

Turning the Tide on Cancer



August, 2020



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 Cardiff Oncology's expectations, strategy, plans or intentions.

These forward-looking statements are based on Cardiff Oncology's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. While the list of factors presented in the 10-K 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.

Company At-A-Glance

Clinical-stage oncology therapeutics company, developing **onvansertib**, an oral and highly-selective Polo-like Kinase 1 (PLK1) inhibitor

- Selectively targets PLK1, a proven therapeutic target; overexpressed in most cancers
- Stops division of cancer cells while limiting impact to normal cells
- Proven safety and preliminary efficacy in 3 clinical programs (mCRC, mCRPC, AML)
- Presentation of efficacy data from all 3 Phase 2 clinical trials in 2020

San Diego, CA

Nasdaq: CRDF

Clinical Development Plan: Complete Phase 2 clinical trials of Onvansertib, in combination with standard-of-care, in colorectal cancer, prostate cancer and acute myeloid leukemia, and advance to registrational trials

Experienced Management Team

Drug Development + Biomarker Technology Expertise



Thomas Adams, PhD
Executive Chairman



Mark Erlander, PhD
Chief Executive Officer



Vicki Kelemen
EVP and Chief Operating Officer



Brigitte Lindsay
Vice President Finance



Investment Highlights



Ovansertib

1st-in-class, 3rd-generation, safe and well-tolerated, oral PLK1 inhibitor; selectively targets PLK1 and blocks cancer cell division



Clinical Efficacy Demonstrated

3 ongoing clinical trials with demonstrated efficacy in patients who have developed resistance to standard-of-care or who have relapsed disease



Predictive Biomarkers

Assessment of response to treatment derived from a simple blood test



Validating Combination Clinical Trials

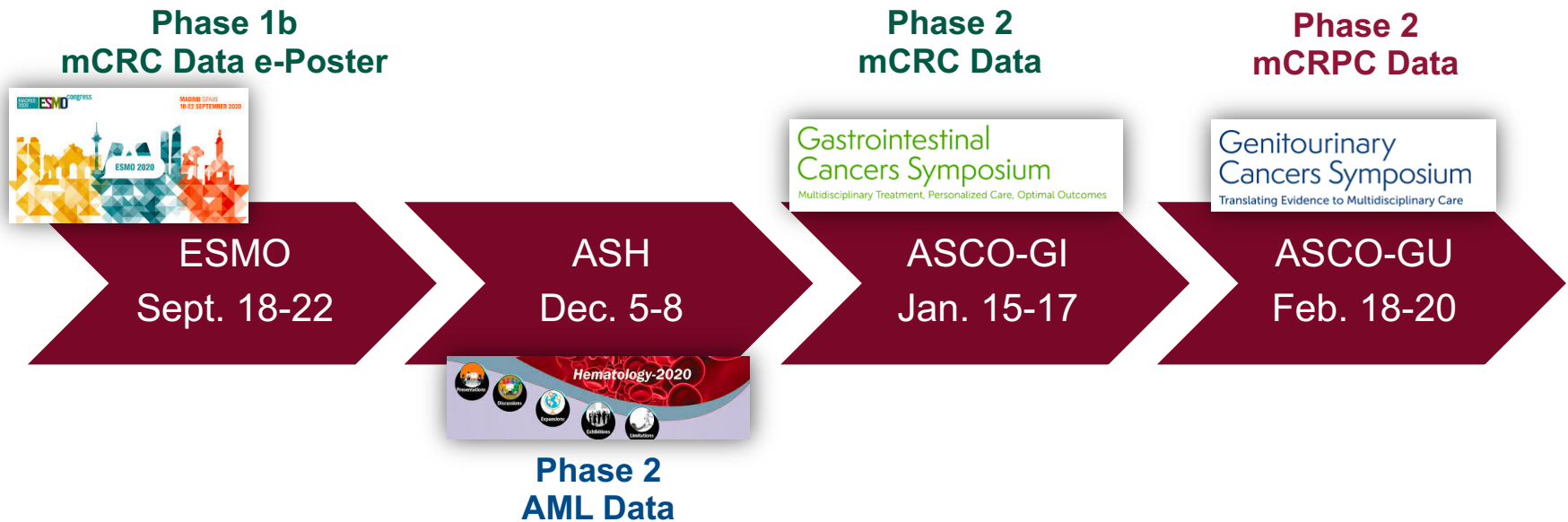
- KRAS-mutated metastatic colorectal cancer (mCRC): onvansertib + FOLFIRI[®]/Avastin[®]
- metastatic castrate-resistant prostate cancer (mCRPC): onvansertib + Zytiga[®]
- acute myeloid leukemia (AML): onvansertib + decitabine



Established Manufacturing and Drug Supply

FDA approved, GMP facility for production of raw material and finished drug

Upcoming Catalysts



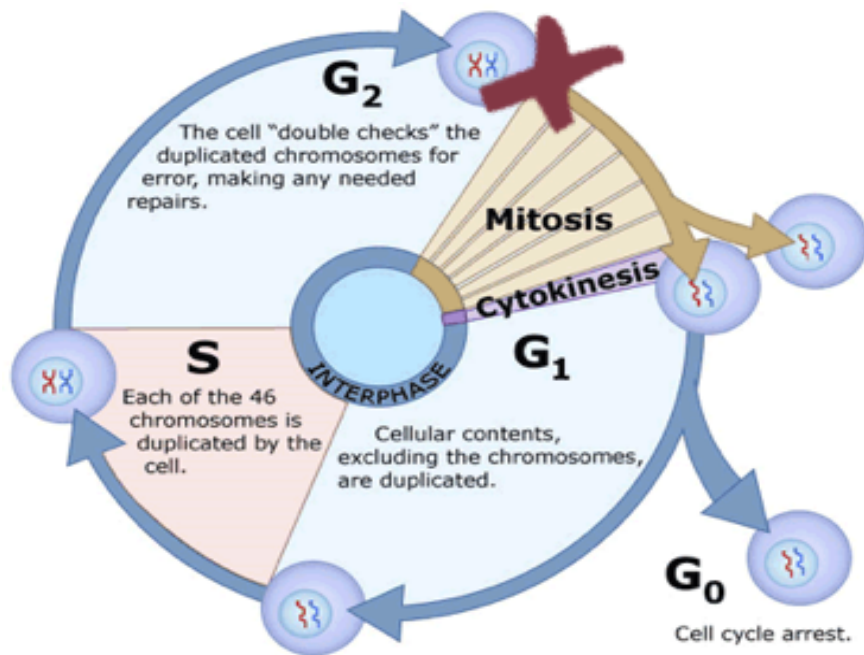
Onvansertib is a Platform for Value Creation

- ▶ **Clinical Programs Based on Scientific Rationale:** supported by preclinical and synergy data, and integration of biomarkers to rapidly assess response to treatment
- ▶ **Addressing Significant Medical Need for New Treatment Options:**
 - Overcome resistance to standard-of-care drugs
 - Extend response to treatment and progression-free survival (PFS)

	Indication	Preclinical	Phase 1b	Phase 2	Next Milestone
Onvansertib Solid Tumors	mCRC	<i>Onvansertib + FOLFIRI/Avastin® in Second-Line KRAS-Mutated Metastatic Colorectal Cancer</i>			Q3 2020 ESMO
	mCRPC	<i>Onvansertib + Zytiga® (abiraterone)/prednisone in Zytiga-Resistant Castration-Resistant Metastatic Prostate Cancer</i>			Q1 2021 ASCO GU
Onvansertib Hematologic	AML	<i>Onvansertib + Decitabine in Relapsed or Refractory Acute Myeloid Leukemia</i>			Q4 2020 ASH

Onvansertib: Stops Cancer Cell Division and is Synergistic in Combination Regimens

Inhibition of PLK1 causes arrest of cell division and subsequent cell death¹

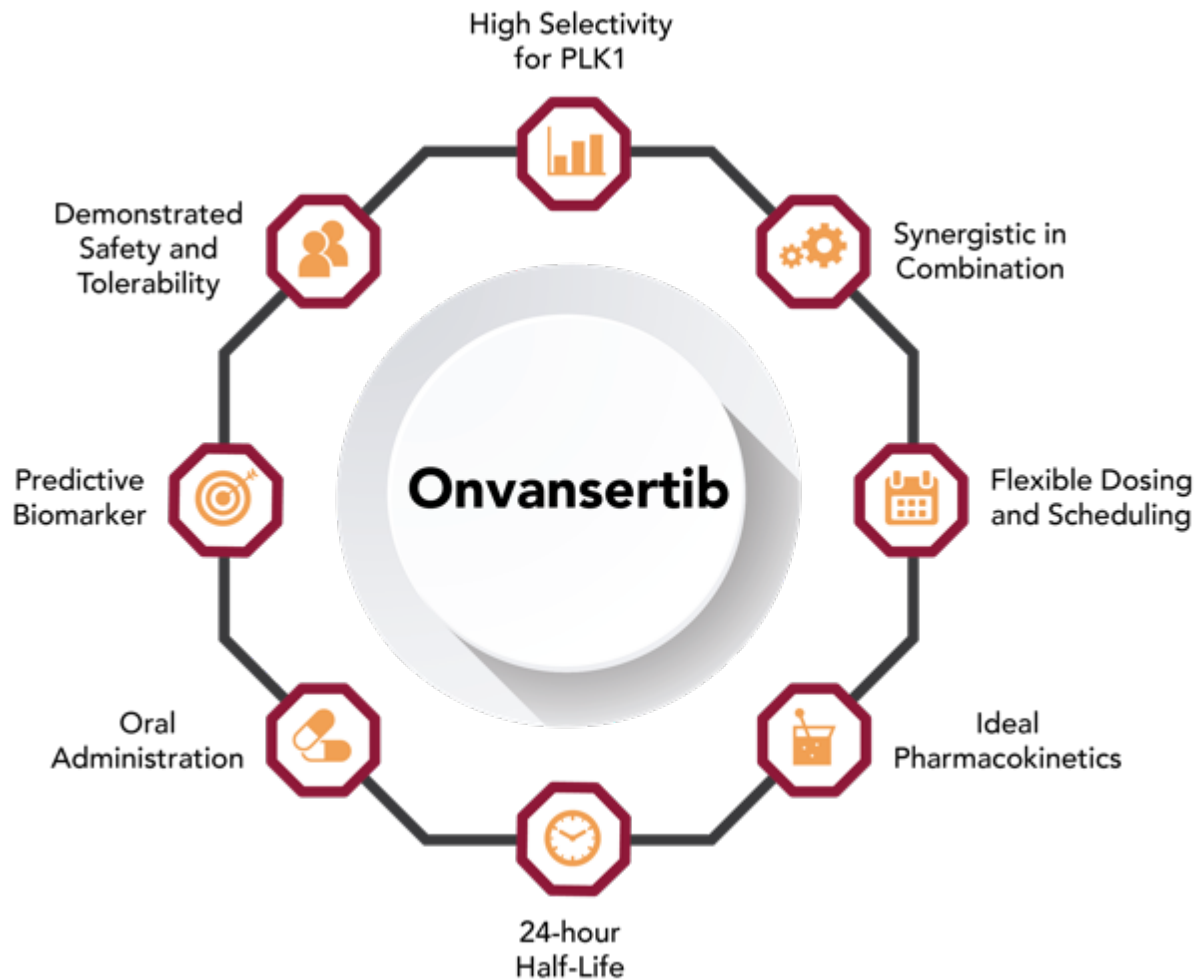


Synergistic in combination with chemotherapies and targeted therapeutics²



¹Zitouni et al., Nat Rev Mol Cell Biol. 2014 Jul;15(7):433-52; ²Data on File – Cardiff Oncology

Optimal Attributes for a Safe and Effective Drug



Indication: Second-Line Treatment of KRAS-Mutated Metastatic Colorectal Cancer (mCRC)

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

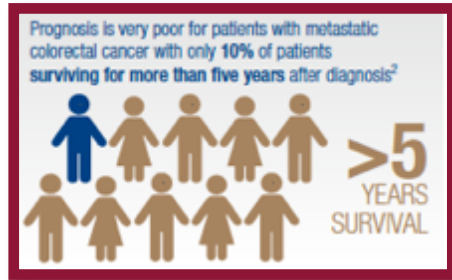
**USC Norris Comprehensive
Cancer Center**
Keck Medicine of **USC**

Principal Investigator
Dr. Heinz-Josef Lenz



Improving Response and Progression-Free Survival

Metastatic Colorectal Cancer (mCRC)



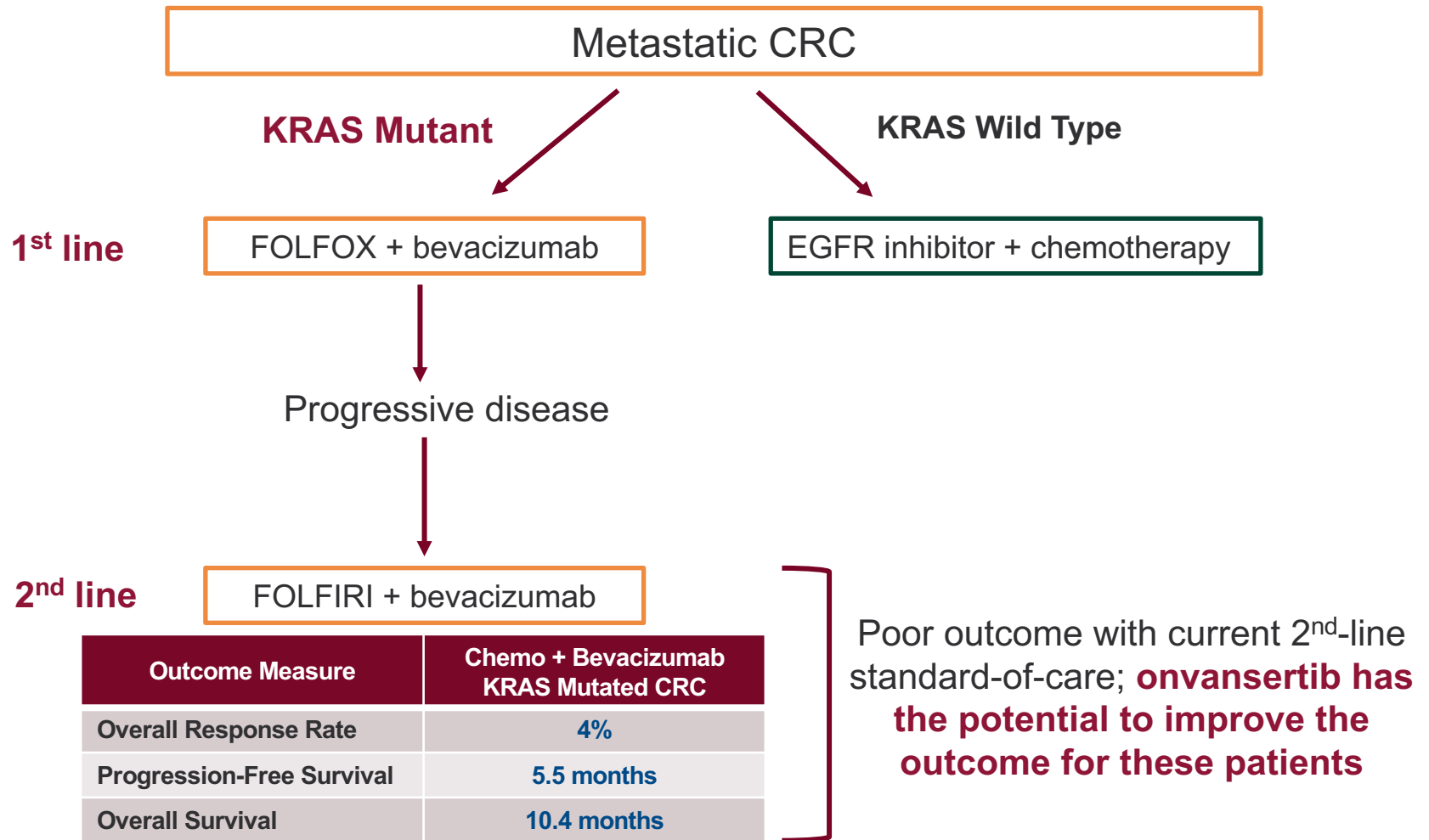
- ▶ Only a 4% response rate to second-line standard-of-care chemotherapy + bevacizumab¹
- ▶ Onvansertib + FOLFIRI® significantly reduces tumor growth²
- ▶ Biomarkers drive therapy decisions³
- ▶ KRAS mutation is a biomarker for clinical response to onvansertib⁴
- ▶ KRAS mutation in 50% of mCRC⁵

Establishing a Successful Path Forward:

- Fast Track Designation granted by FDA
- Positive results from Phase 1b/2 trial may provide an opportunity for Phase 2b registrational trial
- Biomarker increases likelihood of success by enabling rapid assessment of KRAS mutation as an early predictor of response to treatment

¹Kubicka et al, Annals of Oncology 2013; 2342–2349; ²Investigator Brochure, Data-on-file, Cardiff Oncology; ³Van Cutsem E, Borràs JM, Castells A et al. Improving outcomes in colorectal cancer. Where do we go from here? Eur J Cancer. 2013 Jul; 49(11): 2476–85; ⁴Tie et al., 2015, Annals of Oncology 26: 1715–1722; ⁵Cancer Genomic Atlas Genome, Nature, 2012

Onvansertib in mCRC Treatment Paradigm



Fast Track Designation Granted by FDA

May 26, 2020

Facilitate and expedite development, FDA review and approval of Onvansertib for second-line treatment of patients with KRAS-mutated mCRC

1. Demonstrates that onvansertib is effectively addressing an unmet medical need and serious, life-threatening cancer
2. Recognizes the limitations of currently available standard-of-care and the opportunity to bring a new second-line treatment option to patients
3. Insures more frequent and timely accessibility to the FDA including guidance on registrational trial



Rationale for Onvansertib + FOLFIRI® /Avastin® in KRAS-Mutated Metastatic CRC

Onvansertib Targets KRAS Mutations Through Downstream Effects on Tumor Cell Division



Cracking KRAS

► Synthetic Lethality

- CRC tumor cells harboring KRAS mutation are more vulnerable to cell death with PLK1 inhibition¹
- KRAS-mutated cells are more sensitive to onvansertib than KRAS wild-type isogenic cells²

► Synergy

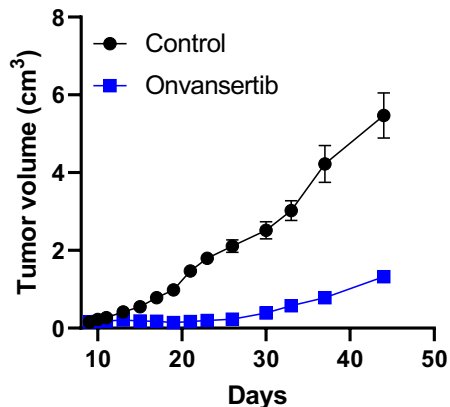
- Onvansertib + irinotecan (the “IRI” in FOLFIRI) are synergistic in CRC cell lines³
- Combination demonstrated significantly greater tumor growth inhibition than either drug alone

► Proof-of-Concept Clinical Response

- Phase 1 trial in solid tumors: 3 of 5 patients with stable disease had KRAS mutation; 2 in CRC and 1 in pancreatic cancer⁴

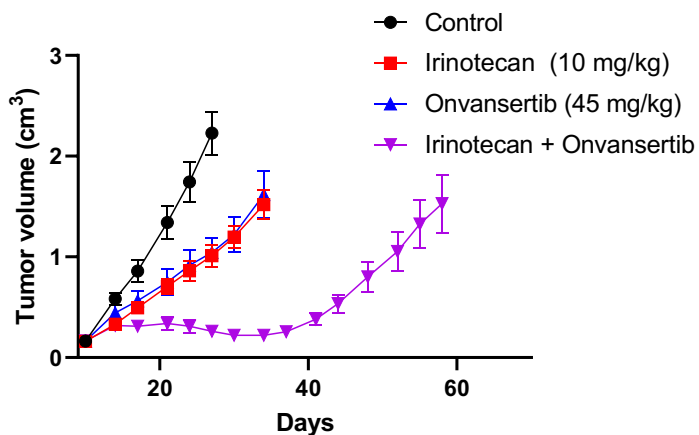
¹Luo J, Elledge SJ, Cell 2009; ²Cardiff Oncology, Investigator Brochure, 2019; ³Valsasina et al., Mol Cancer Ther 2012; ⁴Weiss et al, Invest New Drugs, 2017

Anti-tumor Activity of Onvansertib as Single Agent and Synergy in Combination with Irinotecan

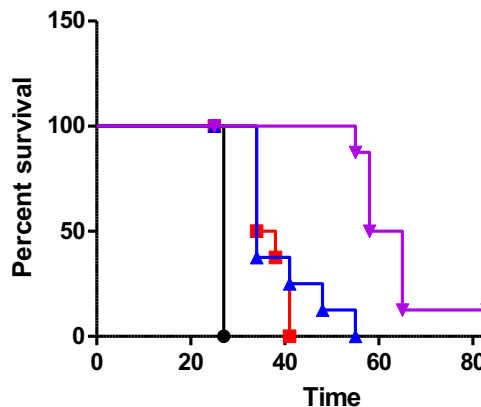


► Anti-tumor activity of onvansertib in a KRAS-mutant CRC xenograft model (HCT116) as single agent and in combination with irinotecan¹⁻³

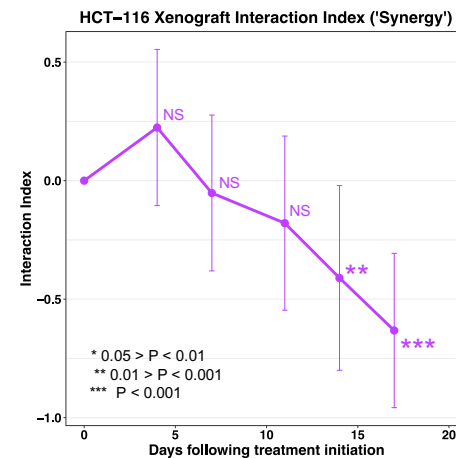
Tumor Growth



Survival



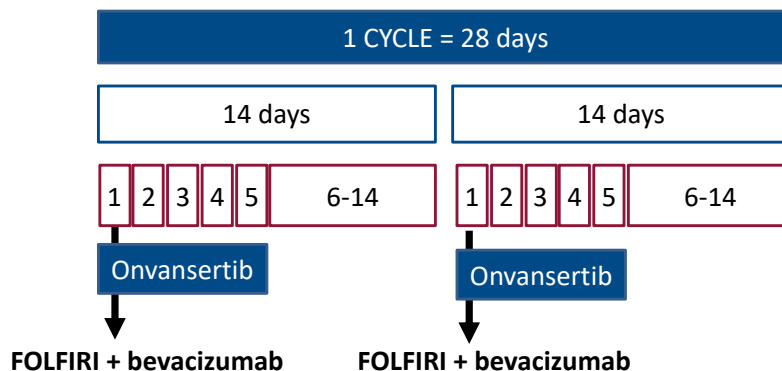
Synergy



¹Valsasina et al., 2012, Mol Cancer Ther, 11: 1006-1016; ²Data on file – Cardiff Oncology; ³Method used for testing synergy: Wu et al., 2012. J Biopharm. Stat. 22(3): 535-543

Demonstrating Clinical Benefit in KRAS-Mutated CRC as New Second-Line Treatment Option

Trial Design: Phase 1b/2, multi-center, open label trial in KRAS-mutated mCRC



Efficacy Endpoints:

Primary: overall response in patients who receive ≥ 1 cycle (2 courses) of treatment

Correlative Biomarker: decreases in KRAS mutation burden and response to treatment

Standard-of-Care FOLFIRI®/Avastin® Clinical Response in 2nd Line KRAS-Mutated CRC Tumors: overall response is 4%; median progression-free survival (PFS) is 5.5 months¹

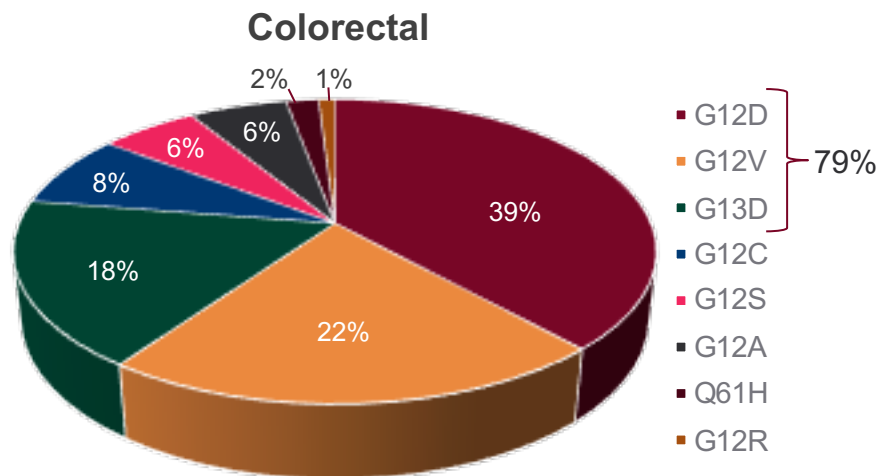
What is Clinical Trial Success:

- ≥ 5 of 26 (~20%) patients achieve clinical response confirmed by radiographic scan
- Patients achieve median progression-free survival (PFS) of ≥ 6 months

¹Kubicka et al, Annals of Oncology 2013; 2342–2349

Clinical Data Shows Onvansertib Effectively Targets Multiple KRAS Mutation Subtypes in CRC

Onvansertib is Agnostic to the Causative KRAS Mutation



- ▶ To date, tumor shrinkage observed in KRAS mutations G12A, G12V, G12D, G13D which make up 85% of KRAS subtypes in CRC¹
- ▶ Other drugs in development target only the KRAS G12C mutation, which accounts for ~8% of the KRAS mutations in CRC

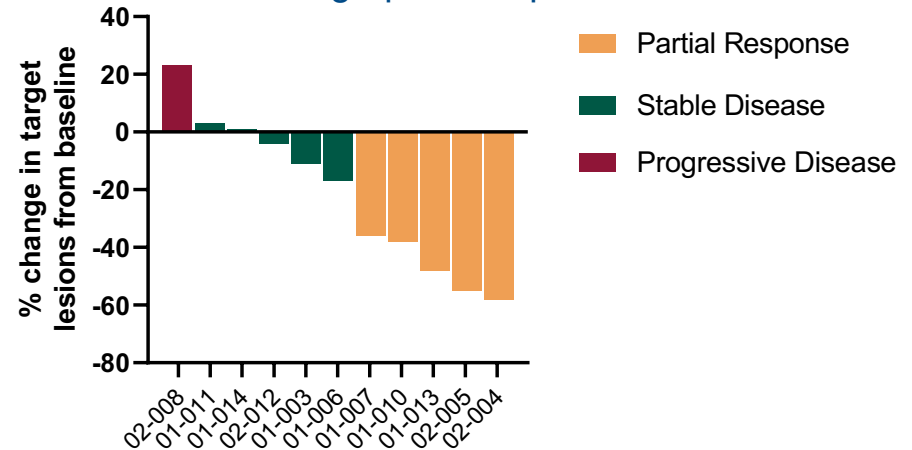
¹Jones et al. Specific Mutations in KRAS Codon 12 are Associated with Worse Overall Survival in Patients with Advanced and Recurrent Colorectal Cancer; BJC Feb. 2017

Response to Treatment Confirmed by Radiographic Scan and Progression-Free Survival

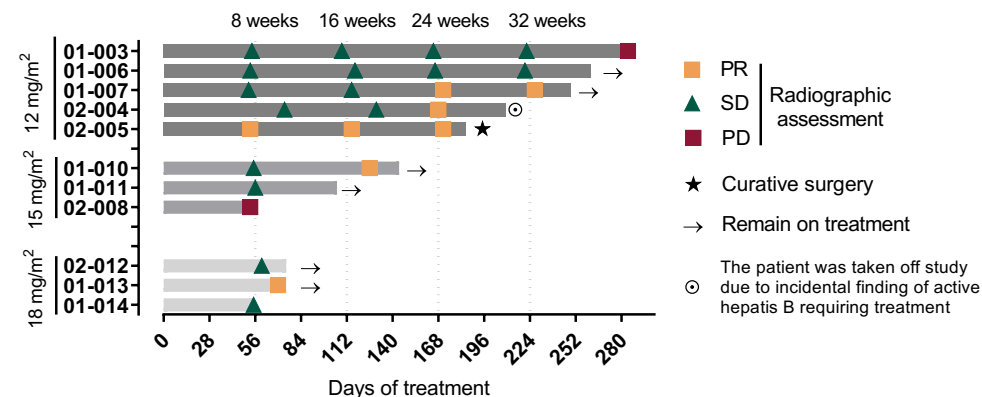
- Of the 11 patients evaluable for efficacy:
 - 10 of 11 (91%) patients had clinical benefit: 5 (45%) partial response (PR) and 5 (45%) stable disease (SD)
 - 2 patients have a confirmed PR (to-date); 1 patient (02-005) went on to have successful curative surgery

- Responses appear durable: progression-free survival (PFS) of >6 months (to-date) with 6 patients continuing on treatment

Radiographic Response

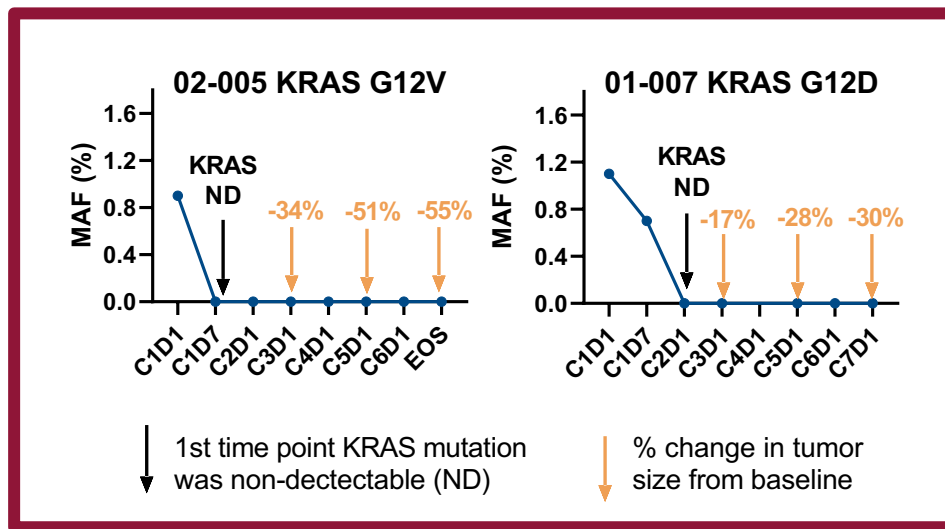


Progression-Free Survival



Response to Onvansertib Correlates with Decreases in KRAS Mutations to Undetectable Levels in Plasma

- ▶ Decreases in plasma KRAS mutation level has been demonstrated to be an early marker for therapeutic response¹
- ▶ 8 of the 9 patients had a KRAS mutation detected by ctDNA analysis at baseline (ddPCR and NGS)
- ▶ Changes in KRAS mutant during cycle 1 of treatment were highly predictive of tumor regression:
 - 5 patients had a decrease in KRAS mutant to non-detectable level in cycle 1 (28 days) and subsequent tumor regression at 8 weeks (Cycle 3 Day 1)



¹Tie et al., 2015, Annals of Oncology 26: 1715–1722; ²BioRad Droplet Digital Assays

Onvansertib is Showing Promise as a New Therapeutic Option for KRAS-Mutated mCRC

- ▶ The 1st two dose levels (onvansertib 12 mg/m² and 15 mg/m²) were cleared for safety; the 3rd dose level (onvansertib 18 mg/m²) is enrolling
- ▶ Clinical benefit (SD + PR) observed in 10 (91%) of the 11 evaluable patients
 - 5 (45%) partial response (PR) and 5 (45%) stable disease (SD)
 - 2 patients have a confirmed PR (to-date); 1 patient (02-005) went on to have successful curative surgery
- ▶ 8 of the 9 patients had a KRAS mutation detected by ctDNA analysis at baseline (ddPCR and NGS)
 - Changes in KRAS mutant during cycle 1 of treatment were highly predictive of tumor regression:
 - 5 patients had a decrease in KRAS mutant to non-detectable level in cycle 1 (28 days) and subsequent tumor regression at 8 weeks (Cycle 3 Day 1)

Indication:
metastatic Castration-Resistant Prostate Cancer (mCRPC)



Dana-Farber/Harvard
Cancer Center



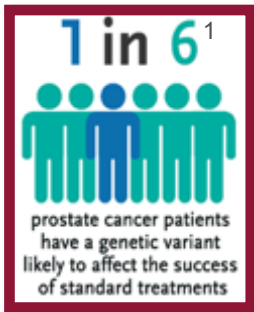
A Cancer Center Designated by the
National Cancer Institute

Principal Investigator
Dr. David Einstein



Overcoming Resistance and Extending Efficacy

Metastatic Castrate-Resistant Prostate Cancer (mCRPC)



- ▶ Resistance develops to standard-of-care therapy, Zytiga® and Xtandi®, within 9-15 months²
- ▶ Onvansertib + Zytiga® are synergistic in combination
- ▶ Combination significantly increase arrest of cell division
- ▶ Up to 40% AR-V7 resistance; very aggressive mutation and no effective treatment options³

Establishing a Successful Path Forward:

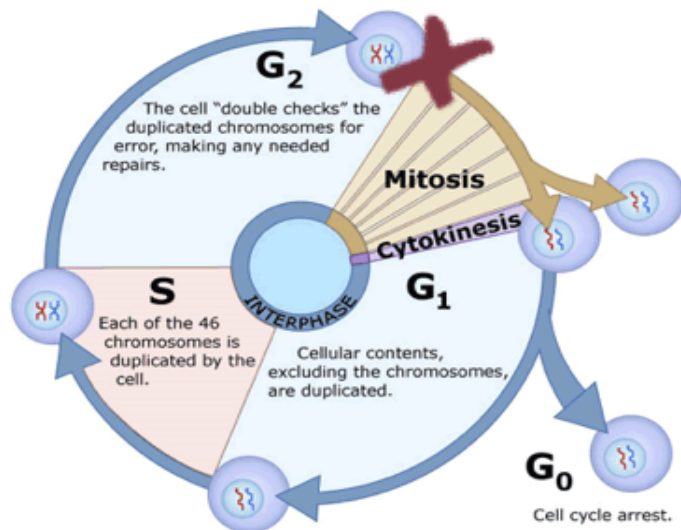
- Positive results from Phase 2 trial may provide an opportunity for a Phase 2b registrational trial
- Proactively assessing AR-V7 enables correlation of status (+/-) with response to onvansertib treatment
- Effective treatment of AR-V7+ patients could lead to Breakthrough Designation

¹Nicolosi P, Ledet E, Yang S et al. Prevalence of germline variants in prostate cancer and implications for current genetic testing guidelines. JAMA Oncol. Published online February 7, 2019; ²Antonarakis, Emmannel – Current Understanding of Resistance to Abiraterone and Enzalutamide in Advanced Prostate Cancer; Clinical Advances in Hematology & Oncology – May 2016 – Volume 14, Issue 5; ³Armstrong et al., 2019, JCO 37: 1120-1129.

Underlying Mechanism of Action (MOA) for Onvansertib + Zytiga® in CRPC

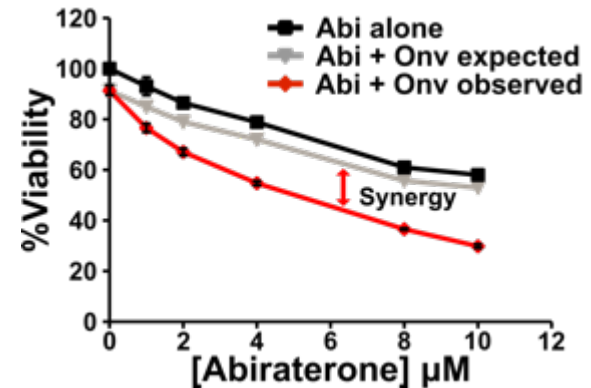
Onvansertib Mechanism of Action

Inhibits tumor cell division (mitosis)
by inducing G2/M arrest

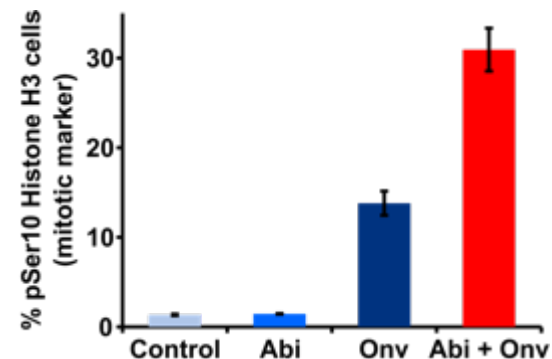


¹Patterson & Yaffe, 2019, MIT

Onvansertib + Zytiga® (abiraterone) demonstrates synergy in mCRPC model (C4-2)¹

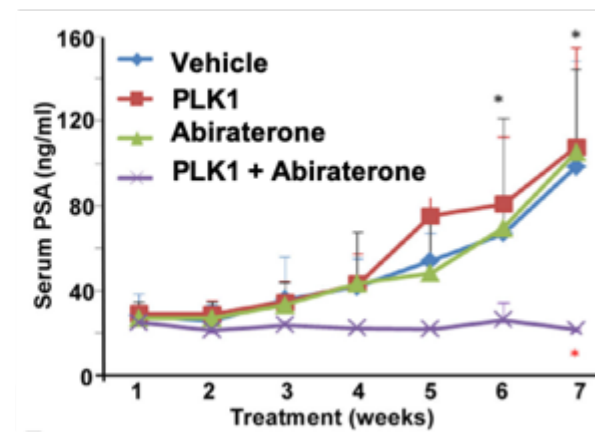
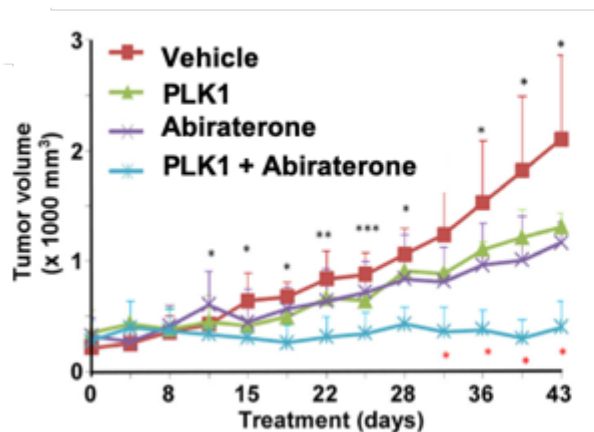


Onvansertib + Zytiga® (abiraterone) significantly increase mitotic arrest¹



PLK1 Inhibition + Abiraterone Efficacy in mCRPC Model

PLK1 Inhibition Enhances the Efficacy of Androgen Signaling Blockade in Castration-Resistant Prostate Cancer



- ▶ The combination of PLK1 inhibition + abiraterone decreases tumor growth and demonstrates a decrease in PSA within an AR-V7 model

¹Zhang et al., 2014, Cancer Res

Phase 2 Clinical Trial in mCRPC

Disease Control Assessed by PSA Stabilization

Trial Design: Phase 2 multi-center, open label trial in mCRPC

	Dosing Schedule	Duration	Efficacy Endpoint
Cohort 1 n=24	Onvansertib 24mg/m ² Days 1-5 (21-day cycle) + Zytiga®	4 Cycles = 12 Weeks	Disease Control PSA Stabilization or Decline
Cohort 2 n=32	Onvansertib 18mg/m ² Days 1-5 (14-day cycle) + Zytiga®	6 Cycles = 12 Weeks	Disease Control PSA Stabilization or Decline
Cohort 3 n=32	Onvansertib 12mg/m ² Days 1-14 (21-day cycle) + Zytiga®	4 Cycles = 12 Weeks	Disease Control PSA Stabilization or Decline

Eligibility Criteria: initial resistance to Zytiga; 2 consecutive rises in PSA levels

Efficacy Endpoint – Internationally Recognized Prostate Cancer Working Group (PCWG)

Primary: disease control evaluated as PSA decline or stabilization (PSA rise <25% over baseline)

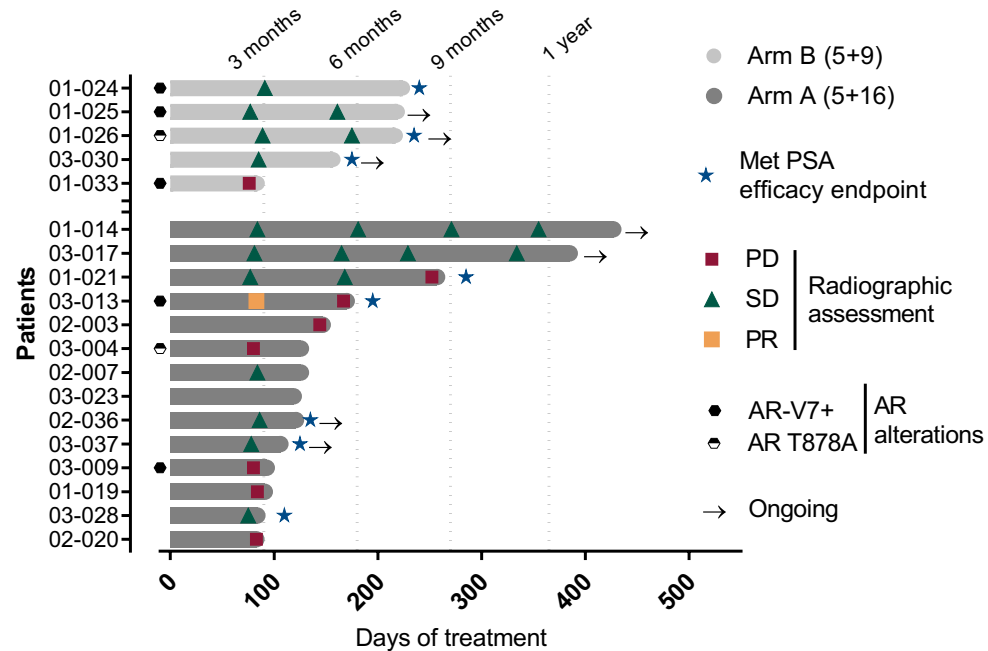
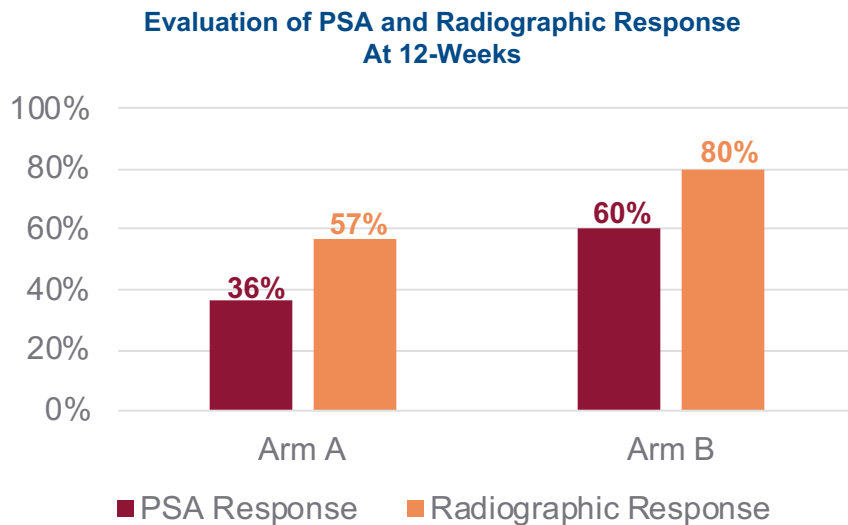
What is Clinical Trial Success:

- ≥6 of 32 (~20%) patients achieve primary efficacy endpoint of disease control at 12 weeks (PSA stabilization or decrease); confirmed by radiographic scan
- Patients achieve median RPFS of ≥6 months

Note: radiographic assessment by RECIST v1.1 [CR = disappearance of all target lesions, PR = ≥30% decrease, PD = ≥20% increase, SD = does not meet criteria for PR nor PD]

Efficacy Demonstrated in Zytiga®-Resistant Patients Treated with Onvansertib

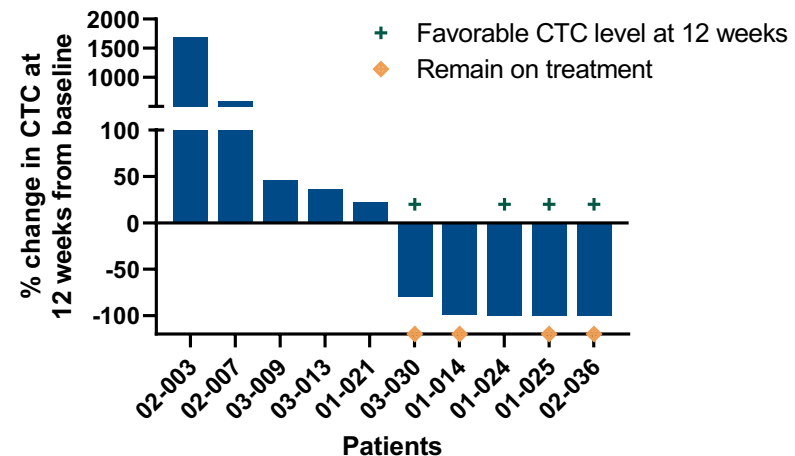
- ▶ Overall, 63% (12 of 19) of evaluable patients achieved partial response (PR) or stable disease (SD) following 12 weeks of treatment with onvansertib + abiraterone
- ▶ Response to treatment was evaluated based on PSA values (primary endpoint) and radiographic scans



Onvansertib-Induced CTC Decrease is Associated with Progression-Free Survival

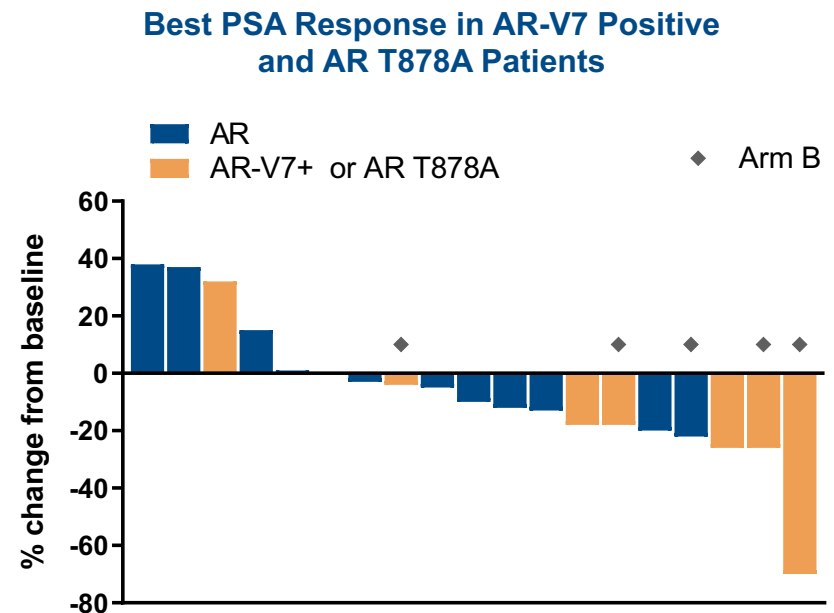
- ▶ CTC count, reported as favorable or unfavorable (<5 versus ≥ 5 CTC/7.5mL of blood, respectively) is a prognostic factor for survival in CRPC and the conversion from unfavorable to favorable is associated with improved survival⁷
- ▶ At baseline, 25 (78%) patients had unfavorable CTC count with median of 19 CTC/7.5mL
- ▶ 10 of the unfavorable patients were re-analyzed after 12 weeks of treatment
 - 5 (50%) patients had a of 80% CTC decrease, including 2 AR-V7+ patients (01-024 and 01-025)
 - 4 (40%) patients converted from unfavorable to favorable CTC level (<5 CTC/7.5mL)
 - 3 (30%) patients had no detectable CTC
 - Median time on treatment for patients with decrease CTC (n=5) is 7 months to-date, with 4 patients remaining on treatment
- ▶ Conversely, median time on treatment for patients with increase CTC (n=5) was 5 months, and none of these patients remain on treatment

% Change in CTC: 12-Weeks vs Baseline in Patients with Unfavorable CTC Level at Baseline



Efficacy Observed in Patients with Abiraterone-Resistant AR Alterations

- ▶ AR mechanisms of resistance to abiraterone include the expression of the constitutively active AR splice variant AR-V7 and the AR gain-of function point mutation T878A⁶
- ▶ Among the 19 patients who completed the 12-week treatment (Arm A + B):
 - 5 patients were AR-V7+ at baseline
 - 2 patients had AR T878A mutations at baseline
- ▶ Onvansertib showed efficacy in patients with AR alterations (N=7):
 - 6 (86%) patients had a decrease in PSA levels with the addition of onvansertib
 - 4 (57%) patients had SD or PR at 12 weeks with 3 (43%) patients achieving the primary efficacy endpoint
 - 3 patients have or had progression-free survival of >7 months, 2 patients remain on treatment



Indication: Acute Myeloid Leukemia (AML)



Principal Investigator
Dr. Amer Zeidan



Addressing the Need for New Treatment Options

Relapsed Acute Myeloid Leukemia (AML)

CHANGING THE TREATMENT PARADIGM

- ▶ 5-year survival rate of only 25%¹
- ▶ Standard-of-care is venetoclax plus azacytidine or decitabine; resistance develops in ~11 months²
- ▶ Onvansertib induces cell death in AML model resistant to Venclexta®³

Establishing a Successful Path Forward:

- Positive results from Phase 2 trial and Orphan Drug Designation may provide an opportunity for a Phase 2b registrational trial
- Opportunity to treat patients who relapse following first-line venetoclax
- Biomarker identifies patients most likely to respond, increasing likelihood of success

¹National Cancer Institute SEER 2016; ²DiNardo et al, Blood, 2019 ²Valsasina et al., Mol Cancer Ther; 11(4) April 2012; ³Data on file – Cardiff Oncology

Providing a New, Safe and Effective Treatment

Trial Design: Phase 2 multi-center, open label trial in AML

Onvansertib +Decitabine

Relapsed or Refractory
Patients (n=32)

Onvansertib 60mg/m² Days 1-5
(21-28 Day Cycle)

Efficacy Endpoint

Primary: safety and preliminary efficacy

Correlative Biomarker: Assess PLK1 inhibition (target engagement) by measuring changes in the PLK1 substrate pTCTP; evaluate predictive biomarkers associated with response to treatment

Current Standard-of-Care Clinical Response: Hypomethylating agents (decitabine and azacytidine) is 16.3% and IDH Inhibitors, ivosidenib (Agiros), is 30.4%; enasidenib (Celgene) is 26.6%¹⁻³

What is Clinical Trial Success:

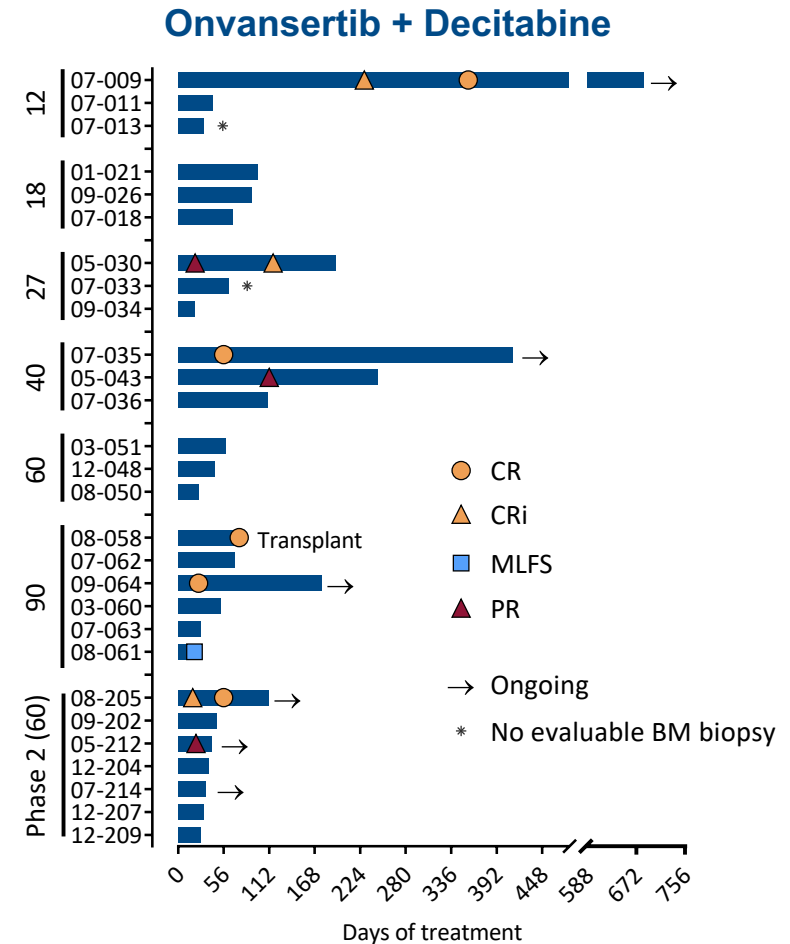
- 10 of 32 (~30%) achieve complete response (CR + CRi)
- Median overall survival of >2 months for relapsed/refractory AML patients

¹Stahl et al., Blood Adv. 2018 Apr 24;2(8):923-932; ²DiNardo et al, N Engl J Med. 2018 Jun 21;378(25):2386-2398; ³Stein et al., Blood. 2017 Aug 10;130(6):722-731

Phase 1b/2 AML Trial Efficacy Summary

Patients Completing 1 Cycle of Treatment

- ▶ Phase 1b: 21 patients completed 1 cycle of treatment
 - 7 (33%) of patients achieved an objective response (CR, CRi, MLFS, PR)
 - 5 (24%) of patients achieved CR/CRi:
 - 3 patients remain on treatment, time since response are 6, 12 and 15 months, respectively
- ▶ Phase 2: 7 patients have completed 1 cycle of treatment (to-date)
 - 2 (28%) of patients achieved an objective response (1 CR and 1 PR)



Conclusions

Completed Phase 1b Study of Onvansertib in AML¹

► **Safety: onvansertib treatment was well tolerated**

- MTD/RP2D was established at 60 mg/m² in both arms and no DLT was observed through this dose level
- Onvansertib-related toxicities were primarily on-target hematological events, in accordance with its mechanism of action and prior Phase 1 clinical study

► **Efficacy: complete response (CR/CRi) was observed in 6 patients**

- At a wide range of onvansertib doses: 27 mg/m² to 90 mg/m²
- CR/CRi rate was 24% through all doses and 31% at the 4 higher dose levels (27 – 90 mg/m²)

► **Pharmacodynamic and biomarker analysis:**

- Decreases in mutant ctDNA after 1 cycle of treatment were highly predictive of clinical response
- Target engagement in circulating blasts was associated with greater decrease in bone marrow blasts

► **Phase 2: enrolling**

- is enrolling and will include 32 patients to further assess the safety, efficacy, target engagement and correlation with response of onvansertib 60 mg/m² in combination with decitabine

¹Zeidan A et al., ASH 2019; Abstract #230

Corporate



Strong Patent Portfolio

► **Core Technology: 3 Issued Patents to 2030 in US, Europe and Asia with extension to 2035 in US**

- Compound (onvansertib): US 8614220
- Salt forms of onvansertib: US 8648078
- Combinations with anti-neoplastic compounds: US 8927530

► **Evergreening: Combination Therapy**

- Exclusive license from MIT for 2 US issued patents with broad method claims for combination of PLK inhibitor + anti-androgen compounds to treat any cancer
 - US 9566280, US 10155006; Expiration 2035

► **Evergreening: Biomarkers**

- Method for assessing PLK1 target phosphorylation status for identifying patients to be treated with Plk1 Inhibitors
 - PCT US1948044, Expiration 2039
- Method for treating patient with a PLK inhibitor when there is a PSA rise
 - Provisional, Expiration 2040

Business Development Strategy

Objective: Joint Development and Commercialization Partnerships

- ▶ Financial and clinical support for company-sponsored and/or investigator sponsored (IST) studies
- ▶ Maintain rights in North America in part or in whole
- ▶ Co-develop and/or out-license specific indications in Japan and Europe
- ▶ Optimize development timelines while efficiently managing resources, internal and outsourced

Co-Research Collaborations

- ▶ [MIT](#) to evaluate combination of Onvansertib with androgen receptor signaling inhibitors; identification of mechanism of action
- ▶ [Nektar Therapeutics](#) to evaluate onvansertib in combination with NKTR-102 in colorectal cancer

Partnering Strategy

- ▶ Successful partnership with US pharma/biotech for co-development
- ▶ Successful partnership with Japan Pharma for co-development and/or out-licensing

Cash Position and Runway

**2020 Capital Raises & Clinical Trial
Funding Commitments to-date**

- \$22.6 million

**Estimated Quarterly
Cash Burn**

- \$4 million

Thank You

for more information contact: ir@cardiffoncology.com

