C4 Therapeutics Presents Preclinical Data on CFT7455, a Novel IKZF1/3 Degrader for the Treatment of Hematologic Malignancies, at the AACR Annual Meeting 2021

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– CFT7455 Demonstrated High Cereblon Binding Affinity and Rapid, Deep IKZF1/3 Degradation Enabling Activity across a Panel of Multiple Myeloma Cell Lines Including IMiD-Resistant Models –

– CFT7455 Promotes Sustained Degradation of IKZF1/3 and Durable Anti-tumor Response, Including Regressions in an IMiD-Insensitive Myeloma Tumor Xenograft Model –

– CFT7455 Phase 1/2 Trial in Multiple Myeloma and Non-Hodgkin Lymphomas On Track for 1H 2021 Initiation –

WATERTOWN, Mass., April 10, 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 preclinical data for CFT7455, the Company's lead program, a MonoDAC ^{TM} degrader targeting IKZF1/3 for the treatment of hematologic malignancies. These results, which support clinical evaluation of CFT7455 in multiple myeloma, were delivered as a late-breaking oral presentation during the first session of the American Association for Cancer Research (AACR) Annual Meeting 2021.

"IKZF1/3 proteins are critical dependencies of B cell malignancies including multiple myeloma and subsets of non-Hodgkin's lymphoma," said Stewart Fisher, Ph.D., chief scientific officer of C4 Therapeutics. "We are pleased to share preclinical data demonstrating that potent catalytic IKZF1/3 degradation activity of CFT7455, coupled with optimized pharmacological properties, can result in regression of multiple myeloma xenograft tumors not responsive to approved IMiD therapies. We are optimistic that the *in vitro* and *in vivo* data we saw preclinically will translate into improved, clinically meaningful outcomes for patients and we look forward to initiating our CFT7455 Phase 1/2 clinical trial in the first half of this year."

Summary of Results

C4T conducted *in vitro* studies to confirm CFT7455's intended mechanism. Notable observations include:

- CFT7455 binds with high affinity to the E3 ligase adapter protein, cereblon (Kd = 0.9 nM);
- *In vitro,* CFT7455 treatment results in deep, rapid degradation of IKZF1/3 proteins, resulting in apoptotic cell death; and
- CFT7455 demonstrated broad, potent anti-proliferative activity in a panel of multiple myeloma cell lines.

In mouse xenograft models of IMiD-insensitive multiple myeloma, data further established CFT7455 as a highly potent, catalytic degrader of IKZF1/3, capable of generating anti-tumor activity as a single agent and in combination with dexamethasone. Notable observations include:

- In the H929 myeloma xenograft tumor model, daily oral administration of CFT7455 at 0.1 mg/kg for three weeks led to partial or complete tumor regression, with the latter being durable even after stopping treatment.
- CFT7455 produced deep and durable degradation of IKZF3 in the RPMI-8226 myeloma xenograft tumor model, which is relatively insensitive to pomalidomide. Tumor regression resulted from treatment with CFT7455 in both naïve RPMI-8226 tumors, as well as those previously exposed, but unresponsive, to pomalidomide.
- The combination of CFT7455 and dexamethasone in the RPMI-8226 tumor xenograft model yielded expected improvements in efficacy and survival outcomes in mice bearing RPMI-8226 xenograft tumors, compared to either agent used alone.

Based in part on these results, C4T plans to explore the therapeutic applications of CFT7455 for the treatment of relapsed or refractory multiple myeloma and non-Hodgkin's lymphomas and expects to initiate a Phase 1/2 clinical study of CFT7455 in the first half of 2021.

C4T's AACR Annual Meeting 2021 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™ (Monofunctional Degradation Activating Compound) degrader designed to bind with high affinity to the E3 ligase adapter protein, cereblon, to target and degrade IKZF1/3 for the treatment of hematologic malignancies such as multiple myeloma and non-Hodgkin's lymphoma, including peripheral T cell lymphoma and mantle cell lymphoma. In preclinical studies, CFT7455 has demonstrated potent and selective protein degradation with favorable pharmacological properties.

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 or safety profile of our therapeutic approaches; the potential timing, design and advancement of our preclinical 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 preclinical studies or clinical trials in any future studies or trials; our current resources and cash runway; 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 and conduct of preclinical and clinical studies and other development requirements for our product candidates 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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