UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **September 8, 2021**

Cardiff Oncology, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-35558**	**27-2004382**
(State or other jurisdiction of incorporation or organization)	(Commission File Number)	IRS Employer Identification No.)

11055 Flintkote Avenue
San Diego, CA 92121
(Address of principal executive offices)

Registrant's telephone number, including area code: **(858) 952-7570**

(Former name or former address, if changed since last report)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class:	Trading Symbol(s)	Name of each exchange on which registered:
Common Stock	CRDF	Nasdaq Capital Market

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

o Written communication pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter). Emerging growth company o

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. o

Item 7.01 Regulation FD Disclosure.

On September 8, 2021, Cardiff Oncology, Inc. (the "Company") issued a press release announcing new data from its lead clinical program evaluating onvansertib in combination with standard-of-care (SOC) FOLFIRI/bevacizumab for second-line treatment of patients with KRAS-mutated metastatic colorectal cancer (mCRC). A copy of the press release is furnished as Exhibit 99.1 to this Form 8-K. In addition, the Company plans to make a presentation to investors at 4:00 pm ET on September 8, 2021 with the Corporate Presentation furnished as Exhibit 99.2 to this Form 8-K.

In accordance with General Instruction B.2 of Form 8-K, the information in this Current Report on Form 8-K is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that Section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits.

99.1	Press Release of Cardiff Oncology, Inc. dated September 8, 2021.
99.2	Corporate Presentation

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: September 8, 2021

CARDIFF ONCOLOGY, INC.

By: /s/ Mark Erlander
Mark Erlander
Chief Executive Officer

Cardiff Oncology Announces New Data from Phase 1b/2 Trial in KRAS-mutated Metastatic Colorectal Cancer Showing Robust Objective Response Rate and Progression Free Survival

- 8 of 19 (42%) patients treated per protocol at the recommended Phase 2 dose (RP2D) of onvansertib 15 mg/m^2 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[1-4]

- 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[1-4]

- The combination regimen of onvansertib plus FOLFIRI/bevacizumab is well tolerated

- Management is hosting key opinion leader webinar to discuss data today at 4:00 PM ET; a replay of the webinar will be available on the events section of the Cardiff Oncology website for 90 days

SAN DIEGO, September 8, 2021 -- Cardiff Oncology, Inc. (Nasdaq: CRDF), a clinical-stage oncology company, developing new precision medicine treatment options for cancer patients in indications with the greatest unmet medical need including KRAS-mutated colorectal cancer, pancreatic cancer, and castrate-resistant prostate cancer, today announced new data from its lead clinical program evaluating onvansertib in combination with standard-of-care (SOC) FOLFIRI/bevacizumab for second-line treatment of patients with KRAS-mutated metastatic colorectal cancer (mCRC).

“Our Phase 1b/2 trial continues to generate data suggesting that the addition of onvansertib to SOC results in an objective response rate and median progression-free survival that substantially exceed those previously achieved with SOC alone,” said Katherine L. Ruffner, M.D., chief medical officer of Cardiff Oncology. “Radiographic responses have been observed across multiple KRAS mutation variants, which speaks to a key advantage of onvansertib over competing agents targeting individual mutations. These impressive results, which have remained consistent across both academic and community trial sites, highlight the potential for onvansertib to address the unmet need for new second-line therapeutic options to treat patients with KRAS-mutated mCRC. I look forward to the trial’s continued advancement and future data readouts.”

Highlights from today’s data announcement include:

Efficacy data in patients evaluable for disease response as of data cutoff date (July 2, 2021):

- *Patients treated per protocol at the recommended Phase 2 dose (RP2D; 15 mg/m^2) across both Phase 1b and Phase 2:*
  - 8 of 19 (42%) achieved an initial partial response (PR) as of the data cutoff date
  - 7 of 19 (37%) have achieved a confirmed PR (based on further follow-up of patients with an initial PR as of data cutoff date)

- Objective response rates observed in historical control trials in similar patient populations treated with standard of care are 5-13%[1-4]

- *Patients evaluable for response treated at all dose levels (12 mg/m^2, 15 mg/m^2, 18 mg/m^2) across both phases of the study*
  - 12 of 32 (38%) achieved an initial PR as of the data cutoff date
  - 10 of 32 (31%) have achieved a confirmed PR (based on further follow-up of patients with an initial PR as of data cutoff date)

Median progression free survival (mPFS)
- mPFS has not yet been reached in patients treated per protocol at the RP2D
- mPFS across all response-evaluable patients (n = 32) is 9.4 months (95% confidence interval: 7.8 – not yet reached)
- mPFS of ~4.5-5.7 months has been reported in trials used as historical controls[1-4]

Biomarker data as of data cutoff date across all patients:
- Partial responses (PRs) were observed across different KRAS mutation variants, including the 3 most common observed in colorectal cancer (G12D, G12V, G13D)
- Patients achieving a best response of PR showed the greatest decreases in plasma KRAS mutant allelic frequency (MAF) after 1 cycle (28 days) of therapy

Safety data as of data cutoff date across all patients:
- The combination of onvansertib and FOLFIRI/bevacizumab was shown to be well-tolerated with only 10% (49/490) of reported treatment-emergent adverse events (TEAEs) being G3/G4
- Most reported treatment-related adverse events (TRAEs) were manageable and reversible with supportive care

Mark Erlander, Ph.D., chief executive officer of Cardiff Oncology, commented, “The strong signal of efficacy and favorable tolerability profile observed in this trial bodes well not only for our lead mCRC program, but for each of our KRAS-focused clinical programs. The meaningful improvements we are seeing in treatment response relative to historical controls demonstrate the value of combination therapy and support the synergistic effect observed preclinically when onvansertib is added to standard-of-care irinotecan and 5-FU (FOLFIRI). We are also seeing compelling biomarker results that highlight the potential utility of plasma KRAS MAF as a predictive tool that could aid in the design of subsequent trials. Looking forward, we anticipate the ongoing Phase 2 portion of the trial to provide additional data catalysts that will advance the clinical development of onvansertib, generate value for shareholders and, most importantly, provide new treatment options for patients.”

Key Opinion Leader Webinar
The newly announced data are being discussed today at 4:00 PM ET as part of a key opinion leader (KOL) webinar being hosted by Cardiff Oncology. The webinar is featuring the clinical trial principal investigator, Heinz-Josef Lenz, M.D., FACP, USC Norris Comprehensive Cancer Center, key clinical advisor Afsaneh Barzi, M.D., Ph.D., City of Hope Comprehensive Cancer Center, and members of the Cardiff Oncology management team.

To attend the webinar, click here. A replay of the webinar will be available by visiting the "Events" section of the Cardiff Oncology website shortly after its conclusion.

About the Phase 1b/2 Trial of Onvansertib in KRAS-mutated mCRC
This is a multi-center, single-arm, Phase 1b/2 trial of onvansertib in combination with standard-of-care FOLFIRI and Avastin® (bevacizumab) to evaluate the safety and preliminary efficacy of the combination regimen in the second-line treatment of patients with KRAS-mutated mCRC. The trial, *A Phase 1b/2 Study of Onvansertib (PCM-075) in Combination with FOLFIRI and Bevacizumab for Second–Line Treatment of Metastatic Colorectal Cancer in Patients with a KRAS Mutation,* is enrolling patients with histologically confirmed metastatic and unresectable colorectal carcinoma harboring a KRAS mutation. Patients must also have failed treatment with, or be intolerant to, FOLFOX (fluoropyrimidine and oxaliplatin) with or without bevacizumab to be eligible. The trial is being conducted at the following cancer centers across the U.S.: USC Norris Comprehensive Cancer Center, The Mayo Clinic (Arizona, Rochester, and Jacksonville), Kansas University Medical Center (KUMC), CARTI Cancer Center and Inova Schar Cancer Institute. For more information on the trial, please visit https://clinicaltrials.gov/ct2/show/NCT03829410.

References

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

About Cardiff Oncology, Inc.
Cardiff Oncology is a clinical-stage 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, a first-in-class, third-generation 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 have three clinical programs currently ongoing: a Phase 1b/2 study of onvansertib in combination with FOLFIRI/Avastin® (bevacizumab) in KRAS-mutated metastatic colorectal cancer (mCRC); a Phase 2 trial of onvansertib in combination with nanoliposomal irinotecan, leucovorin and fluorouracil for the second-line treatment of patients with metastatic pancreatic ductal adenocarcinoma (PDAC); and a Phase 2 study of onvansertib in combination with Zytiga® (abiraterone)/prednisone in metastatic castrate-resistant prostate cancer (mCRPC). For more information, please visit https://www.cardiffoncology.com.

Forward-Looking Statements
Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified using words such as "anticipate," "believe," "forecast," "estimated" and "intend" or other similar terms or expressions that concern Cardiff Oncology's expectations, strategy, plans or intentions. These forward-looking statements are based on Cardiff Oncology's current expectations and actual results could differ materially. There are several factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results; our clinical trials may be suspended or discontinued due to unexpected side effects or other safety risks that could preclude approval of our product candidates; risks related to business interruptions, including the outbreak of COVID-19 coronavirus, which could seriously harm our financial

condition and increase our costs and expenses; uncertainties of government or third party payer reimbursement; dependence on key personnel; limited experience in marketing and sales; substantial competition; uncertainties of patent protection and litigation; dependence upon third parties; and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. There are no guarantees that any of our technology or products will be utilized or prove to be commercially successful. Additionally, there are no guarantees that future clinical trials will be completed or successful or that any precision medicine therapeutics will receive regulatory approval for any indication or prove to be commercially successful. Investors should read the risk factors set forth in Cardiff Oncology's Form 10-K for the year ended December 31, 2020, and other periodic reports filed with the Securities and Exchange Commission. While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and Cardiff Oncology does not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances.

Cardiff Oncology Contact:
Vicki Kelemen
Chief Operating Officer
858-952-7652
vkelemen@cardiffoncology.com

Investor Contact:
Joyce Allaire
LifeSci Advisors
212-915-2569
jallaire@lifesciadvisors.com

Media Contact:
Amy Jobe, Ph.D.
LifeSci Communications
315-879-8192
ajobe@lifescicomms.com

Cardiff Oncology™

New Data Presentation: KRAS-mutated Metastatic Colorectal Cancer (mCRC)

September 8, 2021

Forward-Looking Statements

Certain statements in this presentation are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of words such as "anticipate," "believe," "forecast," "estimated" and "intend" or other similar terms or expressions that concern our expectations, strategy, plans or intentions. These forward-looking statements are based on our current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, our need for additional financing; our ability to continue as a going concern; clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results; our clinical trials may be suspended or discontinued due to unexpected side effects or other safety risks that could preclude approval of our product candidates; risks related to business interruptions, including the outbreak of COVID-19 coronavirus, which could seriously harm our financial condition and increase our costs and expenses; uncertainties of government or third party payer reimbursement; dependence on key personnel; limited experience in marketing and sales; substantial competition; uncertainties of patent protection and litigation; dependence upon third parties; regulatory, and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. There are no guarantees that any of our technology or products will be utilized or prove to be commercially successful. Additionally, there are no guarantees that future clinical trials will be completed or successful or that any precision medicine therapeutics will receive regulatory approval for any indication or prove to be commercially successful. Investors should read the risk factors set forth in our Form 10-K for the year ended December 31, 2020, and other periodic reports filed with the Securities and Exchange Commission. While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and we do not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances.

Agenda

KRAS-mutant Metastatic Colorectal Cancer Remains an Unmet Need for New Therapeutic Options

Afsaneh Barzi, M.D., Ph.D., (City of Hope Comprehensive Cancer Center)
Cardiff Oncology's Key Clinical Advisor

New Data:

Onvansertib in Combination With FOLFIRI and Bevacizumab for Second Line Treatment of Metastatic Colorectal Cancer Patients With a KRAS Mutation

Heinz-Josef Lenz, M.D., FACP (USC Norris Comprehensive Cancer Center)
Cardiff Oncology's mCRC Clinical Trial Principal Investigator

The Cardiff Oncology Opportunity

Mark Erlander, Ph.D., Chief Executive Officer

Question & Answer Session

Katherine Ruffner, M.D. – Chief Medical Officer

- Joined Cardiff as CMO July 6
- Education:
  - BS Biology, Duke University
  - MD, University of Tennessee
  - Internal Medicine residency, University of Michigan
  - Medical Oncology fellowship, Fred Hutch Cancer Research Center/University of Washington
- Academic experience:
  - Assistant Professor, Vanderbilt University, Division of Hematology/Oncology and Nashville VAMC 2002-2007
- Industry experience:
  - VP Clinical Development, ALX Oncology and CTI BioPharma
  - Clinical Development roles at SeaGen, Medivation, Array Biopharma, Pfizer, Biogen-Idec and Amgen
  - Contributed to filing packages for the following approved agents:
    - Crizotinib
    - Bosutinib
    - Brentuximab vedotin

Afsaneh Barzi, M.D., Ph.D. – City of Hope Comprehensive Cancer Center

City of Hope

- Dr. Barzi serves as a key clinical advisor to Cardiff Oncology.
- Academic appointments
  - Current:
    - Associate Professor for GI oncology at City of Hope Comprehensive Cancer Center (COH-CCC)
    - Clinical Director of AccessHope at COH-CCC
  - Previous:
    - Associate Professor of clinical medicine at the Keck School of Medicine of the University of Southern California.
- Education
  - MD, Tehran University of Medical Sciences
  - Masters in Health Informatics, University of Texas Health Sciences Center at Houston
  - PhD, Public Health Management and Policy Sciences, University of Texas Health Sciences Center at Houston
  - Hematology and Oncology fellowship, Cleveland Clinic Taussig Cancer Center
- Academic focus:
  - Research and practice on GI malignancies with a particular focus on colorectal cancer.
  - Use of biomarkers for personalized care.

KRAS-MUTANT METASTATIC COLORECTAL CANCER REMAINS AN UNMET NEED FOR NEW THERAPEUTIC OPTIONS

AFSANEH BARZI, M.D., PH.D.

Associate Clinical Professor of Medical Oncology
GI Oncology and Clinical Director of AccessHope
City of Hope Comprehensive Cancer Center

Objectives

01

Discuss the clinical burden of KRAS-mutated colorectal cancer

02

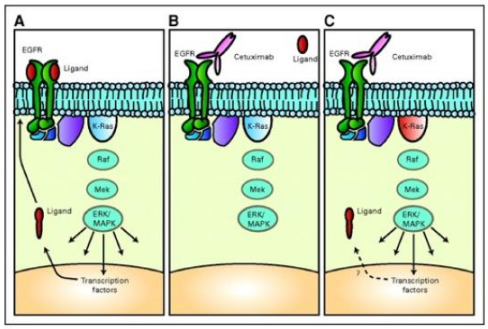
Review ongoing areas of clinical research and their limitations

03

Highlight the opportunity for onvansertib in KRAS-mutated mCRC

Mutated KRAS: a “negative” biomarker to avoid selecting an inappropriate treatment

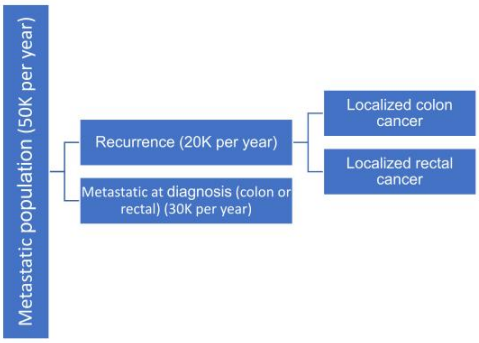
- For most biomarkers, their presence is associated with benefit from a targeted agent
  - BRAF mutation: Encorafenib
- Presence of KRAS is not associated with any benefit from EGFR antibodies (panitumumab and cetuximab)



[1]Khambata-Ford S et al. *Journal of Clinical Oncology* 2007 253230-3237

KRAS mutations are highly prevalent in metastatic CRC

Prevalence of metastatic disease



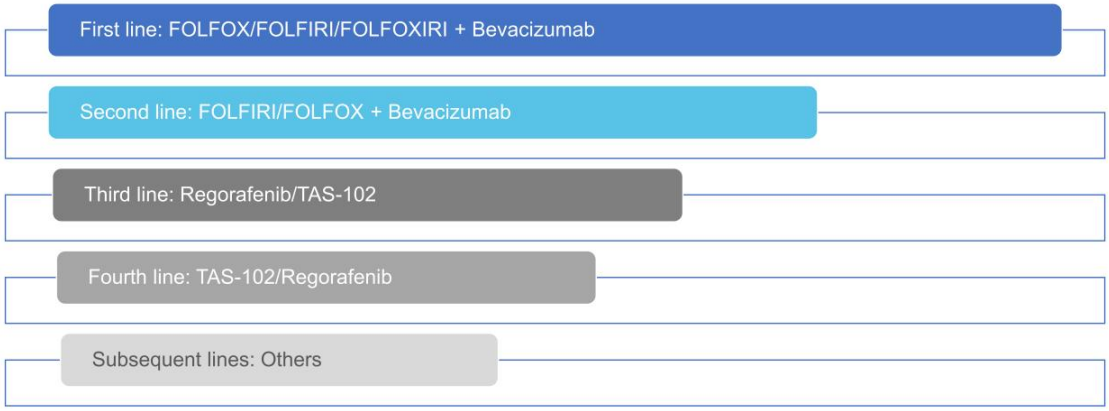
Actionable biomarkers

Actionable Biomarkers	
KRAS	45%
MSI	10%
BRAF	8%
NRAS	5%
HER2	5%
NTRK	1%

City of Hope

[1]Siegel RL et al. CA Cancer J Clin. 2021: 71: 7- 33

Treatment landscape for KRAS mutated CRC



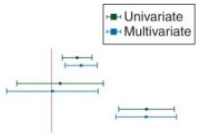
City of Hope

[1]NCCN Recommendations

KRAS mutation, a negative prognostic indicator in metastatic CRC

- A pooled analysis of German Oncology trials included 1239 patients: 664 KRAS wild type and 462 KRAS mutation

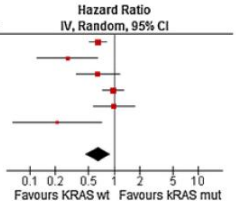
	HR	95% CI	*P*–value
All observations (n = 1239)			
KRAS vs. WT	1.41	(1.17, 1.7)	3e−05
NRAS vs. WT	1.01	(0.6, 1.72)	1
BRAF vs. WT	2.99	(2.1, 4.25)	4e−13



- A meta-analysis of patients who received bevacizumab containing regimen included 2266 patients: 54% KRAS wild type

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI	Year
Diaz Rubio MACRO (2012)	-0.446	0.118	26.0%	0.64 [0.51, 0.81]	
Bruera (2013)	-1.273	0.423	11.0%	0.28 [0.12, 0.64]	
Hurwitz AVF2107 (2009)	-0.446	0.303	15.8%	0.64 [0.35, 1.16]	
Price AGITG MAX (2011)	-0.03	0.143	24.7%	0.97 [0.73, 1.28]	
Saltz (2012)	0	0.296	16.2%	1.00 [0.56, 1.79]	
Stremitzer (2012)	-1.561	0.627	6.3%	0.21 [0.06, 0.72]	
Total (95% CI)			**100.0%**	**0.65 [0.46, 0.92]**	

Heterogeneity: Tau² = 0.11; Chi² = 15.58, df = 5 (P = 0.008); I² = 68%
Test for overall effect: Z = 2.44 (P = 0.01)

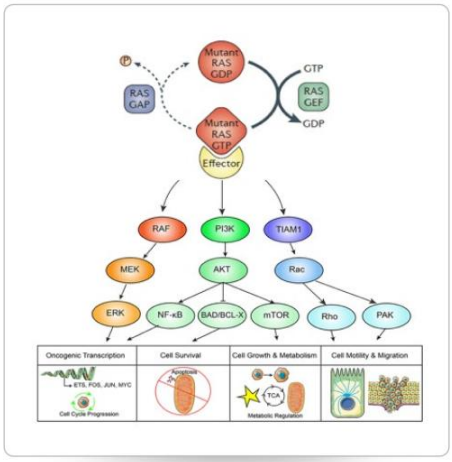


City of Hope

[1]Modest P et al. Ann Oncol 2016 Sep;27(9):1746-53; [2]Petrelli F et al. Med Oncol. 2013;30(3):650

Challenges in targeting KRAS

- Direct targeting (not feasible)
  - RAS high affinity for GTP (activation mechanism) >>> impossible competition as normal functioning will be disrupted
  - Different KRAS mutations result in different conformational change
  - The shape of the conformation in G12C is permissive to inhibition
- Farnesyl transferase: Lonafarnib and tipifarnib (failed due to redundant pathway for prenylation)
- Downstream pathway inhibition (current focus)
  - MEK inhibitor
  - Combination of MEK and PI3K (ongoing)

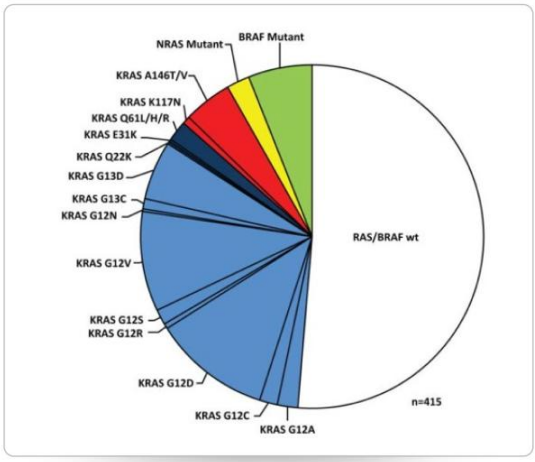


City of Hope

[1]Gimple R and Wang X; Front. Oncol., 24 September 2019, Volume 9 -Article 965

G12C mutation in CRC: a small subset of patients

Somatic Mutations	N (%)
C.35G>A p.G12D	49 (29.2%)
C.35G>C p.G12A	15 (8.9%)
C.34G>T p.G12C	15 (8.9%)
C.34_35delinsTT p.G12F	1 (0.6%)
C.34G>A p.G12S	16 (9.5%)
C.35G>T p.G12V	41 (24.4%)
C.38G>A p.G13D	26 (15.5%)
C.37G>T p.G13C	2 (1.2%)
c.183A>T p.Q61H	4 (2.4%)



City of Hope

[1]Janakiraman M et al. Cancer Res. 2010 Jul 15;70(14):5901-11; [2]Jones R et al. Br J Cancer. 2017 Mar 28;116(7):923-929

Not all G12C's are the same: Colorectal Cancer vs. NSCLC

Table 3. Efficacy of Sotorasib in All Tumor Types.

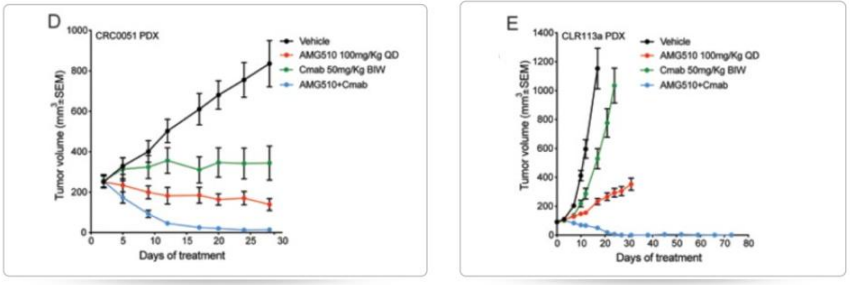
	NSCLC (N=59)	Colorectal Cancer (N=42)	Other (N=28)
Best overall response — no. (%)			
Confirmed complete response	0	0	0
Confirmed partial response	19 (32.2)	3 (7.1)	4 (14.3)
Stable disease	33 (55.9)	28 (66.7)	17 (60.7)
Progressive disease	5 (8.5)	10 (23.8)	4 (14.3)
Could not be evaluated	1 (1.7)	0	1 (3.6)
No assessment*	1 (1.7)	1 (2.4)	2 (7.1)
Objective response — % (95% CI)†	32.2 (20.62–45.64)	7.1 (1.50–19.48)	14.3 (4.03–32.67)
Disease control — % (95% CI)‡	88.1 (77.07–95.09)	73.8 (57.96–86.14)	75.0 (55.13–89.31)

* One patient with NSCLC withdrew consent before tumor assessment. One patient with colorectal cancer and 2 patients with other tumor types had clinical progression.
† Objective response was defined as a complete or partial response.
‡ Disease control was defined as a complete response, a partial response, or stable disease.

[1]DS Hong et al. N Engl. J Med 2020;383:1207-1217

Combination therapy: a requirement in KRAS-mutated CRC

Preclinical Data:



Phase 3 Study: MRTX849 + Cetuximab vs Chemotherapy in Advanced Colorectal Cancer With KRAS G12C Mutation (KRYSTAL-10)

Inclusion Criteria:
Diagnosis of colorectal carcinoma with KRAS G12C mutation in tumor tissue
Prior receipt of 1st line treatment in advanced CRC with documented progression of disease on or after treatment

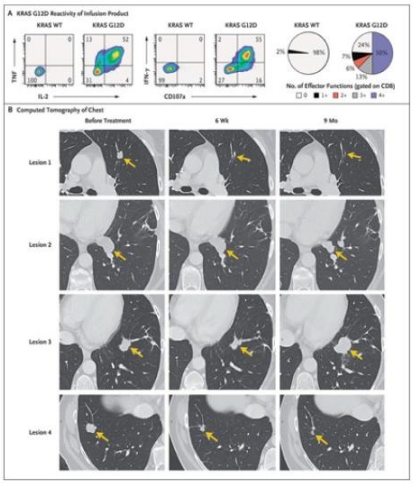
Exclusion Criteria:
Prior treatment with a therapy targeting KRAS G12C mutation (e.g., AMG 510)
Prior treatment with an anti-EGFR antibody (e.g., cetuximab or panitumumab)
Active brain metastasis

City of Hope [1]Amodio V et al. Cancer Discovery, 2020

Other Therapeutic Efforts: Adoptive Transfer of KRAS G12D Specific T Cells

Administering Peripheral Blood Lymphocytes Transduced With a Murine T-Cell Receptor Recognizing the G12D Variant of Mutated RAS in HLA-A*11:01 Patients (NCT03745326).

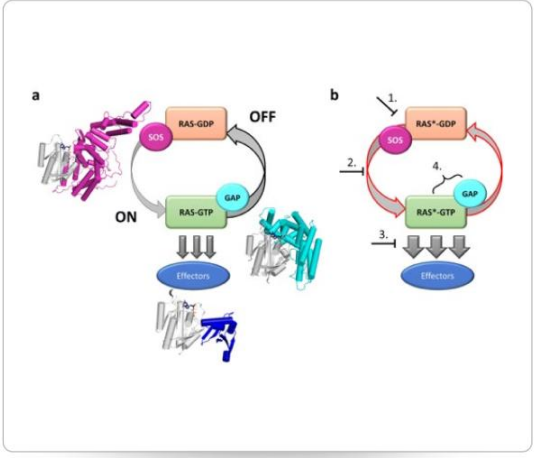
- Metastatic or unresectable RAS G12D-expressing cancer which has progressed after standard therapy (if available).
- HLA-A*11:01 genotype is rare in the US population



City of Hope

[1]Tran E et al. N Engl J Med 2016; [2]Bardi MS et al. Rev Bras Hematol Hemoter. 2012;34(1):25-30

SOS1: Pan KRAS inhibitor



Phase I : BI 1701963 Alone and Combined With Trametinib in Patients With Solid Tumors With KRAS Mutation

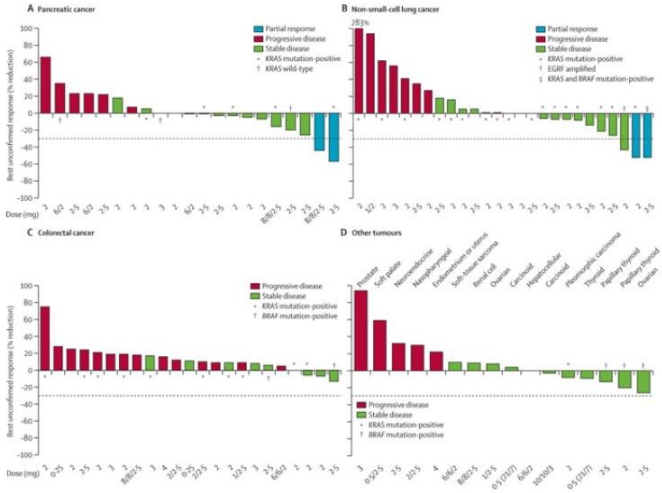
Expansion in NSCLC

Phase I + expansion: BI 1701963 Alone and Combined With Irinotecan in Patients With colorectal cancer Tumors With KRAS Mutation

City of Hope

[1]Nyiri k et al. Cancer and Metastasis Review 2020

MEK-inhibitor (trametinib) has been studied as single agent and in combination in KRAS-mutated cancers



City of Hope

[1]Infante JR et al. Lancet Oncol 2012 Aug;13(8):773-81

Toxicity of MEK Inhibitors (Trametinib)

	Grade 1		Grade 2		Grade 3		Grade 4		Total	
	2 mg once daily (n=70)	Total (n=206)	2 mg once daily (n=70)	Total (n=206)	2 mg once daily (n=70)	Total (n=206)	2 mg once daily (n=70)	Total (n=206)	2 mg once daily (n=70)	Total (n=206)
Any events	20 (29%)	55 (27%)	39 (56%)	102 (50%)	8 (11%)	37 (18%)	0	2 (<1%)	68 (97%)	197 (96%)
Skin-related toxic effects*	34 (49%)	81 (39%)	25 (36%)	74 (36%)	4 (6%)	16 (8%)	0	1 (<1%)	63 (90%)	172 (83%)
Rash or dermatitis acneiform	34 (49%)	81 (39%)	22 (31%)	69 (33%)	3 (4%)	14 (7%)	0	1 (<1%)	59 (84%)	165 (80%)
Diarrhoea	24 (34%)	63 (31%)	7 (10%)	22 (11%)	1 (1%)	2 (<1%)	0	0	32 (46%)	87 (42%)
Fatigue	13 (19%)	37 (18%)	7 (10%)	23 (11%)	1 (1%)	8 (4%)	0	0	21 (30%)	68 (33%)
Peripheral oedema	18 (26%)	47 (23%)	2 (3%)	12 (6%)	0	1 (<1%)	0	0	20 (29%)	60 (29%)
Nausea	14 (20%)	46 (22%)	4 (6%)	11 (5%)	0	0	0	0	18 (26%)	57 (28%)
Vomiting	5 (7%)	23 (11%)	3 (4%)	10 (5%)	1 (1%)	1 (<1%)	0	0	9 (13%)	34 (17%)
Pruritus	10 (14%)	19 (9%)	4 (6%)	10 (5%)	0	0	0	0	14 (20%)	29 (14%)
Dry skin, chapped skin, or skin fissures	11 (16%)	31 (15%)	4 (6%)	7 (3%)	0	0	0	0	15 (21%)	38 (18%)
Decreased appetite	6 (9%)	14 (7%)	1 (1%)	5 (2%)	0	1 (<1%)	0	0	7 (10%)	20 (10%)
Ocular toxic effects†	6 (9%)	26 (13%)	0	4 (2%)	1 (1%)	1 (<1%)	0	0	7 (10%)	31 (15%)
Mucosal inflammation	3 (4%)	11 (5%)	0	4 (2%)	0	0	0	0	3 (4%)	15 (7%)
Constipation	2 (3%)	8 (4%)	1 (1%)	3 (1%)	0	0	0	0	3 (4%)	11 (5%)
Left-ventricular dysfunction or ejection fraction decreased	2 (3%)	5 (2%)	4 (6%)	9 (4%)	1 (1%)	2 (<1%)	0	0	7 (10%)	16 (8%)
Periorbital oedema	5 (7%)	10 (5%)	0	1 (<1%)	0	0	0	0	5 (7%)	11 (5%)
Thrombocytopenia	1 (1%)	8 (4%)	0	1 (<1%)	0	1 (<1%)	0	1 (<1%)	1 (1%)	11 (5%)
Dry mouth	2 (3%)	10 (5%)	0	0	0	0	0	0	2 (3%)	10 (5%)

Data are number of patients (%). The most frequent (≥5%) adverse events are shown. *Includes acne, dermatitis acneiform, dermatitis psoriasiform, erythaema, genital rash, palmar-plantar erythrodysesthesia, rash, erythaematous rash, follicular rash, generalised rash, macular rash, maculopapular rash, pruritic rash, pustular rash, seborrhoeic dermatitis, and skin exfoliation. †Includes blurred vision, central serous retinopathy (chorioretinopathy), dry eye, eye naevus, glaucoma, increased intraocular pressure, photophobia, reduced visual acuity, retinal haemorrhage (retinal vein occlusion), and visual impairment.

City of Hope

[1]Infante JR et al. Lancet Oncol 2012 Aug;13(8):773-81

Toxicity of MEK Inhibitors (CH-5126766/VS-6766)

	Grade 1–2	Grade 3	Grade 4
Rash	39 (68%)	11 (19%)	0 (%)
Creatine phosphokinase elevation	36 (63%)	5 (9%)	1 (2%)
Visual disturbance	24 (42%)	1 (2%)	0
Diarrhoea	22 (39%)	1 (2%)	0
Fatigue	17 (30%)	4 (7%)	0
Peripheral oedema	18 (32%)	0	0
Retinal detachment	16 (28%)	1 (2%)	0
Mucositis	16 (28%)	1 (2%)	0
Dry skin	14 (25%)	0 (%)	0
Hypoalbuminaemia	5 (9%)	6 (11%)	0
Nausea	11 (19%)	0	0
Skin fissure	11 (19%)	0	0
Pain	7 (12%)	0	0
Paronychia	7 (12%)	0	0
Facial oedema	6 (11%)	0	0
Pruritus	6 (11%)	0	0
Dehydration	6 (11%)	0	0
Abdominal discomfort	6 (11%)	0	0
Anaemia	2 (4%)	2 (4%)	0
Bronchial infection	0	1 (2%)	0
Hypokalaemia	0	1 (2%)	0
Hypoxia	0	1 (2%)	0

Data are n (%). 57 patients were included in the safety analysis. Treatment-related grade 1–2 adverse events that occurred in 10% or more of patients and all grade 3 or worse treatment-related adverse events are shown.

City of Hope [1]Guo C et al. Lancet Oncol 2020 Nov; 21(11): 1478-1488

Published in final edited form as:
Cancer Cell. 2014 May 12; 25(5): 697–710. doi:10.1016/j.ccr.2014.03.011.

Disruption of CRAF-mediated MEK activation is required for effective MEK inhibition in KRAS mutant tumors

Piro Lito[1,2,8], **Anna Saborowski**[3,8], **Jingyin Yue**[2], **Martha Solomon**[2], **Eric Joseph**[2], **Sunyana Gadal**[2], **Michael Saborowski**[3], **Edward Kastenhuber**[3], **Christof Fellmann**[7], **Kazuhiro Ohara**[5], **Kenji Morikami**[5], **Takaaki Miura**[5], **Christine Lukacs**[6], **Nobuya Ishii**[5], **Scott Lowe**[3,4,*], and **Neal Rosen**[1,2,*]

[1]Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, 10065, USA

[2]Department of Molecular Pharmacology and Chemistry Program, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, USA

[3]Department of Cancer Biology and Genetics Program, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, USA

[4]Howard Hughes Medical Institute; New York, NY 10065, USA

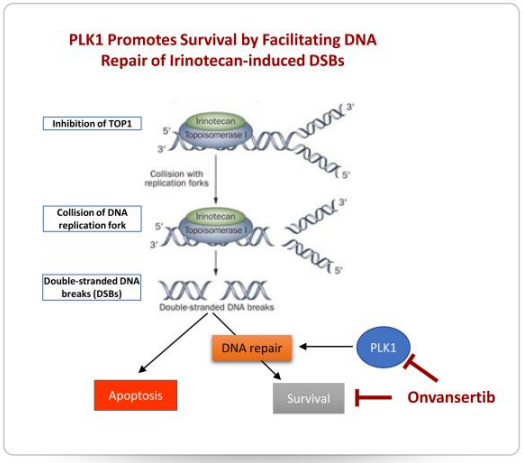
[5]Research Division, Chugai Pharmaceutical; Chuo-ku, Tokyo, 103-8324, JAPAN

[6]Roche Research Center, Hoffmann-La Roche, Nutley, NJ 07110

[7]Cold Spring Harbor Laboratory, Cold Spring Harbor, NY 11724

PLK1 Promotes Cancer Cell Survival by Facilitating DNA Repair of Irinotecan-induced DNA Damage

Onvansertib has the potential to sensitize cancer cells to irinotecan by preventing PLK1-mediated DNA repair

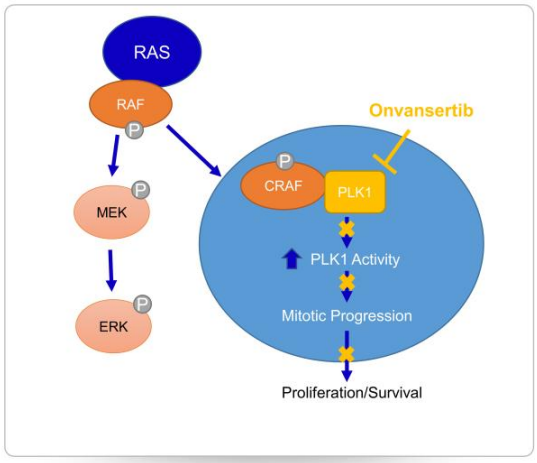


- Topoisomerase I inhibitors such as irinotecan induce double strand DNA breaks (DSBs) during replication (broken replication fork)
- PLK1 is recruited at the broken replication fork to promote DNA repair by homologous recombination (HR)[1]
- PLK1 also facilitates HR by phosphorylating RAD51 and BRCA1 and thereby inducing their recruitment to the DSBs[2,3]
- Repair of the DSBs promotes fork restart and cell survival

City of Hope

[1]Nakamura et al., Mol. Cell 81, 2021; [2]Yata et al. Mol. Cell 45, 2012; [3]Chabalier-Taste et al., Oncotarget 2016 Jan 19; 7(3)

PLK1 and RAS Cooperative Relationship



- RAS activates PLK1 through a MEK/ERK-independent mechanism
- The downstream target of KRAS, pCRAF localizes to the mitotic spindle poles at mitosis where it interacts with PLK1 and promotes PLK1 activation, leading to mitosis and tumor progression[1]
- These data suggest that KRAS-activated cells are dependent on PLK1 for their proliferation and survival, and that inhibition PLK1 by onvansertib could inhibit tumor growth

City of Hope [1]Mielgo et al., Nat. Med. 2011; 17(12):1641-5

Conclusions

- Drug development for KRAS mutated cancers including colorectal cancer has been a long and tortuous way with no success thus far: ***remains an area of unmet need***
- Data suggests that targeting KRAS alone is unlikely to be effective for colorectal cancer: ***combination therapy is being pursued in this space***
- Onvansertib, a PLK1 inhibitor, targets KRAS pathway AND through its impact on DNA repair can enhance the effectiveness of irinotecan
  - The combination is being tested in second line therapy where irinotecan is a standard of care: ***logistical advantage***
  - With >90 patients treated with the combination of onvansertib and irinotecan, the regimen is safe (grade 3-4 treatment emergent AEs = 10% (49 of 490): ***safety and tolerability***
  - Response rate and duration of response in this population is impressive and seen across the most common KRAS subtypes associated with CRC: ***efficacy***

Heinz-Josef Lenz, M.D., FACP – USC Norris Comprehensive Cancer Center

USC Norris Comprehensive Cancer Center
Keck Medicine of USC

- Dr. Lenz is the Principal Investigator for the Phase 1b/2 trial of onvansertib with FOLFIRI-bevacizumab in KRAS-mutated, metastatic colorectal carcinoma.
- Academic appointments at Southern California Norris Comprehensive Cancer Center:
  - Professor of Medicine and Preventive Medicine
  - Section head of Gastrointestinal Oncology, Division of Medical Oncology and co-director of the Colorectal Center
  - Associate Director for clinical research
  - Co-leader of the GI cancers program
- Training:
  - MD, Johannes-Gutenberg Universität in Mainz, Germany
  - Residency, Hematology and Oncology, University Hospital Tübingen, Germany,
  - Clerkship in oncology at George Washington University
  - Clerkship in hematology at Beth Israel Hospital
  - Fellowships in biochemistry and molecular biology at the University of Southern California Norris Comprehensive Cancer Center.
- Honors and committees
  - Member, American Association of Clinical Research, American Gastroenterology Association, and National Society of Genetic Counselors
  - Co-chair of the GI Committee and Correlative Science Committee for SWOG
  - National Cancer Institute (NCI) memberships: Task Force for Gastroesophageal Cancer, the NCI Steering Committee, and the NCI Translational Science Committee.

Onvansertib in Combination With FOLFIRI and Bevacizumab for Second Line Treatment of Metastatic Colorectal Cancer Patients With a KRAS Mutation

Heinz-Josef Lenz, M.D., FACP
Professor of Medicine and Preventive Medicine
Associate Director, Clinical Research
J Terrence Lanni Chair in Cancer Research
Co-Director, USC Center for Molecular Pathways and Drug Discovery

USC/Norris Comprehensive Cancer Center
Los Angeles, California

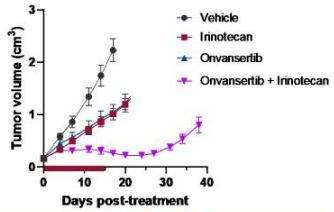
Clinical Trial Rationale Based on Preclinical Data

Synthetic Lethality: KRAS mutant cells are hypersensitive to PLK1 inhibition

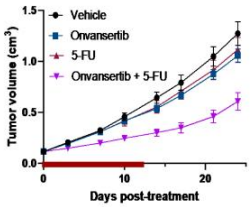
Synergy: onvansertib synergizes with irinotecan and 5-FU in preclinical models

- Onvansertib induced synergistic anti-tumor activity in combination with both standard-of-care chemotherapeutic drugs - irinotecan and 5-FU in a KRAS-mutant xenograft model

Anti-Tumor Activity of Onvansertib in Combination with Irinotecan and 5-FU in the HCT-116 KRAS-Mutant CRC Xenograft Model

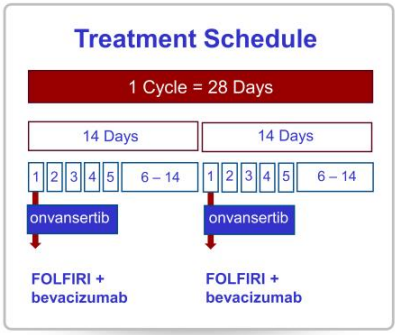


TGI on Day 17	
Onvansertib (Onv)	55%
Irinotecan (Irin)	53%
Onv+Irin	88%



TGI on Day 21	
Onvansertib (Onv)	16%
5-FU	13%
Onv+5FU	56%

Trial Design and Efficacy Endpoints



Primary Endpoints:

- **Phase 1b**: characterization of DLTs, adverse events and tolerability
- **Phase 2:** objective response rate (ORR) in patients who receive at least 1 cycle of treatment and had radiographic scan

Secondary Endpoints:

- Progression-free survival (PFS)
- Reduction in KRAS allelic burden assessed by liquid biopsies

Key Eligibility criteria

- Metastatic and unresectable CRC
- KRAS mutation in primary tumor or metastasis
- Failed or is intolerant to first line treatment of 5-FU and oxaliplatin with or without bevacizumab
- Discontinued first-line treatment because of toxicity and progressed <6 months after last dose
- Received oxaliplatin/fluoropyrimidine-based neoadjuvant or adjuvant therapy and have disease recurrence or progressed >6 months from last dose

Phase 1b/2: Patient Enrollment and Baseline Characteristics

As of 02-Jul-21

Number of patients (N)	Phase 1b Dose Level 0 Onvansertib 12mg/m²	Phase 1b Dose Level +1 Onvansertib 15mg/m²	Phase 1b Dose level +2 Onvansertib 18mg/m²	Phase 2 RP2D Onvansertib 15mg/m²	Total Patients All Doses
Treated	6	6	6	27	45
Currently on Treatment	0	2	1	25	28

Total patients N=45	Median [range] or n (%)
Age, years	58 [36-83]
Sex	
Male	25 (56%)
Female	20 (44%)
ECOG	
0	29 (64%)
1	15 (33%)
Primary tumor site	
Right Colon	16 (36%)
Left Colon	7 (16%)
Rectum	15 (33%)
Other/Unknown/Not Provided	7 (16%)
Liver metastasis	
None	10 (22%)
Liver and other	26 (58%)
Liver only	9 (20%)
Number of metastatic organs	
1	14 (31%)
≥2	31 (69%)
Prior Bevacizumab treatment	
Yes	29 (64%)
No	15 (33%)
Unknown/Not Provided	1 (2%)

Phase 1b/2: Safety and Tolerability of Onvansertib Demonstrated

Most Common Treatment-Emergent Adverse Events (TEAEs) as of 02-July-21

N = 45 Patients

TEAEs*	Grade 1	Grade 2	Grade 3	Grade 4	All Grades
Fatigue	12	3	13	0	28
Neutropenia	1	11	8	5	25
Nausea	15	5	2	0	22
Abdominal Pain	9	5	2	0	16
Diarrhea	8	6	2	0	16
Mucositis	8	5	2	0	15
Alopecia	12	2	0	0	14
WBC Decrease	4	7	1	1	13
Anemia	7	4	0	0	11
Platelet Count Decrease	6	4	0	0	10
Hypertension	2	4	2	0	8
Vomiting	4	3	1	0	8
Headache	6	0	0	0	6
Neuropathy	5	1	0	0	6
ALT increase	3	0	1	0	4
AST Increase	1	1	1	0	3
Palmar-plantar Dysesthesia	0	0	3	0	3
Dehydration	0	2	1	0	3
GERD	3	0	0	0	3

*n=number of patients (total N=45)
WBC=white blood cells; ALT= alanine aminotransferase; AST= aspartate aminotransferase

- 8 patients had a total of 10 G4 adverse events:
  - Neutropenia (n=6); Decreased WBC (n=2); Neutropenic fever (n=1); Hyperphosphatemia (n=1)
- Combination regimen was well tolerated:
  - Of all TEAEs only 10% (49/490) were G3/G4
  - The only G3/G4 AEs reported in ≥2 patients were Neutropenia (n=17 events); Fatigue (n=13); WBC decease (n=3); Nausea (n=2); Abd pain (n=2); Diarrhea (n=2); Mucositis (n=2); and HTN (n=2).
- 5-FU bolus was discontinued due to hematological toxicities in all 16 of the patients in Phase 1b who received more than 1 course of treatment
  - Only 2 of 16 patients continued to have neutropenia following elimination of the 5-FU bolus
- No major/unexpected toxicities were attributed to onvansertib

Summary of Preliminary Efficacy

As of 02-Jul-21

	All Doses of Onvansertib (12 mg/m^2, 15mg/m^2, 18 mg/m^2)	RP2D Dose of Onvansertib (15 mg/m^2)
Response-Evaluable Patients	32*	19**
Partial Response (PRs)	12 (38%)	8 (42%)

Response-Evaluable Patients = completed at least 1 cycle of treatment and had at least 1 post-baseline radiographic scan or had progressive disease within 8 weeks while on treatment

*Of the 45 patients treated with at least 1 dose, 11 patients had not yet reached their first post-baseline scan as of the data cutoff date, and 2 patients came off trial before completing their first cycle of treatment (1 patient at 12 mg/m^2 had a DLT and 1 patient at 18 mg/m^2 had progressive disease) and therefore are not included in the response-evaluable population

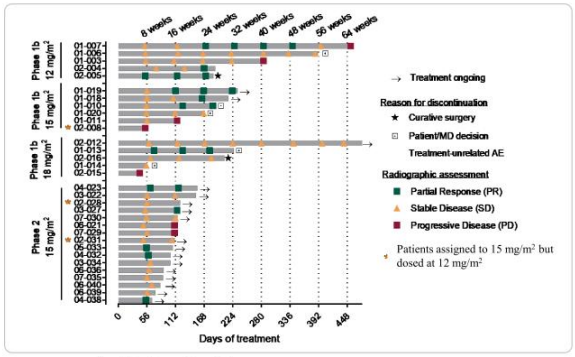
**3 Patients were excluded from the RP2D efficacy evaluation because they received onvansertib 12 mg/m^2 instead of the assigned per protocol dose of 15 mg/m^2

Phase 1b/2: Efficacy and Treatment Duration Demonstrated Across All Dose Levels

As of 02-Jul-21

- Of the 32 patients from Phase 1b/2 evaluable for efficacy*:
  - 12 (38%) achieved a partial response (PR)
    - 6 confirmed and 6 unconfirmed PRs as of 02-Jul-21
    - Further follow-up: 10 confirmed and 2 unconfirmed PRs as of 08-Sept-21
- 2 patients went off study to have potentially curative surgery

Treatment Response and Duration (All Onvansertib Doses)



*Completed at least 1 cycle of treatment and had radiographic scan or progressed within 8 weeks while on treatment

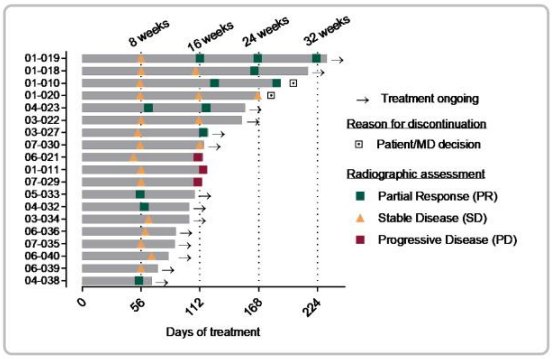
Efficacy at the RP2D of Onvansertib 15 mg/m^2

As of 02-Jul-21

19 of 22 patients treated per protocol* with onvansertib at the RP2D (15 mg/m^2) were evaluable for efficacy:**

- 8 (42%) achieved a partial response (PR)
  - 3 confirmed and 5 unconfirmed PRs as of 02-Jul-21
  - Further follow-up: 7 confirmed and 1 unconfirmed PRs as of 09-08-21

Treatment Response and Duration (Onvansertib 15 mg/m^2)

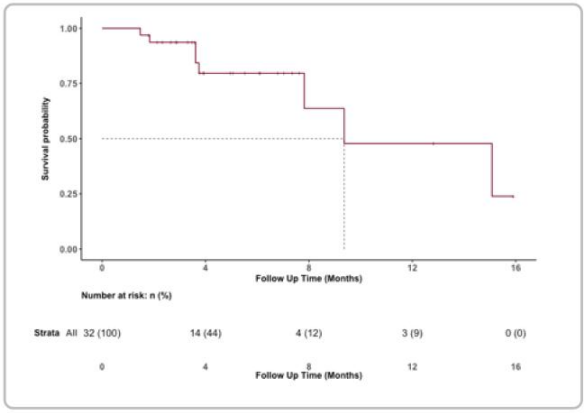


*3 Patients were excluded from the RP2D efficacy evaluation because they received onvansertib 12 mg/m^2 instead of the assigned per protocol dose of 15 mg/m^2
**Completed at least 1 cycle of treatment and had radiographic scan or progressed within 8 weeks while on treatment

Median Progression-Free Survival (mPFS) Has Not Yet Been Reached To-Date

As of 02-Jul-21

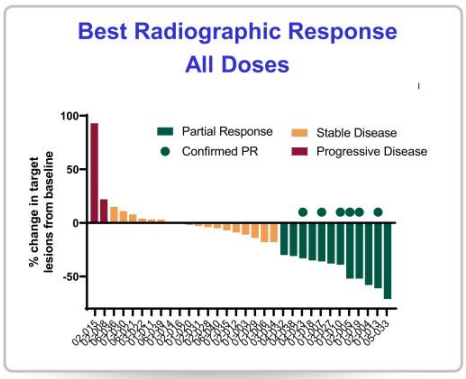
All Phase 1b/2 Evaluable Patients (N=32): mPFS is 9.4 (95% CI 7.8 –NA) Months to-Date

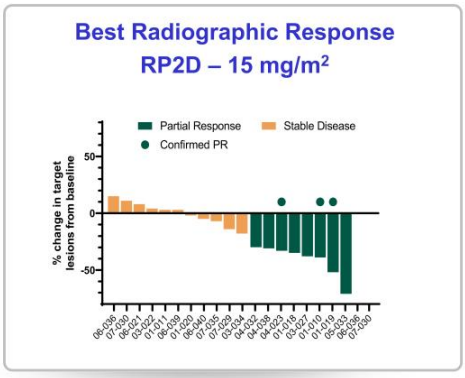


- Patients treated at the RP2D 15 mg/m^2 have not yet reached the mPFS to-date

Best Radiographic Response

As of 02-Jul-21

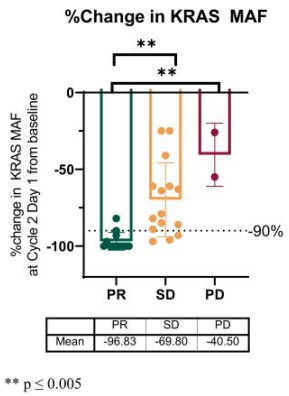




- PRs have been achieved across all dose levels
- 4 additional PRs have been confirmed since the 02-Jul-21 data cutoff date

Changes in KRAS Mutant Allele Frequency (MAF) Correlates with Clinical Responses

% KRAS MAF Decrease Following 1 Cycle of Treatment



	PR	SD	PD
Mean	-96.83	-69.80	-40.50

** $p \leq 0.005$

- KRAS MAF was measured by digital droplet PCR (ddPCR) at baseline (Cycle 1 Day 1, pre-dose) and on-treatment (Day 1 of Cycles 2 to 9)
- 29 of 32 patients evaluable for efficacy had a KRAS mutation detected by ddPCR at baseline
- Clinical responses were observed across patients with different KRAS mutations, including the 3 most prevalent in CRC (G12D, G12V, G13D)
- Decrease in KRAS MAF after 1 cycle of treatment was correlated with clinical response:
  - Decrease in KRAS MAF was significantly higher in patients achieving PR vs patients with SD or PD as best response (P≤ 0.005)
  - 92% (11/12) of PR patients had >90% decrease in KRAS MAF after the 1st cycle, while only 21% (3/14) SD patients and none of the PD patients has such decrease

KRAS Mutation Variants in Treated Patients

- 7 different variants were detected by targeted next-generation sequencing (NGS) in circulating tumor DNA (ctDNA) isolated from patient plasma at baseline
- Clinical responses were observed across different KRAS variants, including the 3 most common (G12D, G12V, G13D) representing 69% of KRAS variants in CRC[1]

	Number of Patients by Best Response			
KRAS Variant	**Partial Response (PR)**	**Stable Disease (SD)**	**Progressive Disease (PD)**	**Total**
G12D	3	4	1	8
G12V	1	5		6
G13D	2	2		4
G12A	3	1		4
A146T	2	2		4
G12S		3		3
G12C	1		1	2
Q61H		1		1
Total	**12**	**18**	**2**	**32**

[1]Jones et al., Br J Cancer 2017; 116 (7):923-929

Conclusions

Safety

- The combination of onvansertib and FOLFIRI/Bev is well-tolerated
- Only 10% (49/490) of reported TEAEs were G3/G4

Efficacy

- Of the 32 Phase 1b/2 patients evaluable for efficacy:
  - 12 (38%) achieved a partial response (PR)
    - 6 confirmed and 6 unconfirmed PRs as of 02-Jul021
    - Further follow-up: 10 confirmed and 2 unconfirmed PRs as of 09-Sept-21
      - Confirmed PRs: 10/32 (31%)
- Of the 19 patients at the RP2D (onvansertib 15 mg/m^2) evaluable for efficacy:
  - 8 (42%) achieved a partial response (PR)
    - 3 confirmed and 5 unconfirmed PRs as of 02-Jul-21
    - Further follow-up: 7 confirmed and 1 unconfirmed PRs as of 08-Sept-21
      - Confirmed PRs: 7/19 (37%)
- Median PFS across Phase 1b/2 evaluable patients (N=32) is 9.4 (95% CI 7.8 – NA) months to-date

KRAS Biomarker

- Clinical responses were observed across different KRAS variants, including the 3 most common in CRC
- Patients achieving a PR showed the greatest decreases in plasma mutant KRAS after 1 cycle of therapy

The Cardiff Oncology Opportunity

Mark Erlander, PhD – Chief Executive Officer

Cardiff Oncology™

Second-Line Treatment of KRAS-Mutated mCRC

Phase 1b/2 open-label trial of onvansertib + FOLFIRI/bevacizumab

Principal Investigator: Dr. Heinz-Josef Lenz

MAYO CLINIC

USC Norris Comprehensive Cancer Center
Keck Medicine of USC

INOVA

KU MEDICAL CENTER
The University of Kansas

CARTI CANCER CENTER
SOUTH ARKANSAS

New Second-Line mCRC Treatment Options are an Unmet Need

Standard-of-Care Second Line mCRC Benchmarks for Median ORR, PFS and OS

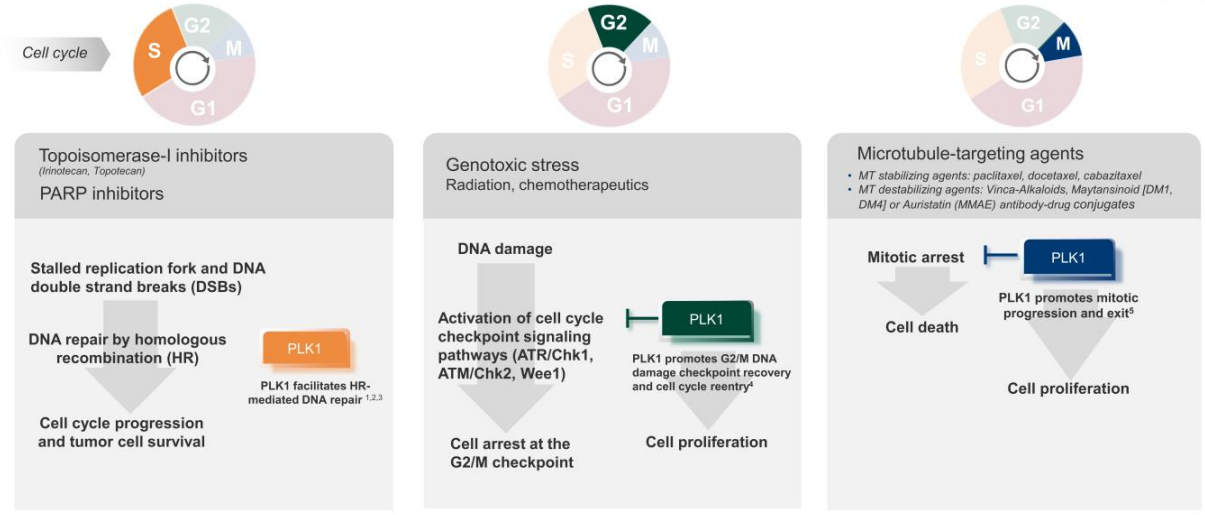
	Objective Response Rate (ORR)	Progression-Free Survival (PFS)	Overall Survival (OS)
ML18147 Phase 3 Registrational Trial of FOLFIRI + bev in second-line[4] (2006 – 2008)	**5%**	5.7 months	11.2 months
Systematic Literature-Based Analysis of 23 Randomized Trials (10,800 Patients) in Second-Line mCRC[1] (2000 – 2013)	**11.4%**	4.5 months	11.5 months
TRIBE2 Randomized Phase 3 Trial: SOC arm FOLFIRI + bev in Second-line following FOLFOX + bev First-line[2,3] (2015 – 2017)	**13%**	5.6 months	Not Reported for Second-line

[1]Giessen et al., Acta Oncologica, 2015, 54: 187-193; [2]Cremolini et al., Lancet Oncol 2020, 21: 497–507; [3]Antoniotti et al., Correspondence Lancet Oncol June 2020; [4]Bennouna et al., Lancet Oncol 2013; 14: 29–37; mCRC: Metastatic colorectal cancer; SOC: Standard-of-care

Efficacy Data Remain Consistent as Patient Numbers Increase

	AS OF APRIL 4	AS OF JULY 2	
	All Doses ($12mg/m^2$, $15 mg/m^2$, $18 mg/m^2$)	All Doses ($12mg/m^2$, $15 mg/m^2$, $18 mg/m^2$)	Phase 2 Dose ($15 mg/m^2$)
Number of Evaluable Patients	**18**	**32**	**19**
Initial PRs as of Data Cutoff Date	**7 of 18 (39%)**	**12 of 32 (38%)**	**8 of 19 (42%)**
Confirmed PRs	**6 of 18 (33%)**	**10 of 32 (31%)**	**7 of 19 (37%)**

Onvansertib's MOA Creates a Broad Opportunity: Inhibit DNA Repair and Mitosis



[1]Yata et al. Mol. Cell 45, 2012; [2]Chabalier-Taste et al., Oncotarget 2016 Jan 19; 7(3), [3]Nakamura et al., Mol. Cell 81, 2021, [4]van Vuget and Yaffe, Cell Cycle 9:11, 2010; [5]Zitouni et al., Nat Rev Mol Cell Biol. 2014; 15(7)

Onvansertib is a Platform Molecule

	Inhibit Ability of PLK1 to Repair DNA			Inhibit Ability of PLK1 to Promote Cell Division (Mitosis)		
	DNA Damaging Agent			Microtubule (MT) Targeting Agents (Disruption of Mitosis)		
	Chemo: Irinotecan & 5-FU	PARP Inhibitors	Radiation	Paclitaxel-MT Stabilizer	Abiraterone	DM4-MT Destabilizer
mCRC	**Phase 1b/2 Trial**					
mPDAC	**Phase 2 Trial**	✓		✓		
mCRPC		✓			**Phase 2 Trial**	
Ovarian		✓		✓		✓
Breast (TNBC and ER$^+$)		✓		✓		
SCLC	✓	✓		✓		
Medulloblastoma			✓			

Cardiff Oncology At-A-Glance

Clinical-stage oncology company, developing new precision medicine treatment options for cancer patients in indications with the greatest unmet medical need

Exchange	Nasdaq: CRDF
Cash, Cash Equivalents and Investments*	$140.1M
Quarterly Net Cash Used in Operating Activities (1H'2021 Average)	$5.1M
Website: www.cardiffoncology.com	

Analyst Coverage
Cowen – Marc Frahm, Ph.D.
Piper – Joseph Catanzaro, Ph.D.
H.C. Wainwright – Raghuram Selvaraju, Ph.D.
Maxim Group – Naureen Quibria, Ph.D.