



SOLVE  
ON.

October 26, 2026

# ESMO 2026 Investor Event

# Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws, including statements regarding Incyte's oncology strategy and the potential of its oncology portfolio; the potential, safety, efficacy and clinical activity of INCA33890 (TGFβR2×PD-1) and INCB161734 (KRAS G12D); the potential for INCA33890 and INCB161734 to serve as backbone therapies and support the development of a multi-product, multi-line oncology franchise; the potential patient populations, market opportunities and commercial opportunities for INCA33890 and INCB161734; the initiation, timing, design, progress and results of ongoing and planned clinical trials, including NEXERA-303 and DAWN-303 and planned studies in adjuvant pancreatic cancer and previously treated colorectal cancer; expectations regarding clinical trial enrollment and anticipated data readouts; plans to evaluate INCA33890 and INCB161734 in additional treatment settings, tumor types and combinations; the potential for clinical data to support further development, regulatory submissions, approvals and commercial launches; expectations regarding Incyte's collaborations and combination strategies; Incyte's aspirations and goals as set forth under the heading "About Incyte"; and 2026 newsflow items.

Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including the preliminary nature of certain clinical data; whether early or interim clinical results will be replicated in later-stage or larger clinical trials; the sufficiency of clinical trial data to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical trials and the ability to enroll subjects in accordance with planned schedules; changes in clinical development plans; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and regulatory approval; the efficacy or safety of Incyte's products; Incyte's ability to successfully develop and commercialize its product candidates; the availability and effectiveness of competing treatments; Incyte's ability to obtain and maintain intellectual property protection for its products and technology; greater than expected expenses, including expenses relating to clinical development, litigation or strategic activities; and those risks and uncertainties discussed in greater detail in Incyte's reports filed with the U.S. Securities and Exchange Commission, including its annual report on Form 10-K for the year ended December 31, 2025 and its quarterly report on Form 10-Q for the quarter ended June 30, 2026. Incyte disclaims any intent or obligation to update these forward-looking statements.

# Today's speakers



*Pablo Cagnoni, M.D.*

President & Global Head of Research and Development



*Steven Stein, M.D.*

Executive Vice President, Chief Medical Officer & Head of Late-Stage Development



*Elena Garralda, M.D., Ph.D.*

Co-director, VHIO Clinical Research Program, Group Leader, VHIO Early Clinical Drug Development Group, Director, Research Unit for Molecular Therapy of Cancer – Caixa Research



*Manuel Hidalgo, M.D., Ph.D., FAACR*

Professor of Medicine, Director, Gastrointestinal Cancer Center, Perlmutter Cancer Center, NYU Grossman School of Medicine

# Agenda

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## **01 Welcome & Solid Tumor Development Strategy**

**Pablo Cagnoni, M.D.**

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## **02 INCA33890 & INCB161734 Development Spotlight**

**Steven Stein, M.D.**

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A first-in-class TGF $\beta$ R2 $\times$ PD-1 bispecific in first-line MSS colorectal cancer

**Elena Garralda, M.D., Ph.D.**

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A novel KRAS G12D inhibitor in pancreatic and colorectal cancer

**Manuel Hidalgo, M.D., Ph.D., FAACR**

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## **03 Closing Remarks**

**Pablo Cagnoni, M.D.**

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## **04 Q&A**

**Incyte Management & Key Opinion Leaders**

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# Solid Tumor Development Strategy

**Pablo Cagnoni, M.D.**  
President and Global Head of R&D

# Three principles guide our oncology strategy

01

## Novel targeted therapies

Pursuing mechanisms with a **clear biological rationale** and **differentiated molecular designs**

02

## High-incidence cancers

Focusing on **large patient populations with limited treatment options**

03

## Front-line treatments & combinations

Prioritizing development in **front-line settings** and pursue **rational combinations** with the goal of establishing new standards of care

# Our late-stage portfolio in solid tumors

**1** Approved medicine

**3** Clinical-stage assets

**4** Distinct mechanisms

**Zynyz**

**Anti-PD-1  
monoclonal**

**MARKETED**

SCAC  
MCC

**INCA33890**

**TGFβR2×PD-1  
bispecific**

**PIVOTAL**

1L MSS CRC

**INCB161734**

**KRAS G12D  
inhibitor**

**PIVOTAL**

1L PDAC

**INCB123667**

**CDK2  
inhibitor**

**PIVOTAL**

Ovarian (CCNE1+)

# High-incidence cancers with poor prognosis

## ASSET

### INCB161734

KRAS G12D inhibitor

**Pancreatic cancer (G12D mutated)<sup>1,2</sup>**

## INCIDENCE

**~47k**

Need for longer survival and durable disease control

## 5-YEAR SURVIVAL

**~3%**

### INCA33890

TGFβR2×PD-1 bispecific

**MSS colorectal cancer<sup>3,4</sup>**

**~174k**

Need to extend immunotherapy benefit to MSS disease

**~13%**

### INCB123667

CDK2 inhibitor

**Ovarian cancer (CCNE1+)<sup>5,6</sup>**

**~25k**

Need for more effective maintenance in CCNE1+ HRD-negative disease

**~22%**

<sup>1</sup>DRG 2026. Lee J.K., et al. npj Precis. Onc. 2022;6(91). <sup>2</sup>For patients with Stage IV disease. CancerMPact® 2026 Treatment Architecture US. <sup>3</sup>DRG 2025. Buchler T, Front. Oncol. 2022;12:888181.

<sup>4</sup>CancerMPact® 2026 Treatment Architecture US. For patients with Stage IV disease. Cremolini C, Lancet, 2015; 16, 1306-1315. <sup>5</sup>DRG -2025. Sisman Y, Cancers, 2025; 17(10). <sup>6</sup>For patients with Stage IV disease. CancerMPact® 2026 Treatment Architecture US.

# Systematic expansion of GI franchise

|                                            | TUMOR<br>TYPES                                                                                                                 | TREATMENT<br>SETTINGS                                                                               | SOC & NOVEL<br>COMBINATIONS                                                                                                                                                      |
|--------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>INCA33890</b><br>TGFβR2×PD-1 bispecific | <ul style="list-style-type: none"><li>• <b>CRC</b></li><li>• HNSCC</li><li>• Ovarian</li><li>• NSCLC</li></ul>                 | <ul style="list-style-type: none"><li>• Adjuvant</li><li>• First line</li><li>• 2L+ lines</li></ul> | <ul style="list-style-type: none"><li>• Chemotherapy ± bevacizumab</li><li>• Muzastotug (anti-CTLA-4 mAb)</li><li>• EGFR Ab</li><li>• ADC combo</li></ul>                        |
| <b>INCB161734</b><br>KRAS G12D inhibitor   | <ul style="list-style-type: none"><li>• <b>PDAC</b></li><li>• <b>CRC</b></li><li>• NSCLC</li><li>• Other G12D tumors</li></ul> | <ul style="list-style-type: none"><li>• Adjuvant</li><li>• First line</li><li>• 2L+ lines</li></ul> | <ul style="list-style-type: none"><li>• Chemotherapy ± cetuximab</li><li>• Navlimetostat (PRMT5i)</li><li>• SNV1521 (PARP1i)</li><li>• Petosemtamab (EGFR x LGR5 bsAb)</li></ul> |

# Five settings addressing 200k+ patients

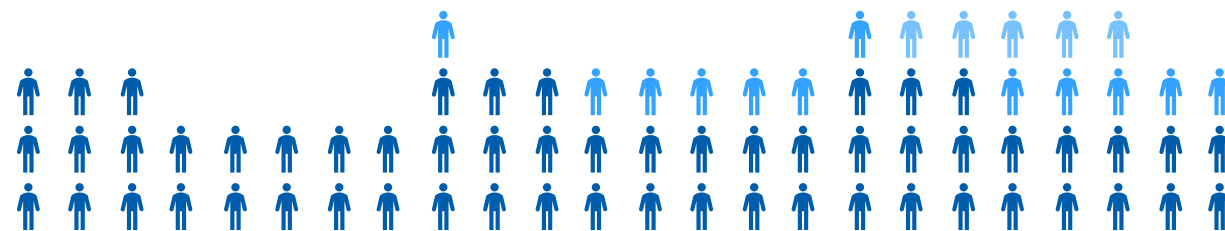
Anticipated data and approvals in 2028+

TGF $\beta$ R2 $\times$ PD-1 TAM<sup>2,3</sup>

200k+

G12D TAM<sup>1,3</sup>

~74k



**INCB161734**

KRAS G12D inhibitor

1L G12D PDAC

~47k

Topline data 2028

Adj. G12D PDAC

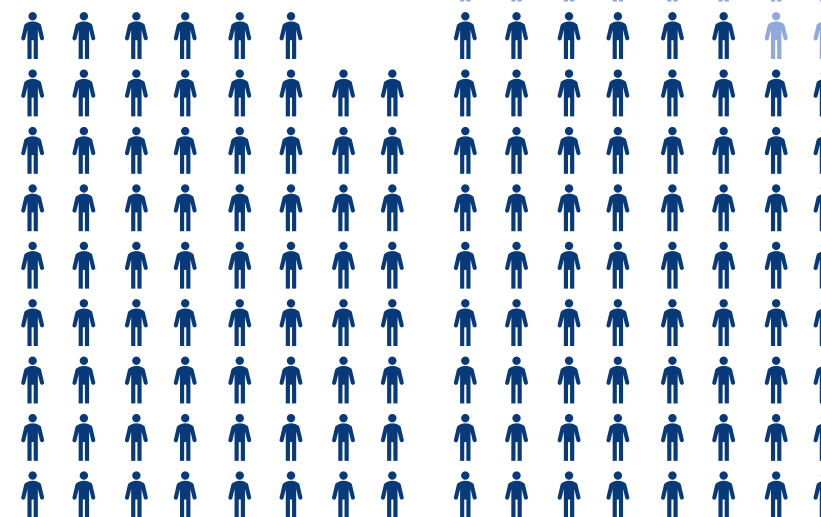
~14k

Phase 3 initiation in 2027

2L/3L G12D CRC

~13k

Phase 3 initiation in 2027



**INCA33890**

TGF $\beta$ R2 $\times$ PD-1 bispecific

1L MSS CRC

~174k

Topline data 2029

Adj. MSS CRC

~27k

Initiated in 2H 2026

 = ~2.5k patients  
Icons are cumulative;  
lighter shade indicates  
additional indications



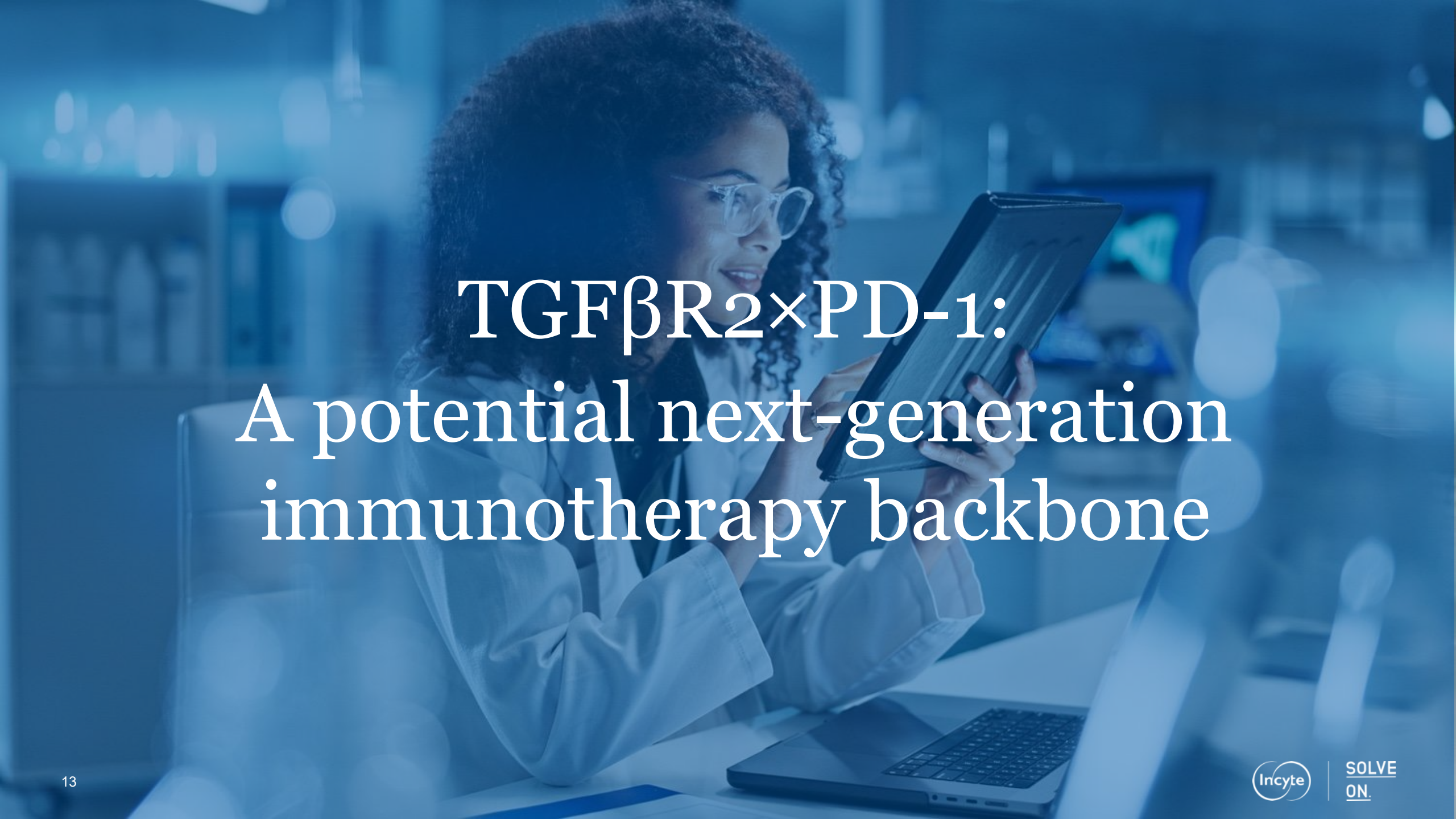
# INCA33890 & INCB161734 Development Spotlight

**Steven Stein, M.D.**

Chief Medical Officer and Head of Late-Stage Development

# Four rapid oral presentations at ESMO

| PRESENTATION                  | ASSET                                         | SETTING            | ABSTRACT TITLE                                                                                                                                                                           |
|-------------------------------|-----------------------------------------------|--------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>RAPID ORAL<br/>#1957RO</b> | <b>INCA33890</b><br>TGFβR2×PD-1<br>bispecific | <b>1L+ MSS CRC</b> | INCA33890, a TGFβR2xPD-1 bispecific antibody, with standard of care (SoC) anticancer therapies for microsatellite stable colorectal cancer (MSS CRC)                                     |
| <b>RAPID ORAL<br/>#3137RO</b> | <b>INCB161734</b><br>KRAS G12D<br>inhibitor   | <b>1L/2L PDAC</b>  | Safety and efficacy of INCB161734, a novel oral KRAS G12D inhibitor, in combination with chemotherapy in patients (pts) with advanced/metastatic pancreatic ductal adenocarcinoma (PDAC) |
| <b>RAPID ORAL<br/>#1007RO</b> | <b>INCB161734</b><br>KRAS G12D<br>inhibitor   | <b>2L+ CRC</b>     | Safety and efficacy of oral KRAS G12D inhibitor INCB161734 as monotherapy or in combination with cetuximab (cetux) in Patients (pts) with advanced/metastatic colorectal cancer (CRC)    |
| <b>RAPID ORAL<br/>#1241RO</b> | <b>INCB123667</b><br>CDK2 inhibitor           | <b>PROC</b>        | Preliminary efficacy of INCB123667 (CDK2 inhibition) with bevacizumab in recurrent epithelial ovarian cancer (rEOC)                                                                      |

A woman with curly hair, wearing glasses and a white lab coat, is holding a tablet and looking at it. She is in a laboratory or office setting with various pieces of equipment and a laptop visible in the background. The entire image has a blue tint.

# TGF $\beta$ R<sub>2</sub>×PD-1: A potential next-generation immunotherapy backbone

# Key takeaways: INCA33890 (TGF $\beta$ R2 $\times$ PD-1 bsAb)

01

## **Potential next-generation immunotherapy backbone**

Ongoing development in MSS CRC, with expansion opportunities in additional solid tumors

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02

## **Encouraging first-line MSS CRC activity supports ongoing Phase 3 development**

Combination with FOLFOX + bev shows response rates above historical benchmarks for SoC

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03

## **Responses in patients with liver metastases support mechanistic rationale**

Activity in difficult-to-treat population is consistent with the potential of dual TGF $\beta$ R2 $\times$ PD-1 inhibition

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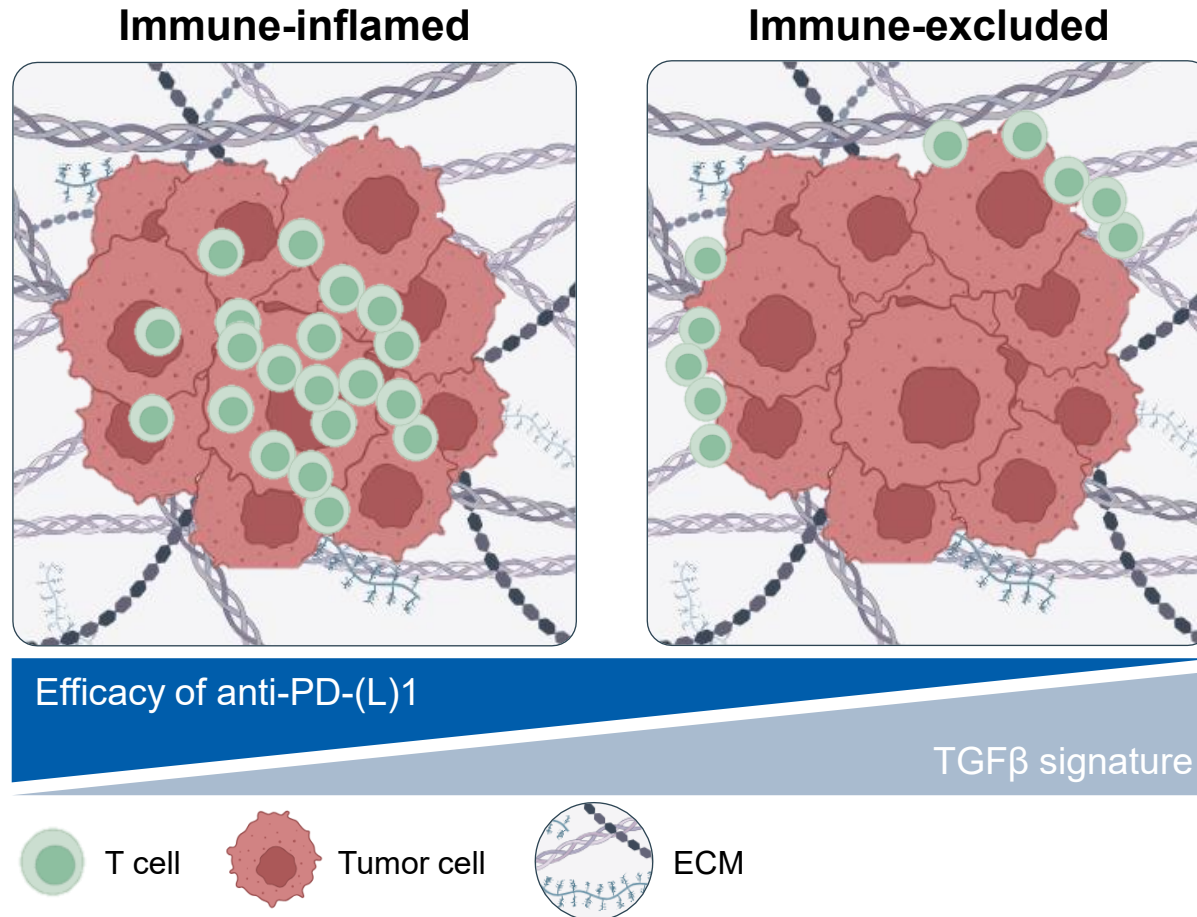
04

## **Expanding into earlier treatment settings with curative intent**

Phase 2 underway in patients with molecular residual disease post-resection and adjuvant chemo

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# High-TGF $\beta$ tumors are PD-(L)1-inhibitor-resistant

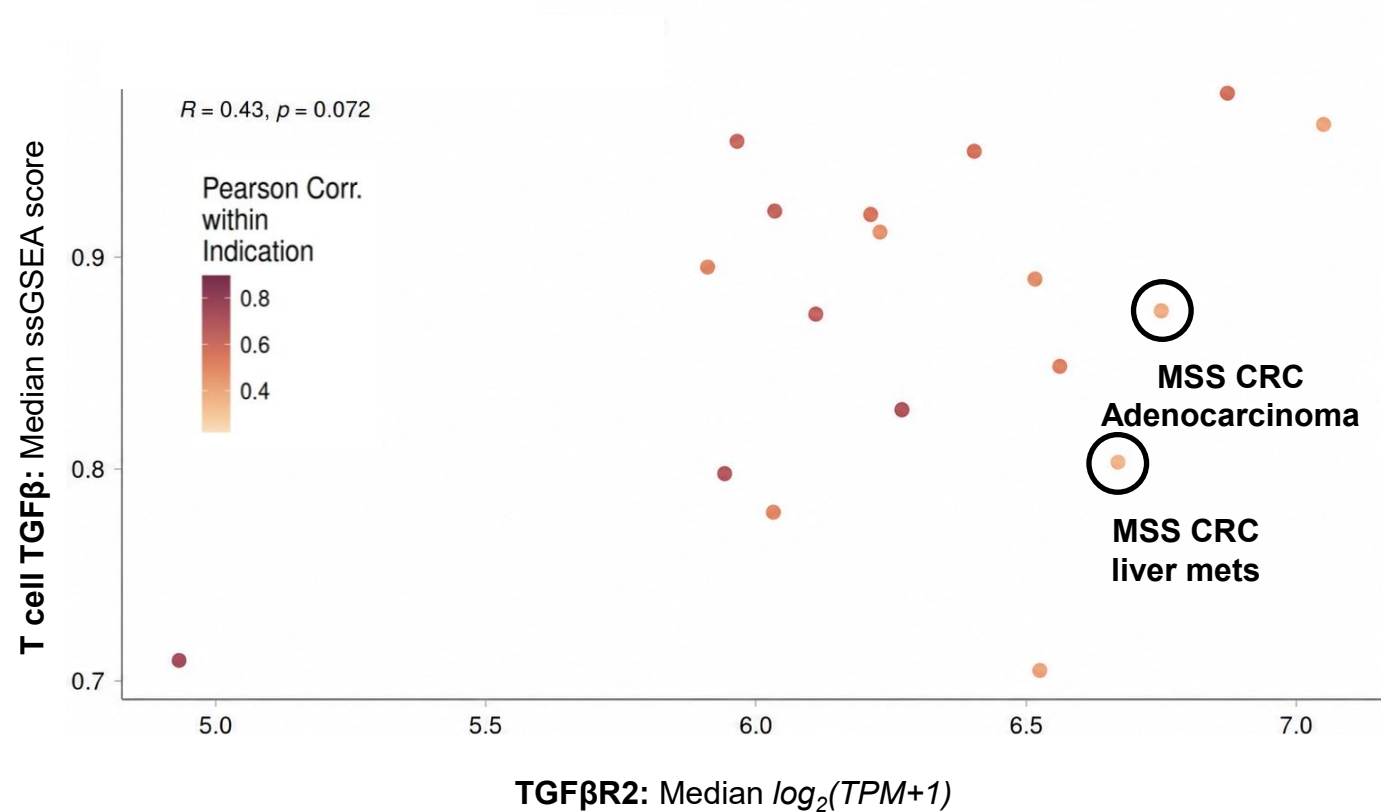


- TGF $\beta$  pathway is hyperactivated in immune-excluded tumors resistant to anti-PD-(L)1 inhibitors<sup>1</sup>
- Binding to TGF $\beta$ R2 leads to suppression of CD8<sup>+</sup> T cells, leading to immune exclusion<sup>2,3</sup>
- Higher TGF $\beta$ R2 expression was shown to be significantly associated with non-response to anti-PD-L1 treatment and reduced survival<sup>1,4</sup>

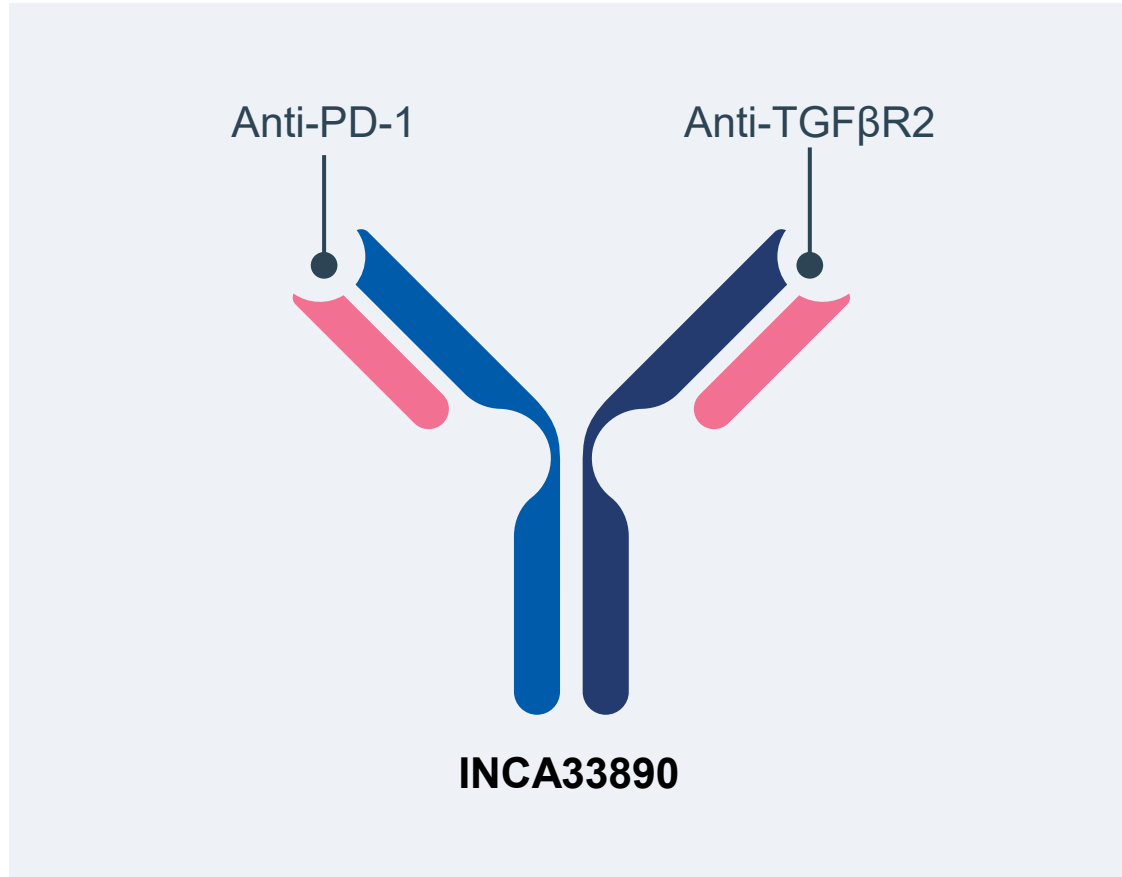
# MSS CRC is one of the highest scoring solid tumors for TGF $\beta$ biology

- MSS CRC liver metastases are enriched for TGF $\beta$  biology

T cell TGF $\beta$  gene expression vs. TGF $\beta$ R2 protein expression in solid tumors<sup>1</sup>



# '890 blocks TGFβR2 and PD-1 signaling



## High-affinity PD-1 arm<sup>1,2,3</sup>

Drives target specificity and efficient binding to PD-1+ cells

## Affinity-tuned TGFβR2 arm<sup>1,2,3</sup>

Minimizes binding to non-target cells and enables TGFβ inhibition only when bound to PD-1

## Spares normal tissues

For where TGFβ signaling is important for normal function, and avoids the known toxicity of broad TGFβ pathway blockade

# '890: A novel immunotherapy backbone in CRC

|         | ADJUVANT                                  | 1L                                                        | 2L+                                                                    |
|---------|-------------------------------------------|-----------------------------------------------------------|------------------------------------------------------------------------|
| CRC     | Mono<br><i>ctDNA+ post-adjuvant chemo</i> | + FOLFOX + bevacizumab<br><i>MSS · Phase 3 NEXERA-303</i> | <div>+ muzastotug<br/>(next-gen CTLA-4)</div> <div>+ bevacizumab</div> |
| Ovarian | —                                         | + CTx +/- bevacizumab                                     | + ADC                                                                  |
| HNSCC   | —                                         | + EGFR Ab                                                 | —                                                                      |
| NSCLC   | —                                         | + CTx                                                     | —                                                                      |



## *Elena Garralda, M.D., Ph.D.*

Co-director, VHIO Clinical Research Program, Group Leader, VHIO Early Clinical Drug Development Group, Director, Research Unit for Molecular Therapy of Cancer – Caixa Research

# MSS CRC remains large, underserved population

174k

1L MSS CRC patients across U.S., Europe and Japan<sup>1</sup>

~45%

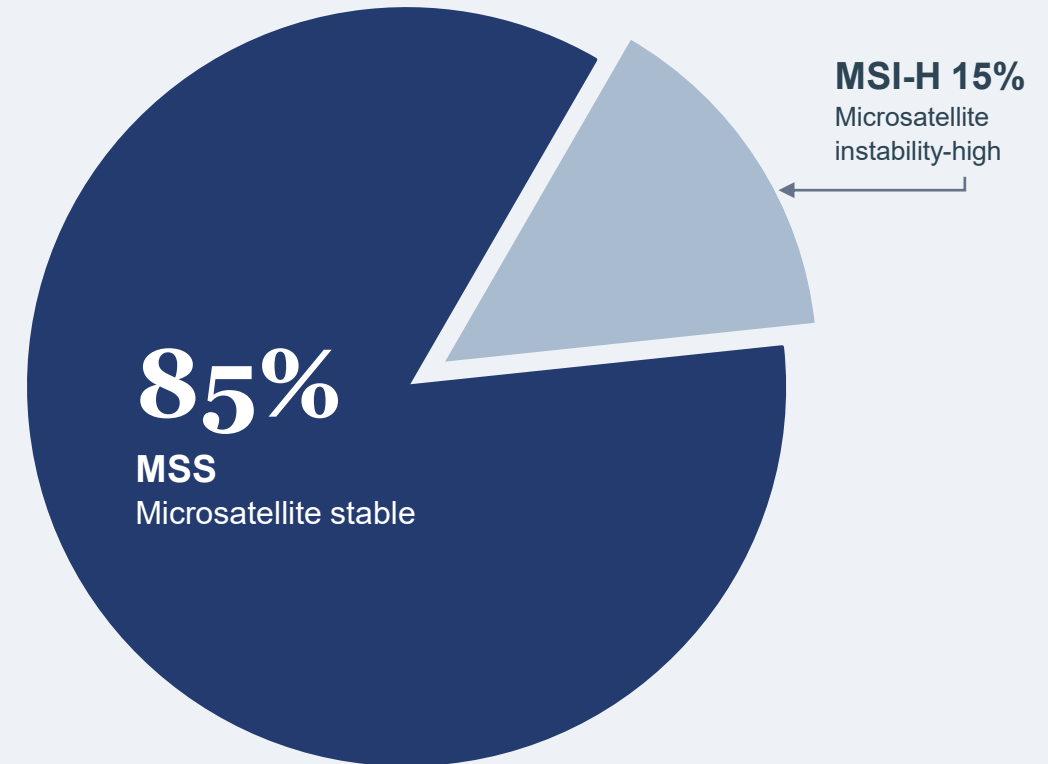
of CRC patients are diagnosed with Stage IV disease<sup>2</sup>

~66%

of CRC with stage IV disease have liver metastases which remain IO-resistant<sup>3</sup>

1L SoC (FOLFOX + bev) has 45-55% ORR, ~10 mo. mPFS and 25-30 mo. mOS in Phase 3 trials<sup>4,5</sup>

DNA mismatch repair profile in CRC<sup>1</sup>



<sup>1</sup>DRG 2025. Buchler T, Front. Oncol. 2022;12:888181. <sup>2</sup>CancerMPact® Treatment Architecture EU5 and US. <sup>3</sup>Väyrynen V, et al. British Journal of Surgery Open, 2020;4(40), 685-692. <sup>4</sup>Cassidy J, et al. British Journal of Cancer, 2011. 105;58-65. <sup>5</sup>Lenz H, et al. JTC. 2024;12e008409.

# INCA33890-101 study design

## INCA33890 monotherapy<sup>1,\*</sup>

**Dose escalation**  
(N=48)  
100-1500 mg q2w and 900 mg q4w IV  
in continuous 28-day cycles

**RDEs (q2w IV)**  
(300, 600, 900, 1200 mg)

**Dose expansion**  
(N=236)  
MSS CRC / PDAC / Gastric / GEJ  
OC / NSCLC / SCCHN

### Selected eligibility criteria

- Aged ≥18 years
- Diagnosis of advanced or metastatic (stage IV) MSS CRC
- ECOG PS 0 or 1

### Primary endpoints

- Safety and tolerability
- DLTs

### Selected secondary endpoints

- ORR, DCR, DOR
- PK

### Dose escalation<sup>†</sup> and expansion in MSS CRC (N=94)

**INCA33890**  
(900 mg q2w IV)  
**+ FOLFOX<sup>‡</sup> + bev<sup>§</sup>**

n=43

No prior  
systemic therapy

**INCA33890**  
(900 mg q2w IV)  
**+ FOLFIRI<sup>||</sup> + bev<sup>§</sup>**

n=6

Prior oxaliplatin  
but no irinotecan

**INCA33890**  
(900 mg q2w IV)  
**+ bev<sup>§</sup>**

n=39

Prior fluoropyrimidine,  
oxaliplatin, & irinotecan

**INCA33890**  
(900 mg q2w IV)  
**+ cetux<sup>¶¶</sup>**

n=6

Prior  
anti-EGFR inhibitor

<sup>1</sup>Garraza E, et al. ESMO 2025. Presentation 1522MO. Enrollment as of August 26, 2026. \*Part 1 of the study investigating INCA33890 monotherapy has been described previously.<sup>1</sup> <sup>†</sup>Dose escalation in part 2 used a statistical hybrid design based on ≥3 DLT-evaluable patients per dose level. <sup>‡</sup>Oxaliplatin: 85 mg/m<sup>2</sup> IV; leucovorin: 400 mg/m<sup>2</sup> IV (levoleucovorin 200 mg/m<sup>2</sup> could be substituted for leucovorin if locally approved); and 5-FU: 400 mg/m<sup>2</sup> IV bolus (optional) followed by 2400mg/m<sup>2</sup> IV infusion. <sup>§</sup>Dosed at 5 mg/kg q2w. <sup>||</sup>Irinotecan: 180 mg/m<sup>2</sup> IV; leucovorin: 400 mg/m<sup>2</sup> IV (levoleucovorin 200 mg/m<sup>2</sup> could be substituted for leucovorin if locally approved); 5-FU: 400 mg/m<sup>2</sup> IV bolus (optional) followed by 2400mg/m<sup>2</sup> IV infusion. <sup>¶¶</sup>Dosed at 500 mg/m<sup>2</sup> q2w.

# Baseline characteristics

| TOTAL (N=94)                                                 |             | 1L                                              | 2L                                              | 3L+                                    | PRIOR anti-EGFR                         |
|--------------------------------------------------------------|-------------|-------------------------------------------------|-------------------------------------------------|----------------------------------------|-----------------------------------------|
|                                                              |             | INCA33890 + FOLFOX + bev<br>(n=43) <sup>†</sup> | INCA33890 + FOLFIRI + bev<br>(n=6) <sup>†</sup> | INCA33890 + bev<br>(n=39) <sup>†</sup> | INCA33890 + cetux<br>(n=6) <sup>†</sup> |
| Age, median (range), years                                   | 56 (20, 89) |                                                 |                                                 |                                        |                                         |
| Male sex, n (%)                                              | 50 (53)     |                                                 |                                                 |                                        |                                         |
| Race, n (%) <sup>*</sup>                                     |             |                                                 |                                                 |                                        |                                         |
| White                                                        | 54 (57)     |                                                 |                                                 |                                        |                                         |
| Black or African American                                    | 6 (6)       |                                                 |                                                 |                                        |                                         |
| Asian                                                        | 23 (25)     |                                                 |                                                 |                                        |                                         |
| ECOG PS, 0/1, %                                              | 55 / 45     |                                                 |                                                 |                                        |                                         |
| INCA33890 + bev<br>(n=39) <sup>†</sup>                       |             |                                                 |                                                 |                                        |                                         |
| Prior therapies, n (%)                                       |             |                                                 |                                                 |                                        |                                         |
| 5-FU, oxaliplatin, and irinotecan                            | 37 (95)     |                                                 |                                                 |                                        |                                         |
| Anti-EGFR                                                    | 11 (28)     |                                                 |                                                 |                                        |                                         |
| Anti-VEGF                                                    | 34 (87)     |                                                 |                                                 |                                        |                                         |
| Trifluridine and tipiracil, regorafenib, and/or fruquintinib | 12 (31)     |                                                 |                                                 |                                        |                                         |
| Anti-PD-(L)1                                                 | 5 (13)      |                                                 |                                                 |                                        |                                         |
| Lines of prior therapy, median (range)                       |             | 0 (0, 1)                                        | 1 (1, 3)                                        | 2 (1, 5)                               | 3 (2, 4)                                |
| Liver metastases, n (%)                                      |             | 29 (67)                                         | 5 (83)                                          | 24 (62)                                | 4 (67)                                  |
| Peritoneal metastases, n (%)                                 |             | 14 (33)                                         | 2 (33)                                          | 13 (33)                                | 1 (17)                                  |
| PD-L1 TAP, n (%) <sup>‡</sup>                                |             |                                                 |                                                 |                                        |                                         |
| <1%                                                          |             | 6 (14)                                          | NA                                              | 8 (21)                                 | NA                                      |
| ≥1%                                                          |             | 26 (61)                                         | NA                                              | 18 (46)                                | NA                                      |
| Sidedness, n (%) <sup>§</sup>                                |             |                                                 |                                                 |                                        |                                         |
| Left                                                         |             | 28 (65)                                         | 4 (67)                                          | 21 (54)                                | 3 (50)                                  |
| Right                                                        |             | 13 (30)                                         | 2 (33)                                          | 15 (39)                                | 0                                       |
| RAS mutant, n (%) <sup>¶</sup>                               |             | 27 (63)                                         | 3 (50)                                          | 27 (69)                                | 0                                       |
| BRAF V600E mutant, n (%) <sup>  </sup>                       |             | 2 (5)                                           | 0                                               | 1 (3)                                  | 0                                       |
| Left-sided, RAS/BRAF WT, n (%)                               |             | 12 (28)                                         | NA                                              | NA                                     | NA                                      |

<sup>\*</sup>Missing values were other race (n=1) or not reported (n=10). <sup>†</sup>Patients enrolled in dose escalation: INCA33890 + FOLFOX + Bev, n=6; INCA33890 + FOLFIRI + Bev, n=6; INCA33890 + Bev, n=6; INCA33890 + Cetux, n=6. <sup>‡</sup>Patients not shown having missing data (INCA33890 + FOLFOX + Bev, n=11; INCA33890 + Bev, n=13); results not reported for all groups due to sparsity of data (INCA33890 + FOLFIRI + Bev, n=2; INCA33890 + Cetux, n=1). <sup>§</sup>Patients not shown have unknown status or missing data (INCA33890 + FOLFOX + Bev, n=2; INCA33890 + Bev, n=3; INCA33890 + Cetux, n=3). <sup>¶</sup>Patients not shown have wild type or unknown status (wild type: INCA33890 + FOLFOX + Bev, n=16; INCA33890 + FOLFIRI + Bev, n=2; INCA33890 + Bev, n=11; INCA33890 + Cetux, n=6; unknown: INCA33890 + FOLFIRI + Bev, n=1; INCA33890 + Bev, n=1). <sup>||</sup>Patients not shown have wild type or unknown status (wild type: INCA33890 + FOLFOX + Bev, n=38; INCA33890 + FOLFIRI + Bev, n=4; INCA33890 + Bev, n=32; INCA33890 + Cetux, n=4; unknown: INCA33890 + FOLFOX + Bev, n=3; INCA33890 + FOLFIRI + Bev, n=2; INCA33890 + Bev, n=6; INCA33890 + Cetux, n=2).

# Safety: Summary

- No DLTs were observed in any cohort and relative dose intensity of SoC was maintained in combination with INCA33890
- INCA33890 discontinuations in the FOLFOX + bev cohort were due to nephritis, myocarditis, rash, and drug-induced liver injury
  - These led to EOT and SoC discontinuation per protocol

|                       | 1L                                    | 2L                                    | 3L+                          | PRIOR anti-EGFR               |
|-----------------------|---------------------------------------|---------------------------------------|------------------------------|-------------------------------|
|                       | INCA33890<br>+ FOLFOX + bev<br>(n=43) | INCA33890<br>+ FOLFIRI + bev<br>(n=6) | INCA33890<br>+ bev<br>(n=39) | INCA33890<br>+ cetux<br>(n=6) |
| TEAE, n (%)           |                                       |                                       |                              |                               |
| Any grade             | 43 (100)                              | 6 (100)                               | 37 (95)                      | 6 (100)                       |
| Grade ≥3              | 31 (72)                               | 5 (83)                                | 13 (33)                      | 4 (67)                        |
| Immune-related        | 23 (54)                               | 2 (33)                                | 16 (41)                      | 5 (83)                        |
| Grade ≥3              | 6 (14)                                | 1 (17)                                | 4 (10)                       | 1 (17)                        |
| Serious               | 19 (44)                               | 3 (50)                                | 9 (23)                       | 1 (17)                        |
| Fatal                 | 0                                     | 0                                     | 0                            | 0                             |
| Leading to INCA33890: |                                       |                                       |                              |                               |
| Dose delay            | 26 (61)                               | 5 (83)                                | 14 (36)                      | 3 (50)                        |
| Discontinuation       | 4 (9)*                                | 0                                     | 0                            | 0                             |
| Leading to SoC:       |                                       |                                       |                              |                               |
| Dose delay            | 29 (67)                               | 5 (83)                                | 16 (41)                      | 3 (50)                        |
| Dose reduction        | 29 (67) <sup>†</sup>                  | 4 (67) <sup>†</sup>                   | 0                            | 0                             |
| Discontinuation       | 3 (7) <sup>‡</sup>                    | 0                                     | 0                            | 0                             |

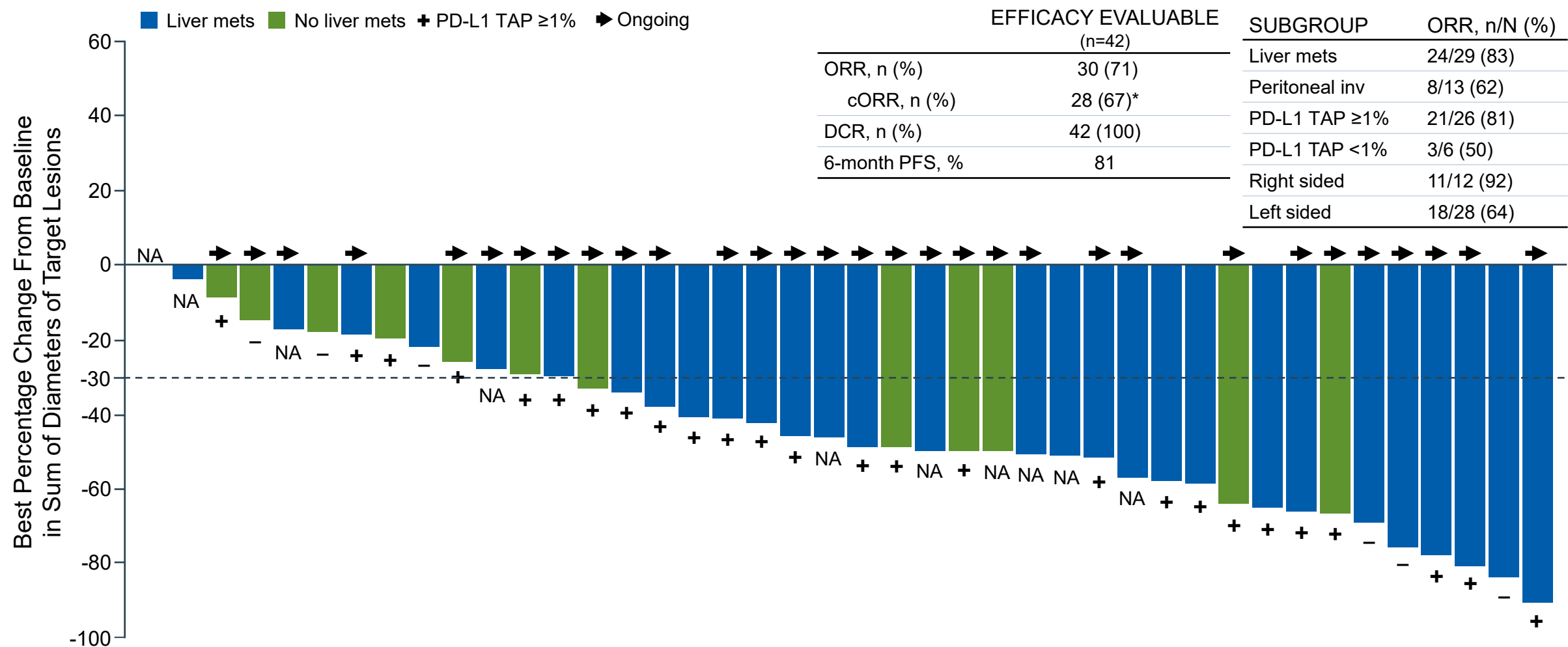
\*All grade 3. Drug-induced liver injury was related to trimethoprim-sulfamethoxazole usage and was not deemed to be related to INCA33890. <sup>†</sup>Dose reduction in INCA33890 + FOLFOX + Bev: 5-FU, n=21 (48.8%); oxaliplatin, n=21 (48.8%); with INCA33890 + FOLFIRI + Bev: 5-FU n=4 (66.7%), folinic acid n=3 (50.0%); irinotecan, n=3 (50.0%). <sup>‡</sup>Discontinuation of individual treatment components: 5-FU, n=3 (7.0%); Bev, n=4 (9.3%); folinic acid, n=5 (11.6%); oxaliplatin, n=23 (53.5%).

# Safety: Most common TEAEs

| TEAEs, n (%) <sup>*</sup> | 1L                                    |          | 2L                                    |          | 3L+                          |          | PRIOR anti-EGFR               |          |
|---------------------------|---------------------------------------|----------|---------------------------------------|----------|------------------------------|----------|-------------------------------|----------|
|                           | INCA33890<br>+ FOLFOX + bev<br>(n=43) |          | INCA33890<br>+ FOLFIRI + bev<br>(n=6) |          | INCA33890<br>+ bev<br>(n=39) |          | INCA33890<br>+ cetux<br>(n=6) |          |
|                           | ANY GRADE                             | GRADE ≥3 | ANY GRADE                             | GRADE ≥3 | ANY GRADE                    | GRADE ≥3 | ANY GRADE                     | GRADE ≥3 |
| Neuropathy <sup>†</sup>   | 33 (77)                               | 1 (2)    | 2 (33)                                | 0        | 0                            | 0        | 0                             | 0        |
| Neutropenia <sup>‡</sup>  | 25 (58)                               | 15 (35)  | 5 (83)                                | 4 (67)   | 1 (3)                        | 0        | 1 (17)                        | 0        |
| Stomatitis                | 20 (47)                               | 3 (7)    | 3 (50)                                | 1 (17)   | 11 (28)                      | 1 (3)    | 3 (50)                        | 0        |
| Nausea                    | 19 (44)                               | 1 (2)    | 1 (17)                                | 1 (17)   | 4 (10)                       | 0        | 3 (50)                        | 0        |
| Diarrhea                  | 18 (42)                               | 1 (2)    | 3 (50)                                | 1 (17)   | 12 (31)                      | 2 (5)    | 1 (17)                        | 0        |
| Fatigue                   | 18 (42)                               | 0        | 4 (67)                                | 0        | 10 (26)                      | 1 (3)    | 4 (67)                        | 1 (17)   |
| Anaemia                   | 15 (35)                               | 1 (2)    | 3 (50)                                | 1 (17)   | 7 (18)                       | 2 (5)    | 0                             | 0        |
| Infusion-related reaction | 15 (35)                               | 1 (2)    | 2 (33)                                | 0        | 2 (5)                        | 0        | 0                             | 0        |
| Related to INCA33890      | 3 (7)                                 | 0        | 2 (33)                                | 0        | 2 (5)                        | 0        | 0                             | 0        |
| Related to SoC            | 12 (28) <sup>§</sup>                  | 1 (2)    | 0                                     | 0        | 1 (3) <sup>¶</sup>           | 0        | 0                             | 0        |
| Vomiting                  | 14 (33)                               | 0        | 1 (17)                                | 0        | 4 (10)                       | 0        | 4 (67)                        | 0        |
| Leukopenia                | 13 (30)                               | 2 (5)    | 4 (67)                                | 3 (50)   | 0                            | 0        | 0                             | 0        |
| Decreased appetite        | 12 (28)                               | 1 (2)    | 3 (50)                                | 1 (17)   | 6 (15)                       | 0        | 0                             | 0        |
| Hypertension              | 12 (28)                               | 4 (9)    | 0                                     | 0        | 4 (10)                       | 1 (3)    | 0                             | 0        |

<sup>\*</sup>TEAEs listed are those occurring in ≥25% of the INCA33890 + FOLFOX + Bev group and ordered by frequency in the INCA33890 + FOLFOX + Bev group. <sup>†</sup>Neuropathy peripheral includes neuropathy peripheral, peripheral sensory neuropathy, and paresthesia. <sup>‡</sup>Neutropenia includes neutropenia and neutrophil count decreased. <sup>§</sup>11 related to oxaliplatin and 1 related to Bev. <sup>¶</sup>Related to Bev.

# Efficacy: INCA33890 + FOLFOX + bev in 1L MSS CRC



25 Median follow-up of 5.6 months. \*1 pending follow-up scan; 1 with target lesion removal (primary tumor resection due to intestinal obstruction, follow-up nonevaluable by RECIST).

# Conclusions

- 01 Tolerable combinations with no DLTs**  
INCA33890 combinations with SoC in patients with MSS CRC were tolerable with no DLTs

---

  - 02 Notable preliminary efficacy in 1L MSS CRC with INCA33890 + FOLFOX + bev**  
With INCA33890 + FOLFOX + bev, ORR was 71%, DCR was 100%, and 6-month PFS was 81%

---

  - 03 Responses in patients with liver or peritoneal metastases, and PD-L1 expression**  
ORR was 83% and 62% in patients with liver metastases and peritoneal metastases, respectively  
ORR was 81% in patients with PD-L1 TAP  $\geq 1\%$

---

  - 04 Data supports ongoing Phase 3 NEXERA-303 study in 1L MSS CRC**  
Study is evaluating the safety and efficacy of 1L FOLFOX + bev  $\pm$  INCA33890 in patients with MSS CRC
-

# '890: Advancing and expanding efforts in MSS CRC

## MSS CRC

Establishing '890 in high incidence tumor type not sensitive to CPI

- **Phase 3 NEXERA-303 study ongoing in 1L MSS CRC**

## ctDNA+ CRC

Exploring potential for '890 to prevent recurrence in patients with minimal residual disease post resection

- **Phase 2 NEXERA-204 study ongoing in adjuvant CRC (ctDNA+)**

## Novel combinations

Evaluate novel combinations to explore pan-tumor potential of '890

- **Phase 1 program evaluating novel combinations ongoing**

# Phase 3 NEXERA-303 topline data expected in 2029

## Select eligibility criteria

- Adults with histologically or cytologically confirmed metastatic CRC not amenable to curative resection
- No prior systemic treatment for unresectable or metastatic CRC
  - Participants who received (neo-) adjuvant therapy may enroll if there was no recurrence within 12 months of the end of treatment
- No MSI-H/dMMR status
- No BRAF V600E mutation
- No ICI treatment within the last 3 years
- ECOG PS of 0 to 1

**N: ~700**

Randomized 1:1

**INCA33890** (900 mg Q2W IV)  
+ **FOLFOX** (Q2W)  
+ **bevacizumab** (5 mg/kg Q2W)

**Placebo** (Q2W)  
+ **FOLFOX** (Q2W)  
+ **bevacizumab** (5 mg/kg Q2W)

## Endpoints/objectives:

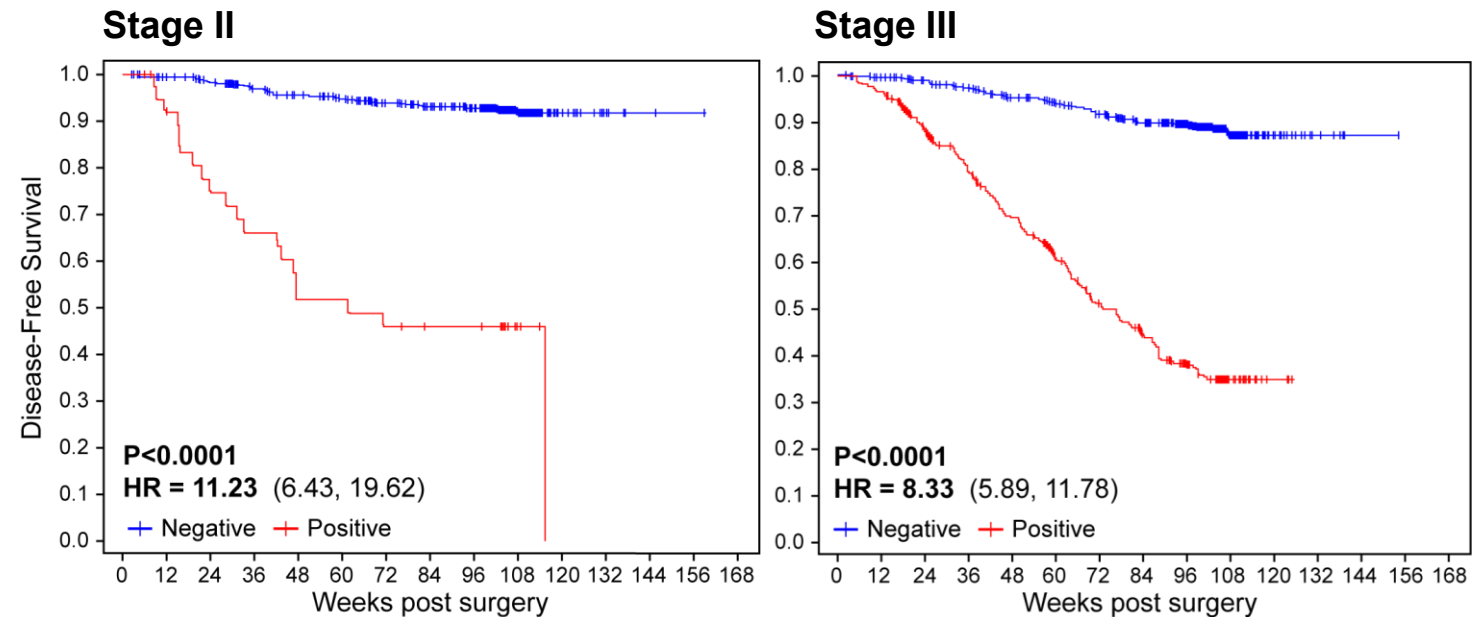
- Primary: PFS (PD-L1+ first)
- Key secondary: OS
- Other secondary: ORR, DOR, safety and tolerability, HRQoL

# Significant unmet need remains for CRC patients with minimal residual disease post surgery

## Biological Rationale

- 15% of Stage II and 30% of Stage III MSS CRC patients experience recurrence<sup>1</sup>
- Patients who remain ctDNA+ post adjuvant chemotherapy are significantly more likely to experience recurrence<sup>1</sup>
- Median DFS of ~12 mo. in ctDNA+ after surgery despite adjuvant chemotherapy<sup>1,2</sup>
- Increasing evidence for ctDNA clearance as biological surrogate for DFS in MSS-CRC<sup>1,2</sup>

## Stage II/III ctDNA+ CRC patients have worse outcomes<sup>2</sup>

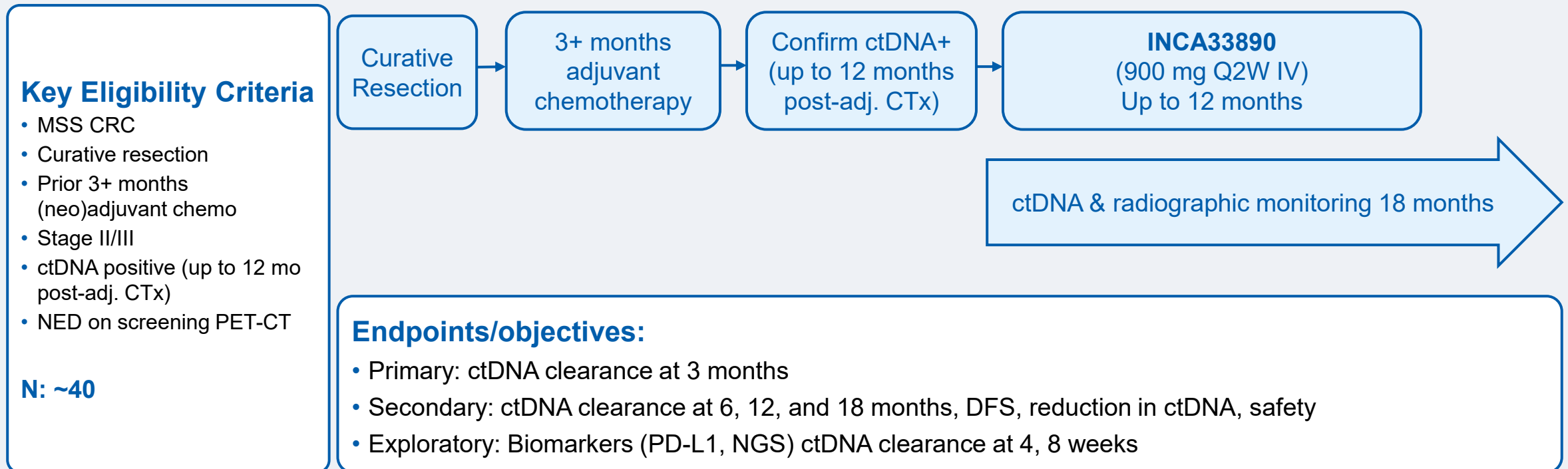


| ctDNA Status | Events | mDFS post surgery, mos | 2-yr DFS post surgery, % |
|--------------|--------|------------------------|--------------------------|
| Negative     | 33     | NE                     | 91.8                     |
| Positive     | 20     | 12.7                   | 45.9                     |

| ctDNA Status | Events | mDFS post surgery, mos | 2-yr DFS post surgery, % |
|--------------|--------|------------------------|--------------------------|
| Negative     | 47     | NE                     | 87.4                     |
| Positive     | 105    | 16.2                   | 35.5                     |

BESPOKE data (n=1,166) includes patients in both observation (n=472) and ACT (n=694) subgroups.

# Moving earlier: Adjuvant POC study in CRC initiated



# Advancing '890 as potential immunotherapy backbone

- 01** Establishing '890 in 1L MSS CRC, with topline data from Phase 3 expected in 2029

---

- 02** Multiple efficacy measures point to clinical activity in MSS CRC  
ORR: 71%; DCR: 100%; 6-month landmark PFS: 81%

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- 03** Activity in difficult-to-treat subgroups strengthens confidence in potential of '890  
ORR (liver metastases): 83%; ORR (peritoneal metastases): 62%; ORR (PD-L1 TAP $\geq$ 1%): 81%

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- 04** Moving earlier into the disease continuum  
Initiated Phase 2 PoC study in adjuvant ctDNA+ Stage II/III MSS CRC

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- 05** Exploring broader potential across solid tumors  
Advancing novel combinations in ovarian, HNSCC, and NSCLC



# KRAS G12D: Building a franchise for 12D mutated tumors

# Key takeaways: INCB161734 (KRAS G12D inhibitor)

01

## **Potential to become a backbone therapy for KRAS G12D-mutated GI cancers**

Ongoing Phase 3 in PDAC, with planned trials in 2L/3L CRC in 1H 2027 and adjuvant PDAC in 2027

---

02

## **First-line PDAC activity in Phase 1 supports ongoing Phase 3 development**

'734 + mFOLFIRINOX or GEMNabP shows response rates above historical benchmarks for SoC

---

03

## **Promising CRC activity supports expansion across lines of therapy**

'734 + cetuximab demonstrates response rates above historical benchmarks for 2L/3L SoC

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04

## **Expanding the potential of '734 through novel combination strategies**

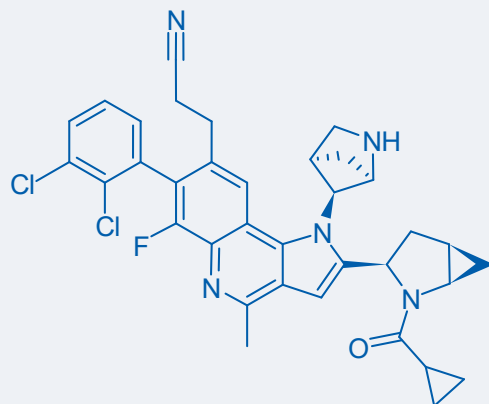
Combination studies with navlimetostat, SNV1521, and petosemtamab planned into 2027

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# '734: Highly selective KRAS G12D ON/OFF inhibitor

**Distinct scaffold that binds KRAS<sup>G12D</sup> at the switch II pocket with picomolar affinity<sup>1</sup>**

- KRAS<sup>G12D</sup> GDP (ON) binding affinity = 0.38 nM
- KRAS<sup>G12D</sup> GTP (OFF) binding affinity = 0.32 nM



**Potent ON/OFF oral KRAS inhibitor with >80-fold selectivity over wild-type KRAS<sup>1</sup>**

- Sustained inhibition of KRAS in both ON and OFF states may translate to more durable efficacy compared to only ON or only OFF inhibitors
- **Only KRAS<sup>G12D</sup> ON/OFF in Phase 3 development**

# '734: Expanding efforts across 12D-mutated tumors

|                                       | ADJUVANT                          | 1L                                                                                                         | 2L+                |                                                        |
|---------------------------------------|-----------------------------------|------------------------------------------------------------------------------------------------------------|--------------------|--------------------------------------------------------|
| PDAC                                  | CTx +/-<br><i>Phase 3 in 2027</i> | CTx (mFFX / GnP) +/-<br><i>Phase 3 DAWN-303 ongoing</i>                                                    | + SNV1521 (PARP1i) | + navlimetostat<br>(PRMT5i)                            |
| CRC                                   | —                                 | <div>+ CTx + cetuximab<br/>(FOLFOX / FOLFIRI)</div> <div>+ CTx + petosemtamab<br/>(LGR5 x EGFR bsAb)</div> | + SNV1521 (PARP1i) | + cetuximab<br>2L/3L Phase 3<br>DAWN-302 in<br>1H 2027 |
| NSCLC and other<br>12D-mutated tumors | —                                 | —                                                                                                          | Monotherapy        |                                                        |



## *Manuel Hidalgo, M.D., Ph.D., FAACR*

Professor of Medicine, Director, Gastrointestinal Cancer Center, Perlmutter Cancer Center, NYU Grossman School of Medicine

# Opportunity for G12D inhibitors to improve outcomes in G12D PDAC patients

~47k

1L G12D PDAC cases<sup>1</sup>

40-50%

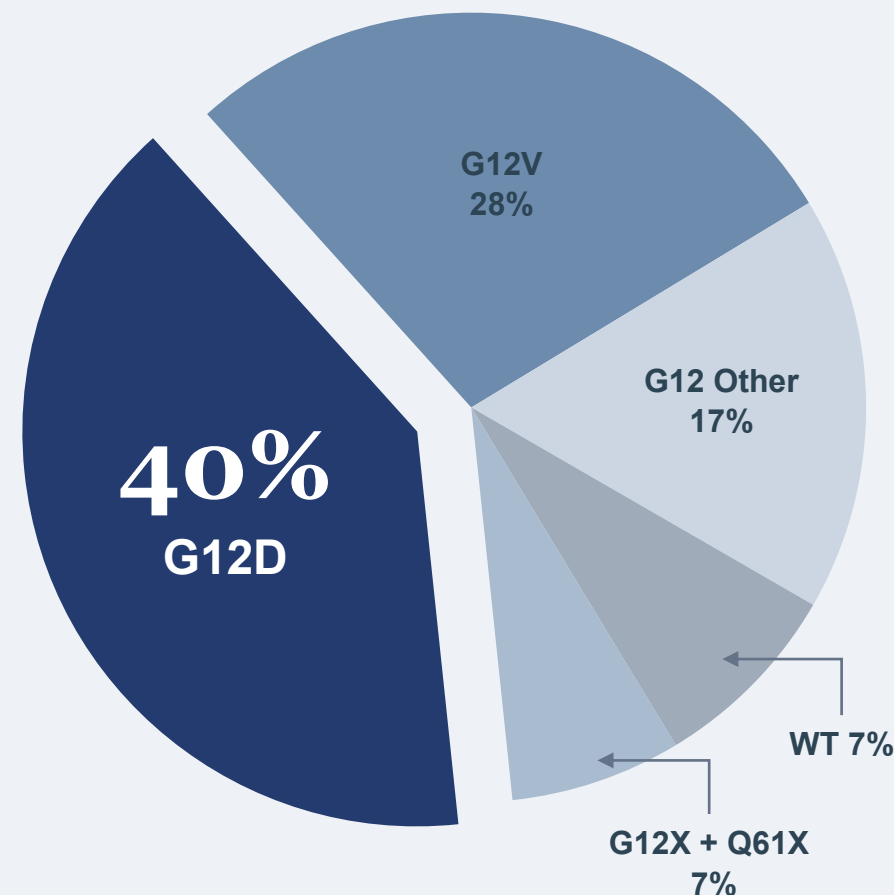
of patients are diagnosed in the metastatic setting<sup>2</sup>

3%

Stage IV 5-year survival<sup>6</sup>

1L SoC (mFFX or GnP) have ORR of 20-30%, mPFS of ~6 mo., mOS of ~11 months in Phase 3 trials<sup>4,5</sup>

KRAS mutations profile in PDAC<sup>3,7</sup>



# Phase 1 evaluating '734 + SoC chemotherapy in PDAC

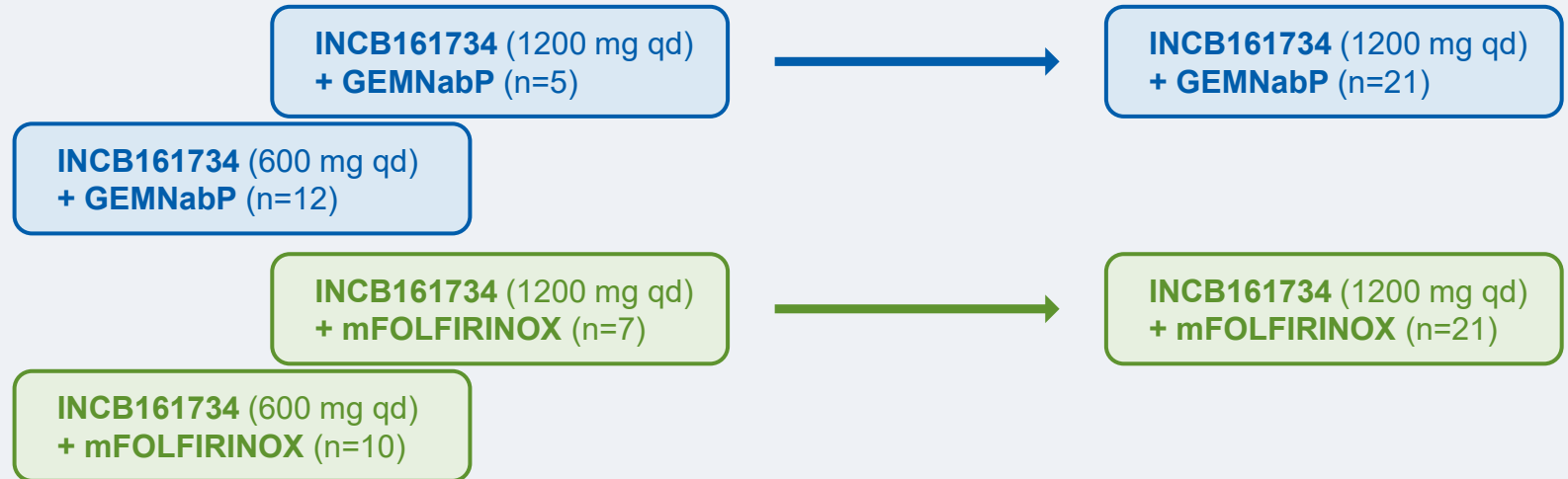
## Key eligibility criteria

- Locally advanced or metastatic PDAC with KRAS G12D mutation\*
- ECOG PS 0 or 1
- No prior treatment with a KRAS G12D selective inhibitor
- Dose escalation: ≤1 prior systemic regimen in the metastatic setting†
- Dose expansion: no prior regimen in the metastatic setting†

## Key endpoints

- Safety and tolerability
- Efficacy (ORR, DCR, DOR, and PFS)

## Dose Escalation‡



## Chemotherapy Regimens

■ **GEMNabP:** D1, D8, D15 of 28D cycle. Gemcitabine 1000 mg/m<sup>2</sup>, nab-paclitaxel 125 mg/m<sup>2</sup>

■ **mFOLFIRINOX:** D1, D15 of 28D cycle. Oxaliplatin 85 mg/m<sup>2</sup>, leucovorin 400 mg/m<sup>2</sup>, irinotecan 150-180 mg/m<sup>2</sup>, fluorouracil 2400 mg/m<sup>2</sup>

Data cut-off date: July 6, 2026. \*Determined by local testing. †Neoadjuvant or adjuvant therapy may be counted as 1 line of therapy if recurrence/development of metastatic disease occurred within 6 months of the last dose of therapy; patients who received no standard systemic therapy for PDAC may have received ≤1 cycle of GEMNabP or mFOLFIRINOX before enrolling. ‡Treated until start of new anticancer therapy, disease progression, unacceptable toxicity, death, withdrawal of consent, discontinuation or the end of the study.

# Patient disposition and baseline characteristics

- As of July 6, 2026, 54 patients with PDAC received INCB161734 1200 mg qd in combination with chemotherapy
- 26 patients received INCB161734 in combination with GEMNabP
  - Median (range) duration of INCB161734 treatment was 7.6 (0.5, 9.1) months
  - Treatment ongoing in 16 (62%)
  - Primary reason for discontinuation was progressive disease (n=8; 31%)\*
- 28 patients received INCB161734 in combination with mFOLFIRINOX
  - Median (range) duration of INCB161734 treatment was 7.0 (0.6, 11.7) months
  - Treatment ongoing in 23 (82%)
  - Primary reason for discontinuation was progressive disease (n=4; 14%)†

|                                                                  | INCB161734 (1200 mg qd) |                         |
|------------------------------------------------------------------|-------------------------|-------------------------|
|                                                                  | + GEMNabP<br>(n=26)     | + mFOLFIRINOX<br>(n=28) |
| Age, median (range), years                                       | 62 (35, 77)             | 63 (37, 77)             |
| ≥65 years, n (%)                                                 | 11 (42)                 | 13 (46)                 |
| ECOG PS, n (%)                                                   |                         |                         |
| 0                                                                | 13 (50)                 | 12 (43)                 |
| 1                                                                | 13 (50)                 | 16 (57)                 |
| Metastatic disease at diagnosis, n (%)                           | 12 (46)                 | 25 (89)                 |
| Liver metastases, n (%)                                          | 22 (85)                 | 24 (86)                 |
| Prior neoadjuvant/adjuvant therapy, n (%)                        | 10 (38)                 | 3 (11)                  |
| Total prior systemic therapy, n (%)                              |                         |                         |
| 0                                                                | 14 (54)                 | 24 (86)                 |
| 1                                                                | 12 (46)                 | 3 (11)                  |
| 2                                                                | 0                       | 1 (4)                   |
| Prior lines of systemic therapy in the metastatic setting, n (%) |                         |                         |
| 0                                                                | 24 (92)                 | 26 (93)                 |
| 1                                                                | 2 (8)                   | 2 (7)                   |

# Safety: '734 in combination with GEMNabP

|                                                  | INCB161734 (1200 mg qd)<br>+ GEMNabP<br>(n=26) | INCB161734 (1200 mg qd)<br>+ GEMNabP<br>(n=26) |           |                         |
|--------------------------------------------------|------------------------------------------------|------------------------------------------------|-----------|-------------------------|
|                                                  |                                                | TRAE, n (%)§                                   | ANY GRADE | GRADE 1/2      GRADE ≥3 |
| Any TRAE, n (%)*                                 | 26 (100)                                       | Diarrhoea                                      | 17 (65)   | 16 (62)      1 (4)      |
| TRAE leading to INCB161734                       |                                                | Nausea                                         | 17 (65)   | 16 (62)      1 (4)      |
| Interruption                                     | 19 (73)                                        | Decreased neutrophil count¶                    | 17 (65)   | 2 (8)      15 (58)      |
| Reduction                                        | 6 (23)                                         | Anaemia                                        | 15 (58)   | 5 (19)      10 (38)     |
| Discontinuation                                  | 1 (4)                                          | Vomiting                                       | 12 (46)   | 9 (35)      3 (12)      |
| TRAE leading to chemotherapy<br>(any component)† |                                                | Fatigue                                        | 12 (46)   | 7 (27)      5 (19)      |
| Interruption                                     | 22 (85)                                        | Pyrexia                                        | 10 (38)   | 9 (35)      1 (4)       |
| Reduction                                        | 18 (69)                                        | Decreased platelet count                       | 9 (35)    | 4 (15)      5 (19)      |
| Discontinuation                                  | 8 (31)                                         | Alopecia                                       | 7 (27)    | 7 (27)      0           |
| RDI, median %‡                                   |                                                | Decreased appetite                             | 7 (27)    | 7 (27)      0           |
| INCB161734                                       | 85                                             | ALT increased                                  | 6 (23)    | 6 (23)      0           |
| GEMNabP (cycles 1-4)                             | 69                                             | Dysgeusia**                                    | 6 (23)    | 6 (23)      NA          |
| GEMNabP†                                         | 49                                             | Oedema peripheral                              | 6 (23)    | 6 (23)      0           |
|                                                  |                                                | Peripheral sensory neuropathy                  | 6 (23)    | 6 (23)      0           |

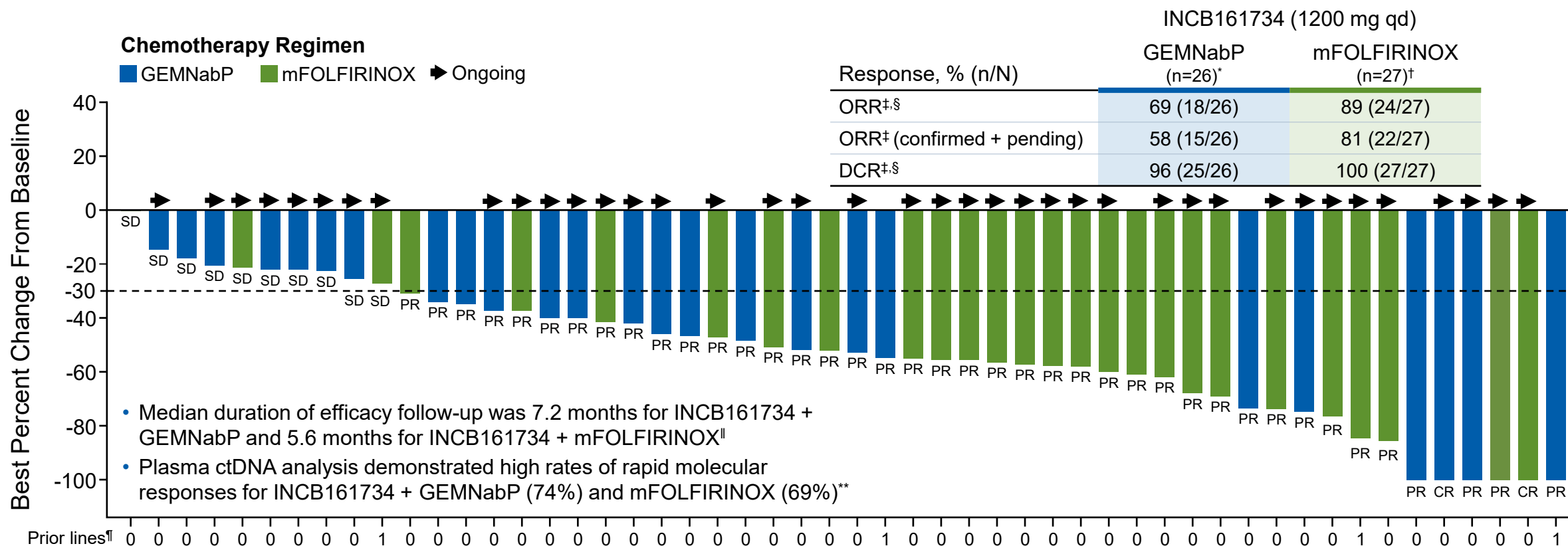
\*Assessed in patients who received ≥1 dose of study drug. †Median duration of treatment was 7.6 months. ‡Chemotherapy dose intensity was derived as the minimum RDI among all chemotherapy components. §Includes any-grade TRAEs that occurred in ≥20% of patients. ¶Includes neutropenia and neutrophil count decreased. ||Includes thrombocytopenia and platelet count decreased. \*\*The maximum possible severity per CTCAE for dysgeusia is grade 2.

# Safety: '734 in combination with mFOLFIRINOX

| INCB161734 (1200 mg qd)<br>+ mFOLFIRINOX<br>(n=28) |          | INCB161734 (1200 mg qd)<br>+ mFOLFIRINOX<br>(n=28)                                                                                                                                                                             |           |           |          |
|----------------------------------------------------|----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|-----------|----------|
|                                                    |          | TRAE, n (%)§                                                                                                                                                                                                                   | ANY GRADE | GRADE 1/2 | GRADE ≥3 |
| Any TRAE, n (%)*                                   | 28 (100) | Diarrhoea                                                                                                                                                                                                                      | 19 (68)   | 16 (57)   | 3 (11)   |
| TRAE leading to INCB161734                         |          | Nausea                                                                                                                                                                                                                         | 18 (64)   | 17 (61)   | 1 (4)    |
| Interruption                                       | 11 (39)  | Vomiting                                                                                                                                                                                                                       | 16 (57)   | 14 (50)   | 2 (7)    |
| Reduction                                          | 6 (21)   | Decreased neutrophil count¶                                                                                                                                                                                                    | 16 (57)   | 6 (21)    | 10 (36)  |
| Discontinuation                                    | 0        | Fatigue                                                                                                                                                                                                                        | 15 (54)   | 12 (43)   | 3 (11)   |
| TRAE leading to chemotherapy<br>(any component)†   |          | Anaemia                                                                                                                                                                                                                        | 11 (39)   | 8 (29)    | 3 (11)   |
| Interruption                                       | 22 (79)  | Decreased platelet count¶                                                                                                                                                                                                      | 9 (32)    | 4 (14)    | 5 (18)   |
| Reduction                                          | 16 (57)  | Peripheral sensory neuropathy                                                                                                                                                                                                  | 9 (32)    | 9 (32)    | 0        |
| Discontinuation                                    | 9 (32)   | Decreased appetite                                                                                                                                                                                                             | 7 (25)    | 7 (25)    | 0        |
| RDI, median %‡                                     |          | Dysgeusia**                                                                                                                                                                                                                    | 7 (25)    | 7 (25)    | NA       |
| INCB161734                                         | 77       | <ul style="list-style-type: none"> <li>• The safety profile of INCB161734 + GEMNabP or mFOLFIRINOX was broadly consistent with the established profiles of the SoC regimens</li> <li>• No fatal TRAEs were recorded</li> </ul> |           |           |          |
| mFOLFIRINOX (cycles 1-4)                           | 67       |                                                                                                                                                                                                                                |           |           |          |
| mFOLFIRINOX†                                       | 53       |                                                                                                                                                                                                                                |           |           |          |

\*Assessed in patients who received ≥1 dose of study drug. †Median duration of treatment was 7.0 months. ‡Chemotherapy dose intensity was derived as the minimum RDI among all chemotherapy components. §Includes any-grade TRAEs that occurred in ≥20% of patients. ¶Includes neutropenia and neutrophil count decreased. †Includes thrombocytopenia and platelet count decreased. \*\*The maximum possible severity per CTCAE for dysgeusia is grade 2.

# Antitumour activity of '734 + SoC chemotherapy in patients with metastatic PDAC

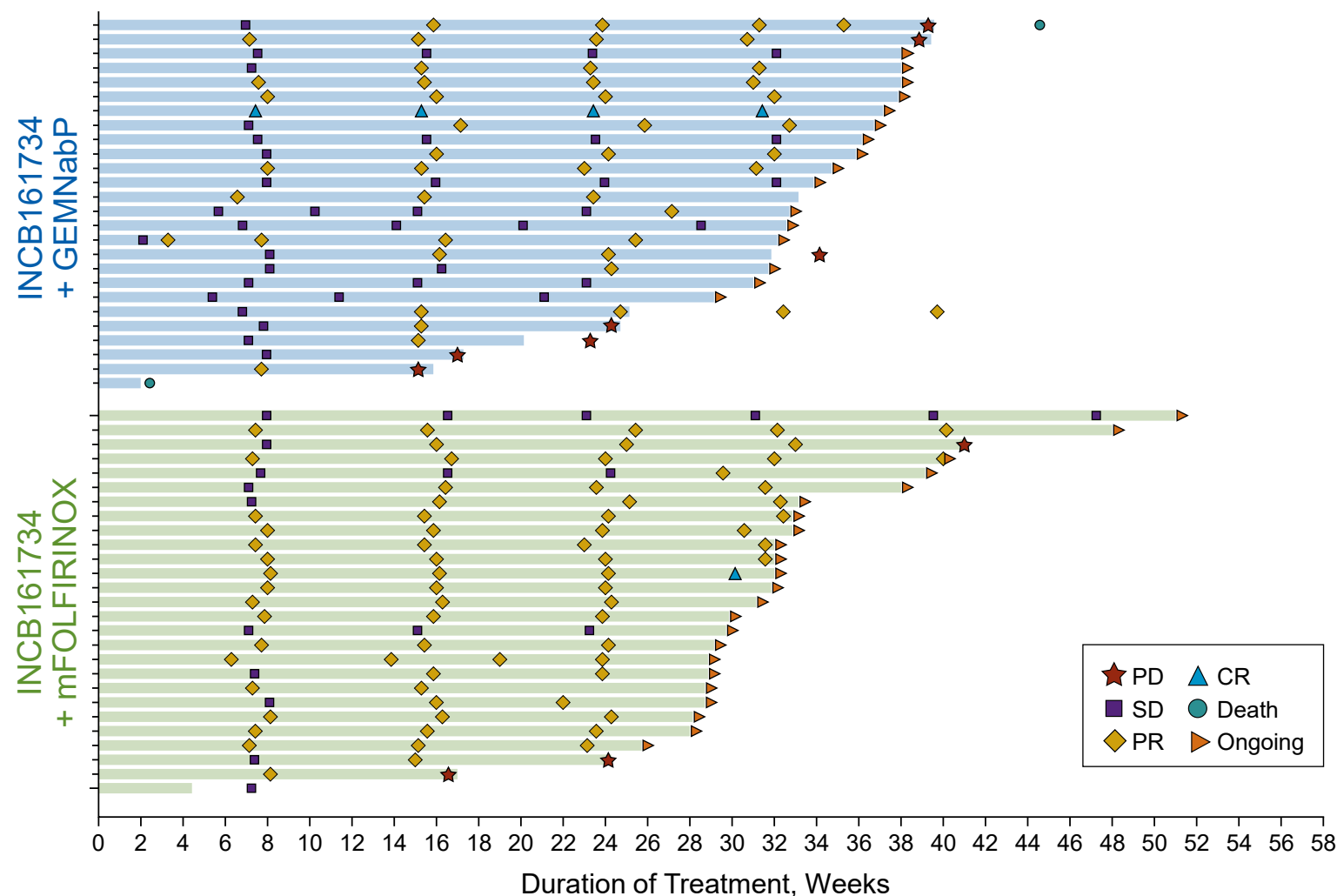


\*1 patient receiving INCB161734 + GEMNabP was included in the efficacy evaluable population but was not included in the waterfall plot due to death before the first scan. †1 patient was removed from the efficacy evaluable population due to an early adverse event. ‡Assessed in patients with a baseline scan and at least 1 of the following: ≥1 postbaseline scan or discontinued treatment due to death or PD. §Data include unconfirmed responses. ¶In the advanced/metastatic setting. †Calculated by the reverse Kaplan-Meier method. \*\*Molecular response: ≥90% reduction in KRASG12D VAF by week 8, assessed by ddPCR or NGS (Predicine) for all patients with baseline G12D VAF and week 8 data.

# Clinical benefit of '734 + SoC is durable in patients with PDAC

## Landmark PFS at 6 months:

- 80% for '734 + GEMNabP
- 90% for '734 + mFOLFIRINOX



Assessed in patients with a baseline scan and at least 1 of the following:  $\geq 1$  postbaseline scan or discontinued treatment due to death or PD. Data include unconfirmed responses.

# Conclusions

## 01 **Favorable safety and tolerability profile for '734 + GEMNabP or mFOLFIRINOX was broadly consistent with established profiles of SoC regimens**

- Incidence of TRAEs leading to '734 discontinuation was low
  - GI TRAEs were mostly Grade 1/2 and improved during treatment
- 

## 02 **Deep and durable treatment responses were observed**

- ORR (DCR) was 69% (96%) for '734 + GEMNabP and 89% (100%) for '734 + mFOLFIRINOX
- 6-month PFS landmark rates were 80% for '734 + GEMNabP and 90% for '734 + mFOLFIRINOX

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## 03 **Encouraging clinical efficacy supports ongoing Phase 3 DAWN-303 study**

- Study is evaluating SoC chemotherapy in combination with '734 or placebo in patients with 1L PDAC

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# KRAS G12D defines a sizable, underserved MSS CRC population

~13k

2L/3L G12D CRC cases in 2026 in the U.S., EU and JP<sup>3</sup>

35–45%

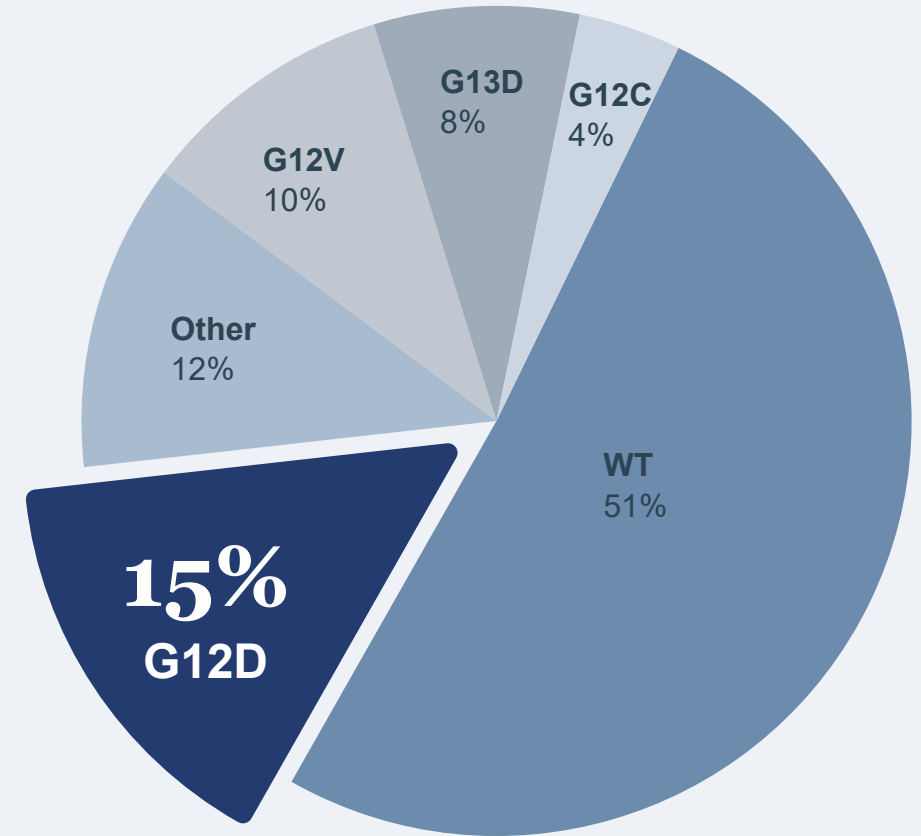
Of CRC patients are diagnosed with Stage IV disease<sup>4</sup>

~13%

5-year survival in Stage IV KRAS-mutant MSS CRC<sup>5</sup>

2L/3L SoC (FTD/TPI + bev) ORR = 6%, mPFS = 5.6 mo., mOS = 10.8 mo. in a Phase 3 trial<sup>6</sup>

KRAS mutations profile in CRC<sup>1,2,7</sup>



# Synergy with EGFR blockade and KRAS inhibition

## **Anti-EGFR is ineffective in KRAS mutated patients**

Blocking EGFR upstream does not shut off mutant KRAS signaling downstream

Historical response rates <5%<sup>1,2</sup>

## **Combination with KRAS G12D inhibitor is synergistic**

Improved early efficacy data in combination vs. monotherapy

Deeper, more durable MAPK pathway suppression than either agent alone

# INCB161734-101: '734 ± cetuximab in patients with metastatic CRC

## Key eligibility criteria

- Locally advanced or metastatic CRC with KRAS G12D mutation\*
- ECOG PS 0 or 1
- Disease progression on prior standard treatment
- No prior treatment with a KRAS G12D selective inhibitor

## Key endpoints

- Safety and tolerability
- Efficacy (ORR, DCR, DOR, and PFS)
- PK

### ■ INCB161734 monotherapy<sup>†</sup>

#### Dose Escalation (All Groups)

**INCB161734**  
(200 mg qd up to 1600 mg qd)

Optimization of Selected RDEs

#### Dose Expansion (CRC)

**INCB161734** (600 mg qd)  
(n=12)

**INCB161734** (1200 mg qd)  
(n=24)

### ■ INCB161734 + cetuximab (500 mg/m<sup>2</sup> IV administered on D1 and D15 of each 28D cycle)

#### Dose Escalation

**INCB161734** (1200 mg qd)  
+ **cetuximab** (n=5)

**INCB161734** (600 mg qd)  
+ **cetuximab** (n=3)

Selected RDE  
No DLTs

MTD not reached

#### Dose Expansion

**INCB161734** (1200 mg qd)  
+ **cetuximab** (n=20)

# CRC patient disposition and baseline characteristics

- As of July 6, 2026, 24 patients with CRC received INCB161734 1200 mg qd monotherapy
  - No patients remained on treatment
  - Primary reason for discontinuation was progressive disease (n=23; 96%)\*
- 25 patients received INCB161734 1200 mg qd in combination with cetuximab
  - Treatment ongoing in 6 (24%)
  - Primary reason for discontinuation was progressive disease (n=14; 56%)†
- All patients had received prior SoC chemotherapy in the metastatic setting

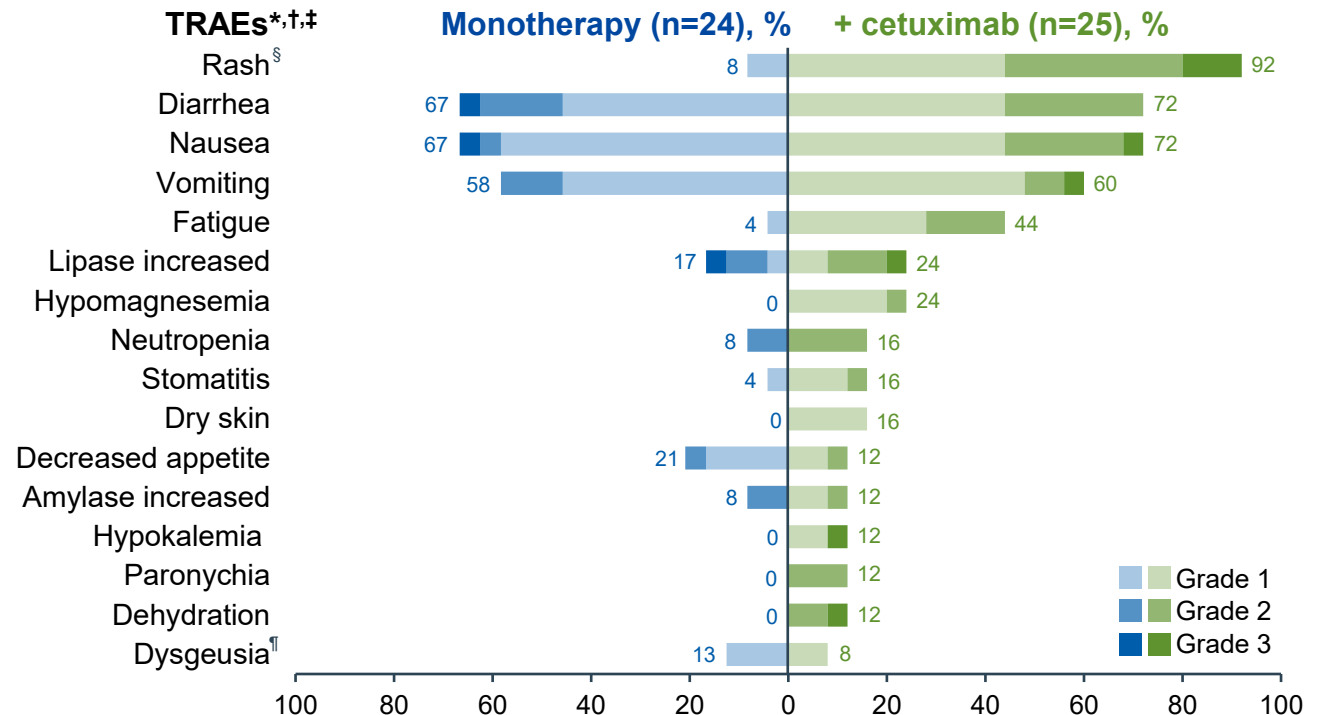
|                                                 | INCB161734 1200 mg qd<br>Monotherapy<br>(n=24) | + cetuximab<br>(n=25) |
|-------------------------------------------------|------------------------------------------------|-----------------------|
| Age, median (range), years                      | 55 (32, 78)                                    | 53 (32, 77)           |
| ≥65 years, n (%)                                | 4 (17)                                         | 7 (28)                |
| Female, n (%)                                   | 13 (54)                                        | 16 (64)               |
| ECOG PS, n (%)                                  |                                                |                       |
| 0                                               | 14 (58)                                        | 16 (64)               |
| 1                                               | 10 (42)                                        | 9 (36)                |
| Liver metastases, n (%)                         | 16 (67)                                        | 15 (60)               |
| Total prior lines of therapy, median (min, max) | 3 (1, 7)                                       | 2 (1, 7)              |
| Prior therapy, n (%)                            |                                                |                       |
| 5-FU/capecitabine                               | 24 (100)                                       | 25 (100)              |
| Oxaliplatin                                     | 21 (88)                                        | 24 (96)               |
| Irinotecan                                      | 24 (100)                                       | 22 (88)               |
| Anti-VEGF chemotherapy combination              | 24 (100)                                       | 21 (84)               |
| Trifluridine and tipiracil                      | 8 (33)                                         | 4 (16)                |
| Primary site of disease, n (%)                  |                                                |                       |
| Right side of colon‡                            | 3 (13)                                         | 8 (32)                |
| Left side of colon§                             | 19 (79)                                        | 16 (64)               |
| Unknown                                         | 2 (8)                                          | 1 (4)                 |

\*1 patient discontinued due to patient withdrawal. †Other reasons for discontinuation were patient withdrawal (n=4) and death (n=1). ‡Includes right side of colon, caecum, and ileocaecal valve. §Includes left side of colon, rectum, sigmoid colon, descending colon, and colon and rectum.

# Safety: '734 ± cetuximab in patients with metastatic CRC

- TRAEs led to INCB161734 dose reductions in 8% of patients with both monotherapy and in combination with cetuximab
- No grade 4 or 5 TRAEs were observed with INCB161734 monotherapy or INCB161734 + cetuximab
- Higher incidences of rash, fatigue, and electrolyte abnormalities were observed with INCB161734 + cetuximab, consistent with the cetuximab safety profile

|                            | INCB161734 (1200 mg qd) |                    |
|----------------------------|-------------------------|--------------------|
| TRAE,*,† n (%)             | Monotherapy (n=24)      | + cetuximab (n=25) |
| Any TRAE                   | 22 (92)                 | 25 (100)           |
| Grade 3 TRAE               | 2 (8)                   | 7 (28)             |
| TRAE leading to INCB161734 |                         |                    |
| Interruption               | 3 (13)                  | 8 (32)             |
| Reduction                  | 2 (8)                   | 2 (8)              |
| Discontinuation            | 0 (0)                   | 0 (0)              |
| TRAE leading to cetuximab  |                         |                    |
| Interruption               | NA                      | 10 (40)            |
| Reduction                  | NA                      | 3 (12)             |
| Discontinuation            | NA                      | 1 (4)              |



\*Assessed in patients who received ≥1 dose of study drug. †Related to INCB161734 monotherapy or related to any study drug for combination therapy. ‡Occurring in ≥10% of patients in either treatment group. §Includes rash, dermatitis acneiform, rash maculo-papular, and rash pustular. ¶The maximum possible severity per CTCAE for dysgeusia is grade 2.

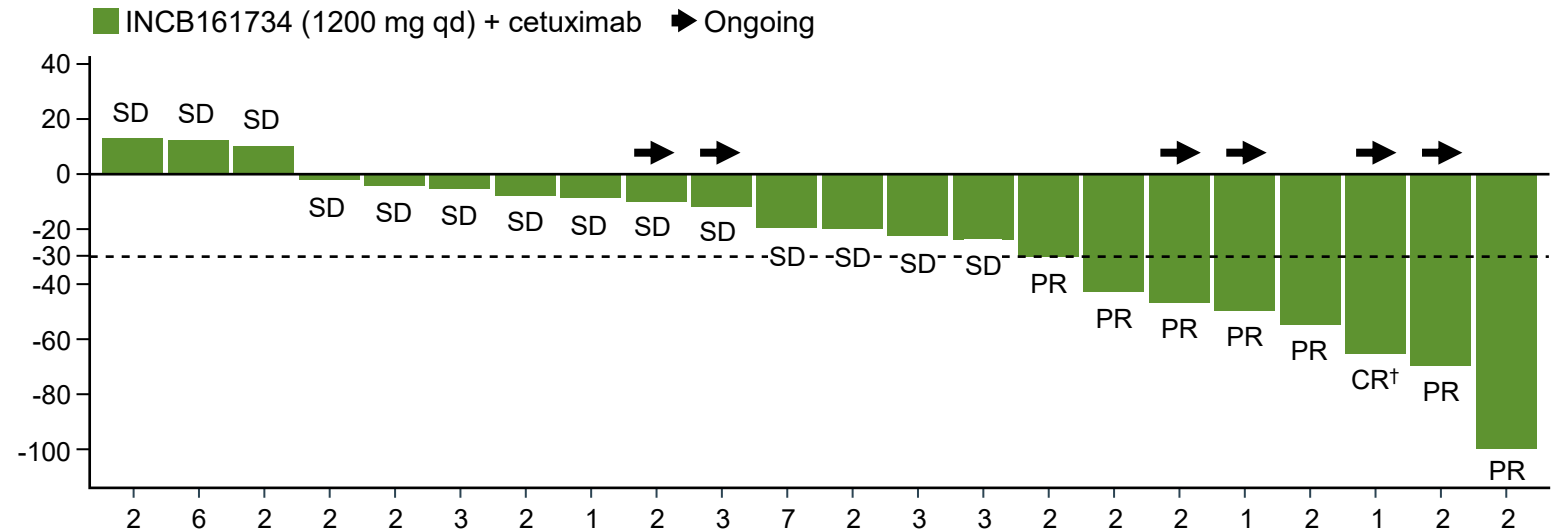
# '734 + cetuximab showed encouraging anti-tumor activity in heavily pretreated patients

- **INCB161734 + cetuximab**

- **ORR\* = 36% (8/22)**
- **DCR\* = 100% (22/22)**

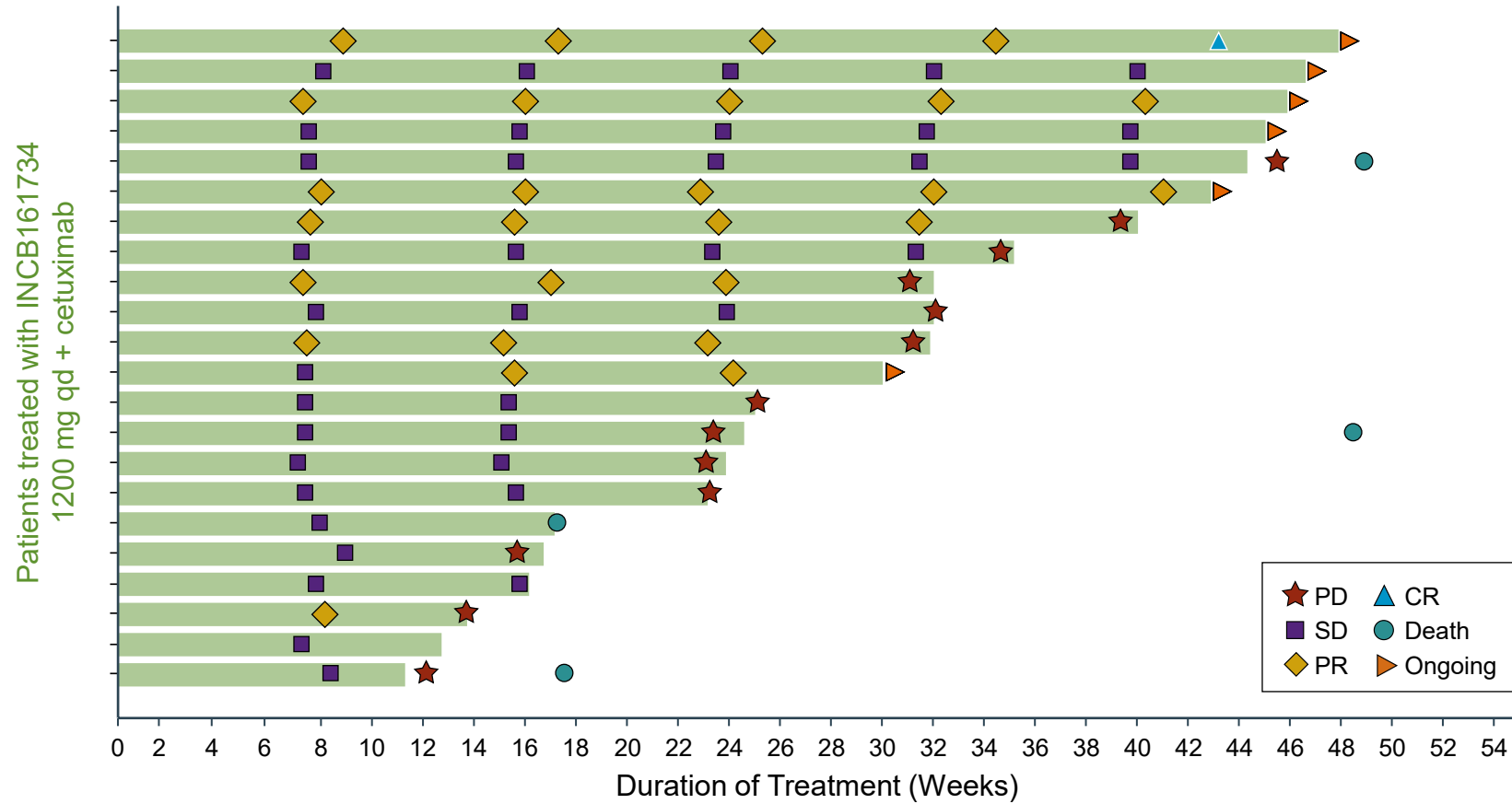
- **INCB161734 monotherapy**

- **ORR\* = 8% (2/24)**
- **DCR\* = 79% (19/24)**



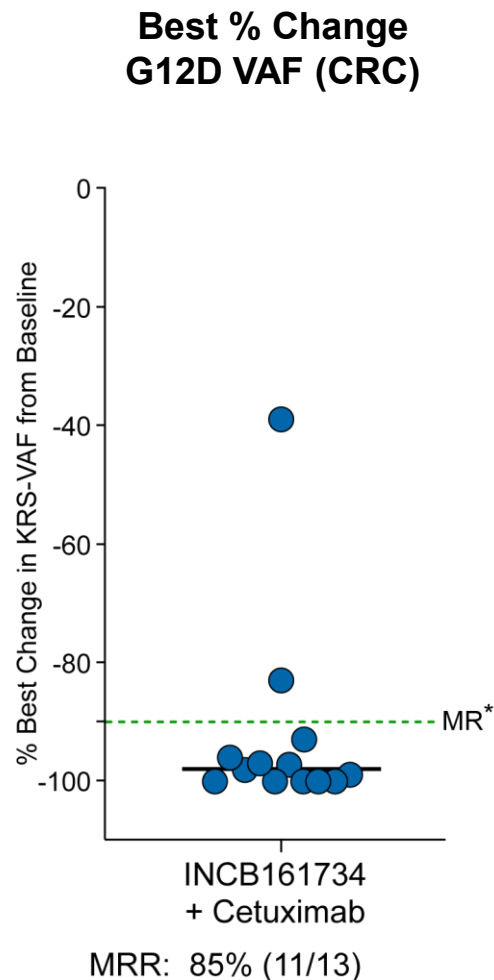
# '734 + cetuximab demonstrated durable responses in heavily pretreated patients

- Median PFS (95% CI) was 7.2 (5.4, NE) months

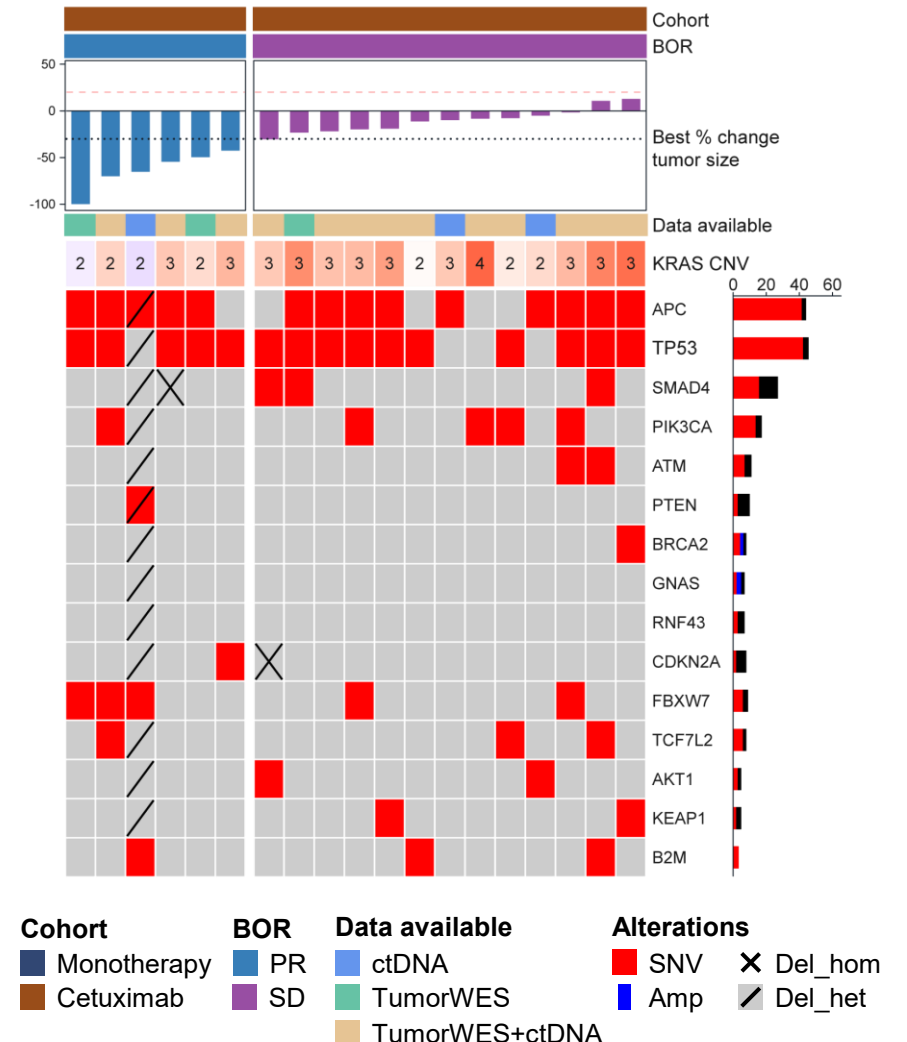


# Measurement of KRAS G12D in plasma ctDNA and early clinicogenomic profiling in patients with CRC

- Higher MR rates were observed in patients with INCB161734 1200 mg + cetuximab
- Baseline genomic analysis found no significant correlations for coalterations with response (ORR or DCR) for INCB161734 monotherapy or in combination with cetuximab



## Baseline genomic analysis by response



\*MR:  $\geq 90\%$  reduction in KRAS G12D VAF by week 8, assessed by ddPCR or NGS (Predicine) for all patients with baseline G12D VAF and 8-week data. Baseline NGS analysis of tumor biopsies (Caris WES) and plasma ctDNA (Predicine WES or Caris WES).

# Conclusions

- 01 Manageable safety profile as monotherapy and in combination with cetuximab**
- No DLTs in combination escalation
  - Low TRAEs leading to discontinuation or dose modification for '734
- 

- 02 Encouraging preliminary efficacy in heavily pretreated metastatic CRC patients**
- '734 + cetuximab: ORR 36%, DCR 100%, median PFS 7.2 months
- 

- 03 Data support further exploration of combination in KRAS G12D CRC**
-

# '734: Expanding across tumors, settings and combinations

## PDAC

Establishing '734 in early settings with high incidence and unmet need

- **Phase 3 DAWN-303 in 1L PDAC ongoing**
- **Phase 3 adjuvant PDAC planned in 2027**

## CRC

Leveraging synergy with EGFR blockade to reach multiple lines of therapy

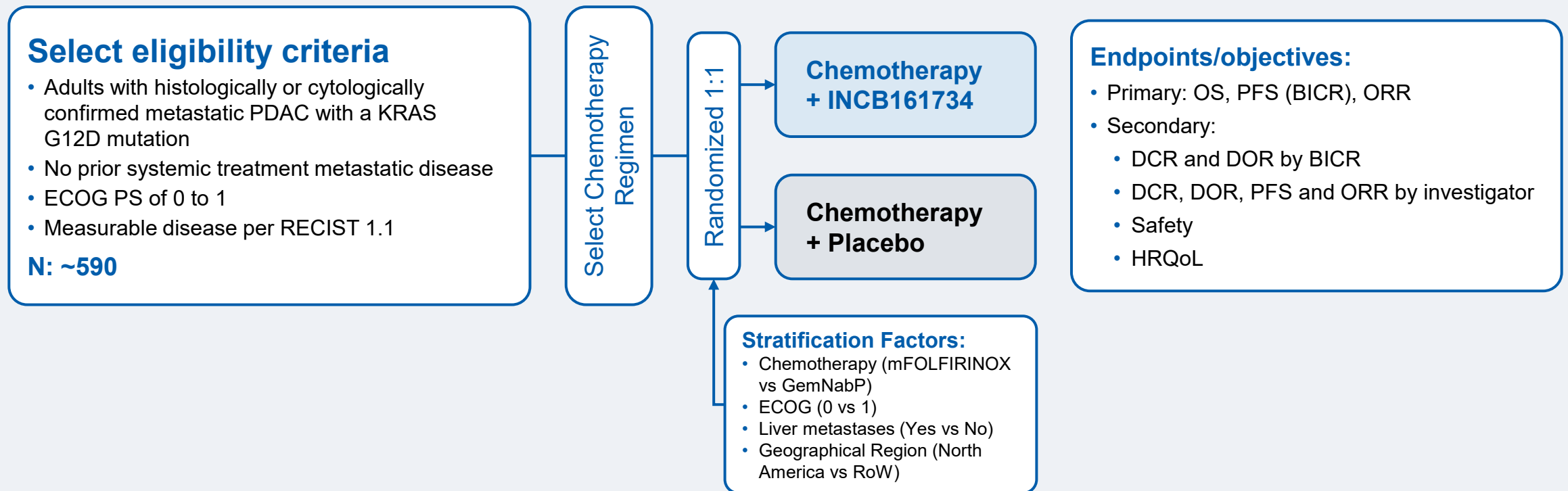
- **Phase 3 2L/3L CRC planned in 1H27**
- **Phase 1 cohort 1L MSS CRC ongoing**

## Novel combinations

Novel combinations to expand reach of '734 and address resistance mechanisms

- **Phase 1 trials evaluating novel combinations ongoing and planned**

# Phase 3 DAWN-303 topline data expected in 2028



# Moving earlier in PDAC treatment

Initiating adjuvant PDAC study in 2027

## Adjuvant Setting

Phase 3 planned

- Chemotherapy +/- '734 in adj. PDAC

Moving  
earlier

## 1L Metastatic Setting

Phase 3 ongoing

- GnP/mFFX +/- '734 in 1L PDAC

## Rationale

- Extends '734 into a curative-intent setting
- Aims to eliminate micro-metastatic disease and extend disease-free survival
- Supported by Phase 1 safety and efficacy data in combination with chemotherapy in metastatic patients

## Study Details

- Setting: Post-resection PDAC
- Regimen: chemotherapy +/- '734
- Status: Phase 3 planned (2027)

# DAWN-302: Establishing '734 in CRC

Initiating Phase 3 study in 1H 2027

## Metastatic Setting

Phase 3 ongoing

- GnP/mFFX +/- '734 in 1L PDAC

Moving into  
an adjacent  
tumor type

## 2L/3L CRC

Phase 3 planned in 1H27

- 'cetuximab + '734 in 2L/3L CRC

## Rationale

- Extends '734 into a high incidence tumor with significant G12D mutated disease
- Aims to take advantage of observed mechanistic synergy with EGFR antibodies
- Supported by Phase 1 in late-line CRC in combination with cetuximab

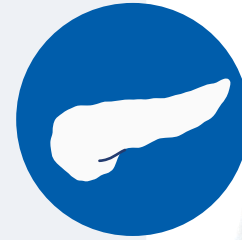
## Study Details

- Setting: 2L/3L CRC (bevacizumab-experienced)
- Regimen: cetuximab + '734
- Status: Phase 3 planned (1H27)

# Building a multi-combination franchise

## Pancreatic combinations

- GNP/mFFX + '734
- '734 + navlimetostat
- '734 + SNV1521



Pancreatic cancer

## Colorectal combinations

- cetuximab + '734
- FOLFIRI/FOLFOX + cetuximab + '734
- FOLFIRI/FOLFOX + petosemtamab + '734



CRC

# Next Steps for establishing '734 in GI oncology

- 01**    **Establishing '734 in 1L PDAC, with topline data from Phase 3 expected in 2028**

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- 02**    **Moving earlier in the disease continuum through adjuvant PDAC**  
Planned Phase 3 study in 2027

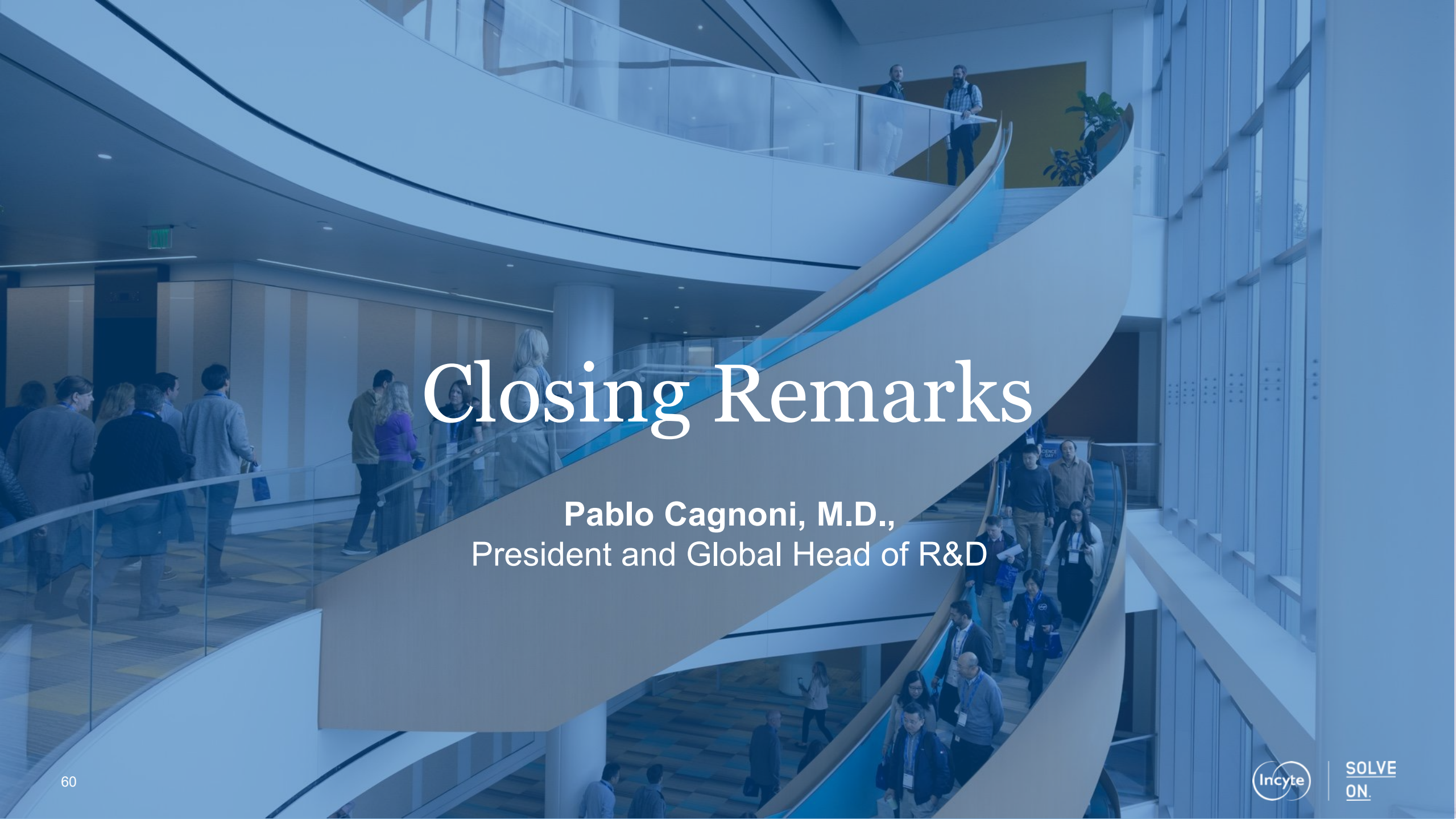
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- 03**    **Expanding into new tumor types with CRC, including pivotal initiation next year**  
Phase 3 DAWN-302 study in pre-treated CRC planned for 1H27; Phase 1 in 1L CRC ongoing

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- 04**    **Expanding the potential of '734 via novel combination strategies across tumor types**  
Combination studies with navlimetostat, SNV1521, and petosemtamab planned in 2027

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# Closing Remarks

**Pablo Cagnoni, M.D.,**  
President and Global Head of R&D

# '734 (G12D) and '890 (TGF $\beta$ $\times$ PD-1) Takeaways

- 01 **Novel compounds in Phase 3 target two major areas in oncology** and anchor Incyte's solid tumor portfolio

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- 02 **Phase 1 results suggest a competitive clinical profile for both assets**, supporting ongoing Phase 3 programs and expansion efforts across tumor types, settings, and combinations

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- 03 **Two ongoing Phase 3 programs approaching major clinical milestones**, with topline readouts beginning in 2028 and potential approvals and launches as early as 2029

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- 04 **Development in the adjuvant setting adds a distinct growth opportunity**, with '890 underway and a Phase 3 adjuvant PDAC study for '734 planned in 2027

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- 05 **Both assets have significant commercial potential**, with the opportunity to contribute meaningfully to Incyte's growth profile into the 2030s

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# Q&A



SOLVE  
ON.

# Thank *you*



# Appendix

# Abbreviation directory (1 of 2)

|                  |                                            |                    |                                                         |                      |                                                             |
|------------------|--------------------------------------------|--------------------|---------------------------------------------------------|----------------------|-------------------------------------------------------------|
| <b>'734</b>      | INCB161734                                 | <b>CRC</b>         | Colorectal cancer                                       | <b>G12D</b>          | KRAS mutation, glycine to aspartate at codon 12             |
| <b>'890</b>      | INCA33890                                  | <b>CSCC</b>        | Cervical squamous cell carcinoma                        | <b>GDP</b>           | Guanosine diphosphate                                       |
| <b>1L / 2L</b>   | First-line / second-line                   | <b>CTCAE</b>       | Common Terminology Criteria for Adverse Events          | <b>GEJ</b>           | Gastroesophageal junction                                   |
| <b>2L+ / 3L+</b> | Second-line or later / third-line or later | <b>ctDNA</b>       | Circulating tumor DNA                                   | <b>GEMNabP / GnP</b> | Gemcitabine plus nab-paclitaxel                             |
| <b>5-FU</b>      | Fluorouracil                               | <b>CTL</b>         | Cytotoxic T lymphocyte                                  | <b>GI</b>            | Gastrointestinal                                            |
| <b>ACT</b>       | Adjuvant chemotherapy                      | <b>CTLA-4</b>      | Cytotoxic T-lymphocyte-associated protein 4             | <b>GTP</b>           | Guanosine triphosphate                                      |
| <b>adj.</b>      | Adjuvant                                   | <b>CTx</b>         | Chemotherapy                                            | <b>HNSCC</b>         | Head and neck squamous cell carcinoma                       |
| <b>ADC</b>       | Antibody-drug conjugate                    | <b>D1, D8, D15</b> | Day 1, day 8, day 15                                    | <b>HR</b>            | Hazard ratio                                                |
| <b>ALT</b>       | Alanine aminotransferase                   | <b>DCR</b>         | Disease control rate                                    | <b>HRD</b>           | Homologous recombination deficiency                         |
| <b>APC</b>       | Antigen-presenting cell                    | <b>ddPCR</b>       | Droplet digital polymerase chain reaction               | <b>HRP</b>           | Homologous recombination proficient                         |
| <b>Bev</b>       | Bevacizumab                                | <b>DFS</b>         | Disease-free survival                                   | <b>HRQoL</b>         | Health-related quality of life                              |
| <b>BICR</b>      | Blinded independent central review         | <b>DLT</b>         | Dose-limiting toxicity                                  | <b>IAI</b>           | Inflammation & Autoimmunity                                 |
| <b>BRAF</b>      | B-Raf proto-oncogene                       | <b>dMMR</b>        | Deficient mismatch repair                               | <b>ICI</b>           | Immune checkpoint inhibitor                                 |
| <b>BRCA</b>      | Breast cancer gene (BRCA1/2)               | <b>DOR</b>         | Duration of response                                    | <b>IDC</b>           | Invasive ductal carcinoma                                   |
| <b>bsAb</b>      | Bispecific antibody                        | <b>EC</b>          | Esophageal carcinoma                                    | <b>inv</b>           | Involvement                                                 |
| <b>CCA</b>       | Cholangiocarcinoma                         | <b>ECM</b>         | Extracellular matrix                                    | <b>IO</b>            | Immuno-oncology                                             |
| <b>CCNE</b>      | Cycle E1                                   | <b>ECOG</b>        | Eastern Cooperative Oncology Group                      | <b>iPR</b>           | Immune partial response                                     |
| <b>CD8</b>       | Cluster of differentiation 8               | <b>EGFR</b>        | Epidermal growth factor receptor                        | <b>IV</b>            | Intravenous                                                 |
| <b>CDK2</b>      | Cyclin-dependent kinase 2                  | <b>EMT</b>         | Epithelial-mesenchymal transition                       | <b>KRAS</b>          | Kirsten rat sarcoma viral oncogene homolog                  |
| <b>Cetux</b>     | Cetuximab                                  | <b>EOT</b>         | End of treatment                                        | <b>KRASm</b>         | KRAS-mutant                                                 |
| <b>CI</b>        | Confidence interval                        | <b>EU4</b>         | France, Germany, Italy and Spain                        | <b>LGR5</b>          | Leucine-rich repeat-containing G protein-coupled receptor 5 |
| <b>CNV</b>       | Copy number variation                      | <b>EU5</b>         | EU4 plus the United Kingdom                             | <b>MAPK</b>          | Mitogen-activated protein kinase                            |
| <b>cORR</b>      | Confirmed objective response rate          | <b>FOLFIRI</b>     | Folinic acid (leucovorin), fluorouracil and irinotecan  | <b>mCRC</b>          | Metastatic colorectal cancer                                |
| <b>CPI</b>       | Checkpoint inhibitor                       | <b>FOLFOX</b>      | Folinic acid (leucovorin), fluorouracil and oxaliplatin | <b>mDFS</b>          | Median disease-free survival                                |
| <b>CR</b>        | Complete response                          | <b>FRα</b>         | Folate receptor alpha                                   | <b>MDS</b>           | Myelodysplastic syndromes                                   |

# Abbreviation directory (2 of 2)

|                       |                                                               |                  |                                                  |               |                                            |
|-----------------------|---------------------------------------------------------------|------------------|--------------------------------------------------|---------------|--------------------------------------------|
| <b>mFFX</b>           | Modified FOLFIRINOX                                           | <b>PDAC</b>      | Pancreatic ductal adenocarcinoma                 | <b>SNV</b>    | Single-nucleotide variant                  |
| <b>mFOLFIRINOX</b>    | Modified leucovorin, fluorouracil, irinotecan and oxaliplatin | <b>PET-CT</b>    | Positron emission tomography-computed tomography | <b>SoC</b>    | Standard of care                           |
| <b>mFOLFOX</b>        | Modified FOLFOX                                               | <b>PFS</b>       | Progression-free survival                        | <b>ssGSEA</b> | Single-sample gene set enrichment analysis |
| <b>mPDAC</b>          | Metastatic pancreatic ductal adenocarcinoma                   | <b>PK</b>        | Pharmacokinetics                                 | <b>STAD</b>   | Stomach adenocarcinoma                     |
| <b>MCC</b>            | Merkel cell carcinoma                                         | <b>PoC</b>       | Proof of concept                                 | <b>TAM</b>    | Total addressable market                   |
| <b>MR</b>             | Molecular response                                            | <b>PR</b>        | Partial response                                 | <b>TAP</b>    | Tumor area positivity                      |
| <b>MRD</b>            | Minimal residual disease                                      | <b>PRMT5i</b>    | Protein arginine methyltransferase 5 inhibitor   | <b>TEAE</b>   | Treatment-emergent adverse event           |
| <b>MRR</b>            | Molecular response rate                                       | <b>PROC</b>      | Platinum-resistant ovarian cancer                | <b>TGCC</b>   | Testicular germ cell cancer                |
| <b>MSI-H</b>          | Microsatellite instability-high                               | <b>PS</b>        | Performance status                               | <b>TGFβ</b>   | Transforming growth factor beta            |
| <b>MSS</b>            | Microsatellite stable                                         | <b>PSOC</b>      | Platinum-sensitive ovarian cancer                | <b>TGFβR2</b> | TGFβ receptor 2                            |
| <b>MTAP</b>           | Methylthioadenosine phosphorylase                             | <b>pts</b>       | Patients                                         | <b>TLS</b>    | Tertiary lymphoid structure                |
| <b>MTD</b>            | Maximum tolerated dose                                        | <b>q2w / q4w</b> | Every 2 weeks / every 4 weeks                    | <b>TME</b>    | Tumor microenvironment                     |
| <b>NA</b>             | Not available                                                 | <b>qd</b>        | Once daily                                       | <b>TPM</b>    | Transcripts per million                    |
| <b>NE</b>             | Not estimable                                                 | <b>RAS</b>       | Rat sarcoma (gene family)                        | <b>TRAE</b>   | Treatment-related adverse event            |
| <b>NED</b>            | No evidence of disease                                        | <b>RDE</b>       | Recommended dose for expansion                   | <b>UEC</b>    | Uterine endometrial carcinoma              |
| <b>NGS</b>            | Next-generation sequencing                                    | <b>RDI</b>       | Relative dose intensity                          | <b>VAF</b>    | Variant allele frequency                   |
| <b>NSCLC</b>          | Non-small cell lung cancer                                    | <b>RECIST</b>    | Response Evaluation Criteria in Solid Tumors     | <b>VEGF</b>   | Vascular endothelial growth factor         |
| <b>OC</b>             | Ovarian cancer                                                | <b>rEOC</b>      | Recurrent epithelial ovarian cancer              | <b>VHIO</b>   | Vall d'Hebron Institute of Oncology        |
| <b>ORR</b>            | Objective response rate                                       | <b>RINA-S</b>    | Rinatabart sesutecan                             | <b>WES</b>    | Whole-exome sequencing                     |
| <b>OS</b>             | Overall survival                                              | <b>RO</b>        | Rapid oral (presentation)                        | <b>WNT</b>    | Wingless-related integration site          |
| <b>PARPi / PARP1i</b> | Poly(ADP-ribose) polymerase (1) inhibitor                     | <b>RoW</b>       | Rest of world                                    | <b>WT</b>     | Wild type                                  |
| <b>PD</b>             | Progressive disease                                           | <b>RP2D</b>      | Recommended phase 2 dose                         |               |                                            |
| <b>PD-1</b>           | Programmed cell death protein 1                               | <b>SCAC</b>      | Squamous cell carcinoma of the anal canal        |               |                                            |
| <b>PD-L1</b>          | Programmed death-ligand 1                                     | <b>SCCHN</b>     | Squamous cell carcinoma of the head and neck     |               |                                            |
| <b>PD-(L)1</b>        | PD-1 or PD-L1                                                 | <b>SD</b>        | Stable disease                                   |               |                                            |