



# Company Overview

## The Onvansertib Opportunity

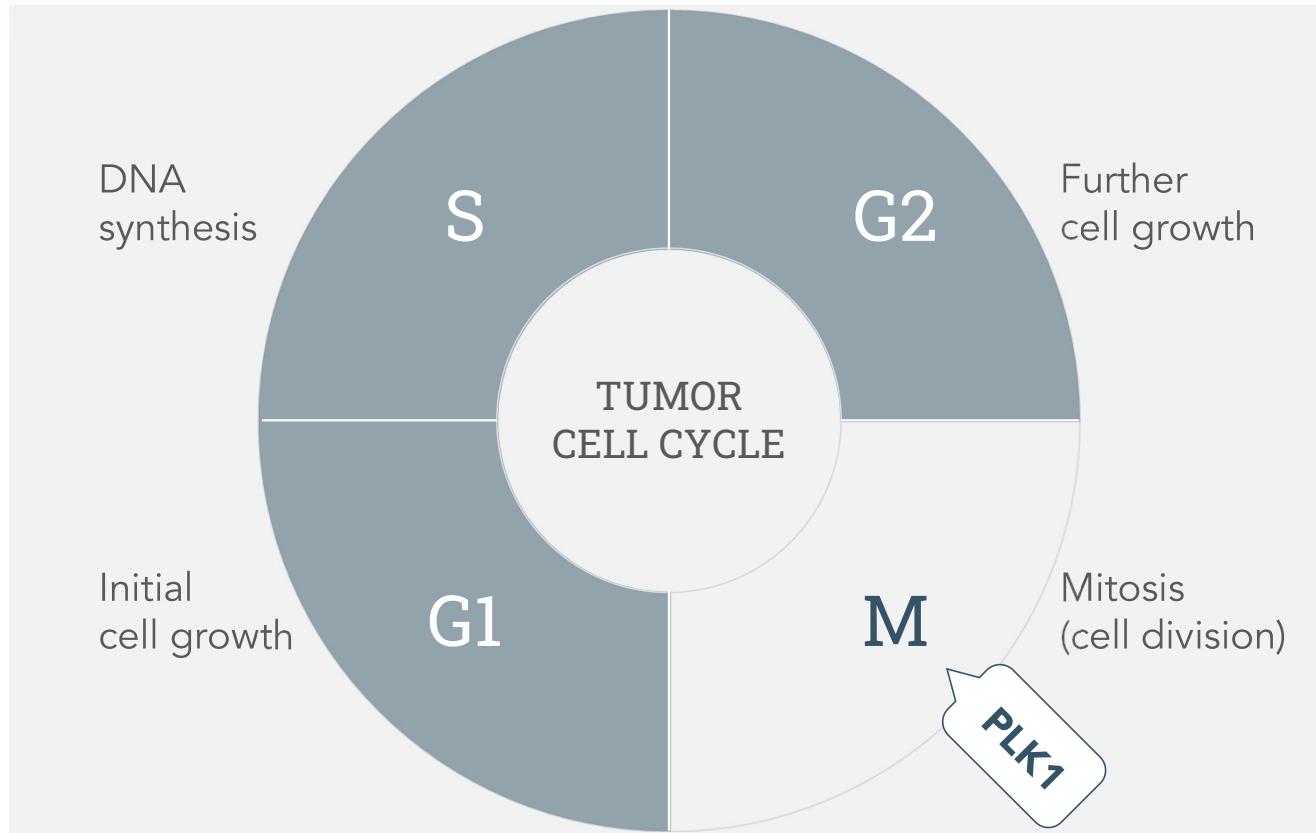
TURNING THE TIDE ON CANCER  
JUNE 2022

# 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; 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.

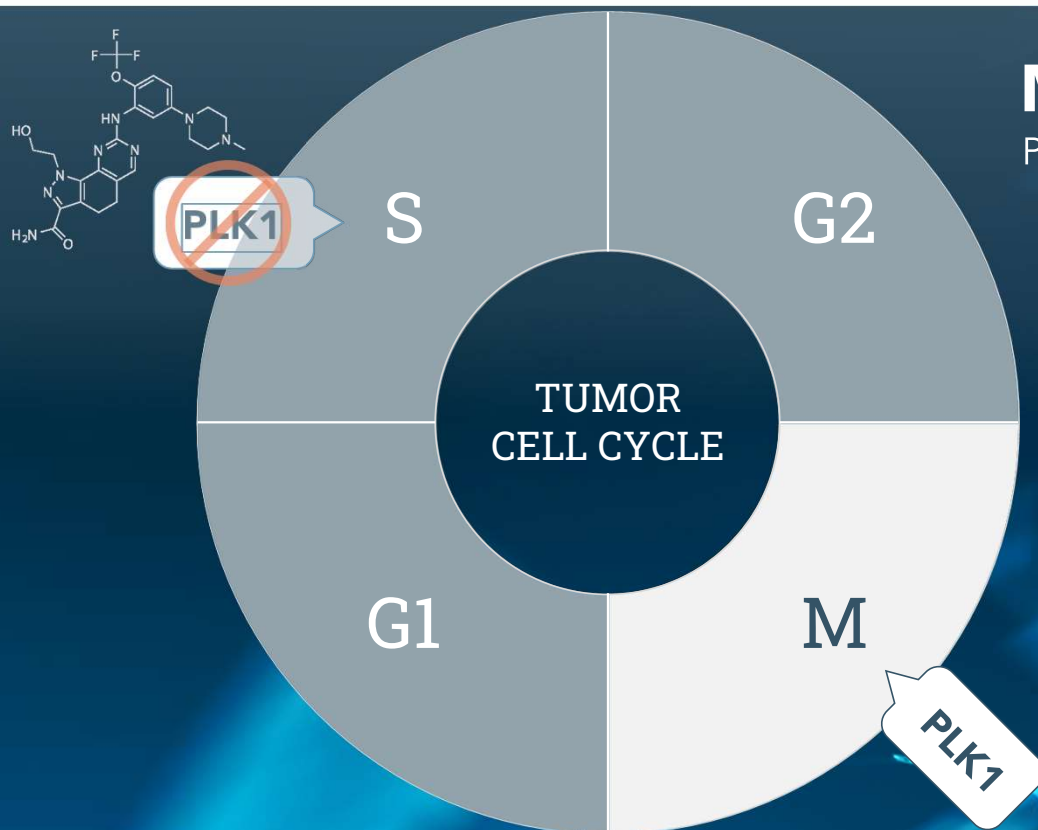
PLK1 is hijacked by tumor cells, allowing uncontrolled growth



# PLK1 repairs damaged DNA, enabling tumor cells to proliferate

**Molecular Cell, March 4, 2021**

PLK1 repairs dsDNA breaks at broken replication forks





# Onvansertib positions Cardiff Oncology to effectively target PLK1

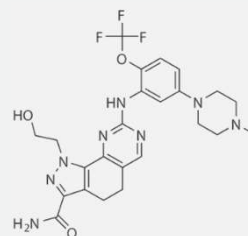
## SPECIFICITY

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<br>and >140 in the Millipore panel | >10                   |

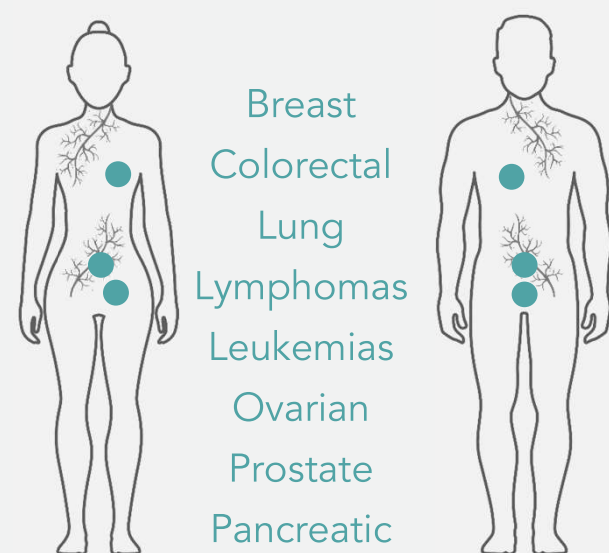
## PROPERTIES

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



## OPPORTUNITY

PLK1 is over-expressed in many cancer types<sup>1</sup>



1. Renner Blood 2009; Mito Leukemia and Lymphoma 2005; 2005; Takai et al., Oncogene (2005) 24, 287–291



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**WHAT**

Onvansertib has achieved

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**WHY**

Onvansertib works

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**WHERE**

Cardiff Oncology can go

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**WHAT**

Onvansertib has achieved

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**WHY**

Onvansertib works

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**WHERE**

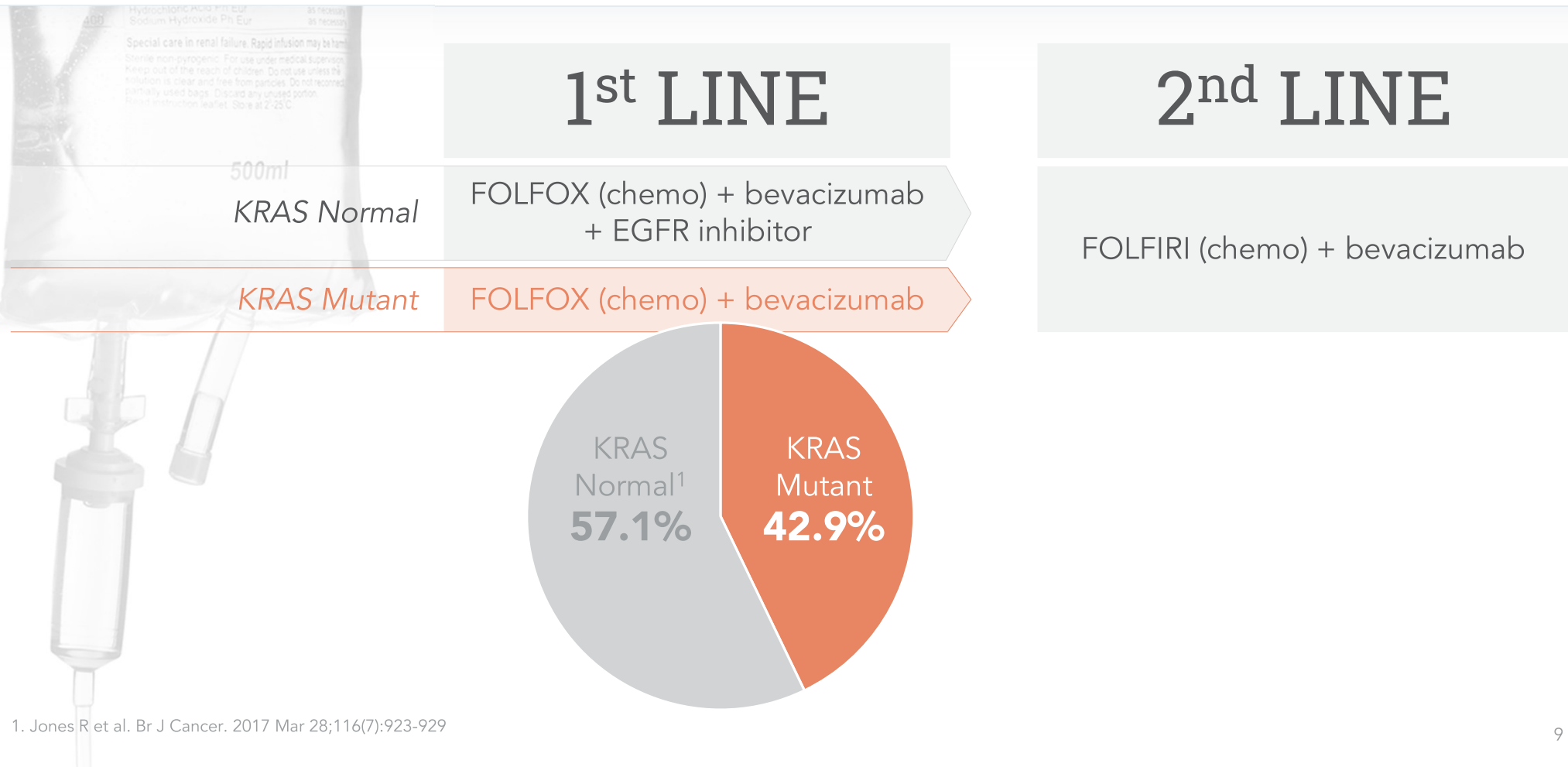
Cardiff Oncology can go

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## Our lead program is in KRAS-metastatic colorectal cancer (mCRC)

|                               |                     | Preclinical | IND En. | Ph 1/2 | Status           | Partners |
|-------------------------------|---------------------|-------------|---------|--------|------------------|----------|
| <b>mCRC</b>                   | <b>FOLFIRI/bev</b>  |             |         |        | <b>Enrolling</b> |          |
| mPDAC                         | Onivyde/5-FU        |             |         |        | Enrolling        |          |
| mCRPC                         | Abiraterone         |             |         |        | Enrolling        |          |
| Ovarian                       | PARP inhibitors     |             |         |        | Planned          |          |
| Investigator-initiated trials |                     |             |         |        |                  |          |
| TNBC                          | Combo w/ Paclitaxel |             |         |        | Planned          |          |
| SCLC                          | Single agent        |             |         |        | Planned          |          |
| CMML                          | Single agent        |             |         |        | Planned          |          |
| Medullo-blastoma              | Combo w/ radiation  |             |         |        | Planned          |          |

# Gaps in current mCRC therapies leave a significant unmet need



# The prognosis for second-line mCRC patients is poor



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

FOLFIRI (chemo) + bevacizumab

5-year survival: 10%

Drugs in development do not address most prevalent KRAS mutations

## HISTORICAL ORR

5%

2006 – 2008

ML18147 Phase 3 Registrational Trial  
FOLFIRI + bev in second-line<sup>1</sup>

11.4%

2000 – 2013

Systematic Literature-Based Analysis of  
23 Randomized Trials (10,800 Patients)  
in Second-Line mCRC<sup>2</sup>

13%

2015 – 2017

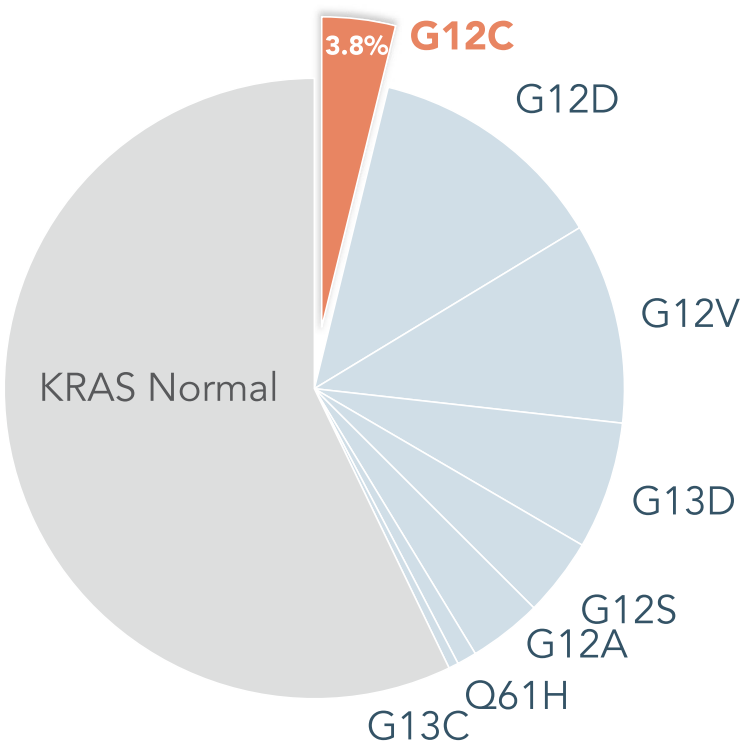
TRIBE2 Randomized Phase 3 Trial: SOC  
arm FOLFIRI + bev in Second-line  
following FOLFOX + bev First-line<sup>3,4</sup>

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



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

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

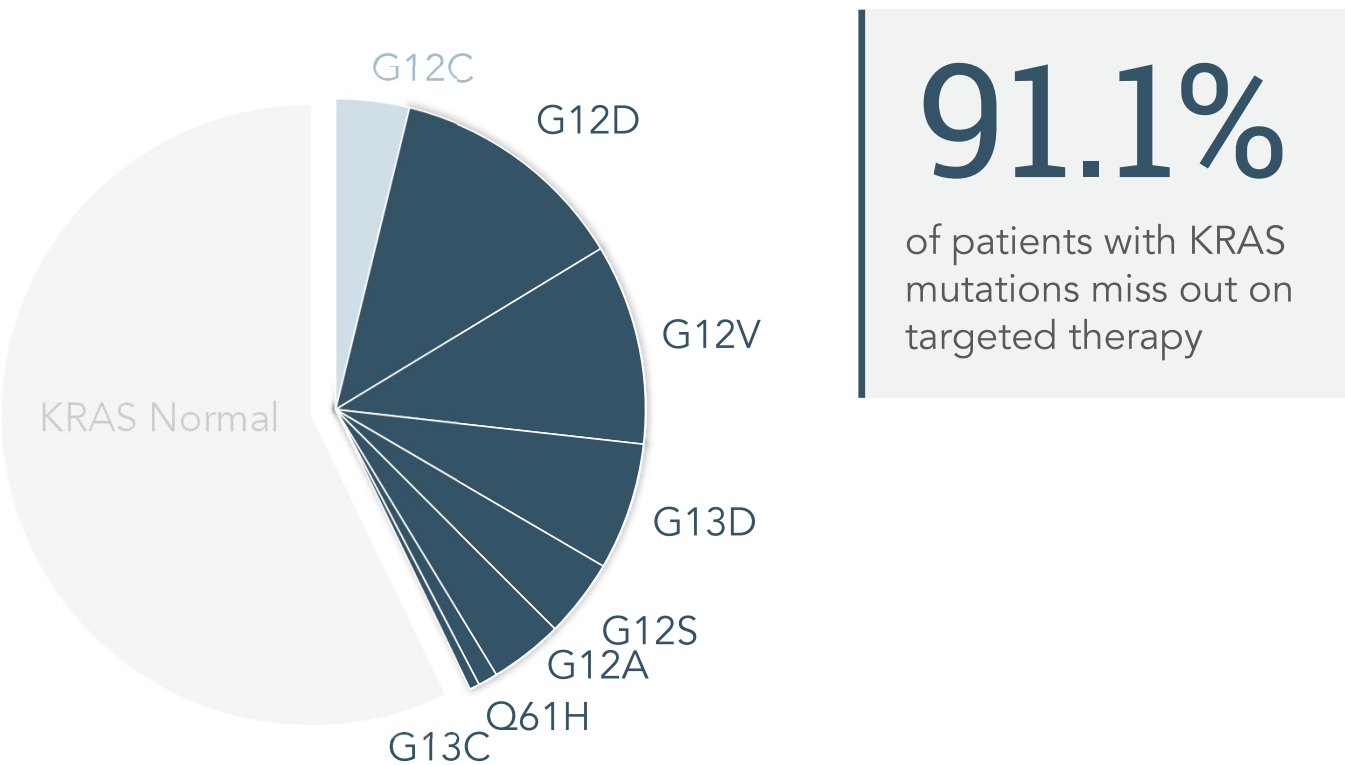


Investigational therapies (Amgen; Mirati) address the G12C KRAS mutation *only*

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

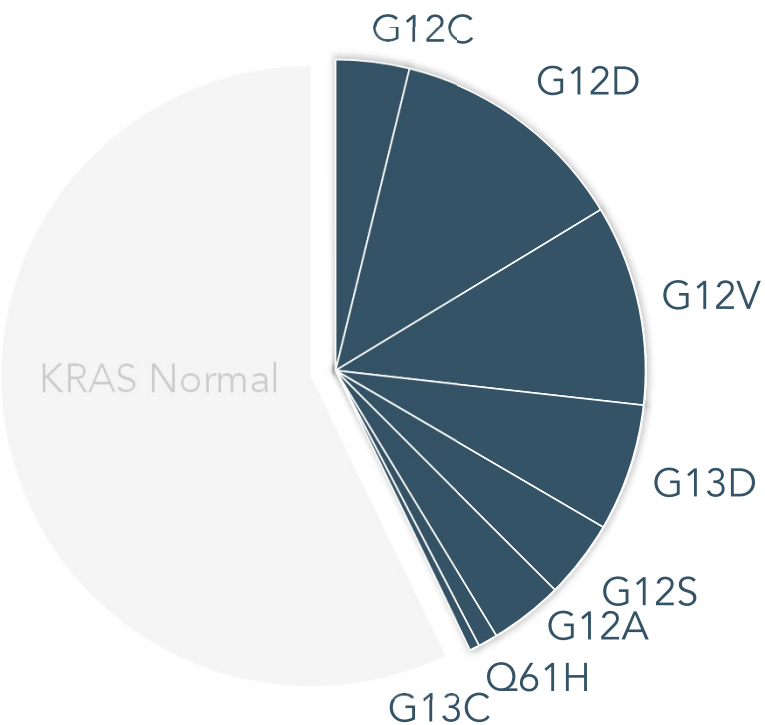
## KRAS Mutations in mCRC<sup>1</sup>



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

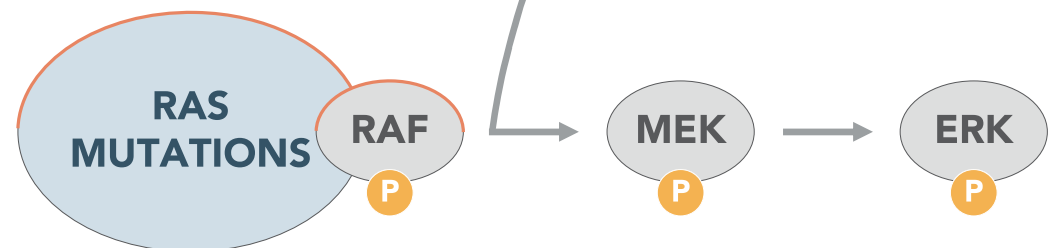
## KRAS Mutations in mCRC<sup>1</sup>



## DOWNSTREAM

### Onvansertib

Addresses all KRAS mutations because PLK1 activation is downstream of RAS

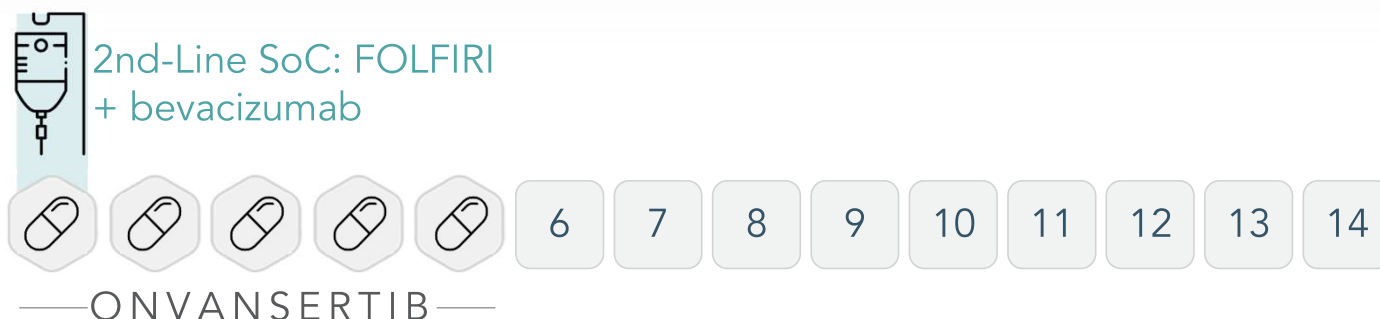


1. Jones R et al. Br J Cancer. 2017 Mar 28;116(7):923-929

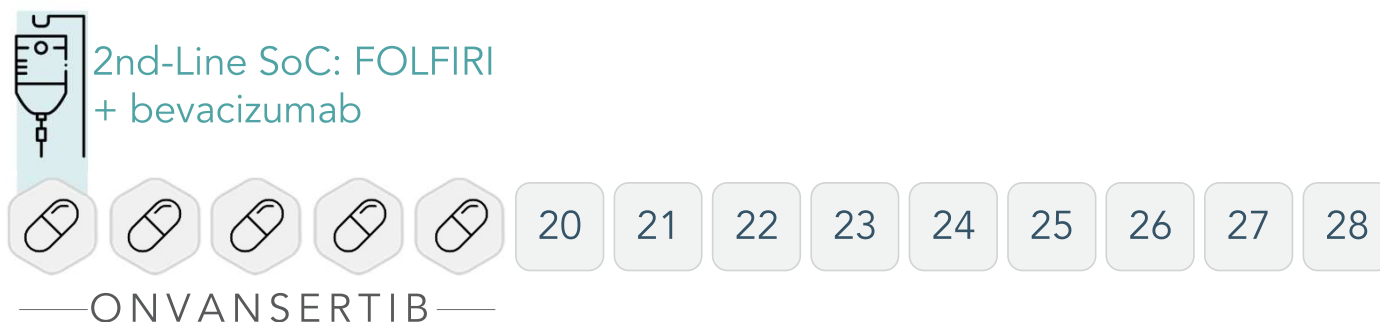
## Our Ph 1b/2 trial in KRAS-mutated mCRC combines onvansertib w/ SoC

One Cycle = 28 Days

WEEKS 1-2



WEEKS 3-4



# Trial endpoints measure tumor response and decrease in KRAS burden

One Cycle = 28 Days

WEEKS 1-2



WEEKS 3-4



## 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

# Endpoints measure tumor response and decrease in KRAS burden



## EVALUABLE PATIENTS AT DEC 3, 2021

### PHASE 1b PHASE 2



1. Three patients were excluded from the RP2D (recommended phase 2 dose) efficacy evaluation because they received onvansertib 12 mg/m<sup>2</sup> instead of the assigned per protocol dose of 15 mg/m<sup>2</sup>

# Proof of concept criteria set to exceed historical ORR and mPFS

## HISTORICAL ORR\*

5%

2006 – 2008

11.4%

2000 – 2013

13%

2015 – 2017

## HISTORICAL mPFS\*

4.5–5.7 mo

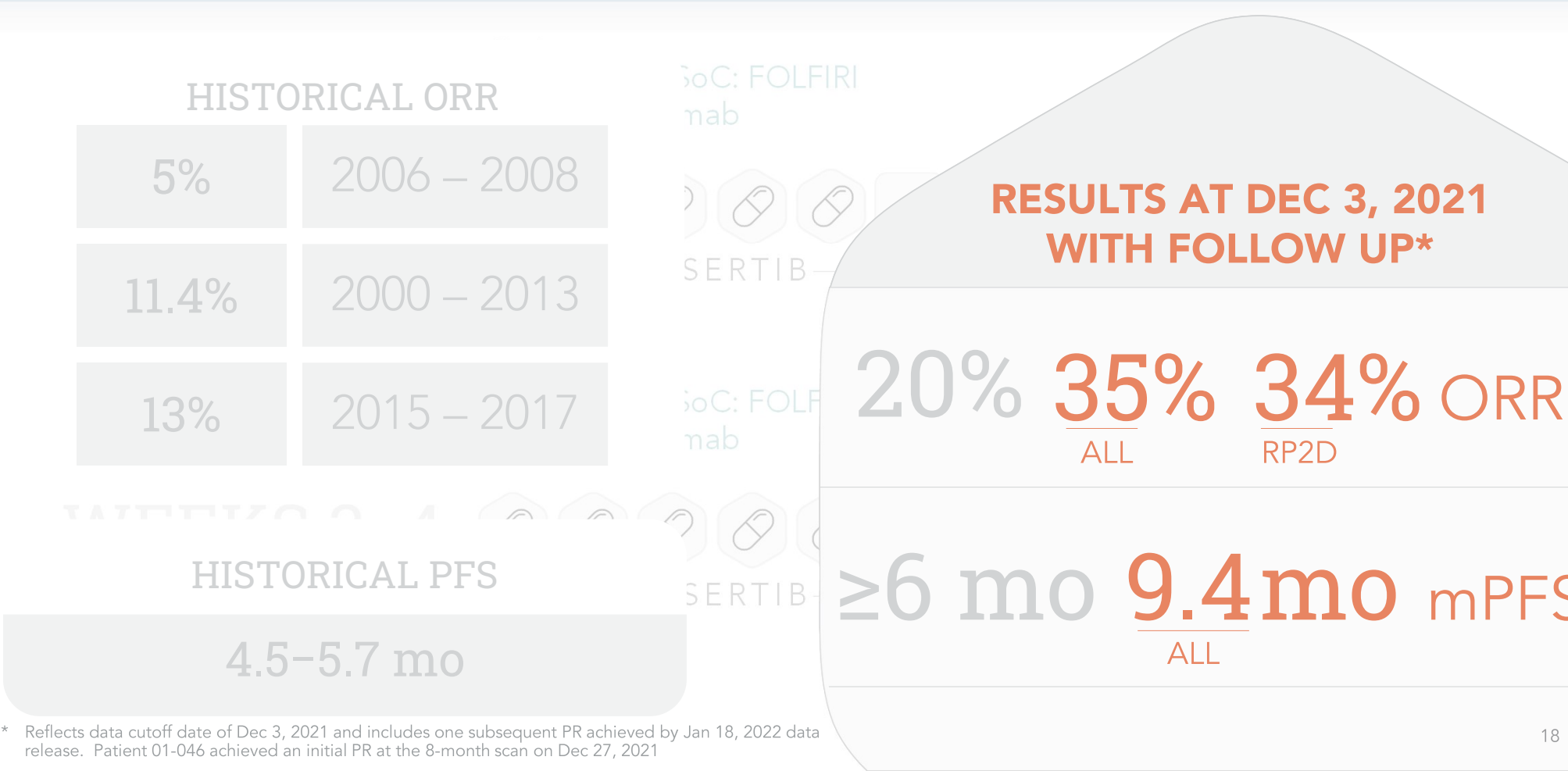
## PROOF OF CONCEPT CRITERIA

20% ORR

≥6 mo mPFS

\* Bennouna et al., Lancet Oncol 2013; 14: 29–37; Giessen et al., Acta Oncologica, 2015, 54: 187–193; Cremolini et al., Lancet Oncol June 2020; ORR: Objective Response Rate; PFS: Progression-Free Survival

# Results from the Ph 1b/2 trial continue to show improvement over SoC





# Our clinical data indicates that onvansertib + SoC 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

les

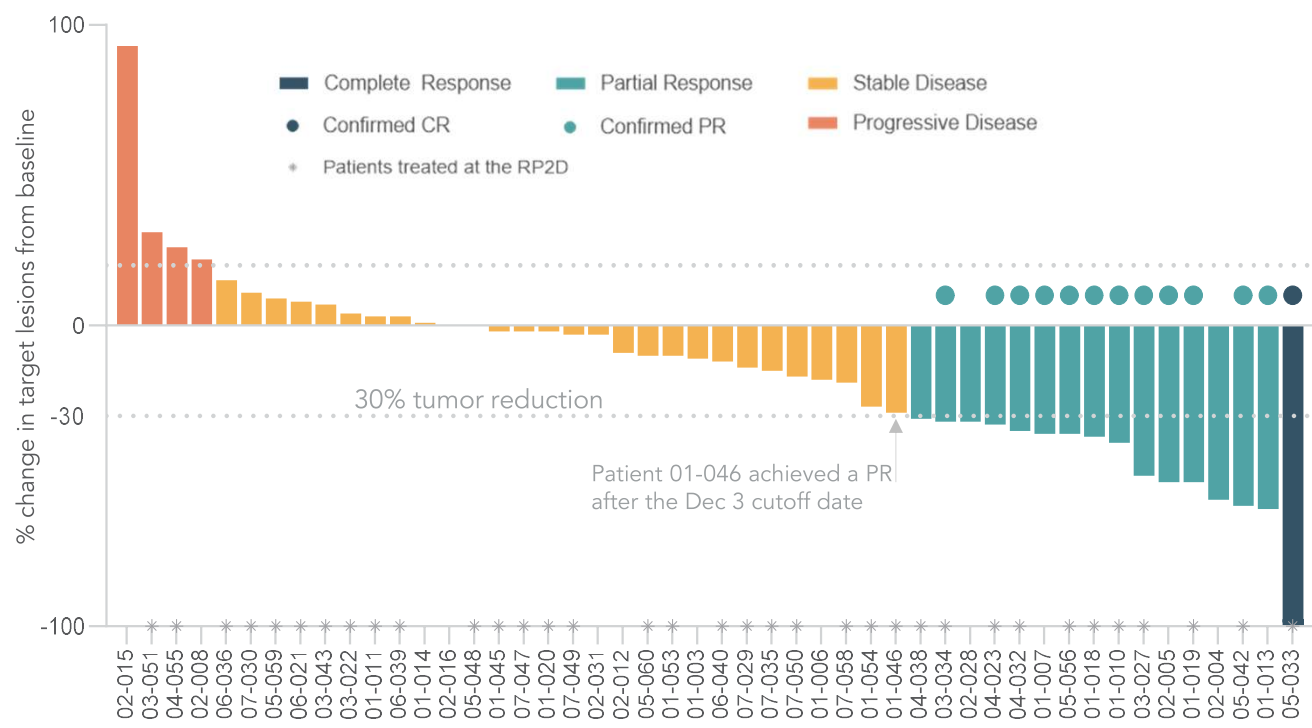
|      |                         | GRADE |    |    |   |     |                   |                                   | GRADE |   |   |   |     |
|------|-------------------------|-------|----|----|---|-----|-------------------|-----------------------------------|-------|---|---|---|-----|
| N=50 | TEAEs*                  | 1     | 2  | 3  | 4 | All |                   | TEAEs*                            | 1     | 2 | 3 | 4 | All |
|      | 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  | as of 03-Dec-2021 |                                   |       |   |   |   |     |

\* Jan 2022 data are interim as of Dec 3, 2021 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

# 92% of patients achieved disease control (CR + PR + SD)

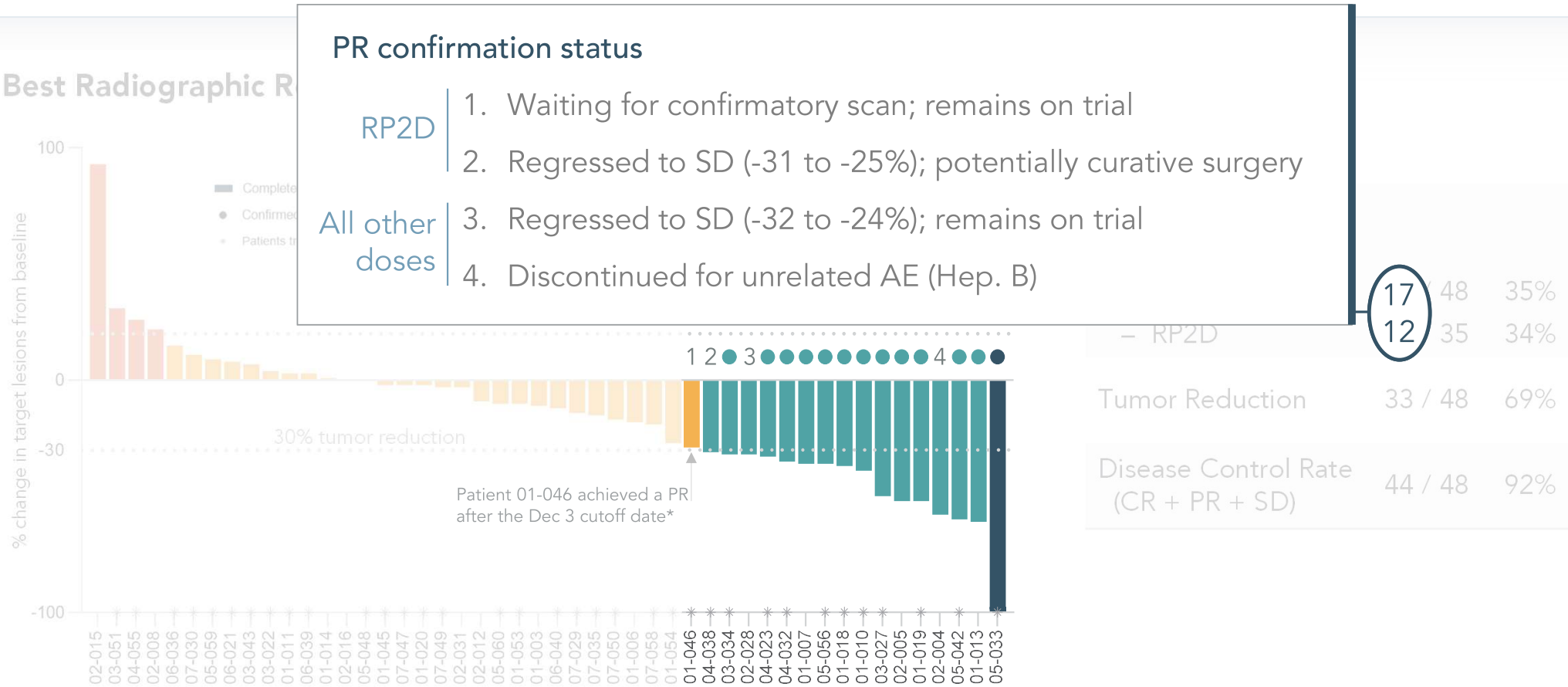
**Best Radiographic Response\*** – all doses (as of Dec 3, 2021)



|                      |         |     |
|----------------------|---------|-----|
| Objective Response*  |         |     |
| (CR + PR)            |         |     |
| – All doses          | 17 / 48 | 35% |
| – RP2D               | 12 / 35 | 34% |
| Tumor Reduction      |         |     |
|                      | 33 / 48 | 69% |
| Disease Control Rate |         |     |
| (CR + PR + SD)       |         |     |
|                      | 44 / 48 | 92% |

\* Waterfall plot and table reflect interim data as of Dec 3, 2021 from an ongoing trial and unlocked database, and indicates one subsequent PR achieved on follow up through Jan 18, 2022 press release 20

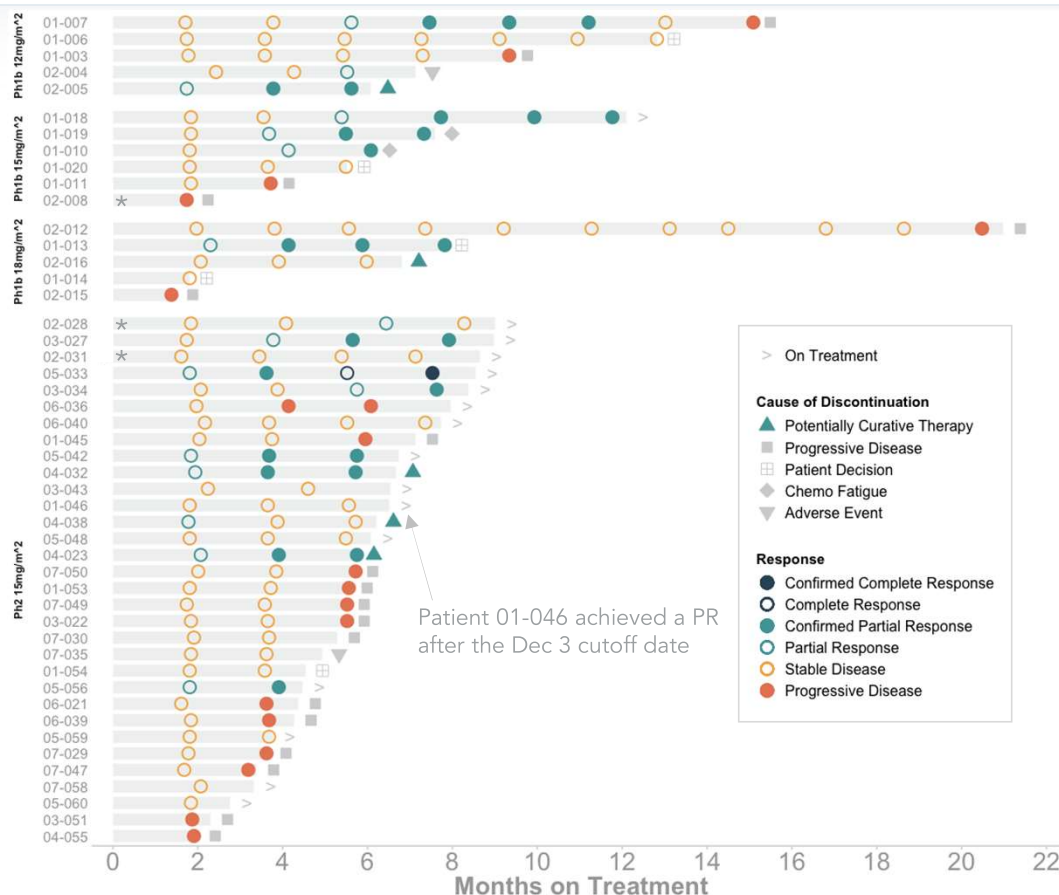
# 92% of patients achieved disease control (CR + PR + SD)



\* Waterfall plot and table reflect interim data as of Dec 3, 2021 from an ongoing trial and unlocked database, and indicates one subsequent PR achieved on follow up through Jan 18, 2022 press release

21

# Across all doses we observe initial PRs up to eight months on treatment



**Swimmer plot<sup>†</sup>** – all doses (as of Dec 3, 2021)

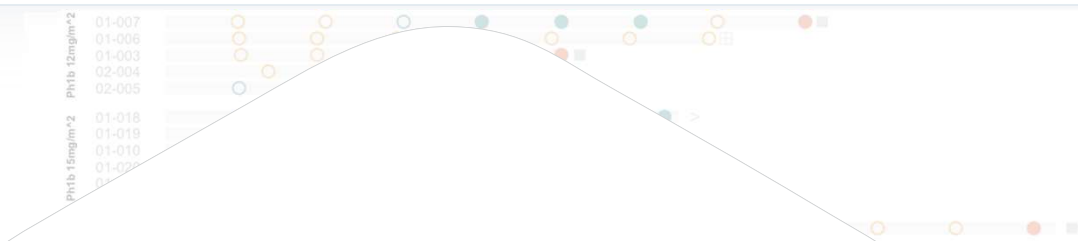
Evaluable Patients – all doses 48

| Time of initial PR        |   |
|---------------------------|---|
| 8-week scan               | 8 |
| 16-week scan              | 3 |
| 24-week scan              | 5 |
| 32-week scan <sup>†</sup> | 1 |

\* Three patients were excluded from the RP2D efficacy evaluation because they received onvansertib 12 mg/m<sup>2</sup> instead of the assigned per protocol dose of 15 mg/m<sup>2</sup>

† Swimmer plot and table reflect interim data as of Dec 3, 2021 from an ongoing trial and unlocked database, and indicates one subsequent PR achieved on follow up through Jan 18, 2022 press release

# Clinical efficacy events of interest



## Clinical benefits observed

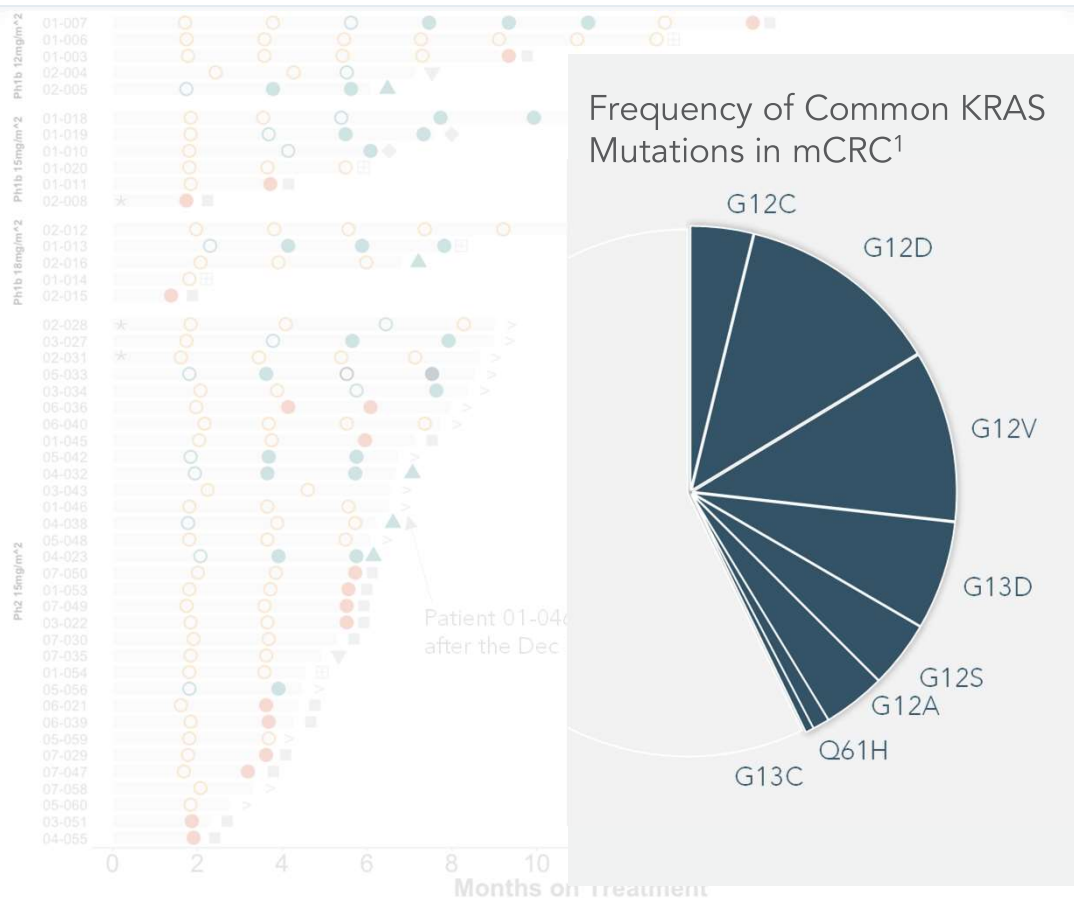
- 1 of 48 (2%) (with 41mm measurable disease) had a **confirmed Complete Response**
- 5 of 48 (10%) left trial for **potentially curative** metastasis-directed therapy
- 1 initial PR occurred at the **8-month scan**

Swimmer plot<sup>†</sup> – all doses (as of Dec 3, 2021)

|                                |    |
|--------------------------------|----|
| Evaluable Patients – all doses | 48 |
| Time of initial PR             |    |
| 8-week scan                    | 8  |
| 16-week scan                   | 3  |
| 24-week scan                   | 5  |
| 32-week scan <sup>†</sup>      | 1  |

<sup>†</sup> 1 patient received cabotegravir 12 mg/m<sup>2</sup> instead of the assigned per protocol dose of 15 mg/m<sup>2</sup> in the clinical trial database, and indicates one subsequent PR achieved on follow up through

# The all-dose cohort achieved responses across several KRAS mutations



Onvansertib responses across KRAS mutations (as of Dec 3, 2021)

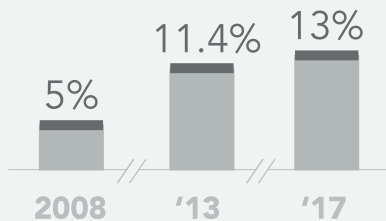
| KRAS Variant | CR+PR | SD  | PD | Total |
|--------------|-------|-----|----|-------|
| G12D         | 6*    | 7*  | 1  | 14    |
| G12V         | 1     | 8   | 1  | 10    |
| G13D         | 4     | 2   |    | 6     |
| G12A         | 3     | 3   |    | 6     |
| A146T        | 1     | 3   |    | 4     |
| 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

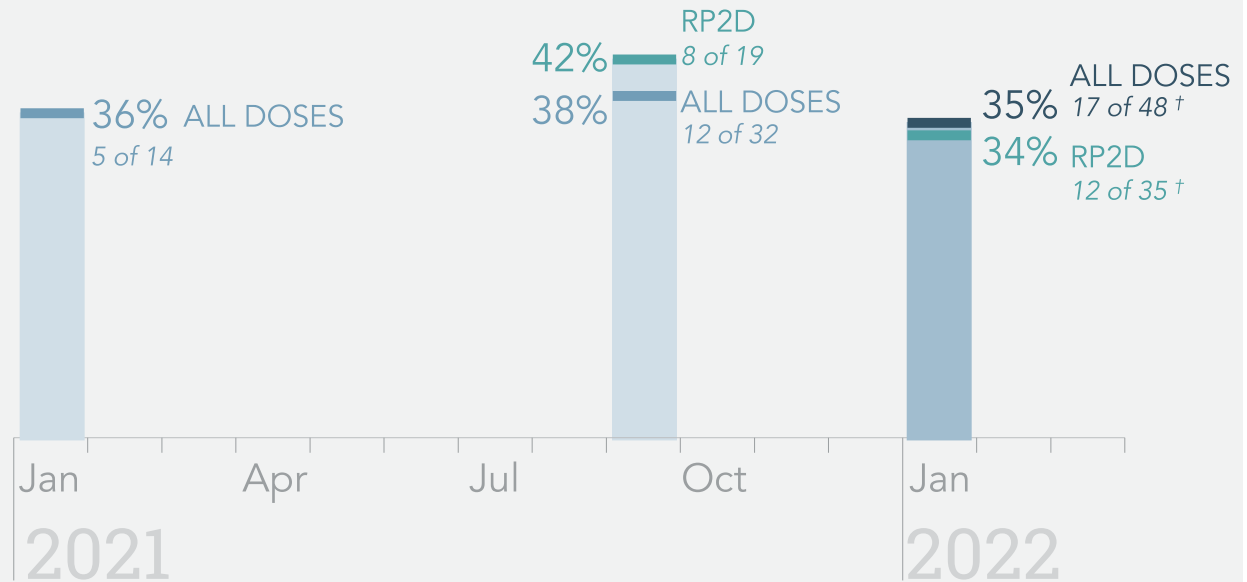
\* Patient 01-046 (with a G12D mutation) achieved a PR after the Dec 3, 2021 data cutoff date and is included in the table above as a 6<sup>th</sup> PR in the G12D line and 17<sup>th</sup> PR in the total line

# Objective response rate for mCRC trial exceeds SoC over time

Historical SoC\* ORR



Onvansertib+SoC ORR over time (as of Dec 3, 2021)

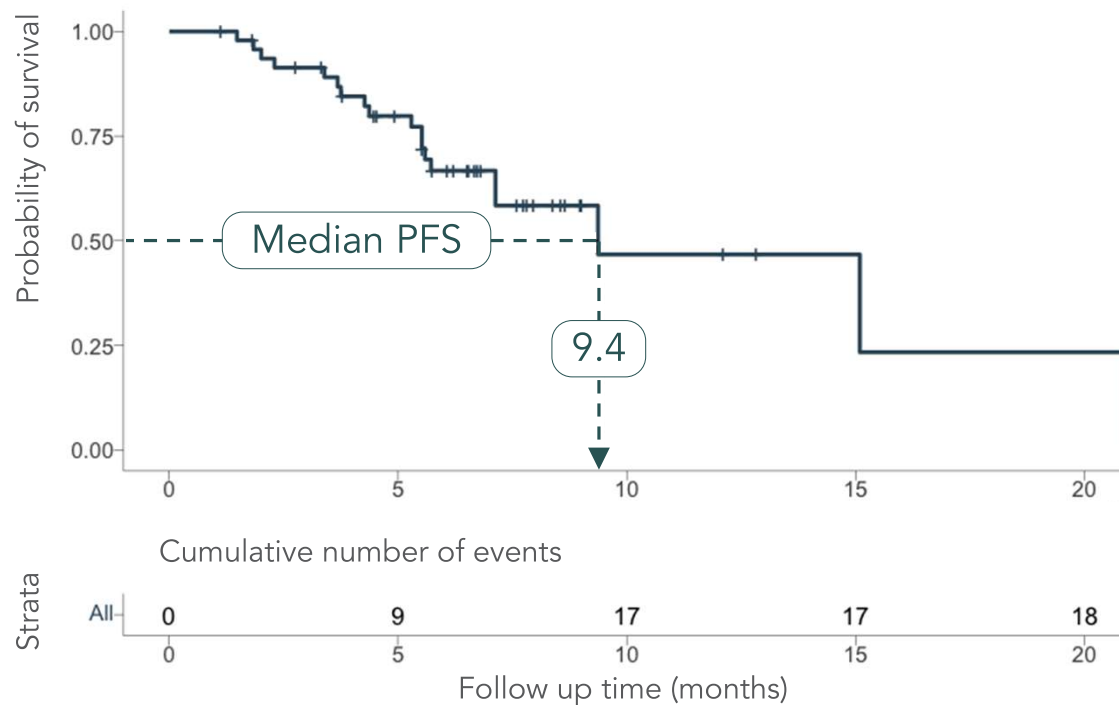


<sup>†</sup> Jan 2022 ORR are interim data as of Dec 3, 2021 from an ongoing trial and unlocked database, and includes one subsequent PR achieved on follow up through Jan 18, 2022 press release

\* 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

# Median progression free survival for mCRC trial exceeds SoC over time

**Progression free survival\*** – all doses (as of Dec 3, 2021)



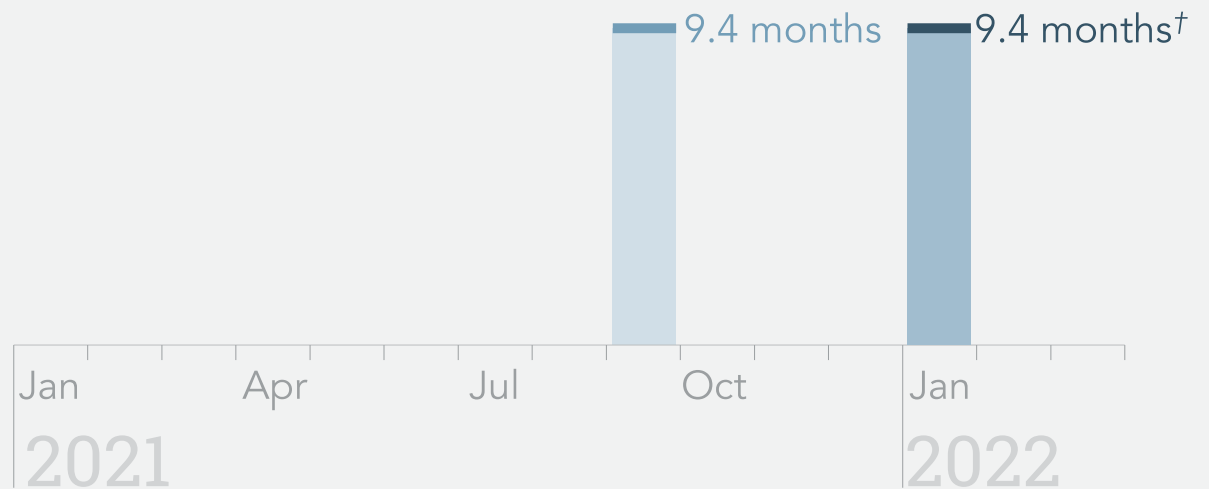
\* mPFS is interim data as of Dec 3, 2021 from an ongoing trial and unlocked database. mPFS for the RP2D is not yet reached as of Dec 3, 2021



# Median progression free survival for mCRC trial exceeds SoC over time



## Onvansertib+SoC mPFS – all doses (as of Dec 3, 2021)



<sup>†</sup> Jan 2022 PFS are interim data as of Dec 3, 2021 from an ongoing trial and unlocked database

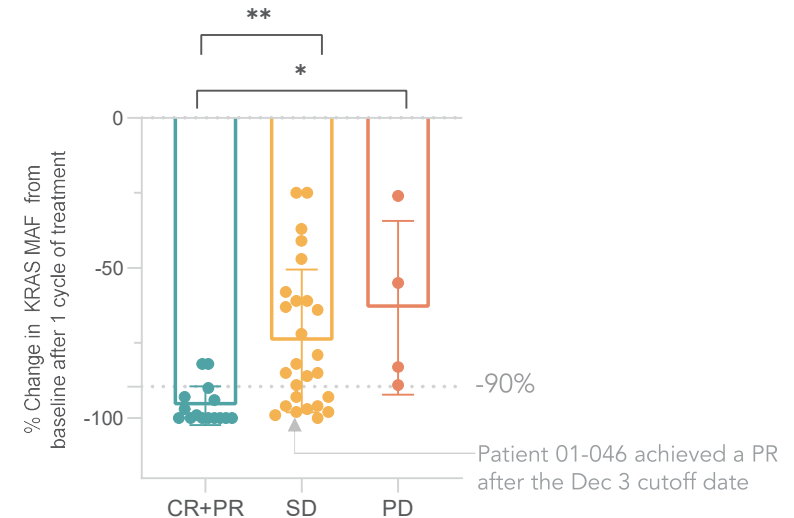
\* 2008: Bennouna et al., Lancet Oncol 2013; 14: 29–37; 2013: Giessen et al., Acta Oncologica, 2015, 54: 187-193; 2017: Cremolini et al., Lancet Oncol 2020, 21: 497–507; and Antoniotti et al., Correspondence Lancet Oncol June 2020. SoC: Standard-of-care. mPFS: median progression free survival

# Early KRAS MAF ctDNA decrease correlates with radiographic response

## Predictive response biomarker

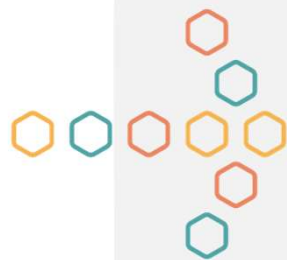
- 87% (13/15) of PR patients had  $\geq 90\%$  decrease in KRAS MAF after the 1st cycle
- 35% (9/26) of SD patients and none of the PD patients (n=4) had such a decrease

**% KRAS Mutant Allelic Frequency (MAF)\***  
decrease after one 28-day treatment cycle  
(as of Dec 3, 2021)



|      | CR+PR | SD  | PD  |
|------|-------|-----|-----|
| Mean | -96   | -74 | -63 |

\* 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). 1 PR and 2 SD patients had undetectable KRAS at baseline. KRAS MAF plot reflects interim data as of Dec 3, 2021 from an ongoing trial and unlocked database, and indicates one subsequent PR achieved on follow up through Jan 18, 2022 press release



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## WHAT

Onvansertib has achieved

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## WHY

Onvansertib works

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## WHERE

Cardiff Oncology can go

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To date, toxicity has prevented regulatory approval of PLK1 inhibitors

## Onvansertib's safety profile

eclipses that of its most promising predecessor

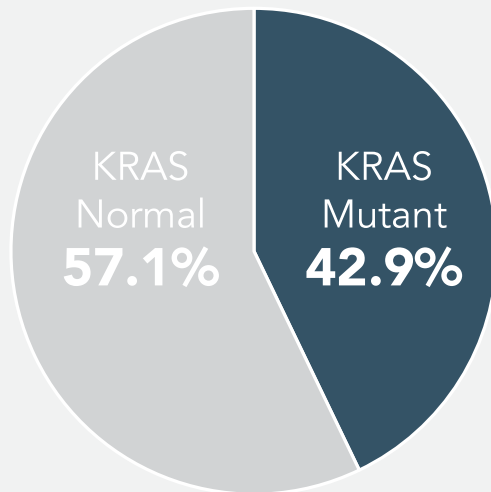
|                         | Onvansertib                     | Volasertib <sup>1</sup>                           |
|-------------------------|---------------------------------|---------------------------------------------------|
| Selectivity for PLK1    | Exclusive for PLK1              | Pan-inhibitor 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<sup>1</sup>

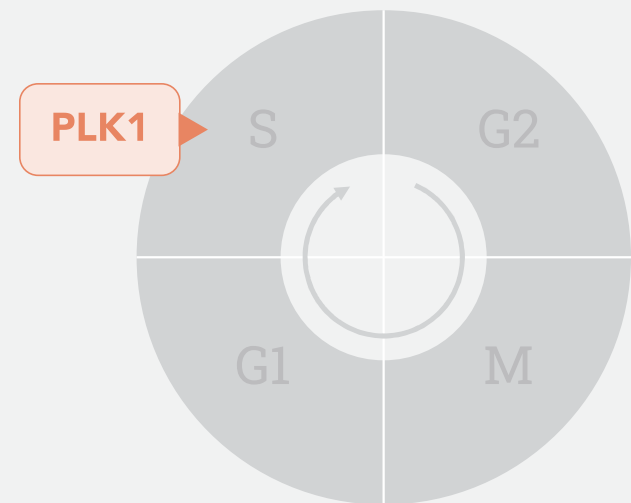
Cells with KRAS mutation are hypersensitive to inhibition of PLK1



**MOA 1**

## SYNERGY WITH CHEMO

Inhibiting PLK1 increases the efficacy of chemotherapy drugs

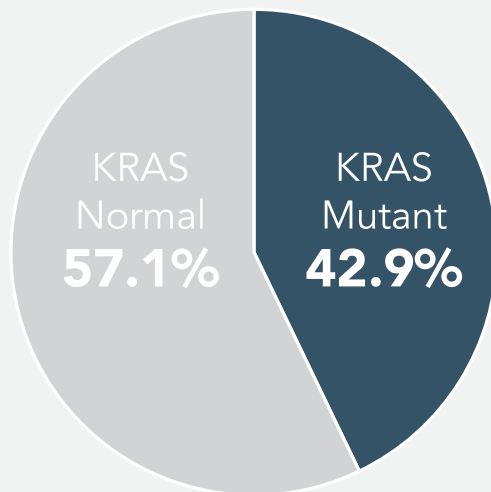


**MOA 2**

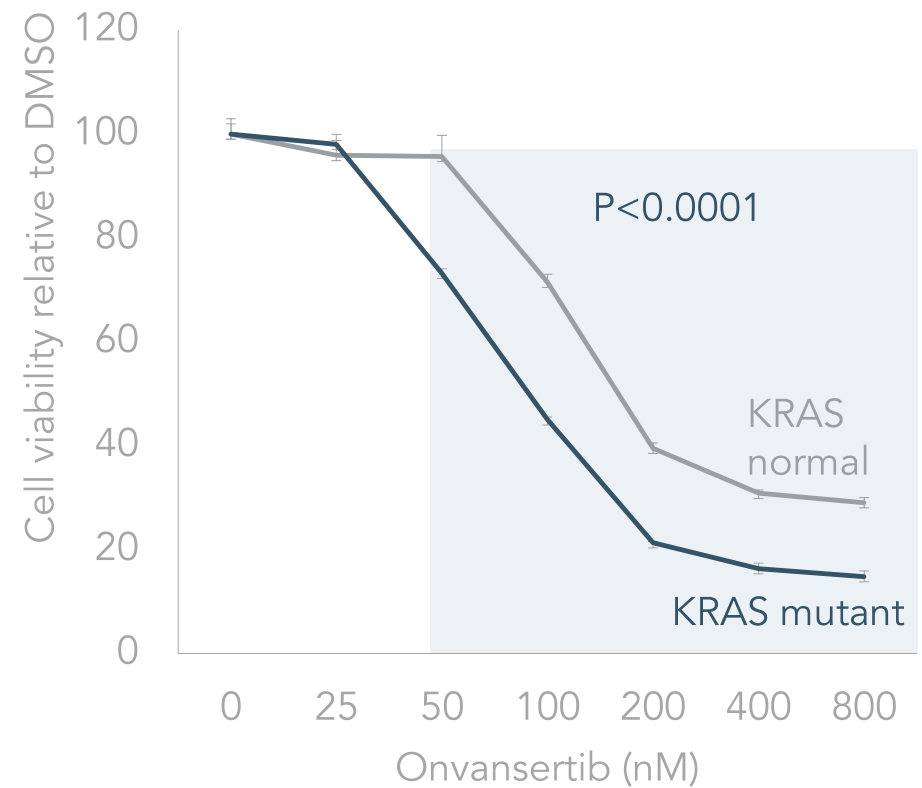
# Onvansertib's PLK1 inhibition is a two-pronged attack of tumor cells

## KRAS HYPERSENSITIVITY<sup>1</sup>

Cells with KRAS mutation are hypersensitive to inhibition of PLK1



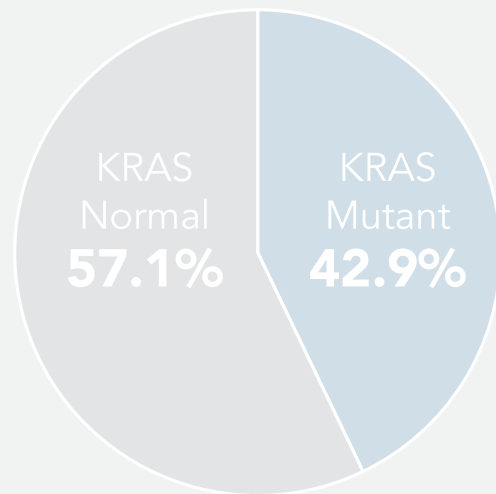
MOA 1



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

## KRAS HYPERSENSITIVITY<sup>1</sup>

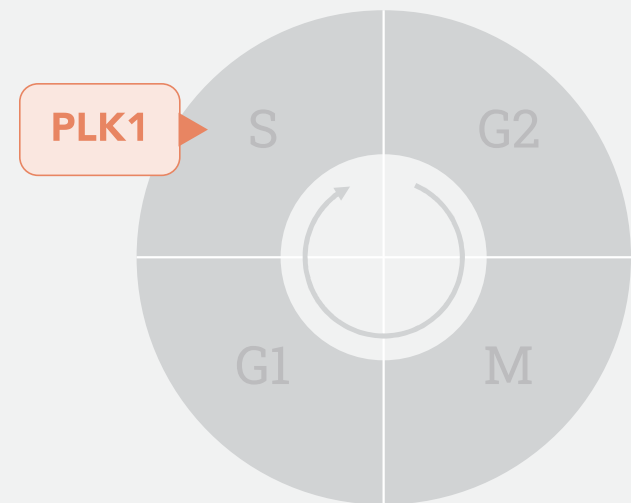
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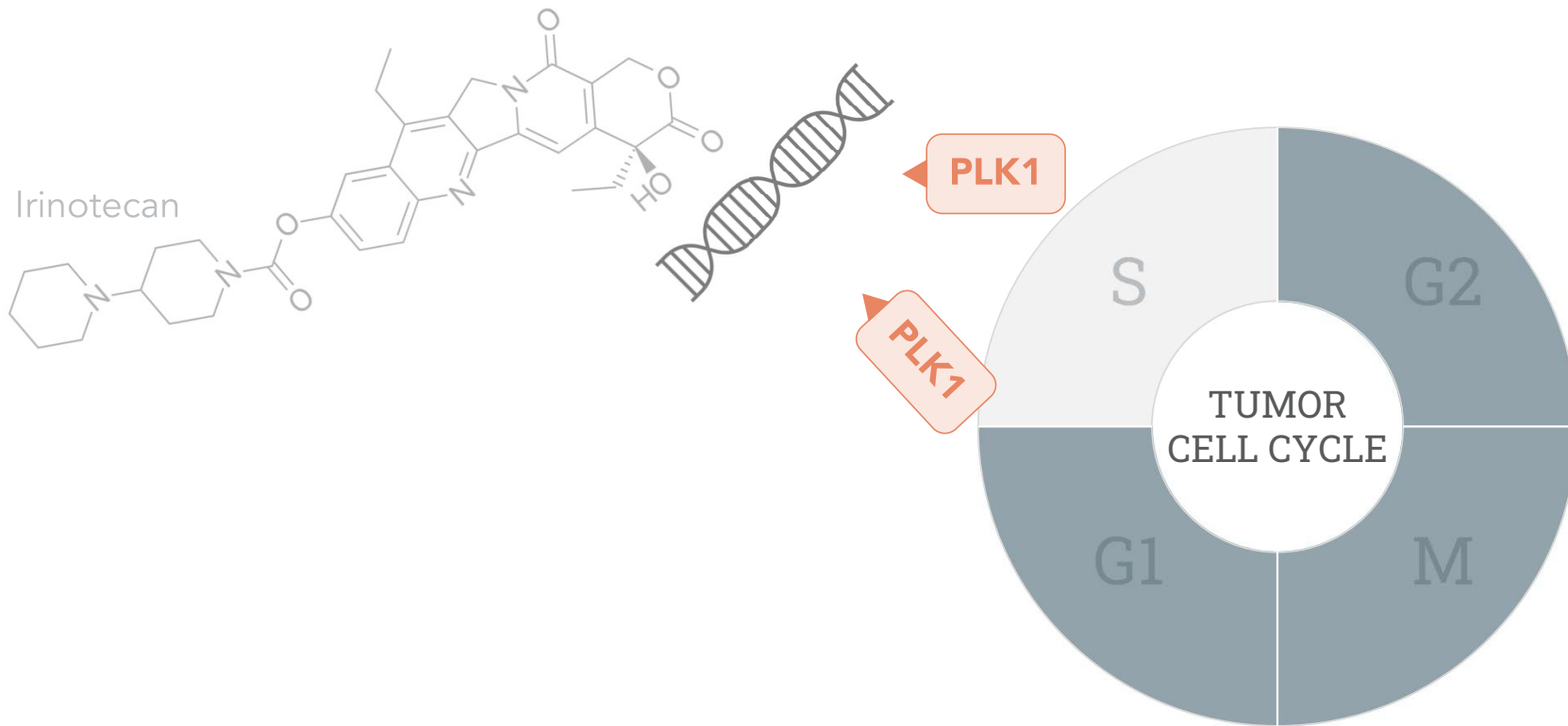


**MOA 2**

# Chemotherapy drugs damage tumor DNA to prevent cell proliferation

DNA Damaging Agent

DNA REPLICATION PHASE



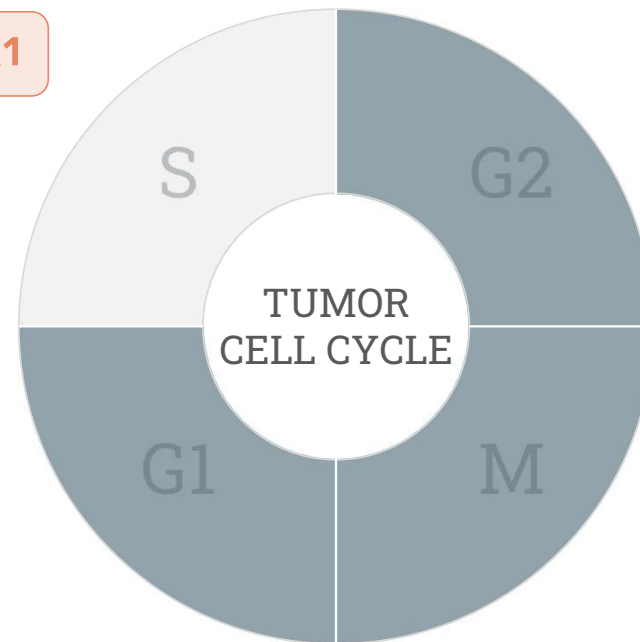
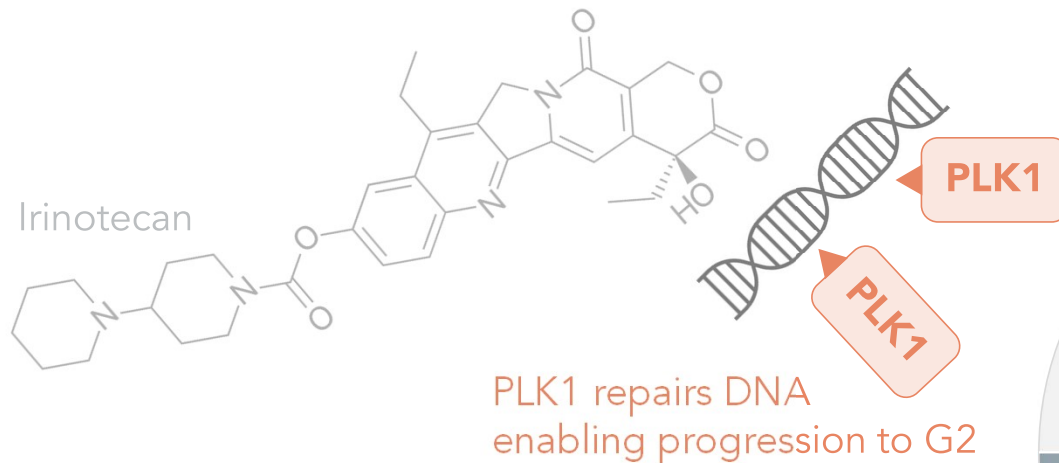


# PLK1's repair of DNA interferes with chemotherapy drugs

DNA Damaging Agent

DNA REPLICATION PHASE

CELL GROWTH PHASE



# Inhibiting PLK1 prevents DNA repair and halts the cell cycle

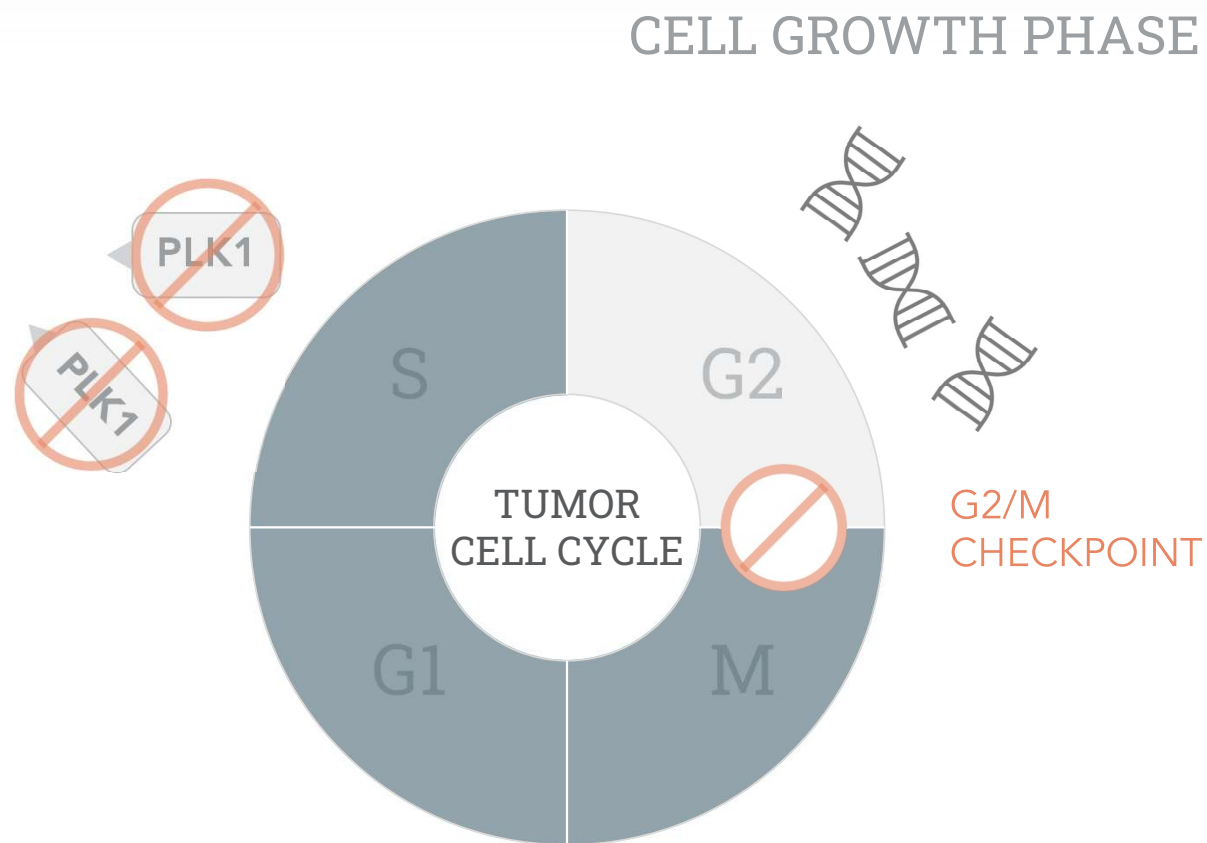
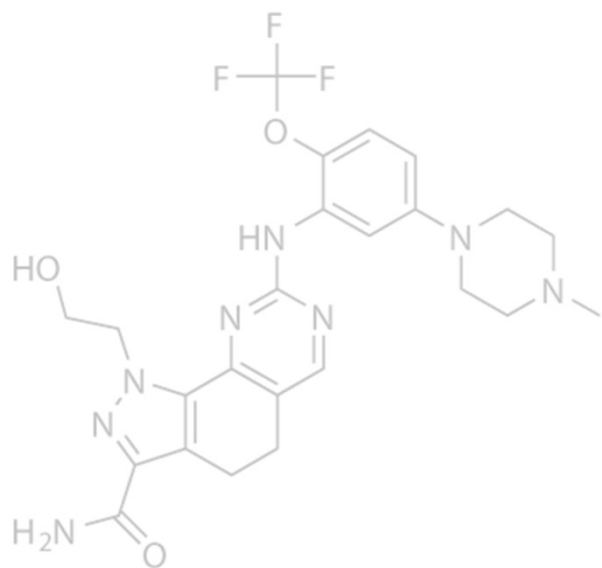
**Onvansertib** inhibits PLK1 preventing DNA repair

CELL GROWTH PHASE



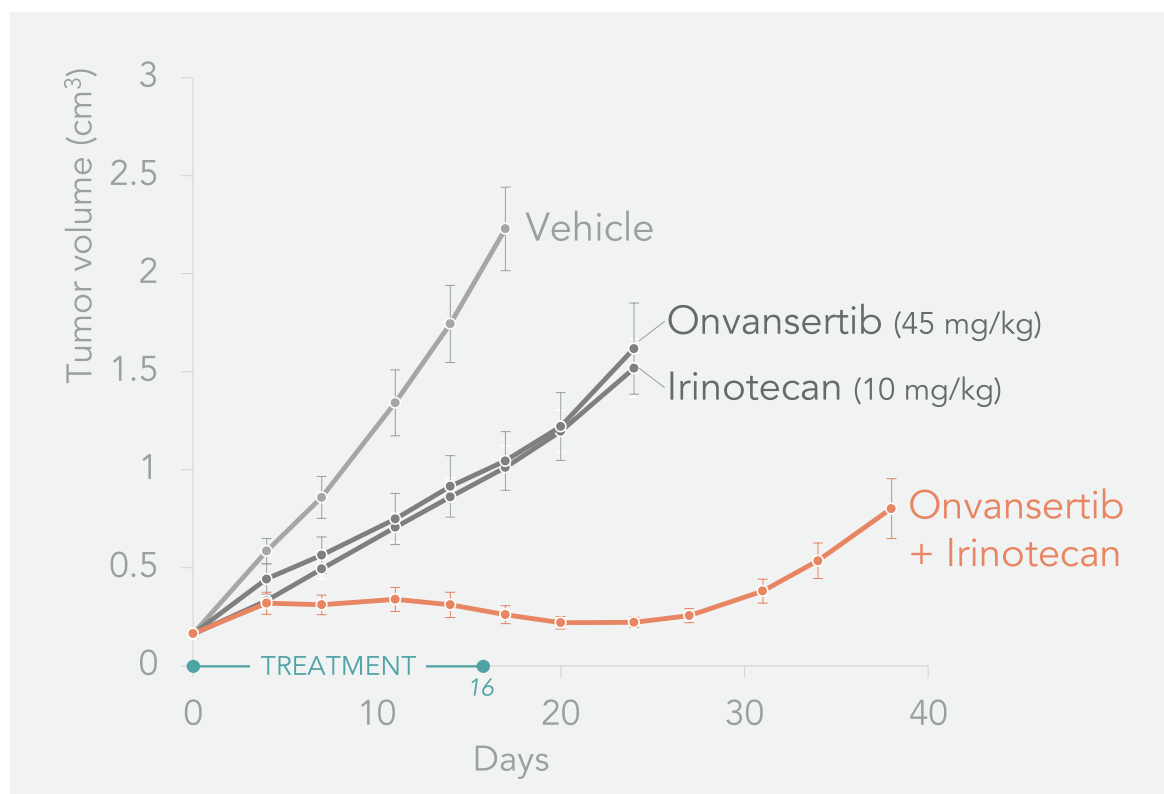
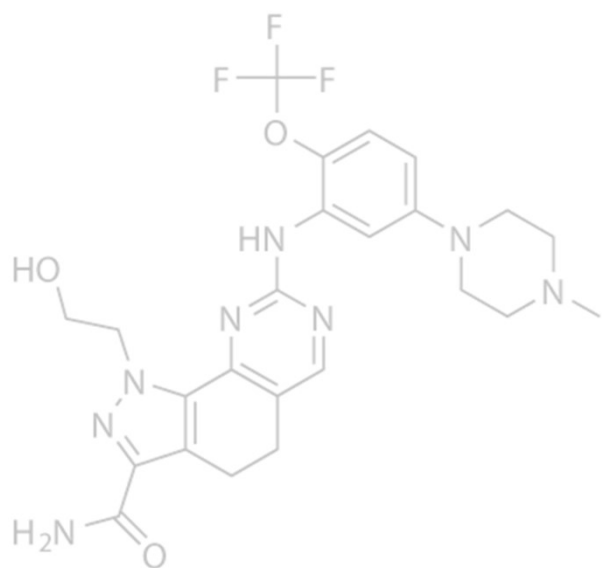
# Inhibiting PLK1 prevents DNA repair and halts the cell cycle

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

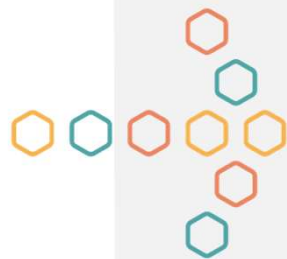


# Combined, onvansertib and irinotecan are profoundly more effective

## Onvansertib + Irinotecan<sup>1</sup> in HCT-116 (with G13D KRAS mutation)



1. Mice were treated with vehicle, onvansertib (4 cycles of 1OFF/3ON), etirinotecan pegol NKTR-102 (days 1, 8, and 15) or the combination



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## WHAT

Onvansertib has achieved

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## WHY

Onvansertib works

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## WHERE

Cardiff Oncology can go

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# Cardiff Oncology has many attractive options

|                  | DNA DAMAGING AGENTS |                 |           | MICROTUBULE TARGETING |           |               | EPIGENETICS     |
|------------------|---------------------|-----------------|-----------|-----------------------|-----------|---------------|-----------------|
|                  | CHEMO-THERAPY       | PARP INHIBITORS | RADIATION | DESTABILIZE           | STABILIZE | DISCONNECT    | LSD1 INHIBITORS |
| mCRC             | Phase 1b/2 Trial    |                 |           |                       |           |               |                 |
| mPDAC            | Phase 2 Trial       |                 |           |                       |           |               |                 |
| mCRPC            |                     |                 |           |                       |           | Phase 2 Trial |                 |
| Ovarian          |                     |                 |           |                       |           |               |                 |
| Breast           |                     |                 |           |                       |           |               |                 |
| SCLC             |                     |                 |           |                       |           |               |                 |
| Medullo-blastoma |                     |                 |           |                       |           |               |                 |

= Cardiff Oncology potential

## Our pipeline opens many attractive opportunities for onvansertib

|                               | Combination with: | Preclinical            | IND En. | Ph 1/2                 | Status    | Partners                                                                              |
|-------------------------------|-------------------|------------------------|---------|------------------------|-----------|---------------------------------------------------------------------------------------|
| mCRC                          | FOLFIRI/bev       | <div><div></div></div> |         | <div><div></div></div> | Enrolling |                                                                                       |
| mPDAC                         | Onivyde/5-FU      | <div><div></div></div> |         | <div><div></div></div> | Enrolling |                                                                                       |
| mCRPC                         | Abiraterone       | <div><div></div></div> |         | <div><div></div></div> | Enrolling |                                                                                       |
| Ovarian                       | PARP inhibitors   | <div><div></div></div> |         |                        | Planned   |                                                                                       |
| Investigator-initiated trials |                   |                        |         |                        |           |                                                                                       |
| TNBC                          | Paclitaxel        | <div><div></div></div> |         | <div><div></div></div> | Planned   |   |
| SCLC                          | Single agent      | <div><div></div></div> |         |                        | Planned   |  |
| CMML                          | Single agent      | <div><div></div></div> |         |                        | Planned   |  |
| Medullo-blastoma              | Radiation         | <div><div></div></div> |         |                        | Planned   |  |

## Anticipated catalysts over the next twelve months

# 2022

### CLINICAL PROGRAMS

*Mid 2022*

mCRC Phase 1b/2 data release

Launch pivotal trial

mPDAC Phase 2 data release

mCRPC Phase 2 data release

### OTHER COMBINATIONS

- **Ovarian** cancer with PARPi
- **Breast** cancer with paclitaxel
- **Medulloblastoma** with radiation (pediatric)



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) with a 180-day lockup
- Right of First Access:  
Pfizer sees onvansertib data 2 days before release

## Cardiff Oncology at a glance

Clinical-stage biotech company developing onvansertib, an oral, highly-selective **PLK1** inhibitor, across a range of cancers

|                                                                                                          | March 31, 2022 |
|----------------------------------------------------------------------------------------------------------|----------------|
| Cash, cash equivalents and investments <sup>1</sup>                                                      | \$129.4M       |
| Net cash used in Operating Activities <sup>1</sup><br>(Rolling two-quarter period ending March 31, 2022) | \$17.6M        |
| Headquarters                                                                                             | San Diego, CA  |
| Exchange                                                                                                 | NASDAQ: CRDF   |

1. As of 3/31/22. The above financial information is derived from our audited financials in Form 10K filed on 2/24/22 and our unaudited financials in Form 10Q filed on 5/4/22.



## KRAS-Mutated Metastatic Colorectal Cancer (mCRC)

# Phase 1b/2 mCRC trial patient enrollment and demographics

## Enrollment\*

| Number of Patients (N) | Phase 1b, Dose Level 0<br>Onvansertib 12 mg/m <sup>2</sup> | Phase 1b, Dose Level +1<br>Onvansertib 15 mg/m <sup>2</sup> | Phase 1b, Dose Level +2<br>Onvansertib 18 mg/m <sup>2</sup> | Phase 2 RP2D<br>Onvansertib 15 mg/m <sup>2</sup> | Total Patients<br>All Doses |
|------------------------|------------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------|--------------------------------------------------|-----------------------------|
| Treated                | 6                                                          | 6                                                           | 6                                                           | 32                                               | 50                          |
| Currently on treatment | 0                                                          | 1                                                           | 0                                                           | 15                                               | 16                          |

| Total Patients N=50             | Median [range] or n (%) |
|---------------------------------|-------------------------|
| Age (years)                     | 61 [35-83]              |
| Sex                             |                         |
| Male                            | 28 (56%)                |
| Female                          | 22 (44%)                |
| ECOG <sup>1</sup>               |                         |
| 0                               | 33 (69%)                |
| 1                               | 15 (31%)                |
| Primary tumor site <sup>2</sup> |                         |
| Colon                           | 27 (55%)                |
| Rectum                          | 17 (35%)                |
| Other                           | 5 (10%)                 |

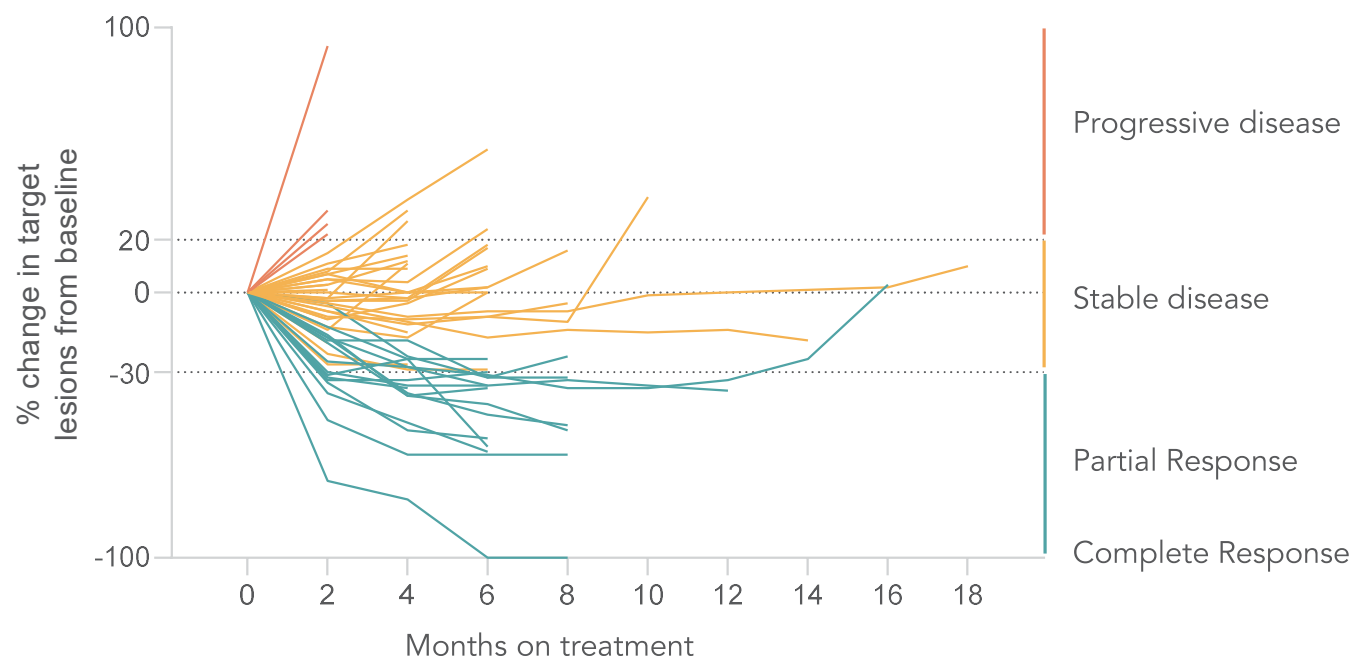
| Total Patients N=50                      | Median n (%) |
|------------------------------------------|--------------|
| Liver metastasis <sup>3</sup>            |              |
| None                                     | 11 (22%)     |
| Liver and other                          | 29 (59%)     |
| Liver only                               | 9 (18%)      |
| Number of metastatic organs <sup>4</sup> |              |
| 1                                        | 17 (35%)     |
| ≥2                                       | 32 (65%)     |
| Prior bevacizumab treatment <sup>5</sup> |              |
| Yes                                      | 33 (67%)     |
| No                                       | 16 (33%)     |

as of 03-Dec-2021

\* Jan 2022 data are interim as of Dec 3, 2021 from an ongoing trial and unlocked database. 1. ECOG not reported for two patients; 2. Primary tumor site not reported for one patient; 3. Liver metastasis presence not reported for one patient; 4. Number of metastatic organs not reported for one patient; 5. Prior bevacizumab treatment not reported for one patient

# Deepening of responses observed as patients remain on treatment

**Change in tumor size from baseline\*** – all doses (as of Dec 3, 2021)

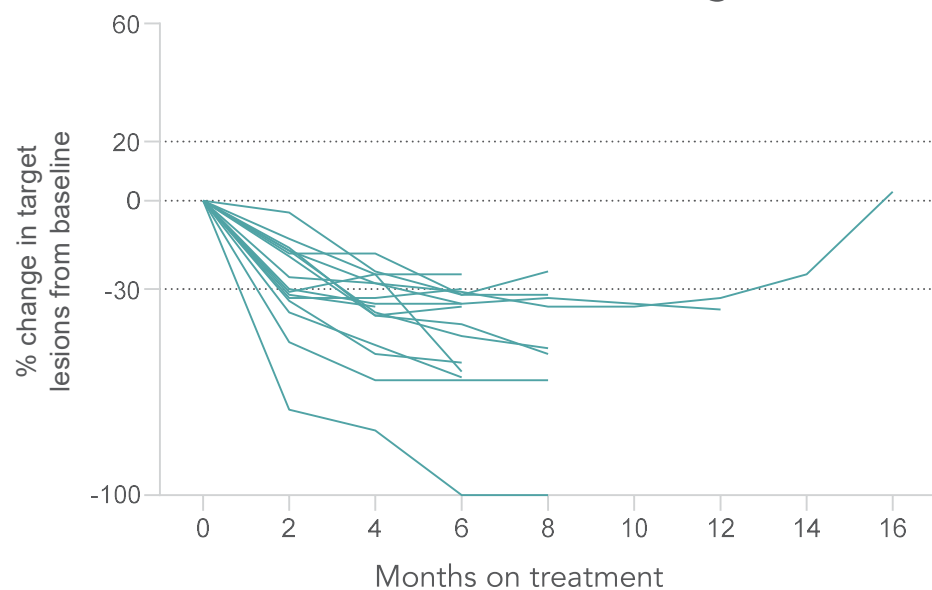


\* Spider plot reflects interim data as of Dec 3, 2021 from an ongoing trial and unlocked database

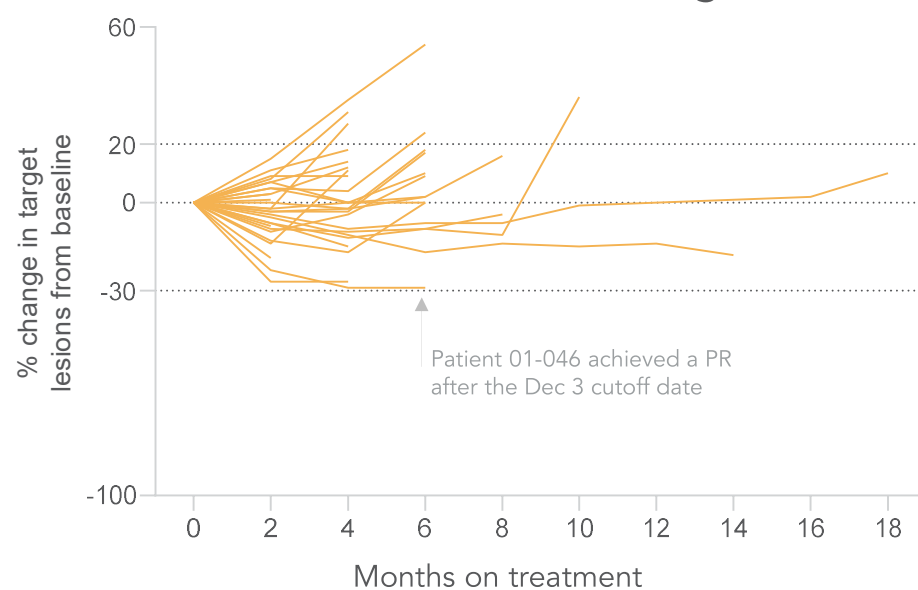
# Deepening of responses observed as patients remain on treatment

**Change in tumor size from baseline\*** – all doses (as of Dec 3, 2021)

## Patients achieving CR+PR



## Patients achieving SD



\* Spider plots reflect interim data as of Dec 3, 2021 from an ongoing trial and unlocked database, and indicates one subsequent PR achieved on follow up through Jan 18, 2022 press release

## Summary of onvansertib mCRC Ph1b/2 trial data over time

|                                    | ASCO GI<br>Jan 2021 | KOL Event<br>Sept 2021 |           | ASCO GI<br>Jan 2022               |          |                |          | Investor Webcast<br>Jan 2022                           |          |
|------------------------------------|---------------------|------------------------|-----------|-----------------------------------|----------|----------------|----------|--------------------------------------------------------|----------|
|                                    |                     |                        |           | Abstract                          |          | Poster         |          |                                                        |          |
| Data Cutoff Date                   | Nov 1, 2020*        | July 2, 2021*          |           | Sep 16, 2021                      |          | Dec 3, 2021    |          | Dec 3, 2021 +<br>efficacy follow up<br>through Jan. 18 |          |
|                                    | All Doses           | All<br>Doses           | RP2D      | All Doses                         | RP2D     | All Doses      | RP2D     | All Doses                                              | RP2D     |
|                                    |                     |                        |           |                                   |          | At data cutoff |          | After data cutoff                                      |          |
| Evaluable<br>Patients              | 14                  | 32                     | 19        | 44                                | 31       | 48             | 35       | 48                                                     | 35       |
| ORR (CR+PR)                        | 36% (5)             | 38% (12)               | 42% (8)   | 36% (16)                          | 35% (11) | 33% (16)       | 31% (11) | 35% (17)                                               | 34% (12) |
| Confirmed PRs                      | 29% (4)             | 31% (10)               | 37% (7)   | Data not disclosed<br>in abstract |          | 27% (13)       | 29% (10) | 1 patient waiting for<br>confirmatory scan             |          |
| mPFS                               | -                   | 9.4 mo                 | NR        |                                   |          | 9.4 mo         | NR       | No change from poster                                  |          |
| Disease control<br>rate (CR+PR+SD) | 86% (12)            | 94% (30)               | 100% (19) |                                   |          | 92% (44)       | 94% (33) |                                                        |          |

\* Data release include certain follow up data. "Investor Webcast Jan 2022" column reflects interim data as of Dec 3, 2021 from an ongoing trial and unlocked database, and indicates one subsequent PR achieved on follow up through Jan 18, 2022 press release. NR: Not reached

## KRAS-mutated mCRC: Cardiff Oncology's next steps

Cardiff Oncology management has decided to expand the activated Phase 2 trial and enroll ~40-50 additional patients as we prepare for initiation of the pivotal trial

- Obtain additional patient data:
  - Safety
  - Efficacy
  - Pharmacokinetic/pharmacodynamic (biomarkers)
- Continue assessing the value of KRAS response biomarker
- Keep current sites activated to lead into pivotal trial



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 <sup>1</sup>                                         |
| 4.5 | 11.5                                          | 2000 – 2013 | Systematic Literature-Based Analysis of 23 Randomized Trials (10,800 Patients) in Second-Line mCRC <sup>2</sup>        |
| 5.6 | —<br>Not reported<br>for 2 <sup>nd</sup> line | 2015 – 2017 | TRIBE2 Randomized Phase 3 Trial: SOC arm FOLFIRI + bev in Second-line following FOLFOX + bev First-line <sup>3,4</sup> |

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



## Metastatic Pancreatic Adenocarcinoma (mPDAC)

## Our Ph 2 trial in KRAS-mutated mPDAC combines onvansertib w/ SoC

One Cycle = 14 Days

WEEKS 1-2



WEEKS 3-4



# Our Ph 2 trial in KRAS-mutated mPDAC combines onvansertib w/ SoC

One Cycle = 14 Days

WEEKS 1-2



ONVA



2nd-Line SoC: NaI-IRI  
+ Leucovorin + 5-FU

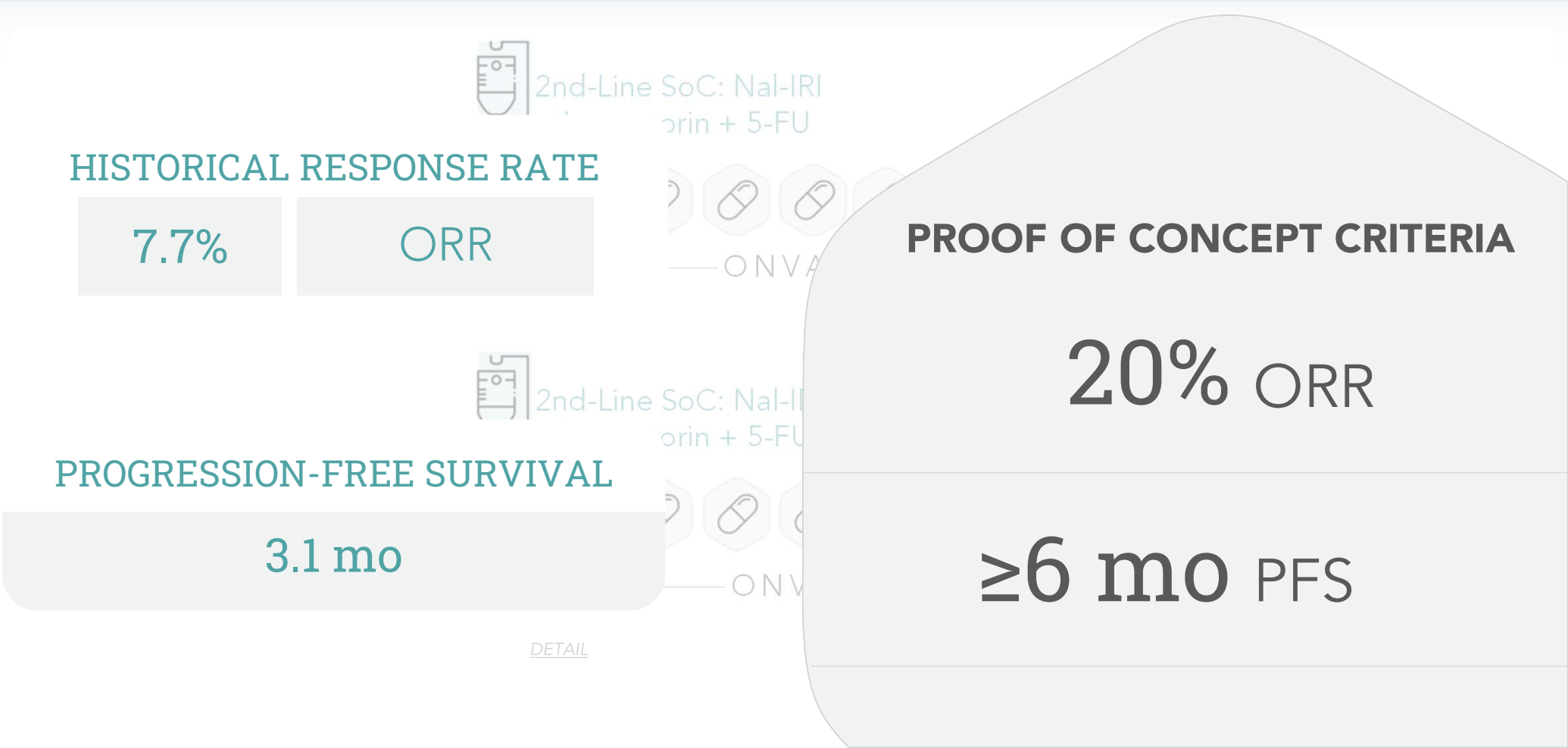


ONV

## EFFICACY END POINTS

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

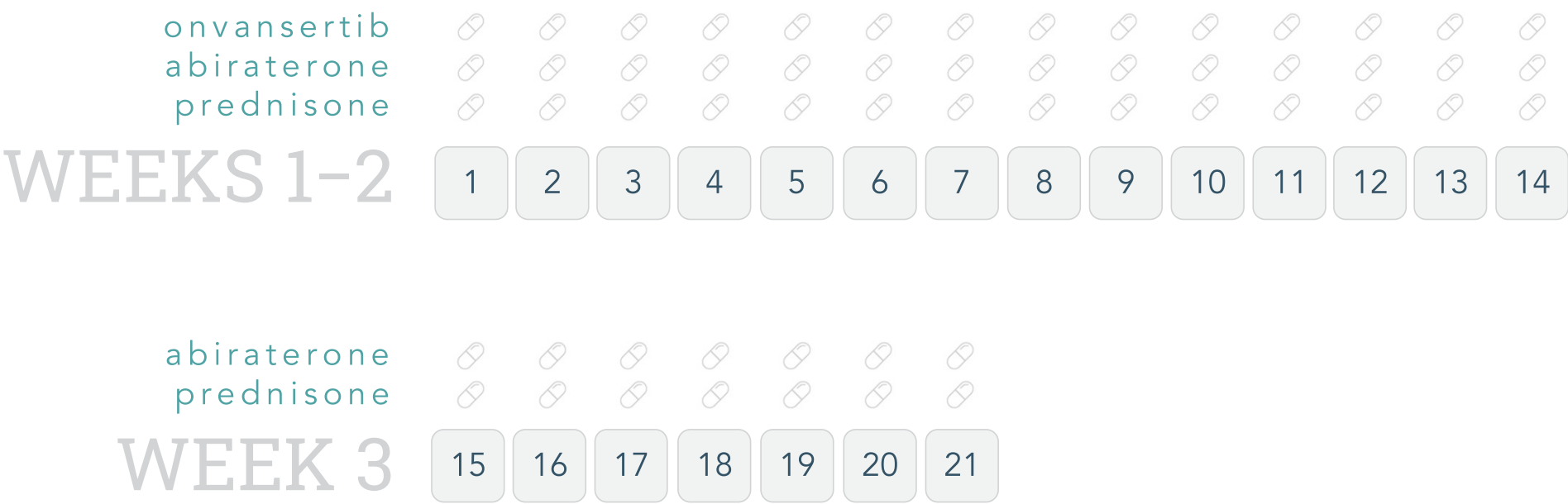
End-points measured tumor response and duration of response





## Metastatic Castrate Resistant Prostate Cancer (mCRPC)

# Our Ph 2 study in mCRPC combines onvansertib with abiraterone



One cycle = 21 days

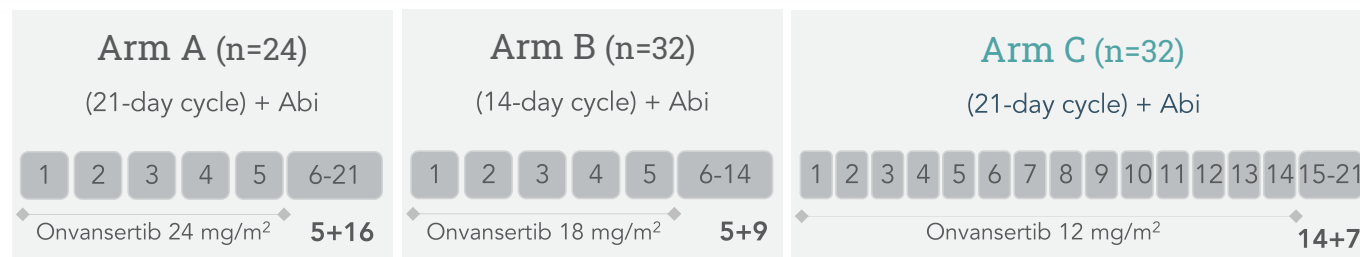
# Arm C in our Ph 2 trial provides the greatest onvansertib dose density

## Key Eligibility Criteria

- Initial signs of abiraterone resistance defined as 2 rising PSAs; one rise of  $\geq 0.3$  ng/mL separated by one week

## Key Exclusion Criteria

- Prior treatment with either enzalutamide or apalutamide
- Rapidly progressing disease or significant symptoms related to disease progression



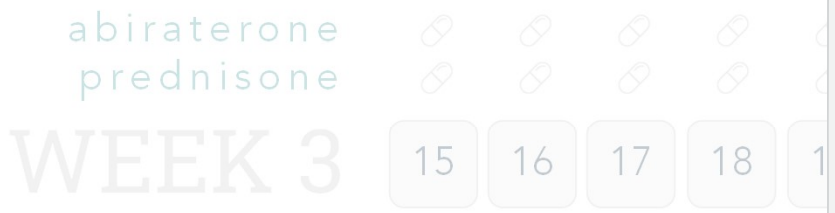
| Number of patients (N)  | Arm A (5+16) | Arm B (5+9) | Arm C (14+7) |
|-------------------------|--------------|-------------|--------------|
| Enrolled                | 24           | 20          | 24           |
| Evaluable for Efficacy* | 17           | 19          | 20           |
| Currently on Treatment  | 0            | 3           | 11           |

Enrollment as of 2-Feb-2022

\*Completed at least 12 weeks of treatment or had radiographic/clinical progression within 12 weeks



# Endpoints measure disease control and time to PSA progression



One cycle = 21 days

## EFFICACY ENDPOINTS

- 1 Primary: Proportion of patients achieving disease control after 12-weeks of treatment, as defined by lack of PSA progression (per PCWG3 criteria)
- 2 Secondary: Radiographic response (per RECIST v1.1); time to PSA progression
- 3 Exploratory: Target inhibition of PLK1 and relevant biomarkers correlated with patient response

End-points measure disease control and time to PSA progression

HISTORICAL RESISTANCE TO ARSi

9-15 mo

Resistance  
to ARSi

OVERALL SURVIVAL BENEFIT

~4 mo

**PROOF OF CONCEPT CRITERIA**

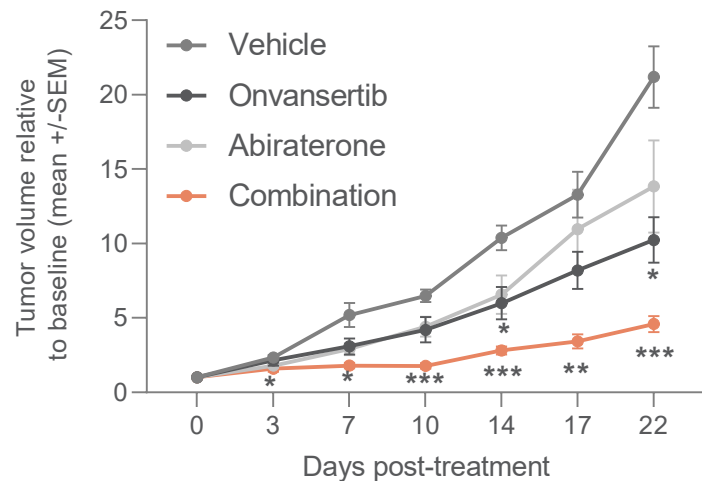
30% disease control rate  
after 12-weeks of treatment

≥6 mo PFS

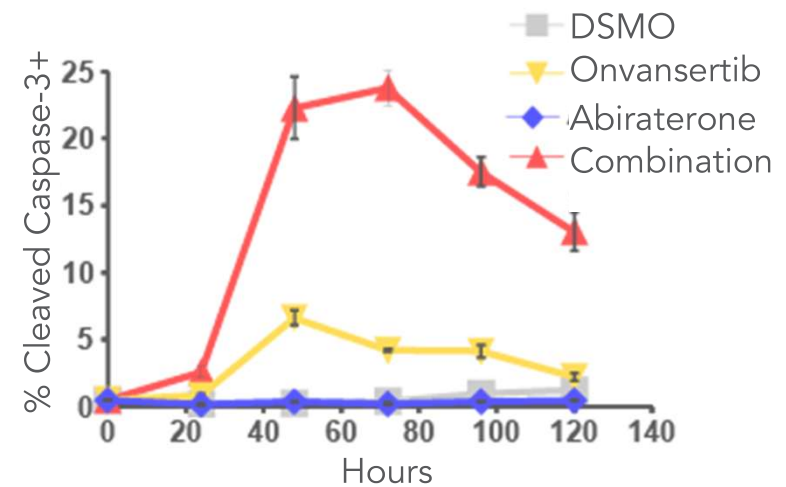
One cycle = 21 days

# Onvansertib demonstrates synergy in an abiraterone-resistant setting

Onvansertib + Abiraterone Demonstrate Synergy in Abi-Resistant Model (LVCaP2CR)<sup>1</sup>



Onvansertib + Abiraterone Significantly Increases Apoptotic Cell Death<sup>1</sup>



- PLK1 is overexpressed in prostate cancer and linked to higher tumor grades<sup>2</sup>
- PLK1 inhibition + abiraterone demonstrated synergy in mCRPC *in vitro* and *in vivo* models: combination induced increased mitotic arrest and apoptosis in comparison with single agents alone
- Preclinical studies suggest that abiraterone sensitizes cells to onvansertib through regulation of mitotic processes

1. Data on-file. In collaboration with Michael Yaffe (MIT) and Jun Luo (John Hopkins University); <sup>2</sup>Weichert et al., Prostate 2004;60(3):240-5  
Abi: Abiraterone; mCRPC: metastatic castrate-resistant prostate cancer

# Arm C of our Phase 2 trial provides the greatest disease control

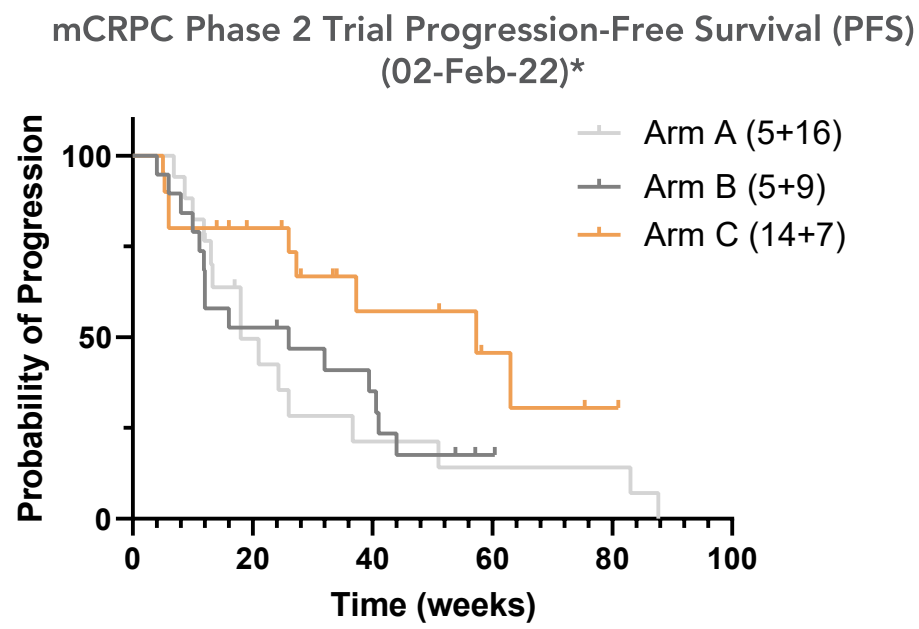
Efficacy Across Arms A, B, and C for Evaluable Patients (02-Feb-22)

|                                                   | Arm A<br>(onv days 1-5 / 21-day cycle) | Arm B<br>(onv days 1-5 / 14-day cycle) | Arm C<br>(onv days 1-14 / 21-day cycle) |
|---------------------------------------------------|----------------------------------------|----------------------------------------|-----------------------------------------|
| Evaluable for efficacy*                           | 17                                     | 19                                     | 20                                      |
| Disease control / PSA Stabilization at 12 weeks** | 5 (29%)                                | 8 (42%)                                | 9 (45%)                                 |
| Radiographic Stable Disease at 12 weeks           | 9 (53%)                                | 11 (58%)                               | 15 (75%)                                |
| Median progression-free survival (months)         | 4.1                                    | 6.0                                    | 13.2                                    |

Increase in rate of patients achieving PSA stabilization and radiographic SD achieved with greater dose-density schedule in Arm C

\* Completed at least 12 weeks of treatment or had radiographic/clinical progression within 12 weeks; \*\*Defined as prostate specific antigen (PSA) stabilization or decline (PSA rise <25% over baseline); SD: Stable Disease 62

# Greater dose density of onvansertib Arm C resulting in longer PFS



| Arm | Median PFS (months) | Log-rank p-value versus Arm C** |
|-----|---------------------|---------------------------------|
| A   | 4.1                 | 0.055                           |
| B   | 6.0                 | 0.057                           |
| C   | 13.2                |                                 |

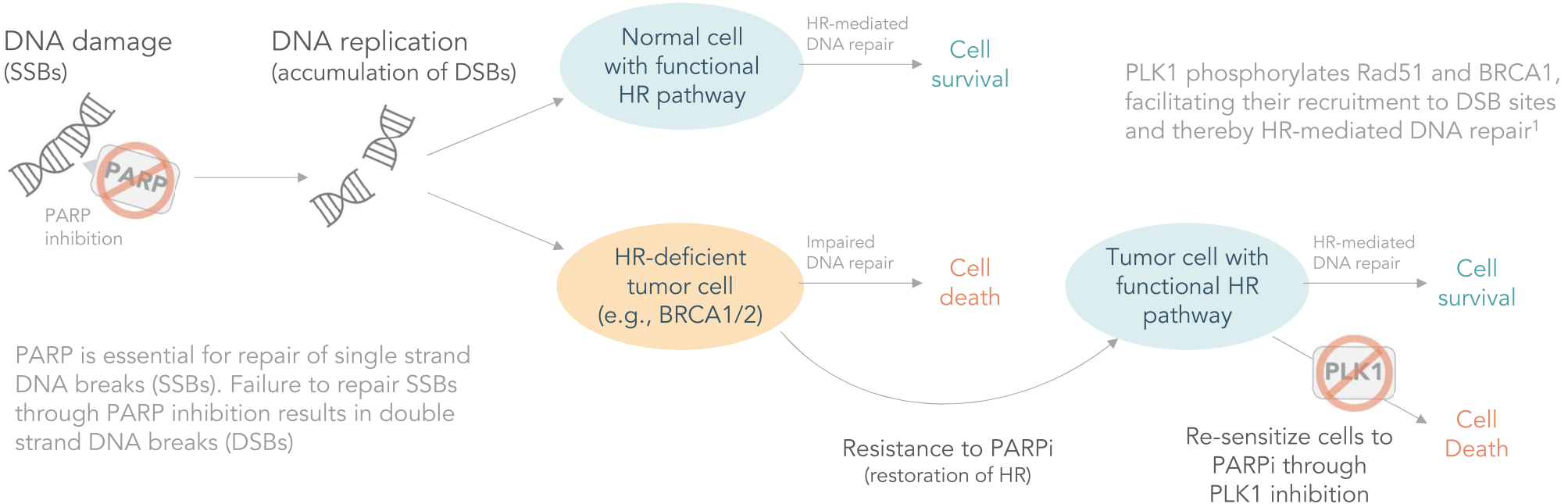
\* 2-Feb-2022 PFS are preliminary data from an ongoing trial and unlocked database



## PARPi Pre-Clinical Data

# PLK1 inhibition re-sensitizes tumor cells to PARP inhibition

## Onvansertib + PARP inhibitors

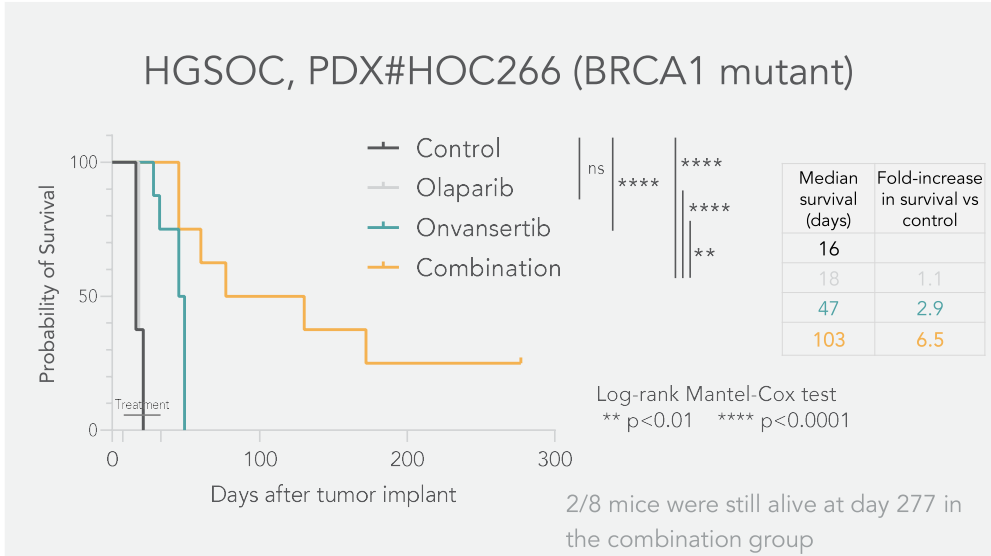
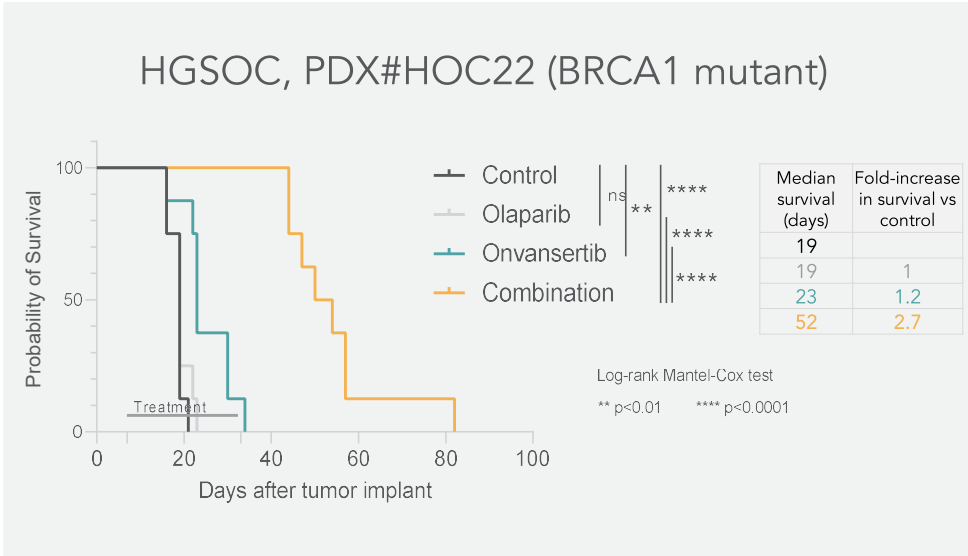


1. Yata et al. Mol. Cell 45, 371-383, 2012; Chabaliere-Taste et al., Oncotarget 2016 Jan 19; 7(3): 2269-83; Peng et al., NAR 2021,49(13):7554-7570. HR: Homologous recombination; PARPi: PARP inhibitor 65

# Preclinical studies demonstrate the benefit of PLK1 + PARP inhibitors

## Onvansertib + PARP inhibitors\*

Ovarian BRCA1 mutant PARPi-resistant PDX models



\* 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