



C4 Therapeutics Presents Pre-clinical Data on CFT7455, a Novel IKZF1/3 Degradator for the Treatment of Hematologic Malignancies, at the 16th Annual International Conference on Malignant Lymphoma

June 21, 2021 12:00 PM EDT

- CFT7455 Demonstrated High Binding Affinity to Cereblon and Target Selectivity in Non-Hodgkin's Lymphoma Cell Models, Producing Rapid and Deep Degradation of IKZF1/3 Proteins –
- CFT7455 Resulted in Improved Efficacy and Potency in Tumor Xenograft Models Compared to Investigational and Approved IMiD Therapies –
- CFT7455 Phase 1/2 Trial in Multiple Myeloma and Non-Hodgkin's Lymphomas Initiated June 2021; Top-line Clinical Data Expected 2022 –

WATERTOWN, Mass., June 21, 2021 (GLOBE NEWSWIRE) -- C4 Therapeutics, Inc. (C4T) (Nasdaq: CCCC), a clinical-stage biopharmaceutical company pioneering a new class of small-molecule medicines that selectively destroy disease-causing proteins through degradation, presented pre-clinical data for CFT7455, the Company's lead program. CFT7455 is an orally bioavailable MonoDAC™ targeting IKZF1/3 for the treatment of multiple myeloma (MM) and non-Hodgkin's lymphomas (NHL), including peripheral T-cell lymphoma (PTCL) and mantle cell lymphoma (MCL). These results, which support clinical evaluation of CFT7455 in non-Hodgkin's lymphomas, were delivered as a poster presentation at the 16th Annual International Conference on Malignant Lymphoma (ICML).

"We are pleased to share these pre-clinical data, which further validate the potential of our lead candidate, CFT7455, to generate deep and durable antitumor responses in non-Hodgkin's lymphomas. IKZF1/3 proteins are essential transcription factors for B cell malignancies, including non-Hodgkin's lymphomas, and we believe there is a compelling opportunity to explore the potential of optimized IKZF1/3 degradation as a much-needed therapeutic alternative," said Adam Crystal, M.D., Ph.D., chief medical officer of C4 Therapeutics. "These results, which are consistent with recent pre-clinical data in multiple myeloma presented at the AACR Annual Meeting 2021, reinforce our belief that CFT7455 will provide significant clinical value in the treatment of hematologic malignancies as we advance the Phase 1/2 trial and prepare to share data in 2022."

Summary of Results

C4T conducted *in vitro* studies which demonstrated that CFT7455 binds to cereblon with high affinity, inducing potent and deep degradation of IKZF1 in pre-clinical NHL models. Notable observations include:

- Cellular competition studies confirmed the high potency of CFT7455 as a cereblon binder (IC₅₀ = 0.4 nM).
- Treatment of the KiJK cell line of anaplastic large cell lymphoma (ALCL) with CFT7455 for 6 hours led to an 89% reduction in IKZF1 protein levels.
- CFT7455 demonstrated potent antiproliferative activity across a panel of NHL cell lines with MYC, BCL2, and/or BCL6 translocations or rearrangements. This includes *in vitro* models of cutaneous T-cell lymphoma (CTCL), anaplastic large cell lymphoma (ALCL), mantle cell lymphoma (MCL), and high-grade B-cell lymphoma.

In xenograft models of NHL, CFT7455 achieved improved *in vivo* potency and efficacy, including deeper and more durable tumor regressions in models of ALCL, diffuse large B-cell lymphoma (DLBCL) and MCL, when compared to approved and investigational IMiD therapies. Notable observations include:

- CFT7455 treatment (100 µg/kg/day, PO) led to durable tumor regression associated with deep IKZF1 degradation and IRF4 downregulation (7% and 25% remaining, respectively) in KiJK xenografts, where pomalidomide treatment was ineffective at a clinically relevant dose (3000 µg/kg/day).
- In the TMD8 DLBCL xenograft model, which proved insensitive to IMiD treatment, CFT7455 (100 µg/kg) promoted tumor regression.
- In the REC1 MCL xenograft model, doses of CFT7455 ≥ 10 µg/kg promoted tumor regression. Pharmacodynamic studies showed that CFT7455 (30 µg/kg) promoted degradation of IKZF1 and downregulation of cyclin D1 and E2F1.
- CFT7455 achieved dose-dependent efficacy in both ALK⁻ (DL-40) and ALK⁺ (KiJK) xenograft

models, from 3-100 µg/kg with regressions at doses ≥ 30 µg/kg. In addition, CFT7455 was shown to be between >30-100 times more potent than other IKZF1/3 degraders in development.

- o Global proteomic studies showed only IKZF1/3 proteins were significantly degraded in DL-40 tumors with treatment of CFT7455, resulting in modulation of IFN-regulated genes.

These results support continued development of CFT7455, which C4T is currently exploring for the treatment of relapsed or refractory multiple myeloma and non-Hodgkin's lymphomas following the initiation of a Phase 1/2 clinical study in June 2021.

C4T's ICML poster presentation will be archived on the "Scientific Publications" page in the Investors section of the Company's website, located at www.c4therapeutics.com.

About CFT7455

CFT7455 is an orally bioavailable MonoDAC™ (Mono-functional Degradation Activating Compound) designed to bind with high affinity to the E3 ligase adapter protein, cereblon, to target and degrade IKZF1/3 for the treatment of multiple myeloma (MM) and non-Hodgkin's lymphomas (NHLs), including peripheral T cell lymphoma (PTCL) and mantle cell lymphoma (MCL). In preclinical studies, CFT7455 has demonstrated potent and selective protein degradation with favorable pharmacological properties. The Company initiated a Phase 1/2 clinical trial for CFT7455 in June 2021. More information about this trial may be accessed at www.clinicaltrials.gov (identifier: NCT04756726).

About C4 Therapeutics

C4 Therapeutics (C4T) is a clinical-stage 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 pre-clinical 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 pre-clinical 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 pre-clinical 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 pre-clinical 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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