C4 Therapeutics Announces Positive Data from CFT7455 Phase 1 Trial in Relapsed/Refractory Multiple Myeloma

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Data Support 14 Days On/14 Days Off as Optimal Dosing Schedule; CFT7455 is Well Tolerated with Promising Signs of Anti-Myeloma Activity

Completed Monotherapy Dose Escalation Demonstrates Anti-Myeloma Activity and Immunomodulatory Effects to Support CFT7455 in Combination with Novel Multiple Myeloma Agents and as a Monotherapy Maintenance Option

CFT7455 in Combination with Dexamethasone Results in IMWG Responses at the First Two Dose Levels Studied in Multi-Refractory Multiple Myeloma Patients

Dose Escalation Continues for CFT7455 in Combination with Dexamethasone in Relapsed/Refractory Multiple Myeloma, and as a Monotherapy in non-Hodgkin's Lymphomas; Complete Phase 1 Dose Escalation Data Expected in 2024

C4T to Host Webcast Today at 4:30 pm ET; Webcast Link Available Here

WATERTOWN, Mass., Dec. 12, 2023 (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 clinical data from the ongoing Phase 1 dose escalation portion of its Phase 1/2 clinical trial of CFT7455, a MonoDAC™ degrader of IKZF1/3, for the potential treatment of multiple myeloma (MM) and non-Hodgkin's lymphomas (NHL). These data include results from CFT7455 as a monotherapy for relapsed/refractory (R/R) MM patients, which has completed dose escalation, and interim results from CFT7455 in combination with dexamethasone for R/R MM patients, which continues to enroll patients. C4T also continues to enroll patients in the Phase 1 dose escalation trial exploring CFT7455 as a monotherapy for NHL patients.

"We are excited CFT7455 monotherapy is showing promising signs of anti-myeloma and immunomodulatory activity and anti-myeloma activity when combined with dexamethasone, particularly in patients who have undergone numerous lines of prior therapy for multiple myeloma, including BCMA therapies," said Len Reyno, M.D., chief medical officer of C4 Therapeutics. "We have established 14 days on/14 days off as the optimal dosing schedule, which is consistent with our preclinical data supporting CFT7455 as a rationally designed IKZF1/3 degrader with the potential to offer a new therapy for patients with relapsed/refractory multiple myeloma."

CFT7455 Phase 1 Dose Escalation
The goal of the CFT7455 Phase 1 dose escalation trial is to define the safety profile of CFT7455, determine the maximum tolerated or administered dose, and identify signs of anti-tumor activity in R/R MM and R/R NHL. The Phase 1 dose escalation portion of the trial includes three arms: CFT7455 as a monotherapy for R/R MM patients, which is complete; CFT7455 in combination with dexamethasone for R/R MM patients, which continues to advance through dose escalation; and CFT7455 as a monotherapy for NHL patients, which also continues to advance through dose escalation. The Phase 1 dose escalation portion of the ongoing Phase 1/2 trial has utilized a 14 days on/14 days off dosing schedule within which both daily dosing and Monday/Wednesday/Friday (MWF) dosing were explored.

CFT7455 as a Monotherapy for R/R MM Patients
Monotherapy dose escalation is complete. As of the November 28, 2023 data cutoff date, 22 patients had received CFT7455 as a monotherapy. The maximum dose administered was 75 µg daily for 14 days on/14 days off. A maximum tolerated dose was not defined. Patients were heavily pretreated, with a median of seven prior therapies. The majority of patients (n=12) received prior CAR-T or T-cell engager therapy.

Pharmacokinetic and Pharmacodynamic Results

- Clearance of CFT7455 is consistent with a 48-hour half-life.
- Daily dosing (14 days on/14 days off) resulted in deep IKZF1/3 degradation.
- After day 14, as plasma concentrations of CFT7455 begin to decline, degraded proteins recover through day 28, enabling neutrophil recovery.

Safety and Evidence of Anti-Tumor Effect

- CFT7455 was well tolerated.
- 22 patients were evaluable for safety. The most common adverse events (AEs) Grade 3 or above were neutropenia (n=11), anemia (n=4) and leukopenia (n=4).
- No dose-limiting toxicities (DLTs) resulted in discontinuation of therapy.
- As of the November 28, 2023 data cutoff date, 20 patients were evaluable for evidence of anti-tumor effect.
- Four patients received the maximum dose administered of 75 µg daily. Three patients were

refractory to BCMA therapies. Responses were measured in accordance with the International Myeloma Working Group (IMWG) criteria for multiple myeloma. All four patients achieved Stable Disease (SD) or better and one patient achieved a Partial Response (PR).

Immunomodulatory Results

- CFT7455 induced CD8+ T-cell activation by increasing the effector memory T-cell subset, as required for effective adaptive immunity.
- T-cell activation was observed at well tolerated monotherapy doses, supporting the potential use of CFT7455 in combination with bi-specific T-cell engagers and monoclonal antibody therapies.

CFT7455 in Combination with Dexamethasone for R/R MM Patients
As of the November 28, 2023 data cutoff date, nine patients had received CFT7455 in combination with dexamethasone across two initial dose escalation cohorts (50 µg MWF for 14 days on/14 days off; or 37.5 µg daily for 14 days on/14 days off). Patients were heavily pretreated, with a median of six prior therapies. The majority of patients (n=5) received prior CAR-T or T-cell engager therapy. This arm is ongoing; patients are currently enrolling in either the 62.5 µg escalation cohort or the 37.5 µg expansion cohort.

Safety and Evidence of Anti-Tumor Effect

- CFT7455 in combination with dexamethasone is well tolerated to date.
- The most common AEs Grade 3 or above were consistent with the monotherapy safety signal.
- No AEs have led to dose reductions, discontinuations or DLTs.
- All three patients evaluable for efficacy at 37.5 µg daily achieved SD or better according to IMWG criteria. These assessments include:
    - One patient achieved a Stringent Complete Response (sCR), after initially achieving a Very Good Partial Response (VGPR). This patient was refractory to BCMA therapies.
    - One patient achieved a PR. This patient was refractory to BCMA therapies.
    - One patient achieved SD.

Upcoming Data Presentations for CFT7455
C4T expects to present the following data on CFT7455 in 2024:

- Complete Phase 1 dose escalation data from the ongoing Phase 1/2 clinical trial in R/R MM.
- Complete Phase 1 dose escalation data from the ongoing Phase 1/2 clinical trial in NHL.

C4T Webcast for Analysts and Investors
C4T will host an investor webcast today, December 12, 2023, at 4:30 pm Eastern Time, to discuss the CFT7455 Phase 1 clinical data in relapsed/refractory multiple myeloma. To join the webcast, please visit this link or the “Events & Presentations” page of the Investors section on the company’s website at www.c4therapeutics.com. A replay of the webcast will be archived and available 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 transforms 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™ degrader designed to be highly potent and selective against its intended targets of Ikaros (IKZF1) and Aiolos (IKZF3) and overcome shortcomings of currently approved therapies to treat multiple myeloma (MM) and non-Hodgkin’s lymphoma (NHL). Initial clinical data show CFT7455 is well tolerated, demonstrates anti-myeloma activity and displays evidence of immunomodulatory effects. The optimal dosing schedule for CFT7455 is 14 days on/14 days off. Dose escalation continues in cohorts exploring CFT7455 in combination with dexamethasone for relapsed/refractory MM patients and as a monotherapy for NHL patients. 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; the design and potential efficacy of our therapeutic approaches; the predictive capability of our TORPEDO® platform in the development of novel, selective, orally bioavailable BiDAC™ and MonoDAC™ degraders; the potential timing, design and advancement of our preclinical studies and clinical trials, including the potential timing for and receipt of regulatory authorization related to clinical trials and other clinical development activities including clinical trial commencement; 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 ability to replicate interim or early-stage results from our clinical trials in the results obtained when those clinical trials are completed or when those therapies

complete later stage clinical trials; regulatory developments in the United States and foreign countries; the potential timing for updates on our clinical and research programs; and our ability to fund our future operations. 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 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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