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Cardiff Oncology, Inc. (CRDF: NASDAQ)

CRDF: Initiating Coverage – Combination Therapy Elicits Superior Response

Our valuation relies on a DCF model and a 15% discount rate applied to our cash flow estimates. Additionally, we apply a success probability of 60% to the onvansertib program in metastatic colorectal cancer (mCRC). The likelihood recognizes regulatory and commercialization risks. The model includes contributions from the United States and the developed world.

Current Price (12/8/2025)	$2.34
Valuation	**$8.50**

INITIATION

Cardiff is a clinical-stage, oncology-focused biotechnology company developing onvansertib against solid tumors including subsets of colorectal (CRC), pancreatic, lung and breast cancers. The company's primary indication is first line metastatic CRC in patients with Rat Sarcoma (RAS) mutations.

Onvansertib is an oral Polo-like kinase 1 (PLK1)-selective inhibitor that has synergies with bevacizumab & various chemotherapy regimens. It is the subject of a Ph2 dose confirmation trial and is anticipated to begin a Ph3 study in 2026. PLK1 is associated with the cell cycle and when dysregulated can allow for uncontrolled mitosis. When inhibited, the cell cycle can be arrested & synthetic lethality can occur especially in combination with other anti-angiogenesis agents and chemotherapy.

While the lead target is in mCRC, onvansertib has potential in other indications. Combination studies with chemotherapy, checkpoint and PARP inhibitors may emerge in future iterations.

SUMMARY DATA

52-Week High	**5.64**
52-Week Low	**1.90**
One-Year Return (%)	**-4.1**
Beta	**1.4**
Average Daily Volume (sh)	**769,701**
Shares Outstanding (mil)	**67.4**
Market Capitalization ($mil)	**157.7**
Short Interest Ratio (days)	**19.8**
Institutional Ownership (%)	**34.3**
Insider Ownership (%)	**6.0**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2025 Estimate	**N/A**
P/E using 2026 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of USD)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2024	$0.2 A	$0.2 A	$0.2 A	$0.2 A	$0.7 A
2025	$0.1 A	$0.1 A	$0.1 A	$0.1 E	$0.4 E
2026					$0.7 E
2027					$0.7 E

Earnings per Share

	Q1	Q2	Q3	Q4	Year
2024	-$0.30 A	-$0.27 A	-$0.23 A	-$0.24 A	-$1.00 A
2025	-$0.20 A	-$0.21 A	-$0.17 A	-$0.18 E	-$0.76 E
2026					-$0.81 E
2027					-$0.77 E

INITIATION

We are initiating coverage of Cardiff Oncology, Inc. (NASDAQ: CRDF) with a valuation of $8.50 per share. This value is based on our estimates for successful development and commercialization of onvansertib for first line treatment of patients with metastatic colorectal cancer (mCRC). Onvansertib is a Polo-Like kinase 1 (PLK1) inhibitor and the subject of a Phase II study which has reported favorable efficacy results. An update on the program is expected in 1Q:26 where further clarity will be provided on the design of a registrational Phase III trial that will support accelerated and full approval.

Cardiff's clinical resources are focused on the indication in mCRC; however, there are investigator-sponsored studies that are evaluating other indications. This includes the University of Kansas Medical Center studies in metastatic pancreatic ductal adenocarcinoma (mPDAC), University of Maryland studies in small cell lung cancer (SCLC) and Dana Farber Cancer Institute work in triple negative breast cancer (TNBC). While we do not expect Cardiff to pursue these in the near term, the indications may become candidates when the mCRC indication has exited the clinic.

Polo-Like Kinase 1 is a serine/threonine kinase enzyme that plays a central role in cell division. If PLK1 is dysregulated it can drive cancer by promoting excessive cell proliferation and overriding cell cycle checkpoints. Patients with high PLK1 expression in tumors have a poor prognosis. Blocking the expression of PLK1 can inhibit the proliferation of tumor cells and induce apoptosis especially in combination with other therapies. This has led to development of numerous inhibitors of the enzyme including onvansertib. Onvansertib builds upon the science underlying previously developed Polo-Box Kinase inhibitors by narrowing its specificity to the PLK1 enzyme. It offers fewer off-target effects than previous generations of PLK inhibitors which were associated with poor tolerability. No other PLK inhibitors have been approved.

We anticipate that the onvansertib mCRC program will begin a Phase III registrational study next year and generate sufficient data to submit a new drug application by 2029. Following FDA review, approval could be granted by 2030 in the United States. We anticipate registrational submissions in other developed regions around the world in subsequent years. Our model assumes approvals in the EU, Asia, Oceania and other countries in 2031 and beyond. We forecast that an established pharmaceutical company will either buy the company or license global commercialization rights to onvansertib and assume commercialization activities.

Cardiff has demonstrated clinical activity and initial safety for onvansertib and is in the process of developing a Phase III study with the FDA that will demonstrate further efficacy and satisfy requirements for both accelerated and full approval. Data to date has shown that both 20 mg and 30 mg doses of onvansertib in combination with bevacizumab and chemotherapy produces a better overall response rate (ORR) and progression free survival (PFS) compared to standard of care. If these results are replicated in a Phase III study, we expect FDA approval following the achievement of the study's accelerated endpoints.

Cardiff is working closely with partners such as Pfizer to develop onvansertib. Pfizer initially invested in Cardiff in 2021 through its Breakthrough Growth Initiative program. It provided $15 million in capital and a Pfizer representative to participate on Cardiff's Scientific Advisory Board. This investment gives Pfizer the right of first access to data prior to publication and could potentially set up this large pharmaceutical company to be an acquiror. In 2023, Pfizer took another step closer to Cardiff by having Pfizer Ignite's clinical development infrastructure provide its expertise to run onvansertib's mCRC trial.

Despite being the 3rd or 4th most common cancer around the globe and in the US, mCRC represents an unmet need especially in the metastatic setting where mortality is high and approved therapies provide progression free survival (PFS) of around a year or less. The addressable market for onvansertib in the current setting for mCRC is just under 30,000 in the United States and about 84,000 in the developed world.

Cardiff has a strong balance sheet with sufficient capital to support the completion of its Phase II trial and begin its registrational Phase III. With over $60 million at the beginning of 4Q:25 and a cash burn rate of about $40 million per year, we see sufficient funds available to support company operations into 2027. In addition to strong relationships with the banking community, Cardiff also has access to an at-the-market (ATM) facility with Jefferies that can augment registered offerings at low cost.

We expect further updates from Cardiff in the new year as Phase II mCRC data continue to mature and as the team has an opportunity to meet with the FDA to design a registrational trial. Assuming the two parties can agree on next

steps, we anticipate the clinical trial to generate registrational data by 2029 which will be subsequently submitted to the FDA for accelerated approval.

Key reasons to own Cardiff Oncology shares:

- **Onvansertib has demonstrated remarkable overall response rate (ORR) in bevacizumab naïve mCRC**
  - **Prior trial in second line KRAS-mutated mCRC showed a material improvement in ORR in combination with standard of care**
    - **ORR of 77% & median PFS of 14.9 months**[1]
    - **Compares with standard of care 2nd line of 20% ORR & PFS of 7 months**
  - **Addresses gap in effective treatments for RAS-mutated mCRC**
  - **Mechanism of action inhibits angiogenesis cascade**
  - **Dose dependent response**
  - **Agent is highly specific to PLK1 with low off target binding affinity**
  - **Brings new treatment to indication lacking innovation for last 20 years**
- **Colorectal cancer is 3rd or 4th (Global and US) most common cancer**
  - **154,000 estimated new cases of CRC in 2025**
  - **Addressable market is approximately 19% of the total**
- **Adverse event profile for combination onvansertib in similar to standard of care**
- **Onvansertib expected to begin registrational Phase III trial 1Q:26**
  - **Designed for accelerated and full approval**
  - **FDA awarded Fast Track designation**
- **Multiple efficacy surrogates predict long term outcome**
  - **Early tumor shrinkage**
  - **Depth of response**
- **Balance sheet provides sufficient cash to support operations until 2027**
- **Robust intellectual property**
  - **Patent portfolio addressing multiple indications and combination therapies**
  - **Patents extend until 2043 with eligibility for five years of patent term extension**

In this initiation report on Cardiff Oncology, we provide the information necessary for an investor to evaluate the company and determine whether or not it is an appropriate investment based upon their tolerance for reward and risk. In the following sections we define the use of targeted therapy in oncology and dive into PLK1 inhibitors and how they work in combination with other agents. We examine they ways in which PLK1 inhibitors differ from other types of targeted therapy and how onvansertib specifically addresses an unmet need in RAS-mutated mCRC.

The report follows with a review of Cardiff's clinical trials for onvansertib in mCRC and summarizes endpoints and safety metrics. The review highlights the unexpected and serendipitous finding that bevacizumab-naïve patients in the second line setting perform better than patients that had received the VEGF inhibitor as part of their prior first line therapy. After the introduction to onvansertib, we take a thorough look at colorectal cancer including the most important types, the incidence and prevalence of the disease, risk factors, screening, symptoms, diagnosis and standard of care. The next section introduces peers and competitors in the space who have developed other PLK1 or Polo Box domain inhibitors or are pursuing new therapies in mCRC.

The report then examines Cardiff's corporate history and milestones achieved, followed by a review of 2025 financial performance. The next section discusses risks faced by life sciences companies in general and for those at the smaller end of the spectrum. This includes financial, partner, regulatory, manufacturing and other risks. The final section of our report discusses the data and assumptions underlying our valuation for onvansertib in first-line, RAS-mutant metastatic colorectal cancer. Our work generates a valuation of $8.50 per share.

[1] Ahn, D. *et al*. Onvansertib in Combination With Chemotherapy and Bevacizumab in Second-Line Treatment of KRAS-Mutant Metastatic Colorectal Cancer: A Single-Arm, Phase II Trial. Gastrointestinal Cancer. October 2024.

Targeted Therapies in Cancer

Targeted therapy is a type of precision or personalized medicine that treats cancer by interfering with specific molecules, proteins, genes or pathways that are critical for cancer cell growth and survival. Unlike traditional chemotherapy, which acts broadly on rapidly dividing cells, targeted therapies focus on features that are primarily found in cancer cells, thereby minimizing damage to normal, healthy cells.[2]

Targeted therapy blocks the growth of cancer cells by interfering with specific features, changes, mutations or substances needed for carcinogenesis and tumor growth. This is in contrast to chemotherapy which attacks all rapidly dividing cells. This precision approach represents a significant advancement in oncology, allowing for more personalized treatment strategies based on the molecular characteristics of individual tumors.[3]

There are a variety of mechanisms that fall under the heading of targeted therapies. This includes interference with growth signals, inducing apoptosis, starving tumors of blood supply, delivering a toxic payload and activating immune responses among other approaches. These are achieved through signal transduction inhibitors, growth factor receptor blockers, angiogenesis inhibitors, epigenetic modulators, hormone pathway inhibitors, DNA damage response (DDR) modulators and other methods.

Biomarkers are commonly used to determine whether or not a patient is appropriate for a type of targeted therapy and can indicate which patients are most likely to benefit. Biomarker guided treatment allows oncologists to match patients with therapies based on their tumor's unique molecular characteristics. Some of the most common actionable targets include EGFR, ALK, ROS1, BRAF, MET, KRAS, NTRK, RET, HER2 and PD-L1. A 2021 study showed that using biomarkers to guide treatment increased overall survival by 8.5% and improved treatment discontinuation compared with non-adherent patients.[4] Beyond identifying patients that should benefit from certain therapies, biomarkers can also help patients avoid therapies that are unlikely to be effective. This can improve patient quality of care, apply appropriate therapies sooner and reduce cost.[5]

Targeted therapies avoid many of the severe side effects associated with traditional cancer treatments such as surgery, radiation and chemotherapy. Targeted therapies are non-invasive, have fewer systemic and off target effects, avoid radiation exposure, nausea and hair loss and reduce immune system effects. However, this class presents other side effects which include skin and nail changes, cardiovascular impacts, gastrointestinal issues and immune related effects. In most cases the reactions subside after treatment ends.

While targeted therapies have generated superior results compared with chemotherapy, radiotherapy and surgery, the cancer can develop resistance to targeted therapies and patients can relapse. To overcome this eventuality, combination approaches are commonly used to attack the cancer from multiple directions and reduce the likelihood of recurrence and resistance. Success of combination approaches in targeted cancer therapy relies on the basic idea that cancer uses multiple redundant survival pathways and that targeting only one often leads to resistance. Therefore, pursuing the disruption of several pathways (or mechanisms) at once can produce deeper, more durable responses. Tumor heterogeneity, escape via alternative pathways and secondary mutations are some of the ways cancer cells persist. Approaches that add immunotherapy can take advantage of agents that make tumors more visible to the immune system and other approaches that employ chemotherapy, sensitize tumors to DNA damage or deliver cytotoxic agents.

Despite the benefits of combination approaches, there are additional risks and considerations. These include toxicity overlap where cumulative adverse effects can affect performance, complex dosing that balances multiple therapies, cost of simultaneous and expensive medicines, and identifying patients that will be most receptive. Many side effects can be addressed through the use of molecular profiling and biomarker analysis. Monitoring, risk management and collaboration with other medical specialties on the treatment team can also minimize problems.

There are several types of targeted therapies. In terms of molecule type, they can be small molecules, monoclonal antibodies (mAbs), peptides and proteins, cell-based therapies and other molecules. There are a variety of classes and mechanisms of action represented by the group. This includes tyrosine kinase inhibitors (TKIs) such as epidermal growth factor receptor (EGFR) inhibitors that block abnormal signaling proteins, vascular endothelial growth

[2] National Institute of Health, National Cancer Institute. Targeted Therapy to Treat Cancer. Accessed October 2025.
[3] American Cancer Society. Targeted Therapy. Accessed October 2025.
[4] John, A., *et al*. Clinical Impact of Adherence to NCCN Guidelines for Biomarker Testing and First-Line Treatment in Advanced Non-Small Cell Lung Cancer (aNSCLC) Using Real-World Electronic Health Record Data. Advances in Therapy. February 2021.
[5] Lawler, M., *et al*. Empowering effective biomarker-driven precision oncology: A call to action. European Journal of Cancer. September 2024.

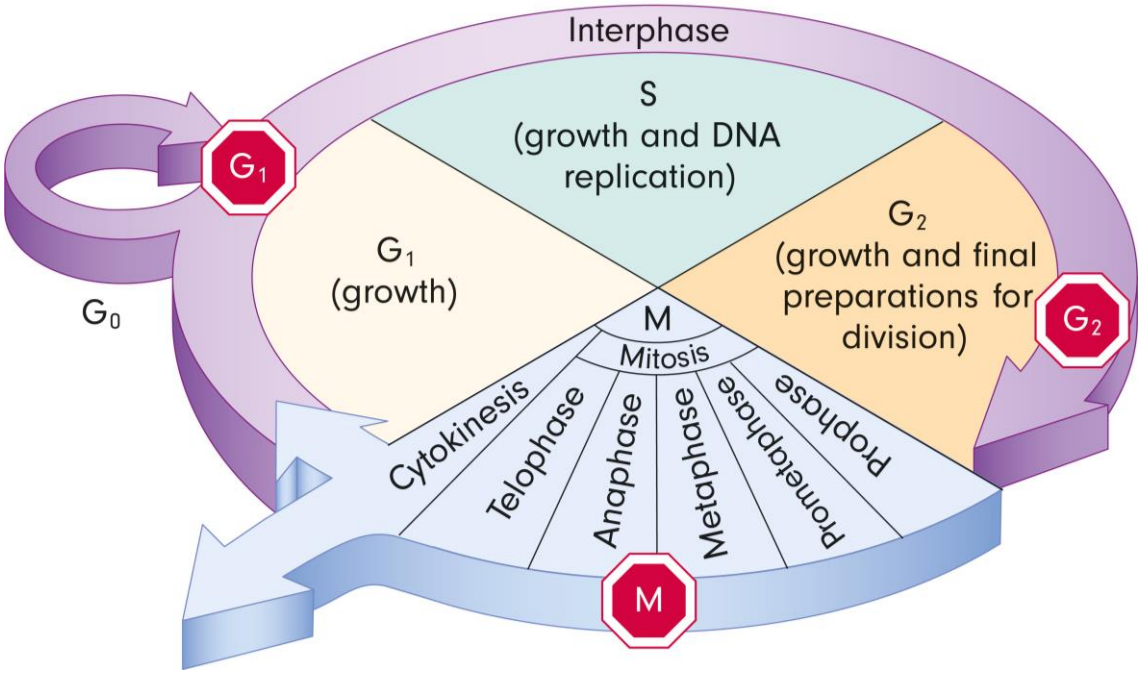
factor (VEGF) inhibitors which prevent the angiogenic signaling cascade, human epidermal growth factor receptor 2 (HER2) targeting mAbs which block downstream growth signals, BCR-ABL fusion protein inhibitors which stop the growth signaling cascade, B-Raf (BRAF) proto-oncogene and serine/threonine kinase inhibitors among many others. Targeted therapies can also be developed into antibody-drug conjugates (ADCs) which link a mAb with a cytotoxic drug to precisely target the cells to be destroyed.

Polo-Like Kinase I (PLK1) Inhibitors

The Polo-Like Kinase I (PLK1) inhibitor represents an important member of the targeted therapy class. The target was first identified in the 1990s during a search for human homologs stemming from work conducted on *Drosophila melanogaster*, the common fruit fly.[6] The work defined PLK1 as a serine/threonine kinase[7] enzyme that plays a central role in cell division. The work found that PLK1 regulates the various steps in the mitotic process. PLK1 has related protein kinases designated PLK2, PLK3, PLK4 and PLK5[8] that are involved in mitosis, DNA damage response and differentiation.

During a normal cell cycle, PLK1 becomes active in late G2 and M phase, orchestrating events that ensure successful chromosome segregation and cell splitting. PLK1 is required for initiating mitosis, proper formation of the mitotic spindle, centrosome maturation and separation, the transition from metaphase to anaphase, and the final steps of cell division (cytokinesis). Continuing the musical metaphor, PLK1 is the conductor that ensures the cell successfully divides and is a key checkpoint kinase for cell cycle progression. PLK1 is expressed in dividing cells and plays a crucial role in mitosis. It is expressed at extremely low levels in quiescent cells and rises sharply during G2/M. It also affects DNA replication, apoptosis and cellular metabolism.[9] PLK1 is overexpressed in many human tumors and is associated with aggressive cancer progression and poor patient prognosis.[10]

Exhibit I – Cell Cycle Phases



Source: Shutterstock. Image 1288735681

PLK1 Activity

In quiescent cells, PLK1 is largely inactive and very low or undetectable in G0 and G1 stages. Cancerous cells, however, overexpress PLK1 and are dysregulated. This overexpression can drive cancerous transformation by

[6] Golsteyn, R.M., *et al*. Cell cycle analysis and chromosomal localization of human Plk1, a putative homologue of the mitotic kinases Drosophila polo and Saccharomyces cerevisiae Cdc5. Journal of Cell Science. June 1994.
[7] A kinase is an enzyme (a biological catalyst) that adds a phosphate group to another molecule, a process called phosphorylation. This action changes the activity of the molecule, often turning it on or off, and plays a crucial role in cell signaling, metabolism, and other cellular processes. For example, many cancer drugs target specific protein kinases involved in cancer cell growth.
[8] Chiappa, M., *et al*. Present and Future Perspective on PLK1 Inhibition in Cancer Treatment. Frontiers in Oncology. June 2022.
[9] Chapagai, D., *et al*. Structural regulation of PLK1 activity: implications for cell cycle function and drug discovery. Cancer Gene Therapy. May 2025.
[10] Liu, Z., *et al*. PLK1, A Potential Target for Cancer Therapy. Translational Oncology. November 2016.

promoting excessive cell proliferation and by overriding cell cycle checkpoints (like the spindle assembly checkpoint or DNA damage checkpoint). This leads to genomic instability, a hallmark of cancer. PLK1 is also a modulator of DNA replication, DNA damage response (DDR), G2 DNA-damage checkpoint, chromosome dynamics, and microtubule dynamics by its interaction with and phosphorylation of several key factors involved in these pathways.

Clinical studies have found that high PLK1 expression in tumors is associated with poor prognosis. Patients whose tumors overproduce PLK1 often have lower disease-free and overall survival, likely reflecting the importance of PLK1 in driving unchecked proliferation. Some of the impacts of PLK1 include:[11]

- Inhibition of cell death pathways such as apoptosis
- Associated with low immune cell infiltration and antitumor activity
- Inhibition of NF-κB transcription, which triggers cytokines essential to inflammation and immunity
- Overexpression in many cancer types

The recognition that PLK1 is overexpressed in many human cancers catalyzed intense interest in the protein as a therapeutic target. Immunohistochemical and transcriptomic analyses demonstrated elevated PLK1 expression in melanoma, breast, ovarian, thyroid, colon, prostate, pancreatic, head and neck and non-small cell lung cancers, as well as non-Hodgkin lymphomas. High PLK1 expression correlates with poor prognosis, decreased survival rates, tumor grade and metastatic potential across multiple cancer types.[12,13,14]

PLK1 Inhibition

Work began to characterize PLK1 as a target for cancer therapy in the early 1990s.[15] By the late 1990s and early 2000s, proof-of-concept experiments demonstrated that inhibition (using RNAi, antisense, or early small-molecule tools) could suppress cancer cell growth or induce apoptosis in tumor cells, while leaving non-malignant cells relatively unaffected.[16,17] This work showed that inhibition of PLK1 could lead to death of cancer cells by interfering with multiple stages of mitosis making it a valuable target for therapy. Researchers compared a patient's overall survival (OS) measured by PLK1 expression. They found that there was a positive correlation between lower PLK1 expression level and OS.

The Mechanism

In cancer cells, PLK1 overexpression drives unchecked proliferation and can inactivate tumor suppressors (PTEN)[18] or stabilize oncogenes (MYC)[19] thereby promoting tumor growth. PLK1 inhibition reverses these oncogenic processes, leading to cell-cycle arrest and apoptosis in rapidly dividing cells.[20] Most clinical PLK1 inhibitors are adenosine triphosphate (ATP)-competitive small molecules that bind the kinase domain, blocking PLK1's catalytic activity. By occupying the ATP-binding pocket, these drugs prevent PLK1 from phosphorylating its substrates, thereby halting cells in the G_2/M phase of the cell cycle. This leads to cell death. In the combination sphere, PLK1 blockade can enhance chemotherapy sensitivity and increase tumor immunogenicity.[21,22]

Previous PLK1 Inhibitors

While there were a number of candidates pursuing PLK targets, many of them were pan inhibitors. This includes Boehringer Ingelheim's BI2536 and volasertib as well as other sponsors' rigosertib and plogosertib. One of the reasons why some of these candidates failed was their lack of specificity. The primary limitation faced by this class was the high structural similarity of the ATP binding pocket across all kinases. Early PLK1 inhibitors often exhibited insufficient isoform selectivity, leading to the concurrent inhibition of PLK2 and PLK3. Evidence suggests that PLK2

[11] Jayachandran, P., *et al*. Pan-RAS inhibitors and polo-like kinase 1: promising targets in colorectal cancer. Oncogene. July 2025.
[12] Cholewa, B.D., *et al*. The role of polo-like kinase 1 in carcinogenesis: cause or consequence? Cancer Research. November 2013.
[13] Gheghiani, L., Zheng, F. The Dark Side of PLK1: Implications for Cancer and Genomic Stability. Oncotarget. 2023.
[14] Takai, N., *et al*. Polo-like kinase (PLK) expression in endometrial carcinoma. Cancer Letters August 2001.
[15] Holtrich, U., *et al*. Induction and down-regulation of PLK, a human serine/threonine kinase expressed in proliferating cells and tumors. Proceedings of the National Academy of Sciences. March 1994.
[16] Zhixian, L, *et al*. PLK1, A Potential Target for Cancer Therapy. Translational Oncology. November 2016.
[17] Degenhardt, Y., Lampkin, T. Targeting Polo-like Kinase in Cancer Therapy. Clinical Cancer Research. January 2010.
[18] PTEN (Phosphatase and TENsin homolog) is an important tumor suppressor genes in human cancer. Its main role is to keep cell growth under control by acting as a brake on a major survival and proliferation pathway called PI3K/AKT/mTOR.
[19] MYC (often referring to c-MYC) is one of the most important and powerful oncogenes in human cancer. It encodes a transcription factor that controls 10–15% of all human genes, making it a master regulator of cell growth. When MYC is overexpressed, amplified or dysregulated, it drives aggressive tumor behavior, uncontrolled proliferation, metabolic rewiring and genomic instability.
[20] Synapse. What are PLK inhibitors and how do they work? June 2024.
[21] Wang, W., *et al*. PLK1 in cancer therapy: a comprehensive review of immunomodulatory mechanisms and therapeutic opportunities. Frontiers in Immunology. June 2025.
[22] Zhou, J., *et al*. PLK1 Inhibition Induces Immunogenic Cell Death and Enhances Immunity against NSCLC. International Journal of Medical Sciences. August 2021.

and PLK3 function as tumor suppressors within the p53 signaling network, protecting against cellular stress.[23] The inhibitors also hit other targets with as yet undefined modes of action.[24] Hematological toxicities (neutropenia and thrombocytopenia) were common. The toxicities severely narrowed the therapeutic window and led to the clinical setbacks suffered by several first-generation assets.[25,26] These toxicities may be attributable to inhibition of bone marrow precursor cell proliferation. Other toxicities in the digestive and nervous system along with those in the blood circulatory system suggest that PLK-class agents should avoid tumors in these locations.[27]

Combination Therapy with PLK1 Inhibitors

Partial responses for PLK1 inhibition-based monotherapies have encouraged the use of combination therapies for cancer management. Adding chemotherapy to PLK1 inhibitors has shown synergistic benefits in both preclinical and clinical settings. PLK1 inhibitors have also been used with targeted therapy including agents such as RhoA/Rho kinase (ROCK), mammalian target of rapamycin (mTOR) and poly (ADP-ribose) polymerase (PARP) inhibitors among others. According to Su *et al*. there are three areas where combination therapy provides advantages over monotherapy: when it is appropriate to the patient's genetic profile, when the primary drug is only effective in a part of a heterogeneous tumor and when the selection pressure from one drug may induce drug resistance.[28]

RAS Mutations

Rat Sarcoma Virus (RAS) proto-oncogenes are found in three human genes designated HRAS, KRAS and NRAS. They encode proteins that promote cell growth, survival and division. Mutations in these genes are associated with worse outcomes and resistance to many therapies. RAS mutation cancer is an area of unmet need and attempts to directly inhibit RAS have not borne fruit.[29] PLK1 inhibition is an effective cancer treatment across many RAS mutations because it relies on synthetic lethality[30] rather than access to difficult binding pockets for tumor cell destruction. PLK1 inhibition can exploit synthetic lethality and is a mechanism that favors RAS-mutant cells over RAS wild-type.

Summary

In summary Polo-like kinase 1 (PLK1) is a mitosis-regulating serine/threonine kinase that becomes active in the late G2/M phase of the cell cycle and is essential for spindle formation, chromosome segregation and successful cell division. The protein is minimally expressed in normal, non-dividing cells but overexpressed across many human cancers and strongly associated with aggressive disease, poor survival and genomic instability. This has raised PLK1 as an attractive therapeutic target. Early studies showed that inhibiting PLK1 triggers G2/M arrest and apoptosis in cancer cells, including those with RAS mutations, where PLK1 dependence creates a synthetic-lethality vulnerability. However, first-generation PLK inhibitors often lacked isoform selectivity and caused hematologic and systemic toxicities due to off-target effects on related kinases (PLK2/PLK3) and bone-marrow precursors. As a result, PLK1 candidates need to be refined to be more selective. Combination regimens also show signs of improved efficacy and overcoming resistance when added to chemotherapy and targeted agents such as mTOR, ROCK, and PARP inhibitors.

[23] Gao, Y., *et al*. Tumor Suppressor PLK2 May Serve as a Biomarker in Triple-Negative Breast Cancer for Improved Response to PLK1 Therapeutics. Cancer Research Communications. December 2021.
[24] Abdelfatah, S., *et al*. A selective inhibitor of the Polo-box domain of Polo-like kinase 1 identified by virtual screening. Journal of Advanced Research. October 2018.
[25] Chiappa, M., *et al*. Present and Future Perspective on PLK1 Inhibition in Cancer Treatment. Frontiers in Oncology. June 2022.
[26] Awada, A., *et al*. Phase I trial of volasertib, a Polo-like kinase inhibitor, plus platinum agents in solid tumors: safety, pharmacokinetics and activity. Investigational New Drugs. March 2015.
[27] Xiao, W., *et al*. Effectiveness, safety and pharmacokinetics of Polo-like kinase 1 inhibitors in tumor therapy: A systematic review and meta-analysis. Frontiers in Oncology. February 2023.
[28] Su, S. *et al*. PLK1 inhibition-based combination therapies for cancer management. Translational Oncology. December 2021.
[29] Jayachandran, P., *et al*. Pan-RAS inhibitors and polo-like kinase 1: promising targets in colorectal cancer. Oncogene. July 2025.
[30] Synthetic lethality is a genetic interaction where the simultaneous loss or inhibition of two different genes or pathways is lethal to cells, whereas the disruption of either gene or pathway alone is not. In the context of cancer therapy, this principle enables selective targeting of tumor cells while minimizing toxicity to healthy tissues, since normal cells typically possess intact copies of both repair genes and remain unaffected.

Therapeutic Candidate

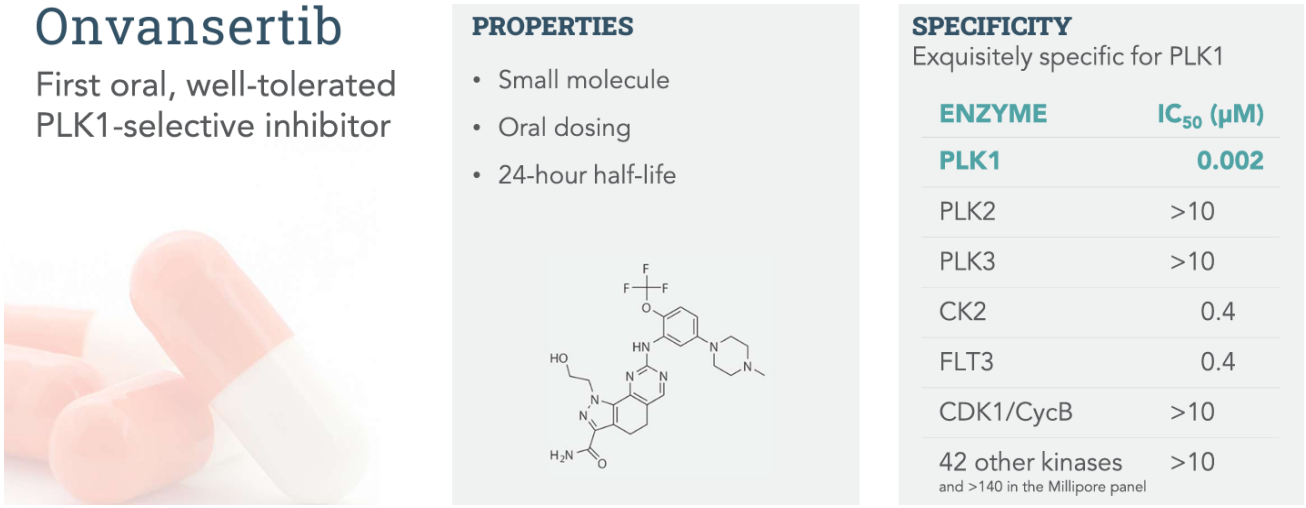
Onvansertib

Onvansertib is a third generation, highly selective, oral Polo-Like Kinase 1 (PLK1) inhibitor, that is designed to target and inhibit cancer cell division (mitosis). It is a small molecule agent with a relatively short 24-hour half-life. It is highly potent against the PLK1 enzyme compared with previous generation of PLK pan inhibitors. It works as an ATP-competitive inhibitor that selectively binds to and inhibits PLK1, a serine/threonine kinase crucial for cell cycle regulation.

Pharmacologically, onvansertib is classified as a targeted small-molecule kinase inhibitor specific for PLK1. It is distinct from earlier PLK inhibitors by its improved selectivity with minimal activity against PLK2 and PLK3. It is also orally delivered in contrast to previous PLK inhibitors that were intravenously administered.

PLK1 plays two critical roles in cancer cells: it controls mitotic progression during the M phase of the cell cycle, and it mediates DNA repair mechanisms during the S phase. By inhibiting PLK1, onvansertib disrupts mitosis and induces G2/M cell-cycle arrest, ultimately leading to apoptosis (programmed cell death) in PLK1 overexpressing tumor cells.

Exhibit II – Onvansertib Characteristics



Source: September 2025 Corporate Presentation

Beyond its direct cell-cycle effects, onvansertib's therapeutic potential is amplified by its ability to disrupt a critical survival pathway in solid tumors: the hypoxia-HIF signaling axis. Onvansertib's activity in hypoxic tumors illustrates how PLK1 inhibition intersects with a fundamental cancer-cell survival pathway driven by HIF-1α. As a tumor expands rapidly, its interior often becomes oxygen-deprived, which stabilizes HIF-1α rather than degrading it. Stabilized HIF-1α then activates a broad transcriptional cascade that supports tumor survival, including induction of vascular endothelial growth factor (VEGF)-A. VEGF-A promotes angiogenesis and the upregulation of genes that activate glycolysis which sustain a cell's energy production in low-oxygen conditions.

Hypoxia arises when cancer cells outgrow their blood supply or when new vessels are poorly formed, leaving the center of the tumor chronically under-oxygenated. In response, cancer cells activate both HIF-1α and HIF-2α, which stimulate VEGF-driven angiogenesis and trigger metabolic and pH-regulatory adaptations that help the cells persist despite oxygen scarcity.

PLK1 is closely linked to this hypoxia–HIF signaling axis, helping regulate hypoxic responses and angiogenic signaling. This creates a hypoxia-PLK1-angiogenesis feedback loop in which HIF activation upregulates PLK1. When PLK1 is inhibited, anti-angiogenic therapies such as bevacizumab can be effective by further disrupting this survival pathway.

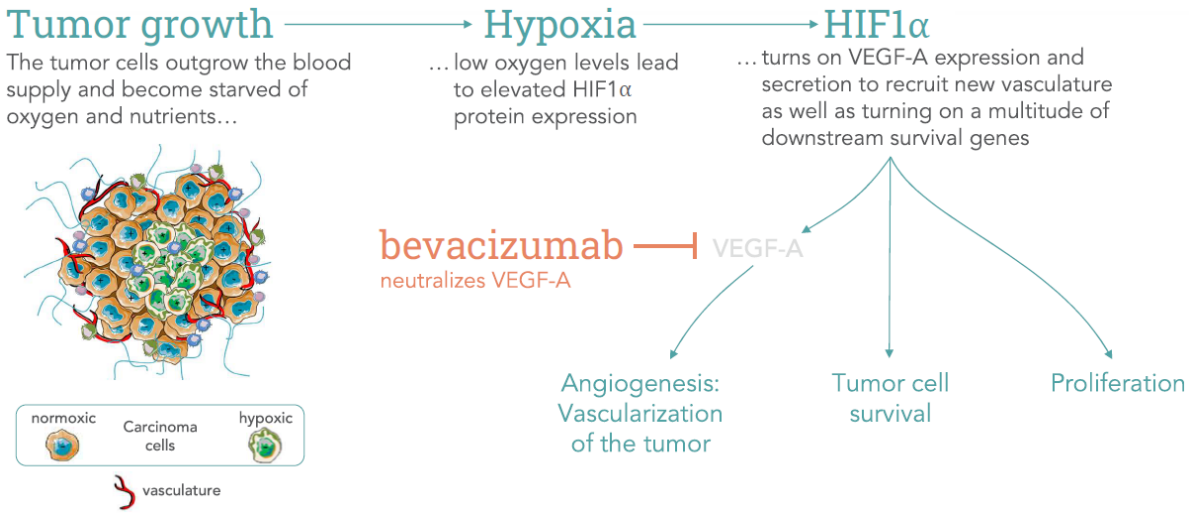
This response to hypoxia is especially important in KRAS-mutant tumors, where glycolytic metabolism is already enhanced by the oncogenic KRAS mutation, making the combination of glycolysis and HIF-1α activation important for tumor survival. A critical dimension of this pathway involves bidirectional regulation between HIF and PLK1. Re-

search has demonstrated that HIF-2α transcriptionally upregulates PLK1 expression through direct binding to hypoxia response elements (HREs) in the PLK1 promoter. This mechanism occurs in clear cell renal cell carcinoma and other hypoxia-driven cancers, creating a series of reactions where hypoxia stabilizes HIF-2α, which then drives PLK1 expression, and elevated PLK1 correlates with metastasis and therapeutic resistance. Furthermore, PLK1 itself can activate the COX-2-HIF-1α-VEGF-A signaling pathway through phosphorylation of downstream mediators, suggesting that PLK1 directly participates in sustaining HIF-1α-driven angiogenesis and hypoxic adaptation.[31]

Preclinical studies show that onvansertib directly downregulates HIF-1α protein levels, particularly in hypoxic conditions that mimic the tumor microenvironment. By inhibiting PLK1, onvansertib disrupts the hypoxia-driven survival pathways through at least two complementary mechanisms:

- Reduced HIF-1α Stabilization and Activity: Onvansertib diminishes HIF-1α protein accumulation in hypoxic tumor cells, thereby suppressing the transcription of HIF-1α target genes, including VEGF-A and pro-survival factors.
- Inhibition of Glycolysis: Onvansertib downregulates glycolysis-related genes, severing a critical lifeline for cancer cells adapting to low-oxygen environments. Glycolysis inhibition is significant in KRAS-mutant colorectal cancer, where the combination of oncogenic KRAS-driven glycolysis plus HIF-1α-mediated hypoxic adaptation creates exceptional metabolic vulnerability.

Exhibit III – Role of HIF-1α In Tumor Survival



Source: September 2025 Corporate Presentation

Anti-angiogenic agents, such as bevacizumab, bind to VEGF, thereby inhibiting downstream signaling that stimulates angiogenesis. VEGF normally triggers a cascade that promotes endothelial cell proliferation, migration, and blood vessel formation. When an antagonist binds to VEGF, the signaling pathway is inhibited and angiogenesis is reduced. Administration of anti-VEGF agents can lead to tumor resistance as the tumor cells seek other pathways to survival and endothelial cells activate survival signals independent of VEGF. Resistance can also emerge from the induction of hypoxia inducible factor (HIF). This may allow tumors to compensate for the loss in blood supply by relying on alternative angiogenic factors, such as FGF2,[32] which may allow for revascularization.[33]

Due to the emergence of resistance, cancer patients can relapse after treatment with kinase inhibitors such as bevacizumab. Following treatment, patient tumors express higher levels of PLK1 compared with primary tumor tissue.[34] This suggests that PLK1 inhibitors may be an appropriate treatment in combination with bevacizumab. Dufies and Pagès[35] write that there may be a benefit of combining angiogenesis and PLK1 inhibition which may prevent metastatic spreading.

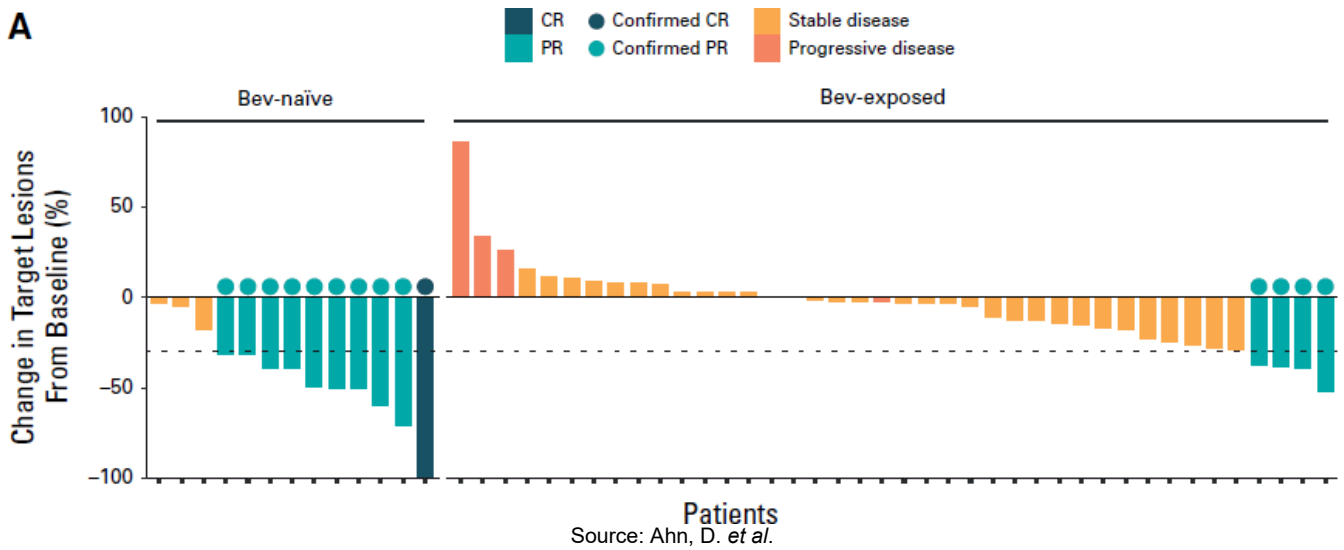
[31] Zhao, S., *et al*. Deciphering the performance of polo-like kinase 1 in triple-negative breast cancer progression according to the centromere protein U-phosphorylation pathway. American Journal of Cancer Research. May 2021.
[32] FGF2 is fibroblast growth factor 2
[33] Mitsuhashi, A., *et al*. Fibrocyte-like cells mediate acquired resistance to anti-angiogenic therapy with bevacizumab. Nature Communications. December 2015.
[34] Ahn, D.H., *et al*. Onvansertib in Combination with FOLFIRI and Bevacizumab in Second-Line Treatment of KRAS-Mutant Metastatic Colorectal Cancer: A Phase Ib Clinical Study. Clinical Cancer Research. January 2024.
[35] Dufies, M., Pagès, G. HIF2-Plk1, an Oncogenic Pathway in Clear Cell Renal Cell Carcinoma - Beyond the Abstract. Urology Today. May 2021.

Onvansertib Phase II Trial in Second Line mCRC

Cardiff ran a Phase II clinical trial which evaluated onvansertib in combination with FOLFIRI and bevacizumab and reported this data from the trial in 2023. The enrolled population included KRAS-mutated metastatic colorectal cancer patients eligible for second line treatment. It was designed as a multicenter, open-label, single-arm study for patients that had previously been treated with oxaliplatin and fluorouracil with or without bevacizumab.[36] The Phase II trial is listed under the NCT03829410 identifier on the clinicaltrials.gov website. The primary endpoint was overall response rate (ORR). Secondary endpoints included progression-free survival (PFS), duration of response (DoR) and tolerability. Study protocol called for administration of several dose strengths of onvansertib (12, 15 and 18 mg/m^2) to subjects on days 1 to 5 and 15 to 19 of a 28-day cycle. Standard of care FOLFIRI and bevacizumab was administered on days 1 and 15. Sixty-eight patients were intent to treat (ITT) patients, sixty-six were evaluable and fifty were enrolled in the Phase II portion at the 15 mg/m^2 dose.

ctDNA Associations
Analysis showed that a greater than 90% decrease in KRAS-mutant circulating tumor (ctDNA) after one cycle of treatment. Patients that generated a complete or partial response (n=12) had a significantly greater decrease in KRAS-mutant ctDNA compared with those with stable or progressive disease (n=35). A greater than 90% reduction in KRAS-mutant ctDNA compared with a less than 90% reduction was also associated with a higher ORR (55.0% vs. 3.7%) and a significantly longer PFS (12.6 months vs. 5.8).

Exhibit IV – Bevacizumab-Naïve vs Exposed Tumor Change in Onvansertib-Treated Patients



Source: Ahn, D. *et al.*

Prior Bevacizumab Treatment Associations
Investigators evaluated patient outcomes based on a number of characteristics including prior use of bevacizumab. The results of the analysis demonstrated that the absence of prior bevacizumab use was associated with clinical benefit. Bevacizumab-naïve patients (n = 13) had an ORR of 76.9% and a median PFS of 14.9 months compared with prior bevacizumab-treated patients with an ORR of 10.0% and median PFS of 6.6 months. An investigation of potential resistance mechanisms suggested that transcriptomic changes after bevacizumab exposure might drive resistance to both bevacizumab and onvansertib.

The study investigators evaluated the antitumor activity of onvansertib and bevacizumab in CRC xenograft models and measured superior inhibition of tumor growth using both of the agents together compared with treatments by each agent alone. The combination produced greater reduction in vascularization compared to the use of an individual agent and tumors were smaller. The use of the combination also produced a reduction in tumor cell proliferation and an increase in apoptosis. Onvansertib treatment generated a dose dependent reduction in hypoxia inducible factor 1α (HIF1α). Active HIF1α triggers the expression of genes promoting angiogenesis, metabolic changes, and cell survival. In other words, onvansertib impedes potentially cancerous cells from spreading. Transcriptomic profiling was also done, showing that onvansertib significantly downregulated the hypoxia pathway and the closely associated glycolysis metabolic pathway in both cell lines. Glycolysis represents another important mode of cell survival which provides essential energy and adaptation to hypoxic tumor cell environments. Other mechanisms be-

[36] Ahn, D. *et al*. Onvansertib in Combination With Chemotherapy and Bevacizumab in Second-Line Treatment of KRAS-Mutant Metastatic Colorectal Cancer: A Single-Arm, Phase II Trial. Gastrointestinal Cancer. October 2024.

sides the use of onvansertib were employed to deplete PLK1 and these approaches produced similar reductions in the HIF1α protein and mRNA expression of hypoxia related genes.

Safety
Cardiff's second line mCRC trial reported at least one treatment emergent adverse event (TEAE) of any grade for each patient. Fatigue, neutropenia, nausea and diarrhea were the most common. Only four Grade 4 TEAEs were observed. Three were severe cases of neutropenia and one was colonic perforation. Four patients discontinued treatment due to an AE, but the discontinuation was not attributed to onvansertib.

While the interim data from the Phase I/II study did not achieve the intended 30% overall response rate, it did identify a bevacizumab-naïve subpopulation that achieved an ORR of 76.9%. Based on this unexpected finding in the naïve population, the second line study was discontinued and a new study was proposed in first line mCRC patients without previous exposure to bevacizumab. The first-line study was designated CRDF-004.

The unexpected finding in the bevacizumab-naïve population directly led to the design of CRDF-004. CRDF-004 was constructed as a first-line study specifically in bevacizumab-naïve KRAS/NRAS-mutant mCRC patients. Not only does the shift allow Cardiff to focus resources on the population most likely to benefit but it is more likely to generate data that will support approval of onvansertib.

CRDF-004 – Metastatic Colorectal Cancer (mCRC)

Cardiff's lead program is evaluating onvansertib in the treatment of first line, RAS-mutated, metastatic colorectal cancer (mCRC). Standard of care (SoC) treatment for mCRC is the anti-VEGF bevacizumab and FOLFOXIRI[37] and bevacizumab. In pivotal trials, bevacizumab added about four months of progression free survival (PFS) to prior SoC, which was equal to 10.6 months for all categories of patients in the trial and 9.3 months for RAS mutant.

Cardiff's CRDF-004 trial's official title is: Study of Onvansertib in Combination With FOLFIRI and Bevacizumab or FOLFOX and Bevacizumab Versus FOLFIRI and Bevacizumab or FOLFOX and Bevacizumab for First-Line Treatment of Metastatic Colorectal Cancer in Adult Participants With a KRAS or NRAS Mutation. It is listed under the designator NCT06106308 on clinicaltrials.gov. It is a Phase II study that enrolled 110 subjects at over 40 sites around the United States.

We start with a summary of CRDF-004 interim results in comparison with other targeted therapies in mCRC.

Exhibit V – Depth of Response Comparison: Onvansertib vs. Other Targeted Therapies in mCRC[38]

		Previous Ph3 1st Line mCRC Trials[1]				
	% of patients with ETS	TRIBE RAS WT/mut.	CRYSTAL RAS WT	OPUS RAS WT	CRDF-004 RAS mut.	
Early Tumor Shrinkage (ETS)	Control Arm	52%	49%	46%	41% (11/27)	
≥20% reduction in tumor size at 2-month scan.	Experimental Arm	63%	62%	69%	Onv 20mg 63% (19/30)	Onv 30mg 69% (22/32)
Final data: All patients on trial have had a 2-month scan.	**ETS Delta** *p-value*	**11%** *0.025*	**13%** *0.02*	**23%** *0.006*	**22%** *0.114*	**28%** *0.038*
	Hazard Ratio	0.79	0.68	0.57		
	Improvement in PFS	2.0 mo	4.4 mo	3.7 mo		

Source: September 2025 Corporate Presentation

[37] FOLFOXIRI: FOL - Folinic acid (leucovorin) F-5-fluorouracil (5-FU) OX – Oxaliplatin IRI - Irinotecan
[38] First-line mCRC trials in which ETS and/or DpR were evaluated as predictors of PFS and OS comparing a control arm of chemo alone vs. an experimental arm of chemo + an active agent including bevacizumab (TRIBE) and cetuximab (CRYSTAL and OPUS). Piessevaux, et al, J Clin Oncol 2013; Cremolini, et al, Ann Oncol 2015; Van Cutsem, et al, N Engl J Med 2009 (HR for CRYSTAL); Bokemeyer et al, Ann Oncol 2011 (HR for OPUS). ETS, early tumor shrinkage; mCRC, metastatic colorectal cancer; WT, wild type; mut, mutated; PFS, progression free survival; bev, bevacizumab; onv, onvansertib.

Exhibit VI – Summary Table for TRIBE, CRYSTAL and OPUS Trials[39,40,41,42]

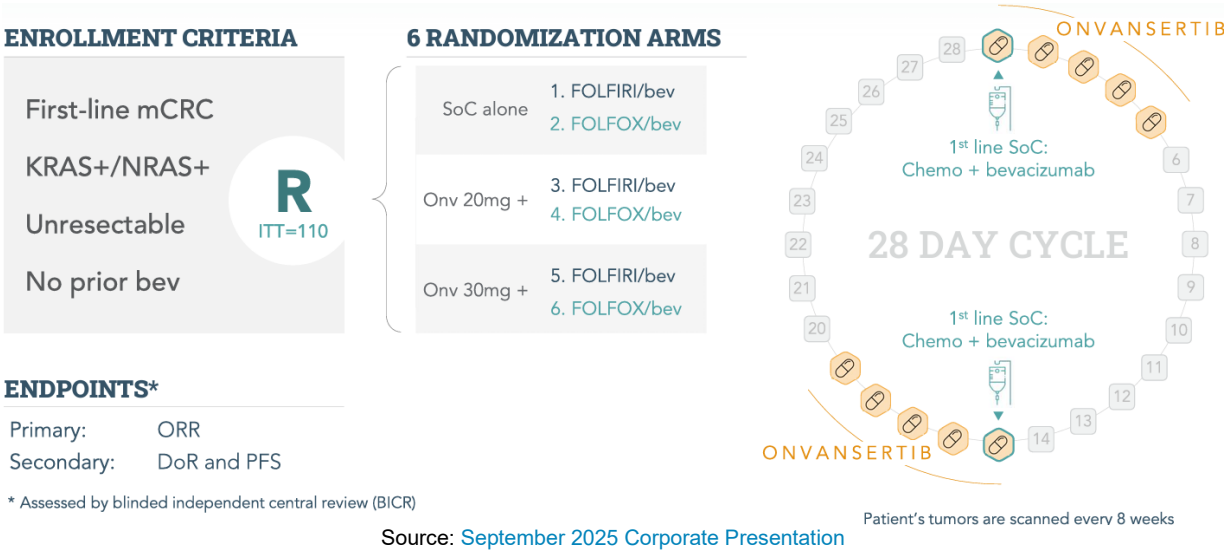
Trial	Chemotherapy Backbone	Targeted Agent	Mechanism	Control Arm
TRIBE	FOLFOXIRI	Bevacizumab	Anti-VEGF	FOLFIRI + Bev
CRYSTAL	FOLFIRI	Cetuximab	Anti-EGFR	FOLFIRI alone
OPUS	FOLFOX4	Cetuximab	Anti-EGFR	FOLFOX4 alone

Source: Zacks Analyst Work

Trial Design

CRDF-004 was designed to enroll first-line mCRC patients that are KRAS or NRAS positive with unresectable tumors and no prior treatment with bevacizumab (bev). It has enrolled six randomization arms. Two arms were standard of care,[43] FOLFIRI+bev[44] and FOLFOX+bev[45]. Two arms evaluated 20 mg of onvansertib with one or the other standard of care arms and two arms evaluated 30 mg of onvansertib with each of the two standard-of-care arms. The primary endpoint is overall response rate (ORR). Secondary endpoints included duration of response (DoR), measurement of adverse events, overall survival (OS) and progression free survival (PFS) as well as several pharmacokinetic and pharmacodynamic metrics.

Exhibit VII – Onvansertib Pipeline



Source: September 2025 Corporate Presentation

Since it began, CRDF-004 has provided two interim readouts. One with data reported in December 2024 and the other with data reported July 2025. As of the latter date, the onvansertib arms produced better ORR compared with standard of care. The 30 mg arm produced an ORR of 49% and the 20 mg an ORR of 42%. This compares to standard of care generating an ORR of 30%. When evaluated by chemotherapy backbone, the FOLFOX combination with onvansertib produced slightly better results.

[39] First-line mCRC trials in which ETS and/or DpR were evaluated as predictors of PFS and OS comparing a control arm of chemo alone vs. an experimental arm of chemo + an active agent including bevacizumab (TRIBE) and cetuximab (CRYSTAL and OPUS). Piessevaux, et al, J Clin Oncol 2013; Cremolini, et al, Ann Oncol 2015; Van Cutsem, et al, N Engl J Med 2009 (HR for CRYSTAL); Bokemeyer et al, Ann Oncol 2011 (HR for OPUS). ETS, early tumor shrinkage; mCRC, metastatic colorectal cancer; WT, wild type; mut, mutated; PFS, progression free survival; bev, bevacizumab; onv, onvansertib.

[40] Loupakis, F., *et al.* Initial Therapy with FOLFOXIRI and Bevacizumab for Metastatic Colorectal Cancer. New England Journal of Medicine. October 2014.

[41] Cutsem, E.V., *et al.* Cetuximab and Chemotherapy as Initial Treatment for Metastatic Colorectal Cancer. New England Journal of Medicine. April 2009

[42] Bokemeyer, C., *et al.* Efficacy according to biomarker status of cetuximab plus FOLFOX-4 as first-line treatment for metastatic colorectal cancer: the OPUS study. Gastrointestinal Tumors. July 2011.

[43] FOLFOX and FOLFIRI are often considered equivalent first-line options for metastatic colorectal cancer. The choice between them may depend on the patient's tolerance for specific side effects (neuropathy and diarrhea), previous treatments received, overall health status and tumor characteristics.

[44] FOLFIRI is a chemotherapy regimen commonly used to treat colorectal cancer: FOL - Folinic acid (leucovorin) F - 5-fluorouracil (5-FU) IRI - Irinotecan

[45] FOLFOX: FOL - Folinic acid (leucovorin) F - 5-fluorouracil (5-FU) OX - Oxaliplatin

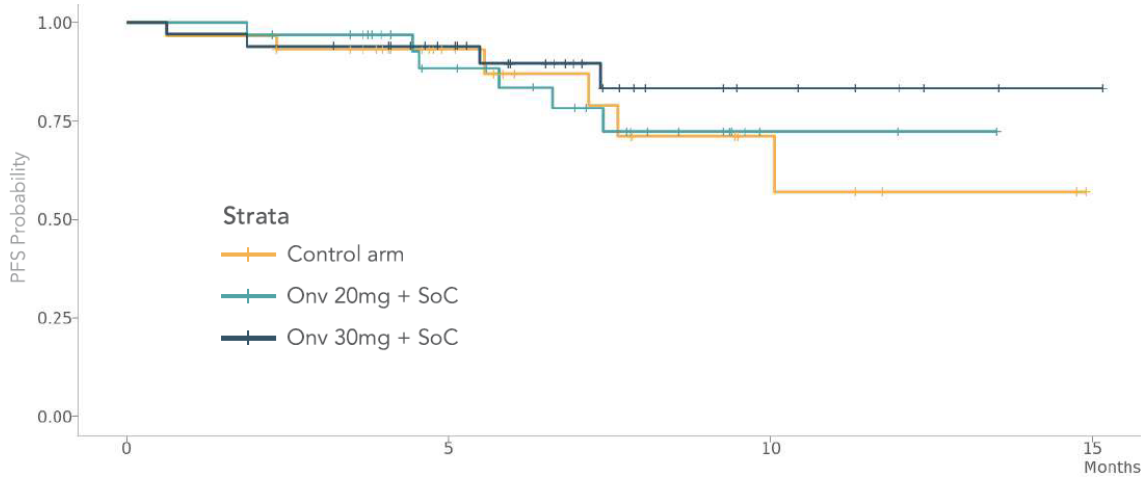
Exhibit VIII – Objective Response Rates per RECIST 1.1

Intent-to-treat (ITT) (N=110)	Control (SoC alone) (n=37)	Onv 20mg + SoC (n=36)	Onv 30mg + SoC (n=37)	Onv 30mg vs. Control
Confirmed ORR[1] n, [95% CI]	30% n=11 [16-47]	42% n=15 [26–59]	49% n=18 [32–66]	19% p=0.018[2]
Confirmed ORR at 6 months	22% n=8	33% n=12	46% n=17	
ORR[3] n, [95% CI]	43% n=16 [27–61]	50% n=18 [33–67]	59% n=22 [42–75]	
Best response on trial				
Complete Response (CR)	1 (3%)	1 (3%)	2 (5%)	
Partial Response (PR)	15 (41%)	17 (47%)	20 (54%)	
Unconfirmed (will not confirm) PR/CR	3 (8%)	3 (8%)	1 (3%)	
Stable Disease (SD)	9 (24%)	10 (28%)	8 (22%)	
Progressive Disease (PD)	0	0	1 (3%)	
Death	1 (3%)	0	1 (3%)	
Not evaluable	8 (22%)	5 (14%)	4 (11%)	

Source: September 2025 Corporate Presentation

As of July 2025, median PFS had not been reached; however, a separation of the curves is apparent (see below). There is a distinct spread between the SoC arm and both investigational arms at 15 months, especially for the 30 mg onvansertib group indicating a dose dependent response. Early responses are indicative of better responses later. This feature was apparent to a greater degree in the 30 mg arm. Details of the interim readout were provided in a July 2025 press release, conference call and slide deck.

Exhibit IX – CRDF-004 Interim Readout: Progression Free Survival (PFS)



Source: September 2025 Corporate Presentation

Cardiff provided a summary of its enrolled population characteristics and we believe that it is representative of the mCRC population in the United States with respect to age, sex, race, stage and other factors. The study population also appears to be evenly distributed across the six study arms. The safety profile for the onvansertib arms compared to the control arms was comparable for Grade 3 and higher adverse events. Onvansertib was also well tolerated when used in combination with bevacizumab and either chemotherapy regimen. Furthermore, none of the patients that discontinued did so due to onvansertib in the opinion of the clinical investigators.

Safety Profile and Summary of Side Effects

Onvansertib has generally demonstrated a manageable safety profile in trials to date, with side effects that are consistent with its mechanism as a cell-cycle inhibitor. Unlike earlier PLK inhibitors, onvansertib's toxicity appears mostly on-target (related to its anti-proliferative effects on dividing cells) and is largely reversible.

Dose-dependent neutropenia and thrombocytopenia are the signature toxicities of the onvansertib cocktail and recognized side effects of the FOLFOX and FOLFIRI regimens. In the first in-human study, the dose-limiting toxicities at high doses were Grade 3 or 4 neutropenia and thrombocytopenia. Across trials, neutropenia is the most frequent

treatment-related adverse event. Some patients experience mild nausea, fatigue, or diarrhea, which are side effects common to many oral anticancer agents, most notably the components of FOLFIRI.[46]

Higher doses of onvansertib of 90 mg/m^2 have been associated with mucosal inflammation yielding dose-limiting mucositis/stomatitis (Grade 3). Skin rash has also been observed; any-grade rash occurred in ~36% of AML patients (mostly mild), and a few Grade 3 and 4 skin reactions emerged at the highest doses. These effects are thought to stem from onvansertib's impact on rapidly renewing cells. They have been relatively infrequent at recommended doses.

Investigator Initiated Onvansertib Trials

Metastatic Pancreatic Ductal Adenocarcinoma (mPDAC)
The University of Kansas Medical Center is running a Phase Ib/II trial of onvansertib in combination with NALIRIFOX[47] for first line treatment of advanced pancreatic cancer. The single site in Kansas City plans to enroll 21 patients and evaluate them for ORR, disease control rate, PFS and OS over the duration of the trial. Further details about the trial are available on clinicaltrials.gov under the designator NCT06736717.

Small Cell Lung Cancer (SCLC)
The University of Maryland is conducting a Phase II clinical trial to evaluate the safety and efficacy of onvansertib to treat patients with small cell lung cancer (SCLC) who have either not responded to or cannot tolerate chemotherapy. This is a single arm, two stage, phase II study of onvansertib in patients with relapsed SCLC who have received not more than 2 lines of prior therapies. The study will enroll 15 patients in stage I. Enrolment into stage II will occur if two or more patients achieve objective response. Subsequent enrolment into stage II will be by biomarker selection if the stage I accrual supports any of the three preliminarily identified biomarkers: TP53 mutation type, SCLC-Y or MYC expression. 37 patients are expected to be enrolled at two sites in Maryland and Pennsylvania. The primary endpoint is ORR and secondary endpoints include adverse events, PFS and OS. Details of the study are on clinicaltrials.gov under the designator NCT05450965.

Triple Negative Breast Cancer (TNBC)
Dana-Farber Cancer Institute has sponsored a triple negative breast cancer (TNBC) study evaluating onvansertib and paclitaxel. The study began in 2022 and has targeted 50 patients for enrollment. It is a Phase Ib/II study in patients with triple negative invasive breast cancer with unresectable locally advanced or metastatic disease. In the first phase, different doses of onvansertib will be studied with a fixed dose of paclitaxel to determine the maximum tolerated dose (MTD) and recommended Phase II dose (RP2D) of onvansertib. In the Phase II, the selected onvansertib RP2D in combination with paclitaxel will be studied following a Simon two-stage design. The trial is expected to complete patient evaluation by next year. Details of the trial are available on the clinicaltrials.gov website under the NCT05383196 designator.

Exhibit X – Onvansertib Pipeline

	Line of Therapy	Trial	IIT*	Ph2	Ph3	Combination with:
mCRC (RAS-mut)	1st line	CRDF-004 (w/Pfizer)		randomized		FOLFIRI/bev and FOLFOX/bev
	2nd line	Ph 1b/2		completed		FOLFIRI/bev
mPDAC	1st line	Ph 2	KU Medical Center, The University of Kansas			NALIRIFOX
	2nd line	Ph 2		completed		Nal-IRI/leucovorin/5-FU
SCLC	2nd line	Ph 2	University of Maryland Marlene and Stewart Greenebaum Comprehensive Cancer Center			None (monotherapy)
TNBC	2nd line	Ph 2	Dana-Farber Cancer Institute			Paclitaxel

Source: Cardiff November 2025 Corporate Presentation

[46] Weiss, G.J., *et al.* Phase I dose escalation study of NMS-1286937, an orally available Polo-Like Kinase 1 inhibitor, in patients with advanced or metastatic solid tumors. Investigational New Drugs. February 2018.
[47] NALIRIFOX is a chemotherapy drug combination approved by the FDA for the first-line treatment of metastatic pancreatic adenocarcinoma. It consists of four drugs: Nal-IRI (liposomal irinotecan, also known as Onivyde), Oxaliplatin, Fluorouracil (5-FU), and Leucovorin (folinic acid). NALIRIFOX works by providing a more sustained release of irinotecan and offers improved survival rates and progression-free survival compared to older treatments.

Intellectual Property

At the end of 2024, Cardiff owned and licensed 57 issued patents and 57 pending patent applications in the U.S. and abroad as summarized in its 2024 Form 10-K filing. Some of the patents related to the company's legacy products. The pending patent applications include multiple international patent applications filed under the Patent Cooperation Treaty (PCT) that may be used as the basis for multiple additional patent applications worldwide.

Cardiff licensed onvansertib from Nerviano Medical Sciences (Nerviano) in March 2017. The license grants Cardiff exclusive, worldwide rights to patents covering three areas:

- Onvansertib composition of matter, related compounds and processes for making compounds; pharmaceutical compositions and methods of treating diseases characterized by dysregulated protein kinase activity;
- Salts and pharmaceutical compositions of onvansertib; methods of treating mammals in need of PLK inhibition; and
- Synergistic combinations of onvansertib and one or more other antineoplastic agents and pharmaceutical compositions of those combinations.

Licensed patents will expire between 2027 and 2030. U.S. patents of this licensed patent portfolio will expire in 2030. Patent term extension may be available until 2035.

Cardiff filed two method-of-use patents after data from the Phase Ib/II trial in second line KRAS-mutated mCRC which demonstrated that bevacizumab-naïve patients achieved higher response rates. These patents ('813 and '173) protect the use of a PLK1 inhibitor in combination with an anti-angiogenic for treating metastatic colorectal cancer in bevacizumab-naïve patients. They expire in 2044 and may be eligible for patent extension of five years.

Another patent family includes a patent application directed to selecting and treating cancers with combination therapies of PLK1 inhibitors. Cardiff and the Massachusetts Institute of Technology (MIT) co-own this family which includes additional licensed patents that expire in 2035 to 2037. These relate to the use of a PLK inhibitor, specifically onvansertib, in combination with an antiandrogen or androgen antagonist, to treat cancer, including metastatic and non-metastatic castrate-resistant prostate cancer. These may be eligible for a patent term extension of five years.

Cardiff owns 28 patent families related to onvansertib. These families include patent applications directed to treating cancer using PLK1 inhibitors and determining efficacy of the treatment, treating benign prostatic hyperplasia using onvansertib, treating prostate cancer using PLK1 inhibitors, determining or predicting efficacies or responsiveness of PLK1 inhibitor treatments based on biomarkers and treating cancers with combination therapies of PLK1 inhibitors. Members of this family of patents will expire between 2039 and 2045.

Exhibit XI – Summary of Cardiff's Key Patents

Compound	Title	Patent #	Filed	Region	Expiry	Assignee
Onvansertib	PLK1 inhibitor in combination with anti-angiogenics for treating metastatic cancer	12,144,813	6/21/2024	US	2043	Cardiff
Onvansertib	PLK1 inhibitor in combination with anti-angiogenics for treating metastatic cancer	12,263,173	6/21/2024	US	2043	Cardiff
PLK inhibitor	Combination therapies and methods of use thereof for treating cancer	9,566,280	1/28/2015	US	1/28/2035	MIT
PLK inhibitor	Combination therapies and methods of use thereof for treating cancer	10,155,006	2/13/2017	US	2/13/2037	MIT
PLK inhibitor	Combination therapies and methods of use thereof for treating cancer	10,772,898	12/17/2018	US	1/28/2035	MIT
PLK inhibitor	Combination therapies and methods of use thereof for treating cancer	12,115,171	6/9/2022	US	1/28/2035	MIT
Onvansertib	Substituted pyrazolo-quinazoline derivatives, process for their preparation and their use as kinase inhibitors	8,614,220	12/17/2007	US	5/6/2030	Nerviano

The FDA’s Fast Track Designation

The FDA's Fast Track is a designation program designed to expedite the development and review of drugs intended to treat serious conditions and fill an unmet medical need. The goal of the fast track award is to accelerate the approval process for promising new drugs by facilitating closer collaboration between the FDA and drug sponsors. A drug can qualify for Fast Track if it treats a serious or life-threatening condition and demonstrates the potential to address an unmet medical need. Benefits of Fast Track include more frequent meetings with the FDA, a rolling review where completed sections of an NDA can be submitted as they are completed, eligibility for Accelerated Approval and Priority Review and a written commitment from the FDA on how disputes will be settled. Cardiff was granted Fast Track status in 2020 for onvansertib in KRAS-mutated metastatic colorectal cancer.

Primary Indications

Colorectal Cancer (CRC)

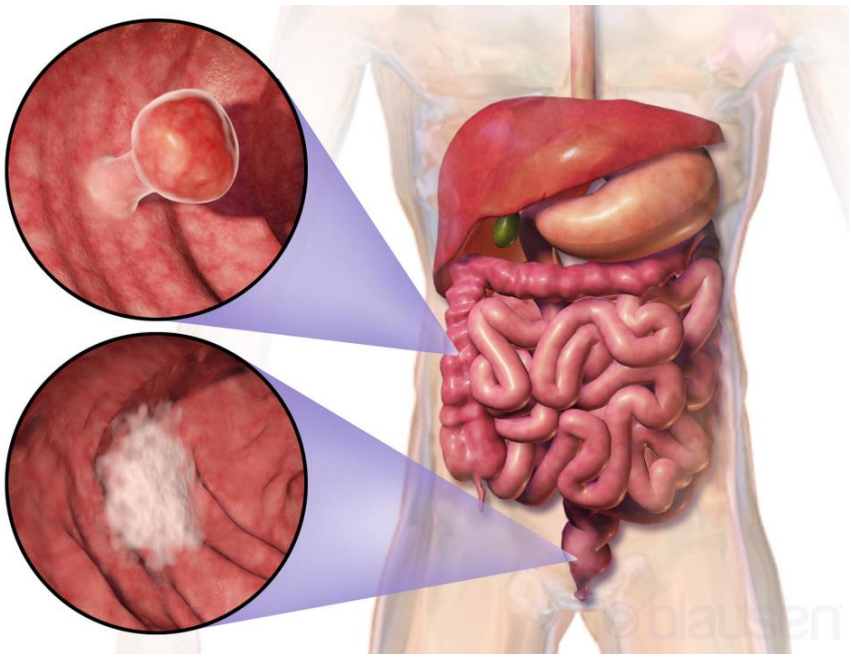
Colorectal Cancer (CRC) is a malignancy which begins the colon and rectum. These organs make up part of the digestive or gastrointestinal system. The colon is the larger of the two and a muscular tube approximately five feet long. It absorbs water and electrolytes from indigestible food matter and processes waste into stool.[48,49]

Colorectal cancers often begin as growths on the inner lining of the colon or rectum which are called polyps. Most polyps are not cancerous; however, some polyps termed adenomas can evolve into cancer. The three types of adenomatous polyps are classified as tubular, villous and tubulovillous. Villous adenomas are the least common type of this polyp but most likely to become cancerous. Sessile serrated polyps and traditional serrated adenomas are also potentially cancerous.[50] Other features of polyps that indicate a higher risk of cancer include large polyp size (>1 cm), a high number of polyps and detection of dysplasia in the polyp.

CRC can spread through metastasis, which is when cancer cells break away from the original tumor and circulate throughout the body via the bloodstream or lymphatic system. In contrast to many other cancers, CRC may disperse soon after the original tumor has developed. These metastatic-prone cancers have certain genetic mutations that are associated with early proliferation.[51] In some cases, CRC may spread through direct invasion as it grows directly through the layers of the colon or rectal wall into nearby tissues or organs. This can lead to the cancer attaching or invading the abdominal lining, bladder or reproductive organs.[52]

CRC Introduction
There are a number of histological categories of tumors that comprise CRC with the dominant one being adenocarcinomas. In the United States there are over 150,000 and worldwide about 1.9 million CRC cases which are identified through screening, examination, biopsy and molecular characterization. Standard of care is biomarker-driven and treated based on type and stage of CRC with frequent use of combination therapies. Molecular testing is especially relevant for mCRC, as systemic targeted therapies are used. The primary biomarkers evaluated include KRAS/ NRAS, BRAF V600E and MSI-high and dMMR.[53]

Exhibit XII – Colorectal Cancer



Source: Wikimedia Commons, Blausen Medical Communications, Inc.

[48] American Cancer Society Webpage, What is Colorectal Cancer?
[49] Cleveland Clinic Webpage, Large Intestine and Colon
[50] American Cancer Society Webpage, What is Colorectal Cancer?
[51] National Cancer Institute. Metastatic Colorectal Cancer May Spread Early in the Disease, Study Finds
[52] Mayo Clinic. Stage 4 (Metastatic) Colon Cancer
[53] Molecular Biomarkers of Colorectal Cancer. Association for Molecular Pathology. June 2025.

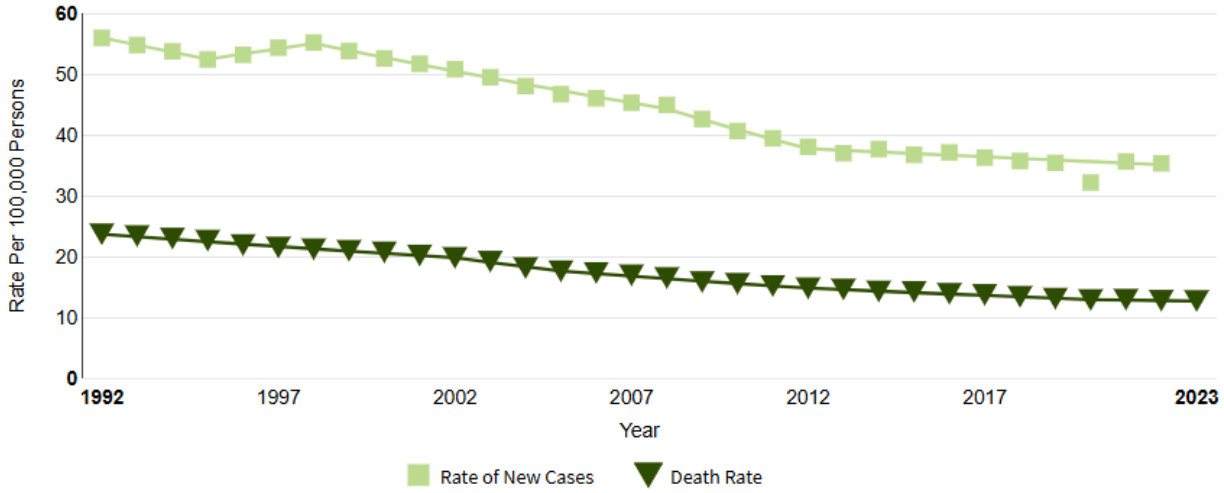
Types of CRC

There are five histological categories of CRC tumors defined by the World Health Organization (WHO). These cancers begin in the cells that make mucus to lubricate the inside of the colon and rectum.[54] About 90 to 95% of cases are classified as adenocarcinomas which commonly arise from benign adenomatous polyps and progress to invasive (malignant) neoplasms.[55] Adenocarcinomas usually develop from these precancerous polyps over a period of several years. Subtypes of adenocarcinoma include mucinous adenocarcinoma (about 25% of cases) and signet-ring cell carcinoma (about 4% of cases) which are less-common variants that can have a poorer prognosis. Classic adenocarcinoma makes up about 70% of cases.[56] References to colorectal cancer typically refer to adenocarcinomas. Other types of CRC include carcinoid tumors (1% of total), gastrointestinal stromal tumors (GISTs), lymphomas and other rare types. Other types of CRC that make up a minority of cases include adenosquamous carcinoma, spindle cell carcinoma, squamous cell carcinoma and undifferentiated carcinoma. Onvansertib is pursuing mCRC with KRAS or NRAS mutations. KRAS mutations occur in approximately 40% of metastatic colorectal cancers and are frequently resistant to anti-EGFR therapy.

Incidence & Prevalence

After breast, prostate and lung, CRC is the fourth most common cancer in the United States with over 1.4 million persons living with the disease. The American Cancer Society (ACS) estimates that there will be about 107,320 new cases of colon cancer and 46,950 new cases of rectal cancer in the United States for 2025. The proportion of cases is slightly tilted towards men. The ACS notes that while the incidence of CRC has declined overall since the mid-1980s, it has increased in people younger than 50.[57] The lifetime risk of developing CRC is about 1:24 for men and 1:26 for women, with several risk factors increasing the likelihood including obesity, type 2 diabetes, smoking, alcohol use and diets high in red meats and low in vegetables. According to the Surveillance, Epidemiology, and End Results (SEER) database, the rate of new colorectal cancer deaths per 100,000 was 12.9 in the United States based on data over the 2019 to 2023 period. Deaths from CRC are expected to be about 52,900 in 2025.[58]

Exhibit XIII – New CRC Cases and Deaths Over the Last 30 Years



National Institute of Health's (NIH) National Cancer Institute (NCI) Cancer Stat Facts: Colorectal Cancer

Worldwide, CRC is the third most commonly diagnosed cancer after lung and breast. In 2020, there were an estimated 1.9 million new cases and 930,000 deaths recorded globally. Incidence was highest in Australia and New Zealand and Europe and lowest in Africa and Southern Asia.[59] North America also has elevated rates of CRC compared with global averages.

Based on US data, about two thirds of patients diagnosed with CRC survive past five years. The rate for an individual is highly dependent on the stage of the disease and if it is classified as localized, regional or distant. Localized disease has a 90-91% survival rate, while regional CRC has a 73-74% rate. If the cancer is distant, only 13-18% of patients are expected to be alive after five years. As shown in the previous exhibit, survival for CRC patients has improved over the last 30 years.[60]

[54] American Cancer Society. What is Colorectal Cancer? Accessed September 2025.
[55] Dubansky, B. *et al*. Classification and Histological Characteristics of Colorectal Cancer. Clinical Laboratory Science. September 2024.
[56] Sheng, H., *et al*. Adenocarcinoma with mixed subtypes is a rare but aggressive histologic subtype in colorectal cancer. BMC Cancer. 2019
[57] Downham L, *et al*. Increase of early-onset colorectal cancer: a cohort effect. Journal of the National Cancer Inst. 23 August 2025
[58] American Cancer Society. Key Statistics for Colorectal Cancer. Accessed September 2025.
[59] World Health Organization, International Agency for Research on Cancer. Colorectal Cancer.
[60] American Cancer Society. Survival Rates for Colorectal Cancer. Accessed September 2025.

Risk Factors
There are both modifiable risks and unmodifiable risks associated with CRC. Individuals can improve their likelihood of avoiding CRC by controlling their body weight and reducing risk factors for diabetes, changing their diet to reduce red and processed meats and increasing consumption of fresh fruits and vegetables, and reducing or eliminating alcohol use and smoking. Risk factors that cannot be changed include age, race, sex, and a history of bowel disease, colorectal polyps, exposure to radiation, diagnosis of other cancers, and several inherited conditions. Generally greater age is associated with greater probability of CRC, with diagnosis more common after age 50. Individuals of Native American and African American descent and Ashkenazi Jews have a higher risk of colorectal cancer. A previous cancer diagnosis and a history of gastrointestinal disease or polyps are other factors that increase the likelihood of having the disease. There are also a number of inherited genetic mutations and conditions that contribute to having the disease including Lynch Syndrome and familial adenomatous polyposis (FAP).[61]

Screening
Early stages of CRC do not have perceptible symptoms; therefore, screening is used to identify it. For the average adult, screening is conducted starting at age 45. For high-risk individuals with family history of CRC or high-risk genetic mutations, screening is advised earlier and up to 10 years prior to other family members being diagnosed. The least invasive and easiest approach is a high-sensitivity fecal immunochemical test or stool DNA-FIT test. If the test results indicate further examination, a colonoscopy or flexible sigmoidoscopy may be administered. Imaging studies may also be appropriate and a Computed Tomography (CT) Colonography may be run.

During a colonoscopy, surgical tools can be passed through the scope to remove polyps or take tissue samples (biopsies) from suspicious areas for lab testing. The tissue from the biopsy is then tested to determine if it is cancerous. Analysis of the tissue allows for histological grading from Grade 1 to Grade 4 ranging from well differentiated to undifferentiated. Molecular markers are measured with the biopsy tissue including the Kirsten Rat Sarcoma (KRAS), Neuroblastoma Rat Sarcoma (NRAS) oncogenes, microsatellite instability-high (MSI) and BRAF.

Symptoms
A patient complaining of change in bowel habits, rectal bleeding, abdominal pain and cramping, weakness and fatigue and/or unintended weight loss should see a physician for further assessment. Bowel habit changes can be manifested in persistent diarrhea or constipation, a change in stool consistency and an urge to have a bowel movement even when there is no need. If present, blood in the stool can be bright red or dark and tarry-colored indicating that the bleeding is occurring earlier in the colon. Some bleeding may not be visible in the stool, but can be observed indirectly in iron-deficiency anemia from slow chronic colonic bleeding. Many of these symptoms are shared with other conditions such as hemorrhoids, irritable bowel syndrome or infection. If these symptoms are observed, the individual should visit a provider for further diagnosis.

Diagnosis
If there are signs that a subject may have CRC, there are a number of initial detection and screening methods that may be used to confirm it. As part of an initial screen, a provider may perform a digital rectal exam looking for abnormal lumps, growths or other irregularities. To confirm a diagnosis, tissue samples from a biopsy are examined by microscope where the cancer is typed and graded. Molecular testing is also conducted to identify any gene mutations present and to help guide the use of targeted therapies. Standard of care calls for all newly diagnosed colorectal cancers to be tested for alterations in the mismatch repair (MMR) genes or assessed for Microsatellite Instability (MSI) status.[62] Once CRC is diagnosed, imaging can determine if it has spread. CT scans, MRI, PET-CT scan and X-ray may identify metastases in the chest, liver, lung and other distant sites.[63]

Current Standard of Care
Treatment for colorectal cancer usually requires a combination of surgery, systemic therapy and sometimes radiotherapy. Surgical resection is the first step for localized colon and rectal cancer. Surgery also provides tissue for pathology and staging. For more advanced cancer, chemotherapy is commonly used. 5-fluorouracil[64] is often administered with leucovorin (folinic acid) to enhance its effect. Oxaliplatin is a platinum-based drug that causes DNA cross-linking and is frequently combined with 5-FU/leucovorin in the FOLFOX regimen. Irinotecan, a topoisomerase I inhibitor that causes DNA breaks, is also used with FOLFIRI. In metastatic CRC, chemotherapy can shrink tumors and alleviate symptoms. While not curative in stage IV (except in rare cases of limited metastases), it can prolong

[61] American Cancer Society. Colorectal Cancer Risk Factors. Accessed October 2025.
[62] Molecular Biomarkers of Colorectal Cancer. Association for Molecular Pathology. June 2025.
[63] NCCN Guideline for Patients, Colon Cancer.
[64] 5-fluorouracil (5-FU) is a pyrimidine analog that interferes with DNA synthesis.

survival.[65] Often combined with targeted drugs, FOLFOX or FOLFIRI are standard in advanced disease and as post-surgery treatment.

Radiation therapy is used to treat rectal cancer and is combined with 5-FU or capecitabine chemotherapy as a radiosensitizer. Radiation shrinks the tumor before surgery and reduces recurrence risk. Radiation is not routinely used for colon cancer due to risk of irradiation of nearby tissue. In some cases, it can be used palliatively to prevent symptoms from metastases or in unresectable recurrences. Modern radiation techniques allow for more precise targeting which increases the number of cases where it may be appropriate.[66]

Targeted therapy has emerged as a component of standard of care over the past two decades. The drugs target specific molecular pathways that cancer cells use. The most important of these approaches include anti-angiogenesis or vascular endothelial growth factor (VEGF) inhibitors, epidermal growth factor receptor (EGFR) inhibitors, B-Raf proto-oncogene, serine/threonine kinase (BRAF) inhibitors, Human Epidermal Growth Factor Receptor 2 (HER2) targeted therapy and Mismatch Repair-Deficient (dMMR) cancers.[67]

For RAS wild type, FOLFOX or FOLFIRI plus anti-EGFR antibodies (cetuximab or panitumumab) are administered. In selected patients that require high response rates, FOLFOXIRI plus bevacizumab is used. RAS mutant diagnosed patients receive FOLFOXIRI plus bevacizumab, FOLFOX or FOLFIRI plus bevacizumab and, for aggressive disease, FOLFOXIRI plus bevacizumab. In BRAF V600E mutant patients, FOLFOXIRI plus bevacizumab is often preferred and alternatively other doublet chemotherapy plus bevacizumab is used. BRAF/EGFR/MEK inhibitor combinations are considered for MSI-high/dMMR.

Second line therapy combines different variations of these agents. Third line and later treatment of mCRC prescribes kinase inhibitors such as regorafenib and anti-VEGFR fruquintinib. For BRAF V600E mutant tumors, Encorafenib, cetuximab and binimetinib are administered.

A diagnosis of oligometastatic CRC calls for aggressive local therapies that provide for long-term survival or a cure. A complete surgical resection of all metastases is required and is appropriate for patients with low tumor burden such as fewer than three metastases and small tumor size. If the metastases are unresectable, intensive systemic chemotherapy is used to downstage the diagnosis, after which resection may be employed. Other approaches for localized disease may employ metastasectomy, ablation of tumor tissue, stereotactic body radiation therapy (SBRT) and regional therapies.

[65] American Cancer Society. Chemotherapy for Colorectal Cancer. Accessed September 2025.
[66] Global Colon Cancer Association. Radiation Therapy for Colorectal Cancer. Accessed September 2025.
[67] American Cancer Society. Targeted Therapy Drugs for Colorectal Cancer. Accessed September 2025.

Peers and Competitors[68]

Targeted therapy is an important modality in oncology with a broad range of therapeutic approaches. The space includes several types of treatments that center on molecular changes in cancer cells. Some of the most visible products include antibody drug conjugates (ADCs), monoclonal antibodies (mAbs), and inhibitors of tyrosine kinase (TKIs), angiogenesis and poly (ADP-ribose) polymerase (PARP) among others. Another target in this category is Polo-Like kinase inhibition which has been pursued by a number of sponsors both large and small. An early innovator in PLK inhibition was Boehringer Ingelheim with BI 2536. The candidate did not advance to pivotal trials but did inspire the development of other PLK1 inhibitors by the pharmaceutical giant including volasertib. Volasertib advanced to a Phase III trial but did not meet its primary endpoint and raised safety concerns. Boehringer discontinued the program but did license the candidate to other sponsors including Notable Labs and Oncoheroes Biosciences.

Other notable PLK1 assets include Cyclacel's ploglosertib (now owned by Tethra Biosciences) a pan inhibitor which has undertaken Phase I/II studies but has not yet provided final data. Another pan-inhibitor is rigosertib which had been sponsored by a predecessor to Traws Pharma, which now owns the asset. The multi-kinase inhibitor targets cell-division proteins such as PLK1 and was the subject of two Phase III trials in myelodysplastic syndromes. However, neither study demonstrated a material overall survival (OS) benefit in patients.

Oric Pharmaceuticals and Repare Therapeutics are both developing competing selective PLK4 inhibitors designed to exploit synthetic lethality in tumors. They are both small molecule inhibitors that have further targeted TRIM37 amplification or overexpression, which is associated with breast cancer and neuroblastoma. Another PLK4 developer is Treadwell Therapeutics which is advancing ocifisertib. Ocifisertib seeks to disrupt cancer cell mitosis and force apoptosis. Treadwell is actively recruiting for a Phase I/II study for blood cancers and is also collaborating with several institutions on investigator-initiated studies in a variety of other solid and liquid tumors. Despite belonging to the same kinase family, PLK4 inhibitors are a distinct therapeutic class as they serve a different biological role. While PLK1 is essential for mitosis, PLK4 controls centrosome copy number and appear to have a narrower therapeutic window.

A number of established pharmaceutical companies have conducted early-stage work on the PLK class. Arbutus Biopharma's former asset was TKM-PLK1, an RNA interference (RNAi) therapeutic encapsulated in a lipid nanoparticle targeting hepatocellular carcinoma (HCC). GlaxoSmithKline's GSK461364 was an early-stage cancer drug candidate that was an ATP-competitive inhibitor of PLK1. The intravenously administered drug was evaluated in Phase I studies but did not advance further because of a high incidence of venous thromboembolism. More than a decade ago, Takeda was developing TAK-960, an oral PLK1 inhibitor. Preclinical data demonstrated tumor growth inhibition and a Phase I was started. However, the project was later terminated

Several PLK programs have been evaluated but later dropped due to toxicities and off-target effects due to poor isoform selectivity. Historically, PLK1 has been the primary target, but inhibition of PLK2 and PLK3, two tumor suppressor isoforms of PLK may counterbalance the effect of PLK1 inhibition. The use of some PLK inhibitors has been associated with cancer cells developing resistance due to upregulation of other kinases or parallel survival pathways.[69] In many cases, the efficacy of the varied PLK1 inhibitors has been modest which has stimulated interest in pursuing combination therapies. This may allow for targeting multiple receptors and provide synergistic effect. Chemotherapies, other targeted therapies such as PARP and MEK inhibitors as well as surgery and radiation when appropriate have all shown incremental benefits.

Next-generation PLK1 inhibitors target the non-catalytic polo-box domain (PBD), offering an allosteric mechanism to bypass the chronic issues associated with ATP-competitive inhibition which can improve PLK1 specificity.[70]

There are many agents used to treat CRC including a number of chemotherapies, anti-VEGF, RAS inhibitors and checkpoint inhibitors among others. There are several bispecifics in development to treat mCRC including PF-08634 sponsored by Pfizer, ivonescimab sponsored by Summit Therapeutics and pumitamig sponsored by Bristol Myers. Each of these products have origins in China and are in very early-stage development for mCRC.

[68] A useful summary of leading PLK1 inhibitors in CRC. Ye, P., *et al*. PLK1 inhibitors for the treatment of colorectal cancer. Annals of Medicine & Surgery. July 2025.
[69] Gutteridge, E.A. *et al*. Plk1 Inhibitors in Cancer Therapy: From Laboratory to Clinics. Molecular Cancer Therapeutics. July 2016.
[70] Park, J.E., *et al*. Specific inhibition of an anticancer target, polo-like kinase 1, by allosterically dismantling its mechanism of substrate recognition. Proceedings of the National Academy of Sciences (PNAS). August 2023.

Exhibit XIV – Peers and Competitors[71]

Ticker	Company	Price	MktCap (MM)	EV (MM)	Therapeutic Area
ABUS	Arbutus	$4.52	$869	$777	TKM-PLK-1 in HCC. siRNA. Abandoned.
AMGN	Amgen	$321.23	$172,976	$218,120	Ph1 AMG900 pan-Aurora kinase inhibitor-cell cycle regulation
AZN	AstraZeneca	$91.28	$283,020	$305,540	Imfinzi, PD-L2, Imjudo CTLA-4
BMY	Bristol-Myers Squibb	$51.67	$105,187	$139,730	Opdivo, Yervoy. Relatlimab, lirilumab in dev.
CGEM	Cullinan Therapeutics	$12.44	$735	$297	CLN081 small molecule in NSCLC w/ exon 20 insertion mutations
FATE	Fate Therapeutics	$1.07	$123	($12)	Multiple targets (CD19/BCMA/HER2) in 5 oncology indications
GILD	Gilead Sciences	$121.19	$150,373	$167,950	Checkpoints: MB272, partnership w/ Arcus anti-TIGIT & PD-L1
GSK	GlaxoSmithKline	$48.47	$98,185	$116,470	GSK461364-IV ATP competitive PLK1 inhibitor Ph1. Inactive.
INCY	Incyte Corp	$96.70	$18,984	$16,100	PD-1 retifanlimab & other PD-1 & PD-L1, TIM-3, LAG-3
IPHA	Innate Pharma	$1.90	$175	$140	Checkpoint: NKG2A target with monalizumab
LLY	Eli Lilly	$997.59	$894,296	$925,450	PD-1 Tyvyt
MGNX	MacroGenics	$1.33	$84	($26)	PD-1, CTLA-4, LAG-3, HER2, ADC, bispecifics,
MRK	Merck & Co.	$98.93	$247,106	$268,710	Keytruda. TIGIT (MK-7684) & LAG-3 (MK-4280) in development
MRKR	Marker Tx	$1.42	$18	$4	I-O: multi-tumor antigen approach
MRNA	Moderna	$27.97	$10,929	$7,160	Individualized neoantigen therapies for cancer
MRUS	Merus	$96.27	$7,302	$6,680	mAb therapeutics for cancer: anti-EGFR bispecific
NKTR	Nektar Tx	$57.28	$1,165	$986	IL-15 receptor agonists in dev. for liquid and solid tumors
NVS	Novartis	$130.17	$249,769	$276,980	Broad oncology portfolio
ORIC	ORIC Pharma	$10.52	$1,025	$741	Oncology assets: ORIC613-PLK4 inhibitor for TRIM37 in BC
PFE	Pfizer	$25.77	$146,521	$192,380	PD-L1 Bavencio, PD-1 sasanlimab
REGN	Regeneron	$703.26	$75,500	$69,760	PD-1 Libtayo, LAG-3 fianlimab, bispecifics
RHHBY	Roche	$48.90	$311,519	$335,610	Broad oncology portfolio: PLK1 RO3280-not active
RPTX	Repare Tx	$2.15	$92	($19)	Ph1 RP1664 PLK4 for TRIM37 overexpression
RVMD	Revolution Medicines	$80.06	$15,477	$13,700	RAS targeting portfolio w/ 3 assets.
SNSE	Sensei Bio	$8.24	$10	($13)	SNS-101: VISTA for solid tumors. Also VSIG4 & CD39 targets
TAK	Takeda	$14.22	$47,321	$70,480	PLK1s TAK960 (oral & discontinued) & MN0905 (preclin)
TRAW	Traws Pharma	$2.16	$17	$11	Pan-inhibitor including PLK1 rigosertib. Divesting.
pvt	Boehringer Ingelheim				Volasertib, BI2536 PLK1 & others discontinued
pvt	Tethra Biosciences				Oral PLK1 plogosertib Ph2 in solid & liquid tumors
pvt	Nerviano MS				PLK1 licensed to Cardiff (NMS-P937)
pvt	Oncoheros Bio				Acquired rights to volasertib from BI
pvt	Treadwell Tx				PLK4 in AML: Ph1/2 ocifisertib
CRDF	Cardiff Oncology	$2.34	$158	$83	Advancing onvansertib in Ph3 for RAS mutated mCRC

[71] Compiled by Zacks' analysts as of December 8, 2025

Financial & Operational Results

Milestones

- Cardiff Oncology predecessor Xenomics, Inc. founded in San Diego – 1999
- Xenomics changed name to Trovagene focused on diagnostics – 2004
- Nerviano Medical Sciences performs preclinical studies on onvansertib – 2010s
- Addition of PLK1 inhibitor to pipeline, later called onvansertib – 2017
- First clinical trials evaluating onvansertib in AML - 2017
- USAN approval of onvansertib as non-proprietary name of the PLK1 inhibitor – August 2018
- Onvansertib expansion into CRC – 2019
- Corporate name changes to Cardiff Oncology - 2020
- Appointment of Mark Erlander as CEO – 2020
- James Levine appointed CFO – July 2021
- Pfizer breakthrough growth initiative $15 mm grant – November 2021
- Tod Smeal, Ph.D. appointed CSO – January 2022
- Lead program in first line mCRC announced (CRDF-004) – August 2023
- Publication of Pivotal mCRC Results – October 2024
- $40 million registered offering – December 2024
- CRDF-004 enrollment completed – April 2025
- Triple negative breast cancer data presented at ASCO – June 2025
- Dr. Roger Sidhu appointed CMO – June 2025
- Interim update on CRDF-004 trial – July 2025
- Poster presentation of investigator-sponsored data in CMML at ASH – December 2025
- Presentation at Sidoti's investor conference – December 2025
- Launch of Phase III onvansertib trial (CRDF-005) - 2026

Origin of Cardiff Oncology

Cardiff's existence as a life sciences company began in 2004 when a corporate shell acquired Xenomics, a company developing transrenal DNA technology. In 2010 the company changed its name to TrovaGene, Inc. with a focus on cancer medicine diagnostics and liquid biopsy platforms. The company's product detected circulating tumor DNA in urine and blood samples using noninvasive technology. In 2012 TrovaGene began trading on the NASDAQ under the ticker TROV. The listing provided access to capital to continue development of its circulating tumor DNA precision cancer monitoring (PCM) tests. In 2017, the company in-licensed onvansertib from Nerviano Medical Sciences, a large oncology-focused research development company in Italy. After the licensing, TrovaGene moved the candidate into clinical trials and shifted its focus exclusively on oncology therapeutics. Initial work centered on acute myeloid leukemia (AML), KRAS-mutated metastatic colorectal cancer (mCRC), and castration-resistant prostate cancer (mCRPC).

In May 2020 the company changed its name to Cardiff Oncology, presumably to credit the seaside town north of San Diego called Cardiff-by-the-Sea, near the company's headquarters. Simultaneously, Dr. Mark Erlander, who had served as the Chief Scientific Officer since 2013, was appointed as Chief Executive Officer. In the following years after the name change, Cardiff narrowed its focus to metastatic CRC, and more recently first line mCRC.

In December 2024 Cardiff Oncology announced positive initial efficacy data from its first-line RAS-mutated mCRC clinical trial (CRDF-004), demonstrating a 64% objective response rate in patients on the 30mg onvansertib dose arm compared to 33% in the control arm. Along with the compelling data, the company raised $40 million through an underwritten registered direct offering at $2.60 per share. The transaction strengthened the balance sheet with support from biotech specialist investors.

As April 2025 rolled around, Cardiff completed enrollment in the CRDF-004 trial and in July 2025 reported confirmed ORR of 49% at the 30 mg dose of onvansertib compared with control generating a 30% ORR. Onvansertib has been well tolerated and provides a dose dependent response which suggests the 30 mg dose is optimal. The favorable data prompted an investor presentation of the CRDF-004 trial data with the newly appointed Chief Medical Officer, Dr. Roger Sidhu along with the report of second quarter results. Several examples of complete responses were shared on the call.

In parallel with the CRDF-004 trial, an investigator-initiated trial of onvansertib was being run in metastatic triple negative breast cancer. Data from the study was presented in a poster at the American Society of Clinical Oncology (ASCO) Annual Meeting in late May and early June. Results showed that onvansertib generated a 40% objective response rate at the highest dose and validate earlier work that demonstrated synergies between onvansertib and paclitaxel.

2025 Financial Results

Cardiff reported results for the first nine months of 2025 in a press release and Form 10-Q filing with the SEC on November 6th, 2025. For the nine-month period ending September 30th, 2025 and versus the comparable prior year period, revenues of $350,000 were reported vs. $533,000 in the same prior year period. Loss for the first nine months totaled ($38.7) million or ($0.58) per share. Operational expenses rose 13% due to increases in both research and development (R&D) and general and administrative (G&A) expenses.

- Revenues of $350,000 compared to $532,000 and represent Cardiff's sales based and usage-based royalties on assets unrelated to onvansertib;
- Research and development expenses totaled $30.3 million, up 11.5% from $27.1 million attributable to greater expenditures for the CRDF-004 clinical trial, clinical programs and outside service costs related to developing onvansertib. Salaries and staff costs rose due to new hires in research and development and clinical operations. Stock compensation was also higher;
- Selling, General & Administrative expenses were $11.2 million, up 19% from $9.5 million. Increases relate to higher salaries and staff costs related to an employee severance agreement and higher professional fees related to strategic advisory services used during the period. Patent fees and stock-based compensation also rose;
- Net interest income of $2.5 million was essentially flat with prior period levels and other income of $6,000 compared to other expense of $37,000;
- Net loss was ($38.7) million vs. ($33.7) million or ($0.58) and ($0.74) per share, respectively.

As of September 30th, 2025, cash totaled $60.6 million. This amount compares to the $91.7 million balance in cash held at the end of 2024. Cash burn for the first nine months of 2025 was ($32.0) million versus ($27.5) million for 2024. Cardiff's cash is expected to support operating activities until 1Q:27.

Management Profiles

Mark Erlander, Ph.D,, Chief Executive Officer

Dr. Erlander has served as Cardiff's Chief Executive Officer since May 2020 and was formerly the Chief Scientific Officer at the company from March 2013 to May 2020. Previously, he was Chief Scientific Officer at bioTheranostics, a subsidiary of bioMérieux, a molecular diagnostic testing company focused on clinical applications in oncology, where he served from 2008 to 2013. From 2000 to 2008, Dr. Erlander was Chief Scientific Officer at Arcturus, Inc. (later AviaraDx), which was acquired by bioMérieux in 2008. Dr. Erlander entered therapeutics as a Group Leader and then Research Fellow in drug discovery at Johnson & Johnson from 1994 to 2000. From 1991 to 1994, Dr. Erlander was a Postdoctoral Fellow and then Assistant Professor at Scripps Research. He has 44 issued patents, over 50 pending applications and has co-authored more than 90 scientific publications. Dr. Erlander holds a B.S. in Biochemistry from the University of California, Davis, an M.S. degree in Biochemistry from Iowa State University, and a Ph.D. in Neuroscience from the University of California, Los Angeles.

James Levine, Chief Financial Officer

Mr. Levine has served as Chief Financial Officer since 2021. Mr. Levine has extensive corporate and investment banking experience with both private and public biotechnology and pharmaceutical companies. Prior to joining Cardiff Oncology, Mr. Levine served as CFO of Cidara Therapeutics, where he led the financial aspects of important pre-clinical and clinical collaborations with Janssen Pharmaceuticals (part of Johnson & Johnson) and Mundipharma with a combined value of over $1.3 billion. Previously, Mr. Levine was the president and chief executive officer of Sapphire Energy Inc., a private industrial biotechnology company that was sold to two private investor groups. He also previously served in the same roles at Verenium Corp., where he negotiated six product commercialization partnerships and asset sales, before selling the company to BASF. He also previously served as a managing director in the investment banking division of Goldman Sachs & Co. in its healthcare and energy groups.

Mr. Levine earned an MBA in finance from the Wharton School of the University of Pennsylvania and a BA in economics from Brandeis University.

Roger Sidhu, M.D., Chief Medical Officer

Dr. Sidhu is an accomplished and seasoned drug developer who joined Cardiff Oncology in 2025 with over 20 years of oncology leadership and clinical experience. Dr. Sidhu has advanced therapeutics across multiple modalities, and from Phase I to Phase III clinical development and through commercial launch. Dr. Sidhu was most recently Acting CEO and Chief Medical Officer at Treadwell Therapeutics, a privately held biotechnology company where he was responsible for advancing a portfolio of small molecules for the treatment of solid tumors and hematologic malignancies. Prior to that role, Dr. Sidhu has held the role of VP of Clinical Development at Kite, a Gilead Company, Chief Medical Officer at Cell Design Labs, Executive Vice President and Chief Medical Officer at Roivant Sciences, and Chief Medical Officer at Eterna Therapeutics (now Ernexa).

Dr. Sidhu spent nearly 10 years at Amgen in roles of increasing responsibility in the Hematology/Oncology therapeutic area where he advanced multiple therapeutic candidates. In metastatic colorectal cancer, he led multiple Phase III clinical trials of panitumumab (Vectibix) in monotherapy and in combination with chemotherapy leading to approvals in the U.S. and globally. Dr. Sidhu was also a leader in advancing the science of RAS biology and therapeutics in metastatic colorectal cancer, which was published in the New England Journal of Medicine.

Dr. Sidhu is a Fellow of the Royal College of Physicians and Surgeons of Canada in both internal medicine and medical oncology. He earned his medical degree from Queen's University in Kingston, Ontario, Canada and his bachelor's degree in biochemistry from the University of Alberta in Edmonton, Alberta.

Tod Smeal, Ph.D., Chief Scientific Officer

Dr. Smeal has served as Chief Scientific Officer since January 2022. Previously he was CSO at Hexagon Bio (2020-2021), CSO of Cancer Biology at Eli Lilly and Company (2015-2020), Director at the Oncology Research Unit of Pfizer (2003-2015), and Senior Group Leader at the SUGEN site of Pharmacia and Upjohn and SUGEN (1998-2003). When Pfizer closed the SUGEN site in 2003, Dr. Smeal continued his oncology research efforts on targeted therapies and their resistance mechanisms with Pfizer at their San Diego oncology research site. Subsequently in 2015, Dr. Smeal joined Eli Lilly where he led their oncology research efforts at Lilly Research Labs in Indianapolis. During his over 20 years in industry working on targeted therapies, Dr. Smeal has played key leadership roles in delivering about 20 FHD/NMEs and several FDA approved or soon to be approved drugs (e.g., Lorbrena, Xalkori, Vizimpro and Nirogacestat). Dr. Smeal's work in developing cancer therapies has been focused on intracellular signaling, kinases, drug pharmacology, and targeted therapies and their resistance mechanisms. He has over 45 publications which includes high impact publications in Cell, Nature, New England Journal of Medicine, Cancer Cell and Cancer Discovery.

From 1994 to 1998, Dr. Smeal was a post-doctoral fellow of the American Cancer Society and a senior post-doctoral fellow of the MIT-Merck fellowship program. Dr. Smeal holds a B.S. in Biology from the Massachusetts Institute of Technology and a Ph.D. in Biology from the University of California, San Diego.

RISKS

All investments contain an element of risk that reflects the uncertainty of a business and what it will ultimately achieve. Some investments exhibit higher predictability, with current cash flows and established sales. These enterprises will have a lower level of perceived risk while other companies that are developing an undefined, new technology have a much higher level of perceived risk.

The biotechnology space includes companies at both ends of the spectrum, from mega-cap pharmaceutical titans that have multiple products generating revenues, to small operations with a handful of employees conducting preclinical studies. Many of the risks faced by the large pharmaceutical companies and smaller biotechnology-focused firms are similar; however, some hazards are specific to smaller companies that have not yet established themselves or their products.

For smaller, early-stage companies, such as Cardiff, investing in drug development is a lengthy process. The timeframe for conducting preclinical research to eventually commercializing a drug can take from 12 to 15 years or even longer given market and company-specific conditions. And with, on average, only one in one thousand compounds eventually making it to the market from the discovery stage, the risks are substantial.

Financing

Even if a company has a strong, experienced team that is developing a therapy with a high likelihood of success and a large addressable market, securing funding may be difficult. Access to financing comes and goes in cycles. During periods of improving confidence, capital may be easy to obtain; however, during a liquidity crisis or a period of heightened risk perception, even companies with bright prospects may be in trouble if they are dependent on the financial markets to fund their work. If capital is needed to sustain operations and it is not readily available, the company may be forced to suspend research and development activities, sell equity at a substantial discount to previous valuations and dilute earlier shareholders. A lack of funding may leave potentially promising therapies without a viable route to progress or force a company to accept onerous terms.

Increases in cost of capital can make previously attractive investments less so. Interest rates have increased over the last several years, materially changing the perceived net present value and reward to risk ratio for many investments, especially those in higher risk categories such as drug development. Early-stage life sciences companies are dependent on a steady flow of capital to support their research and development activities. As capital becomes more dear, previously attractive projects may no longer be, making access to critical capital inflows less certain. In 2024, Cardiff raised over $53 million in a registered direct offering with a consortium of banks and Sales Agreement with Jefferies, LLC that increased cash on hand to over $60 million as of the start of 4Q:25. The company has also had regular access to the capital markets and we expect funding to last until 1Q:27. Additional capital will have to be raised to support the anticipated registrational CRDF-005 trial.

Partners

Contract research organizations (CROs) have assumed a larger role in the development of drug candidates as the complexity and cost of trials has increased. Finding appropriate populations to participate in clinical trials has become increasingly difficult due to the shift to biomarker defined groups, screening for specific mutations, personalized medicine and orphan indications that address small clusters of patients. This shift has increased the dependence on specialized CROs for project management and clinical monitoring services that add additional risks related to third parties. During its early clinical work, Cardiff relied on university partners to conduct research work; but in August 2023, after it was clear that first line use of onvansertib was the most beneficial path forward, Pfizer Ignite took over the management of the CRO services for the CRDF-004 trial. We anticipate that Cardiff will forge a new relationship to manage the Phase III CRDF-005 study.

A CRO partner may face competing demands which can adversely affect the work they are managing on behalf of the client. CROs and subcontractors must abide by strict execution and trial parameters that if violated can jeopardize trial execution or data validity. Patient recruitment may be difficult. Subcontractors supervise and execute research as well as conduct biometric and pharmaco-vigilance, which are complex tasks. Clinical investigational centers need sufficient capacity and the candidate drug needs to be manufactured in compliance with current Good Manufacturing Practices (cGMP) and be available to administer to patients. Finally, the data itself needs to produce results that achieve sufficient statistical significance and clinical relevance to justify regulatory approval.

Regulatory Environment

All drugs must navigate the regulatory approval process in the US, EU, Japan and other countries before commercialization. Success is uncertain and may take years depending upon the needs and desires of the determining authority. Substantial expense is undertaken to bring a molecule or compound through clinical trials and address all of the regulatory agencies' concerns. Companies that offer a history of research success in drug development, with opinion leaders and experts in the field are in a stronger position to mitigate this risk. Companies and management teams that have achieved previous success with the FDA or other regulatory agencies are more attractive than those that are new to the process. Cardiff has multiple team members who have shepherded products through the regulatory process including the Chief Medical Officer, Dr. Roger Sidhu. Accelerated pathways to approval may be appropriate in some cases, such as those outlined in the Orphan Drug Act, Regenerative Medicine Advanced Therapy (RMAT) program and the Breakthrough Therapy designation; however, changes in sentiment or perceived safety for pharmaceuticals drugs could alter the regulatory environment to demand a more thorough process and these pathways may be extended or additional requirements may be put in place. Cardiff was granted a Fast Track designation by the FDA in 2020 for treatment of colorectal cancer which enables onvansertib to be eligible for priority review and accelerated approval.

Exhibit XV – Success of Phased Trials and Regulatory Approval[72]

Phase	I - II	II - III	III - NDA/BLA	NDA/BLA - Approval	I - Approval
Probability	52.0%	28.9%	57.8%	90.6%	7.9%

Competitive Environment

Many firms are developing new oncology products and must compete against established treatments that are entrenched in the health care system. In oncology, for example, there are hundreds of approved agents available. According to Evaluate Pharma there are 459 protein kinase inhibitors marketed in oncology as of October 2025. On the development side, there are 33 of these oncology agents filed, 114 in Phase III and 286 in Phase II. To differentiate itself from other sponsors, Cardiff has focused on a target that is not being broadly pursued by other sponsors in RAS mutated, first line mCRC. Onvansertib also employs a mechanism of action that is selective for the PLK1 kinase with only minimal binding to other isoforms which minimizes off-target toxicity in contrast to the profile exhibited by earlier Polo-Like kinase inhibitors.

Marketing and Commercialization Risk

Successful marketing of approved drug candidates relies on adoption by patients and providers. An approved drug must have convincing clinical trial data and maintain a favorable reputation among prescribers. Marketing is expensive and requires an experienced sales force and a presence in the marketing region. Marketed products remain under surveillance and any unexpected adverse effects may lead regulatory authorities to revoke marketing authorization. Inclusion of the drug in insurance plan offerings is also important. Rapidly obtaining a preferred position on health plan and payor formularies is critical to achieving target penetration rates. If health plans and payors cannot agree on appropriate pricing for the drug and the compound fails to offer a significant benefit above standard of care, sales may be limited. Cardiff is several years away from marketing and commercialization activities. We anticipate that the company will hand off its assets after further development to an established partner who will assume these responsibilities and risks.

Manufacturing

Medical product companies can either produce medicines in-house or rely on third parties to manufacture them. While there are many benefits to owning manufacturing facilities and exercising direct control, in most cases small and medium size biopharmaceutical companies work with partners through supply agreements to make their products. Working with a partner confers several benefits including economies of scale, a management team dedicated to compliance with regulatory requirements and the flexibility of engaging other manufacturers based on changing circumstances. The use of a contract development and manufacturing organization (CDMO) also limits the capital burden of a single product company and more closely aligns volume, costs and their respective timing. While there are numerous benefits to outsourcing manufacturing, a sponsor can also be exposed to several risks. Manufacturing partners may not prioritize client projects and may run afoul of regulatory requirements. The manufacturer may experience quality control or volume constraints that could disrupt demand. Take or pay contracts could force the client to accept more product than can be sold in a reasonable time, impacting cash flow and producing excessive

[72] Summarized from Clinical Development Success Rates 2011-2020. Compiled by Zacks Analysts.

inventory which could expire before sale. Using outside contractors could also allow internally developed trade secrets to be compromised. Nerviano initially manufactured onvansertib for Cardiff but the latter has subsequently secured another source of supply for clinical supply. Onvansertib is a small molecule that does not have any special manufacturing requirements compared with other widely used products, which opens up a broad network of CDMOs around the globe that can satisfy Cardiff's supply needs.

Intellectual Property

Despite the existence of patents, exclusivity and trade secrets, infringement of intellectual property is a risk. Cardiff owns 28 patent families related to onvansertib and owns and licenses 57 issued patents and has 57 patents pending. They include composition of matter and the use of a PLK1 inhibitor and onvansertib in combination with a broad selection of other agents including bevacizumab. The patents also provide protection for the use of onvansertib in treating mCRC and other cancers.

Geopolitical

Trade tensions and the imposition of tariffs by the United States have negatively impacted the global economy, slowed cross-border commerce and limited technology transfer. The conflict may add an additional layer of cost to cross-border distribution of medical products and reduce the availability of capital. It may also limit the formation of partnerships and future development and commercialization deals between countries around the globe. The UK withdrew from the European Union in 2020, creating additional trade, transportation and other barriers between the UK and mainland Europe. Conflict between Ukraine and Russia and between Israel and Gaza has led to disruptions in these countries. Sanctions have been imposed on many Russian businesses which may lead to product shortages. Refugees fleeing the war in Ukraine may also impact nearby nations and their productivity which could affect clinical trials and commercialization in the region. In 2025 there has been a series of tariffs announced that includes pharmaceuticals which may impact sourcing costs and the viability of manufacturing outside the United States. Cardiff relies on clinical stage product manufactured in the United States. However, if commercial quantities of product are needed, high tariffs may impact sourcing decisions.

Inflation

Drug price inflation has gained attention as it and other healthcare costs have risen at a materially faster pace than overall prices. As new therapies have been approved, drug prices have increased to reflect higher development costs and improved pricing power of pharmaceutical and biotech companies. On the demand side, deductibles and co-pays have steadily risen over the last decades, and in some cases, individuals and families must cover several thousand dollars in costs before the benefits of insurance begin. Cost sharing or co-insurance is another component of insurance plans that directly increases a patient's burden. This has resulted in greater elasticity in demand for drugs than was previously the case. Individuals with high deductibles or no insurance may be very sensitive to price and avoid treatments with high cost.

While we have discussed a broad variety of risks above, we believe that our forecast parameters, discount rates, success probabilities and valuation metrics address these potential outcomes and our target price reflects an assumption of these risks faced by life sciences companies in general and Cardiff Oncology specifically.

VALUATION

Cardiff is advancing onvansertib to pursue its primary indication of mCRC. We expect onvansertib to move forward in a Phase III registrational trial in 2026. While there are other indications in development, we focus on the lead. Based on the stage of the mCRC program and the anticipated endpoints, we forecast the start of the Phase III study in 2026, with accelerated approval endpoints reported in 2028, producing a new drug application (NDA) in 2029 and FDA approval in 2030. We anticipate commercialization in late 2030 with a partner. We also see a market in the international developed world. Pursuit of regulatory approval in these regions, which include the European Union, Asia and Oceania among others is expected to begin in 2030 with first sales in 2031. In the interim, we anticipate updates from the trial which are expected to confirm results that we have seen in the Phase II studies.

Colorectal cancer (CRC) is one of the larger indications in oncology as the third or fourth most common tissue site in the global and US populations for cancer to appear. Cardiff is pursuing first line metastatic CRC (mCRC), which makes up about a fifth of the total. This is onvansertib's addressable market. In the United States, the addressable market is approximately one-fifth of the total CRC population or about 30,000 people. In the developed world, we assume a similar incidence of diagnosis, which is equivalent to about 84,000 cases per year.

Onvansertib is expected to start a Phase III trial in early 2026. Cardiff is in discussions with the FDA to finalize the trial design. Designated CRDF-005, we expect that the Phase III study will be constructed to satisfy requirements for both accelerated and full approval, with endpoints of ORR and duration of response (DoR) for accelerated approval and PFS and lack of detriment on OS for full approval. Further details on the design are expected in the coming months. Cardiff has been granted Fast Track for onvansertib in mCRC and we expect this to streamline communications with the agency.

In the first year (2030) of approval, we assume onvansertib to penetrate 1.0% of the addressable market. Year two is expected to jump to 5.0% rising to 20.5% by year seven (2036). This equates to 308 patients in year one and 6,700 by year seven. Ultimately, we think onvansertib can serve about a quarter of the addressable market. Our model assumes that competition begins in 2047, and growth will decline by a terminal rate of 10% annually in subsequent years. In developed international markets, we also see first-year (2031) penetration of 1.0% into the addressable population of mCRC. This is anticipated to grow to 16% penetration by year seven (2037). This equates to about 900 patients treated in year one and 15,000 in year seven. Similar to what we expect for the United States, competition will begin after 2046 and subsequent years will see a 10% annual decline. We assume pricing for onvansertib to be approximately $120,000 per course of treatment in the US, growing at a 3% inflation rate. In markets outside the US, we assume a 50% reduction in revenues which is equivalent to $60,000 per course of treatment. Price inflation in markets outside the US is expected to be 1.5% per year.

Our thesis relies on an established pharmaceutical partner obtaining rights to onvansertib or buying out Cardiff Oncology prior to onvansertib's commercialization. Due to the large unmet need, absence of other competing products with a similarly effective mechanism of action and target, anticipated multiple bidders and combination of favorable safety and efficacy, we assume a royalty (which is inclusive of upfronts and milestones for the purposes of our valuation) of 36%. This represents the entirety of economic value received for the asset. We net out eight percentage points to reflect the royalty owed to Nerviano Medical Sciences. This produces a net royalty of 28% to Cardiff Oncology. These assumptions generate royalty income of $12 million in 2030 and over $580 million by 2036.

Estimates for operational costs call for $39 million in cash expense for 2025, $41 million in 2026 and $42 million in 2027 after which costs are estimated to grow at a low-single-digit per annum rate. Following commercialization, research and development amounts are predicted to fall to zero. After first profits are generated, net operating losses will be consumed. After NOLs are exhausted, we forecast a 25% cash tax rate on earnings. After tax cash flows to the company are discounted at a 15% rate with a terminal growth rate of -10% beginning in 2047. We apply an overall 60% likelihood of success of Cardiff's mCRC program given the stage of development, interim results, safety profile and data generated to date.

Option and warrants are assumed to be exercised if below our target price with proceeds added to cash and exercised shares added to shares outstanding. In addition to the approximately 67 million shares of common stock and 12 million warrant and option shares, we add an additional 13 million shares to reflect anticipated capital raises in 2027. Shares used to calculate our target price are approximately 92 million.

Despite the conservative stance of our assumptions, penetration into addressable markets can potentially be higher for onvansertib if study results demonstrate strong efficacy, synergy with other agents, safety and success in addi-

tional indications. The determinant for many of the variables in our model will be the ultimate performance of onvansertib in pivotal studies. We will update our model accordingly as data is made available and if other indications in the pipeline are advanced towards an anticipated new drug application.

Based on the assumptions identified in our discounted cash flow model, we generate a valuation of $8.50 per share.

PROJECTED FINANCIALS

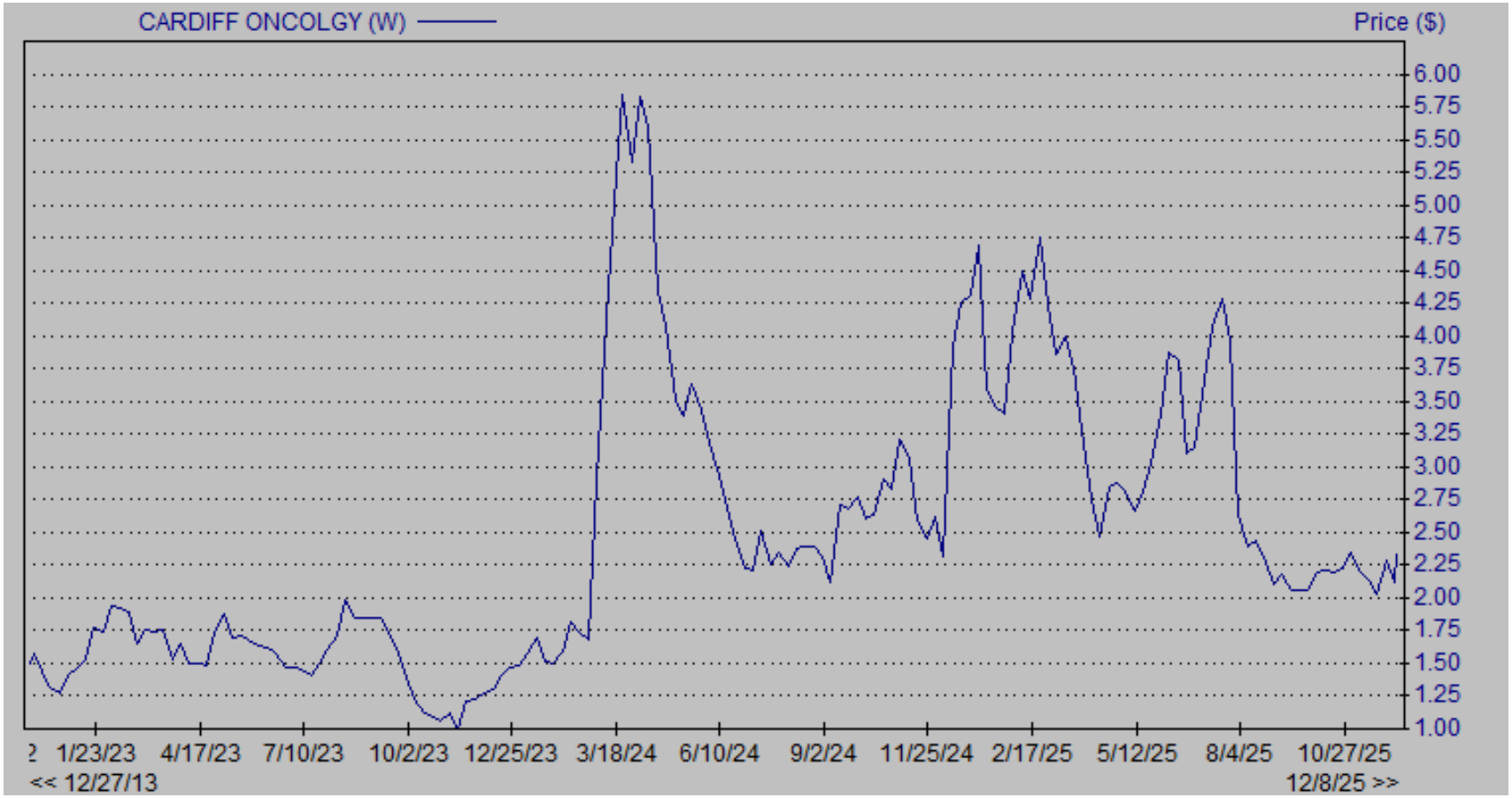
Cardiff Oncology, Inc. - Income Statement

Cardiff Oncology, Inc.	2023 A	2024 A	Q1 A	Q2 A	Q3 A	Q4 E	2025 E	2026 E	2027 E
Total Revenues ($USD)	**$488**	**$683**	**$109**	**$121**	**$120**	**$100**	**$450**	**$695**	**$725**
Research & Development	$32,857	$36,852	$10,477	$11,580	$8,197	$9,000	$39,254	$41,000	$44,000
Selling, General & Administrative	$13,043	$12,482	$4,014	$3,318	$3,897	$3,500	$14,729	$16,000	$17,200
Income from Operations	($45,412)	($48,651)	($14,382)	($14,777)	($11,974)	($12,400)	($53,533)	($56,305)	($60,475)
Interest Income, net	$4,069	$3,259	$941	$835	$716	$602	$3,094	$2,050	
Other Items	($98)	($39)	$7	($1)	$0	$0	$6		
Preferred Stock Dividend	($24)	($24)	($6)	($6)	($6)	($6)	($24)		
Pre-Tax Income	($41,465)	($45,455)	($13,440)	($13,949)	($11,264)	($11,804)	($50,457)	($54,255)	($60,475)
Provision for Income Tax	$0	$0	$0	$0	$0	$0	$0	$0	$0
Net Income	**($41,465)**	**($45,455)**	**($13,440)**	**($13,949)**	**($11,264)**	**($11,804)**	**($50,457)**	**($54,255)**	**($60,475)**
Net Margin									
Reported EPS	**($0.93)**	**($0.95)**	**($0.20)**	**($0.21)**	**($0.17)**	**($0.18)**	**($0.76)**	**($0.81)**	**($0.77)**
YOY Growth									
Basic Shares Outstanding	44,677	47,650	66,524	66,526	66,879	66,987	66,729	67,150	79,000

Source: Company Filing // Zacks Investment Research, Inc. Estimates

HISTORICAL STOCK PRICE

Cardiff Oncology, Inc. – Share Price Chart[73]



[73] Source: Zacks Research System

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