



# Company Overview The Onvansertib Opportunity

SEPTEMBER 2023

# 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; our clinical trials may encounter delays in initiation or enrollment that impact the cost and timing of the trial readout; 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, 2022, 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.

## Cardiff Oncology: Positioned to improve 1<sup>st</sup> line mCRC treatment

### First-in-Class PLK1 inhibitor

- **Onvansertib**: first well-tolerated PLK1-selective inhibitor
- PLK1 inhibition disrupts tumor growth several ways

### Robust clinical data in 2L KRAS-mut mCRC

- **73%** response rate vs **~25%** in SoC
- **15 month** progression free survival vs **~8 month** in SoC

### FDA




- **FDA**-agreed path to 1st line accelerated approval

### Pfizer





- **Pfizer** is equity investor and has seat on SAB
- **Pfizer** provides clinical execution of 1<sup>st</sup> line trial

We expect clinical data from our 1<sup>st</sup> line RAS-mutated mCRC trial in mid-2024  
Runway with current cash extends into 2025

## Our pipeline opens many attractive opportunities for onvansertib

	Line of Therapy	Trial	Ph2	Ph3	Combination with:
mCRC (RAS-mut)	1 <sup>st</sup> line	Ph 2 (w/Pfizer)	 <i>randomized</i>		FOLFIRI/bev and FOLFOX/bev
	2 <sup>nd</sup> line	Ph 1b/2	 <i>completed</i>		FOLFIRI/bev
mPDAC	2 <sup>nd</sup> line	Ph 2			Onivyde <sup>®</sup> /5-FU

### Investigator-initiated trials

TNBC	2 <sup>nd</sup> line	Ph 2  Dana-Farber Cancer Institute			Paclitaxel
SCLC	2 <sup>nd</sup> line	Ph 2  UPMC LIFE CHANGING MEDICINE			None (monotherapy)





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## Fighting mCRC through PLK1 inhibition

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Robust data in lead mCRC program

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Path forward to accelerated approval

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# Onvansertib specifically targets PLK1, a well-established cancer target

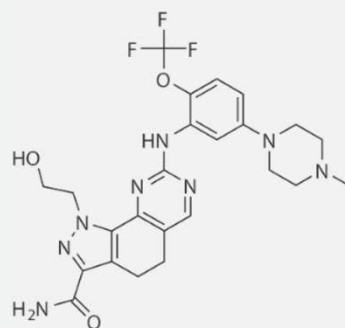
## Onvansertib

First oral, well-tolerated  
PLK1-selective inhibitor



### PROPERTIES

- Small molecule
- Oral dosing
- 24-hour half-life



### SPECIFICITY

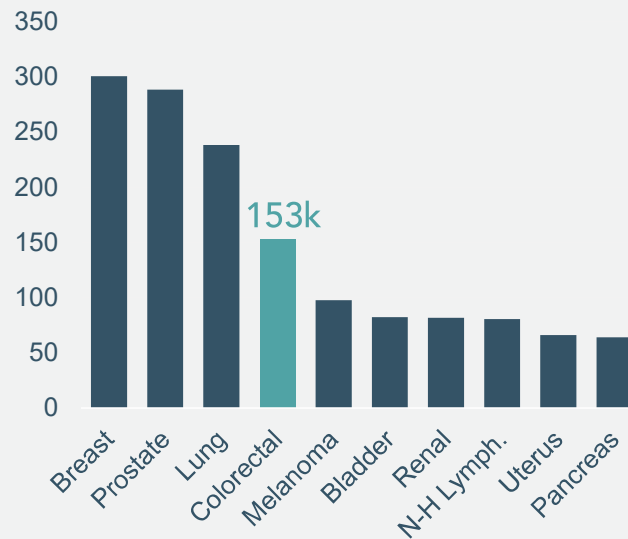
Exquisitely specific for PLK1

ENZYME	IC <sub>50</sub> (μM)
PLK1	0.002
PLK2	>10
PLK3	>10
CK2	0.4
FLT3	0.4
CDK1/CycB	>10
42 other kinases and >140 in the Millipore panel	>10

# Our lead program targets RAS-mutated metastatic colorectal cancer

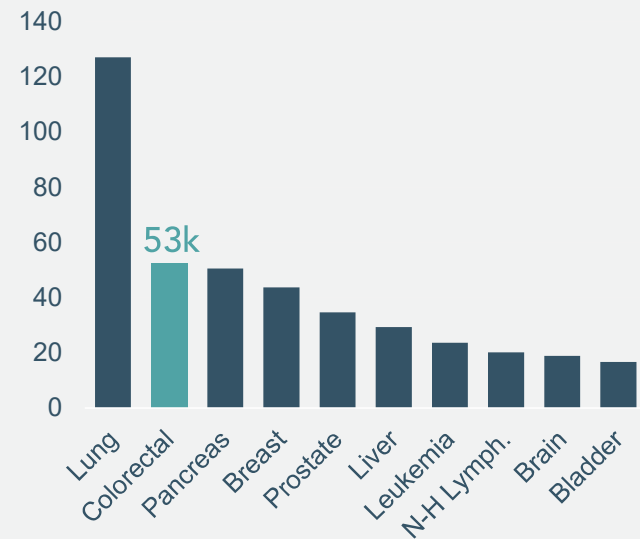
## mCRC is BOTH common...

2023 new US cases ('000s)\*



## ...and challenging to treat


2023 US deaths ('000s)\*



\* National cancer institute SEER data statistics.

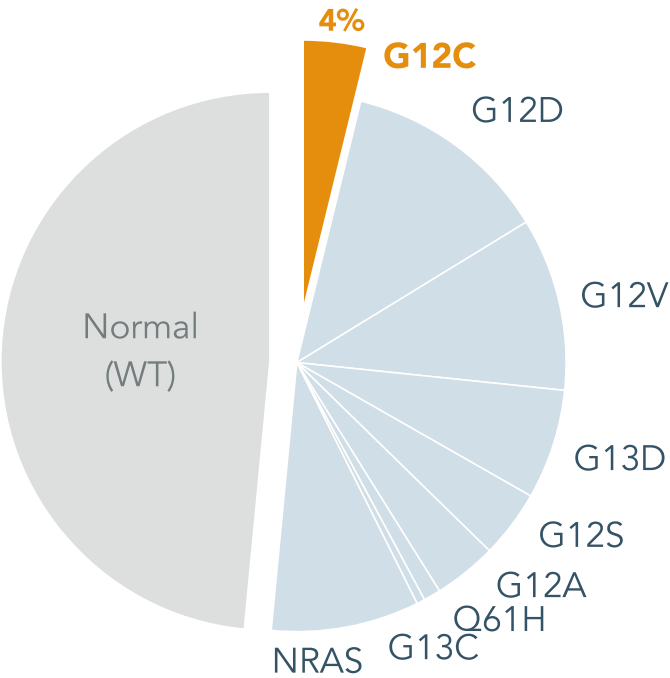
mCRC standard of care leaves a significant unmet need

**Standard of Care** for 1<sup>st</sup> / 2<sup>nd</sup> line RAS-mutated mCRC includes chemo + bevacizumab

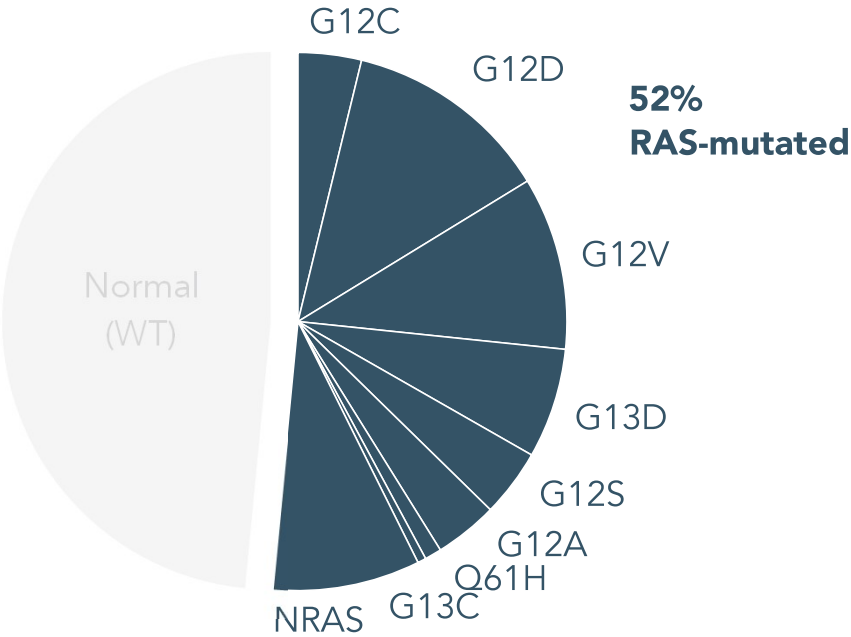
Chemotherapy	FOLFOX (approved 1996) FOLFIRI (approved 2002)
	
Antiangiogenic	Bevacizumab (Avastin®) (approved 2004)
Targeted therapy	None

Other mCRC development programs leave a significant unmet need

**KRAS G12C** therapies would address a small part of the need<sup>1</sup>



**Onvansertib** is targeting all RAS-mutated mCRC<sup>1</sup>



1. Jones R et al. Br J Cancer. 2017 Mar 28;116(7):923-929

# Multiple onvansertib MOAs underlie our focus on RAS-mutated mCRC

## Onvansertib attacks RAS-mutated mCRC in three ways

### 1 Synthetic lethality

RAS-mut mCRC tumor cells are hypersensitive to onvansertib

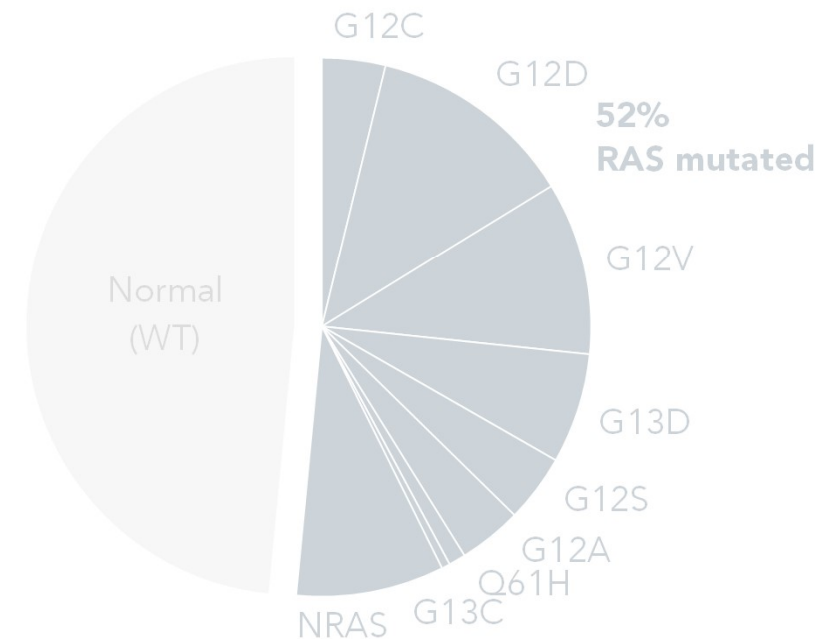
### 2 Inhibit DNA repair

Onvansertib inhibits repair of chemo-induced DNA damage

### 3 Inhibit tumor vasculature

Onvansertib inhibits creation of new blood vessels

**Onvansertib** is targeting all RAS-mutated mCRC<sup>1</sup>



<sup>1</sup> Jones R et al. Br J Cancer. 2017 Mar 28;116(7):923-929

# Targeting PLK1 opens doors to large patient populations

## Targets with oncogenic alterations

ROS1  
RET  
KRAS G12C  
EGFR  
TRK

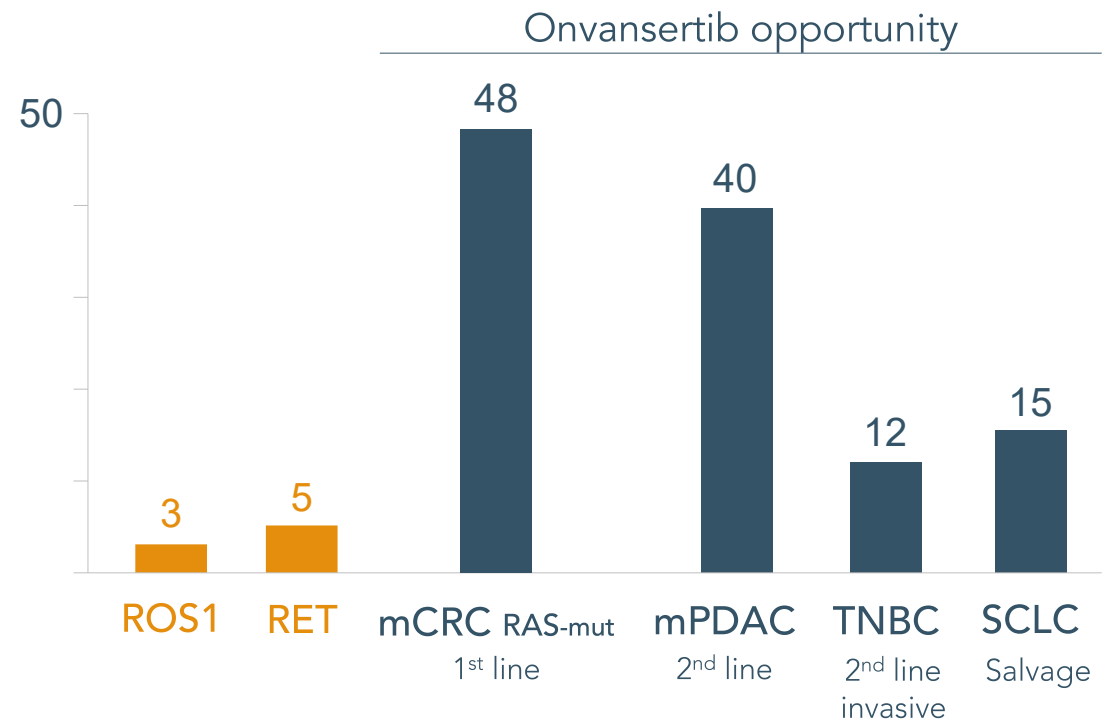
## Targets without oncogenic alterations

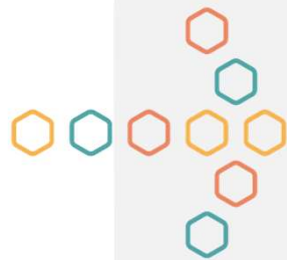
PLK1  
PARP  
CDK4/6  
PD1/PDL1  
VEGF

\*ROS1 estimated eligible patients presented in Turning Point Therapeutics' corporate presentation May 2022 slide 6 (NSCLC disease incidence in the US of 140k of which 2% of patients harbor ROS1 translocation). RET estimated eligible patients presented in Loxo Oncology's corporate presentation January 2018 disclosed on Form 8-K (Jan 8, 2018).

mCRC estimated population includes 2nd line, KRAS- and NRAS-mutated cancers. mPDAC estimated population includes 2nd line PDAC patients. TNBC estimated population includes invasive, 2nd line TNBC patients. SCLC estimated population includes SCLC salvage patients.

## Annual eligible U.S. patients ('000s)\*





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Fighting mCRC through PLK1 inhibition

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Robust data in lead mCRC program

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Path forward to accelerated approval

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# Our focus is RAS-mutated tumors where there are no targeted therapies

## Normal

Standard\*

Targeted

## 1<sup>st</sup> LINE

Chemo + bevacizumab

+ EGFR inhibitor

## 2<sup>nd</sup> LINE

Chemo + bevacizumab

NONE

RAS-mut mCRC is approx.  
half the mCRC population<sup>1</sup>

## RAS Mutated

Standard\*

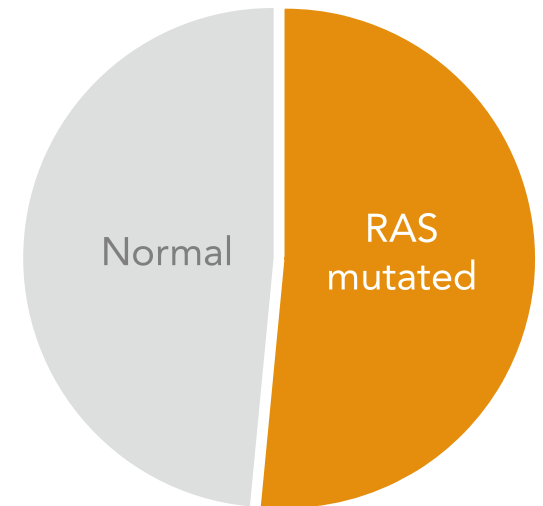
**Targeted**

Chemo + bevacizumab

**NONE**

Chemo + bevacizumab

**NONE**



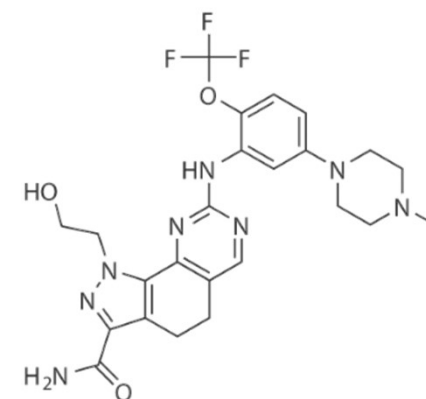
\* FOLFOX and FOLFIRI are interchangeable as SoC chemo for 1<sup>st</sup> and 2<sup>nd</sup> line.  
1. Jones R et al. Br J Cancer. 2017 Mar 28;116(7):923-929

## Our Ph1b/2 trial added onvansertib to SoC in the 2<sup>nd</sup> line setting

	Normal	1 <sup>st</sup> LINE	2 <sup>nd</sup> LINE
Standard		Chemo + bevacizumab	Chemo + bevacizumab
Targeted		+ EGFR inhibitor	NONE

RAS Mutated			
Standard		FOLFOX + bevacizumab	FOLFIRI + bevacizumab
Targeted		NONE	ONVANSERTIB



◀ Our trial explored adding onvansertib to FOLFIRI + bev (SoC)

# Our Ph1b/2 trial combined onvansertib with the current SoC in 2<sup>nd</sup> line

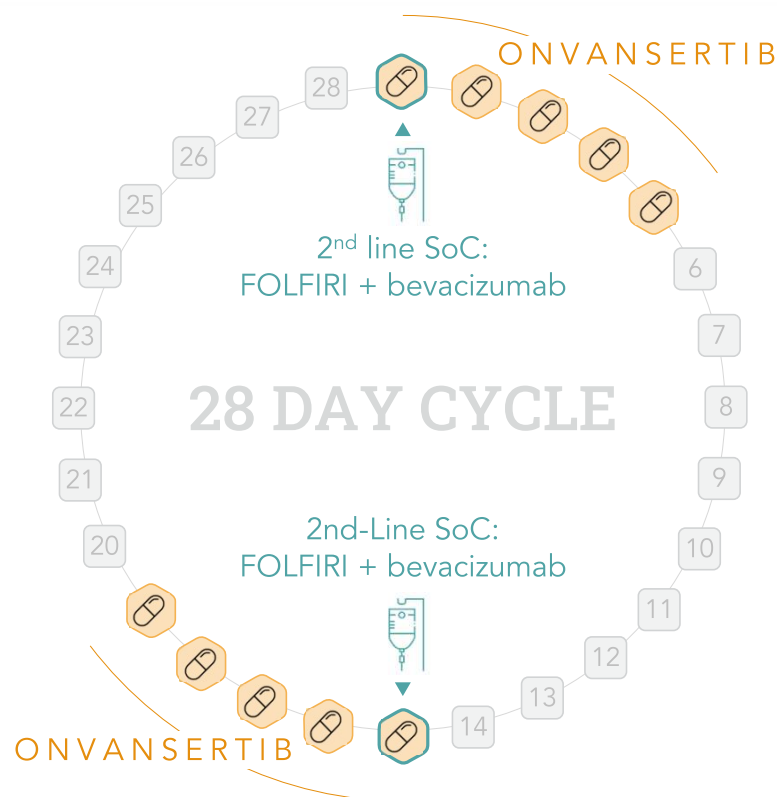
## ENROLLMENT CRITERIA

2<sup>nd</sup> line mCRC

KRAS-mut

Unresectable

N=68 (66 evaluable)



## EFFICACY ENDPOINTS

- 1** Primary: Objective Response Rate (ORR) per RECIST v1.1 in patients who receive  $\geq 1$  cycle of treatment
- 2** Secondary: Progression-Free Survival (PFS) and Duration of Response (DoR)
- 3** Exploratory: decrease in KRAS-mutational burden and response to treatment

## Our 2<sup>nd</sup> line trial patients may or may not have received bev in 1<sup>st</sup> line

### Bev exposed vs bev naïve patients

"Bev naïve" patients who did not receive prior bev in 1<sup>st</sup> line

or

"Bev exposed" patients who received bev in 1<sup>st</sup> line

### 1<sup>st</sup> LINE

FOLFOX

23% (15 of 66)

FOLFOX +  
**bevacizumab**

77% (51 of 66)

### 2<sup>nd</sup> LINE

FOLFIRI +

**bevacizumab**

+

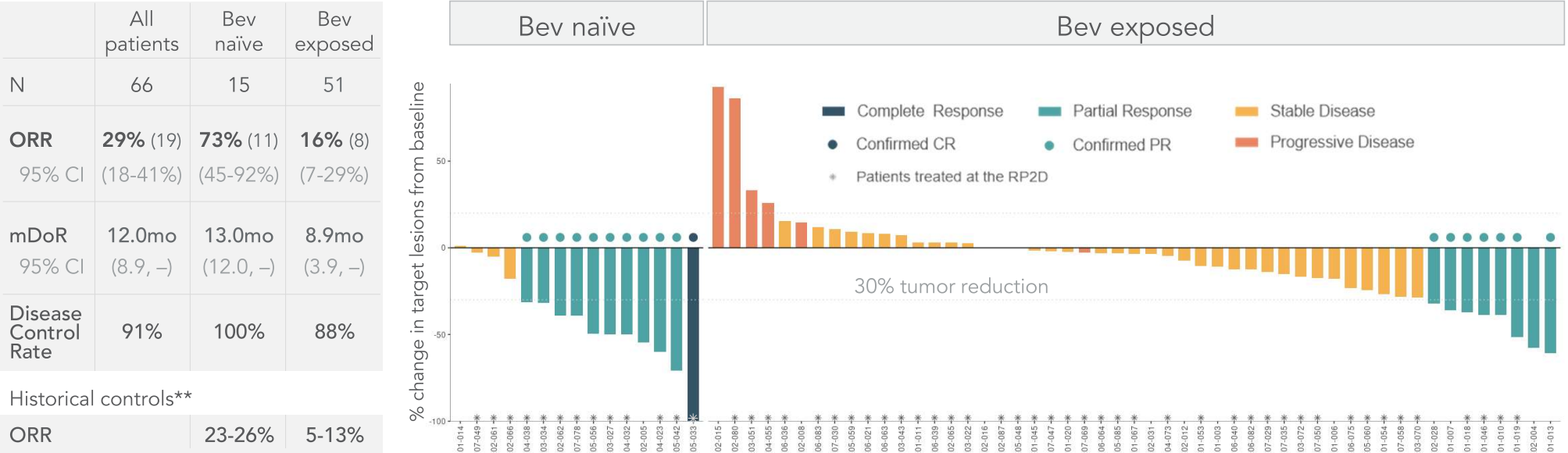
ONVANSERTIB

All patients received  
FOLFIRI + bev + onv  
in our trial

# Bev naïve patients achieved higher response rate with onvansertib+SoC

## Best Radiographic Response and Duration of Response\* – 66 evaluable patients (as of June 16, 2023)

	All patients	Bev naïve	Bev exposed
N	66	15	51
ORR	29% (19)	73% (11)	16% (8)
95% CI	(18-41%)	(45-92%)	(7-29%)
mDoR	12.0mo	13.0mo	8.9mo
95% CI	(8.9, –)	(12.0, –)	(3.9, –)
Disease Control Rate	91%	100%	88%
Historical controls**			
ORR		23-26%	5-13%



\* Radiographic response determined per RECIST 1.1. Waterfall plot and table reflect interim data as of June 16, 2023 from an ongoing trial and unlocked database. Patients 02-008 and 07-029 were categorized as bev naïve in the July 25, 2022 data, but are now determined to have been bev exposed. mDoR CI: “–” means not reached. After external review of the tumor measurements completed May 12, 2023, it was determined that patients 02-028 and 04-038 were confirmed PRs.

\*\* Bennouna et al., Lancet Oncol 2013; 14: 29–37; Giessen et al., Acta Oncologica, 2015, 54: 187-193; Cremolini et al., Lancet Oncol 2020, 21: 497–507; Antoniotti et al., Correspondence Lancet Oncol June 2020. Giantonio et al., 2007, J Clin Oncol 25:1539-1544; Moriwaki et al., Med Oncol, 2012, 29:2842–2848; Beretta et al, Med Oncol 2013, 30:486.

# Patients on our trial achieved responses across KRAS mutations

## Best Radiographic Response a

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Historical controls\*\*

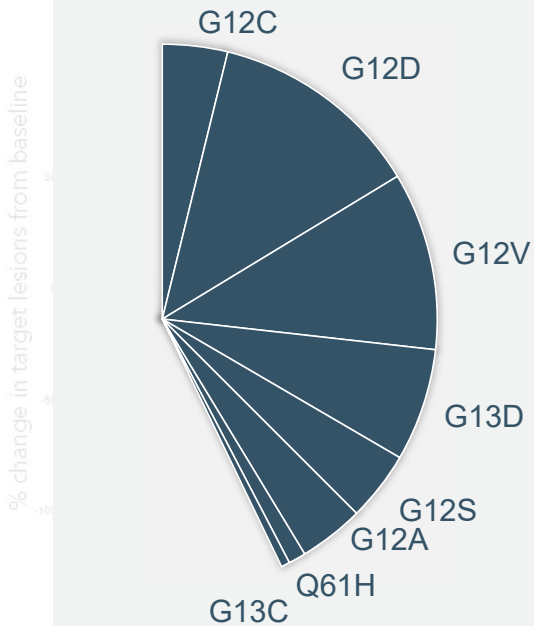
ORR	23-26%	5-13%
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\* Radiographic response determined per RECIST 1.1. Waterfall plot and table not shown. Patients 02-005 and 07-029 were categorized as best response in the July 25, 2022 update. Patients 02-025 and 04-035 were confirmed PRs.

\*\* Benouna et al., Lancet Oncol 2013; 14: 29-37; Giesen et al., Acta Oncologica 2015; 54: 167-173; Gremelmeier et al., Lancet Oncol 2020; 21: 457-507; Antonietti et al., Correspondence Lancet Oncol June 2020; Santoro et al., 2007, J Clin Oncol 25: 1539-1544; Morosak et al., Med Oncol 2012; 29: 2842-2845; Enegetta et al., Med Oncol 2013; 30:485

1. Jones R et al. Br J Cancer. 2017 Mar 28;116(7):923-929

## Frequency of Common KRAS Mutations in mCRC<sup>1</sup>

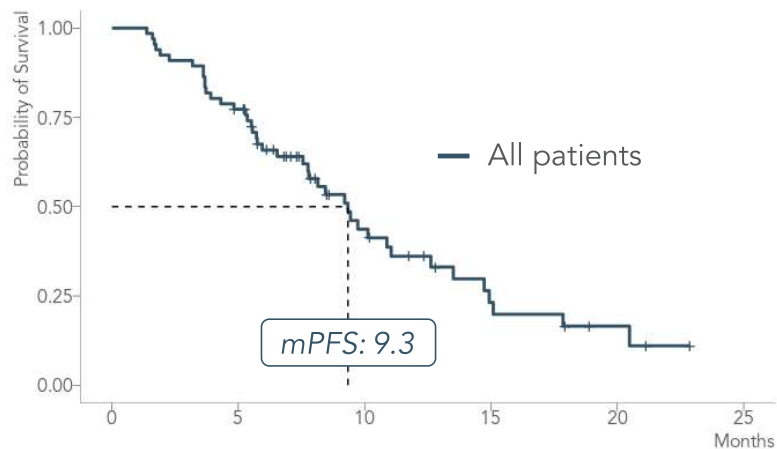


## Onvansertib responses across KRAS mutations (as of June 16, 2023)

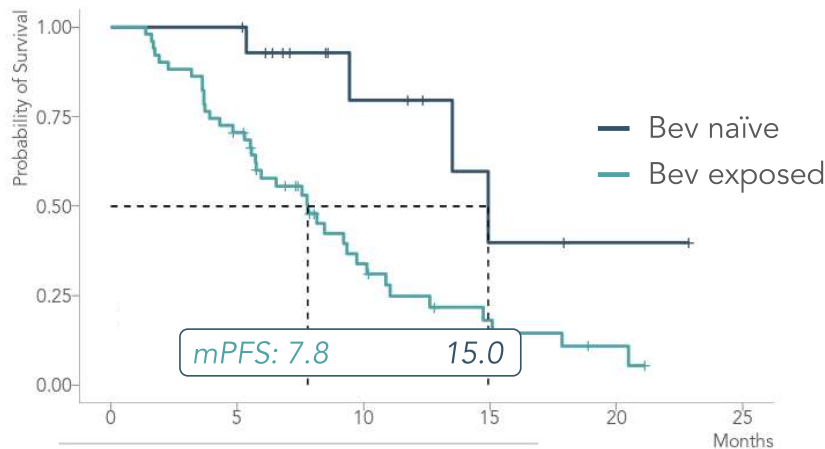
KRAS Variant	CR+PR	SD	PD	Total
G12D	7	13	1	21
G12V	1	10	2	13
G12A	4	4		8
G13D	4	4		8
G12C	1	2	1	4
G12S		3	1	4
A146T	1	2		3
Q61H	1	2		3
K117N		1	1	2
Total	19	41	6	66

# PFS exceeds historical controls for SoC, particularly in bev naïve patients

**Progression free survival\*** – 66 evaluable patients (as of June 16, 2023)



Characteristic	N	Event N	mPFS (95%CI)
Overall	66	42	9.3 (7.8, 14)



Characteristic	N	Event N	mPFS (95%CI)	p-value <sup>†</sup>
prior_chemo	66	42		0.003
Bev Naïve			15 (14, —)	
Prior Bev			7.8 (5.8, 10)	
<sup>†</sup> Log-rank test		CI of “—” means not reached		

Historical controls**		
	Bev exposed	Bev naïve
PFS	4.5 - 6.7mos	6.9 - 8.5mos

\* Onvansertib mPFS are interim data as of June 16, 2023 from an ongoing trial and unlocked database

\*\* Bennouna et al., Lancet Oncol 2013; 14: 29–37; Giessen et al., Acta Oncologica, 2015, 54: 187-193; Cremolini et al., Lancet Oncol 2020, 21: 497–507; Antoniotti et al., Correspondence Lancet Oncol June 2020. Giantonio et al., 2007, J Clin Oncol 25:1539-1544; Moriwaki et al., Med Oncol, 2012, 29:2842–2848; Beretta et al, Med Oncol 2013, 30:486.



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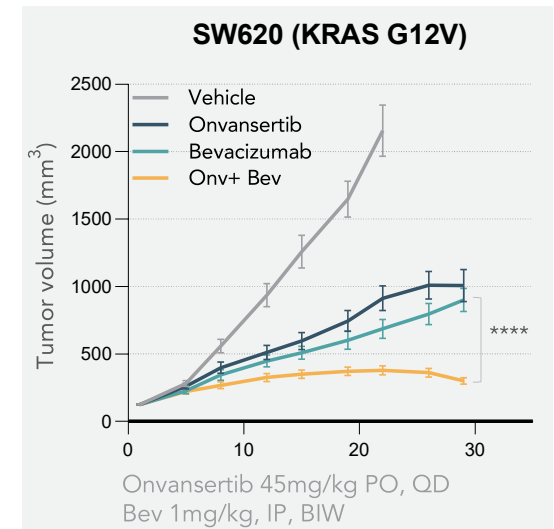
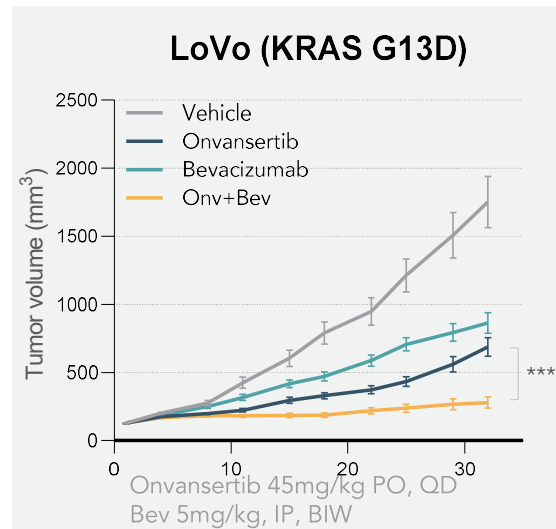
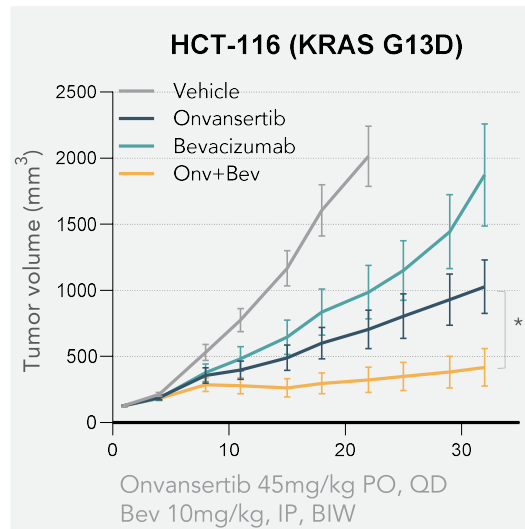
## Scientific basis for clinical findings

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# Onvansertib + bev inhibits tumor growth greater than either agent alone

The combination had significant superior anti-tumor activity compared to the single agents



Three KRAS-mutant xenograft models were treated with vehicle (control), onvansertib, bevacizumab or the combination of onvansertib and bev. 8-9mice/ group. Mean  $\pm$  SEM are represented on graphs. An unpaired t-test was used to test the difference in tumor volume change on the last day of treatment between the combination treatment and the most effective control arm. \*p<0.05, \*\*\*p<0.001, \*\*\*\*p<0.0001

# Onvansertib plays an independent role in antiangiogenesis that complements bev

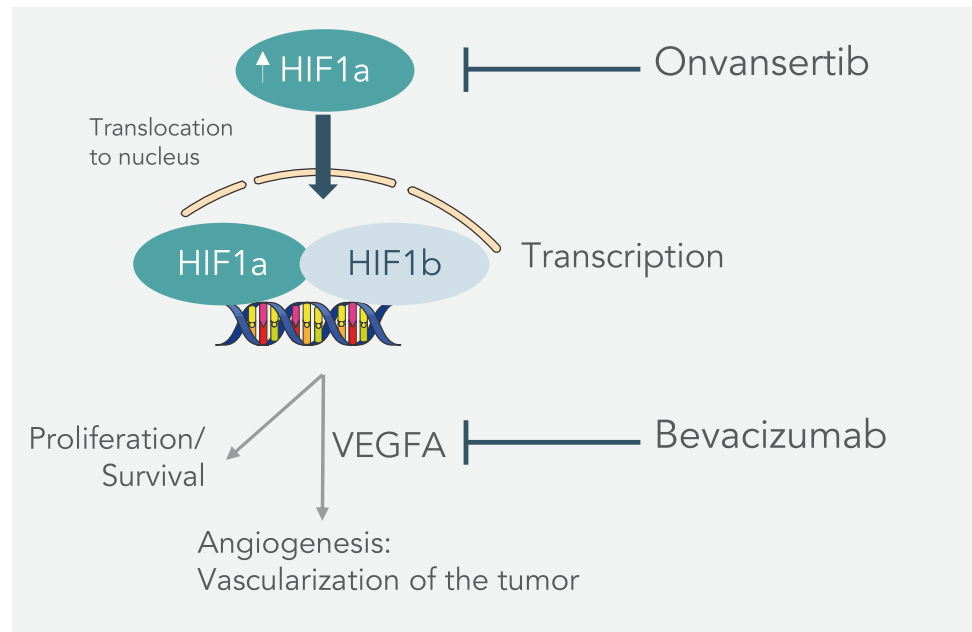
	LoVo (KRAS G13D)*			SW620 (KRAS G12V)*			
Control (vehicle)							
Bevacizumab							<ul style="list-style-type: none"> <li>• Roche drug Avastin®</li> <li>• 8<sup>th</sup> largest global drug in 2019</li> <li>• \$7.1B sales</li> </ul>
Onvansertib							
Onv+Bev							

**KRAS-mut tumors from mice treated with onv + bev appear smaller and pale (less vascularized)**

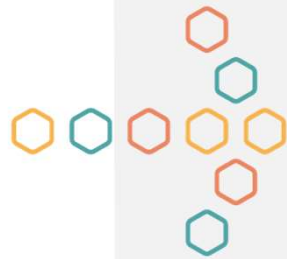
\* Two KRAS-mutant xenograft models were treated with control (vehicle), onvansertib, bevacizumab or the combination of onvansertib and bev. 8-9mice / group. Tumors were removed and photographed at the end of the study. Representative photographs from three mice from each group are shown.

# Onvansertib and bev are complementary inhibitors of the hypoxia signaling pathway

This new MOA, which inhibits a “survival switch” of tumorigenesis, may underlie the increased efficacy observed clinically



In the low oxygen tumor microenvironment (hypoxia), HIF1a is induced by tumors to increase vascularization by secreting VEGF, and to promote proliferation and survival



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Fighting mCRC through PLK1 inhibition

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Robust data in lead mCRC program

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Path forward to accelerated approval

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# mCRC program positions onvansertib for accelerated and full-approval

## mCRC clinical development program agreed with FDA at June 2023 Type C meeting

### CRDF-004

1st line RAS-mutated mCRC trial  
90 patients, randomized, 2 doses of onvansertib

#### Highlights of CRDF-004 exploratory trial

- Provide randomized clinical safety / efficacy data
- Confirm optimal dose in 1<sup>st</sup> line
- Expect to provide interim data readout in mid-2024
- Pfizer Ignite will provide clinical execution

### CRDF-005

1st line RAS-mutated mCRC registrational trial  
320 patients, randomized

#### Highlights of CRDF-005 registrational trial

- Seamless registrational trial for accelerated and full approval, as agreed with FDA
- ORR endpoint: For accelerated approval
- PFS / OS trend endpoint: For full approval

# Trial design of CRDF-004: 1<sup>st</sup> line RAS-mutated mCRC Ph 2 trial

## ENROLLMENT CRITERIA

1<sup>st</sup> line mCRC

KRAS+/NRAS+

Unresectable

No prior bev, FOLFIRI or FOLFOX treatment

**R**

N=90  
1:1:1

Onv 20mg + FOLFIRI/bev or  
FOLFOX/bev  
(n=30)

Onv 30mg + FOLFIRI/bev or  
FOLFOX/bev  
(n=30)

SoC: FOLFIRI/bev or  
FOLFOX/bev  
(n=30)



## ENDPOINTS

Primary ORR

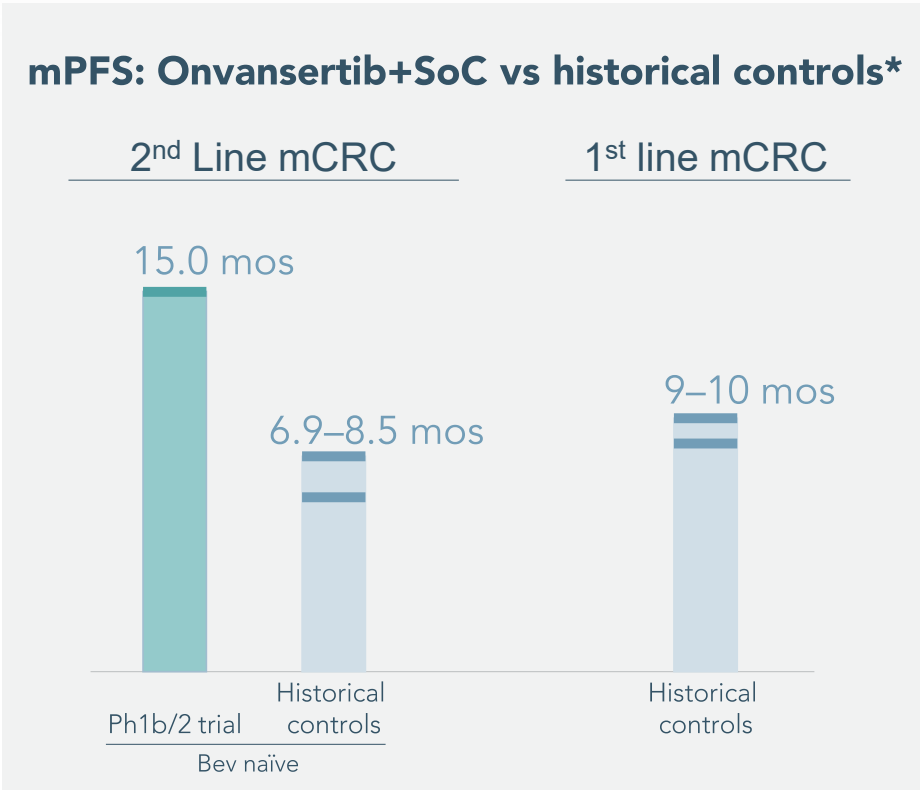
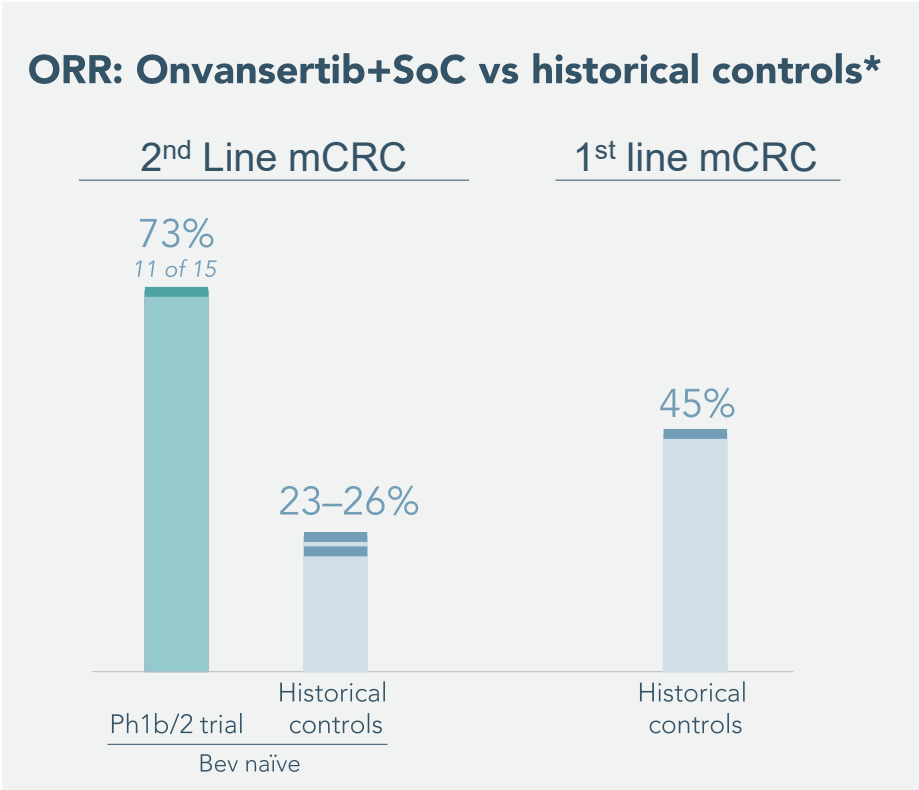
Secondary DoR and PFS

Benchmark of success ORR  $\geq 65\%$

**PFIZER IGNITE** will provide clinical execution for CRDF-004

In CRDF-004, each arm will have an equal number of FOLFIRI/bev and FOLFOX/bev patients.

# ORR/PFS for bev naïve patients exceeds 1<sup>st</sup> and 2<sup>nd</sup> line historical controls



Historical controls reflect RAS-WT and RAS-mut patients  
\* 2008: Bennouna et al., Lancet Oncol 2013; 14: 29–37; 2013: Giessen et al., Acta Oncologica, 2015, 54: 187–193; 2017: Cremolini et al., Lancet Oncol 2020, 21: 497–507; and Antoniotti et al., Correspondence Lancet Oncol June 2020. J. Clin. Med. 2020, 9, 3889; doi:10.3390/jcm9123889.  
ORR and PFS data are interim data from an ongoing trial and unlocked database. Historical controls are from studies in similar anti-angiogenic drugs and restricted geographical areas, and do not all represent purely comparable 2<sup>nd</sup> line mCRC patient populations.

## Pfizer will support clinical execution of 1<sup>st</sup> line mCRC trial

### PFIZER BREAKTHROUGH GROWTH INITIATIVE

November 2021

- \$15M investment
- Adam Schayowitz, Ph.D., MBA, Vice President & Medicine Team Group Lead for Breast Cancer, Colorectal Cancer and Melanoma at Pfizer joins Scientific Advisory Board
- Right of first access to data

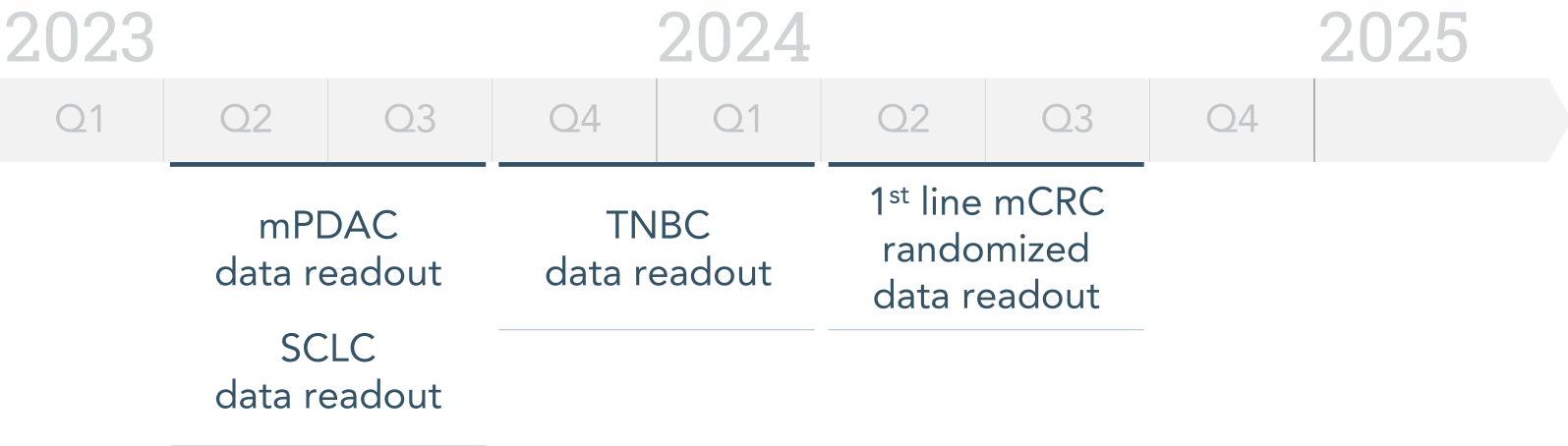
### PFIZER Ignite

August 2023

- Pfizer Ignite will be responsible for the clinical execution of 1<sup>st</sup> line mCRC trial (CRDF-004), including development capabilities, scale and expertise
- Cardiff Oncology retains full economic ownership and control of onvansertib



# We have multiple near-term clinical data read outs



June 30, 2023 cash and investments	\$89.4M
Net cash used in Operating Activities (Rolling two-quarter period ending June 30, 2023)	\$15.8M
Based on our current projections we expect that our capital resources are sufficient to fund our operations into 2025	

\* Financial information above is derived from our unaudited financials in Form 10Q filed on 8/9/23.

## Cardiff Oncology: Positioned to improve 1<sup>st</sup> line mCRC treatment

### First-in-Class PLK1 inhibitor

- **Onvansertib**: first well-tolerated PLK1-selective inhibitor
- PLK1 inhibition disrupts tumor growth several ways

### Robust clinical data in 2L KRAS-mut mCRC

- **73%** response rate vs **~25%** in SoC
- **15 month** progression free survival vs **~8 month** in SoC

### FDA

- **FDA**-agreed path to 1st line accelerated approval

### Pfizer

- **Pfizer** is equity investor and has seat on SAB
- **Pfizer** provides clinical execution of 1<sup>st</sup> line trial

We expect clinical data from our 1<sup>st</sup> line RAS-mutated mCRC trial in mid-2024  
Runway with current cash extends into 2025

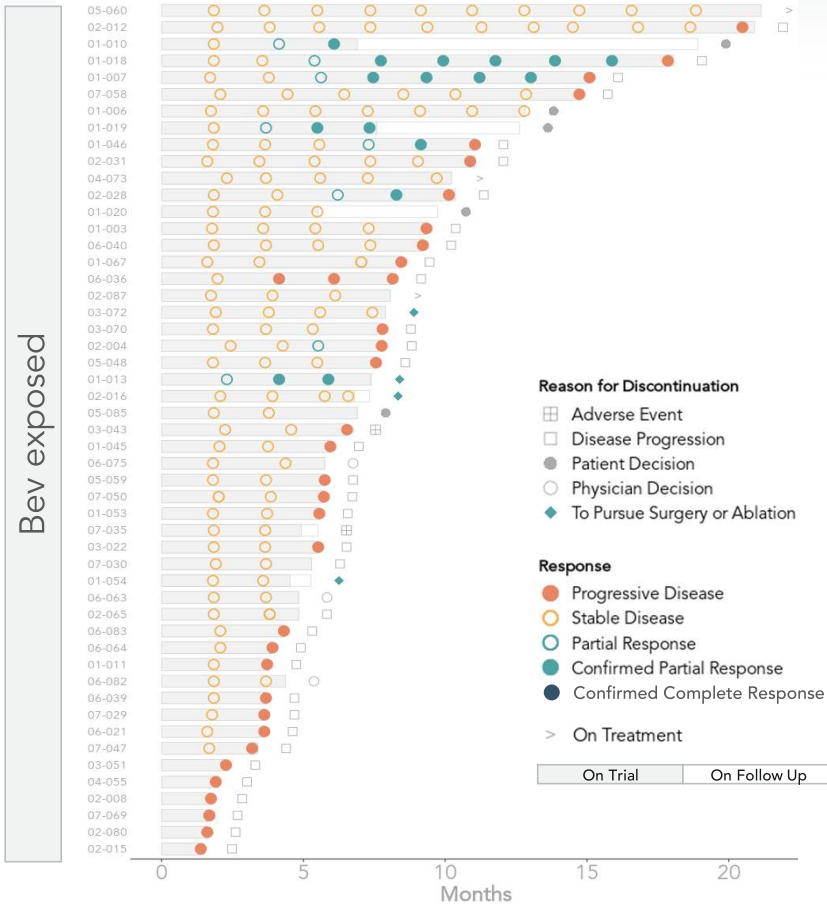


## Additional mCRC Data

# Bev naïve patients experienced more durable responses

**Swimmer plot\*** – 66 evaluable patients (as of June 16, 2023)

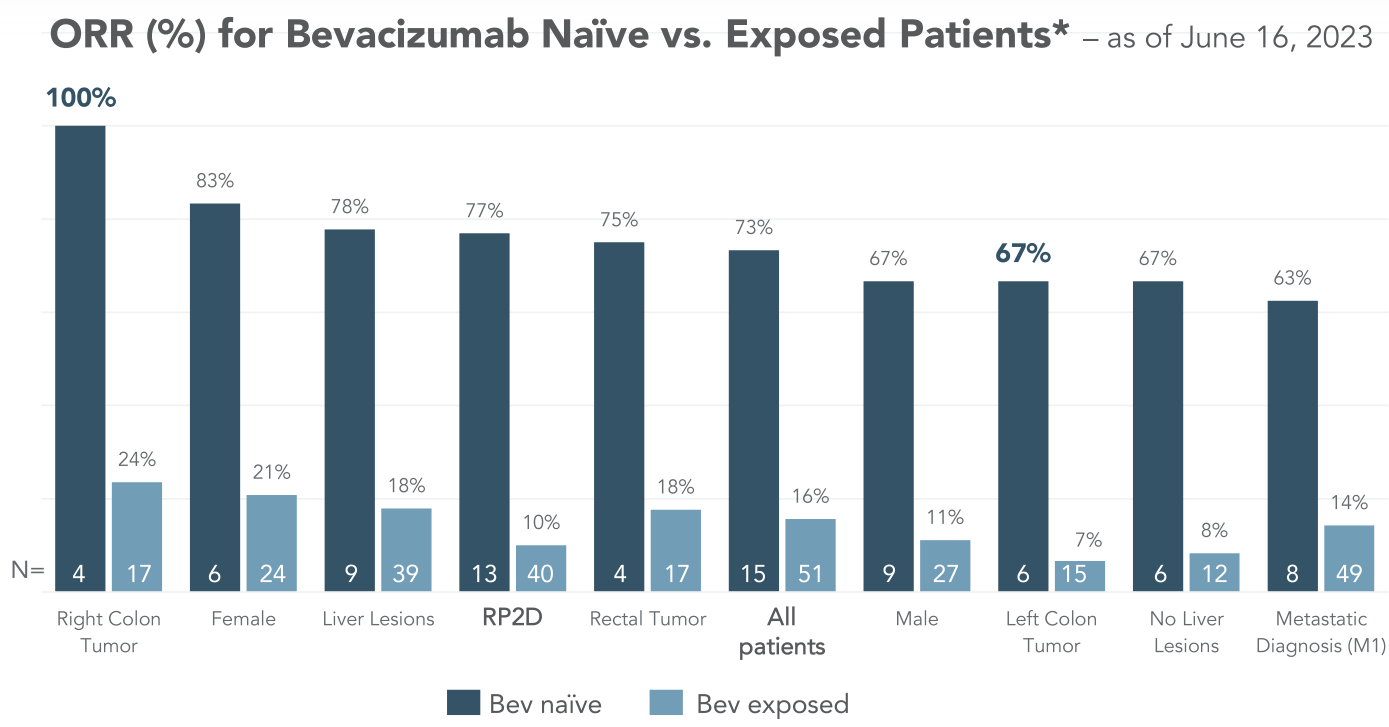
	All patients	Bev naïve	Bev exposed
Pursued surgery / ablation	18% (12/66)	53% (8/15)	8% (4/51)
Initial PR at 8 week scan	9	8	1
Initial PR at 16+ week scan	10	3	7



\* Swimmer plot / table reflect interim data as of June 16, 2023 from an ongoing trial and unlocked database. After external review of the tumor measurements completed May 12, 2023, it was determined that patients 02-028 and 04-038 were confirmed PRs.

# ORR is consistently greater for bev naïve patients across characteristics

No single patient characteristic explains the difference in response rates by prior bev status



\* Onvansertib ORR is interim data as of June 16, 2023 from an ongoing trial and unlocked database.

## Onvansertib in combination with FOLFIRI-bev is well-tolerated\*

- All treated patients (N=68)

- All dose levels (12mg/m<sup>2</sup>, 15mg/m<sup>2</sup>, 18mg/m<sup>2</sup>)

- No major / unexpected toxicities are seen

- 8 patients had a G4 hematologic AE

- All resolved without issue
  - Required dose holds and/or growth factor support
  - None of the 8 patients discontinued treatment due to this AE

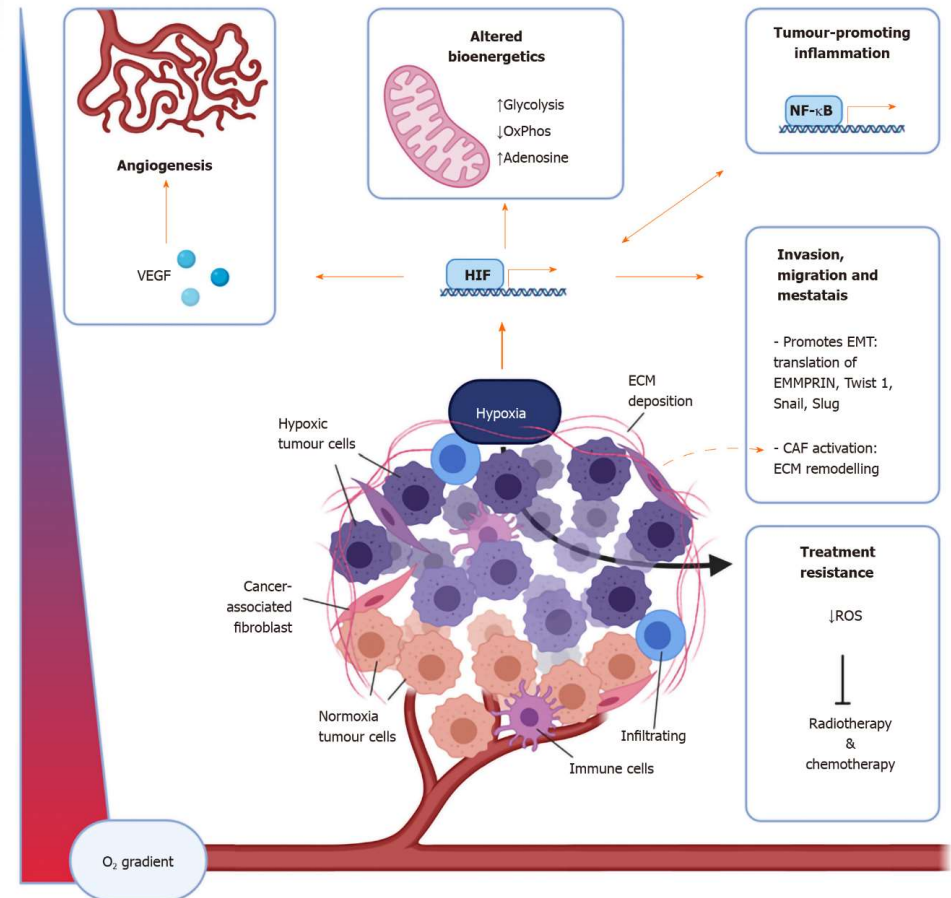
TEAE	GR1	GR2	GR3	GR4	TOTAL	TEAE	GR1	GR2	GR3	GR4	TOTAL
Fatigue	24	22	7	0	53 78%	Cough	11	0	0	0	11 16%
Neutropenia	1	18	23	7	49 72%	Pyrexia	8	1	1	0	10 15%
Nausea	29	13	4	0	46 68%	Dyspnea	7	3	0	0	10 15%
Diarrhea	21	13	4	0	38 56%	AST Increase	7	2	1	0	10 15%
Leukopenia	9	14	5	1	29 43%	Lymphocytopenia	2	7	0	0	9 13%
Anemia	22	5	2	0	29 43%	Dyspepsia	9	0	0	0	9 13%
Alopecia	20	5	0	0	25 37%	ALT Increase	8	0	1	0	9 13%
Abdominal Pain	14	8	3	0	25 37%	Hypocalcemia	9	0	0	0	9 13%
Stomatitis	15	6	3	0	24 35%	Insomnia	9	0	0	0	9 13%
Hypertension	4	10	9	0	23 34%	Dehydration	1	5	2	0	8 12%
Thrombocytopenia	17	5	1	0	23 34%	Hypokalemia	6	2	0	0	8 12%
Constipation	17	2	1	0	20 29%	Arthralgia	6	2	0	0	8 12%
Vomiting	11	6	3	0	20 29%	Hand / Foot Syndrome	5	2	0	0	7 10%
Epistaxis	15	0	0	0	15 22%	Hemorrhoids	5	2	0	0	7 10%
Headache	13	0	0	0	13 19%	Non-Cardiac Chest Pain	6	1	0	0	7 10%
Decreased Appetite	4	6	2	0	12 18%	ALP Increase	5	1	1	0	7 10%
Back Pain	10	2	0	0	12 18%						

\* Data consists of all adverse events entered into the EDC as of June 13, 2023, from an ongoing trial and unlocked database. N: number of patients (total N=68); events shown occurred in ≥10% of patients; numbers indicate number of patients experiencing the event, (regardless of causality); each patient is only counted once and only for the highest grade of a given event. TEAEs: Treatment Emergent Adverse Events; TOTAL shows the absolute # of patients and (%) of the population. COVID, as an AE, is not included as that data is still under review and being tabulated.

# Hypoxia: a hallmark of cancer

In response to hypoxia, cancer cells activate the hypoxia-inducible factor (HIF) pathway, which can promote tumorigenesis through multiple means:

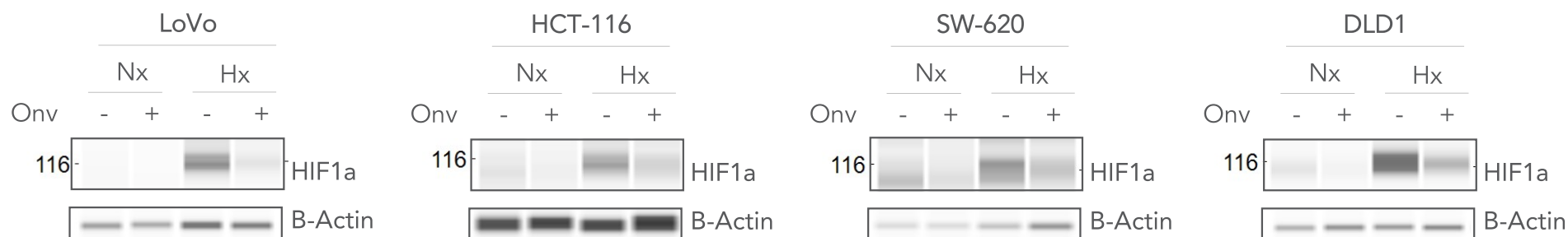
- Angiogenesis
- Cell proliferation and survival
- Highly immunosuppressive and invasive tumor microenvironment
- Hypoxia-induced EMT and acquisition of cancer cell stemness in turn driving metastasis
- Reprogrammed cancer cell metabolism and increased glycolysis
- Delivery of anti-cancer agents rendered more intractable



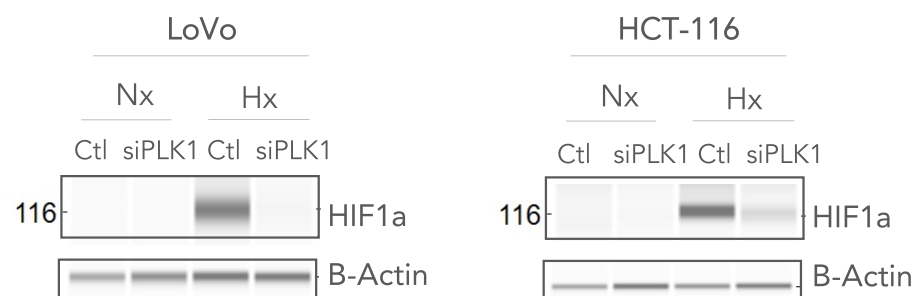
From: King et al., World J Gastrointest Oncol. 2021

# Onvansertib inhibits the hypoxia signaling pathway by downregulating HIF1a expression

In 4 RAS-mutant CRC cell lines\*, onvansertib inhibited hypoxia-induced HIF1a expression



PLK1 inhibition using siRNA against PLK1 (siPLK1) prevented hypoxia-induced HIF1a expression



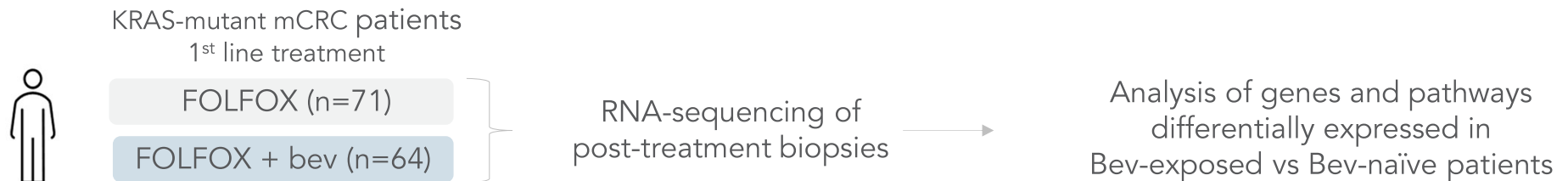
\* Four KRAS-mutant CRC cell lines were cultured under normoxia (20%O<sub>2</sub>, Nx) or hypoxia (1%O<sub>2</sub>, Hx), in the presence (+) or absence (-) of onvansertib. HIF1a expression was strongly induced under hypoxia.



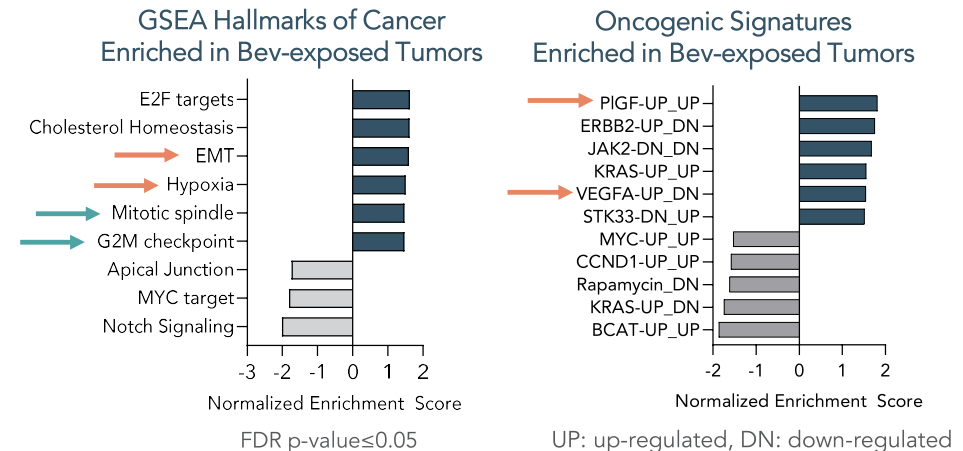
# Prior bev treatment modulates gene pathways that can confer resistance to bev and onvansertib

Aim: to identify potential mechanisms of treatment resistance in bev exposed KRAS-mutant mCRC patients

Method:



- Bev exposed tumors showed up-regulation of pathways associated with:
  - Hypoxia
  - G2/M checkpoint and mitosis
- Up-regulation of these pathways may drive resistance to onvansertib and bev
- Additionally, modulation of oncogenic signatures associated with angiogenic factors (PIGF, VEGFA) were observed in bev exposed tumors and may drive treatment resistance



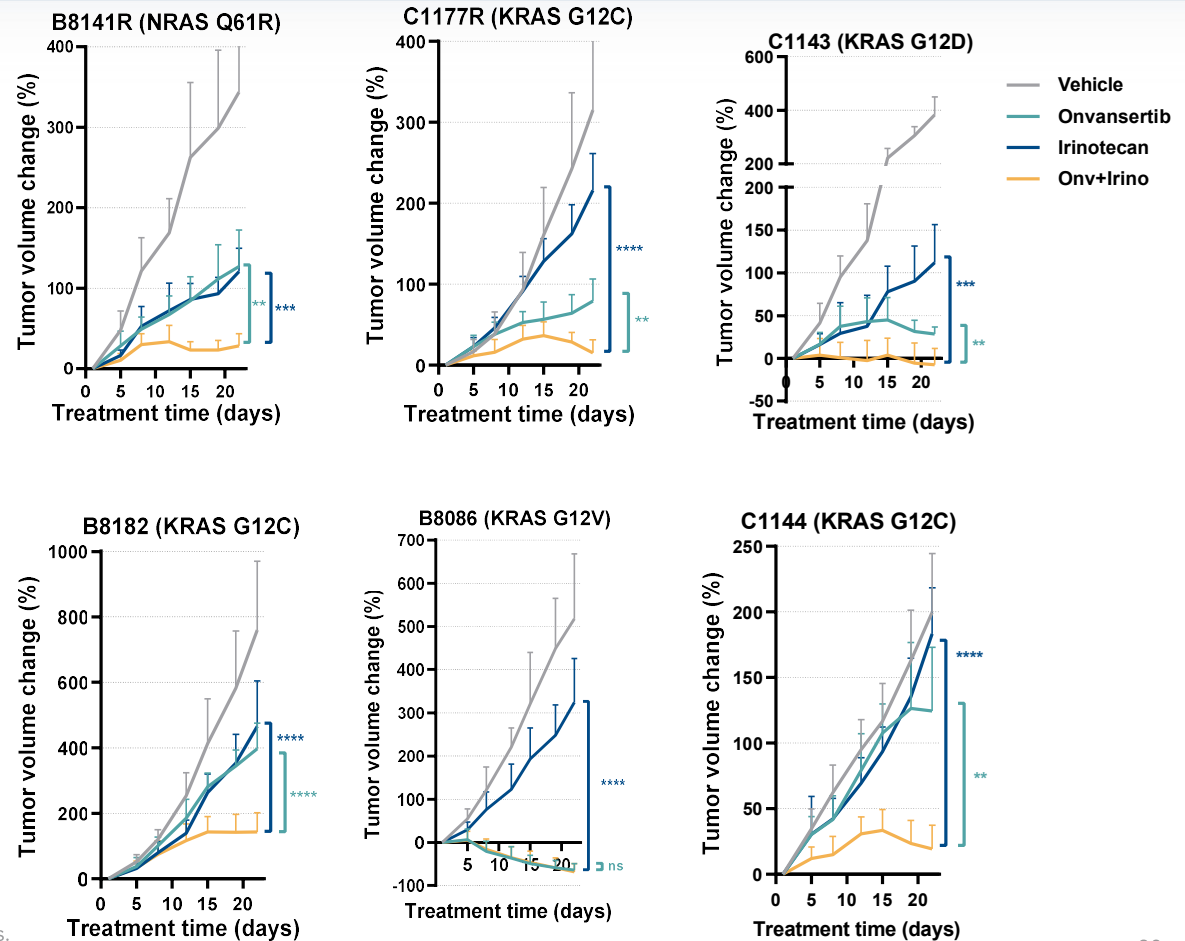
# Onvansertib in combination with irinotecan in RAS-mutant CRC PDXs

The combination of onvansertib and irinotecan showed anti-tumor activity in 6 RAS-mutated PDX models with either acquired or intrinsic resistance to irinotecan.

The combination showed significant increased anti-tumor activity compared to onvansertib single agent in 5 of the 6 models.

These data support that onvansertib + irinotecan is an active combination in RAS-mutated PDX models and that Onvansertib can sensitize tumors to irinotecan.

In collaboration with Dr. Kopetz (MD Anderson)



Dosing schedule: onvansertib 60 mg/kg daily; irinotecan 40mg/kg weekly, for up to 21days. Mean + SD are represented. Unpaired t-test, \*\*p<0.01, \*\*\*p<0.001, \*\*\*\*p<0.0001

# Onvansertib in combination with FOLFOX in RAS-mutant CRC PDXs

The chemotherapeutics oxaliplatin+5FU had no or modest activity in the 6 RAS-mutant PDX models tested.

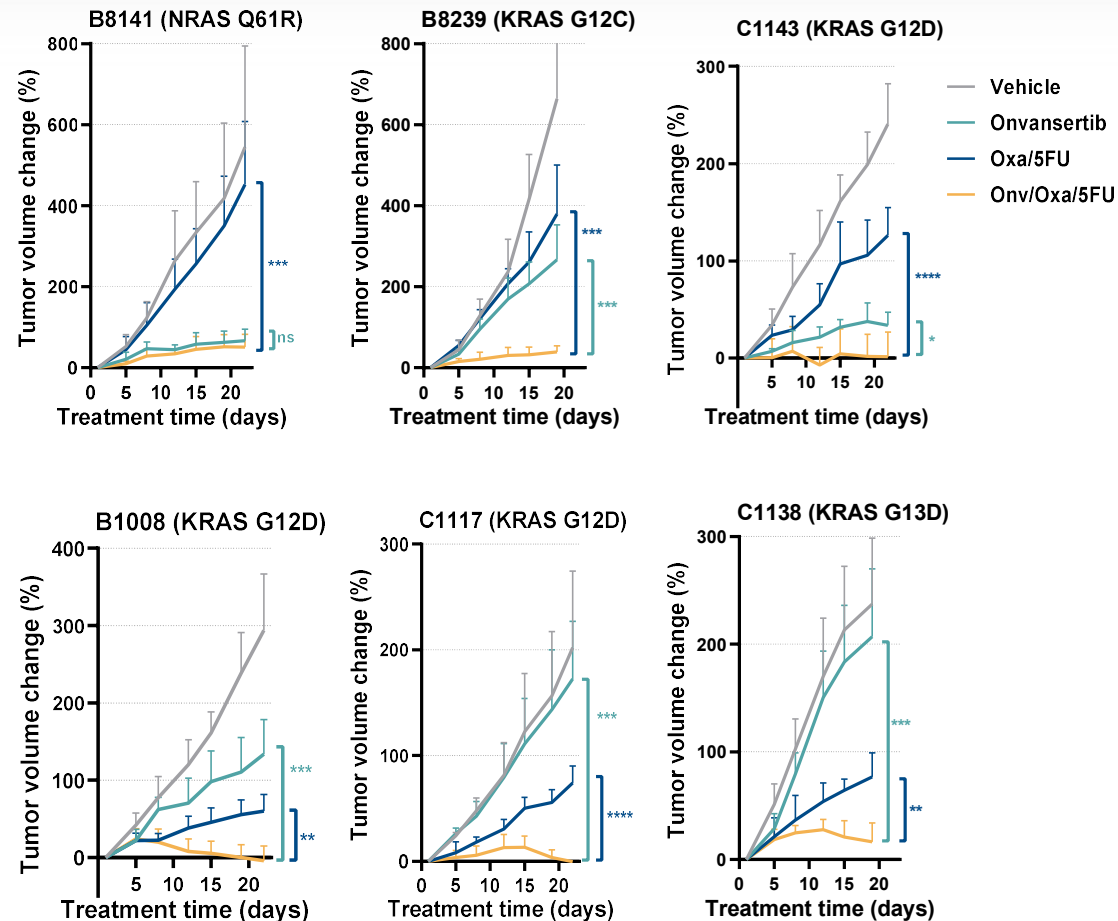
Conversely, the combination of onvansertib with oxaliplatin+5FU was efficacious in all 6 models, resulting in tumor stasis or tumor regression.

In 5 of the 6 models, the combination had significantly superior activity than the single agent treatments.

These data support the efficacy of onvansertib in combination with oxaliplatin+5FU in RAS-mutant CRC PDXs resistant or partially sensitive to oxaliplatin+5FU.

In collaboration with Dr. Kopetz (MD Anderson)

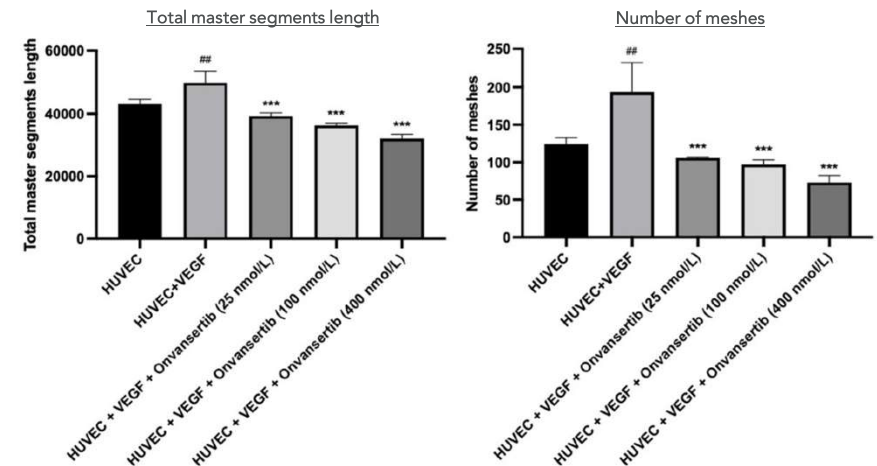
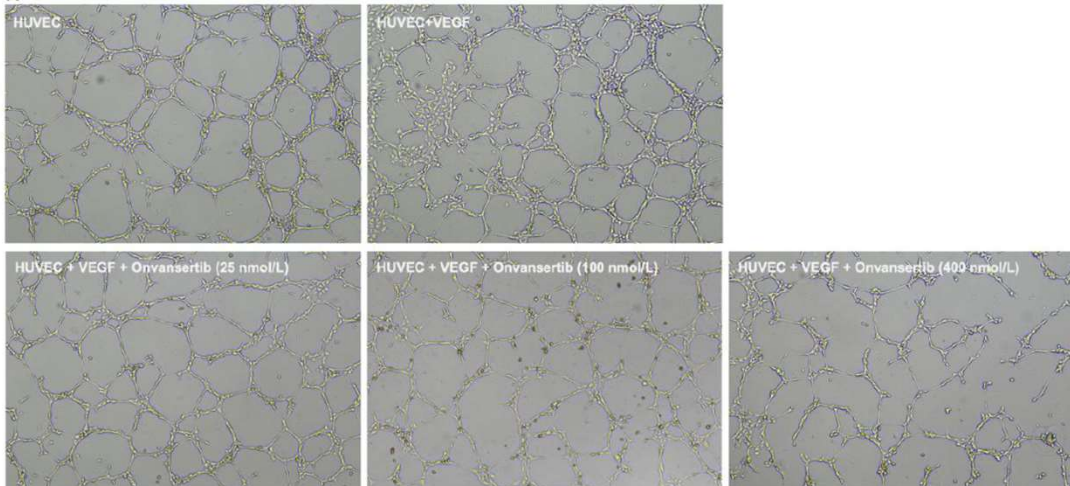
Dosing schedule: onvansertib 45 mg/kg daily; oxaliplatin 10mg/kg weekly; 5-FU 25mg/kg 5times/week for up to 21days. Mean + SD are represented. Unpaired t-test, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001, \*\*\*\*p<0.0001



# Onvansertib inhibits vascularization *in vitro*

Tube formation assay: HUVEC endothelial cells seeded onto a 3D extracellular matrix form tube-like structures upon stimulation with the angiogenic factor VEGFA, simulating the formation of new blood vessels

Treatment with onvansertib (25, 100 and 400nM) for 24h significantly reduced VEGFA-stimulated HUVECs tube formation in a dose-dependent manner, demonstrating that onvansertib inhibits angiogenesis *in vitro*



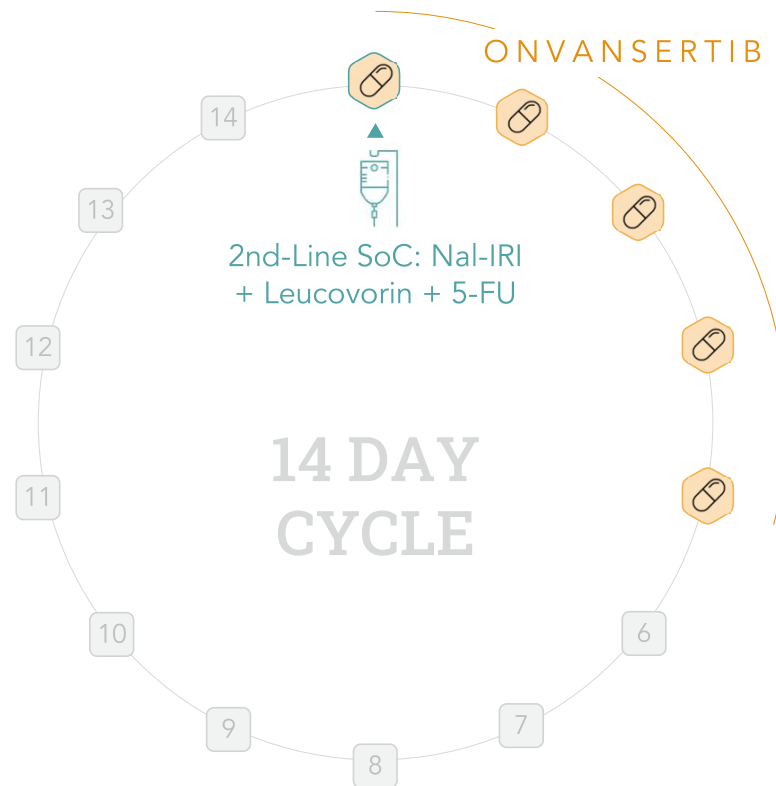


## Metastatic Pancreatic Adenocarcinoma (mPDAC)

# Our mPDAC Ph2 trial combines onvansertib with standard-of-care

## ENROLLMENT CRITERIA

Failed 1st Line  
Gemcitabine / Abraxane



## SINGLE ARM TRIAL

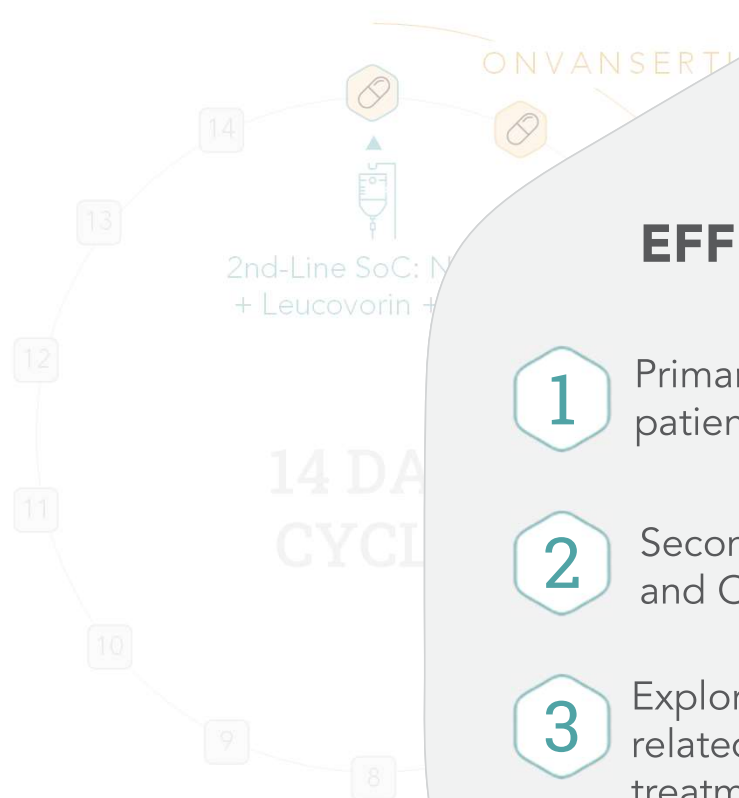
43 patients planned

Can we get a signal that  
onvansertib complements  
and improves SoC?

# The endpoints measure tumor response and duration of response

## ENROLLMENT CRITERIA

Failed 1st Line  
Gemcitabine / Abraxane



## EFFICACY ENDPOINTS

- 1 Primary: Objective Response Rate (ORR) in patients who receive  $\geq 28$ -days of treatment
- 2 Secondary: Duration of Response (DOR) and Overall Survival (OS)
- 3 Exploratory: Identification of biomarkers related to sensitivity and resistance to treatment using patient-derived organoids, blood samples, and archival tissue biopsies

mPDAC trial is designed to demonstrate onvansertib's efficacy vs SoC

## ENROLLMENT CRITERIA

HISTORICAL RESPONSE RATE\*

7.7% ORR

HISTORICAL mPFS\*

3.1 mo

ONVANSERTIB

PROOF OF CONCEPT CRITERIA

20% ORR

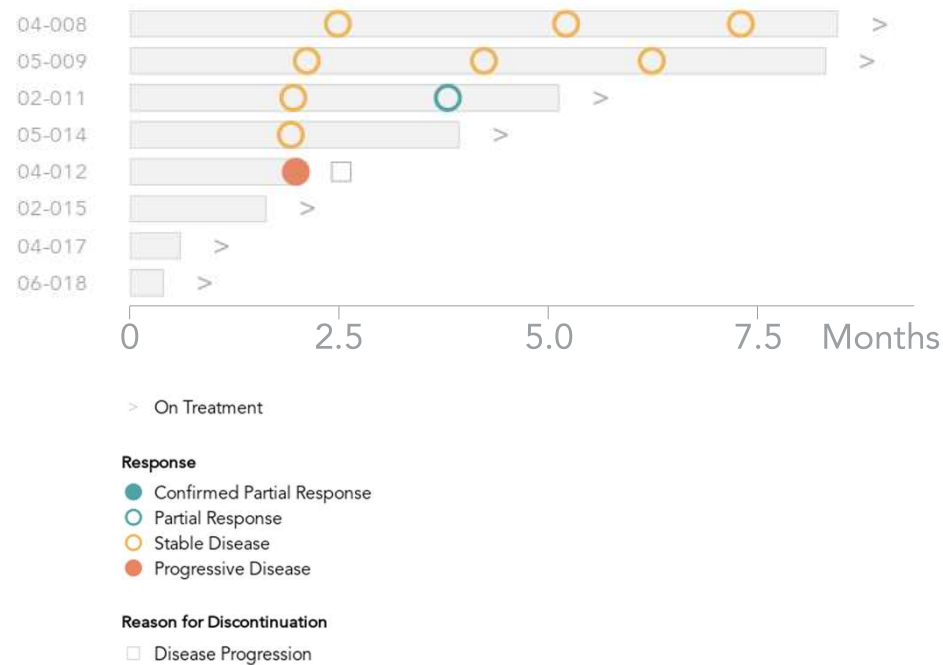
≥6 mo mPFS

\* Wang-Gillam A, Li C-P, Bodoky G, et al. Lancet 2016;387:545-57; Waters AM, Der CJ. Cold Spring Harb Perspect Med 2018;8(9).

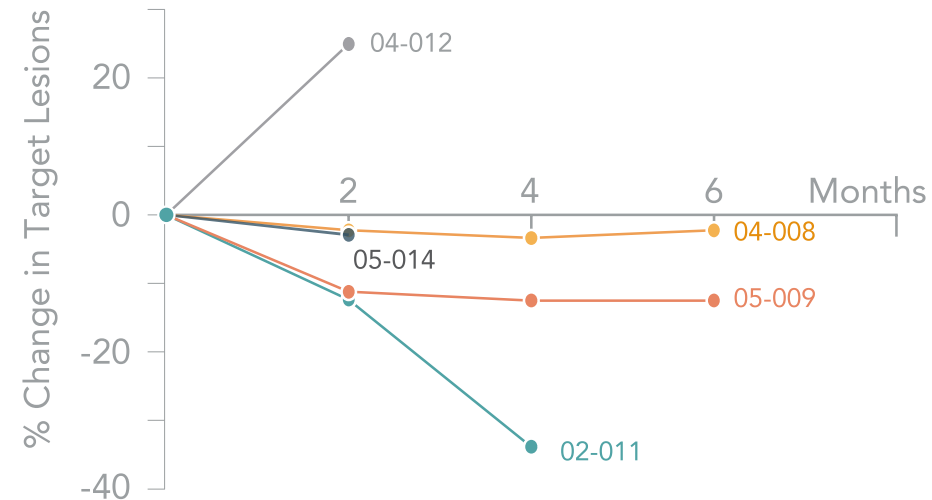


# Early data from our mPDAC trial data is encouraging

## Swimmer plot\* – as of August 30, 2022



## Change in tumor size from baseline\*



\* Swimmer and spider plots reflect interim data as of August 30, 2022 from an ongoing trial and unlocked database



## Investigator-Initiated Trial Small Cell Lung Cancer (SCLC)

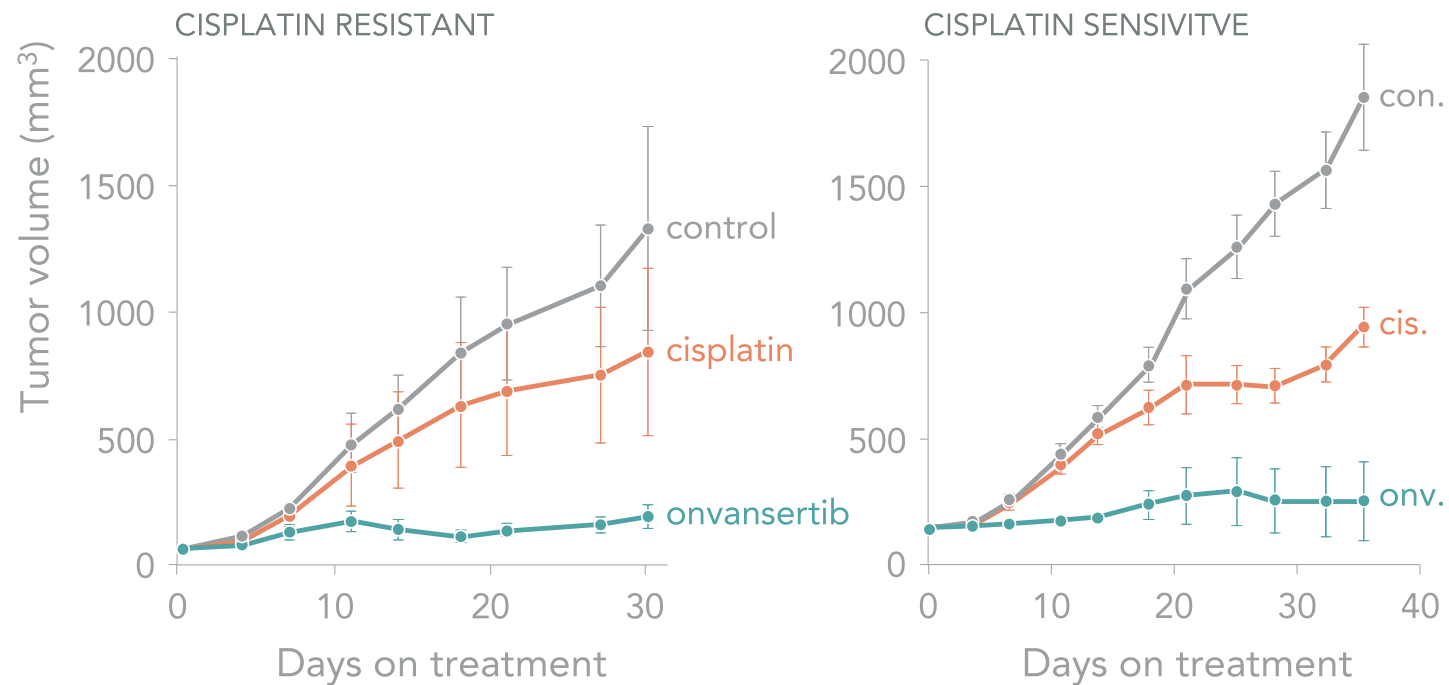
# Onvansertib demonstrates single-agent activity in SCLC

## TRIAL RATIONALE

Onvansertib monotherapy showed significant tumor growth inhibition against platinum-sensitive and -resistant models



## *In vivo* efficacy of onvansertib monotherapy (SCLC xenografts)\*



\* Mice were implanted with SCLC PDX and treated with vehicle, cisplatin 3mg/kg IP weekly, or onvansertib oral 60mg/kg 10 ON / 4 OFF

# This is the first trial to explore onvansertib monotherapy

## ENROLLMENT CRITERIA

Relapsed who have  
received  $\leq 2$  prior therapies

Single-arm trial  
Stage 1: N=15  
Stage 2: N=20

UPMC LIFE  
CHANGING  
MEDICINE

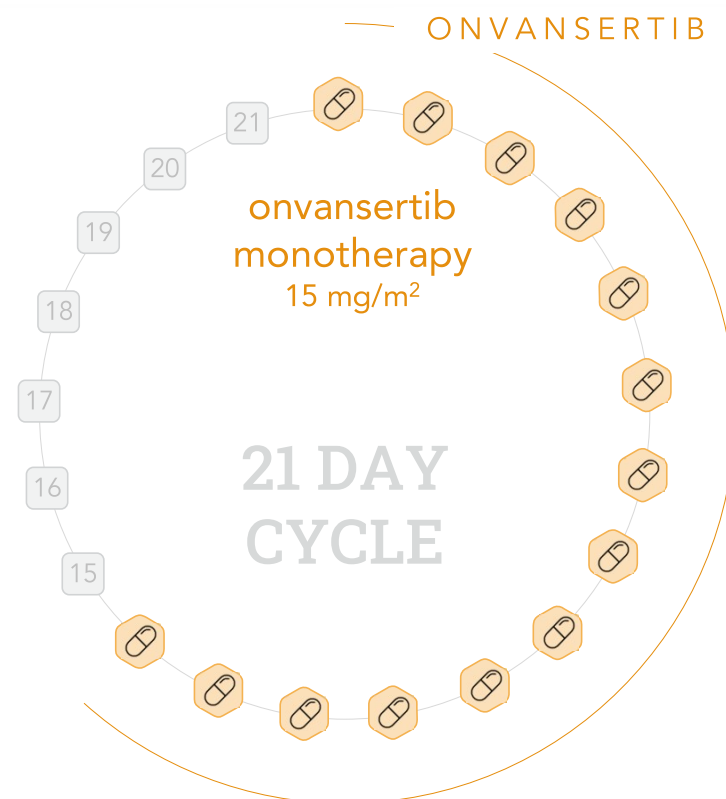


## PRIMARY ENDPOINT

Phase 2  
ORR (RECIST 1.1)

## SECONDARY ENDPOINTS

Phase 2  
Progression-Free Survival (PFS)  
Overall Survival (OS)



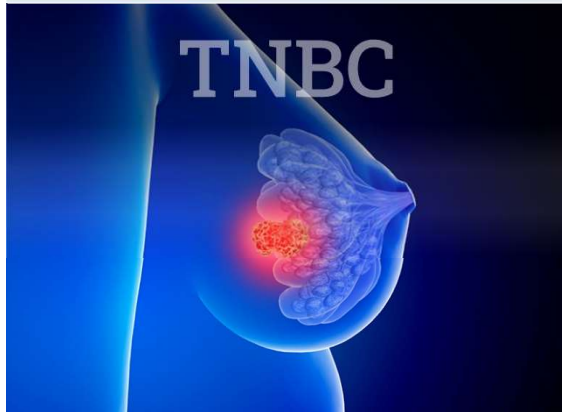


## Investigator-Initiated Trial Triple Negative Breast Cancer (TNBC)

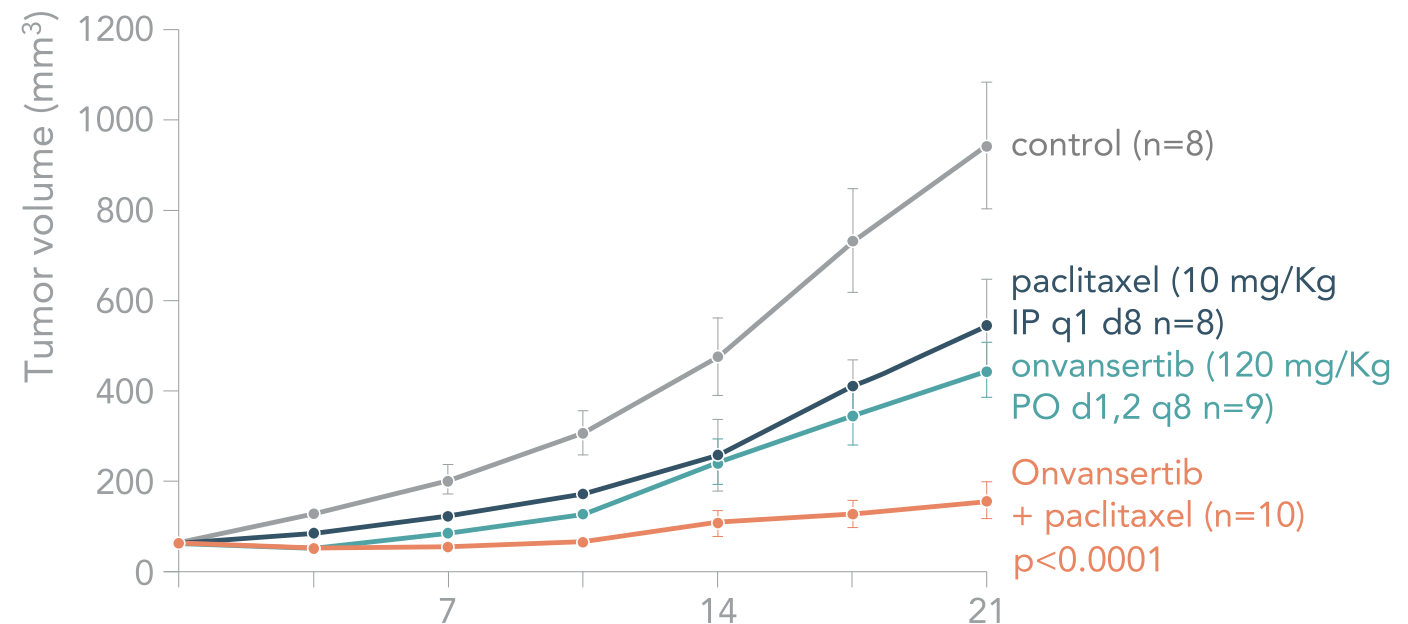
# Onvansertib + paclitaxel is superior to single agent therapy

## TRIAL RATIONALE

The combination of onvansertib + paclitaxel showed significant synergy



## *In vivo* efficacy of onvansertib in combination with paclitaxel Tp53-Mutant SUM159 xenografts\*



\* SUM159 cells were implanted in the mammary fat pad of NOD-scid-IL2 receptor gamma null female mice, and treatments began as follows when tumor volume reached 40 mm<sup>3</sup>: vehicle, onvansertib oral (PO) twice per week (days 1-2), paclitaxel intraperitoneally (IP) weekly (day 1), or the combination.

# This is the first trial to explore onvansertib + paclitaxel combination

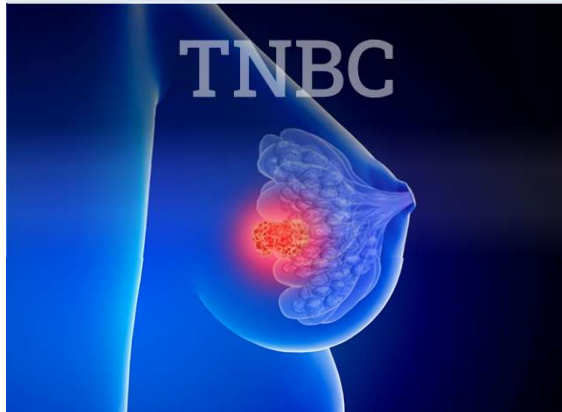
## ENROLLMENT CRITERIA

Metastatic TNBC relapsed or progressed

Single arm trial

Ph 1b: N=14–16

Ph 2: N=34



## PRIMARY ENDPOINTS

### Phase 1b

Safety, characterization of DLTs

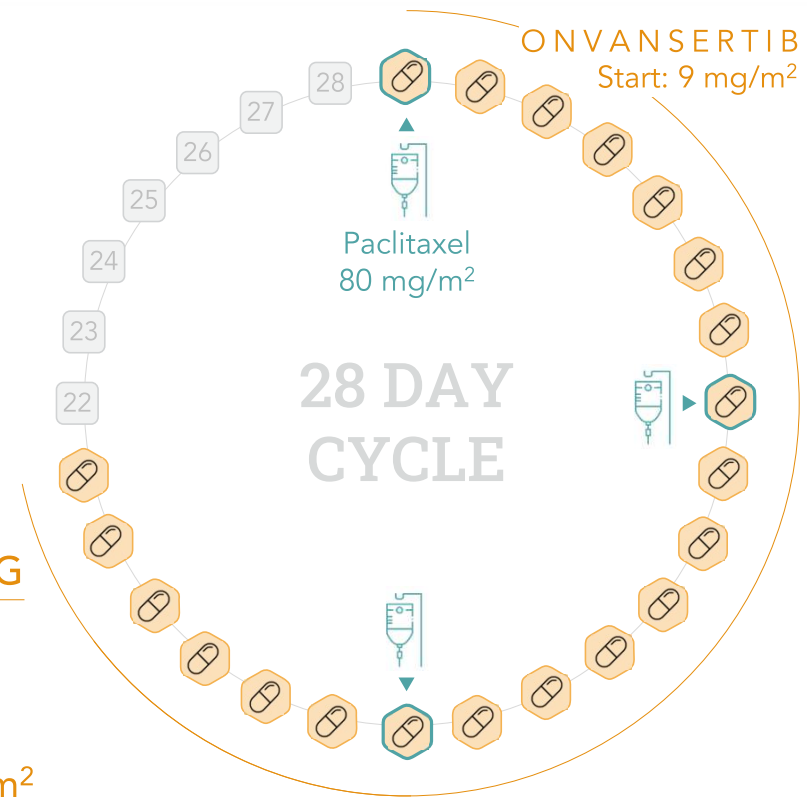
Determination of RP2D

### Phase 2

ORR (RECIST 1.1)

## ONVANSERTIB DOSING

- Escalation: 12 mg/m<sup>2</sup>
- Starting: 9 mg/m<sup>2</sup>
- De-escalation: 6 mg/m<sup>2</sup>

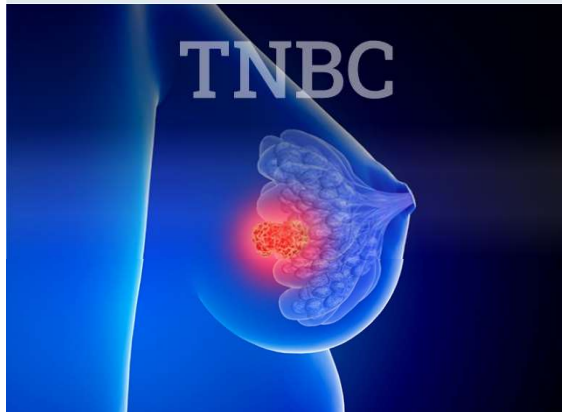


# This is the first trial to explore onvansertib + paclitaxel combination

## ENROLLMENT CRITERIA

Metastatic TNBC relapsed or progressed

Single arm trial  
Ph 1b: N=14–16  
Ph 2: N=34



## PRIMARY ENDPOINTS

Phase 1b  
Safety, characterization of DLTs  
Determination of RP2D

Phase 2  
ORR (RECIST 1.1)

## SECONDARY ENDPOINT

Phase 2  
Progression-Free Survival (PFS)

