Company Overview
The Onvansertib Opportunity

TURNING THE TIDE ON CANCER

MARCH 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.

Why invest in Cardiff Oncology?

Our Drug: Onvansertib

Highly selective and well-tolerated PLK1-inhibitor

WHAT Onvansertib has achieved	Robust clinical proof-of-concept results in Ph 1b/2 KRAS-mutated mCRC trial
WHERE Cardiff Oncology is going	Onvansertib has opportunity to become part of SOC in a wide range of cancer indications
WHY Onvansertib works	Multi-faceted tumor cell cycle inhibitor

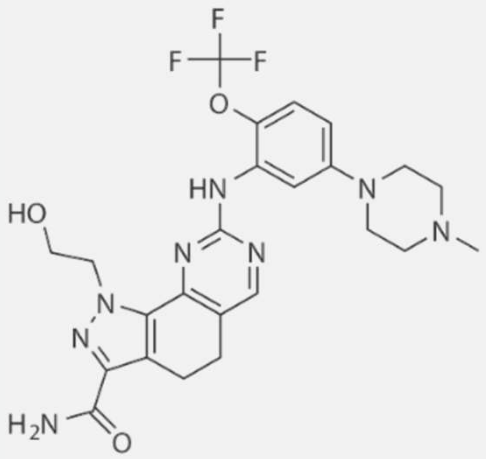
Onvansertib positions Cardiff Oncology to effectively target PLK1

Our Drug: Onvansertib

Highly selective and well-tolerated PLK1-inhibitor

PROPERTIES

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



SPECIFICITY

Exquisitely specific for PLK1

ENZYME	IC_{50} (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

Targeting PLK1 opens doors to large patient populations

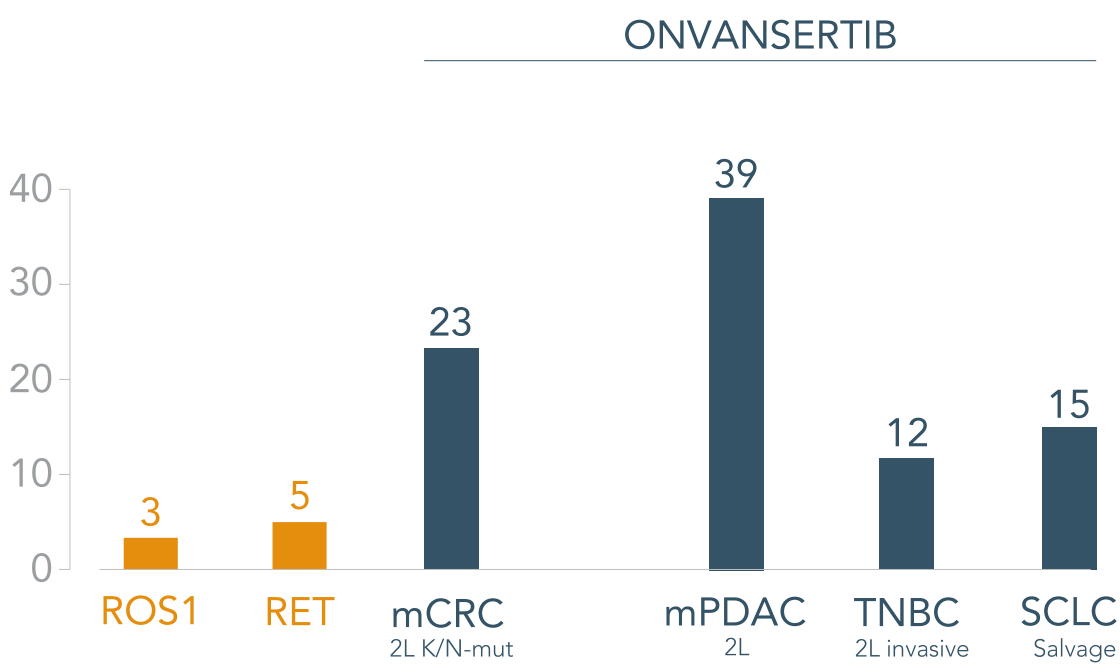
Targets with oncogenic alterations

- ROS1
- RET
- KRAS G12C
- EGFR
- TRK

Targets without oncogenic alterations

- **PLK1**
- PARP
- CDK4/6
- PD1/PDL1
- VEGF

Annual eligible US patients ('000s)*



*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.

Cardiff Oncology™

WHAT	Onvansertib has achieved
WHERE	Cardiff Oncology is going
WHY	Onvansertib works

Cardiff Oncology™

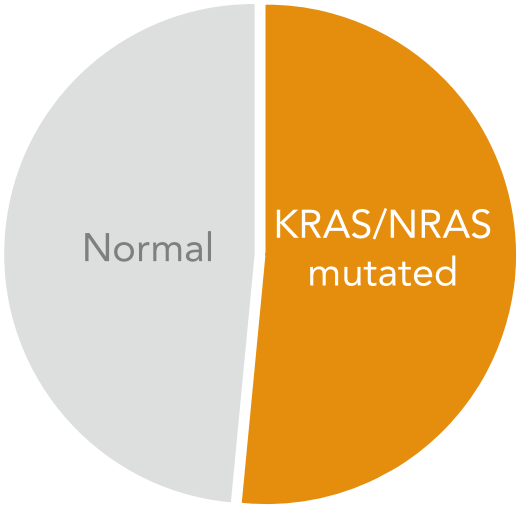
WHAT	Onvansertib has achieved
WHERE	Cardiff Oncology is going
WHY	Onvansertib works

There are no targeted therapies available for KRAS/NRAS mutations

Normal	1st LINE	2nd LINE
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab
Targeted	+ EGFR inhibitor	NONE

Mutated		
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab
Targeted	**NONE**	**NONE**

K/NRAS mut mCRC is approx. half the mCRC population[1]



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

The prognosis for second-line mCRC patients is poor

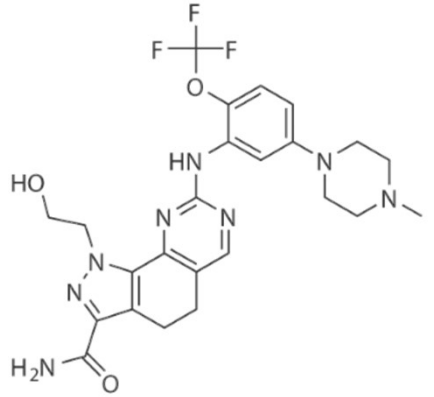
	1st LINE	2nd LINE
Normal		
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab
Targeted	+ EGFR inhibitor	NONE
Mutated		
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab
Targeted	NONE	NONE

HISTORICAL* ORR	
5%	2006 – 2008
11.4%	2000 – 2013
13%	2015 – 2017

* 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. mCRC: metastatic colorectal cancer

Adding onvansertib to SoC could address the unmet need

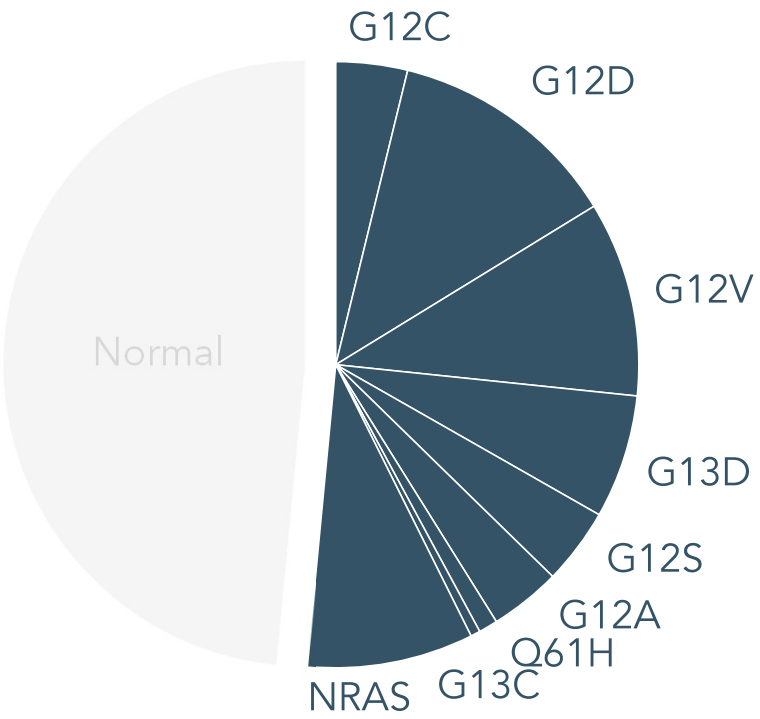
	1st LINE	2nd LINE
Normal		
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab
Targeted	+ EGFR inhibitor	NONE
Mutated		
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab
Targeted	NONE	ONVANSERTIB



◀ Onvansertib has the potential to fill this gap

Onvansertib is positioned to address gaps in KRAS-mutated mCRC

KRAS/NRAS Mutations in mCRC[1]



MOA

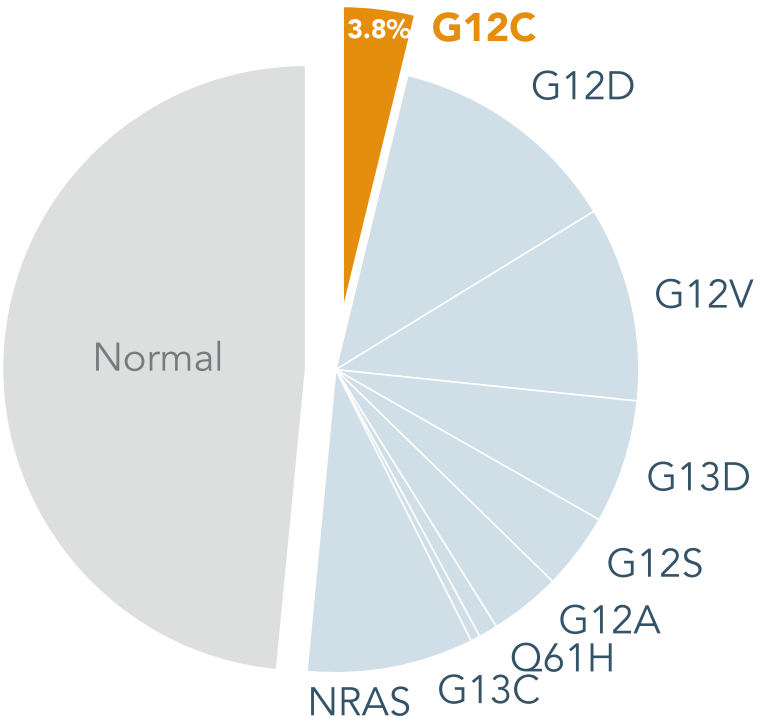
In KRAS-mutated mCRC, onversertib has two mechanisms of action

1. Synthetic lethality in KRAS mutants
2. Synergy with 2nd-line SoC

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

Gaps in KRAS-mutated mCRC therapies leave a significant unmet need

KRAS/NRAS Mutations in mCRC[1]

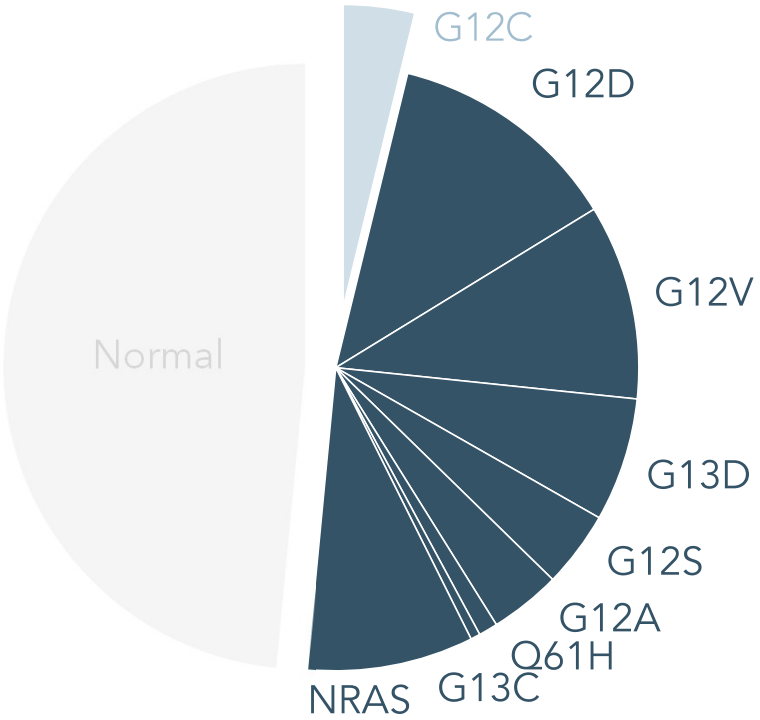


Investigational therapies (Amgen; Mirati) address the G12C KRAS mutation ***only***

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

Gaps in KRAS-mutated mCRC therapies leave a significant unmet need

KRAS/NRAS Mutations in mCRC[1]



93%

of patients with KRAS/NRAS mutations miss targeted therapy

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

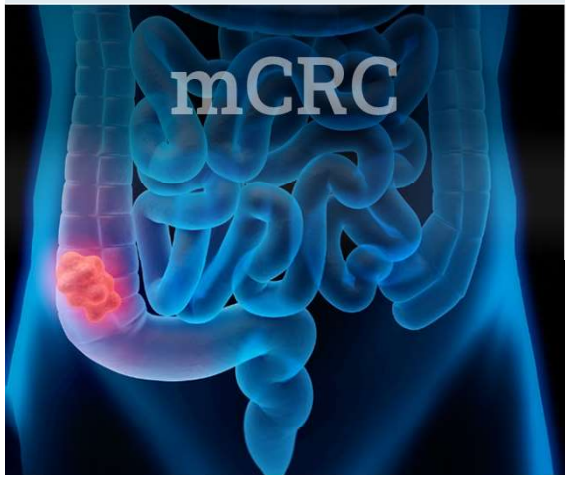
Our Ph1b/2 trial combined onvansertib with the current SoC

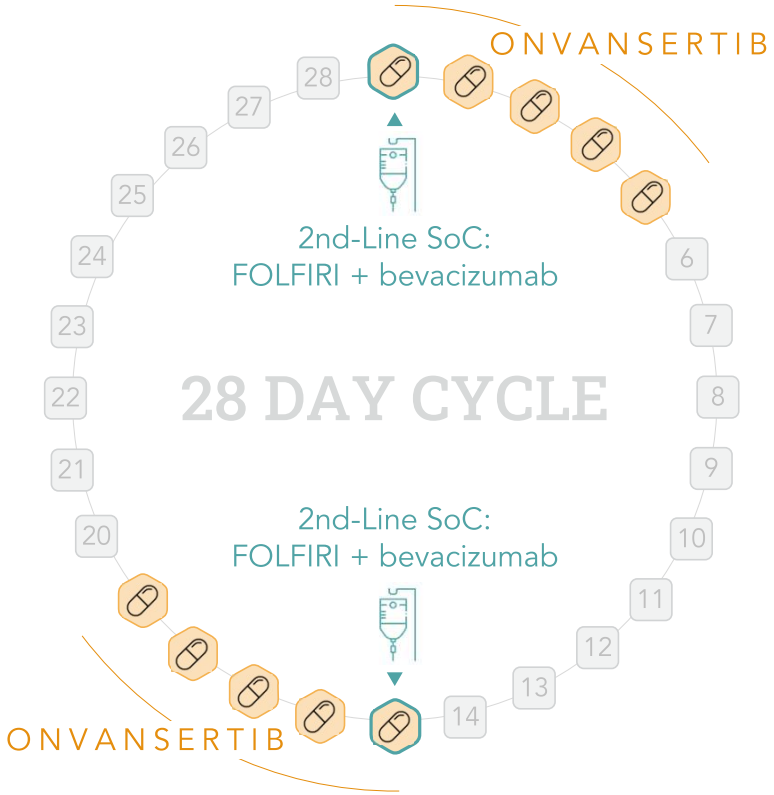
ENROLLMENT CRITERIA

2nd line mCRC

KRAS+

Unresectable





SINGLE ARM TRIAL

N=50 (48 evaluable)

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

Our Ph1b/2 trial assessed safety, efficacy and response biomarker

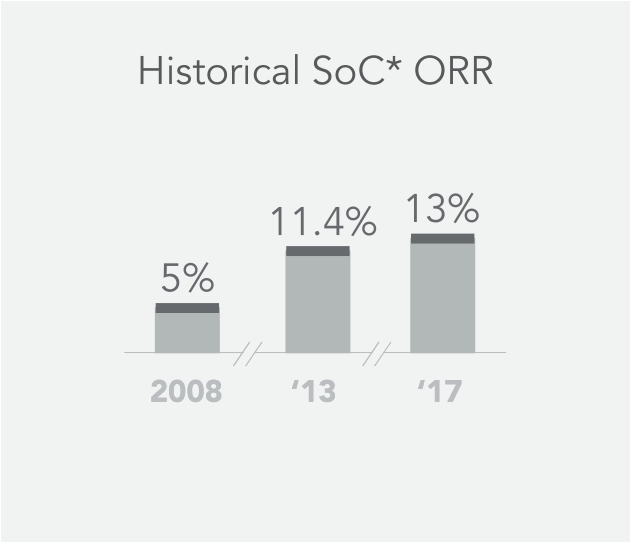
ENROLLMENT CRITERIA

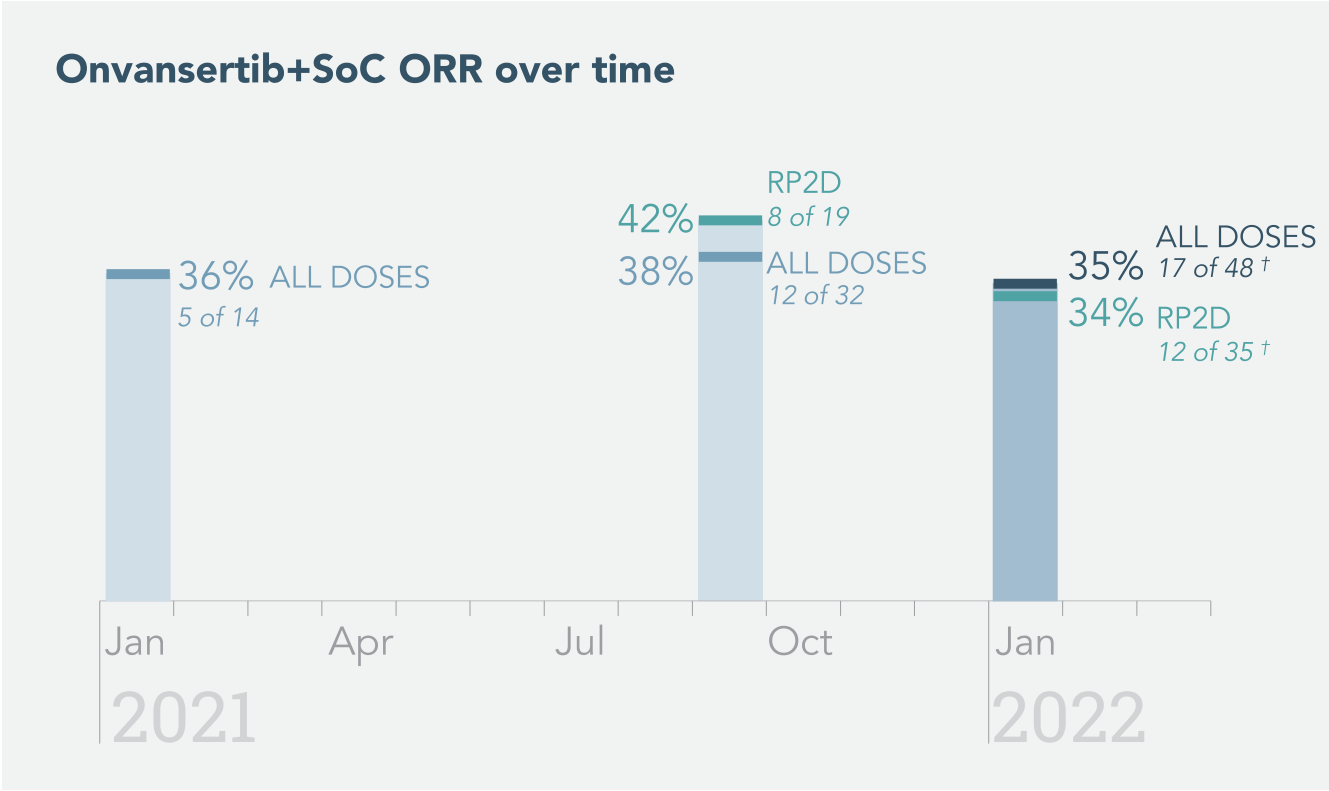
- 2nd line mCRC
- KRAS+
- Unresectable

EFFICACY ENDPOINTS

1. Primary: Objective Response Rate (ORR) per RECIST v1.1 in patients who receive ≥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

Objective Response Rate for mCRC trial exceeds SoC over time



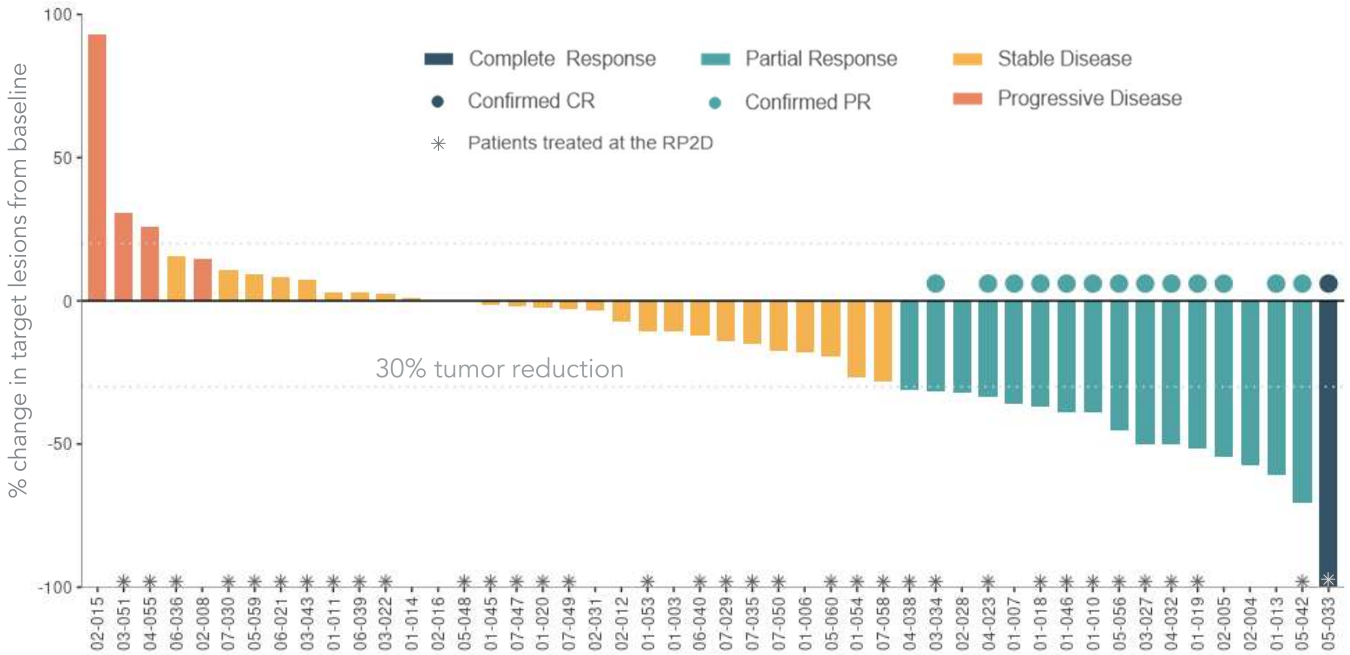


* 2008: Bennouna et al., Lancet Oncol 2013; 14: 29–37; 2013: Giessen et al., Acta Oncologica, 2015, 54: 187-193; 2017: Cremolini et al., Lancet Oncol 2020, 21: 497–507; and Antoniotti et al., Correspondence Lancet Oncol June 2020. SoC: Standard-of-care

† ORR data are interim data from an ongoing trial and unlocked database

Patients achieved a strong, durable response with onvansertib + SoC

Best Radiographic Response* – all doses (as of July 25, 2022)



	All Doses	RP2D
Objective Response Rate* (CR + PR)	35% (17/48)	34% (12/35)
Disease Control Rate (CR + PR + SD)	92% (44/48)	94% (33/35)

Durability

Median Duration of Response	11.7 months	12.5 months

* Radiographic response determined per RECIST 1.1. Waterfall plot and table reflect interim data as of July 25, 2022 from an ongoing trial and unlocked database

We observe initial PRs up to eight months on treatment

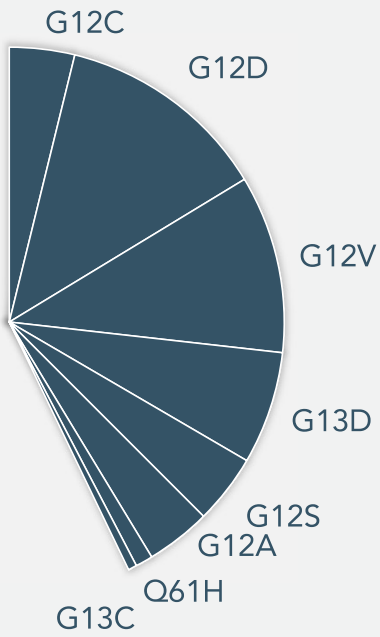
Swimmer plot* – all doses (as of July 25, 2022)

Evaluable Patients – all doses	48
Time of initial PR	
8-week scan	8
16-week scan	3
24-week scan	5
32-week scan	1

* Swimmer plot / table reflect interim data as of July 25, 2022 from an ongoing trial and unlocked database

Patients achieved responses across several KRAS mutations

Frequency of Common KRAS Mutations in mCRC[1]

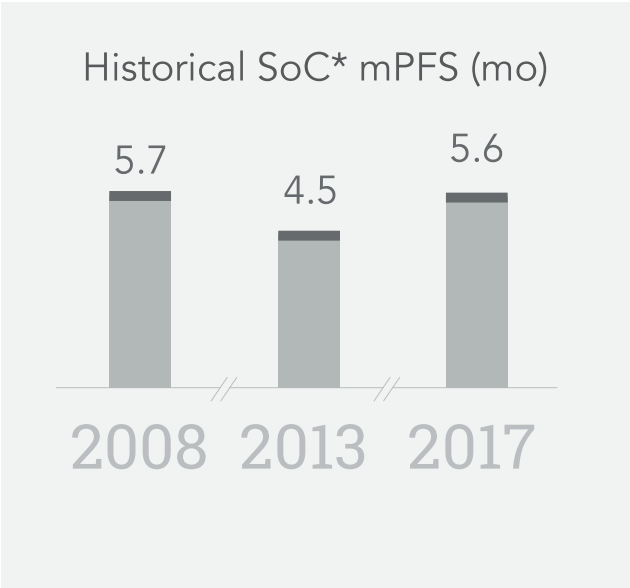


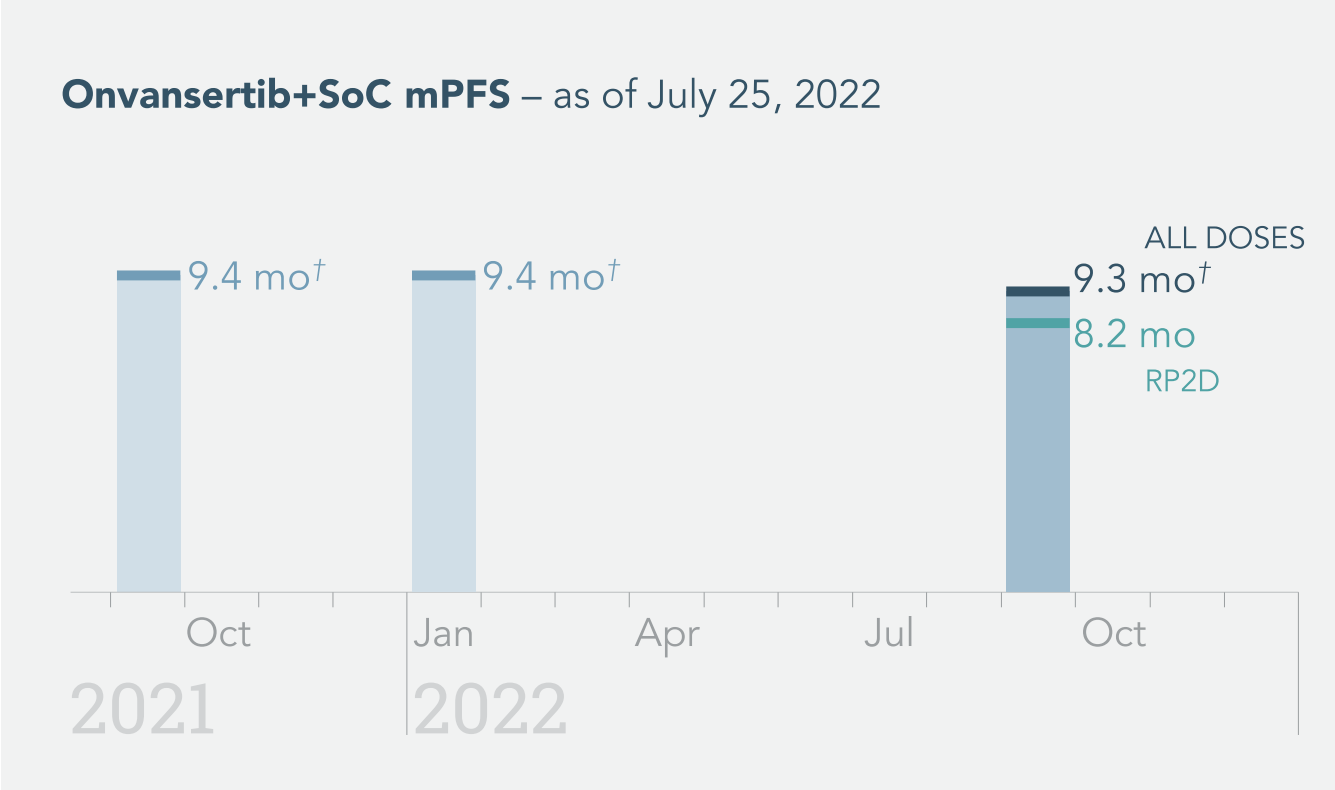
Onvansertib responses across KRAS mutations (as of July 25, 2022)

KRAS Variant	CR+PR	SD	PD	Total
G12D	6	7	1	14
G12V	1	8	1	10
G13D	4	3		7
G12A	3	3		6
A146T	1	2		3
G12S		3	1	4
G12C	1	1	1	3
Q61H	1			1
Total	17	27	4	48

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

Progression Free Survival for mCRC trial exceeds SoC over time

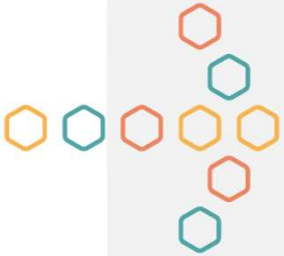




† Onvansertib mPFS are interim data from an ongoing trial and unlocked database

* 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. SoC: Standard-of-care. mPFS: median progression free survival

Cardiff Oncology™



WHAT	Onvansertib has achieved
WHERE	Cardiff Oncology is going
WHY	Onvansertib works

Our clinical development program supports our key goals

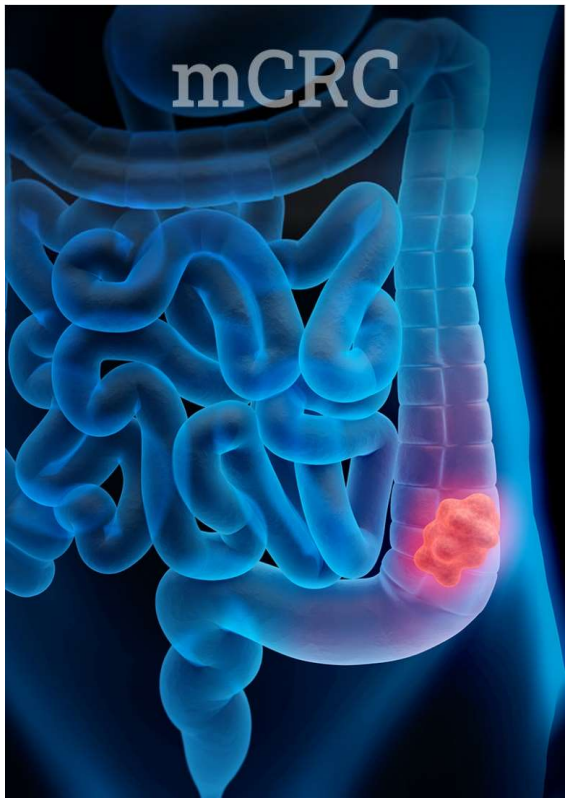
2023				2024				2025	
Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2

GOALS

1 Validate prior mCRC data with a randomized trial

2 Demonstrate clinical POC in additional indications

We approach our current trial, a randomized Ph2, with clear objectives



ONSEMBLE
mCRC Clinical Trial

DEMONSTRATE onvansertib's contribution to SoC

CONFIRM optimal dosing

POSITION for possible accelerated approval opportunity

OPERATE with capital efficiency

Our ONSEMBLE Ph2 trial is designed to demonstrate efficacy

ENROLLMENT CRITERIA

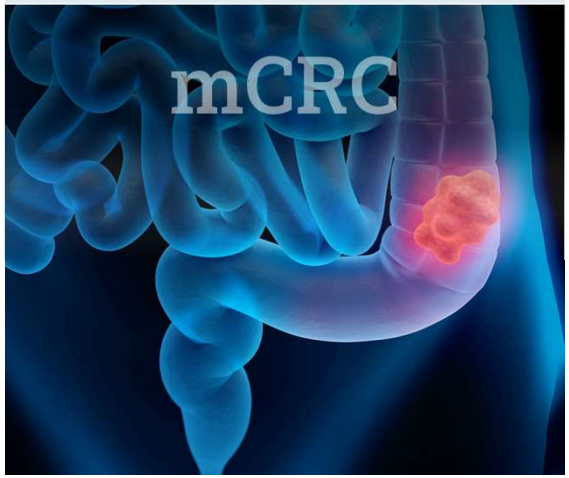
2nd line mCRC

KRAS+/NRAS+

Unresectable

R

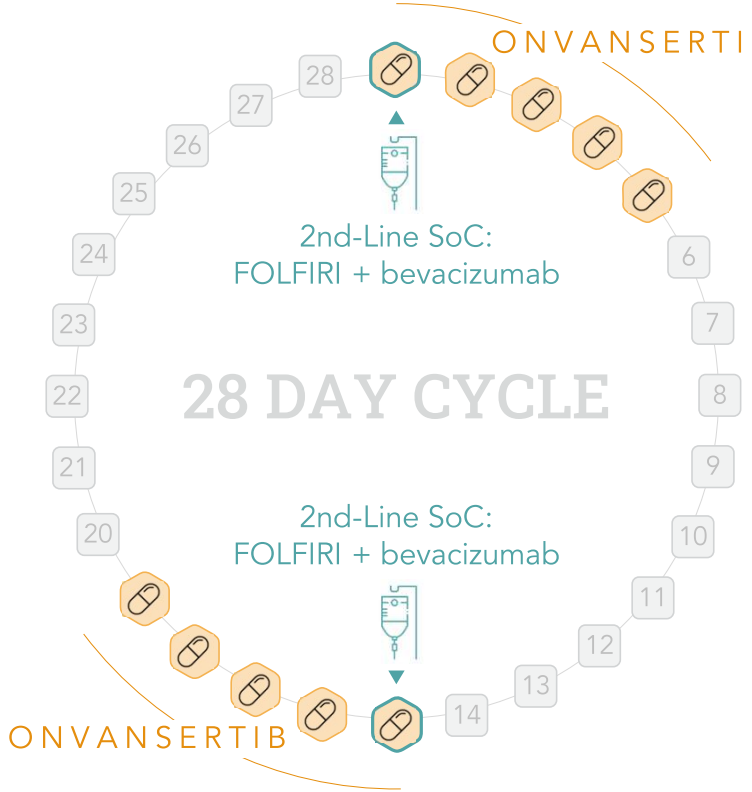
N=150
1:1:1



SoC (FOLFIRI + Bev)

SoC + onvansertib (20mg)

SoC + onvansertib (30mg)



Our ONSEMBLE Ph2 trial is designed to demonstrate efficacy

ENROLLMENT CRITERIA

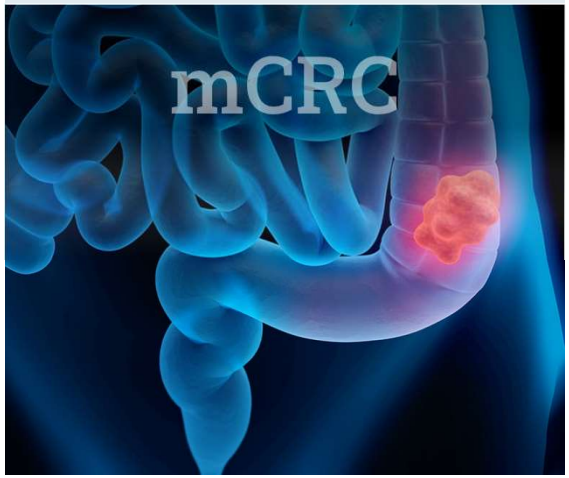
2nd line mCRC

KRAS+/NRAS+

Unresectable

R

N=150
1:1:1



ENDPOINTS

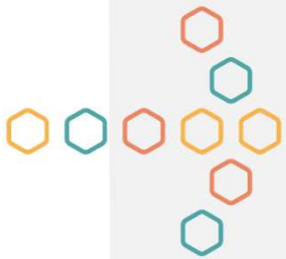
Primary	Objective Response Rate: CR + PR
Key Secondary	Progression-Free Survival
Other Secondary	Disease Control Rate: CR + PR + SD Duration of Response: DoR Overall Survival: OS Reduced MAF association with ORR, PFS, DCR, DoR, OS

ONSEMBLE Stats

Our pipeline opens many attractive opportunities for onvansertib

	Combination with:	Preclinical	Ph1/2	Ph2/3	Status	
mCRC	FOLFIRI/bev			*randomized*	Enrolling	ONSEMBLE mCRC Clinical Trial
mCRC	FOLFIRI/bev		*single-arm*		Enrolled	
mPDAC	Onivyde/5-FU				Enrolling	
Ovarian	PARP inhibitors				Evaluating	

Investigator-initiated trials						Investigator
TNBC	Paclitaxel				Enrolling	Dana-Farber Cancer Institute
SCLC	None (monotherapy)				Enrolling	UPMC LIFE CHANGING MEDICINE



WHAT	Onvansertib has achieved
WHERE	Cardiff Oncology is going
WHY	Onvansertib works

To date, toxicity has prevented regulatory approval of PLK1 inhibitors

Onvansertib's safety profile

eclipses that of its most promising predecessor

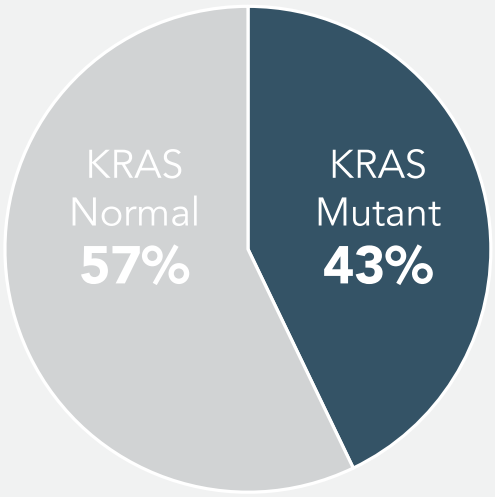
	Onvansertib	Volasertib[1]
Selectivity for PLK1	Exclusive for PLK1	Pan-inhibitor for PLK1, 2, and 3
Dosing	Oral	IV
Half-life	1 day	~5 days
Safety and tolerability	Well tolerated in ~200 patients	Pivotal trial suspended at 371 patients: toxicity

1. Boehringer Ingelheim was developing volasertib plus LDAC for the treatment of AML which did not meet the primary endpoint of ORR (EHA 2016). The data showed an unfavorable overall survival trend with the safety profile of volasertib plus LDAC considered as the main reason. Schoffski et al; European Journal of Cancer 48(2012); 179-186

Onvansertib's PLK1 inhibition is a two-pronged attack of tumor cells

KRAS HYPERSENSITIVITY[1]

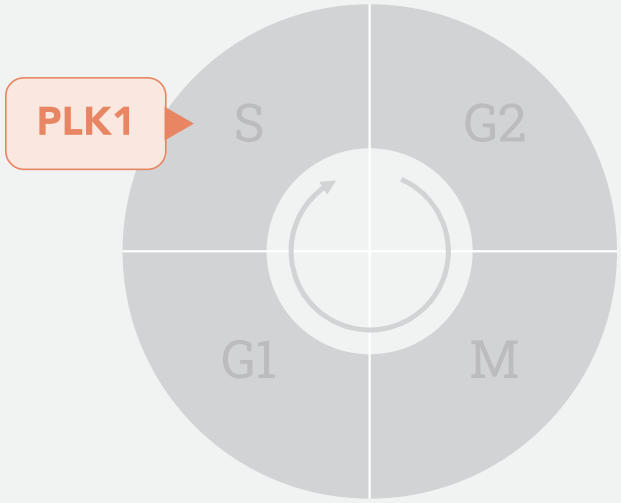
Cells with KRAS mutation are hypersensitive to inhibition of PLK1



MOA 1

SYNERGY WITH CHEMO

Inhibiting PLK1 increases the efficacy of chemotherapy drugs



MOA 2

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

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MOA 1

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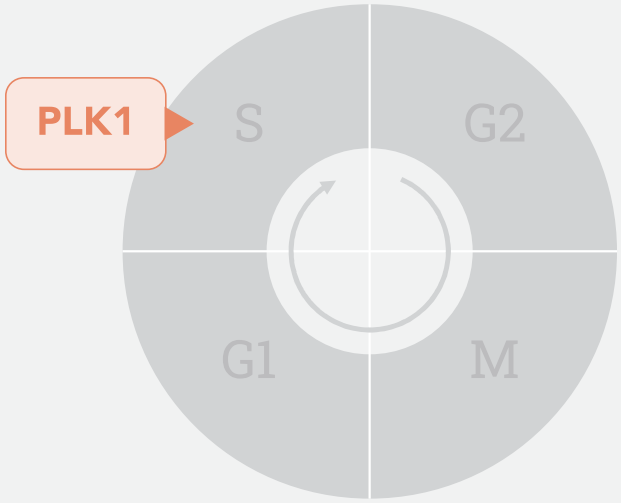
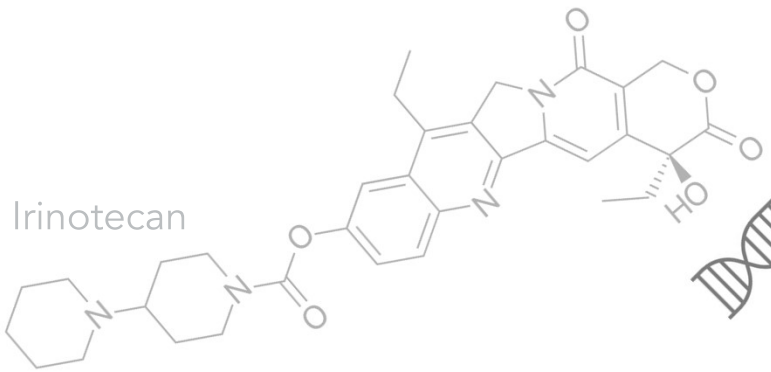


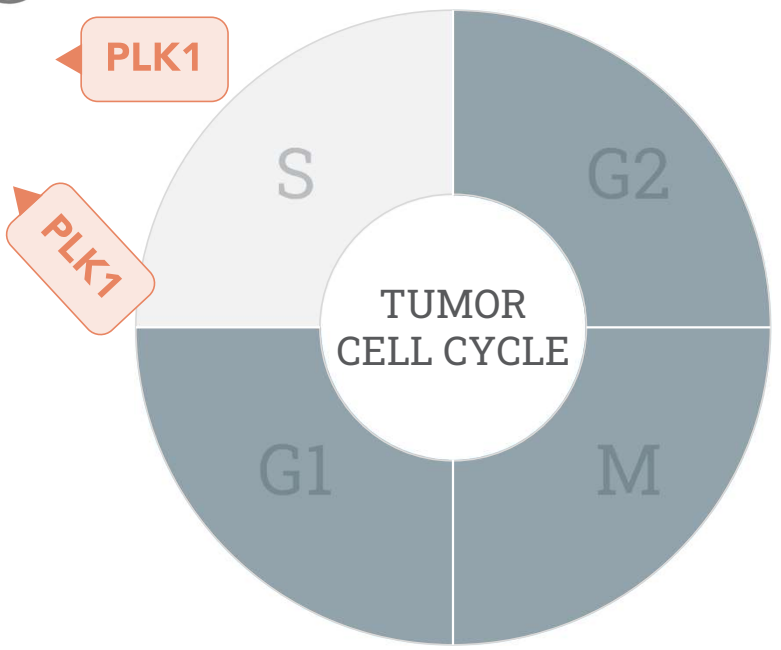
MOA 2

Chemotherapy drugs damage tumor DNA to prevent cell proliferation

DNA Damaging Agent

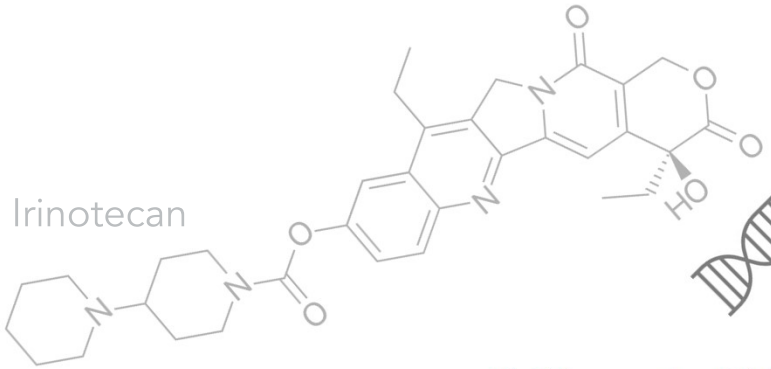


Irinotecan



PLK1's repair of DNA interferes with chemotherapy drugs

DNA Damaging Agent



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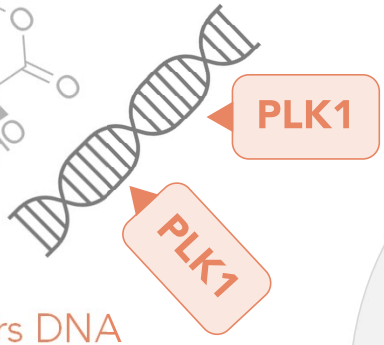
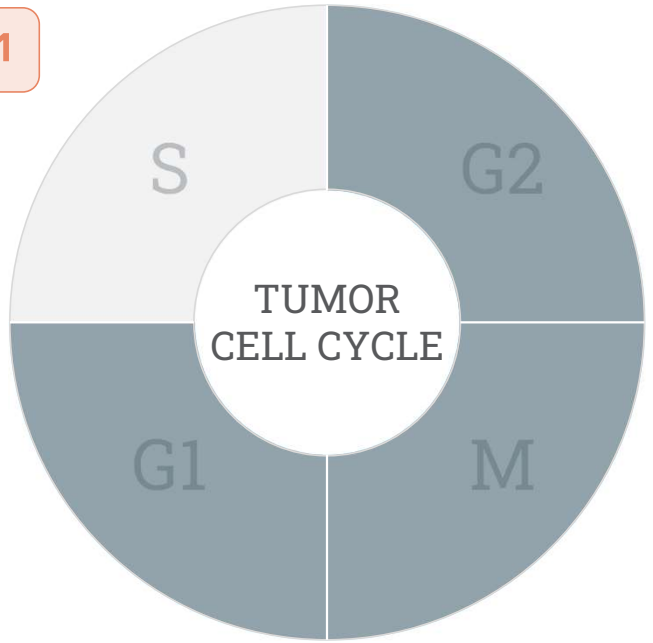


PLK1 repairs DNA
enabling progression to G2

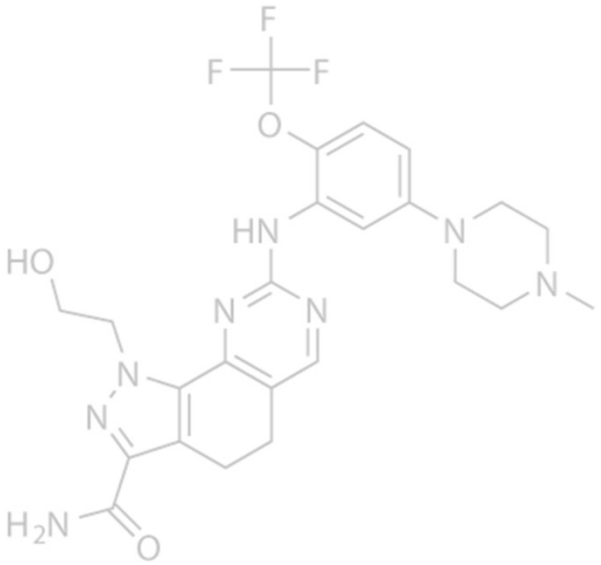
DNA REPLICATION PHASE

CELL GROWTH PHASE

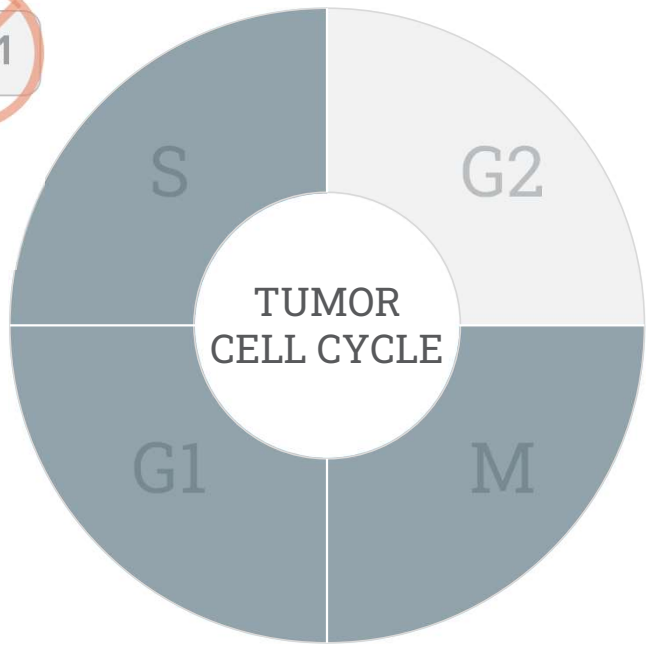


Inhibiting PLK1 prevents DNA repair and halts the cell cycle

Onvansertib inhibits PLK1 preventing DNA repair

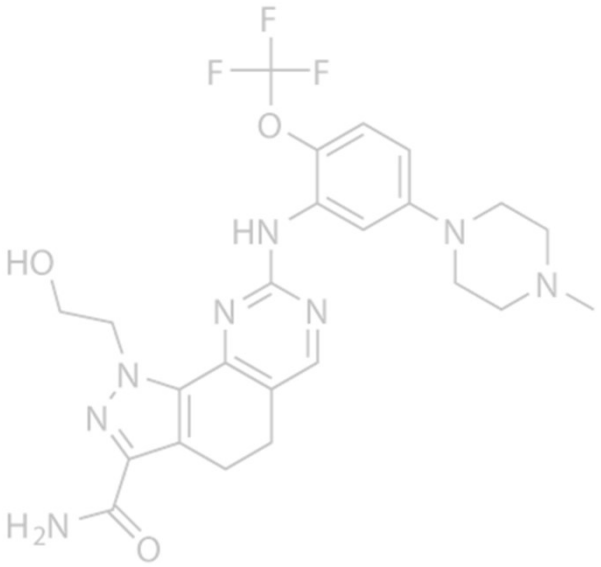


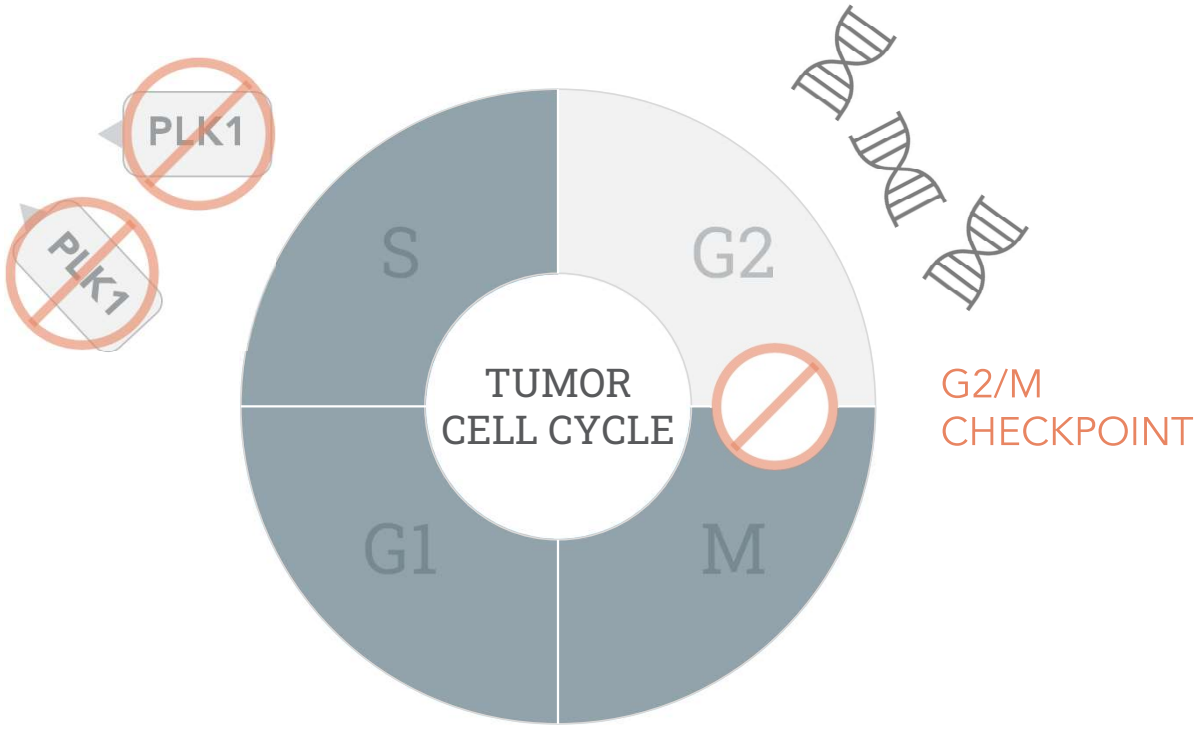
CELL GROWTH PHASE



Inhibiting PLK1 prevents DNA repair and halts the cell cycle

Onvansertib inhibits PLK1 preventing DNA repair and progression from G2 to M





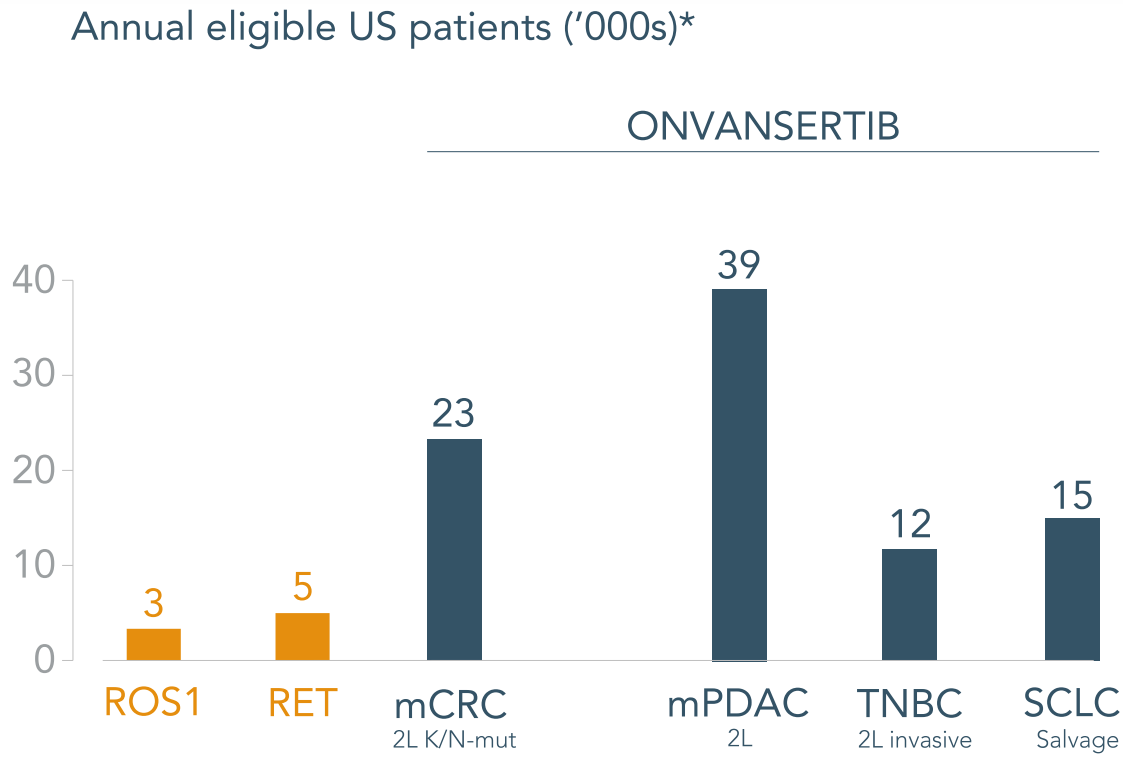
Targeting PLK1 opens doors to large patient populations

Targets with oncogenic alterations

- ROS1
- RET
- KRAS G12C
- EGFR
- TRK

Targets without oncogenic alterations

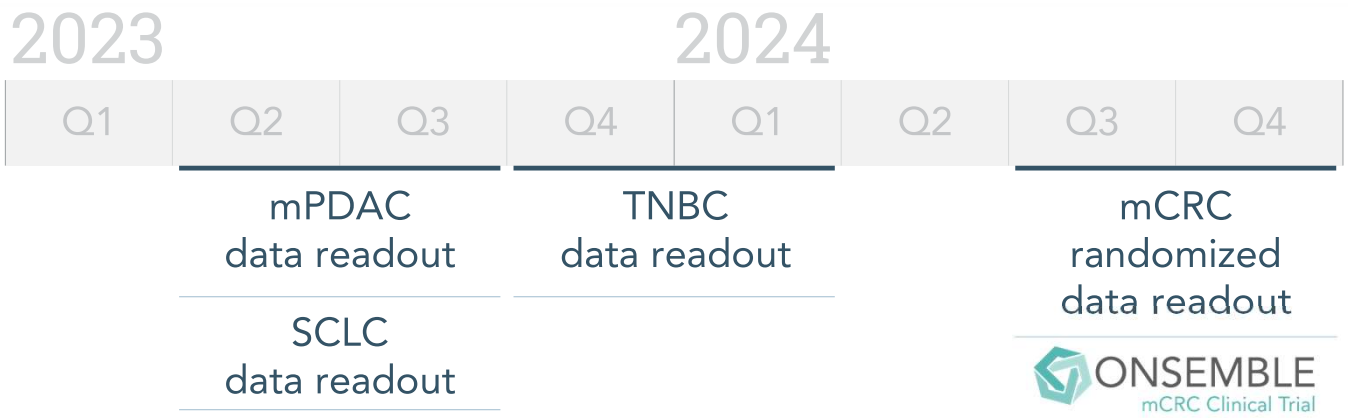
- PLK1
- PARP
- CDK4/6
- PD1/PDL1
- VEGF

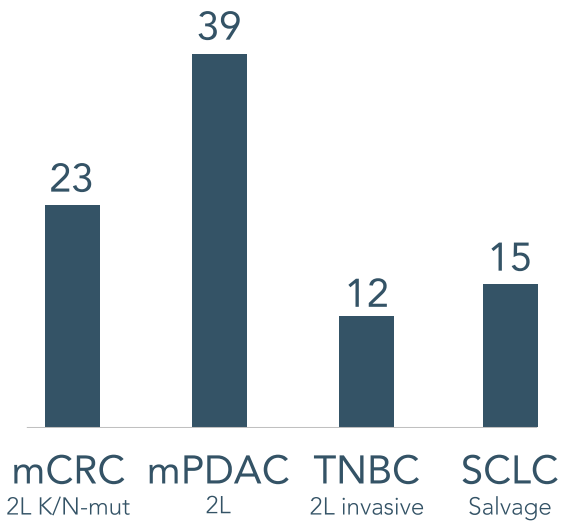


*ROS1 estimated eligible patients presented in Turning Point Therapeutics' corporate presentation May 2022 slide 6 (NSCLC disease incidence in the US of 140k of which 2% of patients harbor ROS1 translocation). RET estimated eligible patients presented in Loxo Oncology's corporate presentation January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

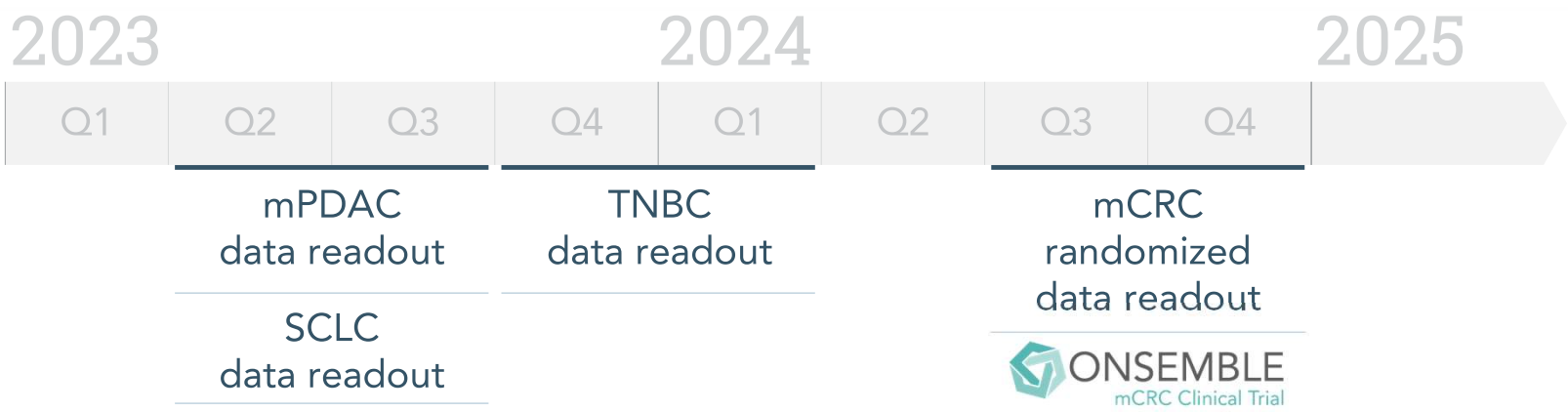
mCRC estimated population includes 2nd line, KRAS- and NRAS-mutated cancers. mPDAC estimated population includes 2nd line PDAC patients. TNBC estimated population includes invasive, 2nd line TNBC patients. SCLC estimated population includes SCLC salvage patients.

We have multiple important catalysts over the next two years





At December 31, 2022, our financial position is robust



December 31, 2022 cash and investments*	$105.3M
Net cash used in Operating Activities* (Rolling two-quarter period ending Dec. 31, 2022)	$16.9M

* Financial information above is derived from our audited financials in Form 10K filed on 3/2/23 and unaudited financials in Form 10Q filed on 11/3/22.

We believe Pfizer relationship validates the opportunity for onvansertib

Pfizer BREAKTHROUGH GROWTH INITIATIVE

- Onvansertib program validation
- Scientific Advisory Board expertise: Adam Schayowitz, PhD
- Financial investment

SUMMARY TERMS

Announced November 18, 2021

- Pfizer invested a total of $15M at $6.22 per share (a 19% premium over prior closing price)
- Right of First Access:
  Pfizer sees onvansertib data 2 days before release

KRAS-Mutated Metastatic Colorectal Cancer (mCRC)

Summary of onvansertib mCRC Ph1b/2 trial data over time

	ASCO GI Jan 2021	KOL Event Sept 2021		Investor Webcast Jan 2022		Investor Webcast Sept 2022	
Data Cutoff Date	Nov 1, 2020*	July 2, 2021*		Dec 3, 2021*		July 25, 2022*	
	All Doses	All Doses	RP2D	All Doses	RP2D	All Doses	RP2D
Evaluable Patients	14	32	19	48	35	48	35
ORR (CR+PR)	36% (5)	38% (12)	42% (8)	35% (17)	34% (12)	35% (17)	34% (12)
Confirmed CR/PRs	29% (4)	31% (10)	37% (7)	27% (13)	29% (10)	29% (14)	31% (11)
Duration of Response						11.7 mos	12.5 mos
mPFS		9.4 mos		9.4 mos		9.3 mos	8.2 mos
Disease control rate (CR+PR+SD)	86% (12)	94% (30)	100% (19)	92% (44)	94% (33)	92% (44)	94% (33)

* Data releases include certain follow up data and reflect interim data from an ongoing trial and unlocked database.

Onvansertib in combination with FOLFIRI-bev is well-tolerated

No major/unexpected toxicities

- Of all TEAEs, only 11% (84/788) were G3/G4
- 7 patients had a total of 11 G4 adverse events:
  - Neutropenia (n=7); Decreased WBC (n=2); Neutropenic fever (n=1); Hyperphosphatemia (n=1)
- Discontinuation of the 5-FU bolus + use of growth factors ameliorated the severity of neutropenia observed

	GRADE				
TEAEs*	1	2	3	4	All
Neutropenia	1	13	15	6	35
Fatigue	15	15	3	0	33
Nausea	24	7	2	0	33
Diarrhea	15	7	2	0	24
Abdominal Pain	13	7	1	0	21
Mucositis	11	6	2	0	19
Alopecia	17	2	0	0	19
WBC Decrease	6	9	2	1	18
Platelet Count Decrease	10	4	1	0	15
Hypertension	2	8	5	0	15

	GRADE				
TEAEs*	1	2	3	4	All
Anemia	9	4	1	0	14
Vomiting	9	3	1	0	13
Musculoskeletal Pain†	11	1	0	0	12
Infection†	3	4	4	0	11
Hemorrhage†	8	0	1	0	9
Headache	7	0	0	0	7
Neuropathy	5	2	0	0	7
GERD	7	0	0	0	7
ALT Increase	4	0	1	0	5

* Data are interim as of July 25, 2022 from an ongoing trial and unlocked database. N: number of patients (total N=50); 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

† Musculoskeletal pain, infection and hemorrhage are pooled terms

Endpoints measure tumor response and decrease in KRAS burden

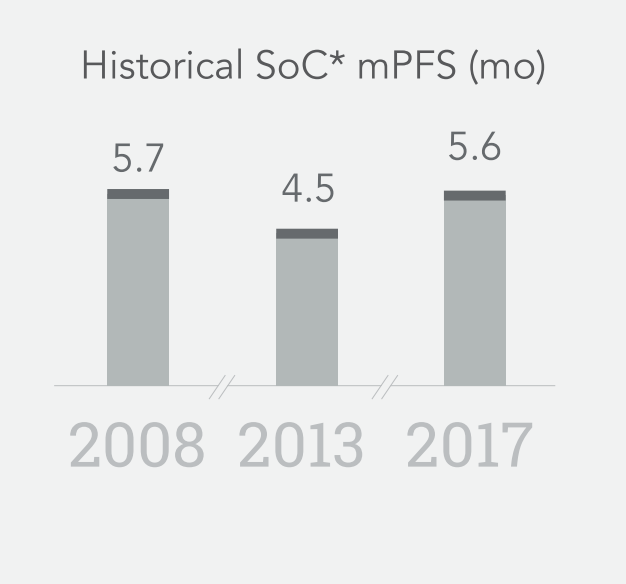
ENROLLMENT CRITERIA

2nd line mCRC
KRAS+
Unresectable

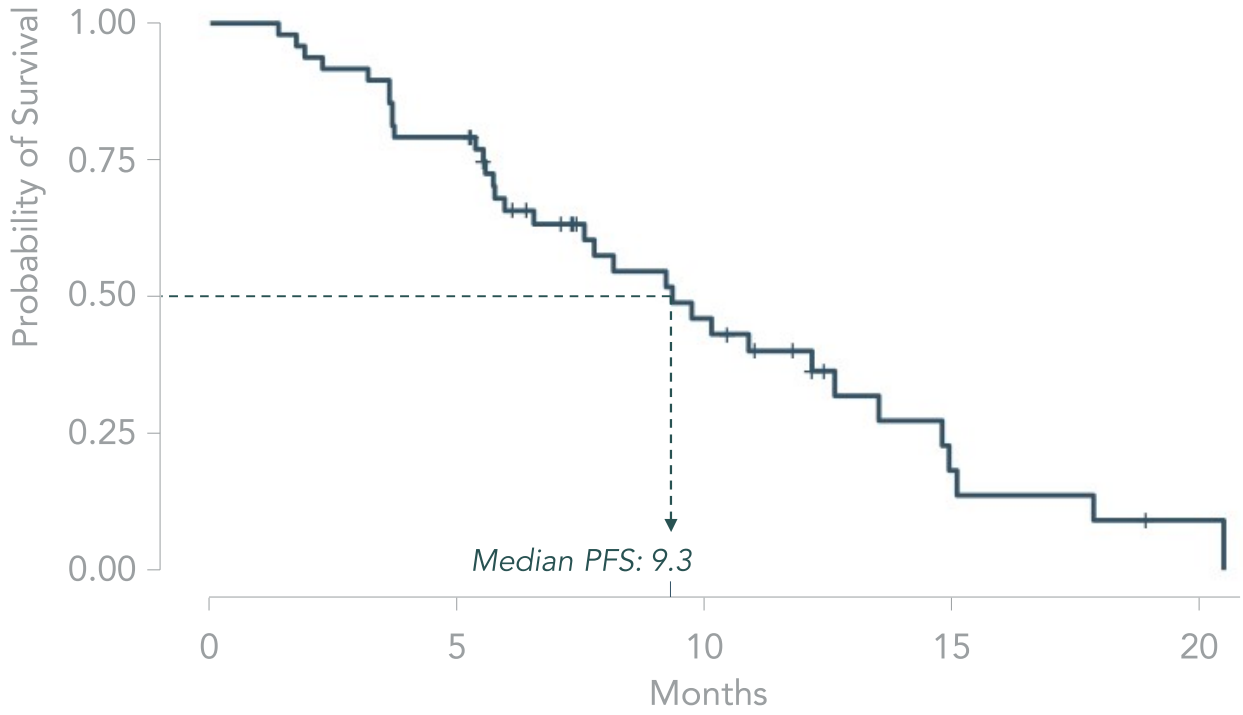
EVALUABLE PATIENTS AT JULY 25, 2022

	PHASE 1b	PHASE 2		
12 mg/m²	5			ALL DOSES N=48
15 mg/m²	6	32	RP2D[1] N=35	ALL DOSES N=48
18 mg/m²	5			ALL DOSES N=48

Progression Free Survival for mCRC trial exceeds SoC over time



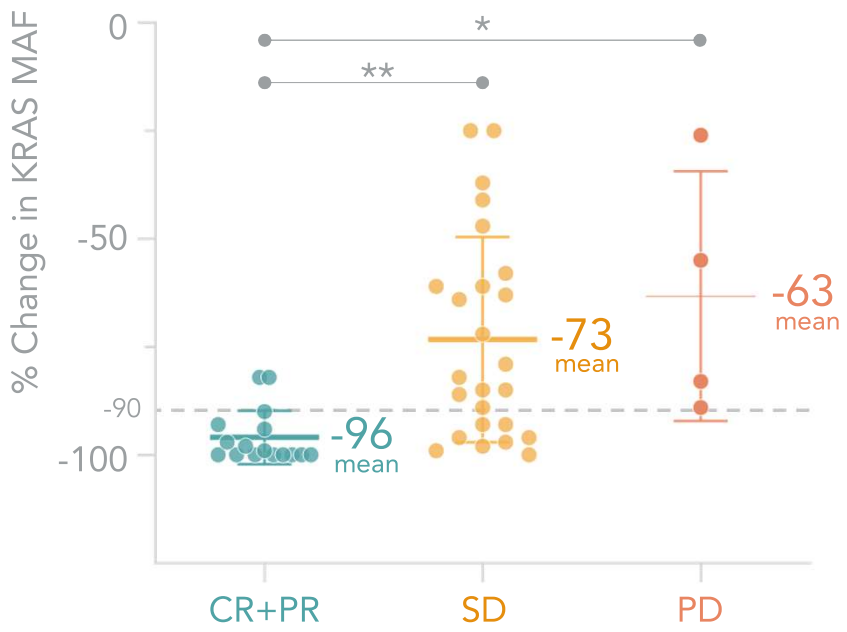
Progression free survival* – all doses (as of July 25, 2022)



* mPFS is interim data from an ongoing trial and unlocked database.

Early KRAS MAF ctDNA decrease correlates w/ radiographic response

% KRAS Mutant Allelic Frequency (MAF)*
decrease after one 28-day treatment cycle
(Mean ±SD, as of July 25, 2022)



Predictive response biomarker

- 45 of the 48 evaluable patients were evaluated for KRAS MAF changes
- 87.5% (14/16) of CR/PR patients had ≥90% decrease in KRAS MAF after the 1st cycle
- 32% (8/25) of SD patients and none of the PD patients (n=4) had such a decrease

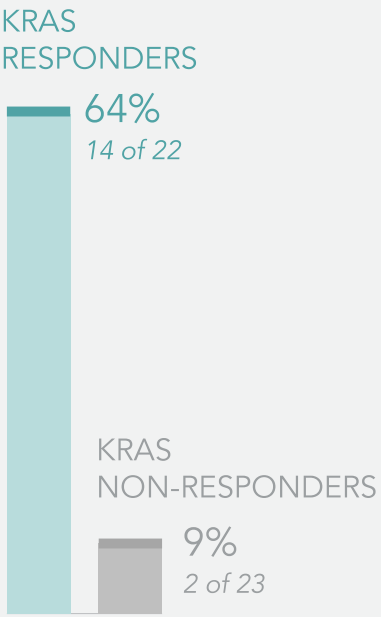
* KRAS MAF measured by droplet digital PCR (ddPCR) at baseline (day 1 of cycle 1, pre-dose) and on-treatment (day 1 of cycle 2 pre-dose). 1 PR and 2 SD patients had undetectable KRAS MAF at baseline.

KRAS MAF plot reflects interim data as of July 25, 2022 from an ongoing trial and unlocked database.

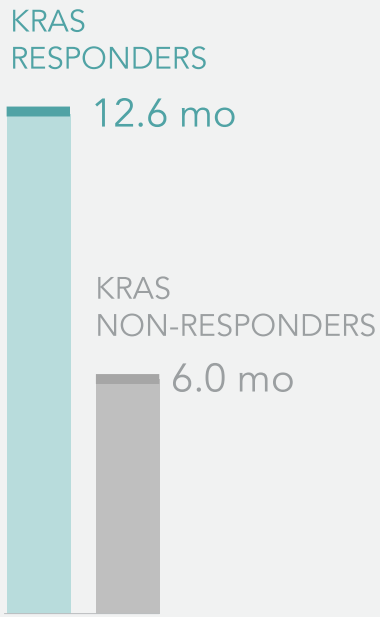
Onvansertib KRAS MAF are interim data as of July 25, 2022 from an ongoing trial and unlocked database.

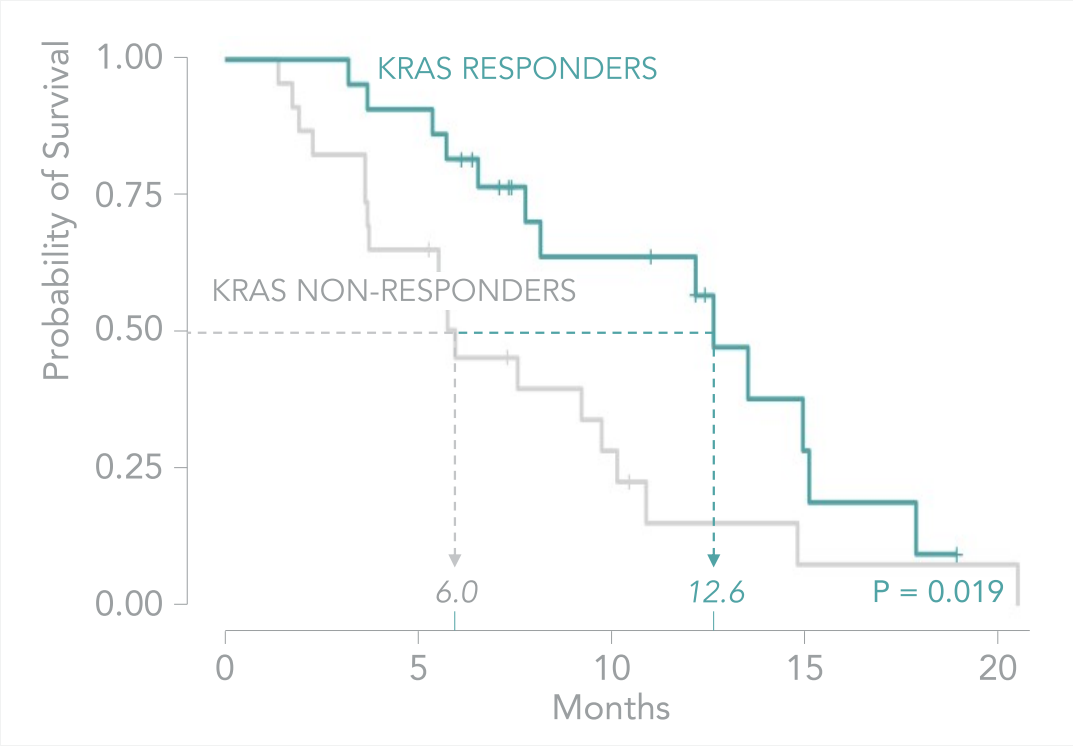
Early Changes in KRAS MAF predicts clinical response

ORR (%)



mPFS (mo)





Onvansertib ORR and mPFS are interim data as of July 25, 2022 from an ongoing trial and unlocked database.

Progression-free survival has ranged from 4.5 – 5.7 months

HISTORICAL REFERENCE

PFS	OS		
5.7	11.2	2006 – 2008	ML18147 Phase 3 Registrational Trial FOLFIRI + bev in second-line[1]
4.5	11.5	2000 – 2013	Systematic Literature-Based Analysis of 23 Randomized Trials (10,800 Patients) in Second-Line mCRC[2]
5.6	— Not reported for 2nd line	2015 – 2017	TRIBE2 Randomized Phase 3 Trial: SOC arm FOLFIRI + bev in Second-line following FOLFOX + bev First-line[3,4]

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

Our ONSEMBLE Ph2 trial will be statistically robust

ENROLLMENT CRITERIA

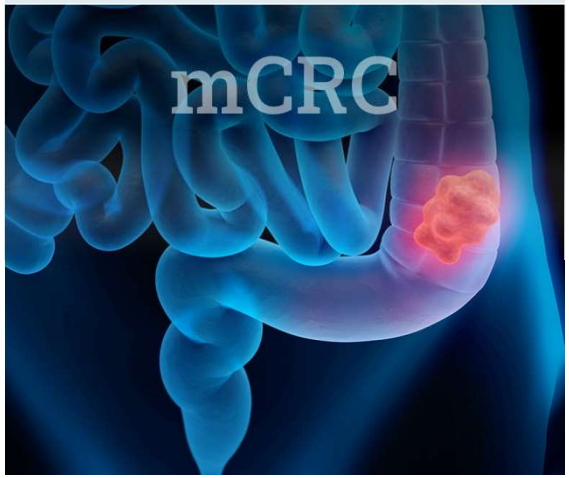
2nd line mCRC

KRAS+/NRAS+

Unresectable

R

N=150
1:1:1



DESIGN

- Randomized with control group exclusively the SoC
- Examine two doses of onvansertib for safety/efficacy
- Stratification within randomization for bev-naïve vs bev exposed
- Efficient and cost effective

STATS

- 80% minimum power to detect a meaningful difference in ORR
- Optimal use of the significance level (alpha 0.045 for each treatment arm vs. control)
- Ability to pool treatment arms for PFS

KRAS-Mutated Metastatic Colorectal Cancer Bevacizumab Subgroup Data

The trial's patient demographics reflects 2nd line mCRC population

Enrollment*

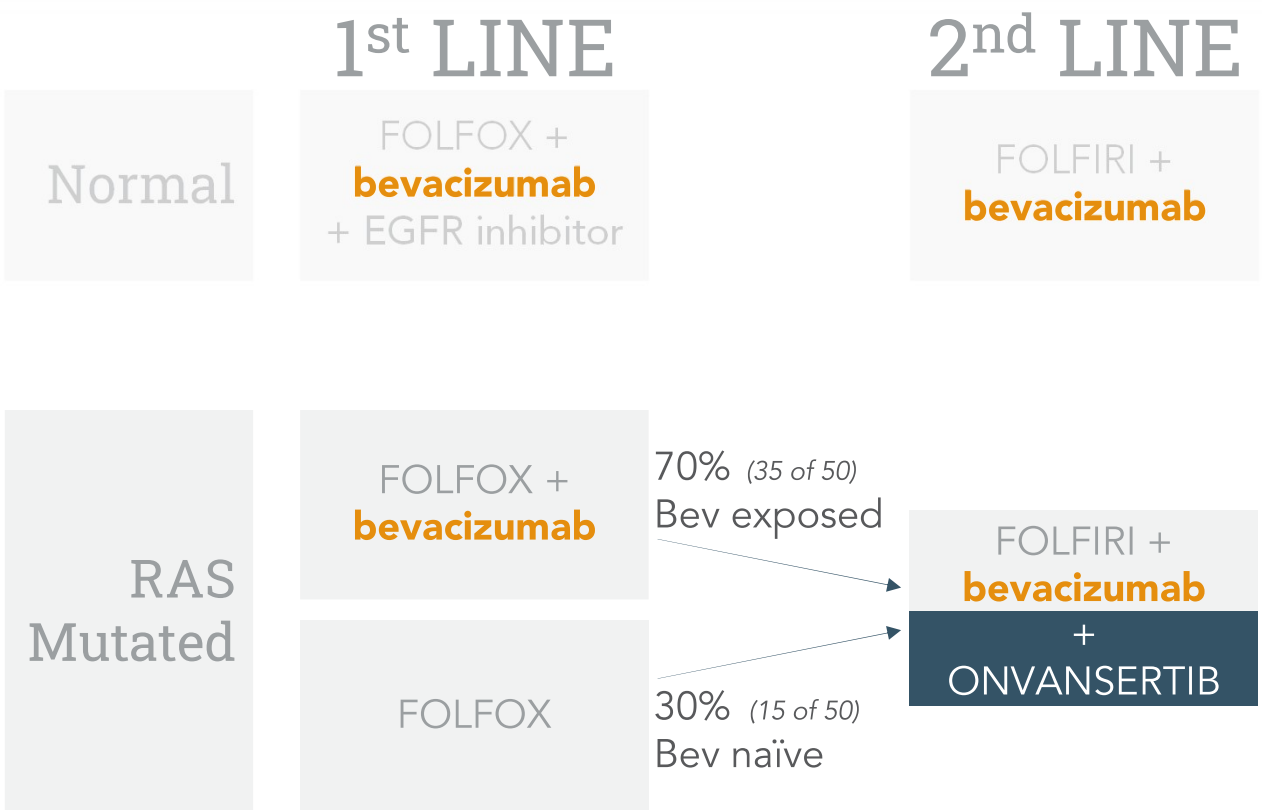
Number of Patients (N)	Phase 1b, Dose Level 0 Onvansertib 12 mg/m^2	Phase 1b, Dose Level +1 Onvansertib 15 mg/m^2	Phase 1b, Dose Level +2 Onvansertib 18 mg/m^2	Phase 2 RP2D Onvansertib 15 mg/m^2	Total Patients All Doses
Treated	6	6	6	32	50
Currently on treatment	0	0	0	3	3

Total Patients N=50	Median [range] or n (%)
Age (years)	61 [35-83]
Sex	
Male	28 (56%)
Female	22 (44%)
ECOG	
0	33 (66%)
1	17 (34%)
Primary tumor site	
Colon	27 (54%)
Rectum	18 (36%)
Other	5 (10%)

Total Patients N=50	Median n (%)
Liver metastasis	
None	13 (26%)
Liver and other	27 (54%)
Liver only	10 (20%)
Number of metastatic organs	
1	16 (32%)
≥2	34 (68%)
Prior bevacizumab treatment[5]	
Yes	**35 (70%)**
No	**15 (30%)**

* Data are interim as of July 25, 2022 from an ongoing trial and unlocked database, for the first 50 subjects.

Anti-angiogenics, like bevacizumab, combine with 1st and 2nd line SoC



mCRC Ph1b/2 trial

N=50 (48 evaluable)

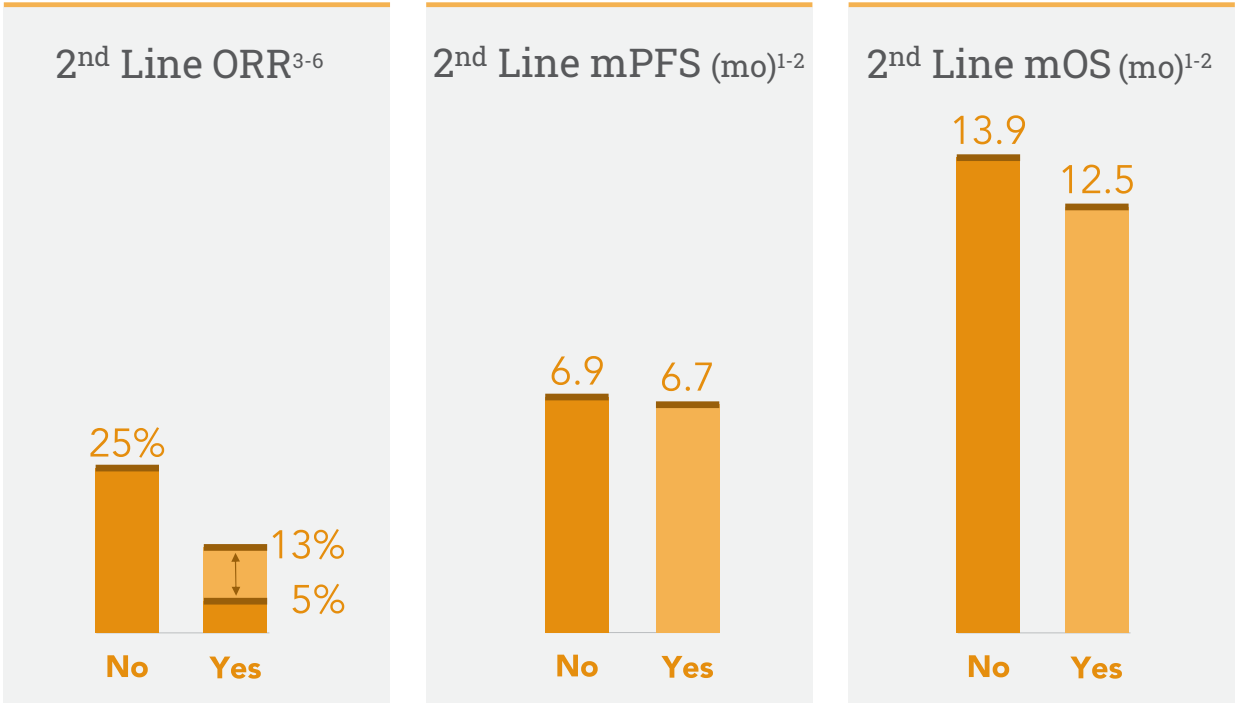
Do 2nd line patients ***naïve*** to bev show better efficacy than 2nd line patients with ***prior*** bev in 1st line?

1st line use of bev in prior trials has minimal impact on 2nd line efficacy

	2nd LINE
Normal	FOLFIRI + **bevacizumab**
RAS Mutated	FOLFIRI + **bevacizumab**

EFFICACY DATA FROM HISTORICAL TRIALS IN mCRC

BEV EXPOSURE IN 1ST LINE?



1. Hansen et al., Cancers 2021, 13, 1031; 2. Tabernaro et al. Eur J Cancer, 2014, 50, 320-332; 3. Bennouna et al., Lancet Oncol. 2013, 14, 29–37; 4. Van Cutsem et al., J. Clin. Oncol. 2012, 30,3499–3506; 5. Tabenaro et al, Lancet Oncol 2015; 16: 499–508; 6. Beretta et al., Med Oncol (2013) 30:486; 7. Moriwakij et al, Med Oncol (2012) 29:2842–2848.

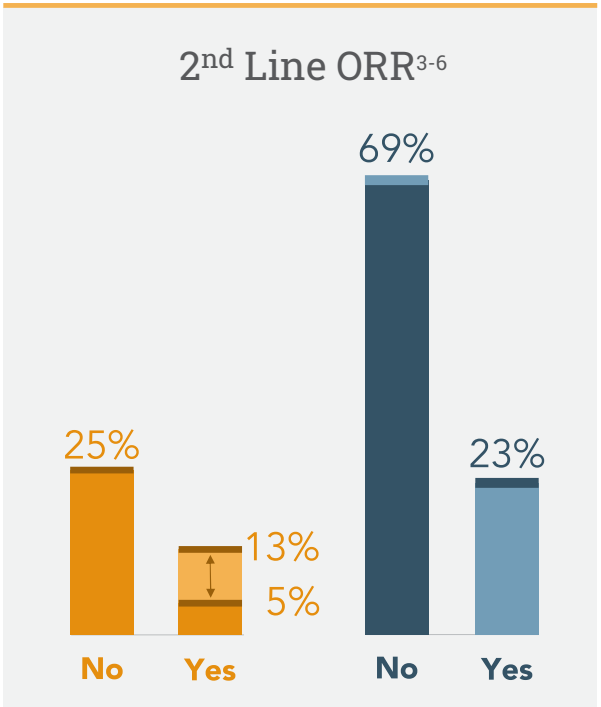
Ph 1b/2 trial bev naïve patients had unexpectedly high ORR and mPFS

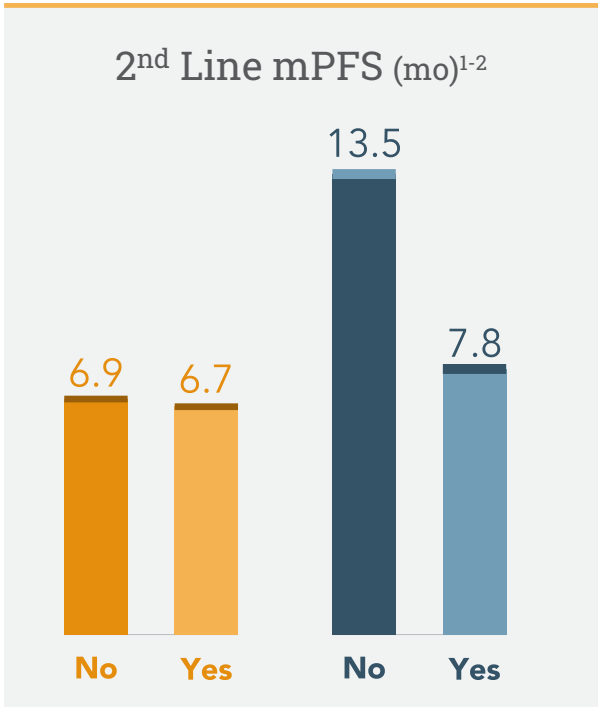
	2nd LINE
Normal	FOLFIRI + **bevacizumab**
RAS Mutated	FOLFIRI + **bevacizumab** + ONVANSERTIB

* Onvansertib ORR and mPFS are interim data as of July 25, 2022 from ongoing trial and unlocked database.

HISTORICAL CONTROLS VS ONVANSERTIB* Ph 1b/2 DATA

BEV EXPOSURE IN 1ST LINE?





1. Hansen et al., Cancers 2021, 13, 1031; 2. Tabernaro et al. Eur J Cancer, 2014, 50, 320-332; 3. Bennouna et al., Lancet Oncol. 2013, 14, 29–37; 4. Van Cutsem et al., J. Clin. Oncol. 2012, 30,3499–3506; 5. Tabenaro et al, Lancet Oncol 2015; 16: 499–508; 6. Beretta et al., Med Oncol (2013) 30:486.

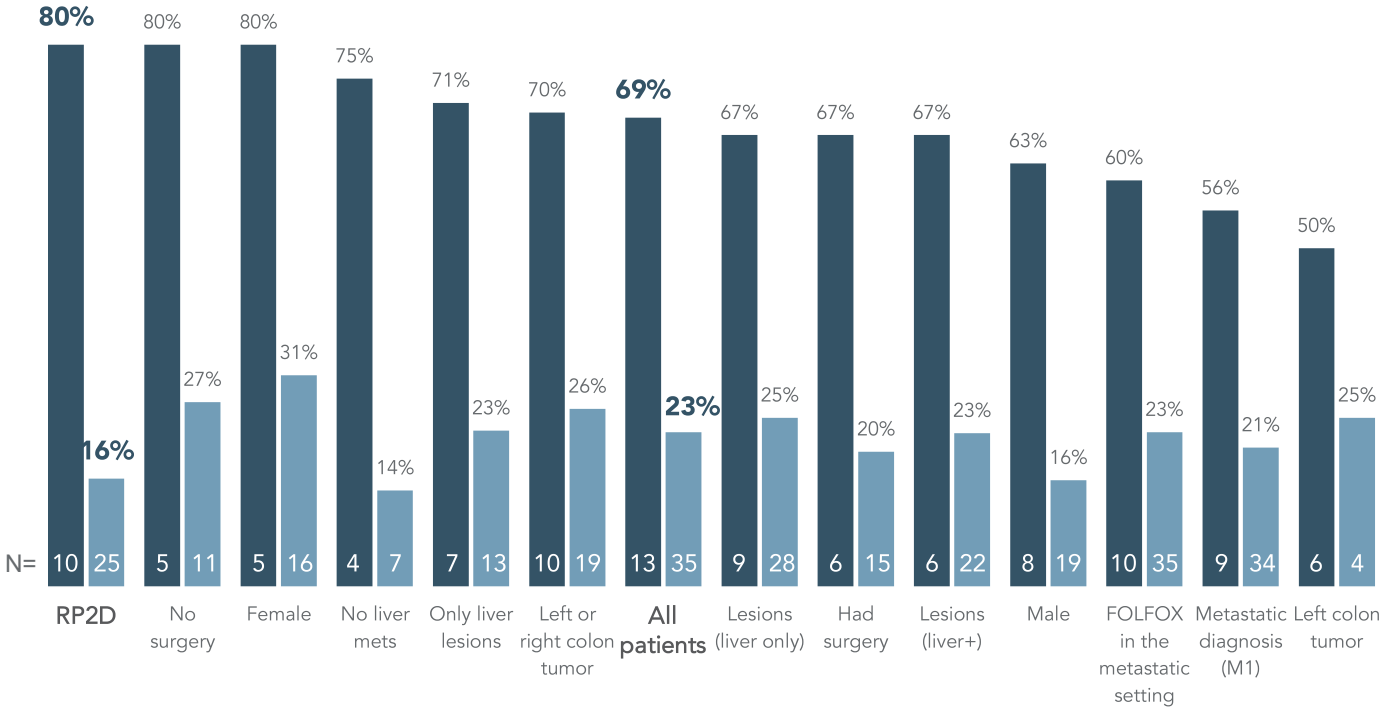
ORR is consistently greater for bev naïve patients across characteristics

No single patient characteristic explains observed ORR difference

BEV EXPOSURE IN 1ST LINE?

	No (naïve)	Yes (exposed)
Range of ORRs	50 – 80%	14 – 31%

ORR (%) for Bevacizumab Naïve vs. Exposed Patients* – as of July 25, 2022



* Onvansertib ORR is interim data as of July 25, 2022 from an ongoing trial and unlocked database.

The potential onvansertib bevacizumab synergy is a new opportunity

How should we respond to this observation?

BEV EXPOSURE IN 1ST LINE?

	No (naïve)	Yes (exposed)
All Patients	69% ORR	23% ORR
RP2D	80% ORR	16% ORR

HYPOTHESIS

Is there a synergy between onvansertib and bevacizumab?

ACTIONS

1. Stratify for prior bev exposure within randomization of next mCRC trial
2. Explore apparent onv / bev synergy in pre-clinical studies
3. Analyze baseline ctDNA in our Ph 1b/2 patients for genomic alterations in bev naïve vs bev exposed

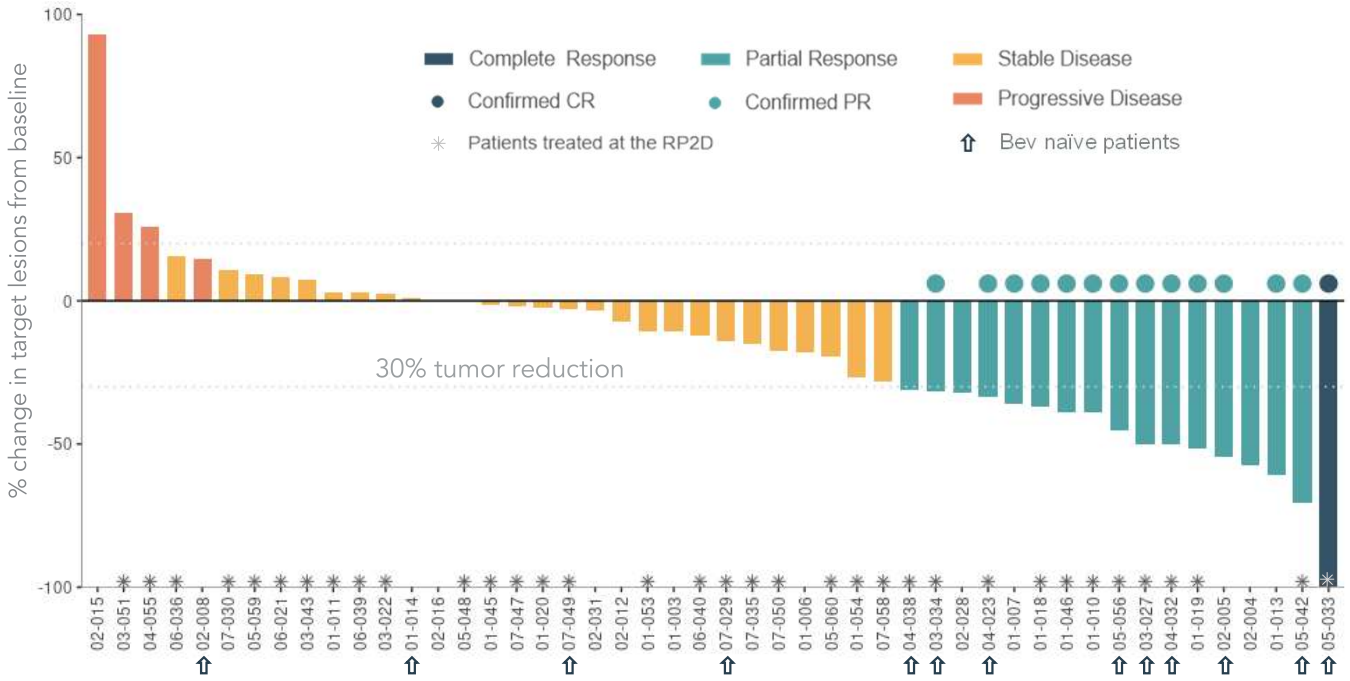
OPPORTUNITY

Conduct a 1st line exploratory mCRC trial of onvansertib + FOLFIRI + bev

* Onvansertib ORR and mPFS are interim data as of July 25, 2022 from an ongoing trial and unlocked database.

Patients achieved a strong, durable response with onvansertib + SoC

Best Radiographic Response* – all doses (as of July 25, 2022)



	All Doses	RP2D
Objective Response Rate* (CR + PR)	35% (17/48)	34% (12/35)
Disease Control Rate (CR + PR + SD)	92% (44/48)	94% (33/35)

Durability

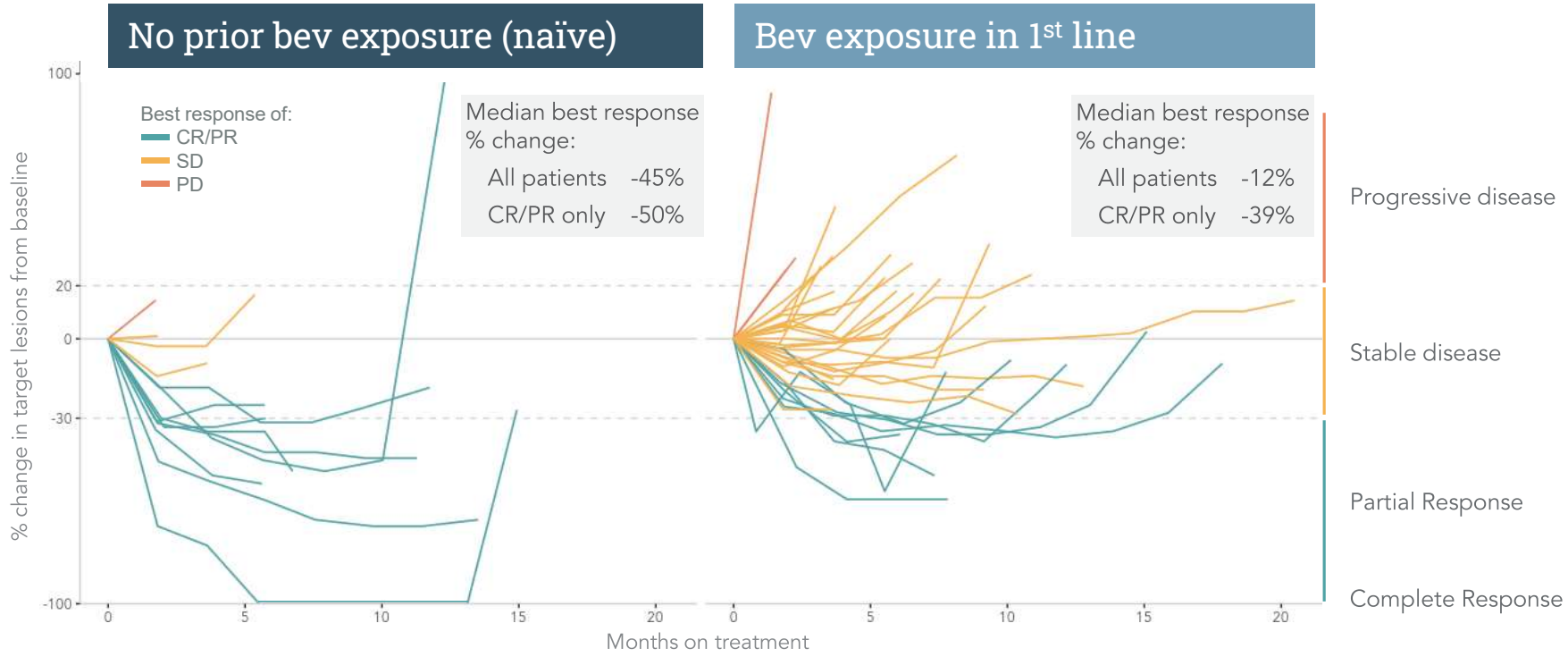
Median Duration of Response	11.7 months	12.5 months†
mDoR bev naive	12.4 months N = 9	12.4 months† N = 8
mDoR bev exposed	8.9 months N = 8	10.7 months† N = 4

* Radiographic response determined per RECIST 1.1. Waterfall plot and table reflect interim data as of July 25, 2022 from an ongoing trial and unlocked database

† mDoR is calculated as the time at which there is a 50% probability of survival based on KM-Curve. This accounts for censorship of patients

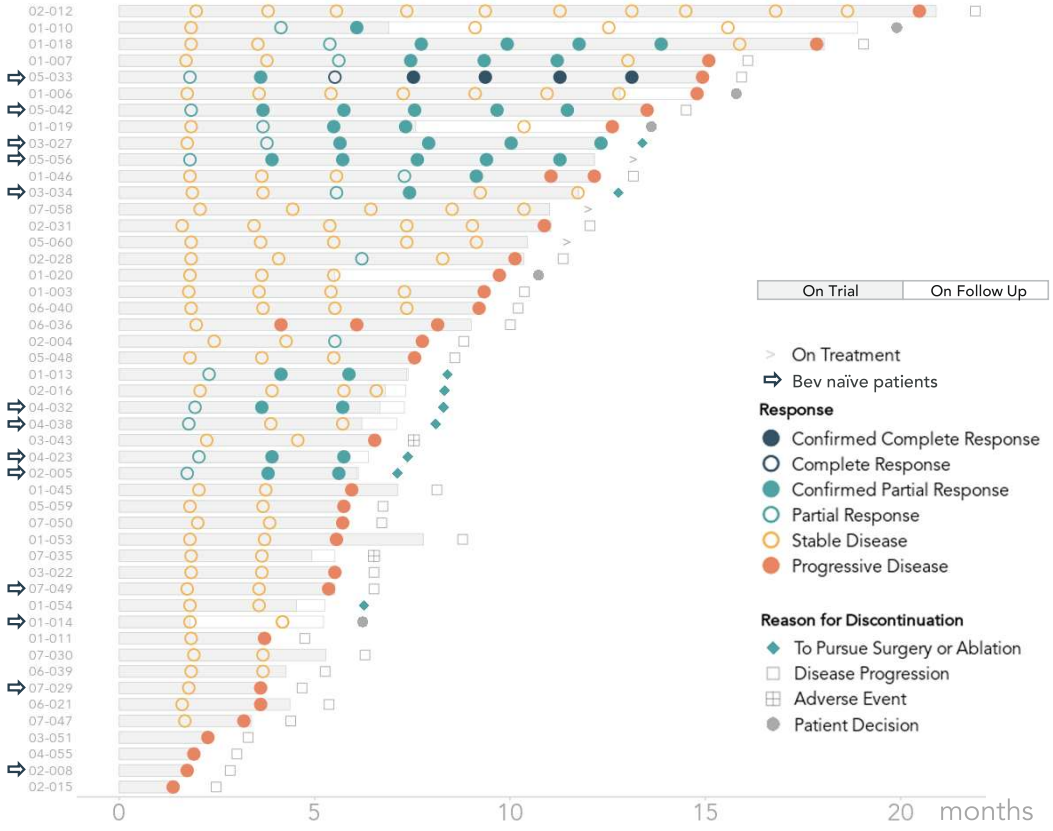
Bev naïve patients experienced deeper tumor regression

Change in tumor size from baseline* – all doses (as of July 25, 2022)



* Spider plots reflect interim data as of July 25, 2022 from an ongoing trial and unlocked database

We observe initial PRs up to eight months on treatment



Swimmer plot* – all doses (as of July 25, 2022)

Evaluable Patients – all doses: 48

Time of initial PR	All patients	Bev naïve	Bev exposed
8-week scan	8	7	1
16-week scan	3	1	2
24-week scan	5	1	4
32-week scan	1		1

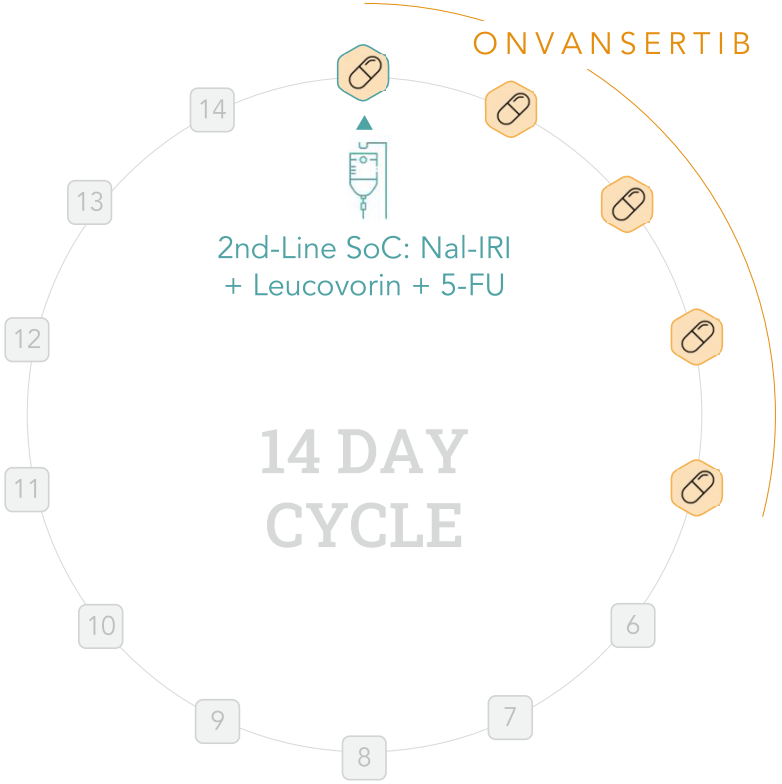
* Swimmer plot and table reflect interim data as of July 25, 2022 from an ongoing trial and unlocked database

Metastatic Pancreatic Adenocarcinoma (mPDAC)

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

ENROLLMENT CRITERIA

Failed 1st Line
Gemcitabine / Abraxane



SINGLE ARM TRIAL

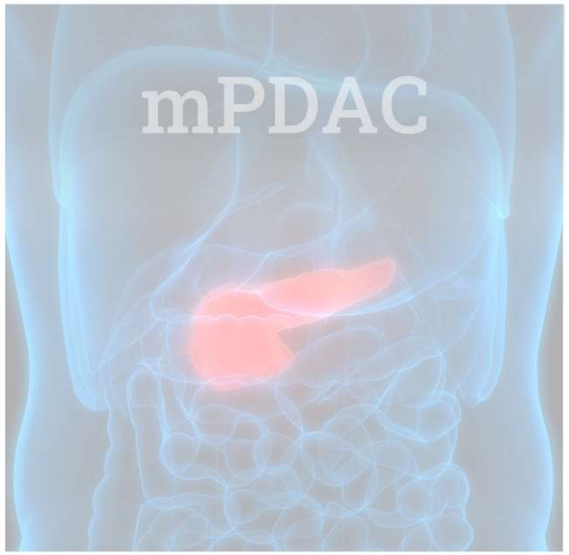
43 patients planned

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 ≥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

PROOF OF CONCEPT CRITERIA

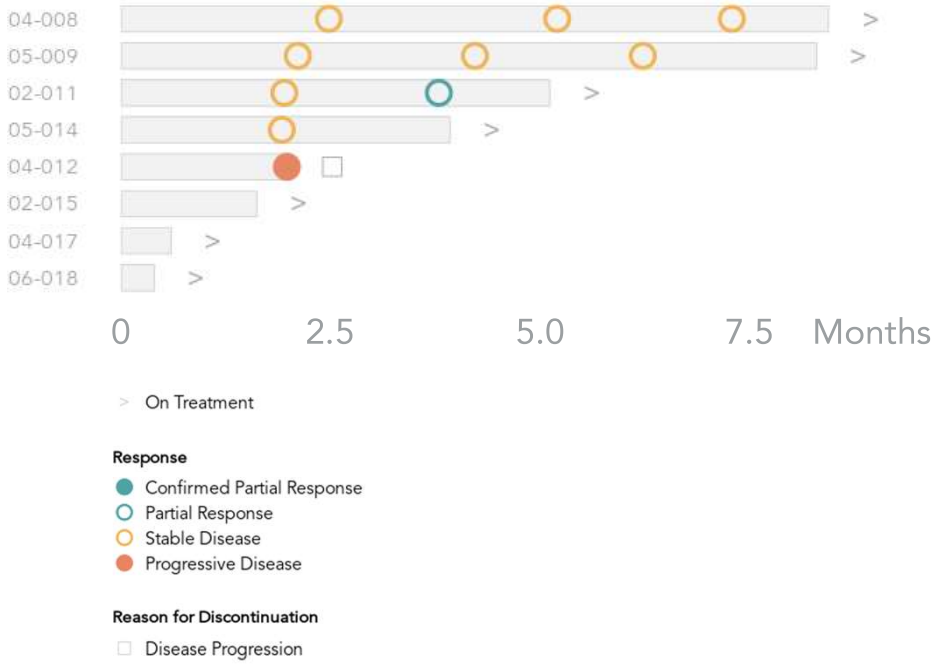
20% ORR

≥6 mo mPFS

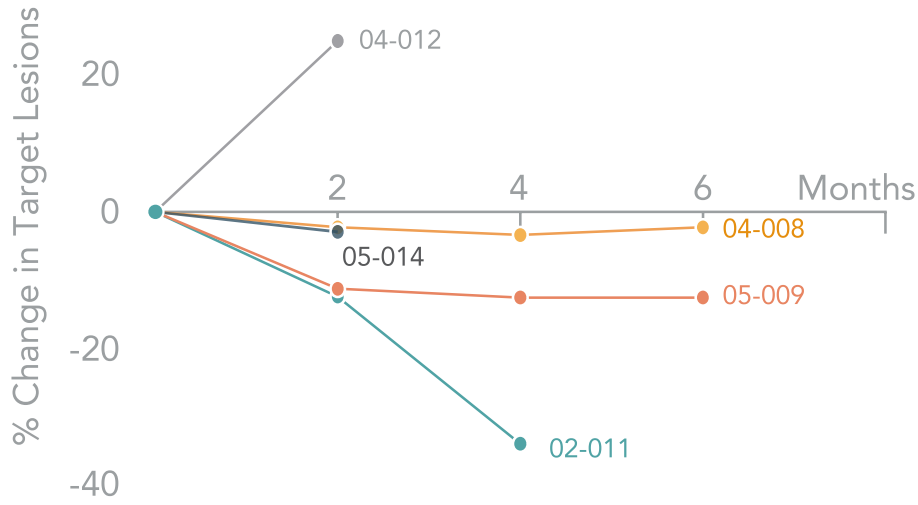
* Wang-Gillam A, Li C-P, Bodoky G, et al. Lancet 2016;387:545-57; Waters AM, Der CJ. Cold Spring Harb Perspect Med 2018;8(9).

Early data from our mPDAC trial data is encouraging

Swimmer plot* – as of August 30, 2022



Change in tumor size from baseline*



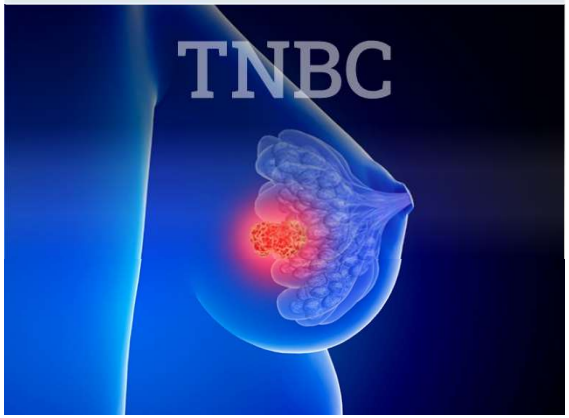
* Swimmer and spider plots reflect interim data as of August 30, 2022 from an ongoing trial and unlocked database

Investigator-Initiated Trial
Triple Negative Breast Cancer (TNBC)

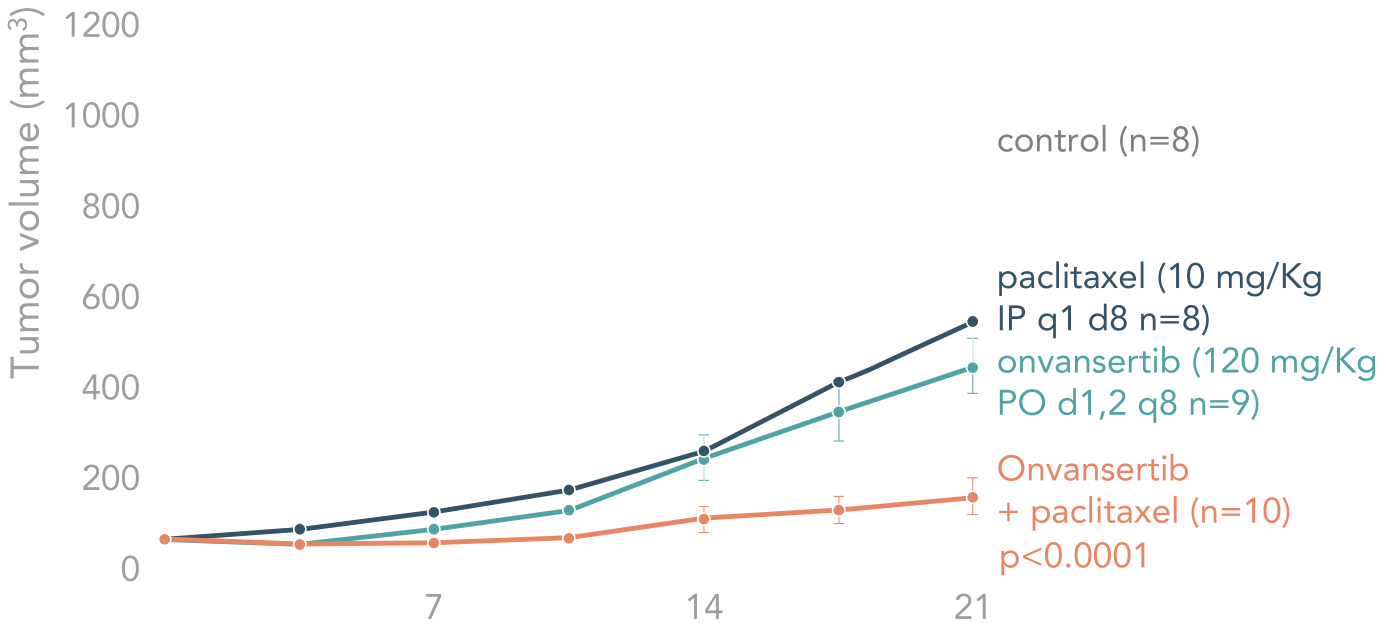
Onvansertib + paclitaxel is superior to single agent therapy

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^3: vehicle, onvansertib oral (PO) twice per week (days 1-2), paclitaxel intraperitoneally (IP) weekly (day 1), or the combination.

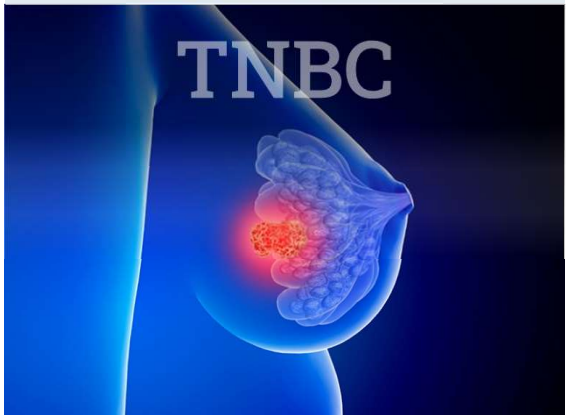
This is the first trial to explore onvansertib + paclitaxel combination

ENROLLMENT CRITERIA

Metastatic TNBC relapsed or progressed

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

Dana-Farber Cancer Institute



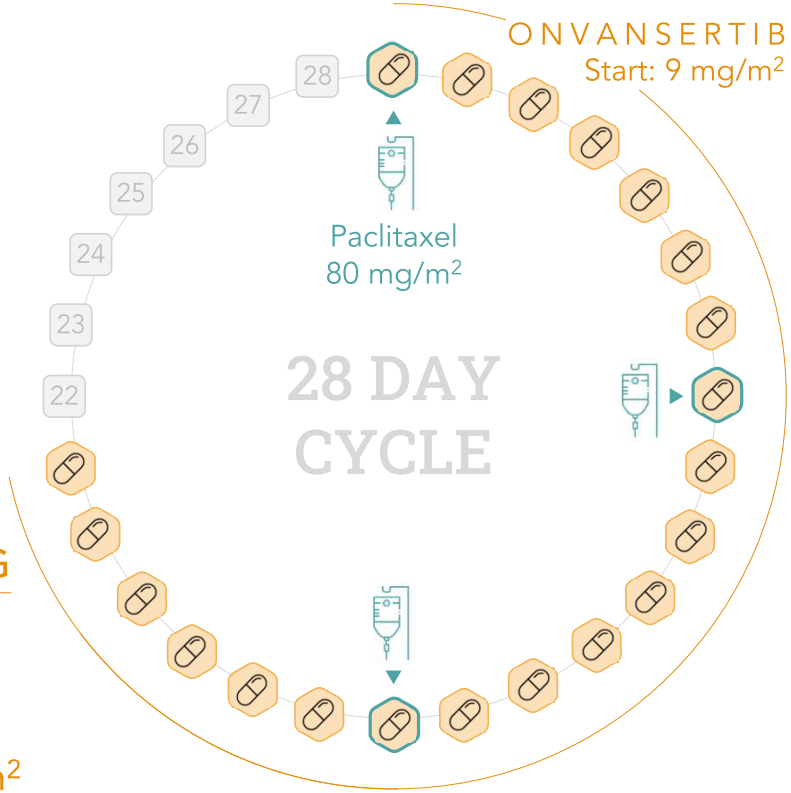
PRIMARY ENDPOINTS

Phase 1b
Safety, characterization of DLTs
Determination of RP2D

Phase 2
ORR (RECIST 1.1)

ONVANSERTIB DOSING

Starting: 9 mg/m²
→ Escalation: 12 mg/m²
→ De-escalation: 6 mg/m²



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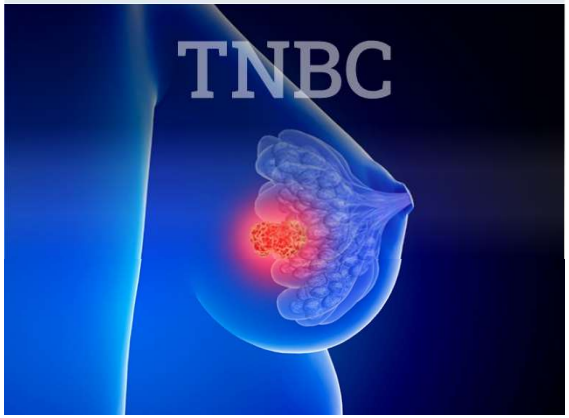


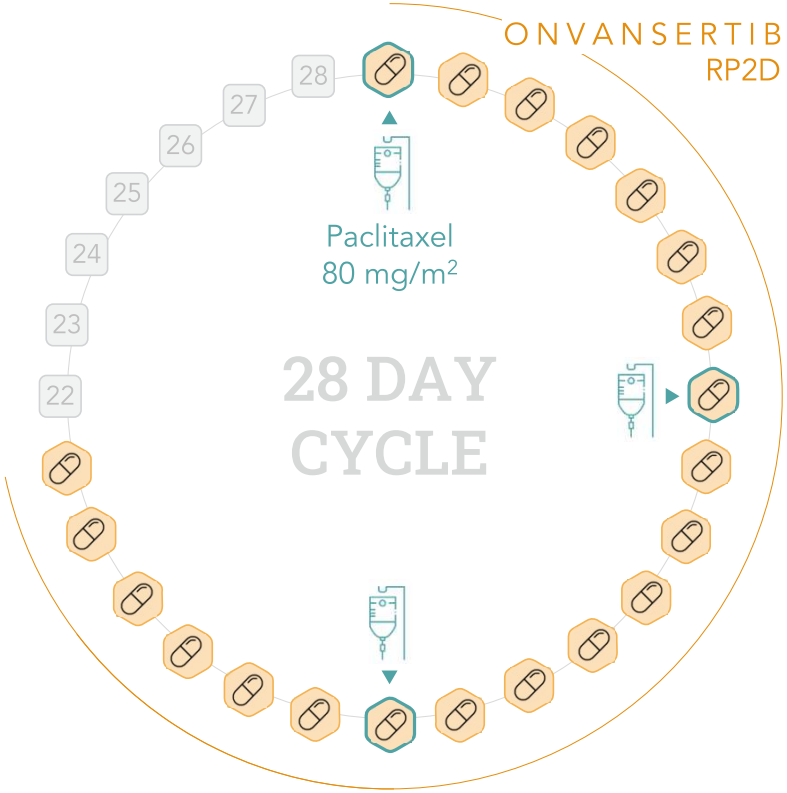
PRIMARY ENDPOINTS

Phase 1b
Safety, characterization of DLTs
Determination of RP2D

Phase 2
ORR (RECIST 1.1)

SECONDARY ENDPOINT

Phase 2
Progression-Free Survival (PFS)



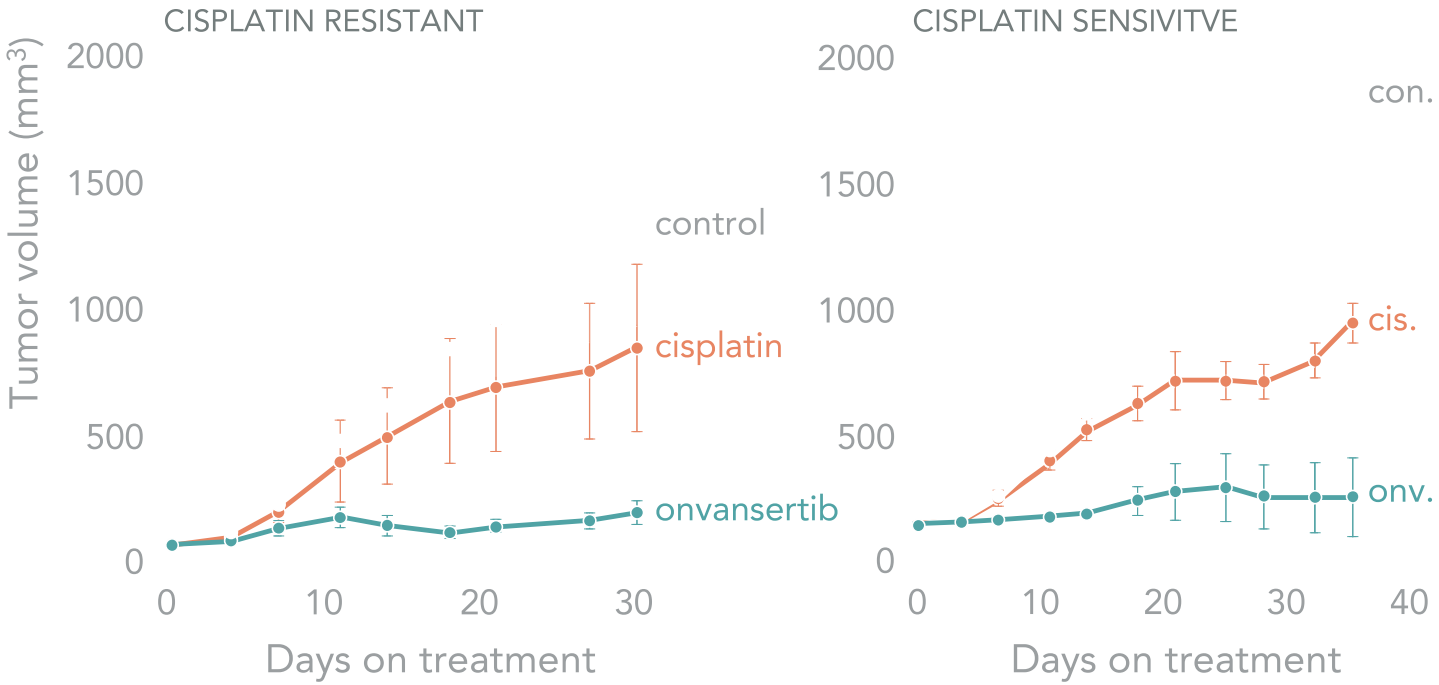
Investigator-Initiated Trial
Small Cell Lung Cancer (SCLC)

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 ≤ 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

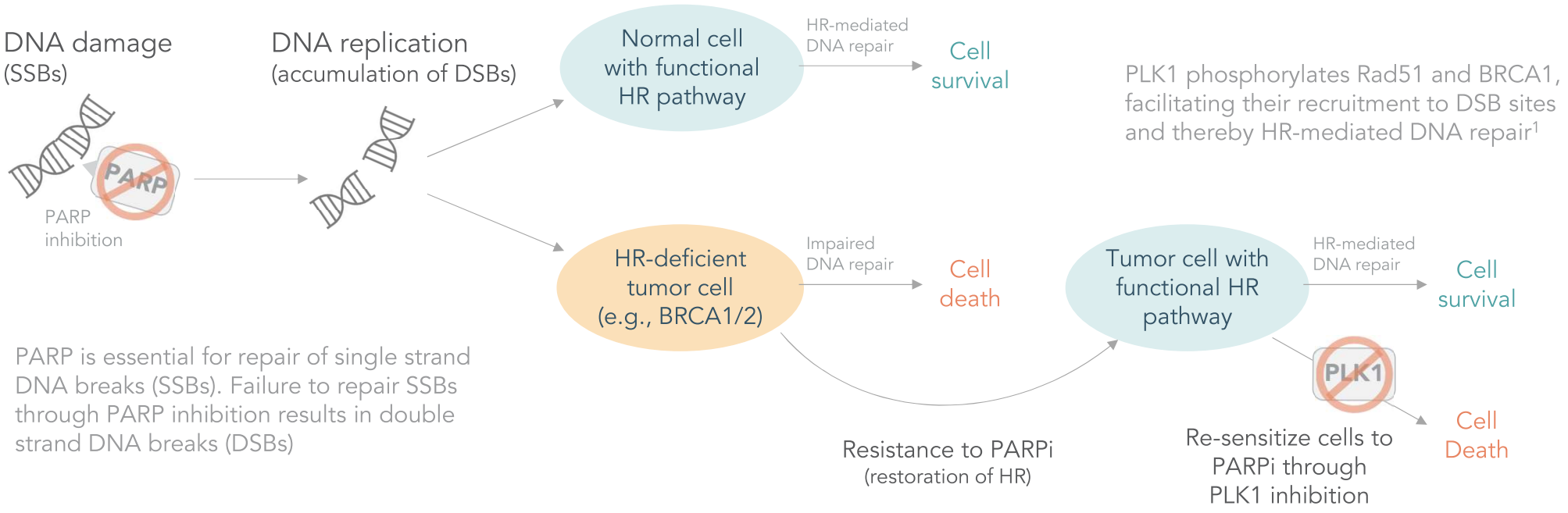
Phase 2
Progression-Free Survival (PFS)

Overall Survival (OS)

PARPi Pre-Clinical Data

PLK1 inhibition re-sensitizes tumor cells to PARP inhibition

Onvansertib + PARP inhibitors



PLK1 phosphorylates Rad51 and BRCA1, facilitating their recruitment to DSB sites and thereby HR-mediated DNA repair[1]

PARP is essential for repair of single strand DNA breaks (SSBs). Failure to repair SSBs through PARP inhibition results in double strand DNA breaks (DSBs)

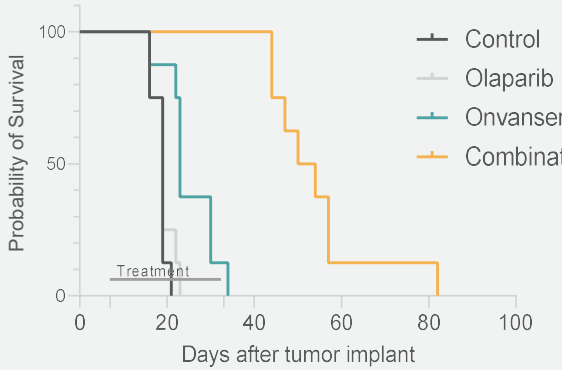
1. Yata et al. Mol. Cell 45, 371-383, 2012; Chabalier-Taste et al., Oncotarget 2016 Jan 19; 7(3): 2269-83; Peng et al., NAR 2021,49(13):7554-7570. HR: Homologous recombination; PARPi: PARP inhibitor

Preclinical studies demonstrate the benefit of PLK1 + PARP inhibitors

Onvansertib + PARP inhibitors*

Ovarian BRCA1 mutant PARPi-resistant PDX models

HGSOC, PDX#HOC22 (BRCA1 mutant)

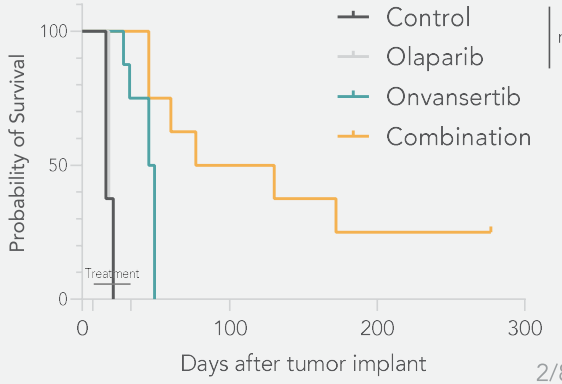


Median survival (days)	Fold-increase in survival vs control
19	
19	1
23	1.2
52	2.7

Log-rank Mantel-Cox test

** p<0.01 **** p<0.0001

HGSOC, PDX#HOC266 (BRCA1 mutant)



Median survival (days)	Fold-increase in survival vs control
16	
18	1.1
47	2.9
103	6.5

Log-rank Mantel-Cox test

** p<0.01 **** p<0.0001

2/8 mice were still alive at day 277 in the combination group

* Tumor cells (#HOC22 and #HOC266) were intraperitoneally transplanted and mice were treated for 4 weeks with vehicle, onvansertib, olaparib or the combination of onvansertib + olaparib. In collaboration with Giovanna Damia (IRFM, Italy). HGSOC: high grade serous ovarian cancer; PARPi: PARP inhibitor