Cardiff Oncology Presents Novel Preclinical Data at AACR Annual Meeting 2024 that Supports Ongoing First-line RAS-mutated mCRC Clinical Study

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RAS-mutated mCRC

– In RAS-mutated mCRC, novel preclinical finding demonstrates onvansertib inhibits the tumor's ability to adapt to hypoxia resulting in a significant decrease in both tumor vascularization and growth –

– Enhanced clinical efficacy signal in bev naïve patients in Phase 1b/2 trial is consistent with results of randomized ONSEMBLE trial providing two independent data sets in second-line mCRC validating our strategy to evaluate onvansertib in combination with chemo/bev in RAS-mutated first-line mCRC –

Therapeutic areas outside of RAS-mutated mCRC

– In RAS-wild type mCRC, onvansertib demonstrates antitumor activity in preclinical models as a single agent and in combination with cetuximab, highlighting that onvansertib activity in mCRC can be independent of RAS mutational status –

– In SCLC and ovarian cancer, robust preclinical data underscore onvansertib's activity in combination treatments across multiple tumors –

SAN DIEGO, April 08, 2024 (GLOBE NEWSWIRE) -- Cardiff Oncology, Inc. (Nasdaq: CRDF), a clinical-stage biotechnology company leveraging PLK1 inhibition to develop novel therapies across a range of cancers, today announced the presentation of five abstracts at the American Association for Cancer Research (AACR), taking place from April 5-10, 2024, in San Diego, California. In combination, the abstracts underscore the significant potential of the company's lead molecule onvansertib in metastatic colorectal cancer (mCRC) and other cancers.

"Overall, the totality of our preclinical and clinical data we are presenting at AACR in mCRC is promising and provides scientific validation of our ongoing first-line RAS-mutated mCRC trial, where all patients have no prior exposure to bevacizumab, meaning they are bev naïve," said Mark Erlander, Ph.D., Chief Executive Officer of Cardiff Oncology. "Furthermore, bev naïve patients in our Phase 1b/2 KRAS-mutated mCRC trial were approximately 4 times (73 % vs 19%) more likely to achieve a clinical response compared to bev exposed patients in the dataset presented at AACR. This is consistent with the data we later generated from our randomized ONSEMBLE trial in RAS-mutated mCRC, which serves as a second independent data set reproducing the robust efficacy signal for onvansertib plus standard of care in bev naïve patients. In addition, we are particularly encouraged by our RAS-mutated mCRC preclinical data highlighting onvansertib's ability to inhibit activation of the hypoxia pathway via the regulation of HIF1α. We believe this mechanism acts complementary to bevacizumab, potentially providing an even greater reduction in tumor vascularization when the two agents are combined."

Key highlights from the company's five poster presentations at AACR are below.

A Phase 1b/2 Clinical Study of Onvansertib in Combination with FOLFIRI/Bev Revealed a New Role of PLK1 in regulating the Hypoxia Pathway in KRAS-mutated Metastatic Colorectal Cancer

- Bev naïve patients treated with onvansertib + FOLFIRI/bev demonstrated a significantly greater overall response rate [odds ratio=13.64, p<0.001] and longer PFS [hazard ratio=0.21, p=0.003] compared to bev exposed patients.
- Onvansertib reduced tumor vascularization as a single agent and onvansertib + bev combination resulted in a greater decrease in tumor vascularization.
- *In vitro*, onvansertib inhibited the activation of the hypoxia pathway through the regulation of the transcription factor HIF1α and its downstream targets.
- Collectively the updated clinical and preclinical data further support the ongoing CRDF-004, Phase 2 trial of onvansertib + chemo/bev for the first-line treatment of RAS-mutated mCRC patients, who by definition are bev naïve.

A Phase 2, Randomized, Open-label Study of Onvansertib in Combination with Standard-of-Care (SoC) Versus SoC Alone for First-line Treatment of RAS-mutated Metastatic Colorectal Cancer

- CRDF-004 is a Phase 2 randomized trial generating preliminary safety and efficacy data and evaluating two different doses of onvansertib to confirm an optimal dose. Onvansertib will be added to standard-of-care consisting of FOLFIRI plus bev, or FOLFOX plus bev.
- A total of 90 patients will be randomized in a 1:1:1 ratio to either 20mg of onvansertib plus standard-of-care, 30mg of onvansertib plus standard-of-care, or standard-of-care alone.
- The primary endpoint of the study includes objective response rate (ORR), and the key secondary endpoints include progression-free survival (PFS) and duration of response (DoR).

The PLK1 Inhibitor Onvansertib is Active as Monotherapy and in Combination with Cetuximab in RAS Wild-type Metastatic Colorectal Cancer Patient-derived Xenografts

- Single agent onvansertib successfully induced tumor stasis or regression in 70% (14/20) of the RAS WT mCRC patient-derived xenograft (PDX) models tested. This included both models sensitive to cetuximab (5/7, 71%) and resistant to cetuximab (9/13, 69%).
- Onvansertib in combination with cetuximab induced tumor stasis or regression in 90% (18/20) of the models tested.
- Overall, the antitumor activity of the combination was superior compared to monotherapy with either agent in both cetuximab sensitive and resistant models.

The PLK1 Inhibitor, Onvansertib, Synergizes with Paclitaxel in Small Cell Lung Cancer (SCLC)

- Onvansertib in combination with paclitaxel was well-tolerated and demonstrated superior efficacy over monotherapies in cisplatin sensitive and resistant SCLC PDX models.

- In cisplatin-resistant models, onvansertib plus paclitaxel led to tumor regression, with effects lasting 2 months post-treatment.
- Collectively, these preclinical findings in SCLC and previous data generated in breast cancer suggest that onvansertib in combination with paclitaxel has the potential to become a highly promising combination strategy across multiple cancer indications.

In vivo anti-tumor activity of onvansertib, a PLK1 inhibitor, combined with gemcitabine or carboplatin in platinum-resistant ovarian carcinoma patient-derived xenograft models

- Onvansertib was synergistic in vitro in combination with carboplatin or gemcitabine in an ovarian cancer cell line.
- Both combinations demonstrated antitumor activity in vivo in platinum-resistant ovarian cancer PDX models and were well tolerated.
- These data support the potential of onvansertib to improve SoC treatments of platinum-resistant ovarian cancer patients.

All the abstracts are available on the AACR Online Program and will be published in the online Proceedings of the AACR. Following the presentation, the posters will be posted to the "Scientific Presentations" section of the Cardiff Oncology website.

About Cardiff Oncology, Inc.

Cardiff Oncology is a clinical-stage biotechnology company leveraging PLK1 inhibition, a well-validated oncology drug target, to develop novel therapies across a range of cancers. The Company's lead asset is onvansertib, a PLK1 inhibitor being evaluated in combination with standard-of-care (SoC) therapeutics in clinical programs targeting indications such as RAS-mutated metastatic colorectal cancer (mCRC) and metastatic pancreatic ductal adenocarcinoma (mPDAC), as well as in investigator-initiated trials in small cell lung cancer (SCLC) and triple negative breast cancer (TNBC). These programs and the Company's broader development strategy are designed to target tumor vulnerabilities in order to overcome treatment resistance and deliver superior clinical benefit compared to the SoC alone. For more information, please visit https://www.cardiffoncology.com.

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