C4 Therapeutics Presents Clinical Data from Cohort A of the Ongoing Phase 1/2 Clinical Trial of CFT7455, a Novel IKZF1/3 Degrader

April 8, 2022

– Single Agent CFT7455 Induces Deep and Durable Degradation of IKZF1/3 and Meaningful Decreases in Serum Free Light Chain at Doses Lower than Expected Based on Pre-clinical Studies –

– CFT7455 Exhibits Differentiated Pharmacokinetics (PK) and Potency Relative to Approved and Investigational IKZF1/3 Degraders –

– On-Target Dose Limiting Toxicity Observed; Modeling Suggests Differentiated Activity and PK Profile Provides Pathway to Increase Therapeutic Index with Alternative Dosing Schedule –

– Company to Host Conference Call and Webcast Today at 2 pm ET –

WATERTOWN, Mass., April 08, 2022 (GLOBE NEWSWIRE) -- C4 Therapeutics, Inc. (C4T) (Nasdaq: CCCC), a clinical-stage biopharmaceutical company dedicated to advancing targeted protein degradation science to develop a new generation of small-molecule medicines and transform how disease is treated, today presented data from Cohort A of its ongoing Phase 1/2 clinical trial of CFT7455, a novel degrader targeting IKZF1/3 for the treatment of multiple myeloma (MM) and non-Hodgkin's lymphomas (NHL). The data will be presented at the American Association for Cancer Research (AACR) Annual Meeting on Tuesday, April 12, 2022, at 9 AM CT by Sagar Lonial, M.D., FACP.

"The early clinical data from the ongoing Phase 1/2 trial demonstrates that CFT7455's differentiated pre-clinical profile, including enhanced PK and increased activity, has translated to the clinical setting," said Dr. Sagar Lonial, professor and chair, department of hematology and medical oncology, Winship Cancer Institute, Emory University. "Single agent CFT7455 has demonstrated preliminary evidence of clinical activity in a population of highly refractory and heavily pre-treated multiple myeloma patients. We continue to enroll patients in the ongoing clinical trial with the goal of providing a new treatment option for myeloma and lymphoma patients."

"We are encouraged by the early clinical observations and the potential of CFT7455 to be a next-generation therapy to treat multiple myeloma and non-Hodgkin's lymphomas," said Adam Crystal, M.D., Ph.D., chief medical officer of C4 Therapeutics. "We believe this initial data highlights the ability of our TORPEDO® platform to develop highly potent and selective degraders that have the potential to demonstrate deep and durable degradation of intended targets in the clinical setting. We will leverage the unique properties of CFT7455 to optimize its schedule and increase the therapeutic index as we progress to a recommended Phase 2 dose."

CFT7455 Phase 1/2 Clinical Trial

C4T designed CFT7455 to be highly potent and selective against its intended targets, IKZF1/3. The Phase 1/2 trial is designed to primarily investigate safety, tolerability, and anti-tumor activity. Secondary and exploratory objectives are to characterize the PK and pharmacodynamic profile of CFT7455. The Phase 1 portion of the study explores CFT7455 as a single agent in patients with relapsed or refractory (RR) MM and NHL, as well as in combination with dexamethasone in patients with RRMM. Following identification of a recommended dose(s) and schedule(s), the Phase 2 portion of the trial is expected to expand to the following four investigational arms: (1) in RRMM, single agent CFT7455; (2) in RRMM, CFT7455 combined with dexamethasone; (3) in peripheral T-cell lymphoma, single agent CFT7455; and (4) in mantle cell lymphoma, single agent CFT7455.

Cohort A, the first cohort in the clinical trial, explored CFT7455 as a single agent and enrolled five patients with MM. All patients in Cohort A were highly refractory and heavily pre-treated, having received a median of five prior lines of therapy (range of 4-14), including both lenalidomide and pomalidomide. The starting dose in the trial was 50 µg and all patients in Cohort A received single agent CFT7455 for 21 days of the 28-day treatment cycle. The data cut-off date was January 14, 2022. At the time of this data cut-off, two patients remained on therapy; however, these patients have since discontinued treatment.

Summary of Data from Cohort A:

Safety

- Four patients received single agent CFT7455 at the starting dose of 50 µg per day. Two of these patients were dose reduced to 25 µg per day due to neutropenia, a known on-target toxicity associated with IKZF1/3 degraders.
- The fifth patient enrolled at a starting dose of 25 µg per day based on the recommendation of the safety review committee.
- Two dose-limiting toxicities (DLTs) were observed at the 50 µg per day starting dose, both consistent with on-target activity:
    1. Grade 4 neutropenia lasting more than 5 days
    2. A delay (more than 7 days) in initiating treatment in Cycle 2, in the setting of persistent Grade 3 neutropenia
- No patient experiencing neutropenia had a concurrent infection or fever.
- There were no serious adverse events reported and no adverse events resulted in death or treatment discontinuation.

Pharmacokinetics and Pharmacodynamics

- CFT7455 was rapidly absorbed, with a plasma half-life of approximately two days. Accumulation of drug was observed up to four-fold by day 15 and achieved exposures at 50 µg that were equivalent to predicted highly active exposures based on pre-clinical studies.
- CFT7455 demonstrated deep and durable degradation of IKZF1/3, as quantified by mass spectrometry, throughout Cycle 1.

Efficacy

- Responsiveness was measured based on International Myeloma Working Group (IMWG) criteria.
- Three patients had best observed reductions in the difference of serum free light chain (dFLC) ranging from 41 percent to 78 percent. One patient had an increase of 56 percent in dFLC.
- The patient who achieved a 78 percent reduction in dFLC did not achieve a partial response under IMWG criteria due to the presence of measurable plasmacytomas, which were assessed as stable.
- Three patients had a best response of stable disease. Two patients had a best response of progressive disease.

Next Steps for CFT7455

C4T has completed modeling of the Cohort A data and believes alternative dosing regimens are expected to increase the therapeutic index by allowing time for adequate neutrophil maturation during the days off drug, with limited impact on efficacy. Patients are enrolling in Cohort B1, exploring CFT7455 as a monotherapy for RRMM, and Cohort C, exploring CFT7455 as a monotherapy for NHL. Cohorts B1 and C have a starting dose of 25 µg per day at an alternative dosing schedule. Each cohort will proceed with dose finding in parallel, with the goal of achieving a recommended Phase 2 dose in each of MM and NHL.

Investor Webcast Information

C4T will host an investor webcast today, Friday, April 8, 2022, at 2 PM ET, with Sagar Lonial, M.D., FACP to discuss the CFT7455 clinical data being presented at AACR. To access the call, please dial 866-374-5140 or 404-400-0571 and provide the conference ID: 66856580. The webcast can be also accessed under “Events & Presentations” in the Investors section of the company’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) (Nasdaq: CCCC) is a clinical-stage biopharmaceutical company dedicated to delivering on the promise of targeted protein degradation science to create a new generation of medicines that transform patients’ lives. C4T is leveraging its TORPEDO ® platform to efficiently design and optimize small-molecule medicines that harness the body’s natural protein recycling system to rapidly degrade disease-causing proteins, offering the potential to overcome drug resistance, drug undruggable targets and improve patient outcomes. C4T is advancing multiple targeted oncology programs to the clinic and expanding its research platform to deliver the next wave of medicines for difficult-to-treat diseases. For more information, please visit www.c4therapeutics.com.

About CFT7455

CFT7455 is an orally bioavailable MonoDAC™ (Monofunctional Degradation Activating Compound) degrader designed to be highly potent and selective against its intended targets of Ikaros (IKZF1) and Aiolos (IKZF3). CFT7455 binds with high affinity to the E3 ligase adapter protein, cereblon, to target and degrade IKZF1/3 for the treatment of multiple myeloma and non-Hodgkin's lymphomas, including peripheral T cell lymphoma and mantle cell lymphoma. In early clinical data, CFT7455 demonstrated deep and durable degradation of IKZF1/3. C4T is actively enrolling patients in its ongoing Phase 1/2 clinical trial. More information about this trial may be accessed at www.clinicaltrials.gov (identifier: NCT04756726).

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; that alternative dosing regimens may increase the therapeutic index of CFT7455 with limited impact on efficacy; 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 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; and regulatory developments in the United States and foreign countries. 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 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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