C4 Therapeutics Presents Pre-clinical Data on CFT8919, A Selective Degrader of EGFR L858R, at Keystone Symposium on Targeted Protein Degradation

June 7, 2021

– CFT8919 Induces Tumor Regression in Pre-clinical Models Resistant to First- and Third-generation EGFR Inhibitors –

– CFT8919 Demonstrates Intracranial Activity Pre-clinically, Indicating the Potential to be Effective Against CNS Metastases –

– Pre-clinical Data Support Plans to Advance CFT8919 to Clinical Development with IND Submission Expected in mid-2022 and Clinical Trial Initiation Expected by YE 2022 –

– Conference Call and Webcast at 8:00 am ET Today –

WATERTOWN, Mass., June 07, 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 presented new pre-clinical data on CFT8919, a novel mutant-selective degrader of epidermal growth factor receptor (EGFR) in non-small cell lung cancer (NSCLC) at the Keystone Symposium on Targeted Protein Degradation. The poster presentation shares pre-clinical data that suggests CFT8919 may be active as a single agent in patients with resistance to EGFR inhibitors 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.

“We are excited to share strong preclinical data that establishes CFT8919 as a potent and selective degrader of EGFR L858R, a mutation responsible for more than a third of mutant EGFR lung cancer diagnoses. Patients with this mutation are commonly treated with approved EGFR inhibitor therapies, but often have worse clinical outcomes than individuals diagnosed with other driver mutations such as Exon19del,” said Adam Crystal, M.D., Ph.D., chief medical officer of C4 Therapeutics. “Across our portfolio, we see the potential for targeted protein degradation to transform patient care. We believe our decision to advance CFT8919 recognizes promising early data that indicate CFT8919 may have the potential to treat patients who develop resistance to first-line EGFR inhibitors as well as a path to inclusion in front-line therapeutic regimens. We look forward to learning more about CFT8919 as we advance the program into IND-enabling studies and initiate the Phase 1 clinical trial in 2022.”

Summary of CFT8919 Pre-clinical Results
C4T conducted *in vitro* and *in vivo* studies that show CFT8919 is a potent and highly selective orally bioavailable degrader of EGFR L858R with broad coverage of on-target resistance mutations as well as intracranial activity. Notable observations include:

- In cancer cell lines, CFT8919 induces degradation of EGFR L858R at low nanomolar concentrations while no degradation of wild type is induced up to 10 µM.
- CFT8919 demonstrates equipotent activity against EGFR mutations resistant to EGFR inhibition, including L858R-C797S, L858R-T790M, and L858R-T790M-C797S compared to L858R single mutation in Ba/F3 cell models in vitro.
- Kinome profiling and global proteomic evaluation did not identify any significant off-target activity of CFT8919. CFT8919 does not induce degradation of known cereblon neo-substrates SALL4 or GSPT1, indicating that the potential associated toxicities will not be liabilities.

Additionally, *in vivo* data demonstrates the following:

- CFT8919 degrades and inhibits mutant EGFR in tumors upon oral administration. In the NCI-H1975 EGFR-L858R-T790M xenograft model, after a single oral dose of CFT8919, up to 85 percent of mutant EGFR was degraded in tumors accompanied with near-complete inhibition of phospho-EGFR.
    - In this model, twice-daily oral administration of CFT8919 showed dose-dependent anti-tumor activity and regressions comparable to osimertinib.
- In BaF3 allograft model expressing EGFR-L858R-T790M-C797S, CFT8919 demonstrates anti-tumor activity resulting in tumor regression, while osimertinib is inactive.
- CFT8919 demonstrates rapid and significant reductions in tumor burden in the H1975-LUC (EGFR L858R-T790M) brain metastasis model after oral dosing, indicating its potential to be active in the central nervous system.

This promising pre-clinical data supports the Company’s decision to advance CFT8919 into investigational new drug (IND)-enabling studies this year. C4T anticipates filing an IND for CFT8919 by mid-2022, with the goal to initiate a Phase 1 clinical trial by year-end 2022.

C4T will host an investor event and webcast today, June 7, 2021, at 8 am E.T. to further discuss the pre-clinical data. Details of this event are included below.

In addition, the poster presentation from the Keystone Symposium on Targeted Protein Degradation will be archived on the “Scientific Publications” page in the Investors section of the Company’s website, located at www.c4therapeutics.com.

Investor Event and Webcast Information
C4T will host a live webcast today, 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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