and Common Resistance Mutations

Drug Naïve, Driver Translocation/Mutation

KIF5B-RET Fusion

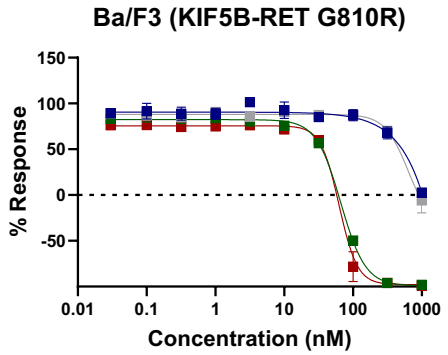


Activating Mutation

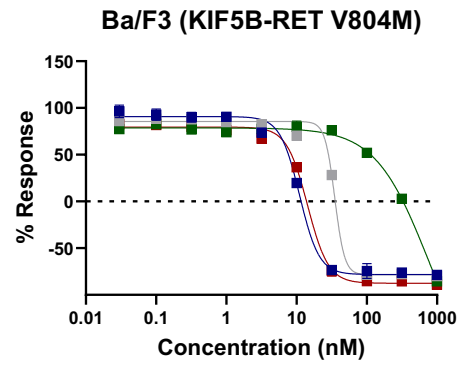


RET Inhibitor Acquired-Resistance Mutants

Solvent Front Mutation



Gatekeeper Mutation



Pralsetinib Selpercatinib 2nd Gen RET TKI CFT RET Degrader

IND Enabling Studies Planned for 2021

Source: C4T data on file

Lead Programs Offer Compelling Opportunities to Address Unmet Need in Multiple Patient Populations

IKZF1/3 CFT7455

NON-HODGKIN's LYMPHOMA

77K cases/year

32K cases/year

MULTIPLE MYELOMA

5-year survival

52%

BRD9 CFT8634

SYNOVIAL SARCOMA

900 cases/year

MEDIAN PFS OF 1L CHEMOTHERAPY

6.3 months

BRAF BiDAC

>70K cases/year

MELANOMA, NSCLC, CRC AND OTHER MALIGNANCIES

PFS across approved BRAF inhibitors

<15 months

RET BiDAC

1-2% of NSCLC

median **PFS**

~16.5 months (selpercatinib)

60% of sporadic medullary thyroid cancer

Sources: National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Database
MM survival: https://seer.cancer.gov/archive/csr/1975_2015/browse_csr.php?sectionSEL=18&pageSEL=sect_18_table.08.html#table2. SS PFS: M. Vlenterie et al. European Journal of Cancer 58 (2016) 62e72; BRAF PFS: Cell Press Review, Trends in Cancer, September 2020, Vol. 6, No. 9; RET PFS: NJEM 383;9 nejm.org 8/27/20

Patient figures represent estimated U.S. annual incidence

C4 Therapeutics

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

	2021	2022
IKZF1/3 (CFT7455)	❑ Phase 1/2 Initiation	❑ Phase 1 Top-line Safety & Efficacy ❑ Proof of Mechanism
BRD9 (CFT8634)	❑ IND Submission	❑ Phase 1 Initiation
BRAF	❑ IND Enabling Studies	❑ Phase 1 Initiation
RET	❑ IND Enabling Studies	❑ Phase 1 Initiation

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

*12/31/20 unaudited cash balance of approximately $370M

C4 Therapeutics

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Thank You