



# Clinical and Corporate Update

SEPTEMBER 12, 2022

# 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;

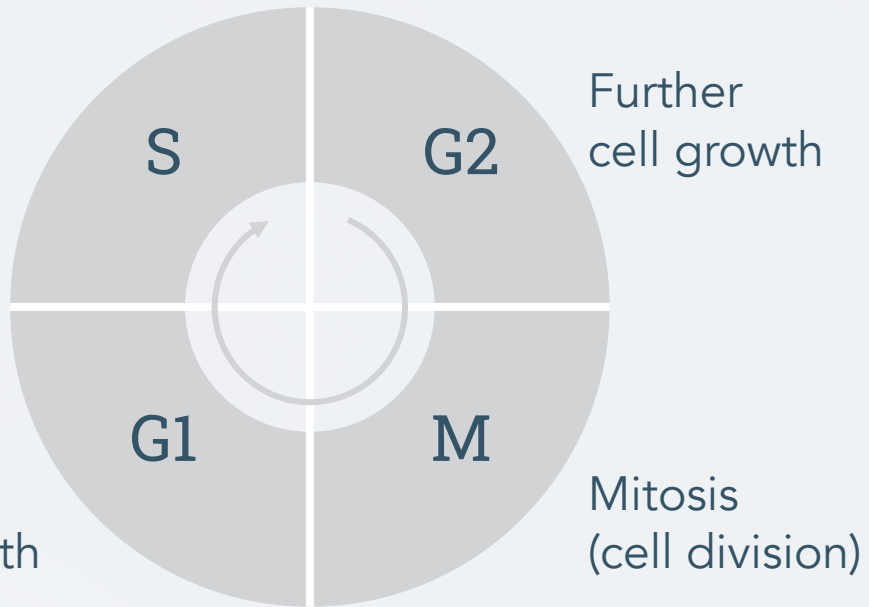
uncertainties of government or third-party payer reimbursement; dependence on key personnel; limited experience in marketing and sales; substantial competition; uncertainties of patent protection and litigation; dependence upon third parties; regulatory, and risks related to failure to obtain FDA clearances 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, 2021, 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.

# Many chemo agents damage a tumor cell's ability to replicate

**Irinotecan**

**5-FU**

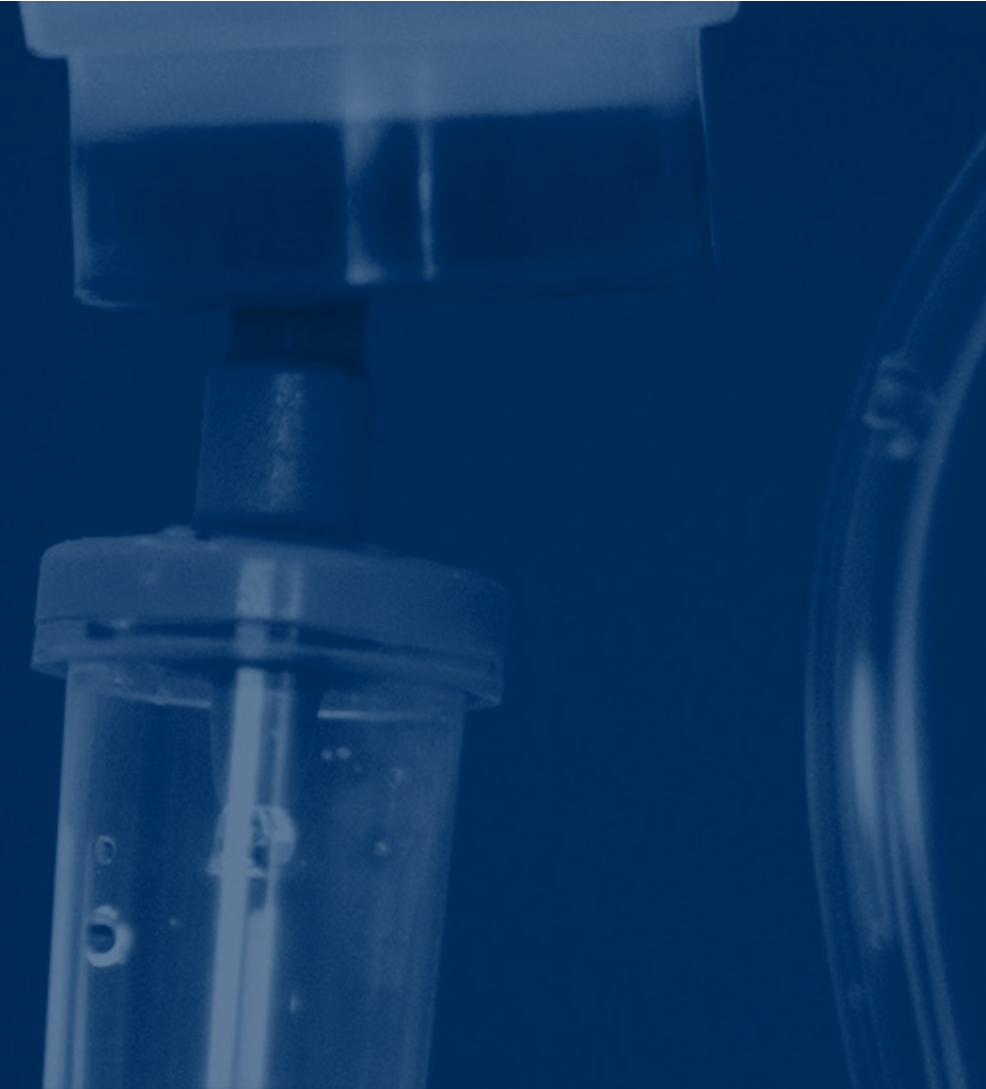
DNA  
synthesis



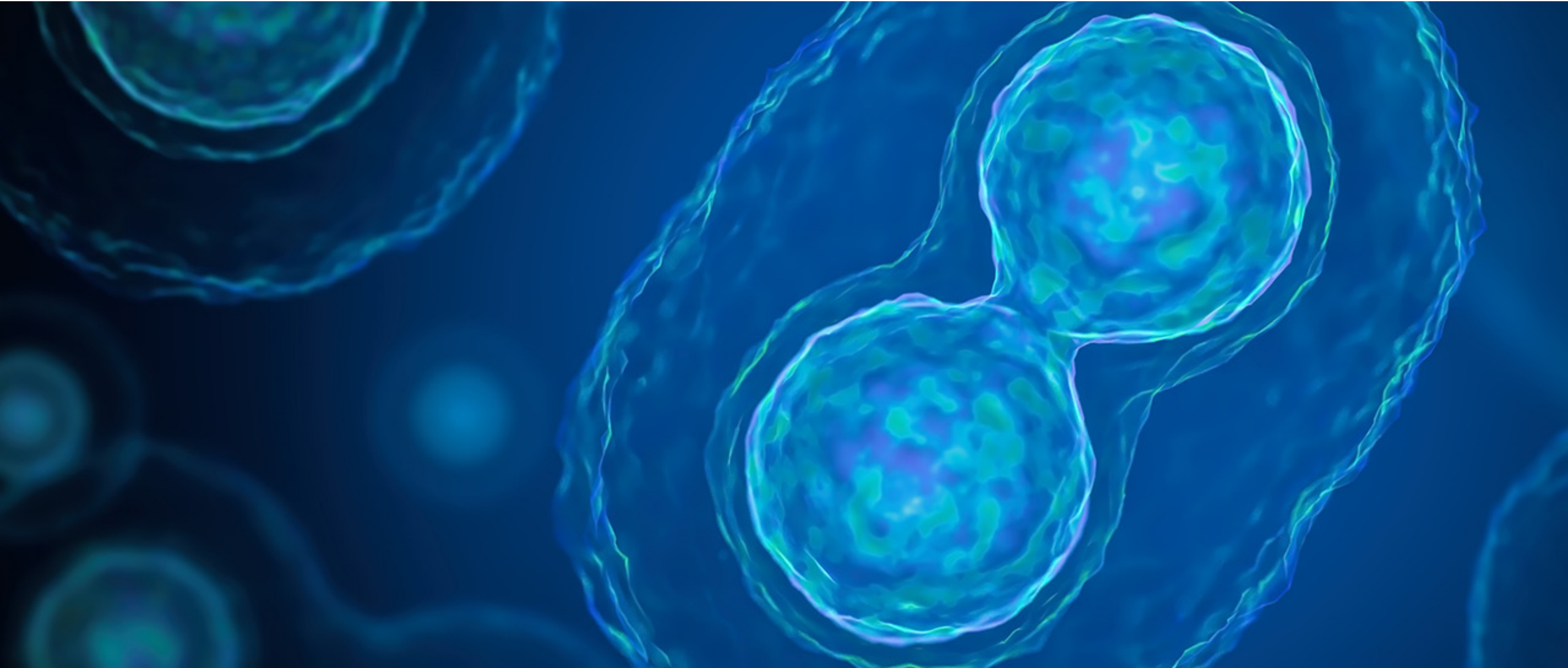
Initial  
cell growth

Mitosis  
(cell division)

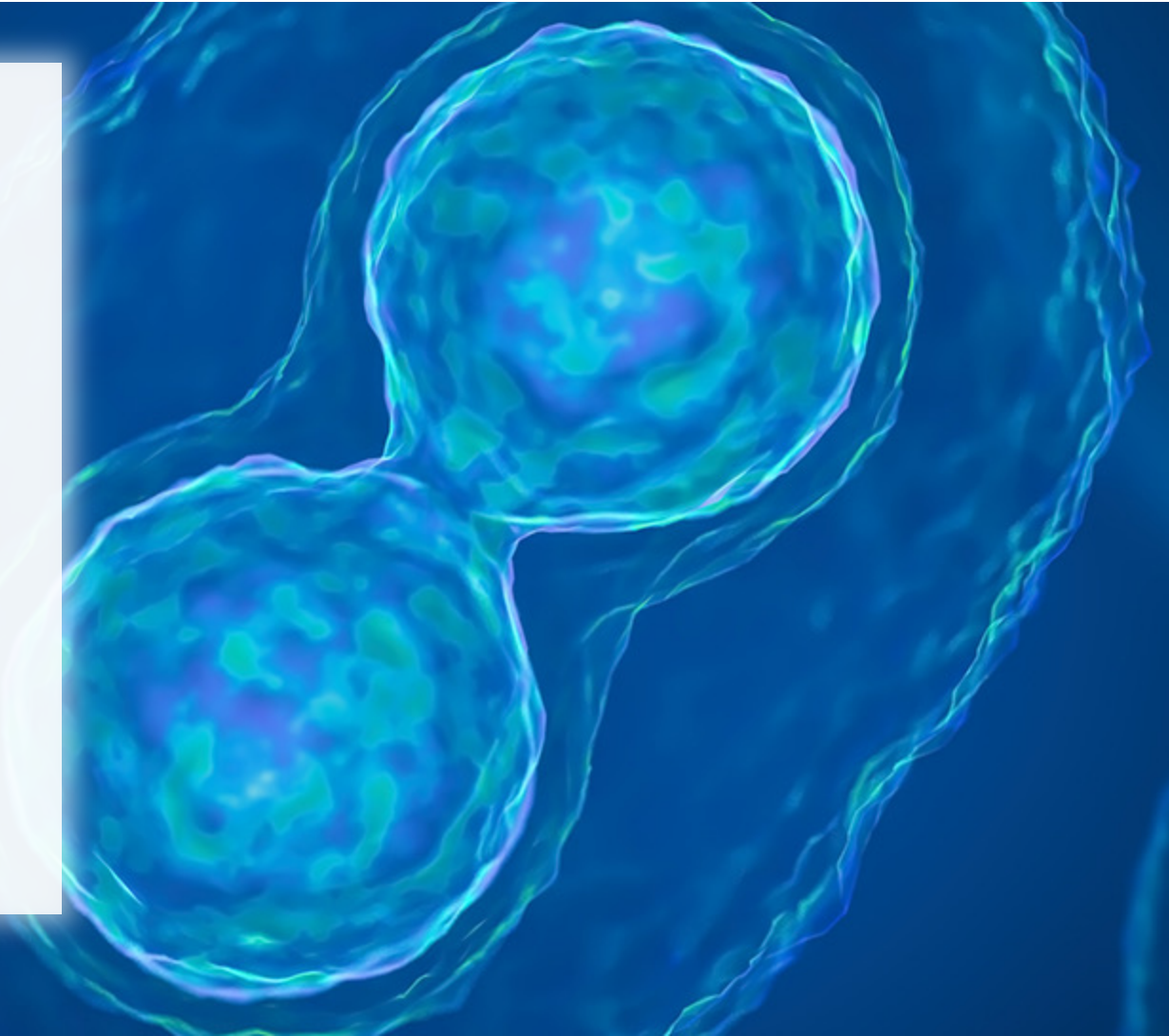
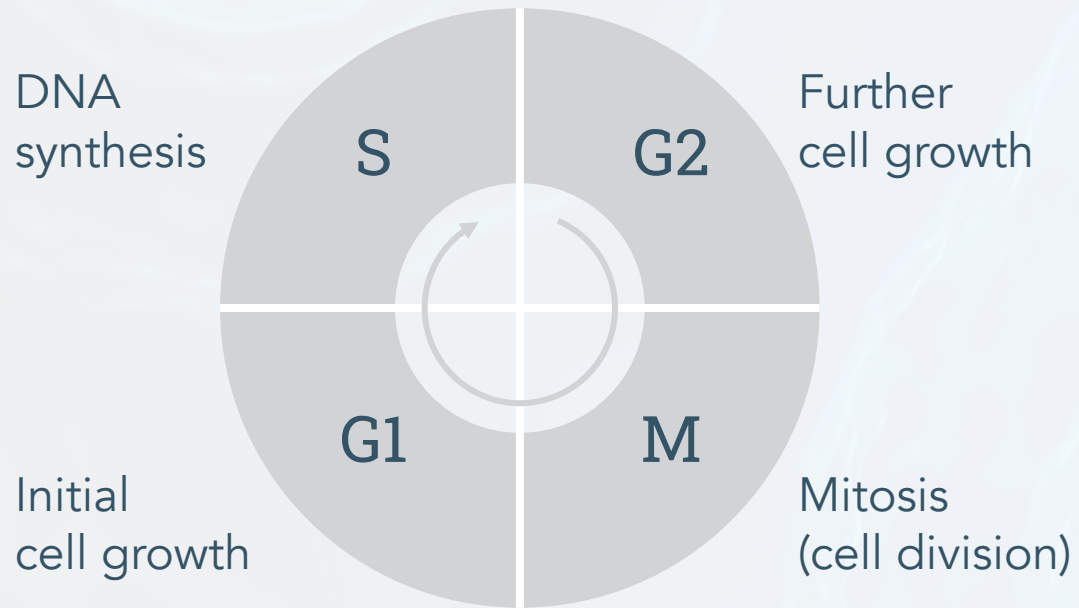
**Taxanes**



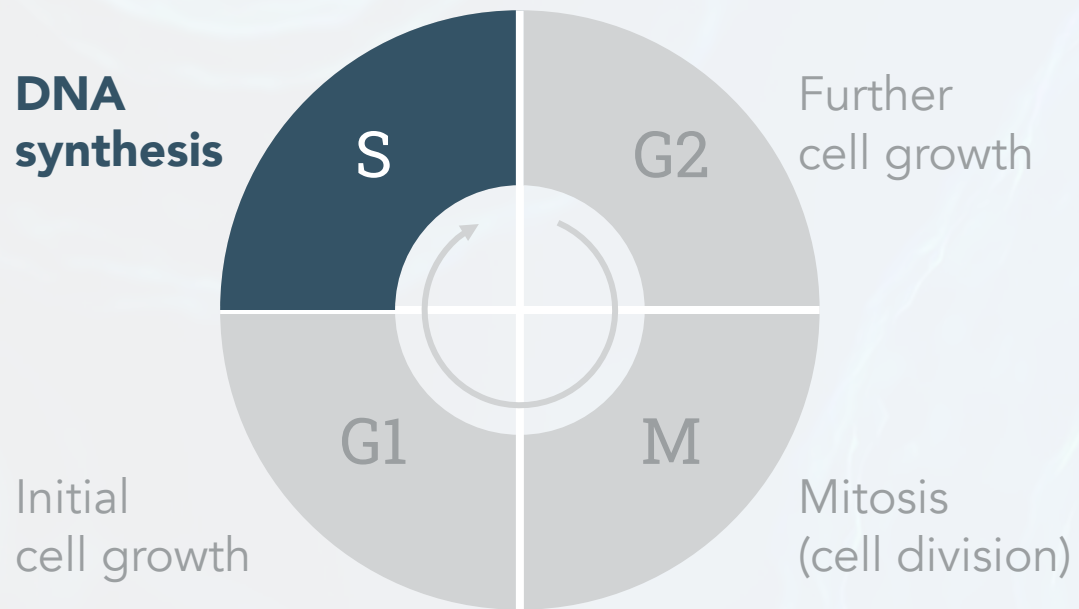
Cancers thrive because they prioritize DNA replication and cell division



# PLK1 is a master regulator of genome integrity during cell replication



# PLK1 is a master regulator of genome integrity during cell replication



## PLK1 plays multiple roles during cell cycle

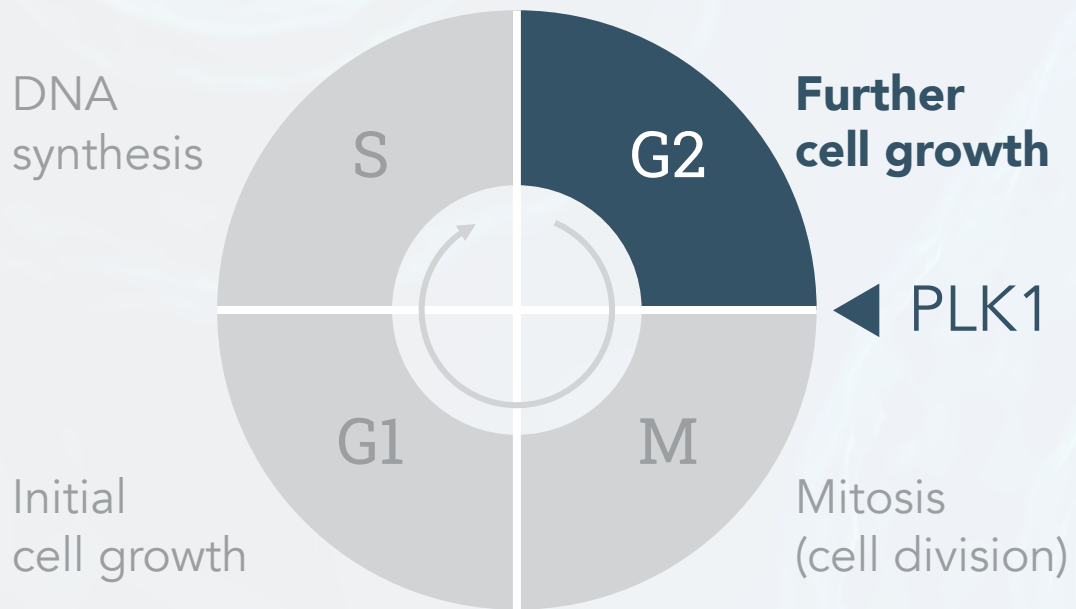
### **S-Phase**

Controls the repair of DNA damage

### G2/M Checkpoint

### M-Phase

# PLK1 is a master regulator of genome integrity during cell replication



## PLK1 plays multiple roles during cell cycle

S-Phase

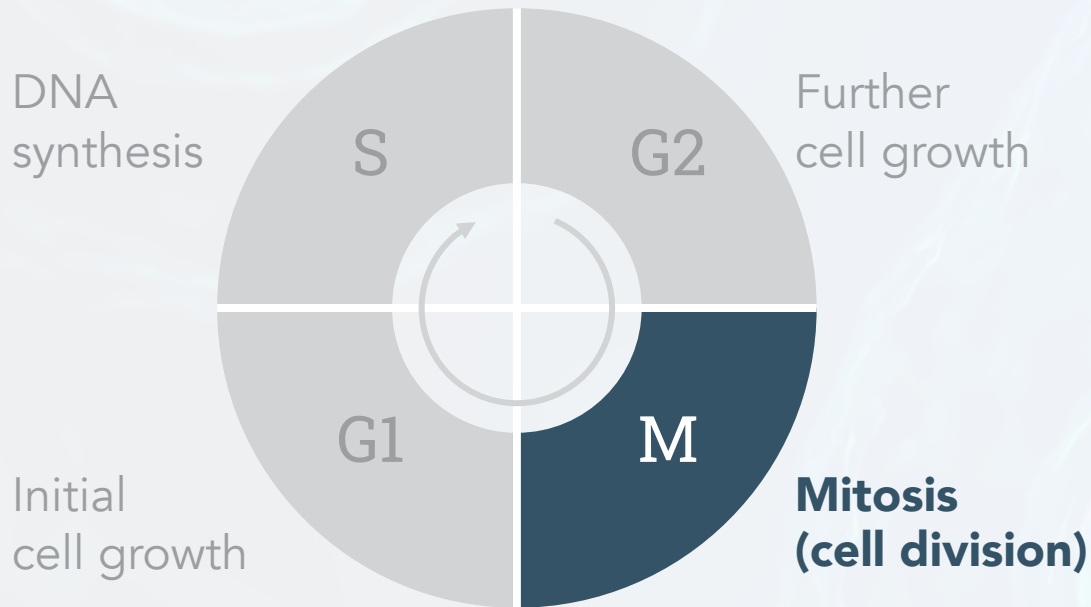
Controls the repair of DNA damage

**G2/M  
Checkpoint**

Controls the checkpoint for DNA quality

M-Phase

# PLK1 is a master regulator of genome integrity during cell replication



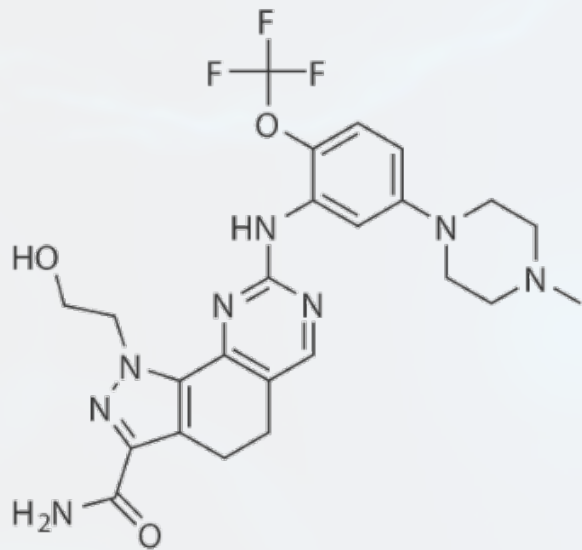
## PLK1 plays multiple roles during cell cycle

<b>S-Phase</b>	Controls the repair of DNA damage
<b>G2/M Checkpoint</b>	Controls the checkpoint for DNA quality
<b>M-Phase</b>	Controls separation of chromosomes

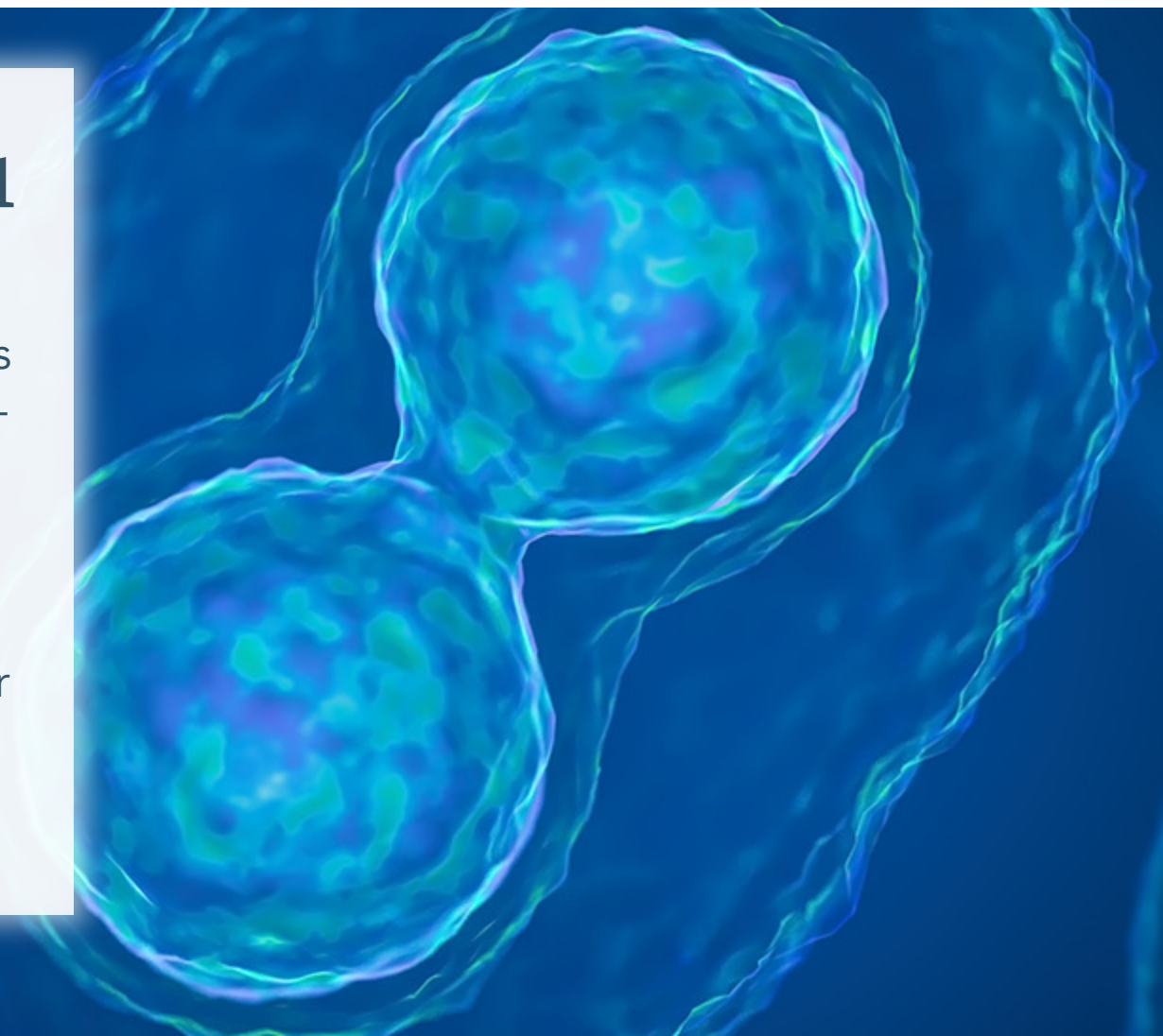


# PLK1 is a master regulator of genome integrity during cell replication

## ONVANSERTIB INHIBITS PLK1



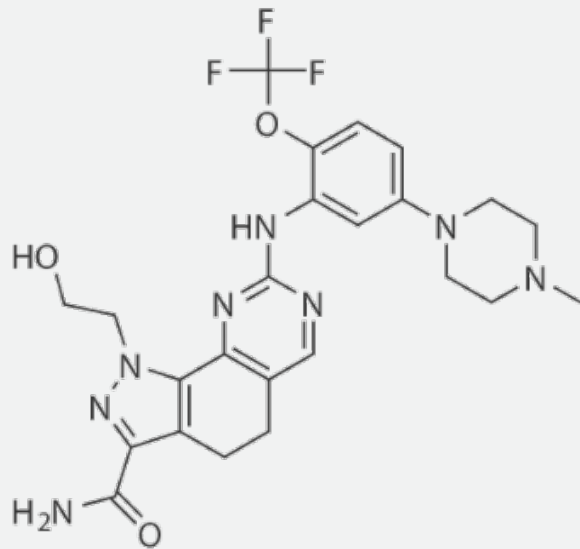
onvansertib shuts down PLK1's cell-preservation mechanisms, enhancing the efficacy of cell-damaging cancer therapies



# Onvansertib positions Cardiff Oncology to effectively target PLK1

## PROPERTIES

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



## SPECIFICITY

Exquisitely specific for PLK1

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



# Two goals drive our near-term clinical development program

2022

Q1

Q2

Q3

Q4

2023

Q1

Q2

Q3

2024

Q4

Q1

Q2

Q3

Q4

## GOALS

1

Validate prior mCRC data with a randomized trial

2

Demonstrate clinical POC in additional indications



# Today we'll see where we are, and where we're going

Accelerating our mCRC program

Additional onvansertib programs

Initial trial: phase 1b/2

Next trial

# Today we'll see where we are, and where we're going

Accelerating our mCRC program

Additional onvansertib programs

Pancreatic cancer (mPDAC)

Prostate cancer (mCRPC)

Triple negative breast cancer (TNBC)

Small cell lung cancer (SCLC)

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Accelerating our mCRC program

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Additional onvansertib programs

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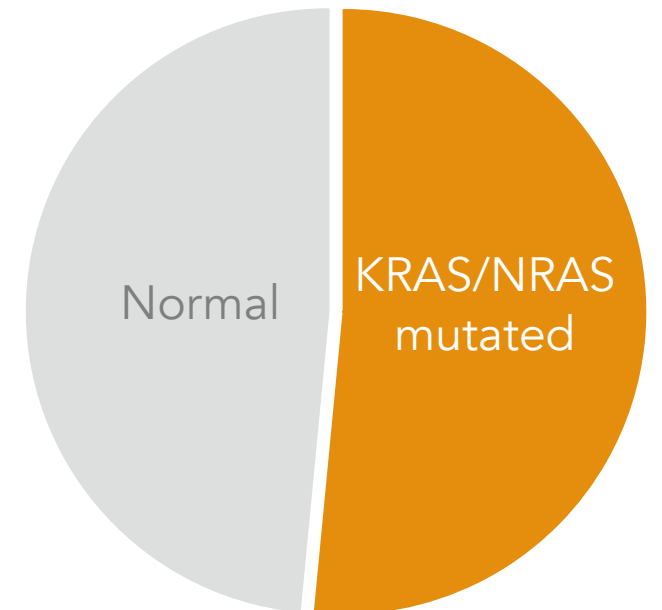
Initial trial: phase 1b/2

Next trial

# There are no targeted therapies available for KRAS/NRAS mutations

	1 <sup>st</sup> LINE	2 <sup>nd</sup> LINE
<b>Normal</b>		
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab
Targeted	+ EGFR inhibitor	NONE
<b>Mutated</b>		
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab
<b>Targeted</b>	<b>NONE</b>	<b>NONE</b>

Mutated mCRC is approx. half the mCRC population<sup>1</sup>



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

# The prognosis for second-line mCRC patients is poor

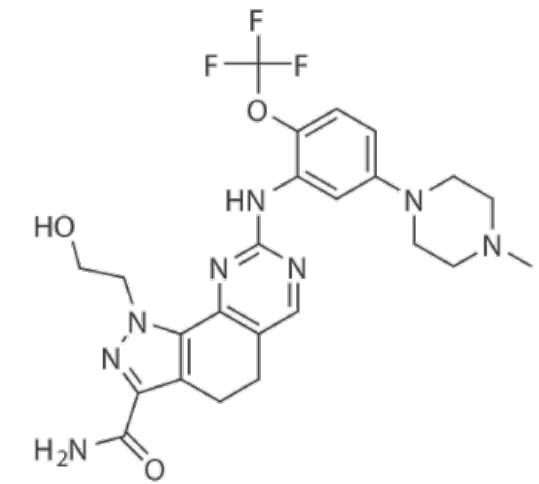
Normal		1 <sup>st</sup> LINE	2 <sup>nd</sup> LINE	HISTORICAL* ORR	
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab	NONE	5%	2006 – 2008
Targeted	+ EGFR inhibitor			11.4%	2000 – 2013
Mutated				13%	2015 – 2017
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab	NONE		
Targeted	NONE				

\* 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

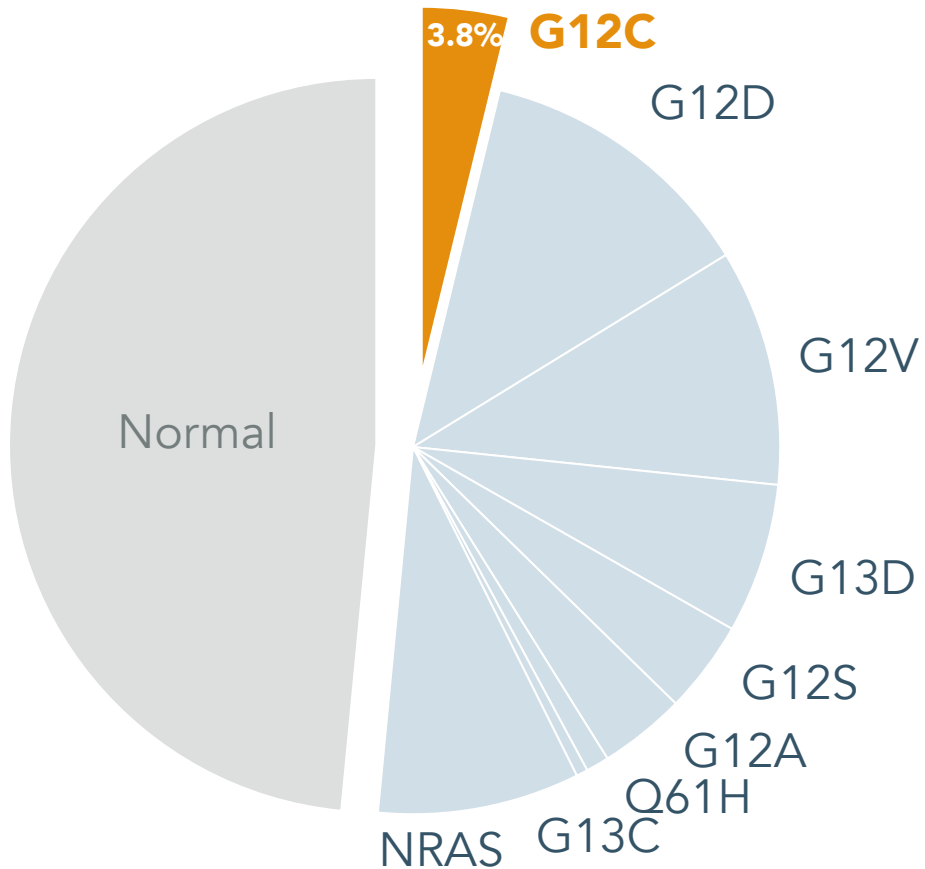
	1 <sup>st</sup> LINE	2 <sup>nd</sup> LINE
<b>Normal</b>		
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab
Targeted	+ EGFR inhibitor	NONE
<b>Mutated</b>		
Standard	FOLFOX + bevacizumab	FOLFIRI + bevacizumab
Targeted	NONE	<b>ONVANSERTIB</b>



◀ Onvansertib has the potential to fill this gap

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

## KRAS/NRAS Mutations in mCRC<sup>1</sup>

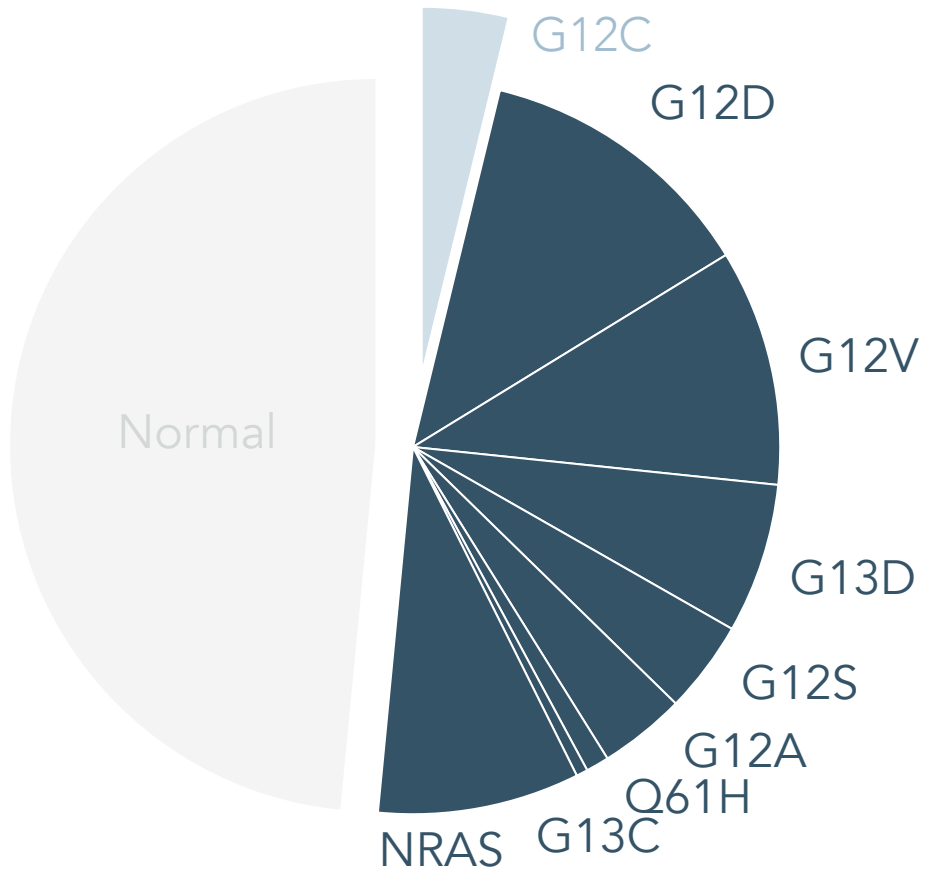


Investigational therapies (Amgen; Mirati) address the G12C KRAS mutation **only**

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<sup>1</sup>

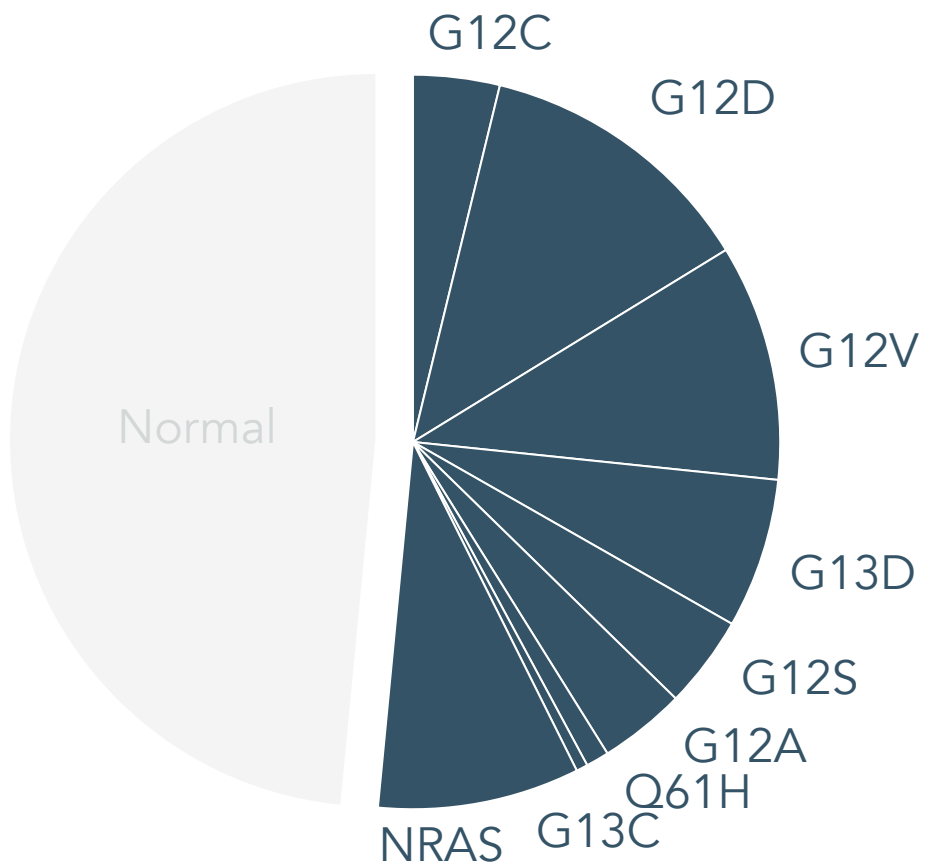


**93%**

of patients with  
KRAS/NRAS mutations  
miss targeted therapy

# Onvansertib is positioned to address gaps in KRAS-mutated mCRC

## KRAS/NRAS Mutations in mCRC<sup>1</sup>



## MOA

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

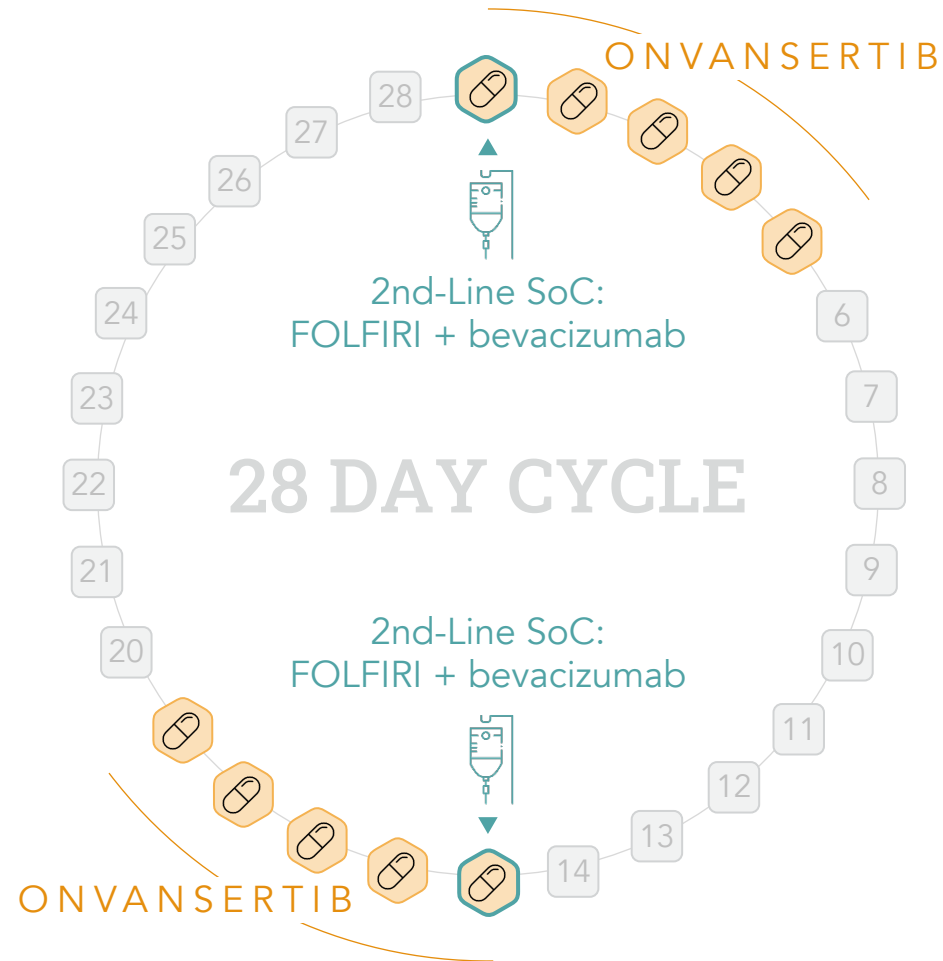
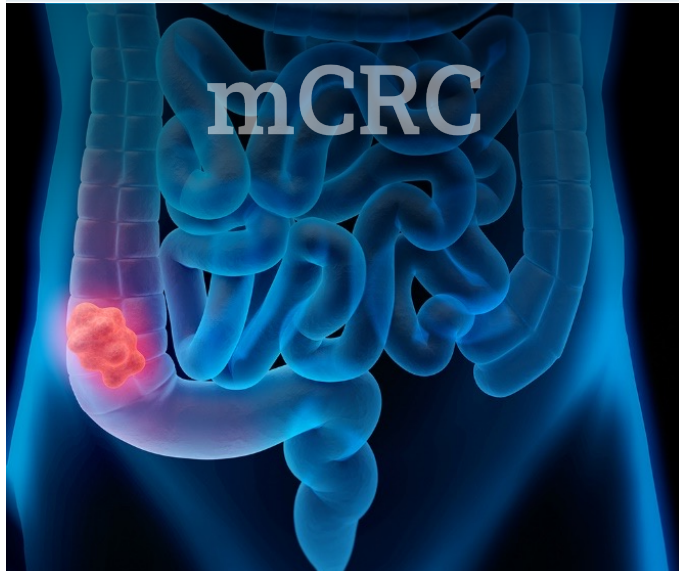
- 1 Synthetic lethality in KRAS mutants
- 2 Synergy with 2<sup>nd</sup>-line SoC

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

# Our Ph1/2b trial combined onvansertib with the current SoC

## ENROLLMENT CRITERIA

2<sup>nd</sup> line mCRC  
KRAS+  
Unresectable



## SINGLE ARM TRIAL

N=50 (48 evaluable)

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

# Our Ph1/2b trial assessed safety, efficacy and response biomarker

## ENROLLMENT CRITERIA

2<sup>nd</sup> line mCRC  
KRAS+  
Unresectable



## EFFICACY ENDPOINTS

1

Primary: Objective Response Rate (ORR) per RECIST v1.1 in patients who receive  $\geq 1$  cycle of treatment

2

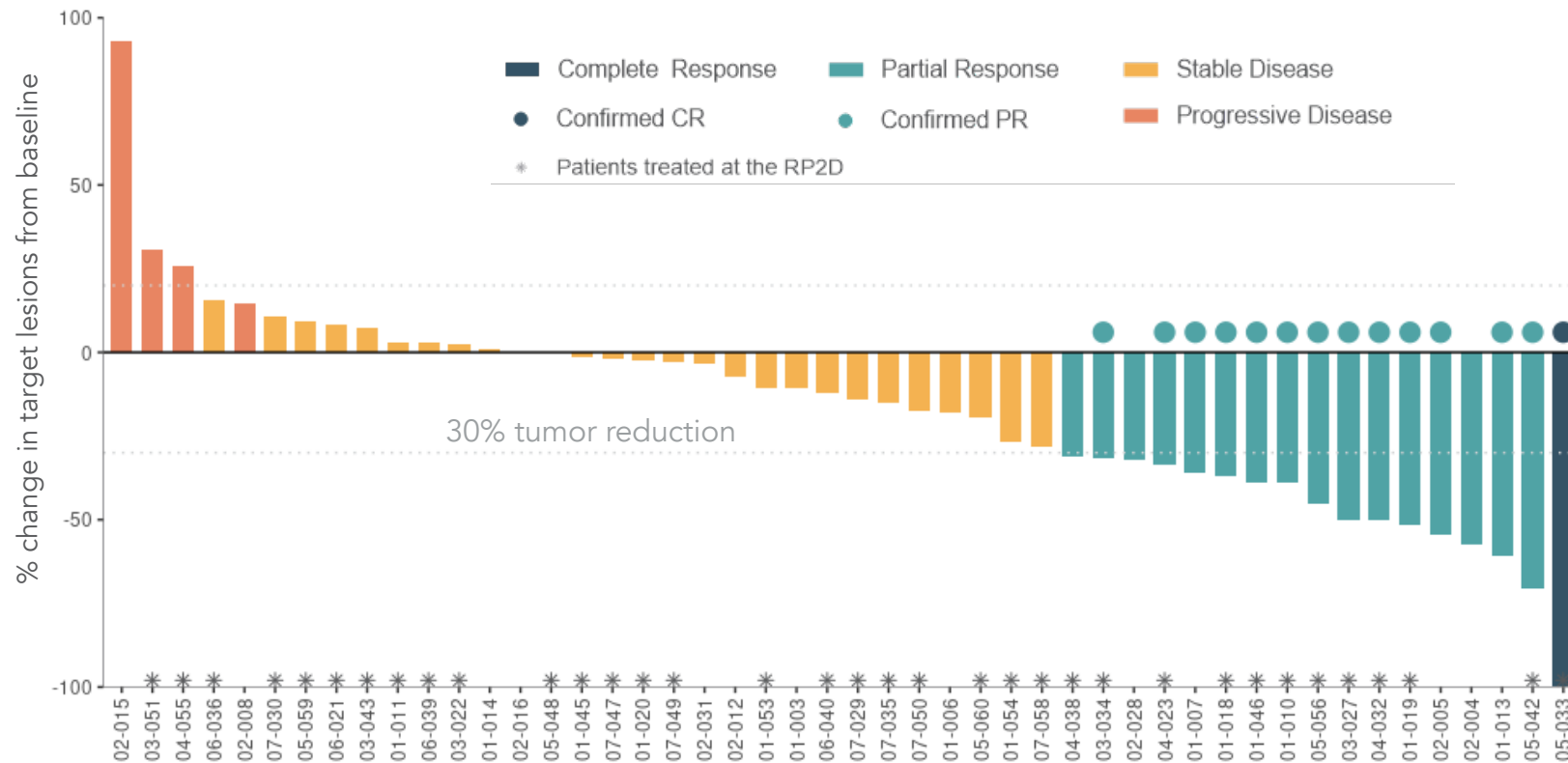
Secondary: Progression-Free Survival (PFS) and Duration of Response (DoR)

3

Exploratory: decrease in KRAS mutational burden and response to treatment

# Patients achieved a strong, durable response with onvansertib + SoC

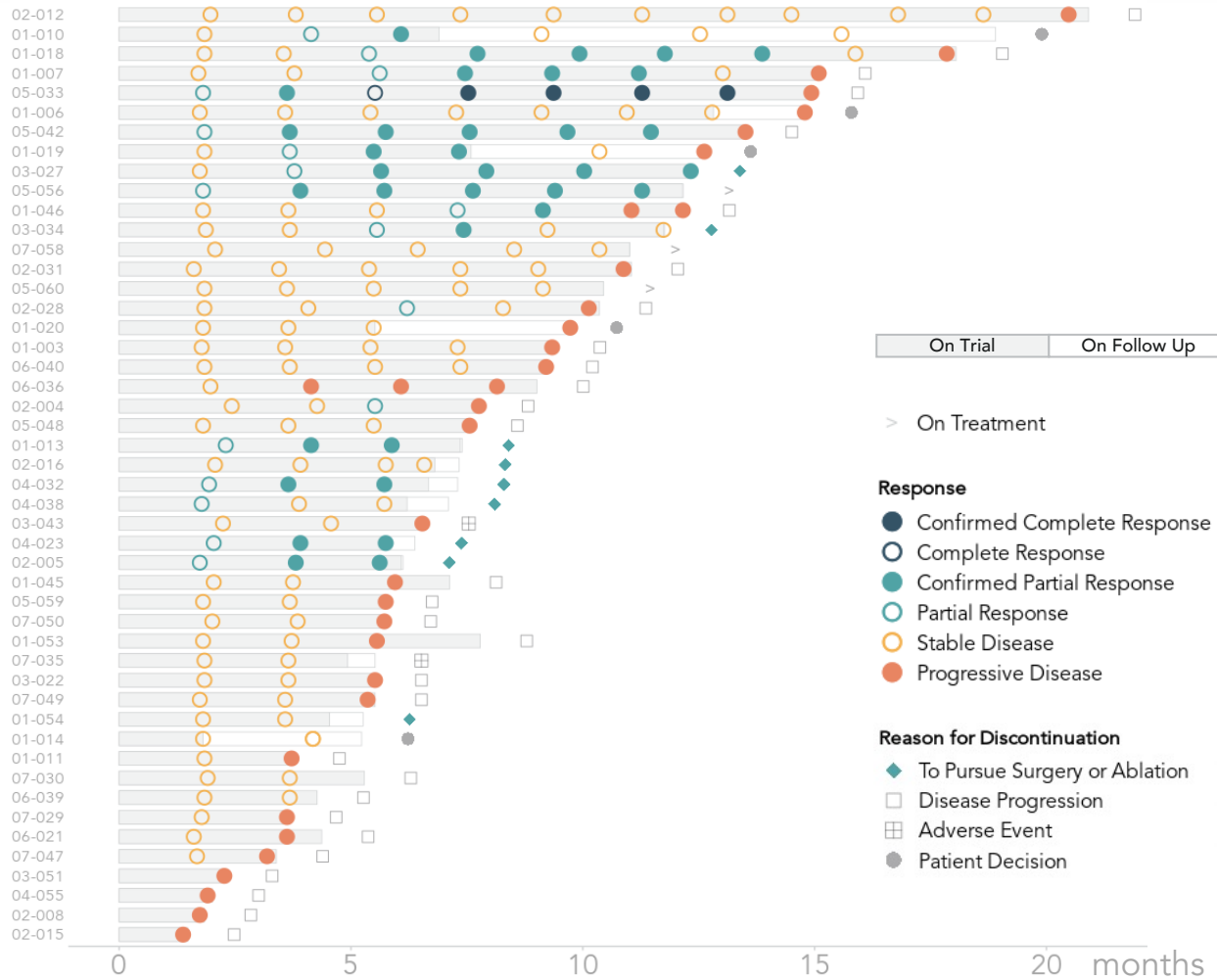
## Best Radiographic Response\* – all doses (as of July 25, 2022)



	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)
<b>Durability</b>		
Median Duration of Response	11.7 months	12.5 months

\* 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



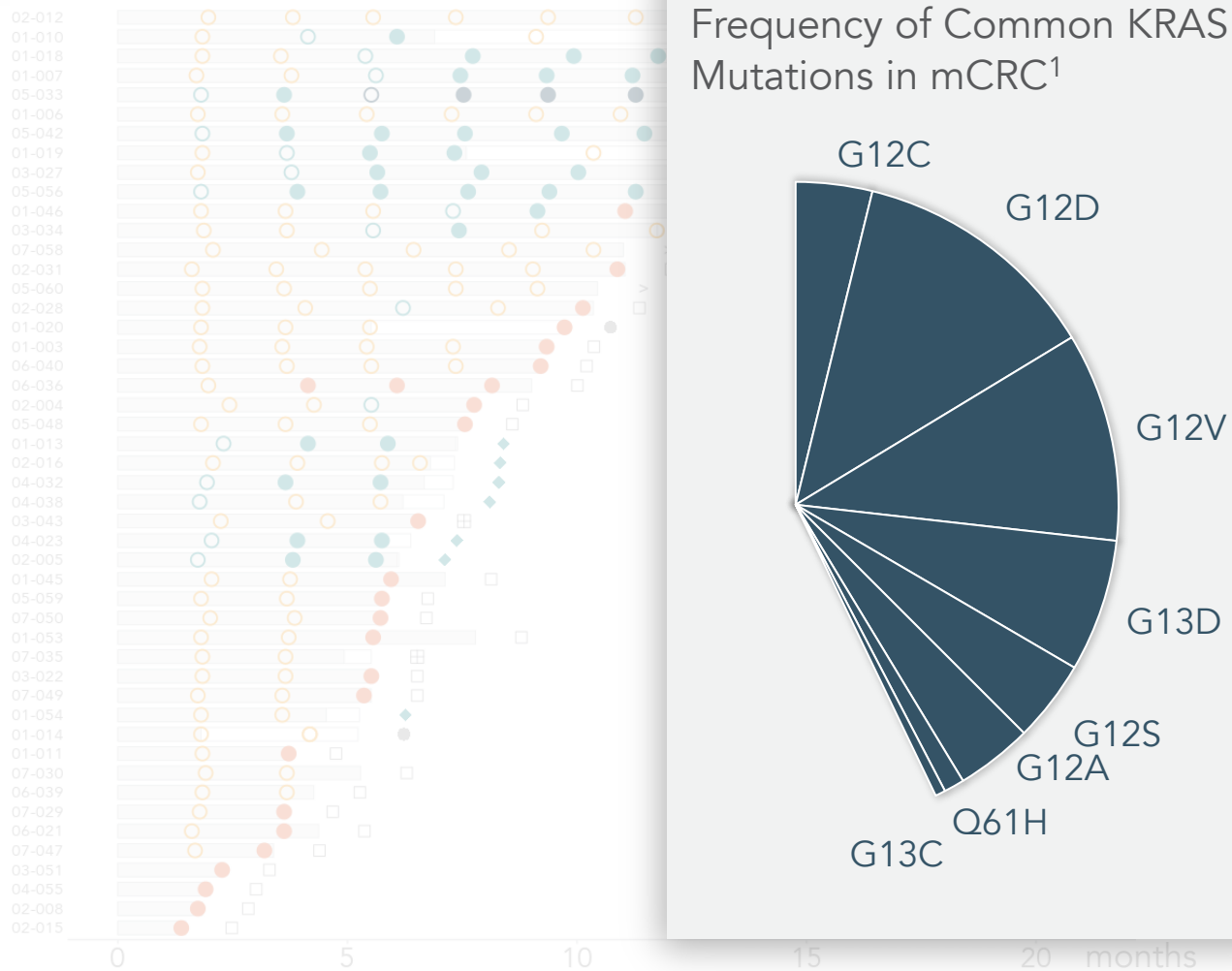
**Swimmer plot\*** – all doses (as of July 25, 2022)

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



# Patients achieved responses across several KRAS mutations

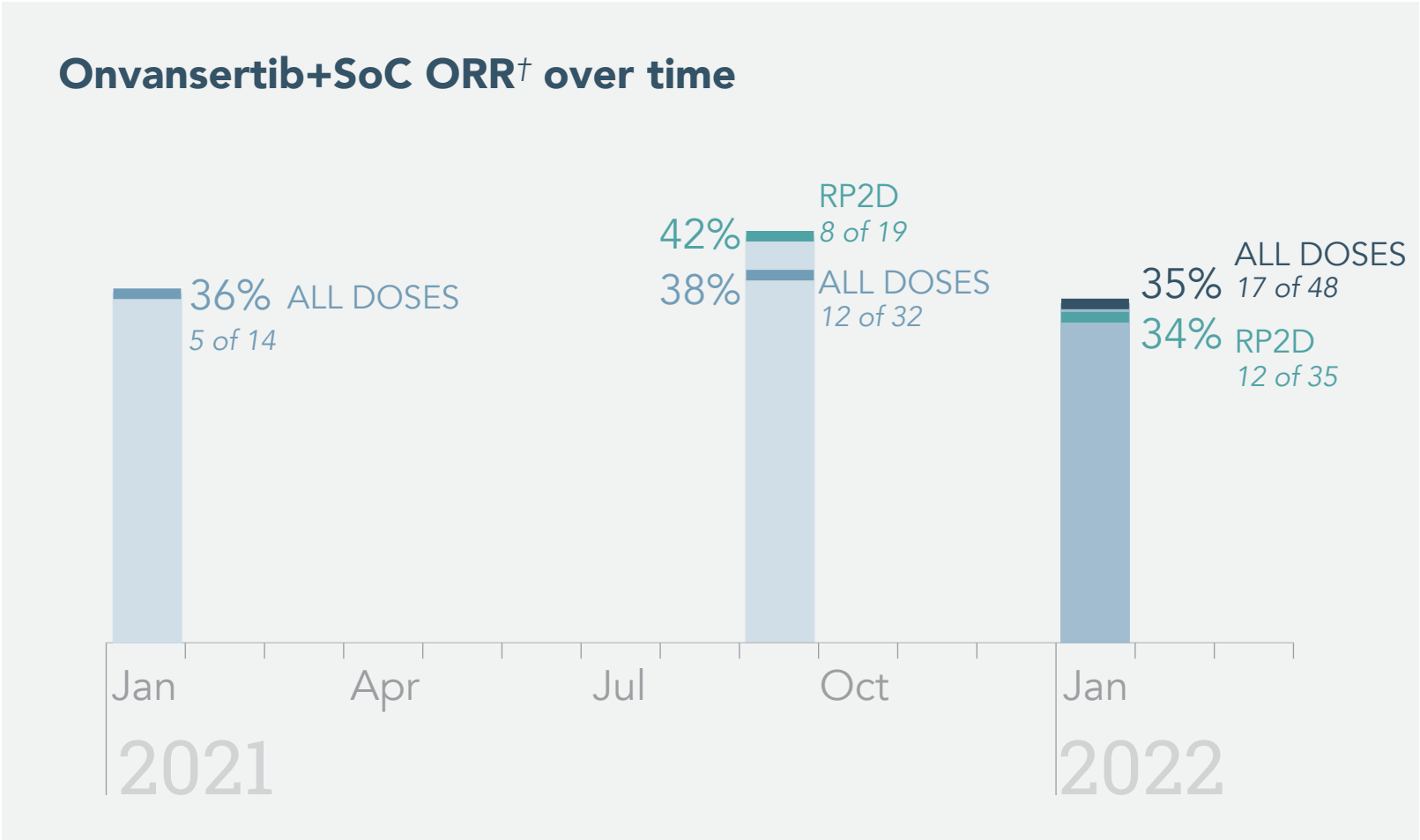
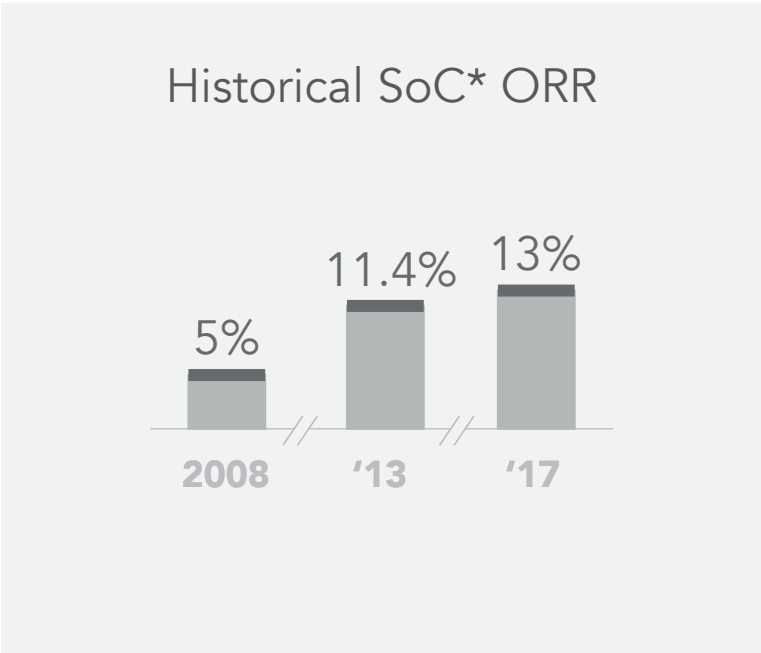


Onvansertib responses across KRAS mutations (as of July 25, 2022)

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
<b>Total</b>	<b>17</b>	<b>27</b>	<b>4</b>	<b>48</b>

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

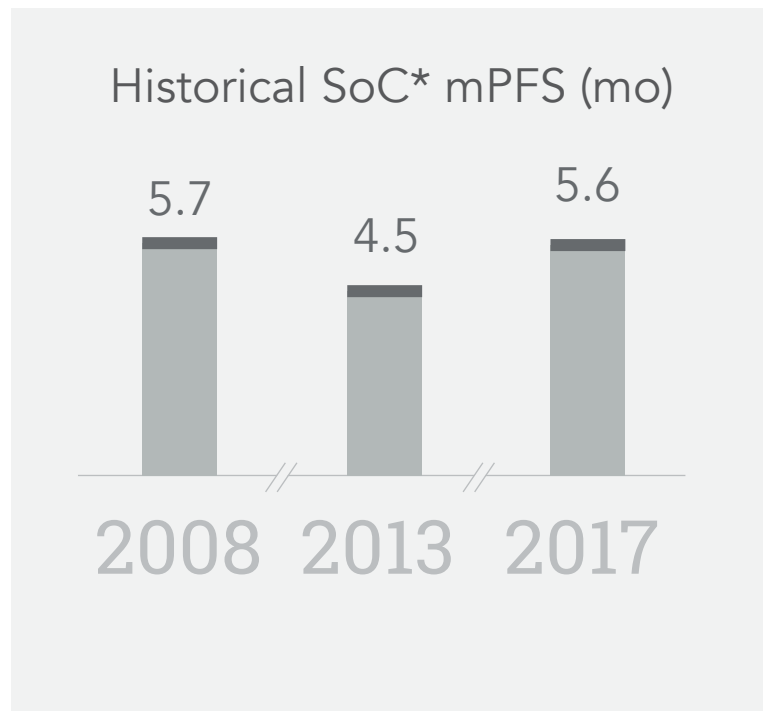
# Objective Response Rate for mCRC trial exceeds SoC over time



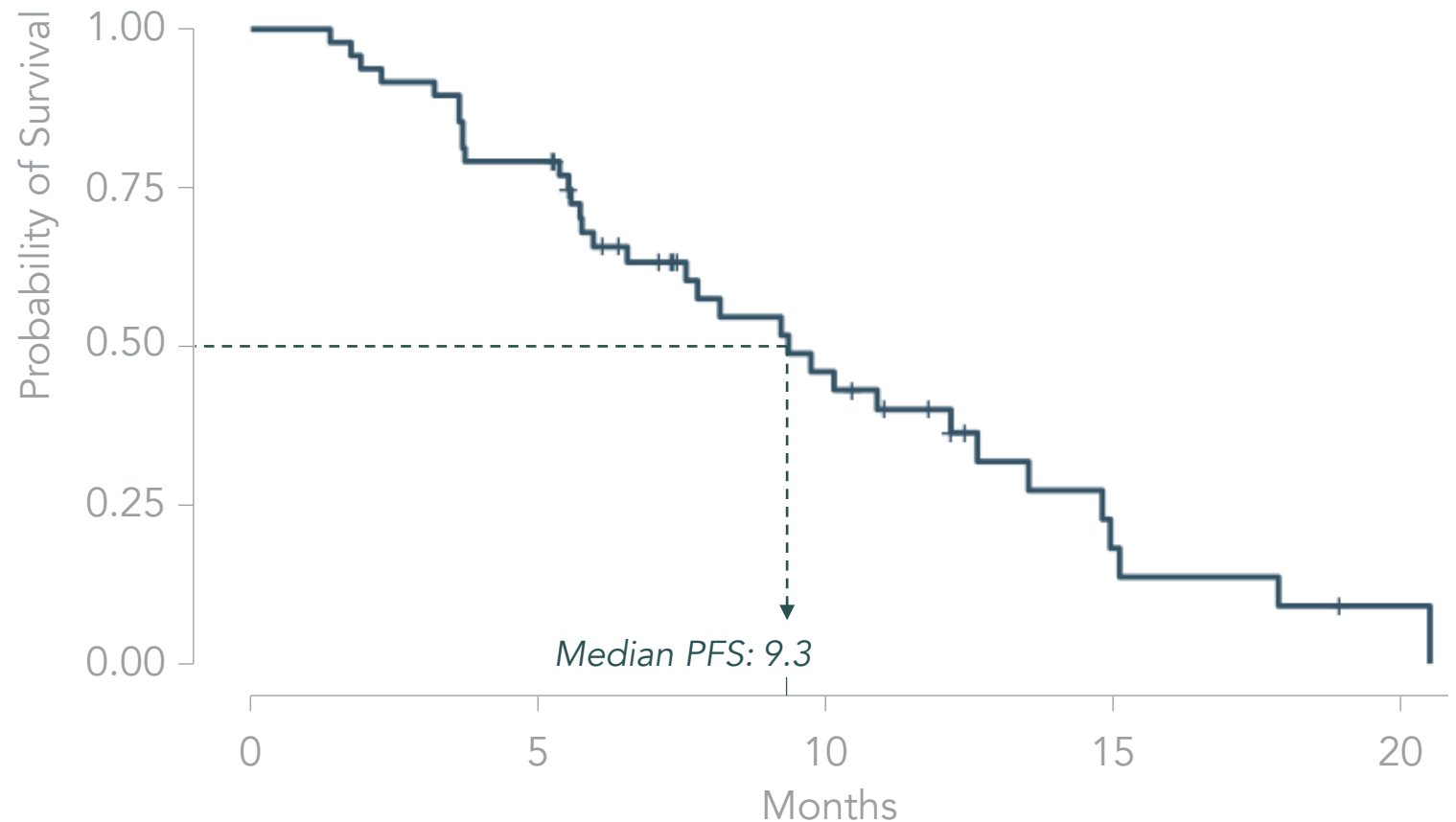
\* 2008: Bennouna et al., Lancet Oncol 2013; 14: 29–37; 2013: Giessen et al., Acta Oncologica, 2015, 54: 187-193; 2017: Cremolini et al., Lancet Oncol 2020, 21: 497–507; and Antoniotti et al., Correspondence Lancet Oncol June 2020. SoC: Standard-of-care

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

# Progression Free Survival for mCRC trial exceeds SoC over time



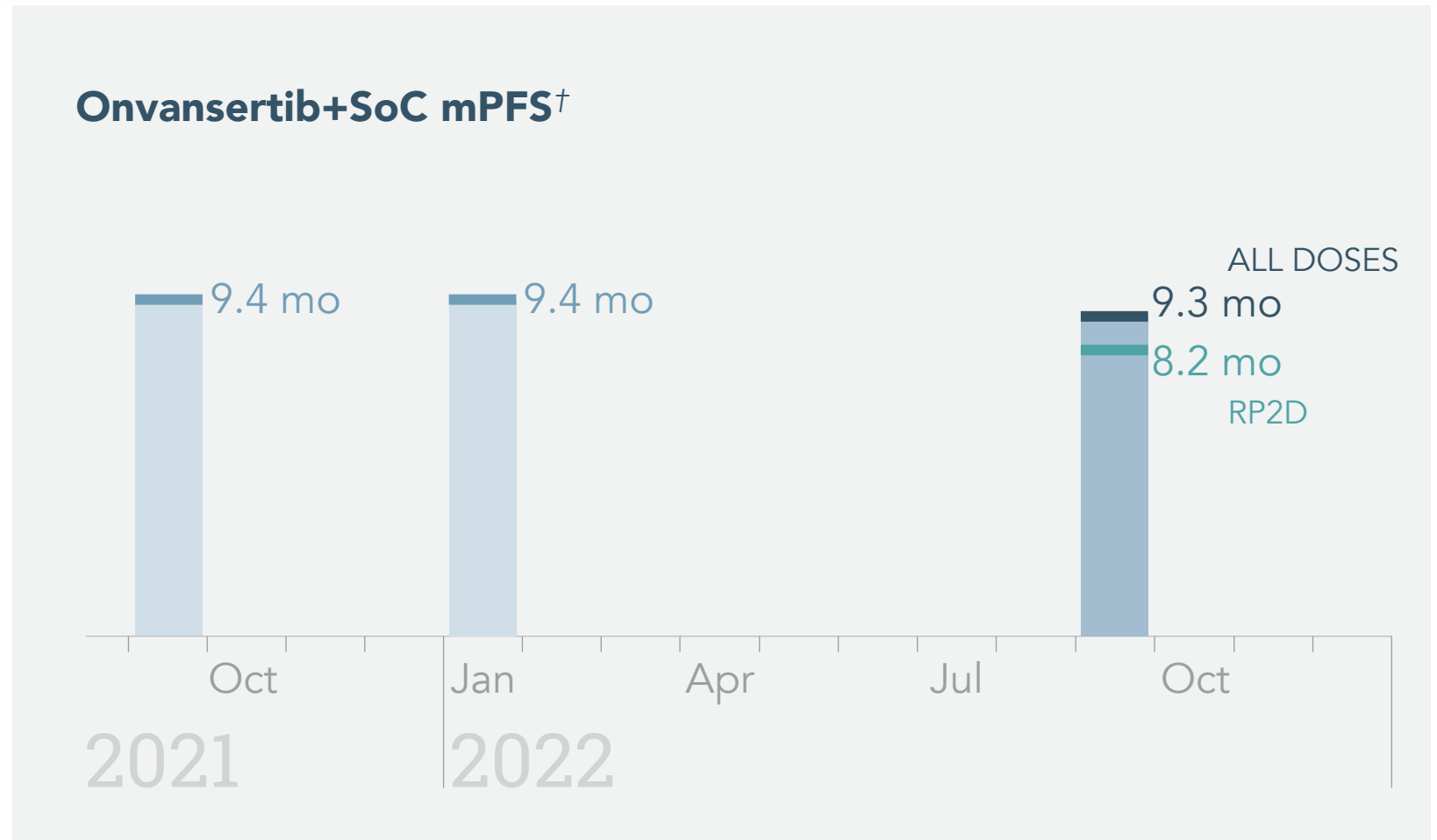
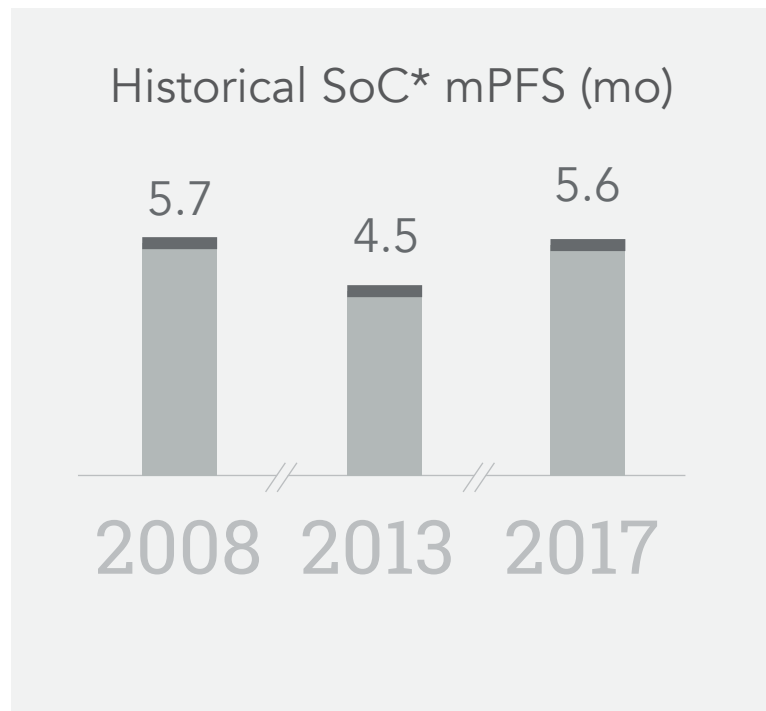
Progression free survival<sup>†</sup> – all doses (as of July 25, 2022)



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

# Progression Free Survival for mCRC trial exceeds SoC over time



<sup>†</sup> Onvansertib mPFS are interim data from an ongoing trial and unlocked database

\* 2008: Bennouna et al., Lancet Oncol 2008; 9: 20-27; 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

# 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

	TEAEs*	GRADE					All		TEAEs*	GRADE					All
		1	2	3	4					1	2	3	4		
	Neutropenia	1	13	15	6	35		Anemia	9	4	1	0	14		
	Fatigue	15	15	3	0	33		Vomiting	9	3	1	0	13		
	Nausea	24	7	2	0	33		Musculoskeletal Pain <sup>†</sup>	11	1	0	0	12		
	Diarrhea	15	7	2	0	24		Infection <sup>†</sup>	3	4	4	0	11		
	Abdominal Pain	13	7	1	0	21		Hemorrhage <sup>†</sup>	8	0	1	0	9		
	Mucositis	11	6	2	0	19		Headache	7	0	0	0	7		
	Alopecia	17	2	0	0	19		Neuropathy	5	2	0	0	7		
	WBC Decrease	6	9	2	1	18		GERD	7	0	0	0	7		
	Platelet Count Decrease	10	4	1	0	15		ALT Increase	4	0	1	0	5		
	Hypertension	2	8	5	0	15									

\* 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

<sup>†</sup> Musculoskeletal pain, infection and hemorrhage are pooled terms

# The trial's patient demographics reflects 2<sup>nd</sup> line mCRC population

## Enrollment\*

Number of Patients (N)	Phase 1b, Dose Level 0 Onvansertib 12 mg/m <sup>2</sup>	Phase 1b, Dose Level +1 Onvansertib 15 mg/m <sup>2</sup>	Phase 1b, Dose Level +2 Onvansertib 18 mg/m <sup>2</sup>	Phase 2 RP2D Onvansertib 15 mg/m <sup>2</sup>	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%)
<b>Prior bevacizumab treatment<sup>5</sup></b>	
<b>Yes</b>	<b>35 (70%)</b>
<b>No</b>	<b>15 (30%)</b>

\* 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 1<sup>st</sup> and 2<sup>nd</sup> line SoC

	1 <sup>st</sup> LINE	2 <sup>nd</sup> LINE
Normal	FOLFOX + <b>bevacizumab</b> + EGFR inhibitor	FOLFIRI + <b>bevacizumab</b>
RAS Mutated	FOLFOX + <b>bevacizumab</b>	FOLFIRI + <b>bevacizumab</b>

## mCRC Ph1b/2 trial

N=50 (48 evaluable)

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

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

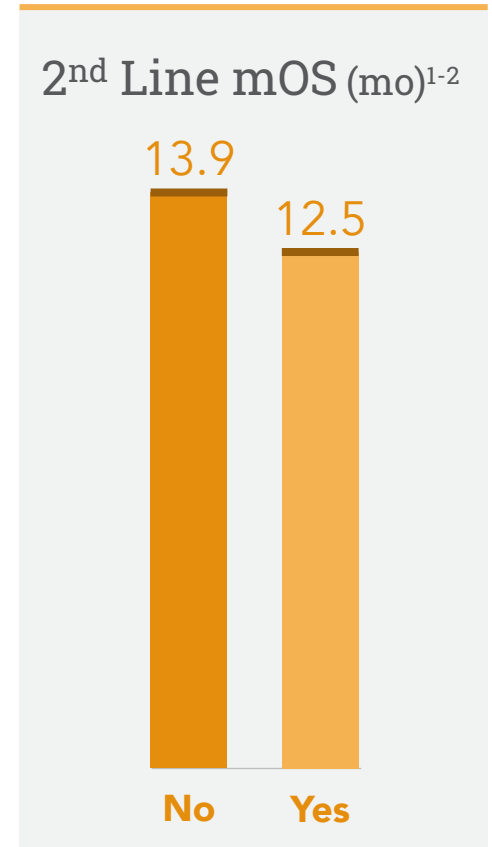
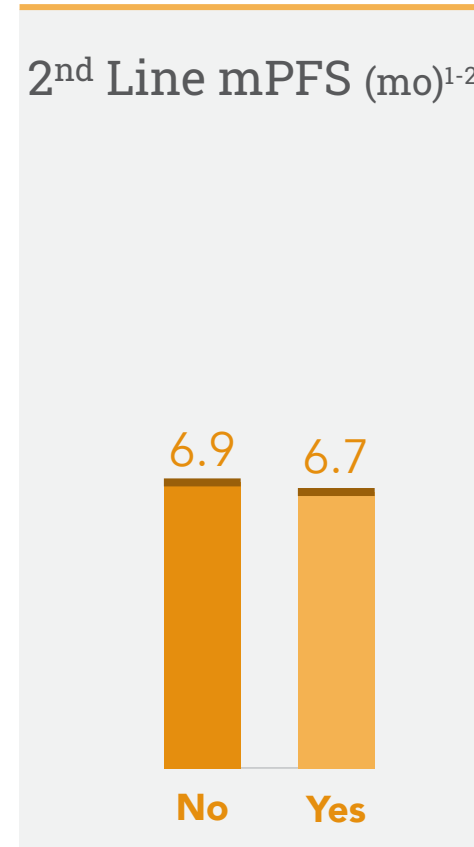
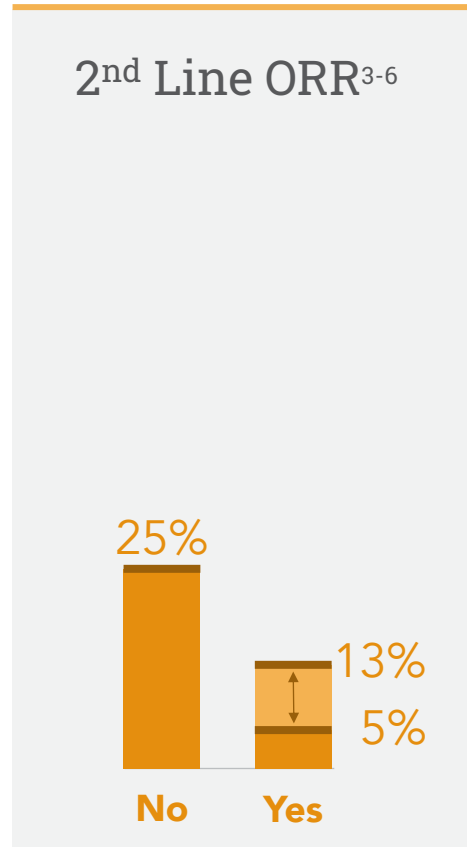
## 2<sup>nd</sup> LINE

### EFFICACY DATA FROM HISTORICAL TRIALS IN mCRC

BEV EXPOSURE IN 1<sup>ST</sup> LINE?

Normal  
FOLFIRI +  
**bevacizumab**

RAS  
Mutated  
FOLFIRI +  
**bevacizumab**



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. Tabernaro 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

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

Normal

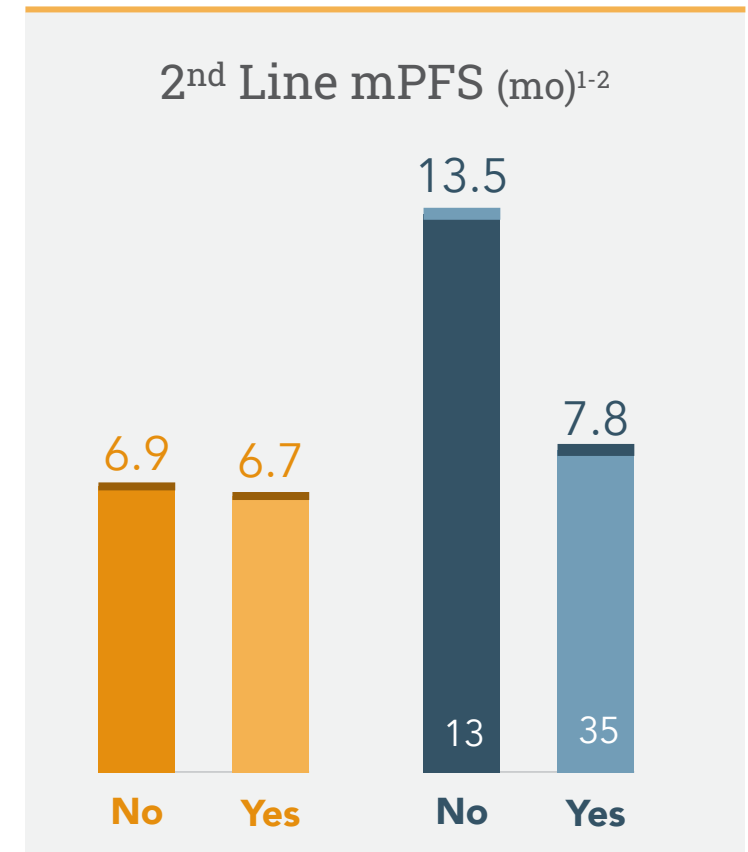
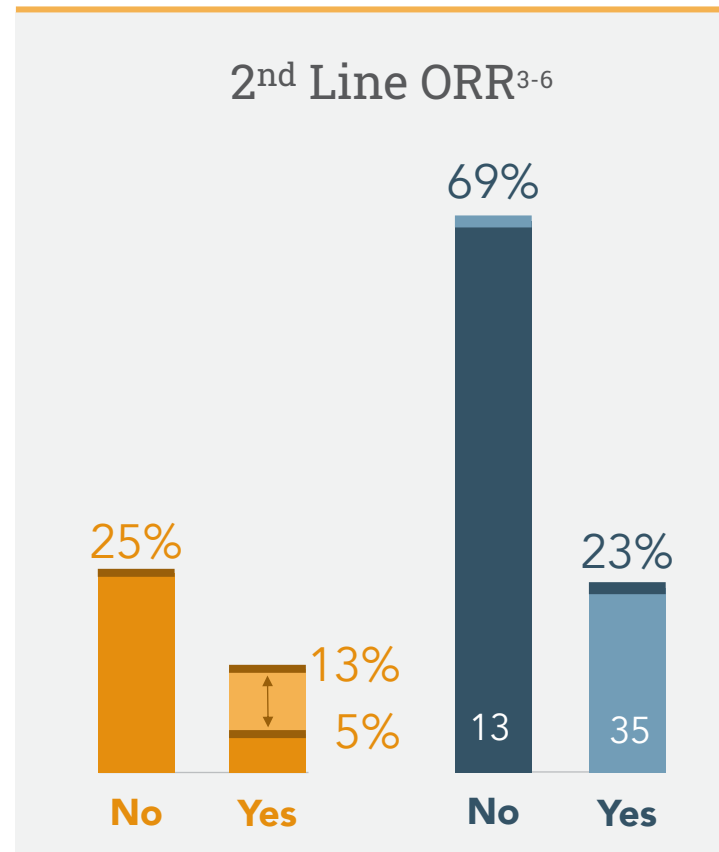
FOLFIRI +  
**bevacizumab**

RAS  
Mutated

FOLFIRI +  
**bevacizumab**  
+  
ONVANSERTIB

### HISTORICAL CONTROLS VS ONVANSERTIB\* Ph 1b/2 DATA

BEV EXPOSURE IN 1<sup>ST</sup> 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. Tabernaro et al, Lancet Oncol 2015; 16: 499-508; 6. Beretta et al., Med Oncol (2013) 30:486.

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

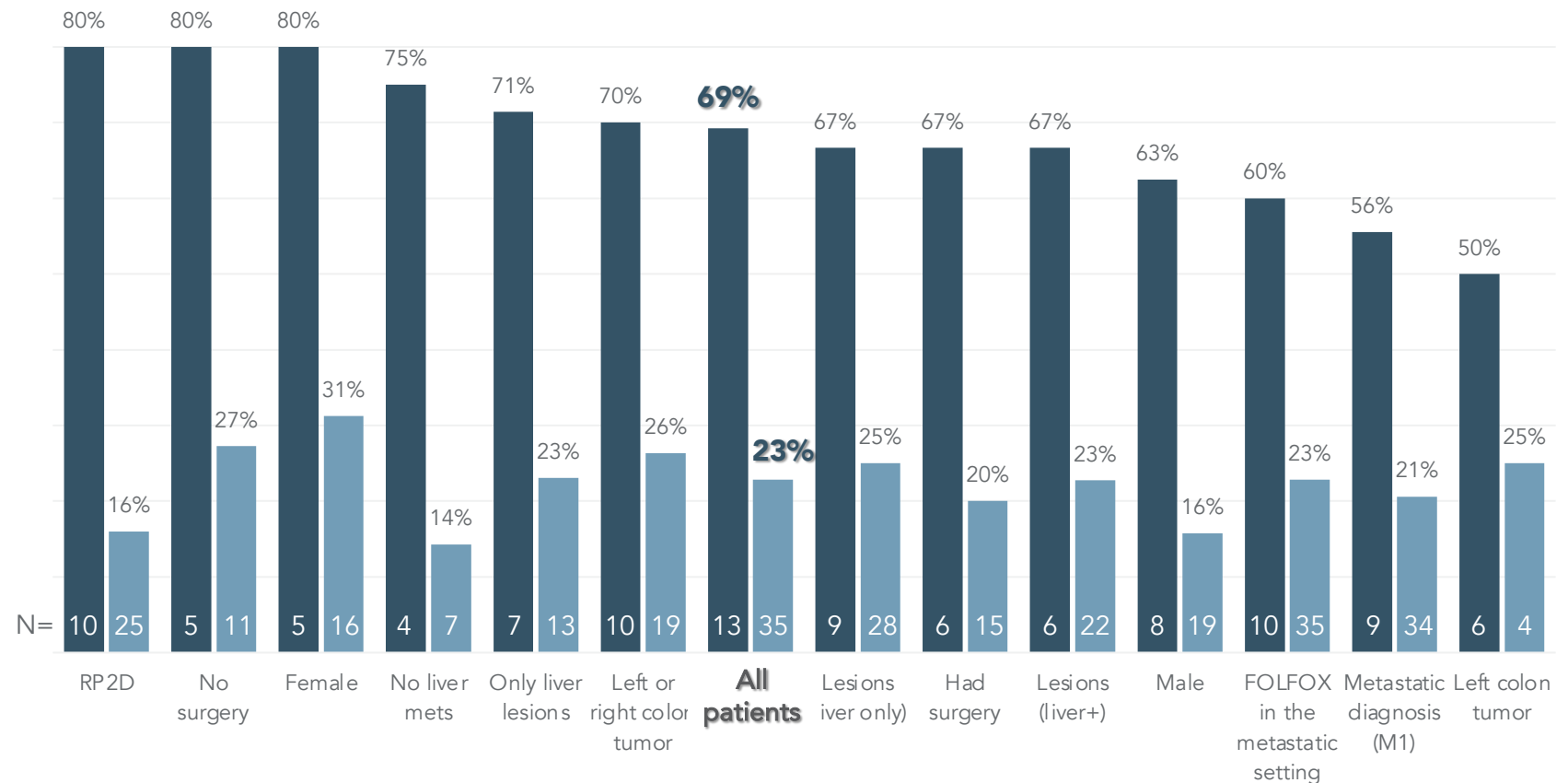
# ORR is consistently greater for bev naïve patients across characteristics

No single patient characteristic explains observed ORR difference

BEV EXPOSURE IN 1<sup>ST</sup> LINE?

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

ORR (%) for Bevacizumab Naïve vs. Exposed Patients\*



\* Onvansertib ORR and mPFS are 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 1<sup>ST</sup> LINE?

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

## HYPOTHESES

- A. This is a statistical anomaly (small n)?
- B. This is due to onv / bev synergy?

## 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 Ph 1b/2 patients for genomic alterations in bev naïve vs bev exposed

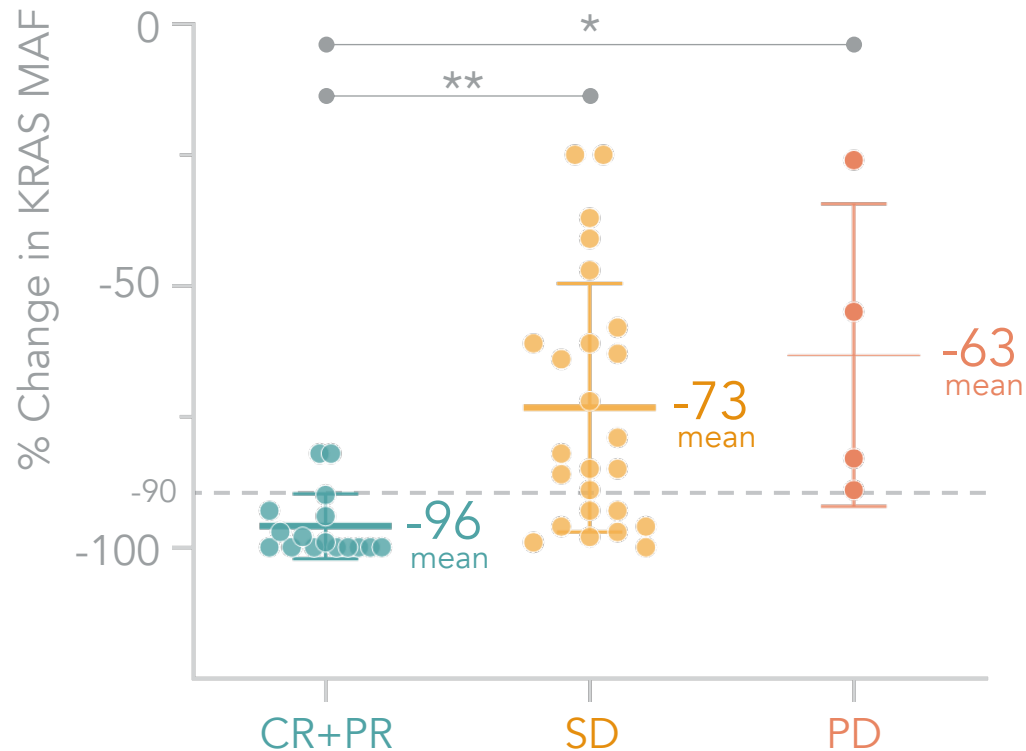
## OPPORTUNITY

Conduct a 1<sup>st</sup> 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.

# Early KRAS MAF ctDNA decrease correlates w/ radiographic response

**% KRAS Mutant Allelic Frequency (MAF)\***  
decrease after one 28-day treatment cycle  
(Mean  $\pm$ 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  $\geq 90\%$  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.

# Early Changes in KRAS MAF predicts clinical response

## ORR (%)

KRAS RESPONDERS

64%  
14 of 22

KRAS NON-RESPONDERS

9%  
2 of 23

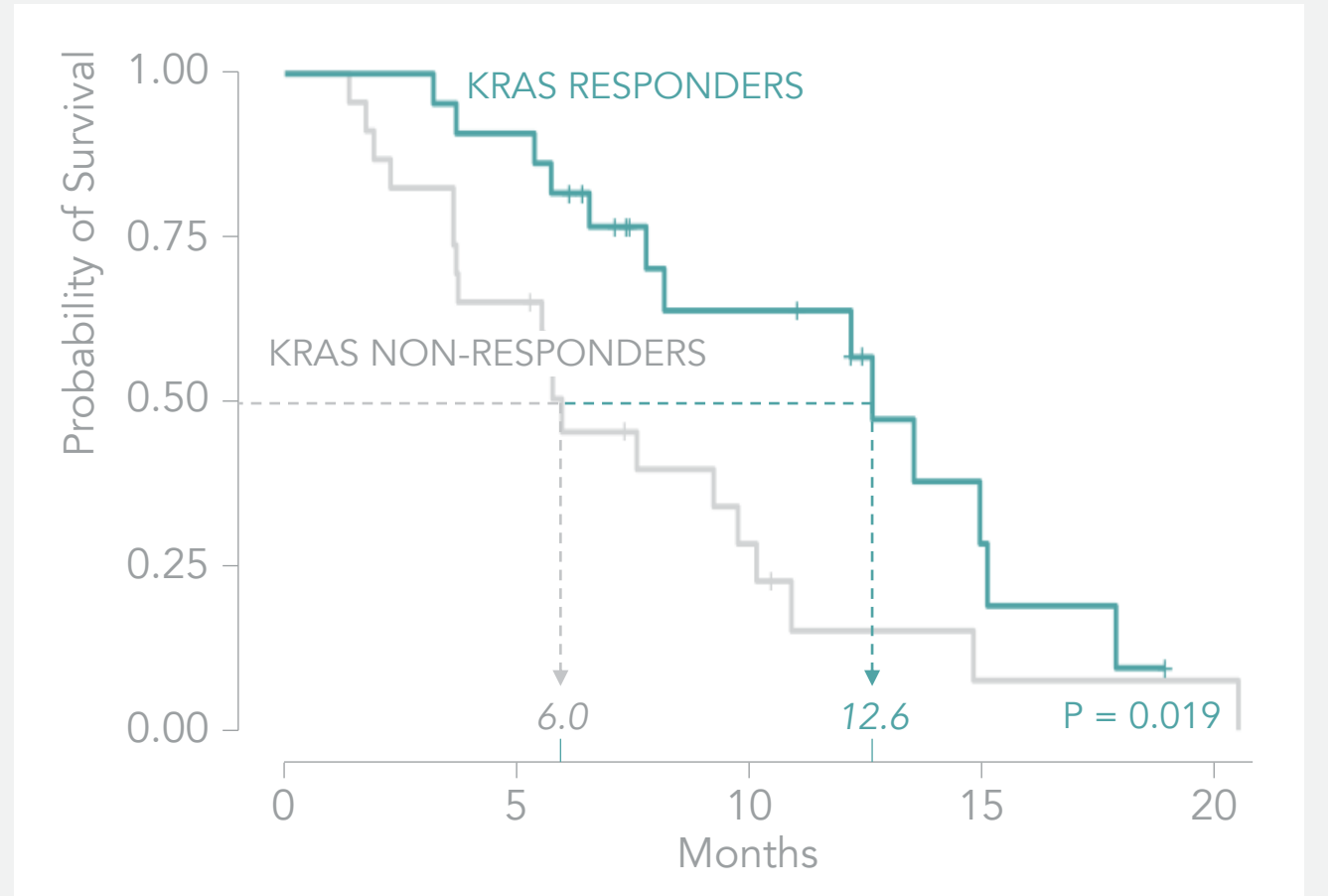
## mPFS (mo)

KRAS RESPONDERS

12.6 mo

KRAS NON-RESPONDERS

6.0 mo



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Accelerating our mCRC program

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Additional onvansertib programs

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Initial trial: phase 1b/2

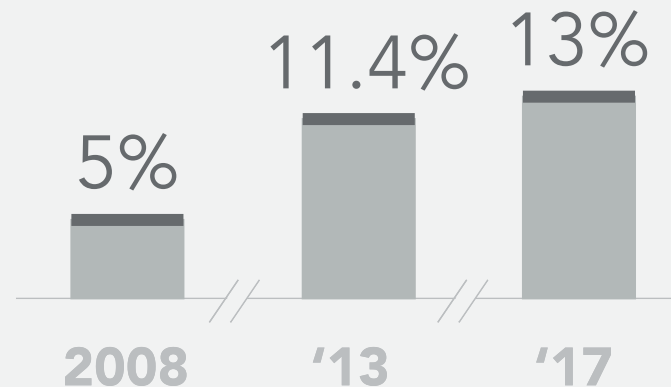
Next trial

# We believe that onvansertib complements and improves SoC

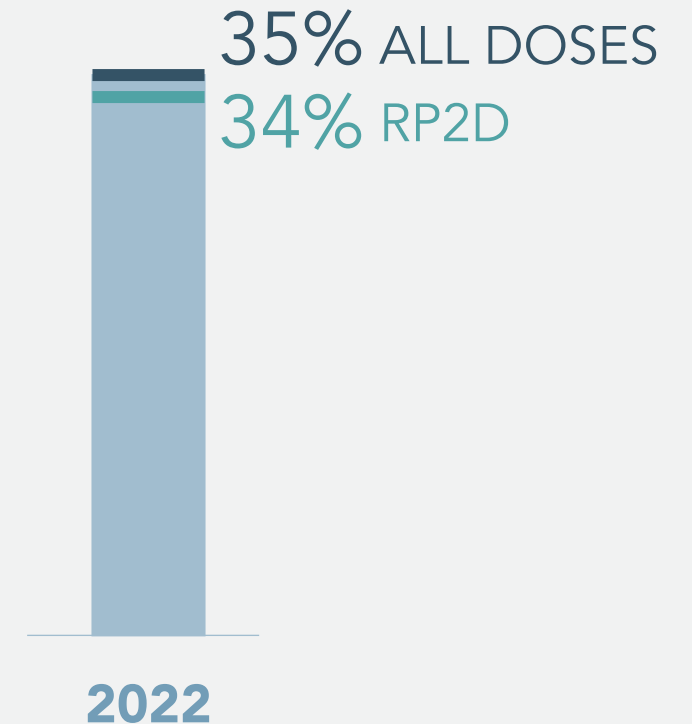
## Our Ph1b/2 Question:

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

### Historical SoC\* ORR



### Ph1b/2 ORR



\* 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

We approach our next trial with four clear objectives



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**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

2<sup>nd</sup> line mCRC  
KRAS+/NRAS+  
Unresectable

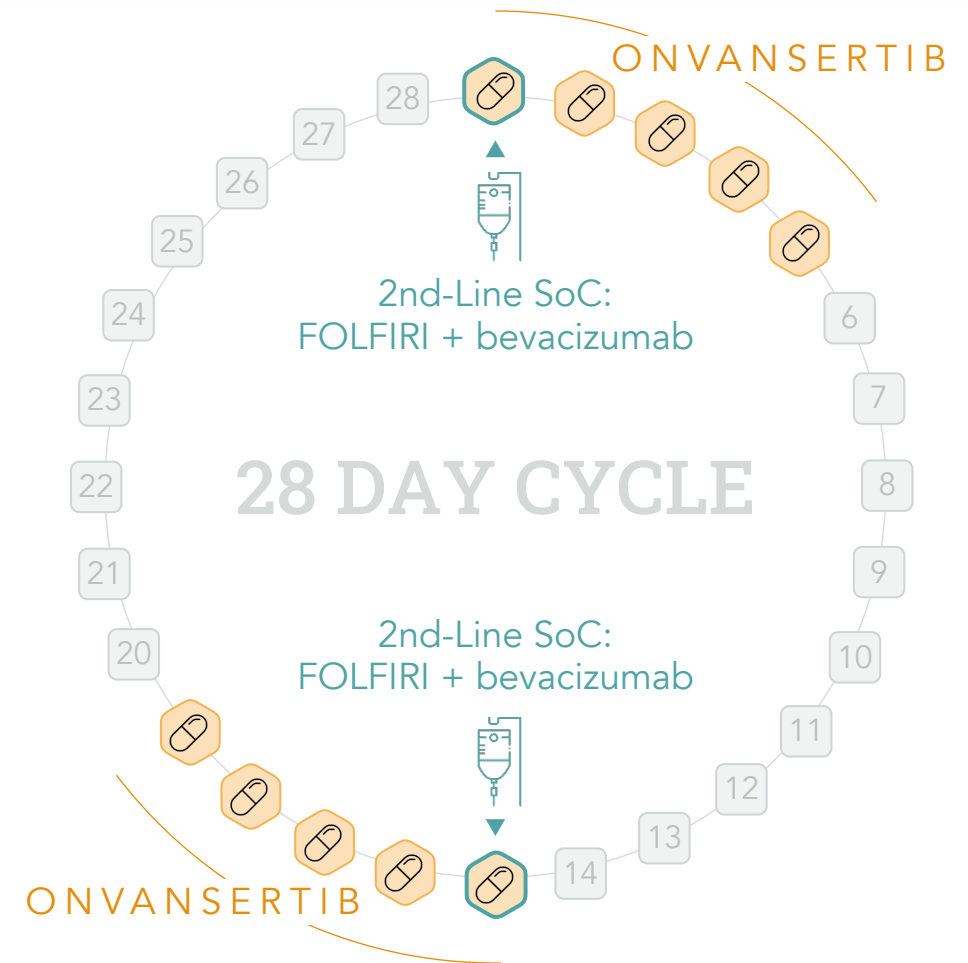
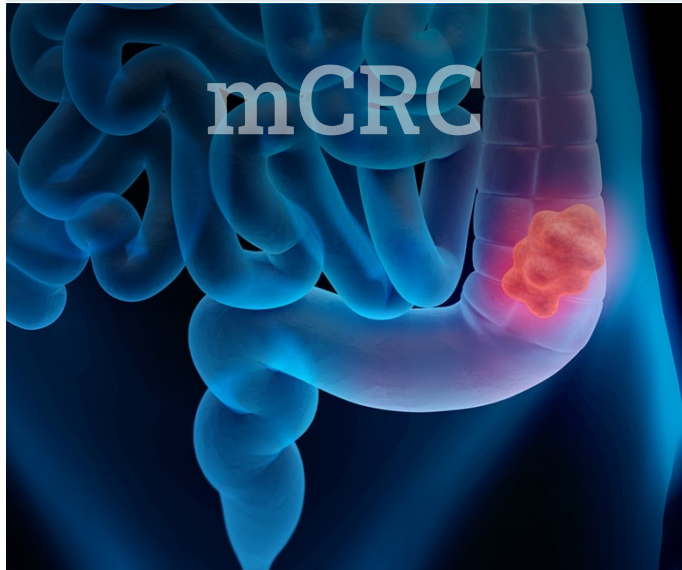
**R**

N=150  
1:1:1

SoC (FOLFIRI + Bev)

SoC + onvansertib (20mg)

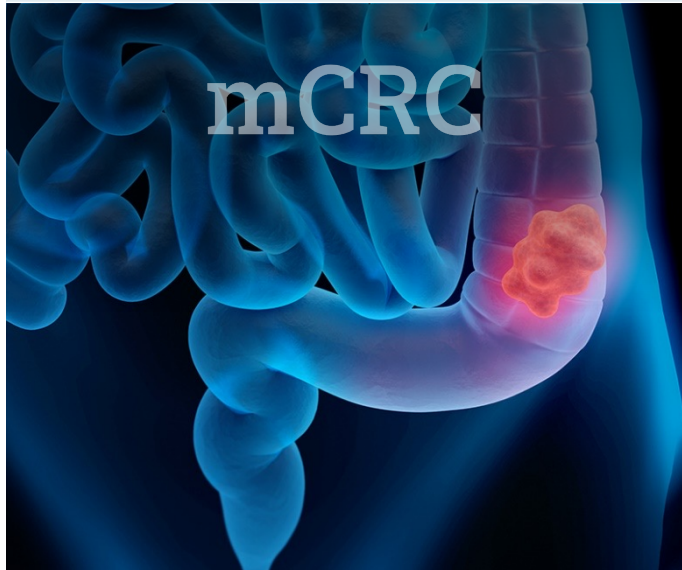
SoC + onvansertib (30mg)



# Our ONSEMBLE Ph2 trial is designed to demonstrate efficacy

## ENROLLMENT CRITERIA

2<sup>nd</sup> line mCRC  
KRAS+/NRAS+  
Unresectable



## ENDPOINTS

Primary Objective Response Rate: CR + PR

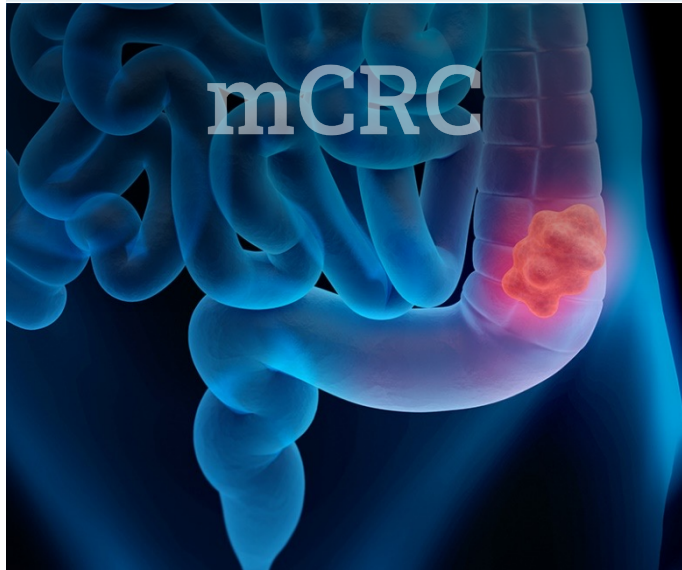
Key Secondary Progression-Free Survival

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

# Our ONSEMBLE Ph2 trial will be statistically robust

## ENROLLMENT CRITERIA

2<sup>nd</sup> line mCRC  
KRAS+/NRAS+  
Unresectable



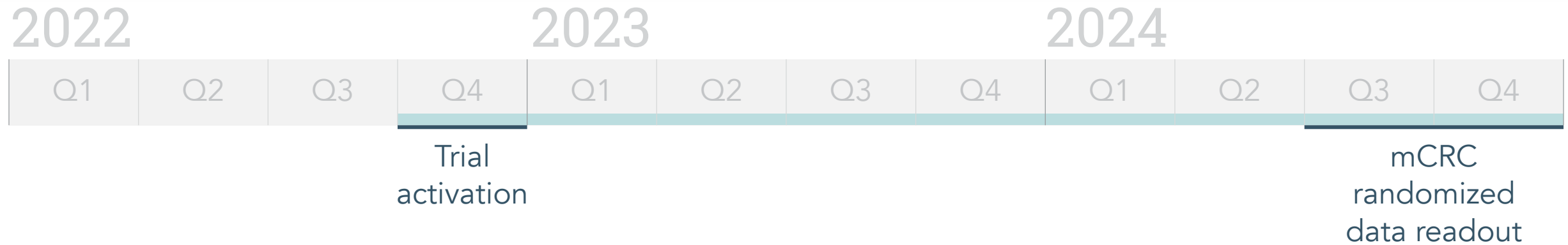
## DESIGN

- 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

# We are optimistic that randomized data will create substantial value



## Opportunity to create value

- Rigorous demonstration of onvansertib's role in increasing efficacy in mCRC vs. SoC alone
- Position for possible accelerated approval opportunity in mCRC
- Early identification of likely responders (MAF)
- Strong indication that onvansertib has potential in other indications

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Accelerating our mCRC program

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Additional onvansertib programs

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Pancreatic cancer (mPDAC)

Prostate cancer (mCRPC)

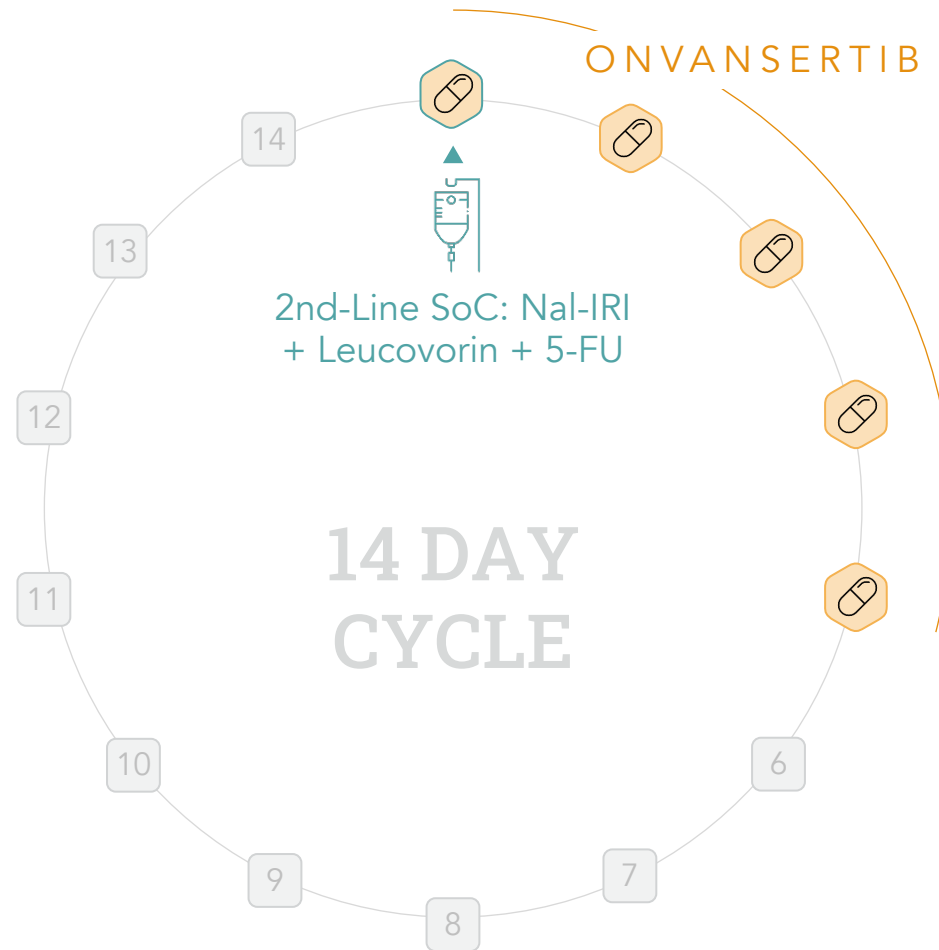
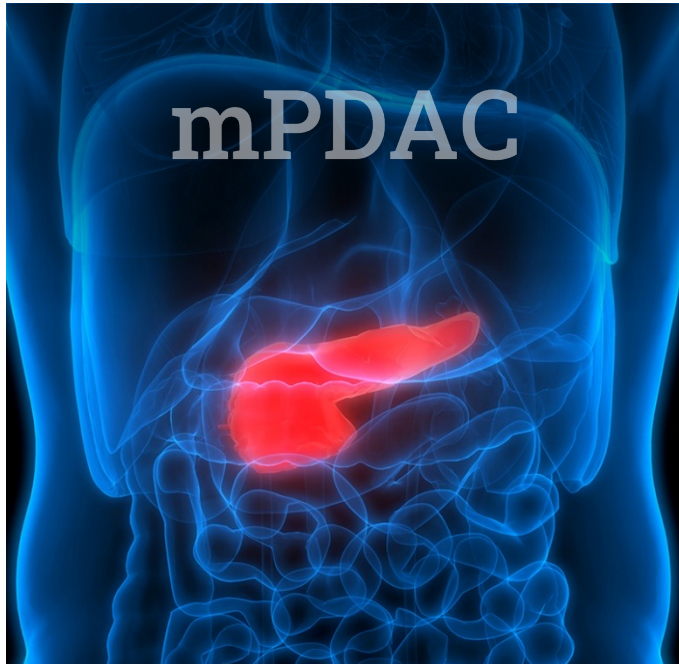
Triple negative breast cancer (TNBC)

Small cell lung cancer (SCLC)

# 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 mPFS, 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

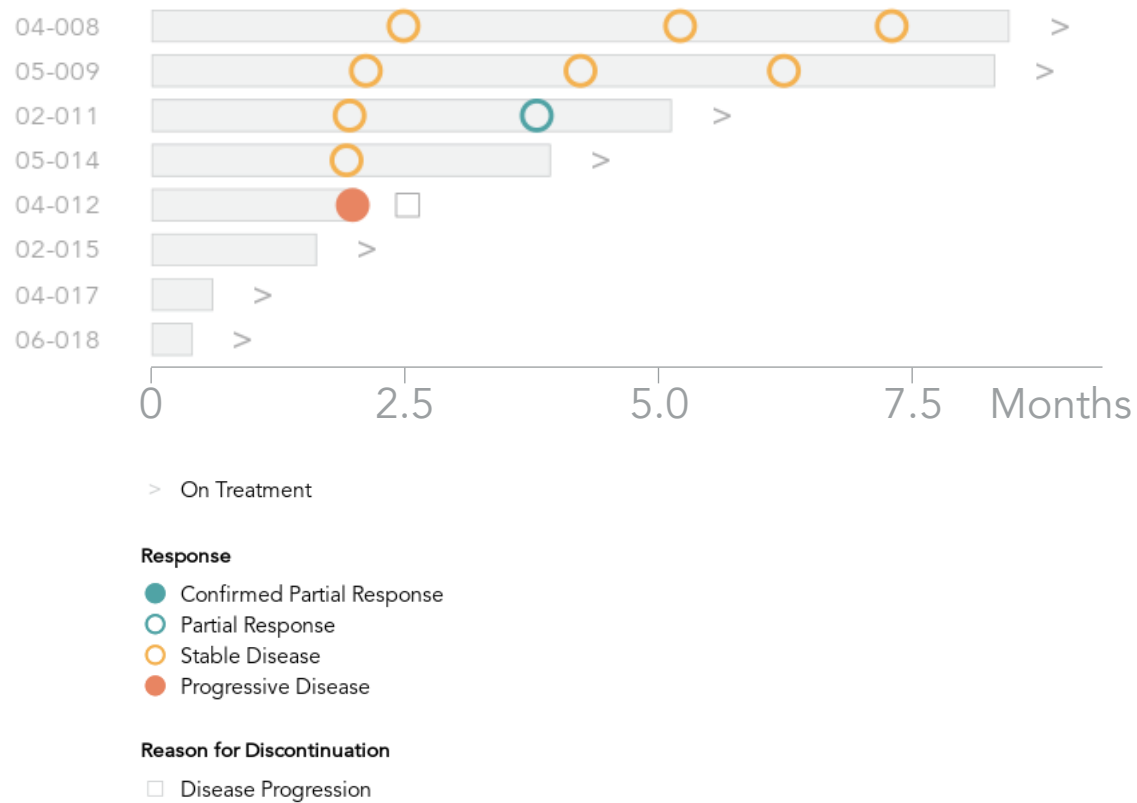
≥6 mo mPFS

\* 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).

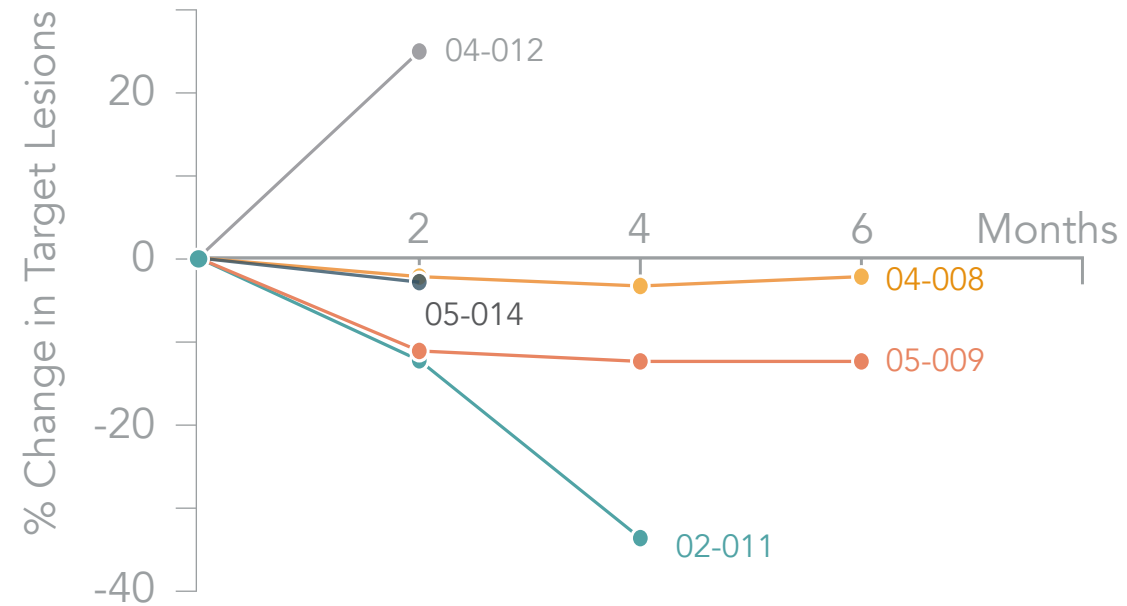


# Early data from our mPDAC trial data is encouraging

## 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

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Accelerating our mCRC program

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Additional onvansertib programs

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Pancreatic cancer (mPDAC)

Prostate cancer (mCRPC)

Triple negative breast cancer (TNBC)

Small cell lung cancer (SCLC)

# AACR data showed disease control increased with dose density

The AACR logo consists of the letters 'AACR' in a bold, sans-serif font. The 'AA' and 'C' are black, while the 'R' is green. A horizontal line is positioned below the letters.

American Association  
for Cancer Research®

FINDING CURES TOGETHER®

APRIL 2022

Evaluated onvansertib + abiraterone / prednisone in mCRPC patients showing initial abiraterone resistance by rising PSA

Disease control increased with onvansertib dose density

- From 29% to 45% of patients achieving PSA stabilization, and
- From 53% to 75% of patients with radiographic stable disease

ctDNA analysis showed a correlation between the PI3K signaling pathway and sensitivity to onvansertib/abiraterone combination

# We are not planning to fund any future mCRPC development activity

## **FINDINGS**

The trial completed enrollment (n=72) and generated important clinical data:

- Negligible toxicities attributed to onvansertib
- Disease control increased with dose density

## **PATH FORWARD**

Cardiff Oncology is not planning for any company-sponsored future steps in mCRPC

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Accelerating our mCRC program

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Additional onvansertib programs

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Pancreatic cancer (mPDAC)

Prostate cancer (mCRPC)

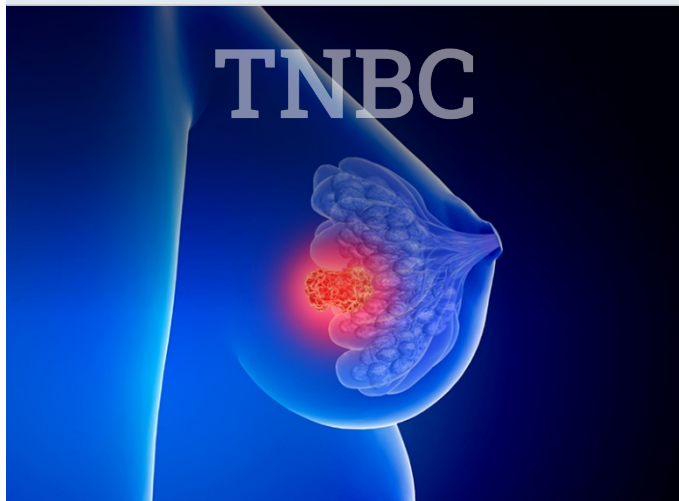
Triple negative breast cancer (TNBC)

Small cell lung cancer (SCLC)

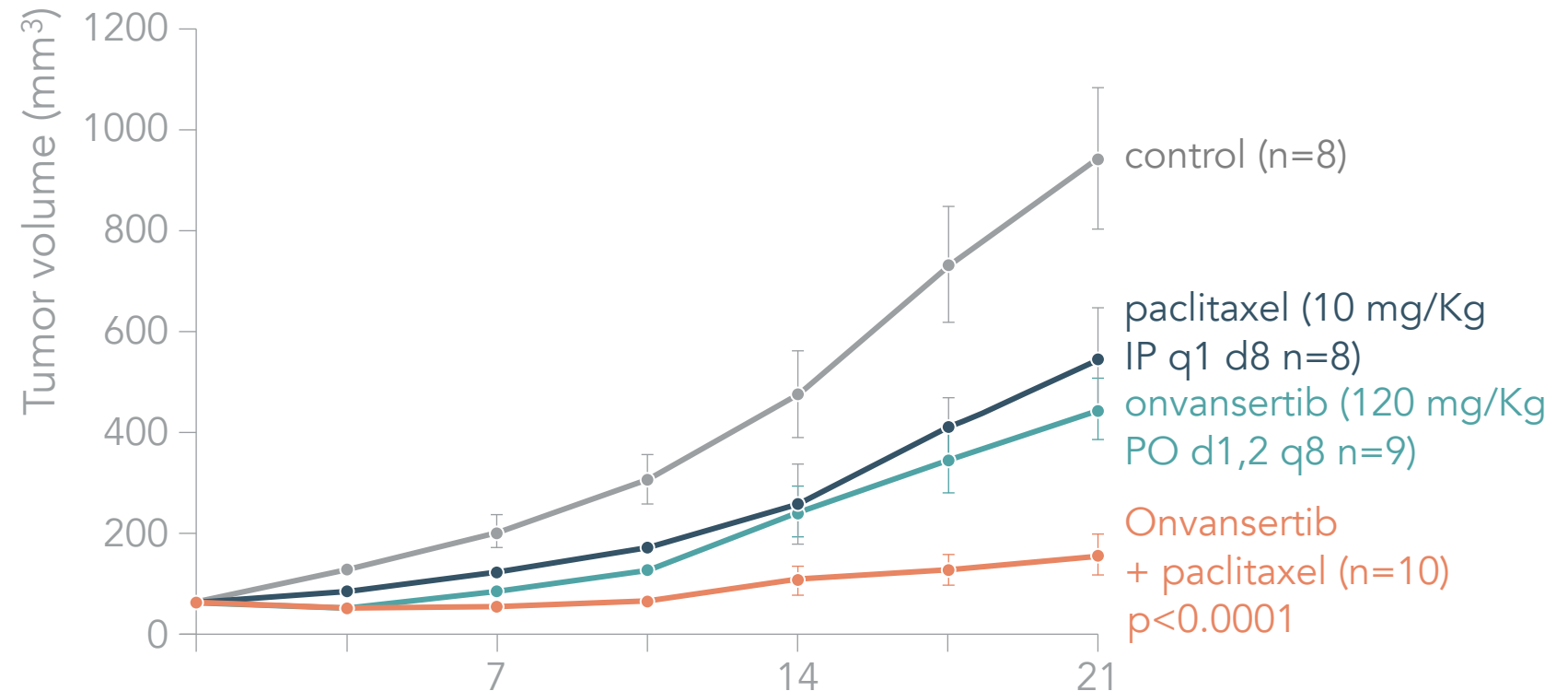
# Onvansertib + paclitaxel is superior to single agent therapy

## 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

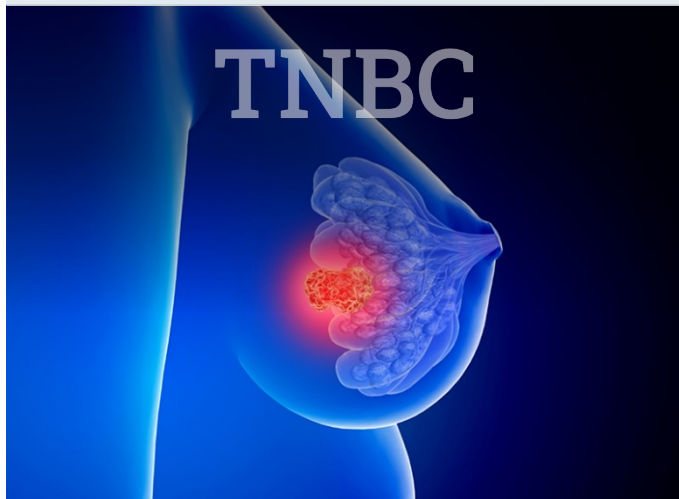
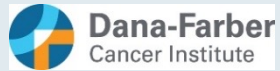
## ENROLLMENT CRITERIA

Metastatic TNBC relapsed or progressed

Single arm trial

Ph 1b: N=14-16

Ph 2: N=34



## PRIMARY ENDPOINTS

### Phase 1b

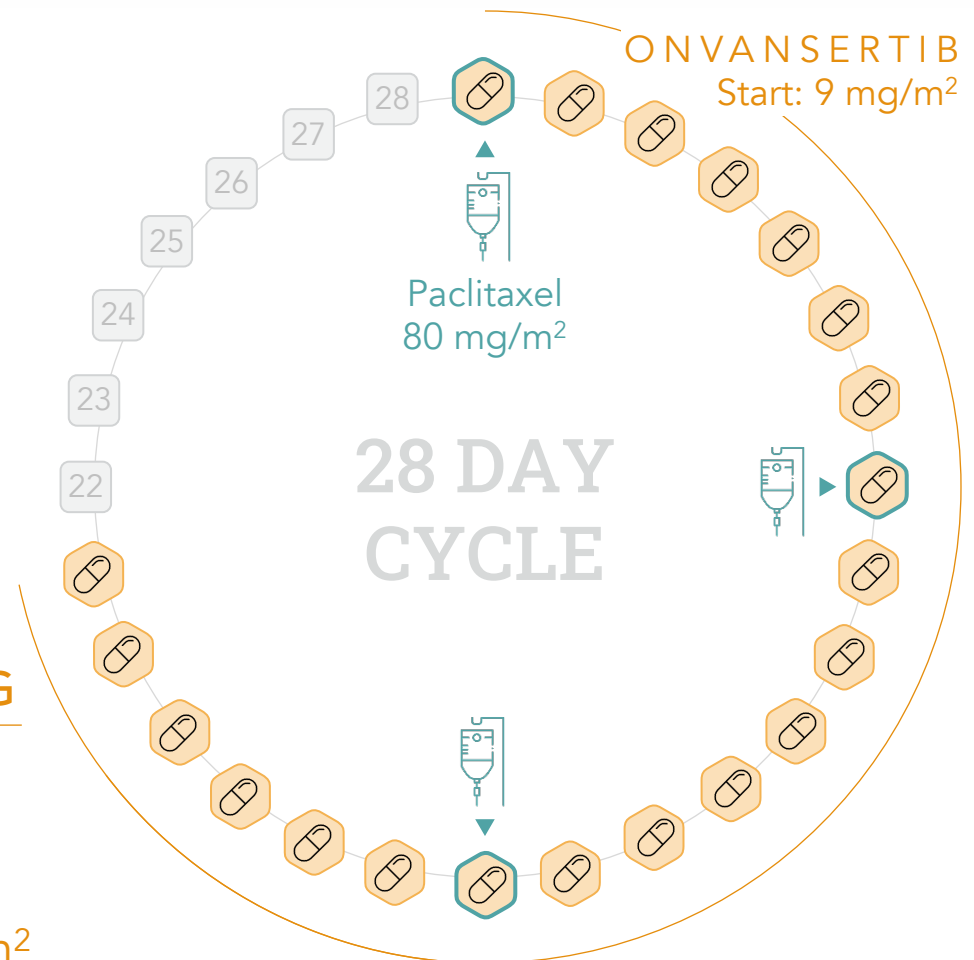
Safety, characterization of DLTs  
Determination of RP2D

### 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

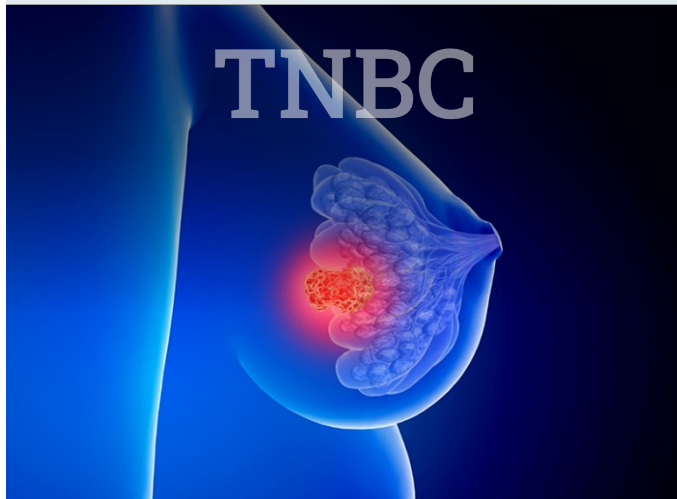
## ENROLLMENT CRITERIA

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

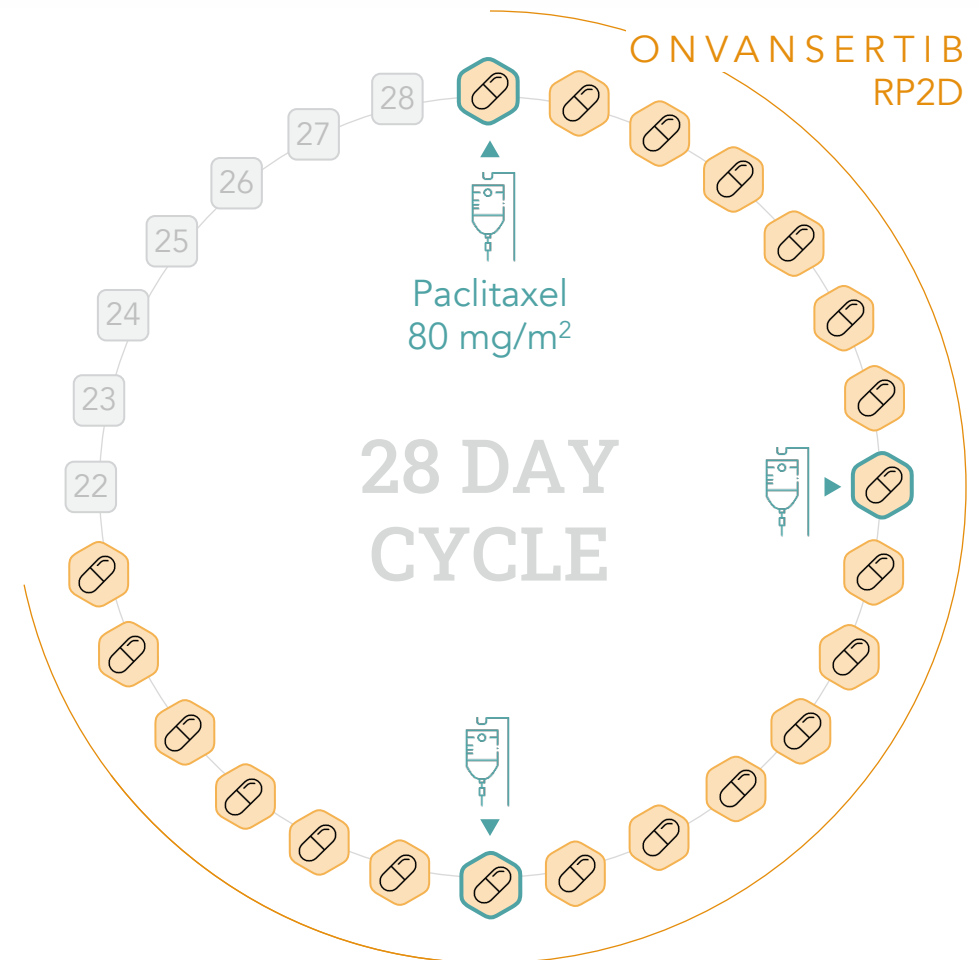
### Phase 2

ORR (RECIST 1.1)

## SECONDARY ENDPOINT

### Phase 2

Progression-Free Survival (PFS)





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Accelerating our mCRC program

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Additional onvansertib programs

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Pancreatic cancer (mPDAC)

Prostate cancer (mCRPC)

Triple negative breast cancer (TNBC)

Small cell lung cancer (SCLC)

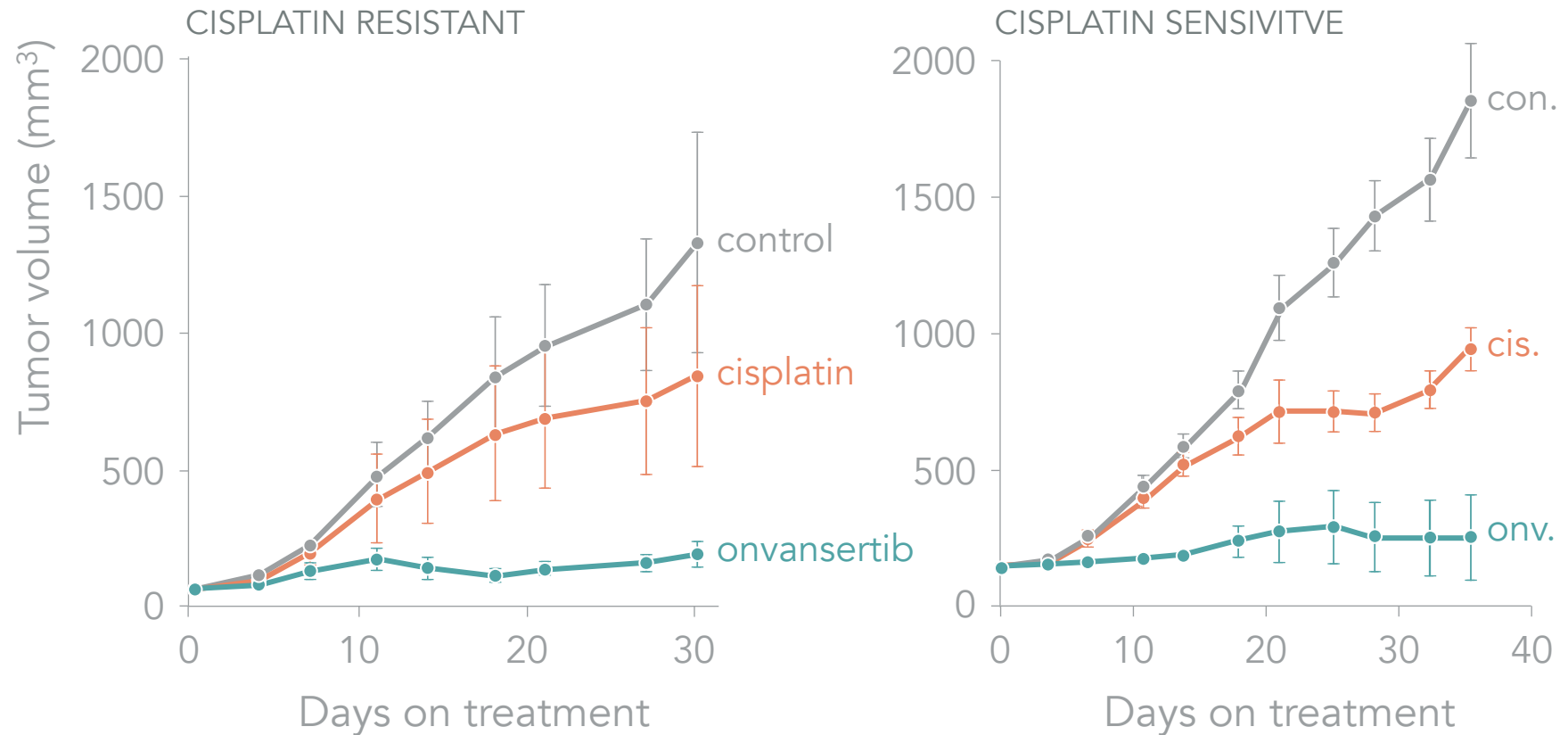
# Onvansertib demonstrates single-agent activity in SCLC

## 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

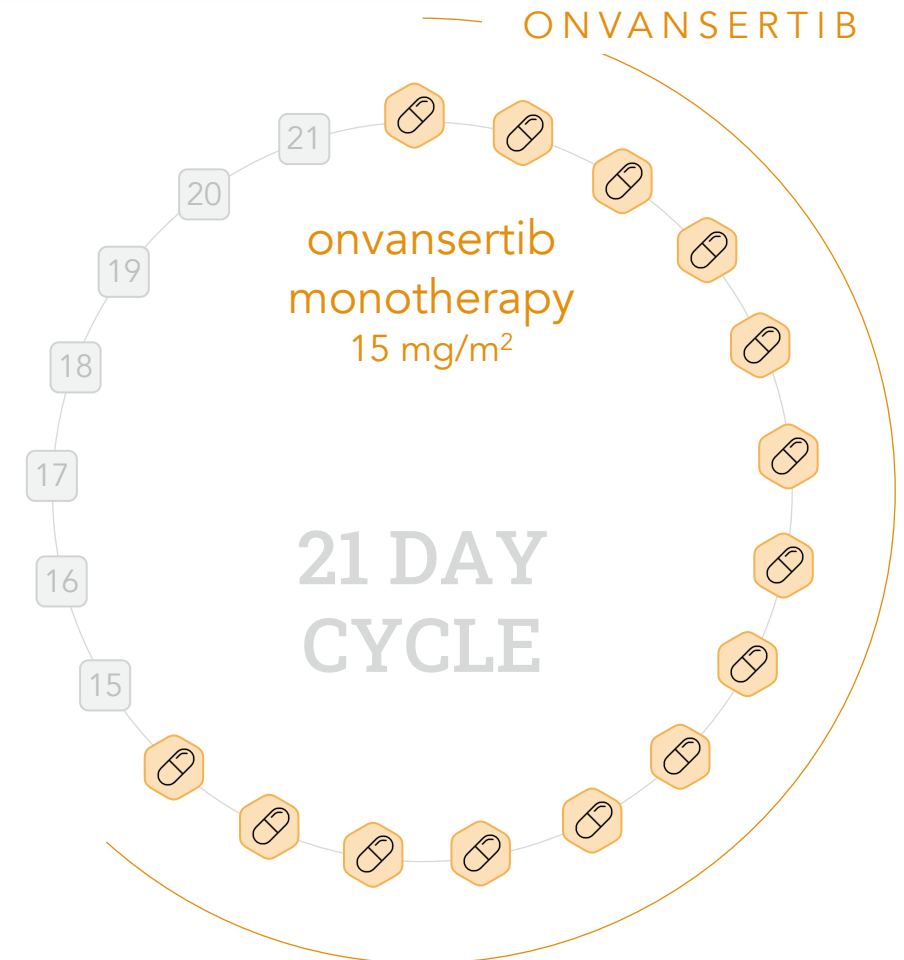


## PRIMARY ENDPOINT

Phase 2  
ORR (RECIST 1.1)

## SECONDARY ENDPOINTS

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



# Our pipeline opens many attractive opportunities for onvansertib

	Combination with:	Preclinical	Ph1/2	Ph2/3	Status		
mCRC	FOLFIRI/bev				<i>randomized</i>	Activation	
mCRC	FOLFIRI/bev			<i>single-arm</i>	Enrolling		
mPDAC	Onivyde/5-FU				Enrolling		
Ovarian	PARP inhibitors				Evaluating		

## Investigator-initiated trials

					Status	Investigator
TNBC	Paclitaxel				Enrolling	
SCLC	None (monotherapy)				Enrolling	

# Targeting PLK1 opens doors to large patient populations

## Targets with oncogenic alterations

ROS1  
RET  
KRAS G12C  
EGFR  
TRK

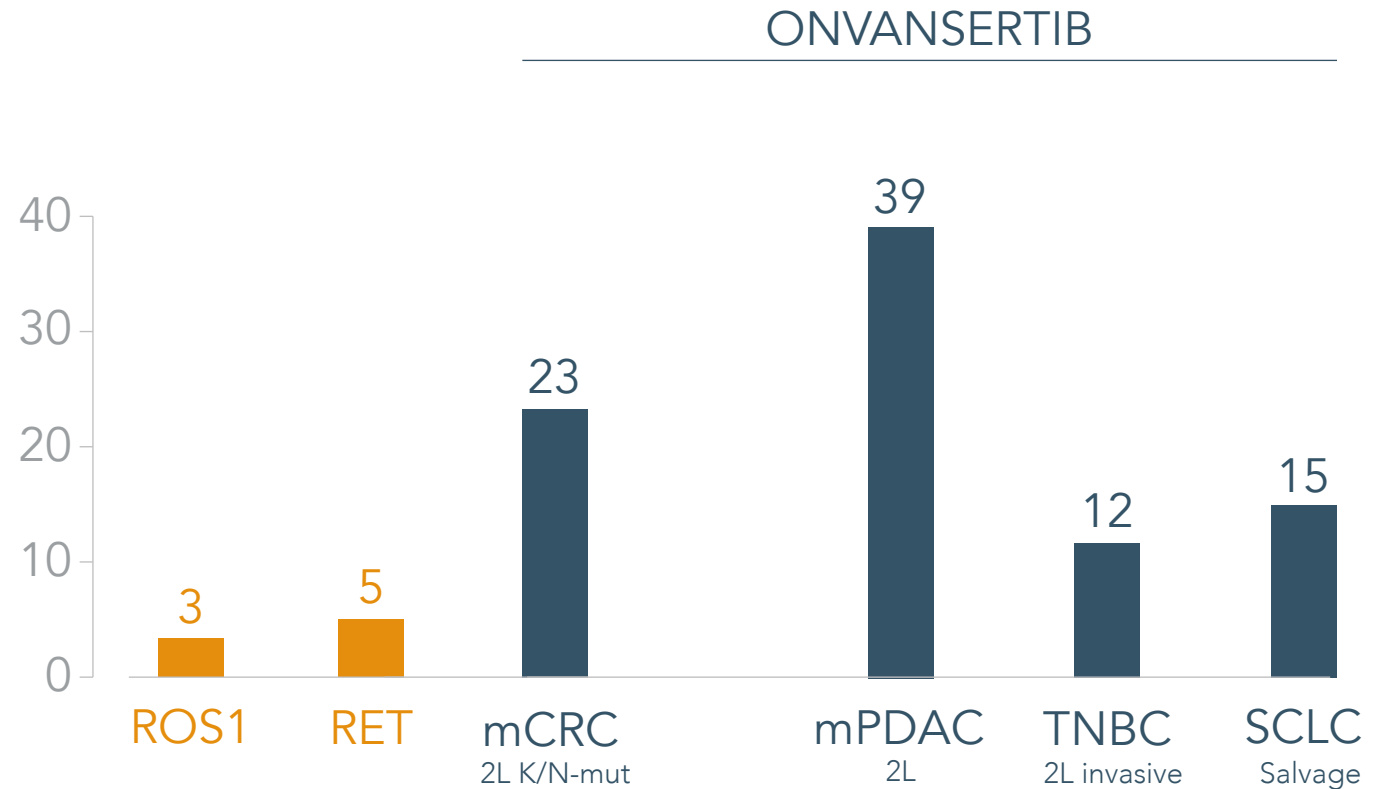
## Targets without oncogenic alterations

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.

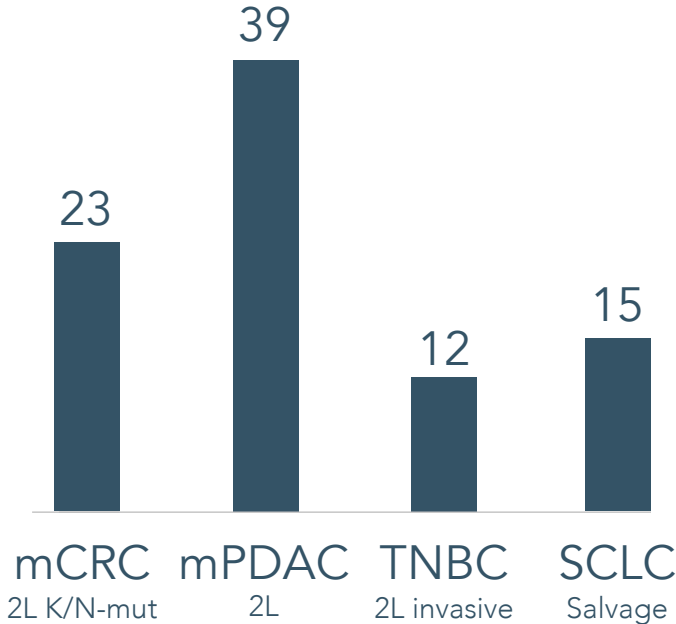
Annual eligible US patients ('000s)\*



# We have multiple important catalysts over the next two years

2023

2024



# At June 30, 2022, our financial position is robust



June 30, 2022 cash and investments\*

\$122.0M

Net cash used in Operating Activities\*  
(Rolling two-quarter period ending June 30, 2022)

\$16.9M

\* Financial information above is derived from our unaudited financials in Form 10Q filed on 8/4/22.

# 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



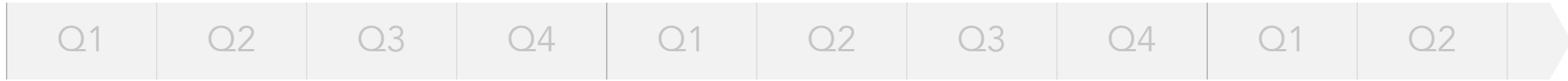


# Our clinical development program supports our key goals

2023

2024

2025



## GOALS

**1** Validate prior mCRC data with a randomized trial

**2** Demonstrate clinical POC in additional indications

## OUR STRATEGY

### Phase 1b/2 single arm

Strong ORR + DoR + PFS  
MAF biomarker opportunity

### Phase 2 randomized

Efficient design  
Confirm dose; stratify bev

Signal finding

# Q&A

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