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

May 26, 2021

– 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 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.

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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