

Cardiff Oncology in Collaboration with MIT Presents Gene Signature Analyses Data Identifying Androgen-Independent Mechanism for Onvansertib-Abiraterone Synergy in mCRPC

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- Onvansertib and the androgen receptor (AR) signaling inhibitor abiraterone synergize in an AR-independent manner in in-vitro and in-vivo metastatic castrate-resistant prostate cancer (mCRPC) models
- AR-independent effects of abiraterone include the upregulation of a mitosis-related gene signature and disruption of mitotic spindle orientation, rendering cancer cells more susceptible to onvansertib induced cell death
- Ongoing analyses of archived tissue from patients enrolled in the ongoing Phase 2 mCRPC trial aims to determine if the identified gene signature is predictive of patient response to onvansertib-abiraterone combination therapy
- The identified gene signature could support a precision medicine approach to treatment by enabling the identification of patients most likely to benefit from the combination

SAN DIEGO, April 10, 2021 /PRNewswire/ -- **Cardiff Oncology, Inc.** (Nasdaq: CRDF), a clinical-stage biotechnology company developing onvansertib to treat cancers with the greatest medical need for new treatment options, including KRAS-mutated colorectal cancer, pancreatic cancer and castrate-resistant prostate cancer, in collaboration with scientists in the Center for Precision Cancer Medicine at the Massachusetts Institute of Technology (MIT), today announced that new gene signature and mechanistic analyses related to its ongoing Phase 2 trial of onvansertib in metastatic castrate-resistant prostate cancer (mCRPC) were featured in a virtual oral poster presentation at the American Association for Cancer Research (AACR) Annual Meeting 2021.

Analyses presented in the poster suggest that the androgen receptor signaling inhibitor (ARSi) abiraterone sensitizes certain prostate cancer cells to onvansertib by upregulating a set of mitosis related genes and disrupting mitotic spindle orientation. These results are consistent with previous findings showing that onvansertib and abiraterone synergize in an androgen receptor (AR)-independent manner in-vitro and in-vivo.

"The latest results from our collaborative studies with Cardiff Oncology provide important insight into the mechanisms of synergy between onvansertib and abiraterone in mCRPC," said Michael B. Yaffe, M.D., Ph.D., David H. Koch Professor of Science and Professor of Biology and Biological Engineering at the Massachusetts Institute of Technology. "Data showing a cellular mechanism for how these two compounds synergize in an AR-independent manner provide a strong scientific rationale for Cardiff Oncology's ongoing Phase 2 trial and explain how the addition of onvansertib can improve clinical outcomes in patients showing initial abiraterone resistance. We have also identified a set of genes that appear to drive this mechanism of onvansertib-abiraterone synergy as well as predict patient response and archived clinical trial tissue from patients enrolled in the ongoing trial are being analyzed to confirm this hypothesis."

Mark Erlander, Ph.D., chief executive officer of Cardiff Oncology added, "The identification of a gene signature that appears to predict patient response to onvansertib-abiraterone combination therapy is encouraging, as is the finding that this signature is enriched in mCRPC patients with the known molecular basal tumor subtype. We look forward to continuing to work with our collaborators at MIT and Decipher Biosciences to validate this gene set as a predictive response biomarker. Validation of such a biomarker would be significant, as it would allow us to take a precision medicine approach to future trials by enabling the identification of patients most likely to benefit from therapy with onvansertib."

Highlights from the AACR presentation include:

- Inhibition of polo-like kinase 1 (PLK1) sensitizes CRPC cells to abiraterone, but not the ARSi enzalutamide, indicating that abiraterone and PLK1 inhibitors synergize in an AR-independent manner.
- In vitro experiments and RNA sequencing analyses indicate that abiraterone's AR-independent effects include the disruption of mitotic spindle orientation and the induction of a mitosis related gene signature.
- Data suggest that the identified mitosis related gene signature may be predictive of patient response to onvansertib-abiraterone combination therapy, a hypothesis that is being further assessed in an ongoing Phase 2 trial evaluating the all-oral regimen of onvansertib, abiraterone and prednisone in mCRPC patients.
- The identified mitosis related gene signature was found to be significantly enriched in the basal molecular subtype of prostate cancer.

The virtual poster, "*The selective polo-like kinase (Plk1) inhibitor onvansertib and the antiandrogen abiraterone synergistically kill cancer cells through disruption of mitosis independently of androgen receptor signaling*" by Patterson et al, is available for on-demand viewing on the AACR Annual Meeting 2021 e-poster website and is also posted on the "Scientific Presentations" section of the Cardiff Oncology website at <https://cardiffoncology.com/scientific-presentations/>.

About the Phase 2 Trial of Onvansertib in Metastatic Castrate-Resistant Prostate Cancer

This trial is a Phase 2 open-label study of onvansertib in combination with abiraterone and prednisone, all administered orally, in patients with metastatic castration-resistant prostate cancer showing signs of early progressive disease (demonstrated by two rising prostate-specific antigen values separated by at least one week with no or minimal symptoms) while on Zytiga®/prednisone therapy. The primary efficacy endpoint is the proportion of patients achieving disease control after 12 weeks of study treatment, as defined by a lack of prostate-specific antigen (PSA), radiographic, or symptomatic progression. The trial is being conducted by Beth Israel Deaconess Medical Center (BIDMC), Dana-Farber Cancer Institute (DFCI), and Massachusetts General Hospital Cancer Center (MGH). David Einstein, M.D., Genitourinary Oncology Program at BIDMC, is the principal investigator for the trial. For more information on the trial, please visit <https://www.clinicaltrials.gov/ct2/show/NCT03414034>.

About Cardiff Oncology, Inc.

Cardiff Oncology is a clinical-stage biotechnology company with the singular mission of developing new treatment options for cancer patients in

indications with the greatest medical need. Our goal is to overcome resistance, improve response to treatment and increase overall survival. We are developing onvansertib, a first-in-class, third-generation Polo-like Kinase 1 (PLK1) inhibitor, in combination with standard-of-care chemotherapy and targeted therapeutics. Our clinical development programs incorporate tumor genomics and biomarker technology to enable assessment of patient response to treatment. We have three clinical programs currently in process: a Phase 1b/2 study of onvansertib in combination with FOLFIRI/Avastin® (bevacizumab) in KRAS-mutated metastatic colorectal cancer (mCRC); a Phase 2 study of onvansertib in combination with Zytiga® (abiraterone)/prednisone in metastatic castration-resistant prostate cancer (mCRPC); and a Phase 2 study of onvansertib in combination with decitabine in relapsed or refractory acute myeloid leukemia (AML). A new Phase 2 trial of onvansertib in combination with nanoliposomal irinotecan, leucovorin and fluorouracil for the second-line treatment of patients with metastatic pancreatic ductal adenocarcinoma (PDAC) is planned for initiation in the first half of 2021. 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 by the use of 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 a number of 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; our ability to develop tests, kits and systems and the success of those products; regulatory, financial and business risks related to our international expansion and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. There are no guarantees that any of our technology or products 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, 2020, 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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