

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered ⁽¹⁾	Proposed Maximum Aggregate Offering Price per share ⁽¹⁾	Aggregate Maximum Offering Price ⁽¹⁾	Amount of Registration Fee
Common stock, par value \$0.0001 per share	2,411,575	\$ 6.22	\$ 14,999,997	\$ 1,391

(1) The Company is offering for sale 2,411,575 shares of the Company's common stock at \$6.22 per share.

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-254217

PROSPECTUS SUPPLEMENT (TO PROSPECTUS DATED MARCH 12, 2021)



Cardiff Oncology, Inc.

2,411,575 Shares of Common Stock

We are offering 2,411,575 shares of our common stock, or Shares, to Pfizer Inc.

Our common stock is listed on the Nasdaq Capital Market under the symbol "CRDF" On November 17, 2021, the last reported sale price of our common stock on the Nasdaq Capital Market was \$5.23 per share.

Investing in our securities involves risks. See "Risk Factors" beginning on page S-6 of this prospectus supplement, page 10 of the accompanying prospectus and under similar headings in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

Delivery of the securities offered hereby is expected to be made against payment therefor on or about November 18, 2021.

The date of this prospectus supplement is November 18, 2021

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ABOUT THIS PROSPECTUS SUPPLEMENT

You should rely only on the information contained in or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information in this prospectus supplement, the accompanying prospectus, and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety before making an investment decision. You also should read and consider the information in the documents to which we have referred you in the section of this prospectus supplement entitled "Information Incorporated by Reference" and the sections of the accompanying prospectus entitled "Information Incorporated by Reference" and "Where You Can Find More Information."

This prospectus supplement and the accompanying prospectus form a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the "Commission") utilizing a "shelf" registration process. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts combined. This prospectus supplement may add to, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference herein or therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference herein and therein.

For investors outside the United States, we have not done anything that would permit this offering or possession or distribution of this prospectus supplement in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus supplement outside of the United States.

As permitted by the rules and regulations of the Commission, the registration statement, of which this prospectus supplement and the accompanying prospectus form a part, includes additional information not contained in this prospectus supplement or the accompanying prospectus. You may read the registration statement and the other reports we file with the Commission at the Commission's web site or at the Commission's offices described below under the heading "Where You Can Find Additional Information."

Trademarks, service marks or trade names of any other companies appearing in this prospectus supplement are the property of their respective owners. Use or display by us of trademarks, service marks or trade names owned by others is not intended to and does not imply a relationship between us and, or endorsement or sponsorship by, the owners of the trademarks, service marks or trade names.

PROSPECTUS SUPPLEMENT SUMMARY

The following summary highlights certain of the information contained elsewhere in or incorporated by reference into this prospectus supplement. Because this is only a summary, however, it does not contain all the information you should consider before investing in our securities and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information included elsewhere in or incorporated by reference into this prospectus supplement. Before you make an investment decision, you should read this entire prospectus supplement and the accompanying prospectus carefully, including the risks of investing in our securities discussed under the section of this prospectus supplement entitled "Risk Factors" and similar headings in the other documents that are incorporated by reference into this prospectus supplement. You should also carefully read the information incorporated by reference into this prospectus supplement, including our financial statements, and the exhibits to the registration statement of which this prospectus supplement is a part.

Unless the context otherwise requires, references to "we," "our," "us," "Cardiff" or the "Company" in this prospectus supplement mean Cardiff Oncology, Inc.

Overview

We are a clinical-stage oncology company, developing new precision medicine treatment options for cancer patients in indications with the greatest unmet medical need. Our goal is to target tumor vulnerabilities with treatment combinations that overcome disease resistance and improve disease response to standard treatment regimens and to increase overall survival. We are developing onvansertib, an oral highly-selective Polo-like Kinase 1 ("PLK1") inhibitor, in combination with standard-of-care anti-cancer therapeutics. Our clinical development programs incorporate tumor genomics and biomarker technology to refine assessment of patient response to treatment.

We licensed onvansertib from Nerviano Medical Sciences ("NMS") pursuant to a license agreement with NMS dated March 13, 2017. This exclusive, world-wide license agreement includes 3 issued patents for onvansertib which cover composition of matter, salt forms of onvansertib and combination of onvansertib with other drugs.

Onvansertib is a novel PLK1 selective adenosine triphosphate ("ATP") competitive inhibitor with oral bioavailability, and a relatively short drug half-life of 24 hours. Onvansertib is highly potent against the PLK1 enzyme (concentration for 50% inhibition [IC₅₀]=5±3 nM), whereas low or no activity was observed on a panel of 63 kinases (IC₅₀>500 nM), including the PLK members PLK2 and PLK3 (IC₅₀>10 µM).

PLK1, a serine/threonine kinase, is a master regulator of mitotic progression with various roles and localizations during the different mitotic phases. Upon PLK1 depletion in cancer cells by RNA interference ("RNAi"), inhibition of proliferation, and decreased viability, resulting from cell cycle arrest with 4N DNA content followed by apoptosis, are observed. PLK1 depletion also results in an increase in the number of cells containing abnormal spindle formation and misaligned chromosomes. Expression of PLK1 is seen in all proliferating normal tissues, and PLK1 is overexpressed in a number of tumors (including colorectal, pancreatic, prostate, ovary, breast and lung cancer), as well as in hematologic cancers.

Although 5 different PLK family members are described in humans, the inhibition of the enzymatic activity or the depletion of PLK1 is sufficient to induce a G2/M cell cycle block and apoptosis in tumor cell lines and tumor regression in xenograft models. In addition, a tumor suppressor function has been described for PLK2 and PLK3 (but not PLK1), and they are reported to be expressed in non-proliferating, differentiated postmitotic cells, such as neurons, indicating a potentially better safety profile for a PLK1-selective compound.

Onvansertib is a highly selective inhibitor of PLK1. The fumarate salt of the compound was formulated for oral administration and is in clinical development for the treatment of a wide range of tumor types. There are 3 ongoing clinical studies of onvansertib in combination treatment: second line treatment in patients with KRAS-mutated metastatic colorectal cancer ("mCRC"), second line treatment in patients with metastatic pancreatic ductal adenocarcinoma ("mPDAC"), and in patients with metastatic castration-resistant prostate cancer ("mCRPC") showing resistance to abiraterone.

In vitro studies have shown synergistic effects when onvansertib was administered in combination with different cytotoxic agents including antimicrotubule agents, topoisomerase 1 inhibitors, antimetabolites, alkylating agents, proteasome inhibitors, kinase inhibitors, BCL-2 inhibitors, and androgen biosynthesis inhibitors.

In addition, in vivo combination studies have confirmed the positive results obtained in vitro and synergistic effects have been observed in xenograft models of onvansertib in combination with abiraterone, 5-fluorouracil (5 FU), irinotecan

(including NKTR-102), quizartinib, venetoclax, and paclitaxel, while additive effects in combination with cytarabine or bevacizumab have been demonstrated.

We believe the high-selectivity of onvansertib to PLK1, its 24-hour half-life, oral bioavailability, and flexible dosing schedule, as well as evidence of favorable safety and clinical benefit, with expected on-target, easy to manage and reversible side effects, may prove beneficial in addressing clinical therapeutic needs across a variety of cancers.

Ongoing Clinical Programs Update:

- TROV-054 is a Phase 1b/2 open-label multi-center clinical trial of onvansertib in combination with FOLFIRI and bevacizumab ("Avastin®") for the second line treatment of patients with KRAS-mutated mCRC, which is being conducted at 7 clinical trial sites across the U.S. - USC Norris Comprehensive Cancer Center, The Mayo Clinic Cancer Centers (Arizona, Minnesota and Florida), Kansas University Medical Center, Inova Schar Cancer Institute and CARTI Cancer Center;
- CRDF-001 is a Phase 2 open-label multi-center clinical trial of onvansertib in combination with nanoliposomal irinotecan ("Onivyde®"), leucovorin, and fluorouracil for second line treatment of patients with mPDAC, which is being conducted at 6 clinical trial sites across the U.S. – The Mayo Clinic Cancer Centers (Arizona, Minnesota and Florida), Kansas University Medical Center, University of Nebraska Medical Center and Inova Schar Cancer Institute;
- TROV-053 is a Phase 2 open-label multi-center clinical trial of onvansertib in combination with abiraterone acetate (Zytiga®) and prednisone in patients with mCRPC, which is being conducted at 3 clinical trial sites - Beth Israel Deaconess Medical Center, Dana-Farber Cancer Institute, and Massachusetts General Hospital.

KRAS-mutated mCRC

TROV-054 is a Phase 1b/2 clinical trial of onvansertib for the second-line treatment of patients with KRAS-mutated metastatic colorectal cancer ("mCRC") in combination with standard-of-care FOLFIRI and bevacizumab (Avastin®).

The primary objective of this trial is to evaluate the dose-limiting toxicities ("DLTs") and maximum tolerated dose ("MTD") or recommended Phase 2 dose ("RP2D") of onvansertib in combination with FOLFIRI and bevacizumab (Phase 1b) and to continue to assess the safety and preliminary efficacy of onvansertib in combination with FOLFIRI and bevacizumab (Phase 2).

The rationale for this clinical trial is based on three key principles including synthetic lethality, synergy and proof-of-concept clinical benefit. Synthetic lethality arises when a combination of deficiencies in the expression of two genes leads to cell death, whereas a deficiency in only one of these genes does not. The deficiencies can arise through mutations, epigenetic alterations or inhibitors of the protein encoded by one of the genes. In reference to onvansertib, CRC tumor cells harboring KRAS mutations are more vulnerable to cell death with PLK1 inhibition versus KRAS wild-type isogenic cells. Synergy occurs when the combination of two drugs results in an unexpected greater activity than an expected additive effect of the two drugs. Onvansertib in combination with irinotecan and in combination with 5-FU (components of FOLFIRI) demonstrate synergy in colorectal cancer cell lines and both combinations have demonstrated significantly greater tumor growth inhibition than either drug alone. Proof-of-concept clinical response has been demonstrated in a previously completed Phase 1 trial in solid tumors in which 3 of 5 patients showing stable disease had tumors with a KRAS mutation; 2 in colorectal cancer and 1 in pancreatic cancer.

Data presented on September 8, 2021, at a key opinion leader webinar, provided an update of the ongoing phase 1b/2 clinical trial in KRAS-mutated metastatic colorectal cancer.

- 8 of 19 (42%) patients treated per protocol at the recommended Phase 2 dose ("RP2D") of onvansertib 15 mg/m² who were evaluable for disease response as of the data cut-off achieved a partial response ("PR"). Historically, objective response rates ("ORR") of 5-13% have been reported in a similar patient population treated with standard of care chemotherapy;
- 12 of 32 (38%) patients evaluable for response as of data cutoff date across all dose levels achieved a PR;

- Median progression-free survival ("mPFS") across all response-evaluable patients is 9.4 months and has not yet been reached in those treated per protocol at the RP2D. Historically, mPFS of ~4.5-5.7 months has been reported in a similar patient population treated with standard of care chemotherapy;
- The combination regimen of onvansertib plus FOLFIRI/bevacizumab is well tolerated.

mPDAC

CRDF-001 is a Phase 2 clinical trial of onvansertib in combination with nanoliposomal irinotecan and 5-FU for the second line treatment of patients with metastatic pancreatic ductal adenocarcinoma ("mPDAC"). The first patient was dosed in June 2021.

The objective of this trial is to assess the safety and preliminary efficacy of onvansertib in combination with nanoliposomal irinotecan (Onyvite®), 5-FU and leucovorin as a second-line treatment in patients with mPDAC who have failed first-line gemcitabine-based therapy. The trial is expected to enroll approximately 45 patients across six sites in the U.S. including the three Mayo Clinic Cancer Centers (Arizona, Minnesota and Florida), Kansas University Medical Center, University of Nebraska Medical Center and Inova Schar Cancer Institute.

mCRPC

TROV-053 is a Phase 2 clinical trial of onvansertib in combination with Zytiga® (abiraterone) and prednisone for the treatment of patients with metastatic castration resistant prostate cancer ("mCRPC").

The primary objective of this trial is to observe the effects of onvansertib in combination with abiraterone and prednisone on disease control as assessed by prostate specific antigen ("PSA") decline or stabilization after 12 weeks of treatment in patients with mCRPC showing early signs of resistance to abiraterone.

The rationale for this trial is based on the mechanism of action ("MOA") of onvansertib and Zytiga® and the synergy of these two drugs when used in combination in pre-clinical experiments. Onvansertib inhibits tumor cell division (mitosis) by inducing G2/M arrest of tumor cells and the combination of onvansertib and Zytiga® significantly increases mitotic arrest and is synergistic when used in combination. Additionally, PLK1 inhibition appears to enhance the efficacy of androgen signaling blockade in castration-resistant prostate cancer.

Data as of July 2, 2021, as follow-up to the data presented on February 11, 2021, at the American Society of Clinical Oncology Genitourinary Cancers Symposium ("ASCO-GU") provided evidence of the safety and efficacy of onvansertib in combination with abiraterone. Arms A (n=17) and B (n=20) and C (13) showed 29%, 40% and 54% of patients, respectively, achieving the primary endpoint of disease control at 12 weeks. The more continuous dosing schedule of Arm C has shown an increase in the rate of patients achieving disease stabilization, to-date. Evidence of efficacy was observed in patients harboring AR alterations across all 3 arms. ctDNA analysis revealed differences in baseline genomic profiles of patients achieving SD at 12 weeks vs. patients progressing before or at 12 weeks. Mutations exclusively present in patients with SD were associated with cell cycle and DNA repair pathways that may result in increased sensitivity to onvansertib and efficacy of the combination. Onvansertib plus abiraterone has demonstrated safety across all 3 dosing schedules.

Company Information

We were incorporated in the State of Florida on April 26, 2002. On July 2, 2004, we acquired Xenomics, a California corporation, which was in business to develop and commercialize urine-based molecular diagnostics technology. In 2007, we changed our fiscal year end from January 31 to December 31 and in January 2010, we re-domesticated our state of incorporation from Florida to Delaware and our name was changed to Trovogene, Inc. On May 6, 2020, we announced a change in our company name from Trovogene, Inc. to Cardiff Oncology, Inc. We have trademarks for the name TROVAGENE, TROVAGENE ONCOLOGY, and CARDIFF ONCOLOGY. Our principal executive offices are located at 11055 Flintkote Avenue, San Diego, CA 92121, and our telephone number is 858-952-7570. Our website address is www.cardiffoncology.com. The information on our website is not part of this prospectus. We have included our website address as a factual reference and do not intend it to be an active link to our website.

THE OFFERING

Securities being offered	2,411,575 shares
Common stock to be outstanding after this offering	41,963,704 shares
Use of proceeds	We intend to use the net proceeds from this offering for clinical development of our product candidate, working capital and other general corporate purposes. See “Use of Proceeds” on page S-7.
Risk factors	See the “Risk Factors” section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to invest in our securities.
Nasdaq Capital Market symbol	“CRDF”

Unless we indicate otherwise, all information in this prospectus supplement is based on 39,552,129 shares of common stock outstanding as of September 30, 2021 and excludes as of that date:

- 877 shares of common stock issuable upon conversion of outstanding Series A Convertible Preferred Stock;
- 2,684,607 shares of common stock issuable upon conversion of outstanding Series E Convertible Preferred Stock;
- 3,566,832 shares of our common stock issuable upon exercise of outstanding stock options under our stock incentive plans at a weighted average exercise price of \$7.22 per share;
- 4,490,159 shares of our common stock issuable upon exercise of outstanding warrants at a weighted average exercise price of \$5.80 per share; and
- 2,289,902 shares of common stock reserved for future grants and awards under our stock incentive plans.

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below and discussed under the section captioned “Risk Factors” in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, which are each incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, as well as any amendment or update to our risk factors reflected in subsequent filings with the SEC, together with other information in this prospectus supplement, the accompanying prospectus, and the information and documents incorporated by reference that we have authorized for use in connection with this offering. If any of these risks actually occur, our business, financial condition, results of operations or cash flows could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related to this Offering

You will experience immediate dilution in the net tangible book value per share of the common stock you purchase.

The public offering price per Share is substantially higher than our net tangible book value per share of common stock. After giving effect to the sale of 2,411,575 Shares in this offering at the public offering price of \$6.22 per Share, and based on our net tangible book value as of September 30, 2021, if you purchase Shares in this offering you will suffer substantial and immediate dilution of \$2.68 per share in the net tangible book value of the common stock. This dilution figure deducts the estimated offering expenses payable from the public offering price. See “Dilution.”

Because we will have broad discretion and flexibility in how the net proceeds from this offering are used, we may use the net proceeds in ways in which you disagree.

We intend to use the net proceeds from this offering for clinical development of our product candidate, working capital and other general corporate purposes. See “Use of Proceeds” on page S-7. We have not allocated specific amounts of the net proceeds from this offering for any of the foregoing purposes. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds of this offering. You will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the net proceeds are being used appropriately. It is possible that the net proceeds will be invested in a way that does not yield a favorable, or any, return for us. The failure of our management to use such funds effectively could have a material adverse effect on our business, financial condition, operating results and cash flow.

You may experience future dilution as a result of future equity offerings and other issuances of our securities. In addition, this offering and future equity offerings and other issuances of our common stock or other securities may adversely affect our common stock price.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per Share in this offering. We may not be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per Share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our Common Stock or securities convertible into common stock in future transactions may be higher or lower than the price per share in this offering. You will incur dilution upon exercise of any outstanding stock options, warrants or upon the issuance of shares of common stock under our stock incentive programs. In addition, the sale of shares in this offering and any future sales of a substantial number of shares of our common stock in the public market, or the perception that such sales may occur, could adversely affect the price of our common stock. We cannot predict the effect, if any, that market sales of those shares of common stock or the availability of those shares of common stock for sale will have on the market price of our common stock.

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the securities offered under this prospectus supplement, after deducting estimated offering expenses payable by us will be approximately \$14.96 million.

We intend to use the net proceeds from the sale of the shares for clinical development of our product candidate, working capital and for other general corporate purposes. The amounts and timing of our use of proceeds will vary depending on a number of factors, including the amount of cash generated or used by our operations. As a result, we will retain broad discretion in the allocation of the net proceeds of this offering. In addition, while we have not entered into any agreements, commitments or understandings relating to any significant transaction as of the date of this prospectus supplement, we may use a portion of the net proceeds to pursue acquisitions, joint ventures and other strategic transactions.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain our future earnings, if any, for use in our business and therefore do not anticipate paying cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs and plans for expansion. Pursuant to the terms of the Series A Convertible Preferred Stock, dividends cannot be paid to the holders of our common stock so long as any dividends due on the Series A Convertible Preferred Stock remain unpaid.

DILUTION

If you purchase Shares in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per security you will pay in this offering and the as adjusted net tangible book value per share of our common stock after giving effect to this offering. Net tangible book value per share is determined by dividing the number of outstanding shares of our common stock into our net tangible book value, which consists of total tangible assets (total assets less intangible assets) less total liabilities. As of September 30, 2021, we had a historical net tangible book value of \$133.5 million, or approximately \$3.38 per share.

Purchasers participating in this offering will incur immediate, substantial dilution. After giving effect to the sale of securities in this offering at the public offering price of \$6.22 per security, and after deducting estimated offering expenses payable by us, our as adjusted net tangible book value per share of our common stock at September 30, 2021 would have been approximately \$148.5 million, or \$3.54 per share. This represents an immediate increase in net tangible book value per share of our common stock of approximately \$0.16 per share to existing stockholders and an immediate dilution of approximately \$2.68 per share to purchasers in this offering. The following table illustrates this per share dilution:

Public offering price per Share		\$	6.22
Net tangible book value per share as of September 30, 2021	\$	3.38	
Increase per share attributable to this offering	\$	0.16	
As adjusted net tangible book value per share as of September 30, 2021		\$	3.54
Dilution in net tangible book value per share to new investors in this offering		\$	2.68

The above discussion and table is based on 39,552,129 shares of common stock outstanding as of September 30, 2021 and excludes as of that date:

- 877 shares of common stock issuable upon conversion of outstanding Series A Convertible Preferred Stock;
- 2,684,607 shares of common stock issuable upon conversion of outstanding Series E Convertible Preferred Stock;
- 3,566,832 shares of our common stock issuable upon exercise of outstanding stock options under our stock incentive plans at a weighted average exercise price of \$7.22 per share;
- 4,490,159 shares of our common stock issuable upon exercise of outstanding warrants at a weighted average exercise price of \$5.80 per share; and
- 2,289,902 shares of common stock reserved for future grants and awards under our stock incentive plans.

DESCRIPTION OF SECURITIES WE ARE OFFERING

Common Stock

The holders of our common stock are entitled to one vote per share. Our certificate of incorporation does not provide for cumulative voting. The holders of our common stock are entitled to receive ratably such dividends, if any, as may be declared by our board of directors out of legally available funds; however, the current policy of our board of directors is to retain earnings, if any, for operations and growth. Upon liquidation, dissolution or winding-up, the holders of our common stock are entitled to share ratably in all assets that are legally available for distribution. The holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of any series of preferred stock, which may be designated solely by action of our board of directors and issued in the future.

PLAN OF DISTRIBUTION

Pursuant to this prospectus supplement and the accompanying prospectus, we are offering 2,411,575 Shares at a public offering price of \$6.22 per Share. The securities are being offered directly to Pfizer Inc. pursuant to a securities purchase agreement without a placement agent, underwriter, broker or dealer.

The transfer agent and registrar for our common stock is Philadelphia Stock Transfer, Inc. Our common stock is listed on The Nasdaq Capital Market under the symbol "CRDF."

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Sheppard, Mullin, Richter & Hampton, New York, New York.

EXPERTS

The financial statements as of December 31, 2020 and 2019 and for the years then ended incorporated by reference in this prospectus supplement and in the registration statement have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement constitutes a part of the registration statement on Form S-3 that we have filed with the SEC under the Securities Act. As permitted by the SEC's rules, this prospectus supplement and any accompanying prospectus, which forms a part of the registration statement, do not contain all of the information that is included in the registration statement. You will find additional information about us in the registration statement. Any statement made in this prospectus supplement or any accompanying prospectus concerning legal documents are not necessarily complete and you should read the documents that are filed as exhibits to the registration statement or otherwise filed with the SEC for a more complete understanding of the document or matter.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at <http://www.sec.gov>. We also maintain a website at www.cardiffoncology.com, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of this prospectus.

You may also read and copy any document we file with the SEC at its public reference facilities at 100 F Street, N.E., Room 1580, Washington, DC 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities. You may also request a copy of these filings, at no cost, by writing or telephoning us at: 11055 Flintkote Avenue, San Diego, California, 92121, (858) 952-7570.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

This prospectus supplement is part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. The SEC permits us to “incorporate by reference” the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus supplement. Information that is incorporated by reference is considered to be part of this prospectus supplement and you should read it with the same care that you read this prospectus supplement and the accompanying prospectus. Information that we file later with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus supplement, and will be considered to be a part of this prospectus supplement from the date those documents are filed.

We incorporate by reference the documents listed below, all filings filed by us pursuant to the Exchange Act after the date of the registration statement of which this prospectus supplement and the accompanying prospectus forms a part, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the time that all securities covered by this prospectus supplement have been sold; provided, however, that we are not incorporating any information furnished under either Item 2.02 or Item 7.01 of any current report on Form 8-K:

- [our Annual Report on Form 10-K for the year ended December 31, 2020 filed with the SEC on February 25, 2021](#);
- our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2021 filed with the SEC on [May 6, 2021](#), for the quarter ended June 30, 2021 filed with the SEC on [August 5, 2021](#), and for the quarter ended September 30, 2021 filed with the SEC on [November 4, 2021](#);
- our Current Reports on Form 8-K filed with the SEC on [January 15, 2021](#), [January 26, 2021](#), [February 11, 2021](#), [February 16, 2021](#), [February 24, 2021](#), [March 3, 2021](#), [March 11, 2021](#), [April 8, 2021](#), [April 12, 2021](#), [May 20, 2021](#), [June 1, 2021](#), [June 8, 2021](#), [June 10, 2021](#), [June 28, 2021](#), [July 6, 2021](#), [July 12, 2021](#), [August 25, 2021](#), [September 7, 2021](#), [September 8, 2021](#), [November 10, 2021](#) and [November 18, 2021](#);
- [our definitive Proxy Statement on Schedule 14a for our 2021 Annual Meeting of Stockholders, filed with the SEC on April 28, 2021](#); and
- [the description of our common stock contained in our Registration Statement on Form 8-A filed with the Commission on May 23, 2012](#).

Any statements made in a document incorporated by reference in this prospectus supplement are deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement in this prospectus supplement or in any other subsequently filed document, which is also incorporated by reference, modifies or supersedes the statement. Any statement made in this prospectus supplement is deemed to be modified or superseded to the extent a statement in any subsequently filed document, which is incorporated by reference in this prospectus supplement, modifies or supersedes such statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

The information relating to us contained in this prospectus supplement should be read together with the information in the documents incorporated by reference. In addition, certain information, including financial information, contained in this prospectus supplement, the accompanying prospectus or incorporated by reference in this prospectus supplement and the accompanying prospectus should be read in conjunction with documents we have filed with the SEC.

We will provide to each person, including any beneficial holder, to whom a prospectus supplement is delivered, at no cost, upon written or oral request, a copy of any or all of the information that has been incorporated by reference in the prospectus supplement but not delivered with the prospectus supplement. Requests for documents should be by writing to or telephoning us at the following address: Cardiff Oncology, Inc., 11055 Flintkote Avenue, San Diego, CA 92121; (858) 952-7570. Exhibits to these filings will not be sent unless those exhibits have been specifically incorporated by reference in such filings.



**Common Stock
Preferred Stock
Debt Securities
Warrants
Units**

We may offer and sell, from time to time in one or more offerings, any combination of common stock, preferred stock, debt securities, warrants to purchase common stock, preferred stock or debt securities, or any combination of the foregoing, either individually or as units comprised of one or more of the other securities.

This prospectus provides a general description of the securities we may offer. Each time we sell a particular class or series of securities, we will provide specific terms of the securities offered in a supplement to this prospectus. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. You should read carefully this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference herein or therein before you invest in any of our securities.

The specific terms of any securities to be offered, and the specific manner in which they may be offered, will be described in one or more supplements to this prospectus. This prospectus may not be used to consummate sales of any of these securities unless it is accompanied by a prospectus supplement. Before investing, you should carefully read this prospectus and any related prospectus supplement.

Our common stock is presently listed on The Nasdaq Capital Market under the symbol "CRDF." On March 11, 2021, the last reported sale price of our common stock was \$10.69 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on The Nasdaq Capital Market or any securities market or other exchange of the securities, if any, covered by the prospectus supplement. Prospective purchasers of our securities are urged to obtain current information as to the market prices of our securities, where applicable.

These securities may be sold directly by us, through dealers or agents designated from time to time, to or through underwriters, dealers, or through a combination of these methods on a continuous or delayed basis. See "*Plan of Distribution*" in this prospectus. We may also describe the plan of distribution for any particular offering of our securities in a prospectus supplement. If any agents, underwriters or dealers are involved in the sale of any securities in respect of which this prospectus is being delivered, we will disclose their names and the nature of our arrangements with them in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from any such sale will also be included in a prospectus supplement.

Investing in our securities involves various risks. See "*Risk Factors*" contained herein for more information on these risks. Additional risks will be described in the related prospectus supplements under the heading "*Risk Factors*." You should review that section of the related prospectus supplements for a discussion of matters that investors in our securities should consider.

Neither the U.S. Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or passed upon the adequacy or accuracy of this prospectus or any accompanying prospectus supplement. Any representation to the contrary is a criminal offense.

The date of this prospectus is March 12, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement on Form S-3 that we filed with the U.S. Securities and Exchange Commission, or SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration statement, we may sell from time to time in one or more offerings of common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or as units comprised of a combination of one or more of the other securities in one or more offerings. This prospectus provides you with a general description of the securities we may offer. Each time we sell any type or series of securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering.

This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. We may add, update or change, in a prospectus supplement or free writing prospectus, any of the information contained in this prospectus or in the documents we have incorporated by reference into this prospectus. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. This prospectus, together with the applicable prospectus supplement, any related free writing prospectus and the documents incorporated by reference into this prospectus and the applicable prospectus supplement, will include all material information relating to the applicable offering. You should carefully read both this prospectus and the applicable prospectus supplement and any related free writing prospectus, together with the additional information described under “*Where You Can Find More Information*,” before buying any of the securities being offered.

We have not authorized any dealer, agent or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus, any accompanying prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or an accompanying prospectus supplement, or any related free writing prospectus that we may authorize to be provided to you. This prospectus, the accompanying prospectus supplement and any related free writing prospectus, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus, the accompanying prospectus supplement or any related free writing prospectus, if any, constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference (as our business, financial condition, results of operations and prospects may have changed since that date), even though this prospectus, any applicable prospectus supplement or any related free writing prospectus is delivered or securities are sold on a later date.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus may not be used to consummate sales of our securities, unless it is accompanied by a prospectus supplement. To the extent there are inconsistencies between any prospectus supplement, this prospectus and any documents incorporated by reference, the document with the most recent date will control.

As permitted by the rules and regulations of the SEC, the registration statement, of which this prospectus forms a part, includes additional information not contained in this prospectus. You may read the registration statement and the other reports we file with the SEC at the SEC’s web site or at the SEC’s offices described below under the heading “*Where You Can Find More Information*.”

Company References

In this prospectus “the Company,” “we,” “us,” and “our” refer to Cardiff Oncology, Inc., a Delaware corporation, and its subsidiaries, unless the context otherwise requires.

SUMMARY

Overview

We are a clinical stage biotechnology company, developing new treatment options for cancer patients in indications with the greatest medical need. Our goal is to overcome resistance, extend duration of response and increase overall survival. We are developing onvansertib, a first-in-class, third-generation Polo-like Kinase 1 ("PLK1") inhibitor, in combination with standard-of-care chemotherapy and targeted therapeutics. Our clinical development programs incorporate tumor genomics and biomarker technology to enable assessment of patient response to treatment.

We licensed onvansertib from Nerviano Medical Sciences ("NMS") pursuant to a license agreement with NMS dated March 13, 2017. This exclusive, world-wide license agreement includes 3 issued patents for onvansertib which cover composition of matter, salt forms of onvansertib and combination of onvansertib with other drugs.

Onvansertib is highly potent against the PLK1 enzyme (concentration for 50% inhibition [IC_{50}] = 2nM), whereas low or no activity was observed on a panel of 63 kinases (IC_{50} >500 nM), including the PLK members PLK2 and PLK3 (IC_{50} >10 μ M). Onvansertib was developed to have ideal pharmacokinetics, including oral bioavailability and administration and a drug half-life of approximately 24 hours, allowing for flexible dosing and scheduling, and is well tolerated and safe with only mild to moderate side effects reported to-date. A Phase 1 safety study of onvansertib was successfully completed in patients with advanced metastatic solid tumors and published in 2017 in *Investigational New Drugs*. Throughout this prospectus, where we make statements of demonstrated safety or efficacy from our clinical trials, we refer only to the conclusions of the investigators performing such trials and not to the standards of demonstrating safety and efficacy as are imposed by the U.S. Food and Drug Administration and will be required to be in order for approval of any future New Drug Application.

PLK1, a serine/threonine kinase, is a master regulator of mitotic progression with various roles and localizations during the different mitotic phases. Upon PLK1 depletion in cancer cells by RNA interference ("RNAi"), inhibition of proliferation and decreased viability, resulting from cell cycle arrest with 4N DNA content followed by apoptosis, are observed. PLK1 depletion also results in an increase in the number of cells containing abnormal spindle formation and misaligned chromosomes. Expression of PLK1 is seen in all proliferating normal tissues, and PLK1 is overexpressed in a number of tumors (including breast, prostate, ovary, lung, gastric and colon cancers), as well as in hematologic cancers.

Onvansertib has been tested for antiproliferative activity on a panel of 148 tumor cell lines and appeared highly active with an IC_{50} (a measure concentration for 50% target inhibition) below 100 nM in 75 cell lines and IC_{50} values below 1 μ M in 133 out of 148 cell lines. Onvansertib also appears active in cells expressing multi-drug resistant ("MDR") transporter proteins and we believe its apparent ability to overcome the MDR transporter resistance mechanism in cancer cells could prove useful in broader drug combination applications. Additionally, onvansertib has been tested in in-vivo xenograft and transgenic models of different cancer types with the demonstration of tumor growth inhibition or tumor regression.

Onvansertib has been evaluated preclinically in combination with several different chemotherapies, including irinotecan, cisplatin, cytarabine, doxorubicin, gemcitabine and paclitaxel, and with targeted therapeutics such as abiraterone, histone deacetylase ("HDAC") inhibitors, fms-like tyrosine kinase 3 ("FLT3") inhibitors, and bortezomib. These therapies are used clinically for the treatment of many hematologic and solid cancers, including acute myeloid leukemia ("AML"), non-Hodgkin's lymphoma ("NHL"), metastatic CRC, metastatic castration resistant prostate cancer ("mCRPC"), adrenocortical carcinoma ("ACC"), triple negative breast cancer ("TNBC"), small cell lung cancer ("SCLC"), and ovarian cancer.

We believe the high-selectivity of onvansertib to PLK1, its 24-hour half-life and oral bioavailability, as well as its demonstrated safety and tolerability, with expected on-target, easy to manage and reversible side effects, may prove beneficial in addressing clinical therapeutic needs across a variety of cancers.

Clinical Program Updates

We currently have three active clinical trials:

- TROV-054 is a Phase 1b/2 open-label clinical trial of onvansertib in combination with FOLFIRI and bevacizumab ("Avastin[®]") for the second line treatment of patients with KRAS-mutated mCRC, which is being conducted at 6 clinical trial sites across the U.S. - USC Norris Comprehensive Cancer Center, The Mayo Clinic Cancer Centers (Arizona, Minnesota and Florida), Kansas University Medical Center ("KUMC") and CARTI Cancer Center;

- TROV-053 is a Phase 2 open-label clinical trial of onvansertib in combination with abiraterone acetate (Zytiga[®]) and prednisone in patients with mCRPC, which is being conducted at Beth Israel Deaconess Medical Center ("BIDMC"), Dana-Farber Cancer Institute ("DFCI"), and Massachusetts General Hospital ("MGH"); and
- TROV-052 is a Phase 2 open-label clinical trial of onvansertib in combination with standard-of-care chemotherapy, decitabine, in patients with relapsed or refractory AML, which is being conducted at nine sites across the U.S. The Phase 1b portion of the AML trial was completed in the fourth quarter of 2019 and enrollment in Phase 2 was completed in October 2020.

KRAS-mutated mCRC

TROV-054 is a Phase 1b/2 study of onvansertib for the second-line treatment of patients with KRAS-mutated metastatic colorectal cancer ("mCRC") in combination with standard-of-care FOLFIRI and bevacizumab (Avastin[®]).

The primary objective of this study is to evaluate the dose-limiting toxicities ("DLTs") and maximum tolerated dose ("MTD") or recommended Phase 2 dose ("RP2D") of onvansertib in combination with FOLFIRI and bevacizumab (Phase 1b) and to continue to assess the safety and preliminary efficacy of onvansertib in combination with FOLFIRI and bevacizumab (Phase 2).

The rationale for this clinical trial is based on three key principles including synthetic lethality, synergy and proof-of-concept clinical benefit. Synthetic lethality arises when a combination of deficiencies in the expression of two genes leads to cell death, whereas a deficiency in only one of these genes does not. The deficiencies can arise through mutations, epigenetic alterations or inhibitors of the protein encoded by one of the genes. In reference to onvansertib, CRC tumor cells harboring KRAS mutations are more vulnerable to cell death with PLK1 inhibition versus KRAS wild-type isogenic cells. Synergy occurs when the combination of two drugs results in an unexpected greater activity than an expected additive effect of the two drugs. Onvansertib in combination with irinotecan and 5-FU (components of FOLFIRI) demonstrate synergy in colorectal cancer cell lines and the combination has demonstrated significantly greater tumor growth inhibition than either drug alone. Proof-of-concept clinical response has been demonstrated in a previously completed Phase 1 trial in solid tumors in which 3 of 5 patients showing stable disease had a KRAS mutation; 2 in colorectal cancer and 1 in pancreatic cancer.

Data presented on January 15, 2021, at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium ("ASCO-GI"), demonstrated the safety and efficacy of onvansertib. Of the 12 patients evaluable for efficacy, 5 (42%) achieved a partial response ("PR"); 4 patients had a confirmed PR; 1 patient went on to curative surgery; 1 patient with a non-confirmed PR went off study due to an unrelated event prior to their 16-week confirmatory scan. 8 (67%) patients showed a durable response to treatment of >6 months with a range from 6.1 to 13.7 months. Time to achieving a PR ranges from 2 to 6 months in patients on treatment. 10 of 12 patients had a KRAS variant detected by ddPCR at baseline (all had a KRAS mutation detected by NGS). Clinical responses were observed across different KRAS variants, including the 3 most common in colorectal cancers ("CRC"). The greatest decreases in KRAS mutant allelic frequency ("MAF") after 1 cycle of treatment were observed in patients achieving a PR (ranging from -78% to -100%), while the 2 patients who progressed showed a more modest reduction in KRAS MAF (-55% and -26%). Patients with PR and stable disease (SD) tended to have lower on-treatment KRAS MAF than patients with early progressive disease ("PD"). Onvansertib in combination with FOLFIRI/bevacizumab is safe and well tolerated with only 9% of all adverse events ("AEs") being grade 3 or 4. Grade 4 adverse events were attributed to the 5-FU bolus component of the combination regimen, which was eliminated in subsequent cycles of treatment per protocol and institutional guidelines. The only G3/G4 AEs reported in ≥2 patients were neutropenia (n=8), which were managed by dose delay, growth factor therapy and/or discontinuation of the 5-FU bolus; no patients went off trial due to neutropenia. No major or unexpected toxicities were attributed to onvansertib.

Key News Releases

On January 15, 2021, we announced an electronic poster presentation of clinical data further demonstrating the clinical benefit of onvansertib in KRAS-mutate mCRC and initial findings from our Expanded Access Program (EAP) in mCRC.

On September 17, 2020, we announced an electronic poster presentation of clinical data further demonstrating the safety, efficacy and durability of response of onvansertib in KRAS-mutated mCRC patients at the European Society of Medical Oncology ("ESMO") Virtual Congress 2020.

On June 9, 2020, we announced the initiation of our EAP for onvansertib, in combination with standard-of-care FOLFIRI and bevacizumab, for second-line treatment of patients with KRAS-mutated mCRC. This announcement followed the FDA granting Fast Track Designation for onvansertib in KRAS-mutated mCRC.

mCRPC

TROV-053 is a Phase 2 study of onvansertib in combination with Zytiga® (abiraterone) and prednisone for the treatment of patients with metastatic castration resistant prostate cancer ("mCRPC").

The primary objective of this study is to observe the effects of onvansertib in combination with abiraterone and prednisone on disease control as assessed by prostate specific antigen ("PSA") decline or stabilization after 12 weeks of study treatment in patients with mCRPC showing early signs of resistance to abiraterone.

The rationale for this trial is based on the mechanism of action ("MOA") of onvansertib and Zytiga® and the synergy of these two drugs when used in combination. Onvansertib inhibits tumor cell division (mitosis) by inducing G2/M arrest of tumor cells and the combination of onvansertib and Zytiga® significantly increases mitotic arrest and is synergistic when used in combination. Additionally, PLK1 inhibition appears to enhance the efficacy of androgen signaling blockade in castration-resistant prostate cancer.

Data presented on February 11, 2021, at the American Society of Clinical Oncology Genitourinary Cancers Symposium ("ASCO-GU") demonstrated safety and efficacy of onvansertib in combination with abiraterone. Arms A (n=17) and B (n=12) showed similar efficacy with 29% and 25% of patients achieving the primary endpoint and 53% and 42% of patients with SD at 12 weeks, respectively. The more continuous dosing schedule of Arm C (n=8) has shown a higher response rate with 63% of patients, to-date, achieving the primary endpoint and 75% with SD at 12 weeks. Efficacy was observed in patients harboring AR alterations across all 3 arms. ctDNA analysis revealed differences in baseline genomic profiles of patients achieving SD at 12 weeks vs patients progressing before or at 12 weeks. Mutations exclusively present in patients with SD were associated with cell cycle and DNA repair pathways that may result in increased sensitivity to onvansertib and efficacy of the combination. Onvansertib + abiraterone has demonstrated safety across all 3 dosing schedules.

Key News Releases

On February 11, 2021, we announced an electronic poster presentation of clinical data further demonstrating the safety, efficacy and durability of response in patient with mCRPC at the American Society of Clinical Oncology Genitourinary Cancers Symposium ("ASCO-GU").

AML

TROV-052 is a Phase 2 Study of onvansertib in combination with standard-of-care chemotherapy, decitabine, for the treatment of patients with relapsed or refractory acute myeloid leukemia ("AML"). The Phase 1b portion of this trial was completed in the fourth quarter of 2019.

The objective of this trial is to evaluate the DLTs and MTD or RP2D of onvansertib (Phase 1b – completed in October 2019). In Phase 2, the objective is to assess the safety, tolerability and preliminary efficacy of the combination of onvansertib at the RP2D and decitabine in patients with relapsed or refractory AML (Phase 2 enrollment completed in October 2020). Additionally, as a correlative objective, this trial is evaluating potential pharmacodynamic and diagnostic biomarkers of onvansertib in patients with AML. We were granted Orphan Drug Designation ("ODD") for onvansertib for the treatment of AML from the FDA and the European Commission.

Data presented on December 6, 2020 at the 62nd American Society of Hematology ("ASH") conference, demonstrated the safety, tolerability and anti-leukemic activity of onvansertib in combination with decitabine in patients with difficult-to-treat relapsed/refractory AML. Nine of 45 (20%) patients achieved a complete remission with or without hematologic count recovery (CR/CRi – 5 in Phase 1b and 4 in Phase 2); 55% of responders had a mutation in a splicing factor. Two patients proceeded to transplant following CR and four patients remain on treatment with duration of response of 9, 10, 17 and 20 months, respectively. Together with data demonstrating the safety and tolerability of the combination therapy, these findings highlight onvansertib's potential to address critical unmet needs in hematologic malignancies.

Key News Releases

On December 6, 2020, we announced an electronic poster presentation of data from the Phase 1b/2 trial in AML demonstrating the safety and efficacy of onvansertib in relapsed or refractory patients at the annual American Society of Hematology ("ASH") conference.

Risks Associated with Our Business

- We are a clinical stage company and may never earn a profit.
- We will need to raise substantial additional capital to develop and commercialize onvansertib and our failure to obtain funding when needed may force us to delay, reduce or eliminate our product development programs or collaboration efforts.
- Our product candidate, onvansertib, is in the early stages of clinical development and its commercial viability remains subject to current and future preclinical studies, clinical trials, regulatory approvals and the risks generally inherent in the development of a pharmaceutical product candidate. If we are unable to successfully advance or develop our product candidate, our business will be materially harmed.
- If the results of preclinical studies or clinical trials for our product candidate, including those that are subject to existing or future license or collaboration agreements, are unfavorable or delayed, we could be delayed or precluded from the further development or commercialization of our product candidate, which could materially harm our business.
- If third party vendors upon whom we intend to rely on to conduct our preclinical studies or clinical trials do not perform or fail to comply with strict regulations, these studies or trials of our product candidate may be delayed, terminated, or fail, or we could incur significant additional expenses, which could materially harm our business.
- We, and our collaborators, must comply with extensive government regulations in order to advance our product candidate through the development process and ultimately obtain and maintain marketing approval for our products in the U.S. and abroad.
- We have limited experience in the development of therapeutic product candidates and therefore may encounter difficulties developing our product candidate or managing our operations in the future.
- Clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.
- Delays in clinical testing could result in increased costs to us and delay our ability to generate revenue.
- The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidate, our business will be substantially harmed.
- If our product candidate is unable to compete effectively with marketed drugs targeting similar indications as our product candidate, our commercial opportunity will be reduced or eliminated.
- If the manufacturers upon whom we rely fail to produce our product candidate, in the volumes that we require on a timely basis, or fail to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the development and commercialization of our product candidate.
- If we materially breach or default under terms of our license agreement with Nerviano Medical Sciences S.r.l. Nerviano Medical Sciences S.r.l. will have the right to terminate the agreement and we could lose critical license rights, which would materially harm our business.

- The outbreak of the novel coronavirus disease, COVID-19, could materially adversely impact our business, results of operations and financial condition, including our clinical trials.
- If we are unable to protect our intellectual property effectively, we may be unable to prevent third parties from using our technologies, which would impair our competitive advantage.
- Our common stock price may be volatile and could fluctuate widely in price, which could result in substantial losses for investors.
- Delaware law and our corporate charter and bylaws contain anti-takeover provisions that could delay or discourage takeover attempts that stockholders may consider favorable.

Company Information

We were incorporated in the State of Florida on April 26, 2002. On July 2, 2004, we acquired Xenomics, a California corporation, which was in business to develop and commercialize urine-based molecular diagnostics technology. In 2007, we changed our fiscal year end from January 31 to December 31 and in January 2010, we re-domesticated our state of incorporation from Florida to Delaware and our name was changed to Trovagene, Inc. On May 6, 2020, we announced a change in our company name from Trovagene, Inc. to Cardiff Oncology, Inc. We have trademarks for the name TROVAGENE, and TROVAGENE ONCOLOGY and we have applied for the trademark for CARDIFF ONCOLOGY. Our principal executive offices are located at 11055 Flintkote Avenue, San Diego, CA 92121, and our telephone number is 858-952-7570. Our website address is www.cardiffoncology.com. The information on our website is not part of this prospectus. We have included our website address as a factual reference and do not intend it to be an active link to our website.

The Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any of such securities, either individually or in units, from time to time under this prospectus, together with any applicable prospectus supplement and related free writing prospectus, at prices and on terms to be determined by market conditions at the time of offering. If we issue any debt securities at a discount from their original stated principal amount, then, for purposes of calculating the total dollar amount of all securities issued under this prospectus, we will treat the initial offering price of the debt securities as the total original principal amount of the debt securities. Each time we offer securities under this prospectus, we will provide offerees with a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities being offered, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;
- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking;
- restrictive covenants, if any;
- voting or other rights, if any; and
- important United States federal income tax considerations.

A prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update, or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

We may sell the securities to or through underwriters, dealers or agents or directly to purchasers. We, as well as any agents acting on our behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. Each prospectus supplement will set forth the names of any underwriters, dealers or agents involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them, details regarding any over-allotment option granted to them, and net proceeds to us. The following is a summary of the securities we may offer with this prospectus.

Common Stock

We currently have authorized 150,000,000 shares of common stock, par value \$0.0001 per share. As of March 11, 2021, 37,552,129 shares of common stock were issued and outstanding. We may offer shares of our common stock either alone or underlying other registered securities convertible into or exercisable for our common stock. Holders of our common stock are entitled to such dividends as our board of directors (the “Board of Directors” or “Board”) may declare from time to time out of legally available funds, subject to the preferential rights of the holders of any shares of our preferred stock that are outstanding or that we may issue in the future. Currently, we do not pay any dividends on our common stock. Each holder of our common stock is entitled to one vote per share. In this prospectus, we provide a general description of, among other things, the rights and restrictions that apply to holders of our common stock.

Preferred Stock

We currently have authorized 20,000,000 shares of preferred stock, par value \$0.001, of which 277,100 shares are designated as Series A Convertible Preferred Stock, of which 60,600 shares are issued and outstanding as of March 11, 2021; 8,860 shares are designated as Series B Convertible Preferred Stock, of which no shares are issued and outstanding as of March 11, 2021; 200,000 shares are designated as Series C Convertible Preferred Stock, of which no shares are issued and outstanding as of March 11, 2021; 154,670 shares are designated as Series D Convertible Preferred Stock, of which no shares are issued and outstanding as of March 11, 2021; and 865,824 shares are designated Series E Convertible Preferred Stock, of which 655,044 shares are issued and outstanding as of March 11, 2021.

Any authorized and undesignated shares of preferred stock may be issued from time to time in one or more additional series pursuant to a resolution or resolutions providing for such issue duly adopted by our Board of Directors (authority to do so being hereby expressly vested in the Board of Directors). The Board of Directors is further authorized, subject to limitations prescribed by law, to fix by resolution or resolutions the designations, powers, preferences and rights, and the qualifications, limitations or restrictions thereof, of any wholly unissued series of preferred stock, including without limitation authority to fix by resolution or resolutions the dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions), redemption price or prices, and liquidation preferences of any such series, and the number of shares constituting any such series and the designation thereof, or any of the foregoing.

The rights, preferences, privileges, and restrictions granted to or imposed upon any series of preferred stock that we offer and sell under this prospectus and applicable prospectus supplements will be set forth in a certificate of designation relating to the series. We will incorporate by reference into the registration statement of which this prospectus is a part the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of shares of that series of preferred stock. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities

We may offer general debt obligations, which may be secured or unsecured, senior or subordinated, and convertible into shares of our common stock or preferred stock. In this prospectus, we refer to the senior debt securities and the subordinated debt securities together as the “debt securities.” We may issue debt securities under a note purchase agreement or under an indenture to be entered between us and a trustee. The indentures do not limit the amount of securities that may be issued under it and provide that debt securities may be issued in one or more series. The senior debt securities will have the same rank as all of our other indebtedness that is not subordinated. The subordinated debt securities will be subordinated to our

senior debt on terms set forth in the applicable prospectus supplement. In addition, the subordinated debt securities will be effectively subordinated to creditors and preferred stockholders of our subsidiaries. Our Board of Directors will determine the terms of each series of debt securities being offered. This prospectus contains only general terms and provisions of the debt securities. The applicable prospectus supplement will describe the particular terms of the debt securities offered thereby. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of debt securities being offered, as well as the complete note agreements and/or indentures that contain the terms of the debt securities. The forms of senior and subordinated indentures have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of debt securities being offered will be incorporated by reference into the registration statement of which this prospectus is a part from reports we file with the SEC.

Warrants

We may offer warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue the warrants by themselves or together with common stock, preferred stock or debt securities, and the warrants may be attached to or separate from any offered securities. Any warrants issued under this prospectus may be evidenced by warrant certificates. Warrants may be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. Our Board of Directors will determine the terms of the warrants. This prospectus contains only general terms and provisions of the warrants. The applicable prospectus supplement will describe the particular terms of the warrants being offered thereby. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of warrants being offered, as well as the complete warrant agreements that contain the terms of the warrants. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference into the registration statement of which this prospectus is a part from reports we file with the SEC.

Units

We may offer units consisting of our common stock or preferred stock, debt securities and/or warrants to purchase any of these securities in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units. This prospectus contains only a summary of certain general features of the units. The applicable prospectus supplement will describe the particular features of the units being offered thereby. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and will be incorporated by reference into the registration statement of which this prospectus is a part from reports we file with the SEC.

RISK FACTORS

An investment in our securities involves a high degree of risk. This prospectus contains, and the prospectus supplement applicable to each offering of our securities will contain, a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading “*Risk Factors*” in this prospectus and the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under Item 1A, “*Risk Factors*,” in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020, filed with the SEC on February 25, 2021, and any updates described in our Quarterly Reports on Form 10-Q, all of which are incorporated herein by reference, and may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future and any prospectus supplement related to a particular offering. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. The occurrence of any of these known or unknown risks might cause you to lose all or part of your investment in the offered securities.

DISCLOSURE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any accompanying prospectus supplement, any related free writing prospectus and the documents incorporated by reference herein or therein contain, in addition to historical information, certain forward-looking statements within the meaning of Section 27A of the Securities Act or 1933, as amended (the “Securities Act”), and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), that include information relating to future events, future

financial performance, strategies, expectations, competitive environment, regulation and availability of resources. Such forward-looking statements include those that express plans, anticipation, intent, contingency, goals, targets or future development and/or otherwise are not statements of historical fact. These forward-looking statements are based on our current expectations and projections about future events and they are subject to risks and uncertainties known and unknown that could cause actual results and developments to differ materially from those expressed or implied in such statements.

In some cases, you can identify forward-looking statements by terminology, such as “expects,” “anticipates,” “intends,” “estimates,” “plans,” “believes,” “seeks,” “may,” “should”, “could” or the negative of such terms or other similar expressions. Accordingly, these statements involve estimates, assumptions and uncertainties that could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus supplement or incorporated herein by reference.

Risks, uncertainties and other factors that may cause our actual results, performance or achievements to be different from those expressed or implied in our written or oral forward-looking statements may be found in this prospectus supplement under the heading “Risk Factors” and in our Annual Report on Form 10-K for the year ended December 31, 2020 under the headings “Risk Factors” and “Business,” as updated in our Quarterly Report(s) on Form 10-Q.

Forward-looking statements speak only as of the date they are made. You should not put undue reliance on any forward-looking statements. We assume no obligation to update forward-looking statements to reflect actual results, changes in assumptions or changes in other factors affecting forward-looking information, except to the extent required by applicable securities laws. If we do update one or more forward-looking statements, no inference should be drawn that we will make additional updates with respect to those or other forward-looking statements.

New factors emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. We qualify all of the information presented in this prospectus supplement and incorporated herein by reference, and particularly our forward-looking statements, by these cautionary statements.

USE OF PROCEEDS

Except as described in any prospectus supplement and any free writing prospectus in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered under this prospectus for general corporate purposes, including the development and commercialization of our products, research and development, general and administrative expenses, license or technology acquisitions, and working capital and capital expenditures. We may also use the net proceeds to repay any debts and/or invest in or acquire complementary businesses, products, or technologies, although we have no current commitments or agreements with respect to any such investments or acquisitions as of the date of this prospectus. We have not determined the amount of net proceeds to be used specifically for the foregoing purposes. As a result, our management will have broad discretion in the allocation of the net proceeds and investors will be relying on the judgment of our management regarding the application of the proceeds of any sale of the securities. Pending use of the net proceeds, we intend to invest the proceeds in short-term, investment-grade, interest-bearing instruments.

Each time we offer securities under this prospectus, we will describe the intended use of the net proceeds from that offering in the applicable prospectus supplement. The actual amount of net proceeds we spend on a particular use will depend on many factors, including, our future capital expenditures, the amount of cash required by our operations, and our future revenue growth, if any. Therefore, we will retain broad discretion in the use of the net proceeds.

DESCRIPTION OF CAPITAL STOCK

General

The following description of our capital stock, together with any additional information we include in any applicable prospectus supplement or any related free writing prospectus, summarizes the material terms and provisions of our common stock and the preferred stock that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future common stock or preferred stock that we may offer, we will describe the particular terms of any class or series of these securities in more detail in the applicable prospectus supplement. For the complete terms of our common stock and preferred stock, please refer to our amended and restated certificate of incorporation, as amended (“Certificate of Incorporation”), and our bylaws that are incorporated by reference into the registration statement of which this prospectus is a part or may be incorporated by reference in this prospectus or any applicable prospectus supplement. The terms of these

securities may also be affected by Delaware General Corporation Law (the “DGCL”). The summary below and that contained in any applicable prospectus supplement or any related free writing prospectus are qualified in their entirety by reference to our Certificate of Incorporation and our bylaws.

As of the date of this prospectus, our authorized capital stock consisted of 150,000,000 shares of common stock, \$0.0001 par value per share, and 20,000,000 shares of preferred stock, \$0.001 par value per share. Our Board may establish the rights and preferences of the preferred stock from time to time. As of March 11, 2021, there were 37,552,129 shares of our common stock issued and outstanding, 60,600 shares of our Series A Convertible Preferred Stock issued and outstanding and 655,044 shares of our Series E Convertible Preferred Stock issued and outstanding.

Common Stock

We are authorized to issue up to a total of 150,000,000 shares of common stock, par value \$0.0001 per share. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of our stockholders. Holders of our common stock have no cumulative voting rights. All shares of common stock offered hereby will, when issued, be fully paid and nonassessable, including shares of common stock issued upon the exercise of common stock warrants or subscription rights, if any.

Further, holders of our common stock have no preemptive or conversion rights or other subscription rights. Upon our liquidation, dissolution or winding-up, holders of our common stock are entitled to share in all assets remaining after payment of all liabilities and the liquidation preferences of any of our outstanding shares of preferred stock. Subject to preferences that may be applicable to any outstanding shares of preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our Board of Directors out of our assets which are legally available. Such dividends, if any, are payable in cash, in property or in shares of capital stock.

The holders of a majority of the shares of our capital stock, represented in person or by proxy, are necessary to constitute a quorum for the transaction of business at any meeting. If a quorum is present, an action by stockholders entitled to vote on a matter is approved if the number of votes cast in favor of the action exceeds the number of votes cast in opposition to the action, with the exception of the election of directors, which requires a plurality of the votes cast.

Preferred Stock

Our Board of Directors has the authority, without further action by the stockholders, to issue up to 20,000,000 shares of preferred stock in one or more series and to fix the designations, powers, preferences, privileges, and relative participating, optional, or special rights as well as the qualifications, limitations, or restrictions of the preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, and liquidation preferences, any or all of which may be greater than the rights of the common stock. Our Board of Directors, without stockholder approval, can issue preferred stock with voting, conversion, or other rights that could adversely affect the voting power and other rights of the holders of common stock. Preferred stock could be issued quickly with terms calculated to delay or prevent a change of control or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of our common stock, and may adversely affect the voting and other rights of the holders of common stock. At present, we have no plans to issue any shares of preferred stock following this offering.

Anti-Takeover Effects of Certain Provisions of our Certificate of Incorporation, Bylaws and the DGCL

We are governed by the provisions of Section 203 of the DGCL. In general, Section 203 prohibits a publicly traded Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. A business combination includes mergers, asset sales or other transactions resulting in a financial benefit to the stockholder. An interested stockholder is a person who, together with affiliates and associates, owns (or within three years, did own) 15% or more of the corporation’s voting stock, subject to certain exceptions. The statute could have the effect of delaying, deferring or preventing a change in control of our Company.

Our Certificate of Incorporation and bylaws contain provisions that could have the effect of discouraging potential acquisition proposals or making a tender offer or delaying or preventing a change in control, including changes a stockholder might consider favorable. In particular, our Certificate of Incorporation and bylaws, as applicable, among other things:

- provide our Board of Directors with the ability to alter our bylaws without stockholder approval; and

- provide that vacancies on our Board of Directors may be filled by a majority of directors in office, although less than a quorum.

Such provisions may have the effect of discouraging a third-party from acquiring us, even if doing so would be beneficial to our stockholders. These provisions are intended to enhance the likelihood of continuity and stability in the composition of our Board of Directors and in the policies formulated by them, and to discourage some types of transactions that may involve an actual or threatened change in control of our Company. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal and to discourage some tactics that may be used in proxy fights. We believe that the benefits of increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure our Company outweigh the disadvantages of discouraging such proposals because, among other things, negotiation of such proposals could result in an improvement of their terms.

However, these provisions could have the effect of discouraging others from making tender offers for our shares that could result from actual or rumored takeover attempts. These provisions also may have the effect of preventing changes in our management.

Listing

Our common stock is listed on the Nasdaq Capital Market under the trading symbol “CRDF.”

Transfer Agent and Registrar

The Transfer Agent and Registrar for our common stock is Philadelphia Stock Transfer, Inc.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements or free writing prospectuses, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement or free writing prospectus. The terms of any debt securities we offer under a prospectus supplement may differ from the terms we describe below. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness. As of the date of this prospectus, we have no outstanding registered debt securities. Unless the context requires otherwise, whenever we refer to the “indentures,” we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue any senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue any subordinated debt securities under the subordinated indenture and any supplemental indentures that we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement, of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The indentures will be qualified under the Trust Indenture Act of 1939, as amended (the “Trust Indenture Act”). We use the term “trustee” to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all of the provisions of the indenture and any supplemental indentures applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indentures that contains the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our Board of Directors and set forth or determined in the manner provided in an officers’ certificate or by a supplemental indenture. Debt securities

may be issued in separate series without limitation as to aggregate principal amount. We may specify a maximum aggregate principal amount for the debt securities of any series. We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title;
- the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;
- any limit on the amount that may be issued;
- whether or not we will issue the series of debt securities in global form, and, if so, the terms and who the depositary will be;
- the maturity date;
- whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;
- the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- the terms of the subordination of any series of subordinated debt;
- the place where payments will be made;
- restrictions on transfer, sale or other assignment, if any;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- provisions for a sinking fund purchase or other analogous fund, if any, including the date, if any, on which, and the price at which we are obligated, pursuant thereto or otherwise, to redeem, or at the holder's option, to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- whether the indenture will restrict our ability or the ability of our subsidiaries, if any, to:
 - incur additional indebtedness;
 - issue additional securities;
 - create liens;
 - pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;
 - redeem capital stock;
 - place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;
 - make investments or other restricted payments;
 - sell or otherwise dispose of assets;
 - enter into sale-leaseback transactions;

- engage in transactions with stockholders or affiliates;
 - issue or sell stock of our subsidiaries; or
 - effect a consolidation or merger;
- whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;
 - a discussion of certain material or special United States federal income tax considerations applicable to the debt securities;
 - information describing any book-entry features;
 - the applicability of the provisions in the indenture on discharge;
 - whether the debt securities are to be offered at a price such that they will be deemed to be offered at an “original issue discount” as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;
 - the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
 - the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and
 - any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms under which a series of debt securities may be convertible into or exchangeable for our common stock, our preferred stock or other securities (including securities of a third party). We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock, our preferred stock or other securities (including securities of a third party) that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for our other securities or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended;
- if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable at maturity, upon redemption or repurchase or otherwise, and the time for payment has not been extended;

- if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or we and the trustee receive notice from the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and

- if specified events of bankruptcy, insolvency or reorganization occur.

We will describe in each applicable prospectus supplement any additional events of default relating to the relevant series of debt securities.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default arises due to the occurrence of certain specified bankruptcy, insolvency or reorganization events, the unpaid principal, premium, if any, and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity or security satisfactory to it against any loss, liability or expense. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and

- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

The indentures will provide that if an event of default has occurred and is continuing, the trustee will be required in the exercise of its powers to use the degree of care that a prudent person would use in the conduct of its own affairs. The trustee, however, may refuse to follow any direction that conflicts with law or the indenture, or that the trustee determines is unduly prejudicial to the rights of any other holder of the relevant series of debt securities, or that would involve the trustee in personal liability. Prior to taking any action under the indentures, the trustee will be entitled to indemnification against all costs, expenses and liabilities that would be incurred by taking or not taking such action.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;

- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made a written request and such holders have offered reasonable indemnity to the trustee or security satisfactory to it against any loss, liability or expense or to be incurred in compliance with instituting the proceeding as trustee; and

- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities, or other defaults that may be specified in the applicable prospectus supplement.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indentures.

The indentures will provide that if a default occurs and is continuing and is actually known to a responsible officer of the trustee, the trustee must mail to each holder notice of the default within the earlier of 90 days after it occurs and 30 days after it is known by a responsible officer of the trustee or written notice of it is received by the trustee, unless such default has been cured or waived. Except in the case of a default in the payment of principal or premium of, or interest on, any debt security or certain other defaults specified in an indenture, the trustee shall be protected in withholding such notice if and so long as the Board of Directors, the executive committee or a trust committee of directors, or responsible officers of the trustee, in good faith determine that withholding notice is in the best interests of holders of the relevant series of debt securities.

Modification of Indenture; Waiver

Subject to the terms of the indenture for any series of debt securities that we may issue, we and the trustee may change an indenture without the consent of any holders with respect to the following specific matters:

- to fix any ambiguity, defect or inconsistency in the indenture;
- to comply with the provisions described above under “*Description of Debt Securities — Consolidation, Merger or Sale;*”
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;
- to add to, delete from or revise the conditions, limitations and restrictions on the authorized amount, terms or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to provide for the issuance of, and establish the form and terms and conditions of, the debt securities of any series as provided under “*Description of Debt Securities — General,*” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment hereunder by a successor trustee;
- to provide for uncertificated debt securities and to make all appropriate changes for such purpose;
- to add such new covenants, restrictions, conditions or provisions for the benefit of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred to us in the indenture; or
- to change anything that does not adversely affect the interests of any holder of debt securities of any series in any material respect.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, subject to the terms of the indenture for any series of debt securities that we may issue or otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may only make the following changes with the consent of each holder of any outstanding debt securities affected:

- extending the stated maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that, subject to the terms of the indenture and any limitation otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we may elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we will deposit with the trustee money or government obligations sufficient to pay all the principal of, and any premium and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indentures will provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series. See “*Legal Ownership of Securities*” below for a further description of the terms relating to any book-entry securities.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture and is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur. However, upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest payment.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Ranking Debt Securities

The subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

The senior debt securities will be unsecured and will rank equally in right of payment to all our other senior unsecured debt. The senior indenture does not limit the amount of senior debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and free writing prospectuses, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and may be issued in one or more series. Warrants may be offered independently or together with common stock, preferred stock or debt securities offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants that we may offer in more detail in the applicable prospectus supplement and any applicable free writing prospectus. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We may issue the warrants under a warrant agreement that we will enter into with a warrant agent to be selected by us. If selected, the warrant agent will act solely as an agent of ours in connection with the warrants and will not act as an agent for the holders or beneficial owners of the warrants. If applicable, we will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from a Current Report on Form 8-K that we file with the SEC, the form of warrant agreement, including a form of warrant certificate, that describes the terms of the particular series of warrants we are

offering before the issuance of the related series of warrants. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. We urge you to read the applicable prospectus supplement and any applicable free writing prospectus related to the particular series of warrants that we sell under this prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms relating to a series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- United States federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or
- in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration

date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to us or the warrant agent as applicable.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Enforceability of Rights by Holders of Warrants

If selected, each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

DESCRIPTION OF UNITS

The following description, together with the additional information we may include in any applicable prospectus supplements and free writing prospectuses, summarizes the material terms and provisions of the units that we may offer under this prospectus.

While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from a Current Report on Form 8-K that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we sell under this prospectus, as well as the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units comprised of one or more debt securities, shares of common stock, shares of preferred stock and warrants in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under “*Description of Capital Stock*,” “*Description of Debt Securities*” and “*Description of Warrants*” will apply to each unit and to any common stock, preferred stock, debt security or warrant included in each unit, respectively.

Unit Agent

The name and address of the unit agent, if any, for any units we offer will be set forth in the applicable prospectus supplement.

Issuance in Series

We may issue units in such amounts and in numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

We, the unit agents and any of their agents may treat the registered holder of any unit certificate as an absolute owner of the units evidenced by that certificate for any purpose and as the person entitled to exercise the rights attaching to the units so requested, despite any notice to the contrary. See “*Legal Ownership of Securities*.”

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee or depositary or warrant agent maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary’s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Global securities will be registered in the name of the depositary or its participants. Consequently, for global securities, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a global security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary’s book-entry system or

holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities that are not issued in global form. In these cases, investors may choose to hold their securities in their own names or in “street name.” Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable trustee or depository will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any such trustee or depository will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not legal holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee or third party employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with its participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of an indenture, or for other purposes. In such an event, we would seek approval only from the legal holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders’ consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a legal holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depository’s rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depository. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we issue to, deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depository. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, NY, known as DTC, will be the depository for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under “— *Special Situations When A Global Security Will Be Terminated.*” As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued as a global security, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations For Global Securities

As an indirect holder, an investor’s rights relating to a global security will be governed by the account rules of the investor’s financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only as global securities, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in the global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depositary’s policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor’s interest in the global security. We and any applicable trustee have no responsibility for any aspect of the depositary’s actions or for its records of ownership interests in the global security. We and the trustee also do not supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in the global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depositary’s book-entry system, and through which an investor holds its interest in the global security, may also have their own policies affecting payments, notices and other matters relating to the securities. There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries

Special Situations When A Global Security Will Be Terminated

In a few special situations described below, a global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own names, so that they will be direct holders. We have described the rights of holders and street name investors above.

A global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and neither we, nor any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities being offered hereby in one or more of the following ways from time to time:

- through agents to the public or to investors;
- to underwriters for resale to the public or to investors;
- negotiated transactions;
- block trades;
- directly to investors; or
- through a combination of any of these methods of sale.

As set forth in more detail below, the securities may be distributed from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We will set forth in a prospectus supplement the terms of that particular offering of securities, including:

- the name or names of any agents or underwriters;
- the purchase price of the securities being offered and the proceeds we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any initial public offering price;
- any discounts or concessions allowed or re-allowed or paid to dealers; and
- any securities exchanges or markets on which such securities may be listed.

Only underwriters named in an applicable prospectus supplement are underwriters of the securities offered by that prospectus supplement.

If underwriters are used in an offering, we will execute an underwriting agreement with such underwriters and will specify the name of each underwriter and the terms of the transaction (including any underwriting discounts and other terms constituting compensation of the underwriters and any dealers) in a prospectus supplement. The securities may be offered to the public either through underwriting syndicates represented by managing underwriters or directly by one or more investment banking firms or others, as designated. If an underwriting syndicate is used, the managing underwriter(s) will be specified on the cover of the prospectus supplement. If underwriters are used in the sale, the offered securities will be acquired by the underwriters for their own accounts and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Any public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time. Unless otherwise set forth in the prospectus supplement, the obligations of the underwriters to purchase the offered securities will be subject to conditions precedent and the underwriters will be obligated to purchase all of the offered securities if any are purchased.

We may grant to the underwriters options to purchase additional securities to cover over-allotments, if any, at the public offering price, with additional underwriting commissions or discounts, as may be set forth in a related prospectus supplement. The terms of any over-allotment option will be set forth in the prospectus supplement for those securities.

If we use a dealer in the sale of the securities being offered pursuant to this prospectus or any prospectus supplement, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. The names of the dealers and the terms of the transaction will be specified in a prospectus supplement.

We may sell the securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, any agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

In connection with the sale of the securities, underwriters, dealers or agents may receive compensation from us or from purchasers of the common stock for whom they act as agents in the form of discounts, concessions or commissions. Underwriters may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions from the purchasers for whom they may act as agents. Underwriters, dealers and agents that participate in the distribution of the securities, and any institutional investors or others that purchase common stock directly and then resell the securities, may be deemed to be underwriters, and any discounts or commissions received by them from us and any profit on the resale of the common stock by them may be deemed to be underwriting discounts and commissions under the Securities Act.

We may provide agents and underwriters with indemnification against particular civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to such liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties (including the writing of options), or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with such a transaction, the third parties may, pursuant to this prospectus and the applicable prospectus supplement, sell securities covered by this prospectus and the applicable prospectus supplement. If so, the third party may use securities borrowed from us or others to settle such sales and may use securities received from us to close out any related short positions. We may also loan or pledge securities covered by this prospectus and the applicable prospectus supplement to third parties, who may sell the loaned securities or, in an event of default in the case of a pledge, sell the pledged securities pursuant to this prospectus and the applicable prospectus supplement. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement or in a post-effective amendment.

To facilitate an offering of a series of securities, persons participating in the offering may engage in transactions that stabilize, maintain, or otherwise affect the market price of the securities. This may include over-allotments or short sales of the securities, which involves the sale by persons participating in the offering of more securities than have been sold to them by us.

In those circumstances, such persons would cover such over-allotments or short positions by purchasing in the open market or by exercising the over-allotment option granted to those persons. In addition, those persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to underwriters or dealers participating in any such offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. Such transactions, if commenced, may be discontinued at any time. We make no representation or prediction as to the direction or magnitude of any effect that the transactions described above, if implemented, may have on the price of our securities.

Unless otherwise specified in the applicable prospectus supplement, each class or series of securities will be a new issue with no established trading market, other than our common stock, which is listed on The Nasdaq Capital Market. We may elect to list any other class or series of securities on any exchange or market, but we are not obligated to do so. It is possible that one or more underwriters may make a market in a class or series of securities, but the underwriters will not be obligated to do so and may discontinue any market making at any time without notice. We cannot give any assurance as to the liquidity of the trading market for any of the securities.

In order to comply with the securities laws of some U.S. states or territories, if applicable, the securities offered pursuant to this prospectus will be sold in those states only through registered or licensed brokers or dealers. In addition, in some states securities may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and complied with.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of these activities at any time.

Any underwriters who are qualified market makers on The Nasdaq Capital Market may engage in passive market making transactions in the securities on The Nasdaq Capital Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security. If all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

LEGAL MATTERS

The validity of the issuance of the securities offered hereby will be passed upon for us by Sheppard, Mullin, Richter & Hampton LLP, New York, NY. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements as of December 31, 2020 and 2019 and for the years then ended incorporated by reference in this prospectus and in the registration statement have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus constitutes a part of the registration statement on Form S-3 that we have filed with the SEC under the Securities Act. As permitted by the SEC's rules, this prospectus supplement and any accompanying prospectus, which forms a part of the registration statement, do not contain all of the information that is included in the registration statement. You will find additional information about us in the registration statement. Any statement made in this prospectus supplement or any accompanying prospectus concerning legal documents are not necessarily complete and you should read the documents that are

filed as exhibits to the registration statement or otherwise filed with the SEC for a more complete understanding of the document or matter.

We are subject to the reporting requirements of the Exchange Act and file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at www.sec.gov. We also maintain a website at www.cardiffoncology.com, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of this prospectus.

You may also request a copy of these filings, at no cost, by writing or telephoning us at: 11055 Flintkote Avenue, San Diego, California, 92121, (858) 952-7570.

INCORPORATION OF DOCUMENTS BY REFERENCE

This prospectus supplement is part of the registration statement, but the registration statement includes and incorporates by reference additional information and exhibits. The SEC permits us to "incorporate by reference" the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus supplement. Information that is incorporated by reference is considered to be part of this prospectus supplement and you should read it with the same care that you read this prospectus supplement and the accompanying prospectus. Information that we file later with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus supplement, and will be considered to be a part of this prospectus supplement from the date those documents are filed.

We incorporate by reference the documents listed below, all filings filed by us pursuant to the Exchange Act after the date of the registration statement of which this prospectus supplement and the accompanying prospectus forms a part, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the time that all securities covered by this prospectus supplement have been sold; provided, however, that we are not incorporating any information furnished under either Item 2.02 or Item 7.01 of any current report on Form 8-K:

- [our Annual Report on Form 10-K for the year ended December 31, 2020 filed with the SEC on February 25, 2021](#);
- our Current Reports on Form 8-K filed on [January 15, 2021](#), [January 26, 2021](#), [February 11, 2021](#), [February 16, 2021](#), [February 24, 2021](#), [March 3, 2021](#) and [March 11, 2021](#);
- [our definitive Proxy Statement on Schedule 14a for our 2020 Annual Meeting of Stockholders, filed with the SEC on March 4, 2020](#); and
- [the description of our common stock contained in our Registration Statement on Form 8-A filed with the Commission on May 23, 2012, including any amendments or reports filed with the SEC for the purposes of updating such description](#).

Any statements made in a document incorporated by reference in this prospectus supplement are deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement in this prospectus supplement or in any other subsequently filed document, which is also incorporated by reference, modifies or supersedes the statement. Any statement made in this prospectus supplement is deemed to be modified or superseded to the extent a statement in any subsequently filed document, which is incorporated by reference in this prospectus supplement, modifies or supersedes such statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

The information relating to us contained in this prospectus supplement should be read together with the information in the documents incorporated by reference. In addition, certain information, including financial information, contained in this prospectus or incorporated by reference in this prospectus should be read in conjunction with documents we have filed with the SEC.

We will provide to each person, including any beneficial holder, to whom a prospectus is delivered, at no cost, upon written or oral request, a copy of any or all of the information that has been incorporated by reference in the prospectus but not delivered with the prospectus. Requests for documents should be by writing to or telephoning us at the following address:

Cardiff Oncology, Inc., 11055 Flintkote Avenue, San Diego, CA 92121; (858) 952-7570. Exhibits to these filings will not be sent unless those exhibits have been specifically incorporated by reference in such filings.

2,411,575 Shares of Common Stock



Cardiff Oncology, Inc.

PROSPECTUS SUPPLEMENT

November 18, 2021