

Cardiff Oncology Announces New Preclinical and Clinical Data from Program in KRAS-mutated Metastatic Colorectal Cancer (mCRC) at the ESMO Congress 2022

September 10, 2022

Durable responses to treatment, with a median duration of response (mDoR) of 11.7 months, reported in Phase 1b/2 clinical trial of onvansertib plus FOLFIRI/bevacizumab in second-line KRAS-mutated mCRC

Observed mDoR is supported by preclinical findings that demonstrate onvansertib in combination with irinotecan can overcome intrinsic and refractory resistance to irinotecan in patient-derived xenograft models

Patients with a $\geq 90\%$ decrease in KRAS mutant allele frequency (MAF), a response biomarker, in the first cycle of treatment had significantly higher ORR and longer PFS in Phase 1b/2 trial and an Expanded Access Program (EAP)

SAN DIEGO, Sept. 10, 2022 /PRNewswire/ -- Cardiff Oncology, Inc. (Nasdaq: CRDF), a clinical-stage biotechnology company leveraging PLK1 inhibition to develop novel therapies across a range of cancers, today announced new preclinical and clinical data from its program in KRAS-mutated mCRC. The data are featured in two posters being presented at the European Society for Medical Oncology (ESMO) Congress 2022, which is taking place at the Paris Expo Porte de Versailles in Paris, France, and virtually.

Poster 397P: Early Decreases in KRAS Mutant Allele Frequency (MAF) Predict Clinical Benefit to the PLK1 Inhibitor Onvansertib in Combination with FOLFIRI/bev in 2L Treatment of Metastatic Colorectal Carcinoma (mCRC)

Poster 397P includes updated data (data cut-off date: July 25, 2022), as well as the results of correlative biomarker analyses from a Phase 1b/2 clinical trial of onvansertib plus FOLFIRI/bevacizumab in second-line KRAS-mutated mCRC. Measures of clinical response were compared between subsets of patients defined as KRAS responders or non-responders. KRAS responders were defined as patients with a $\geq 90\%$ decrease in KRAS mutant allele frequency (MAF) in circulating tumor DNA (ctDNA) after one treatment cycle.

"The data from this trial show onvansertib plus FOLFIRI and bevacizumab outperforming historical controls on multiple key endpoints and are highly encouraging," said Heinz-Josef Lenz, MD, FACP, professor of medicine at USC Norris Comprehensive Cancer Center and the trial's principal investigator. "They suggest trial participants with various KRAS mutations experience durable clinical benefits and that the onvansertib-FOLFIRI combination is avoiding the mechanisms that typically drive rapid acquired resistance to the standard-of-care (SoC). This highlights onvansertib's potential to fill a crucial gap in mCRC's therapeutic paradigm, as there are currently limited options available for second line patients. In addition, the significant increases between response rates and progression-free survival in KRAS responders point to changes in MAF as a potential blood-based biomarker that could aid in treatment decisions."

Key data and conclusions presented in the poster include:

Overall response rate (ORR) and median progression-free survival (mPFS) reported in Phase 1b/2 trial substantially exceed those reported in historical control trials

- ORR across all evaluable patients was 35%, with 17 of 48 evaluable patients achieving an objective response and responses have been observed across multiple KRAS variants
- Median duration of response (mDoR) across all evaluable patients was 11.7 months (95% confidence interval (CI): 8.9 – not reached)
- mPFS across all evaluable patients was 9.3 months (95% CI: 7.6 – 13.5)
- Historical control trials of different drug combinations, including the standard-of-care (SOC) of FOLFIRI with bevacizumab, in similar patient populations have shown ORR and mPFS of 5 – 13% and ~4.5 – 5.7 months, respectively¹⁻⁴

KRAS responders showed significantly greater ORR and mPFS compared to non-responders

- ORR in KRAS responders vs. KRAS non-responders: 63.6% (14/22) vs. 8.7% (2/23) ($p = 0.00014$)
- mPFS in KRAS responders vs. KRAS non-responders: 12.6 months vs. 6.0 months ($p = 0.019$)

Poster 366P: The PLK1 Inhibitor Onvansertib Overcomes Irinotecan Resistance in RAS-mutated Metastatic Colorectal Cancer (mCRC) In Vivo and in Patients

Poster 366P includes findings (as of August 5, 2022) from Cardiff Oncology's EAP of onvansertib in KRAS-mutated mCRC, as well as data from murine studies evaluating onvansertib in combination with irinotecan in 6 PDX models of irinotecan-resistant, RAS-mutated CRC. Clinical findings reported in the Expanded Access Program (EAP) were compared between KRAS responders and non-responders. To enroll in the EAP, a patient must have been ineligible for the Phase 1b/2 clinical trial having received prior treatment with irinotecan or failed or progressed on multiple prior lines of standard-of-care therapy. EAP patients are treated with the same treatment regimen (onvansertib 15 mg/m² plus FOLFIRI and bevacizumab) and dosing schedule as patients in the Phase 1b/2 clinical trial.

Scott Kopetz, MD, PhD, FACP, professor, Department of Gastrointestinal Medical Oncology, Division of Cancer Medicine at The University of Texas MD Anderson Cancer Center commented, "Currently available third-line or later treatment options for patients are severely limited, due in large part to the high prevalence of tumors that show resistance to irinotecan. Based on the findings being presented at ESMO, combining onvansertib with the current SOC appears to be an innovative strategy that can overcome irinotecan resistance and address a broad and pressing unmet need. This hypothesis is further supported by onvansertib's mechanism of action, which targets DNA damage repair pathways underlying resistance to irinotecan and other chemotherapeutic agents."

Key findings and conclusions presented in the poster include:

EAP patients with prior irinotecan treatment (43 out of a total of 51 EAP patients) showed clinical benefit following treatment with onvansertib plus FOLFIRI/bevacizumab

- mPFS was 4.04 months (95% CI: 2.96 – 8.38); 6-month PFS rate was 37.3% (95% CI: 24.9 – 55.8)

Of EAP patients with prior irinotecan treatment, KRAS responders had significantly longer PFS compared to non-responders.

- mPFS in KRAS responders vs. KRAS non-responders: 11.18 months vs. 3.25 months (p=0.0014)

The combination of onvansertib and irinotecan showed significantly greater anti-tumor activity compared to onvansertib monotherapy in 5 of 6 tested PDX models of irinotecan-resistant, RAS-mutated CRC.

The ESMO posters are currently available for viewing on the congress's virtual platform and will also be presented by Drs. Lenz and Kopetz during Poster Sessions 8 and 7, respectively, on September 11, 2022. Following the congress, the posters will be available on the "Scientific Presentations" section of the Cardiff Oncology website at <https://cardiffoncology.com/scientific-presentations/>.

Clinical and Corporate Update Conference Call and Webcast

Cardiff Oncology will host a webcast and conference call to provide a clinical and corporate update to the investment community on Monday, September 12, 2022 at 4:30 PM ET. The event will feature discussions on the planned development pathway for onvansertib in KRAS-mutated metastatic colorectal cancer and updates on other development programs. In addition, company management will provide data updates from ongoing clinical trials. To access the call, please dial 1-877-407-9208 (domestic) or 1-201-493-6784 (international) and refer to conference ID 13731618. The conference call will also be webcast live and a link to the webcast can be accessed [here](#). A replay of the webcast will be available by visiting the "[Events](#)" section of the Cardiff Oncology website after its conclusion.

About the Phase 1b/2 Trial of Onvansertib in the Second-Line Treatment of KRAS-mutated mCRC

This is a multi-center, single-arm, Phase 1b/2 trial of onvansertib in combination with standard-of-care FOLFIRI and Avastin® (bevacizumab) to evaluate the safety and preliminary efficacy of the combination regimen in the second-line treatment of patients with KRAS-mutated mCRC. The trial, *A Phase 1b/2 Study of Onvansertib (PCM-075) in Combination with FOLFIRI and Bevacizumab for Second-Line Treatment of Metastatic Colorectal Cancer in Patients with a KRAS Mutation*, is enrolling patients with histologically confirmed metastatic and unresectable colorectal carcinoma harboring a KRAS mutation. Patients must also have experienced disease progression or treatment intolerance to first-line treatment with fluoropyrimidine and oxaliplatin (FOLFOX or CapeOx) with or without bevacizumab to be eligible. The trial is being conducted at the following cancer centers across the U.S.: USC Norris Comprehensive Cancer Center, The Mayo Clinic (Arizona, Rochester, and Jacksonville), Kansas University Medical Center (KUMC), CARTI Cancer Center and Inova Schar Cancer Institute. For more information on the trial, please visit [NCT03829410](#).

About the EAP for Onvansertib in KRAS-mutated mCRC

Sometimes called "compassionate use", expanded access is a potential pathway for a patient with a serious or life-threatening disease to gain access to an investigational drug for treatment outside of a clinical trial, particularly when no comparable or satisfactory alternative therapy options are available. The Cardiff Oncology EAP in KRAS-mutated mCRC is using the same combination treatment regimen (onvansertib 15 mg/m² + FOLFIRI and bevacizumab) and dosing schedule as the ongoing Phase 1b/2 clinical trial and is intended for patients that have progressed on prior therapy and do not meet the second line eligibility criteria for enrollment in the clinical trial. The program has reached capacity and is no longer open to enrollment.

References:

1. Giessen et al., *Acta Oncologica* 2015, 54: 187-193
2. Cremolini et al., *Lancet Oncol* 2020, 21: 497–507
3. Antoniotti et al., *Correspondence Lancet Oncol* June 2020
4. Bennouna et al., *Lancet Oncol* 2013; 14: 29–37

About Cardiff Oncology, Inc.

Cardiff Oncology is a clinical-stage biotechnology company leveraging PLK1 inhibition to develop novel therapies across a range of cancers. Our lead asset is onvansertib, a PLK1 inhibitor we are evaluating in combination with standard-of-care (SOC) therapeutics in clinical programs targeting indications such as KRAS-mutated metastatic colorectal cancer, metastatic pancreatic ductal adenocarcinoma, and metastatic castrate-resistant prostate cancer. These programs and our broader development strategy are designed to target tumor vulnerabilities in order to overcome treatment resistance and deliver superior clinical benefit compared to the SOC. For more information, please visit <https://www.cardiffoncology.com>.

Forward-Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified using words such as "anticipate," "believe," "forecast," "estimated" and "intend" or other similar terms or expressions that concern Cardiff Oncology's expectations, strategy, plans or intentions. These forward-looking statements are based on Cardiff Oncology's current expectations and actual results could differ materially. There are several factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results; our clinical trials may be suspended or discontinued due to unexpected side effects or other safety risks that could preclude approval of our product candidates; risks related to business interruptions, including the outbreak of COVID-19 coronavirus, which could seriously harm our financial condition and increase our costs and expenses; uncertainties of government or third party payer reimbursement; dependence on key personnel; limited experience in marketing and sales; substantial competition; uncertainties of patent protection and litigation; dependence upon third parties; and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. There are no guarantees that our product candidate will be utilized or prove to be commercially successful. Additionally, there are no guarantees that future clinical trials will be completed or successful or that any precision medicine therapeutics will receive regulatory approval for any indication or prove to be commercially successful. Investors should read the risk factors set forth in Cardiff Oncology's Form 10-K for the year ended December 31, 2021, and other periodic reports filed with the Securities and Exchange Commission. While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and Cardiff Oncology does not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances.

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