

VS-7375: Potential Best-in-Class KRAS G12D (ON/OFF) Inhibitor

R&D Update

October 14, 2026



FORWARD-LOOKING STATEMENTS

This presentation includes forward-looking statements about, among other things, Verastem Oncology's (the "Company") programs and product candidates, strategy, future plans and prospects, including statements related to the potential safety, efficacy and therapeutic profile of VS-7375, including as a monotherapy and in combination with other agents, and the timing of clinical trial initiations, enrollment and data readouts for VS-7375, approval and commercialization of AVMAPKI® FAKZYNJA® CO-PACK (avutometinib capsules; defactinib tablets) as a treatment for adult patients with Kirsten rat sarcoma viral oncogene homolog (KRAS) mutant-type (mt) recurrent Low-Grade Serous Ovarian Cancer (LGSOC), the expected outcome and benefits of collaborations, including with GenFleet Therapeutics (Shanghai), Inc. (GenFleet), including the conduct of a Phase 1/2a study and subsequent studies with respect to VS-7375, the potential of the results of the RAMP 301 Phase 3 trial to confirm the results of the RAMP 201 study specific to KRAS mutant patients and to expand the indication for AVMAPKI FAKZYNJA CO-PACK regardless of KRAS mutation status, the structure and potential clinical value of our completed, planned and pending clinical trials, the potential clinical value of various of the Company's clinical trials, including the RAMP 201, RAMP 201J, RAMP 205, RAMP 301 and VS-7375 trials, the timing of commencing and completing trials, including topline data reports, our interactions with regulators, the timeline and indications for clinical development, regulatory submissions and the potential for and timing of commercialization of our product candidates and potential for additional development programs involving the Company's lead compound and the potential market opportunities thereof; and the estimated addressable markets for, and anticipated market opportunities of our drug candidates. The words "anticipate," "believe," "estimate," "expect," "may," "plan," "target," "would," "could," "should," "continue," "potential," "can" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to: the assumptions underlying the forward-looking statements; risks related to the development and successful commercialization of our product candidates; obtaining and maintaining regulatory approvals, including, but not limited to, potential regulatory delays or rejections; the challenges with the commercialization of a new product; our history of operating losses and the possibility that we may never achieve or maintain profitability; risks associated with meeting the objectives of Verastem's clinical trials, including, but not limited to Verastem's ability to achieve enrollment objectives concerning patient numbers (including an adequate safety database), outcomes objectives and/or timing objectives for Verastem's trials; any delays or failures in enrollment and the occurrence of adverse safety events; our ability to successfully commercialize AVMAPKI FAKZYNJA CO-PACK in the U.S. including our ability to generate market demand for and acceptance of AVMAPKI FAKZYNJA CO-PACK; the potential inability to raise sufficient capital to fund ongoing operations as currently planned or to obtain financing on acceptable terms or to fund operations from revenues generated by the sales of AVMAPKI FAKZYNJA CO-PACK; actions or advice of regulatory agencies to maintain regulatory approval of AVMAPKI FAKZYNJA CO-PACK; the impact of current and future healthcare reforms, including those affecting the delivery of or payment for healthcare products and services; uncertainties related to the activities and initiatives of the current U.S. presidential administration, including regulatory and policy changes that may adversely affect our business; risks related to our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates; decisions by regulatory authorities regarding trial design, labeling and other matters that could affect the timing, availability or commercial potential of our product candidates; whether preclinical studies and any positive preliminary, initial "top-line," and interim data, from our clinical trials of our product candidates may not necessarily be predictive of the results of ongoing or later clinical trials; that the timing, scope and rate of reimbursement for our product candidates is uncertain; that the market opportunities of our drug candidates are based on internal and third-party estimates which may prove to be incorrect; that third-party payors (including government agencies) may not reimburse; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that enrollment of clinical trials may take longer than expected; the risks that we will not satisfy our post-marketing requirements and commitments established and agreed to as part of the FDA's approval of AVMAPKI FAKZYNJA CO-PACK; that our marketed product candidates may cause adverse safety events and/or unexpected concerns may arise from additional data or analysis, or result in unmanageable safety profiles as compared to their levels of efficacy; that we may not be able to confirm the results from the RAMP 201 study or expand the approved indication for AVMAPKI FAKZYNJA CO-PACK; that our product candidates may experience manufacturing or supply interruptions or failures; that any of our third-party contract research organizations, contract manufacturing organizations, clinical sites, or contractors, among others, which we rely on may fail to fully perform; that we face substantial competition, which may result in others developing or commercializing products before or more successfully than we do which could result in reduced market share or market potential for our product candidates; that we may be unable to successfully initiate or complete the clinical development and eventual commercialization of our product candidates; that the development and commercialization of our product candidates may take longer or cost more than planned, including as a result of conducting additional studies or our decisions regarding execution of such commercialization; that we may not attract and retain high quality personnel; that we or Pfizer, Inc. may fail to fully perform under the license agreement covering certain Pfizer FAK inhibitors, including defactinib; that we or Chugai Pharmaceutical Co., Ltd. may fail to fully perform under the avutometinib license agreement; that we or GenFleet may fail to fully perform under the collaboration and option agreement covering VS-7375 and other assets we may decide to option in; that our total addressable and target markets for our product candidates might be smaller than we are presently estimating; that we or Secura Bio, Inc. may fail to fully perform under the asset purchase agreement with Secura Bio, Inc., including in relation to milestone payments; that we may not be able to establish new or expand on existing collaborations or partnerships, including with respect to in-licensing of our product candidates, on favorable terms, or at all; that we may be unable to obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we may not pursue or submit regulatory filings for our product candidates; that, due to the current presidential administration's significant reduction in the FDA's workforce and potential reductions to the FDA's budget, we may experience a material impact to the FDA's ability to engage in a variety of activities that may affect our business, including routine regulatory and oversight activities; and that our product candidates may not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients.

Other risks and uncertainties include those identified under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2025, as filed with the Securities and Exchange Commission ("SEC") on March 04, 2026, the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2026, as filed with the SEC on August 6, 2026 and in any subsequent filings with the SEC, which are available at www.sec.gov and investor.verastem.com. The forward-looking statements in this presentation speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these statements whether as a result of new information, future events or otherwise, except as required by law. Our business is subject to substantial risks and uncertainties, including those referenced above. Investors, potential investors, and others should give careful consideration to these risks and uncertainties.

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Certain information contained in this presentation, including industry and market data and other statistical information, relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or other jurisdiction.

AGENDA

➤ **Welcome and Agenda**

JULISSA VIANA

Senior Vice President, Corp. Comms, IR, Patient Advocacy

➤ **Delivering on the Strategic Vision for VS-7375**

DAN PATERSON

President and Chief Executive Officer

➤ **Defining the Opportunity for VS-7375:** Where Current & Emerging Therapies Fall Short

MICHAEL G. KAUFFMAN, MD, PHD

President, Development

➤ **Clinical Activity of VS-7375:** Pancreatic, Colorectal, and Lung Cancers

MICHAEL G. KAUFFMAN, MD, PHD

President, Development

➤ **Expert Perspective:** The Evolving RAS Treatment Landscape and the Potential Role of VS-7375

MANUEL HIDALGO MEDINA, MD, PHD

GI Medical Oncologist, TARGET-D Investigator

➤ **Safety, Tolerability, and Combination Potential**

TING-HUI WU, MD

Vice President, Clinical Development

➤ **The Path Forward**

MICHAEL G. KAUFFMAN, MD, PHD

President, Development

➤ **Q&A**

Delivering on the Strategic Vision for **VS-7375**

Dan Paterson
President & CEO



VS-7375 is Emerging with Potential Best-in-Class Profile Across Tumors*

Differentiated by Design^{1,2}

- Selective KRAS G12D targeting
- Potent, equal ON/OFF inhibition
- Dose proportional clinical exposures that are at or above the preclinical target for maximal antitumor efficacy

Emerging Potential Best-in-Class Profile Across Tumors

- PDAC: Best ORR with CRs
- CRC: Early and robust combo activity in hard-to-treat patients
- NSCLC: Antitumor activity in line with competitors who excluded prior taxanes
- Significant VAF reductions in PDAC and NSCLC

Favorable Safety Profile

- Predominantly Gr1-2 GI AE's with limited hepatic and heme AE's
- 97% dose intensity at 900 mg
- 2% discontinuation rate due to AEs at 900 mg QD
- Combinability with EGFR mAb, GemNabP and chemo/IO

BUILDING CLINICAL EVIDENCE POSITIONS VS-7375 TO BECOME THE PREFERRED AGENT FOR KRAS-G12D-MUTATED CANCERS

Defining the Opportunity for **VS-7375**: Where Current & Emerging Therapies Fall Short

Michael G. Kauffman, MD, PhD
President of Development



Limitations of Current Chemotherapy SoC, panRASi, and Emerging RAS Therapies Across Metastatic KRAS G12D-Mutated Cancers

We believe that **no current approach fully addresses the need** for meaningful, durable control across KRAS G12D-mutated PDAC, CRC, & NSCLC cancers



Current treatment burden & **toxicity remain high** with chemotherapy SoC and recently approved PanRASi



Other G12D inhibitors appear to have **limited to moderate single agent activity** likely due to limited exposure that may leave **some patients underserved**



1L is the Goal: Establishing **VS-7375** as Potential Best-in-Class KRAS G12D Inhibitor

1L POTENTIAL

A strong standalone profile can support earlier-line use and combination strategies with potential for long-term disease control with good tolerability



Strategic destination

2L ENTRY POINT

Potential initial registration opportunity (accelerated approval pathway) across multiple tumor types

SINGLE-AGENT & COMBO POTENTIAL

Efficacy and tolerability

ROBUST ANTITUMOR ACTIVITY AND A TOLERABLE, COMBINATION-READY PROFILE DRIVES MEANINGFUL AND BROAD OPPORTUNITY

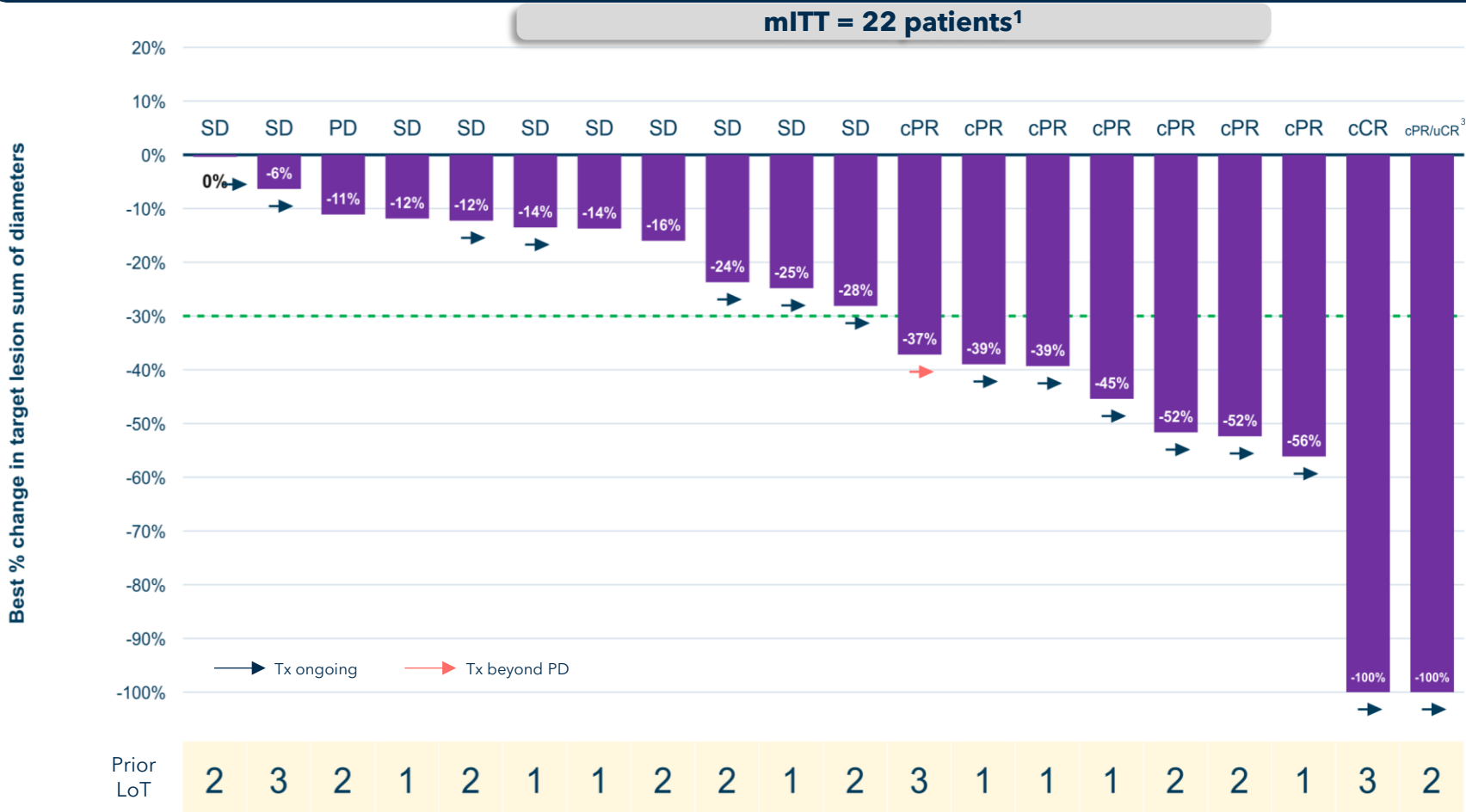
Clinical Activity of **VS-7375**: Pancreatic Ductal Adenocarcinoma

Michael G. Kauffman, MD, PhD
President of Development



VS-7375 900 mg Emerging as Potential Best-in-Class KRAS G12D Inhibitor in Previously Treated (2L-4L) KRAS G12D mPDAC

41% cORR (9/22) 2L+² | 50% cORR (4/8) 2L² | 36% cORR (5/14) 3-4L²



66.5
Median age (years)

2
Median prior lines of
therapy (range 1-3)

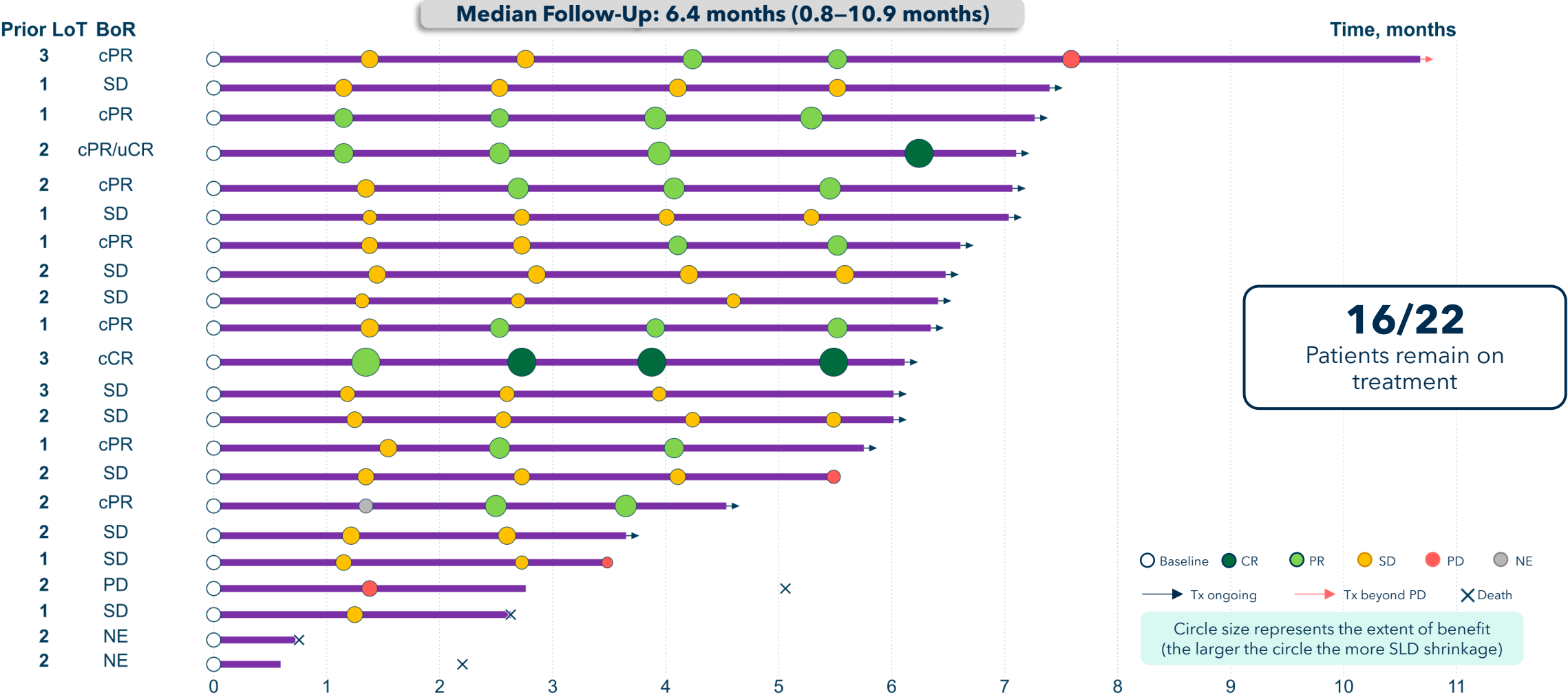
16/22
Patients remain on
treatment

**All Responses
Confirmed**

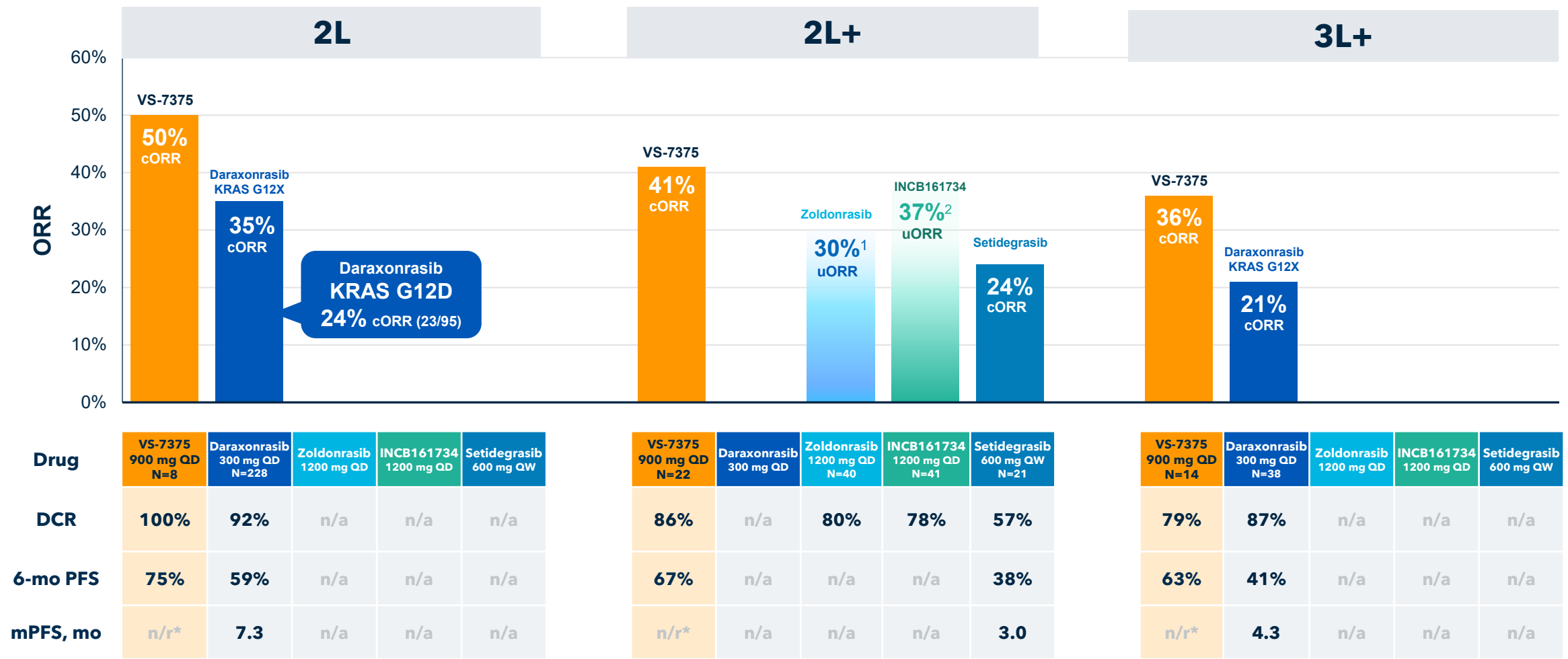
**Deep Responses;
No Target Lesions Grew**

VS-7375: First KRAS G12D Inhibitor to Demonstrate Favorable Monotherapy Durability in mPDAC

67% Landmark 6-month PFS rate | 80% Landmark 6-month OS in 2L/3L/4L



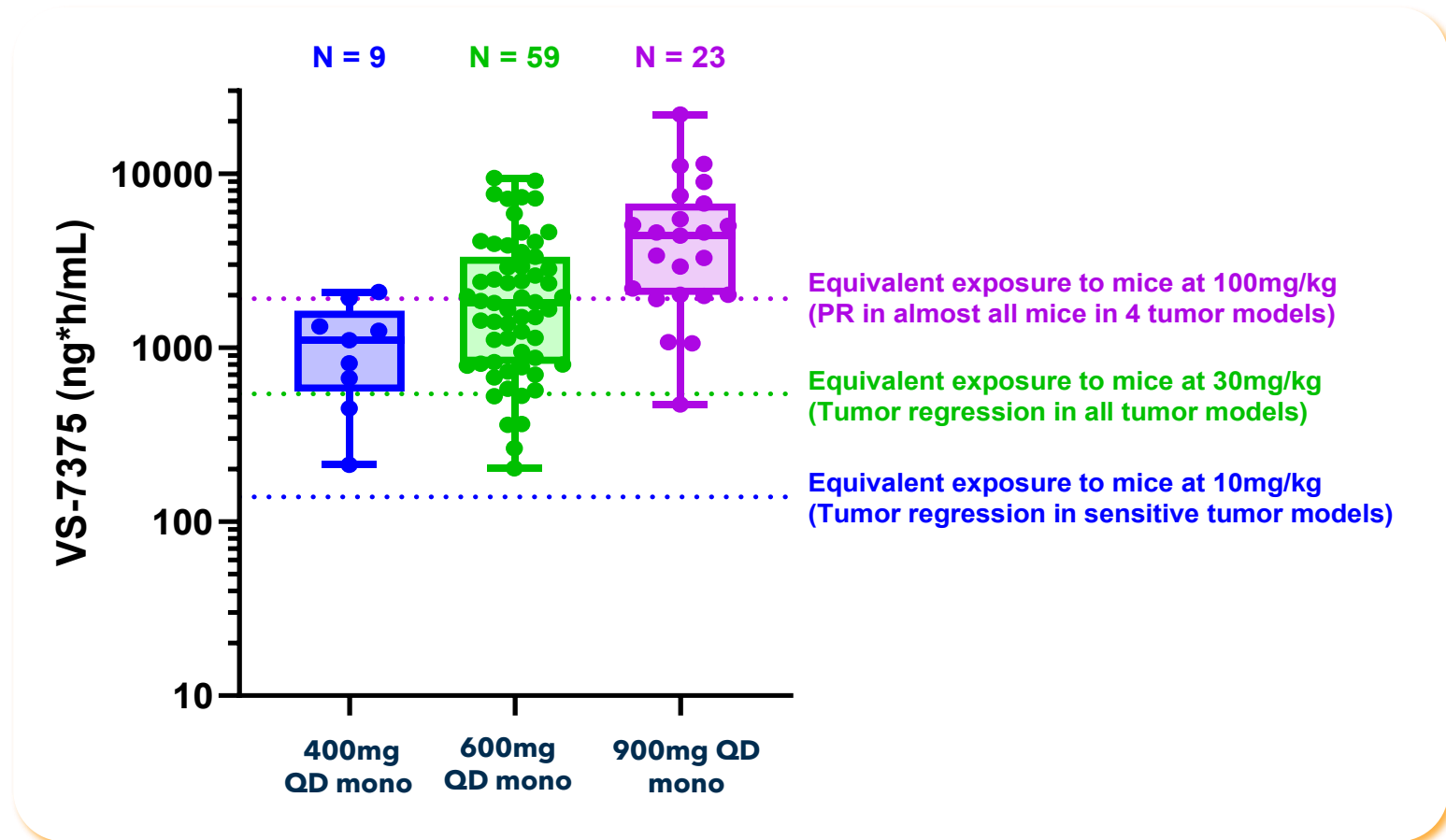
VS-7375 is Emerging as Potential Best-in-Class RAS Inhibitor for Patients with KRAS G12D-Mutated Pancreatic Cancer



Comparisons based on historical published data; no head-to-head studies have been conducted and cross-trial comparisons may not be reliable due to differences in trial design and patient population/characteristics.

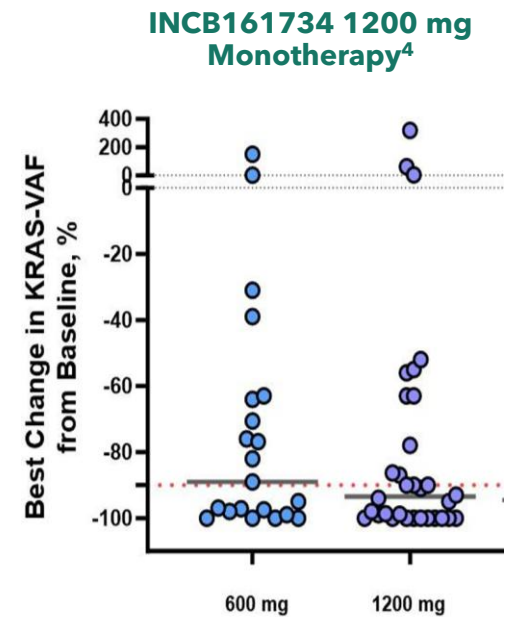
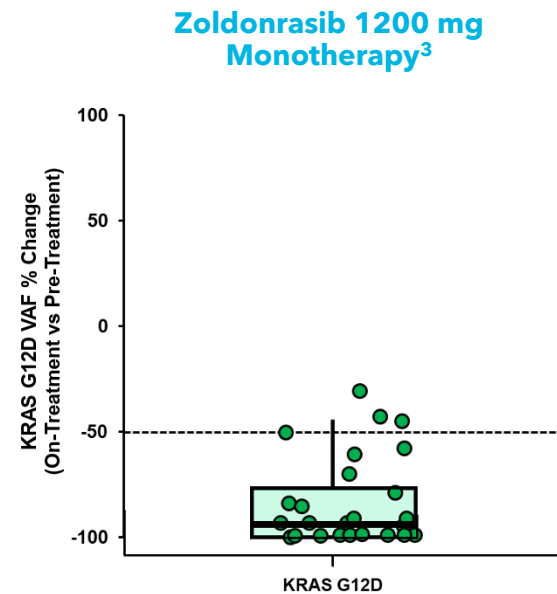
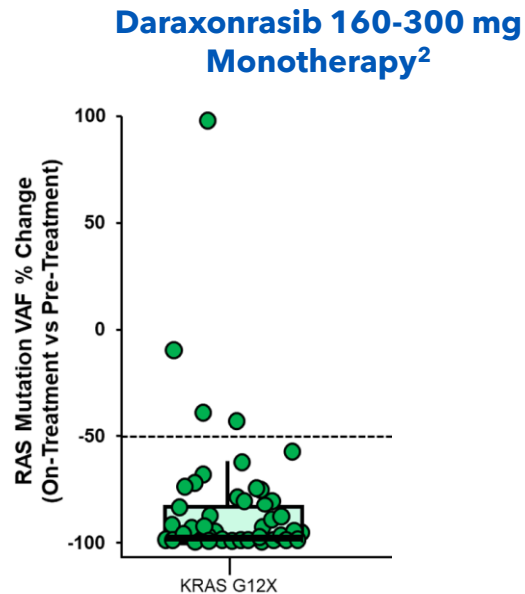
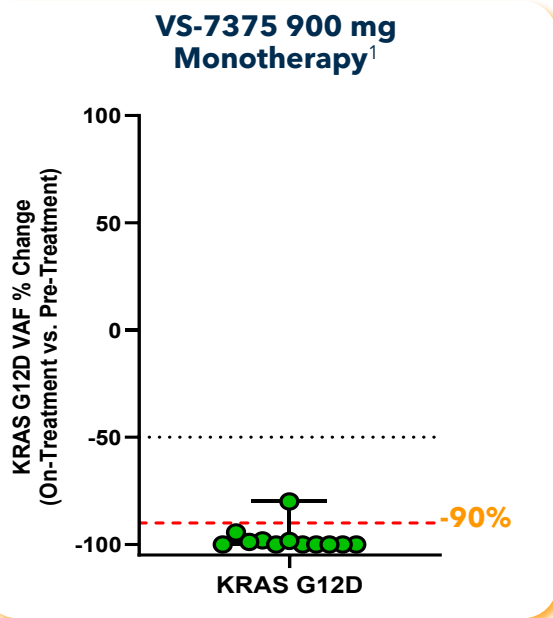
* Not reportable: Insufficient event number to report mPFS
1. ORR calculation included confirmed responses + unconfirmed responses with potential to be confirmed; 6 of the 12 responses were confirmed at time of data cutoff
2. Reported unconfirmed response rate; 8 of the 15 responses were confirmed at time of data cutoff; 3 responses unlikely to be confirmed according to swimmer plot; ORR ~29% if uses the same method as zoldonrasib
Sources: VS-7375 - Verastem data on file (data cutoff Oct 7, 2026). Daraxonrasib 2L - RASolute 302, RAS G12X (n=228); 24% ORR in KRAS G12D subgroup (23/95). Zoldonrasib 2L+ - Revolution Medicines update, Sep 2024 (n=40). INCB161734 2L+ - ASCO GI 2026 (n=41). Setidegrasib 2L+ - NEJM 2026 (n=21). Daraxonrasib 3L+ - Phase 1/2 study (n=38).
QD: daily; QW: once weekly; DCR, disease control rate

VS-7375 900 mg QD Monotherapy Delivers More Complete KRAS G12D Inhibition With a Favorable Therapeutic Window



VS-7375 900 mg QD Monotherapy Achieves the Target Human AUC_{ss} in the Majority of Patients Corresponding to Maximal Tumor Regression Across Mouse Models

VS-7375 at 900mg Achieves High Rates (>90%) of KRAS G12D VAF Clearance in Patients with mPDAC*



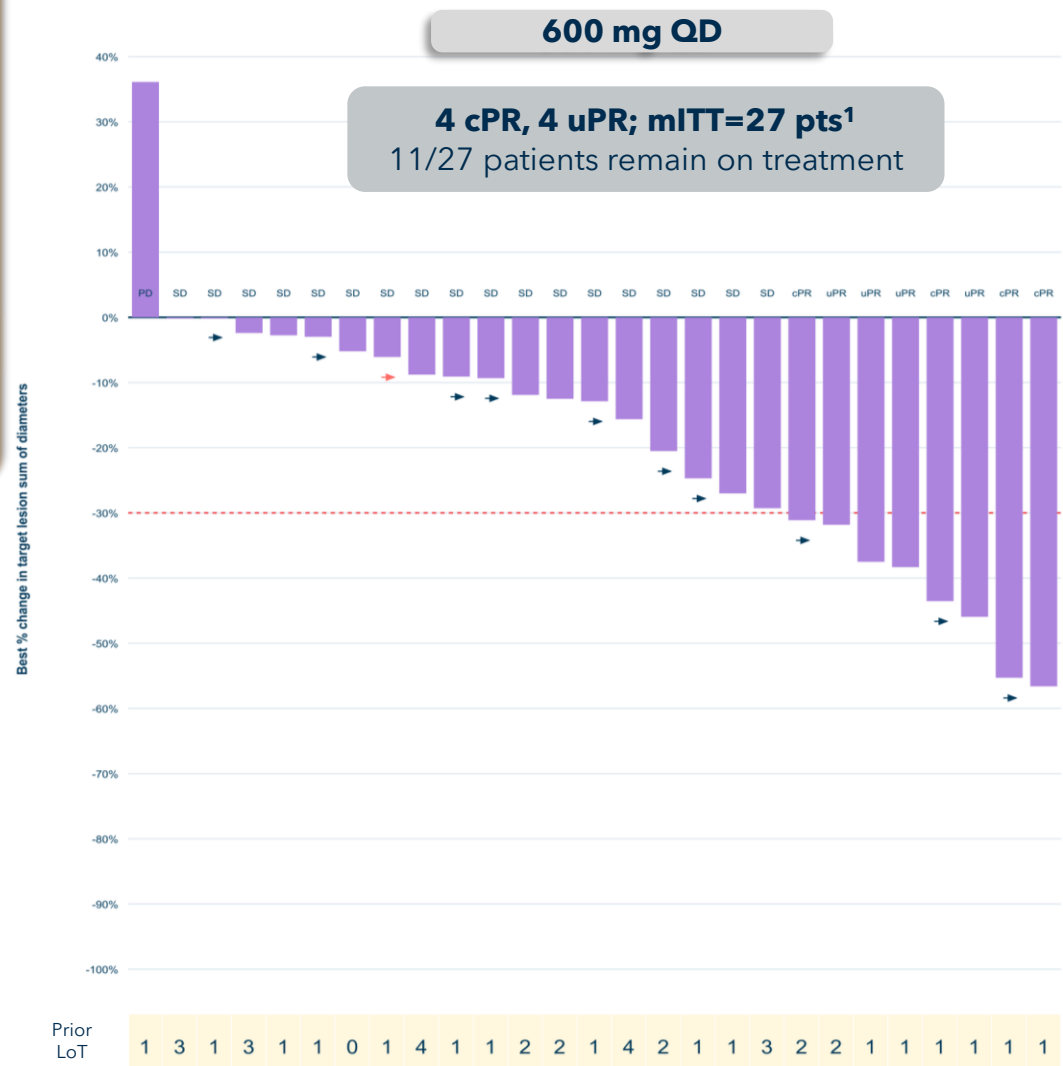
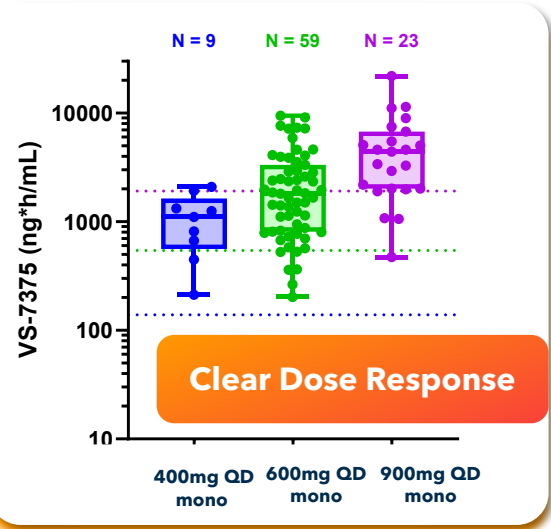
KRAS G12D VAF Clearance	VS-7375 (N = 12)
≥50% KRAS G12D VAF decrease from pre-treatment, n (%)	12 (100%)
≥90% KRAS G12D VAF decrease from pre-treatment, n (%)	11 (92%)
100% KRAS G12D VAF decrease from pre-treatment, n (%)	7 (58%)

RAS VAF Clearance in KRAS G12X patients	Daraxonrasib (N = 60)
≥50% RAS VAF decrease from pre-treatment, n (%)	56 (93%)
≥90% RAS VAF decrease from pre-treatment, n (%)	N.R.
100% RAS VAF decrease from pre-treatment, n (%)	29 (48%)

KRAS G12D VAF Clearance	Zoldonrasib (N = 28)
≥50% KRAS G12D VAF decrease from pre-treatment, n (%)	24 (86%)
≥90% KRAS G12D VAF decrease from pre-treatment, n (%)	N.R.
100% KRAS G12D VAF decrease from pre-treatment, n (%)	11 (39%)

KRAS G12D VAF Clearance	INCB161734 (N = 32)
≥50% KRAS G12D VAF decrease from pre-treatment, n (%)	N.R.
≥90% KRAS G12D VAF decrease from pre-treatment, n (%)	21 (66%)
100% KRAS G12D VAF decrease from pre-treatment, n (%)	N.R..

VS-7375 2L+ PDAC Monotherapy: 900 mg Achieves Higher Exposure and Deeper Tumor Reductions Than 600 mg



Clinical Activity of **VS-7375**: Colorectal Cancer

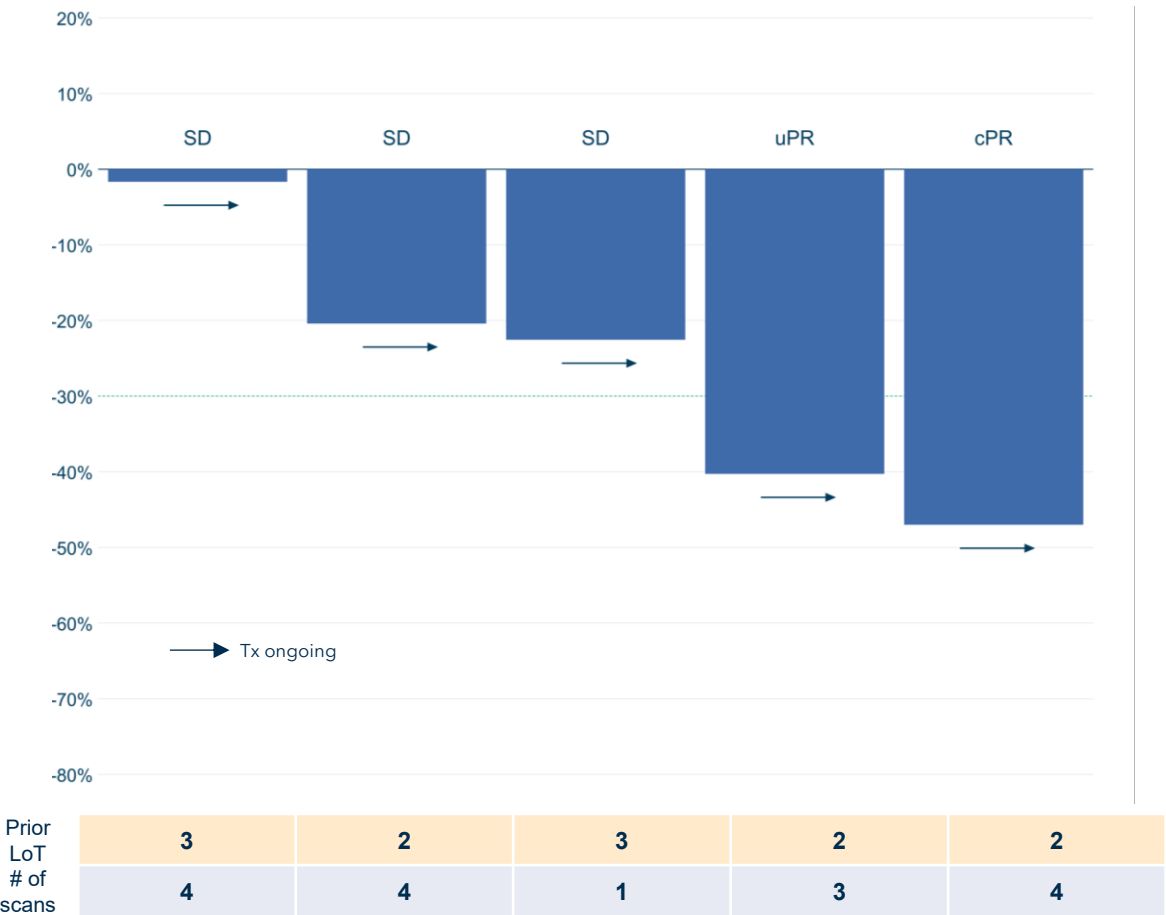
Michael G. Kauffman, MD, PhD
President of Development



VS-7375 900mg Combo with anti-EGFR Demonstrates Promising Antitumor Activity in mCRC

33% ORR* (2/6) 3L+ CRC

miTT = 6 patients¹ | Median Follow-Up: 6.1 months (0.4–7.0 months)



55

Median age (years)

2

Median prior lines of therapy (range 2–3)

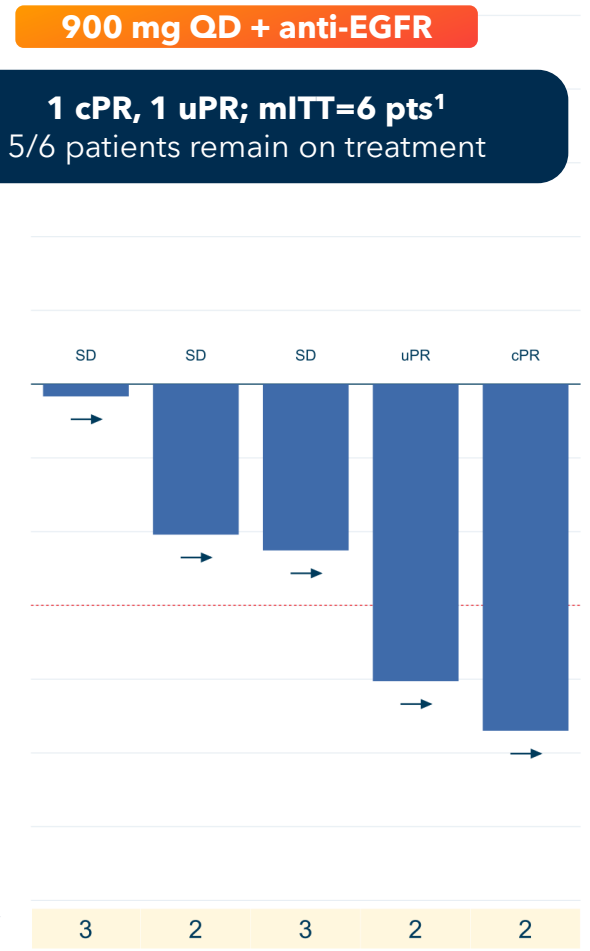
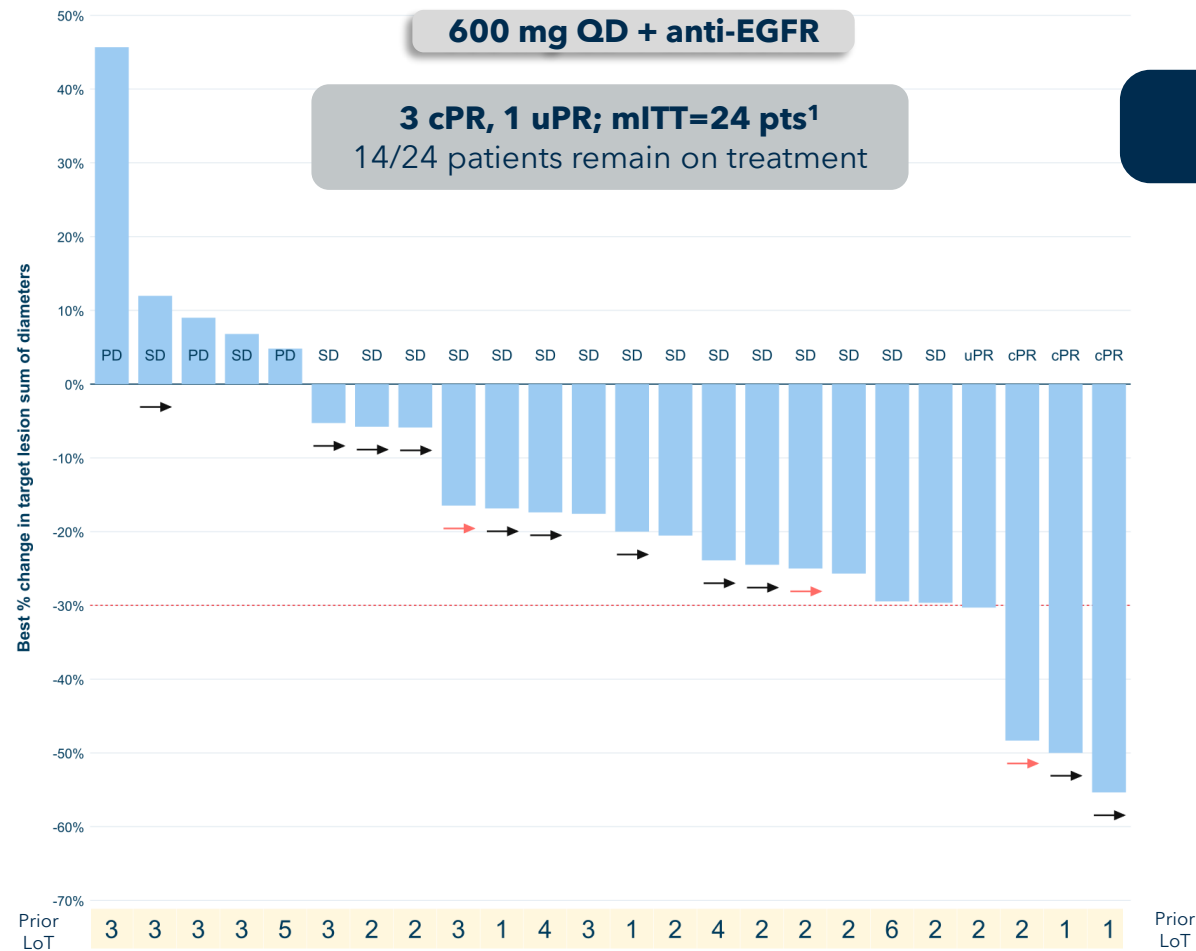
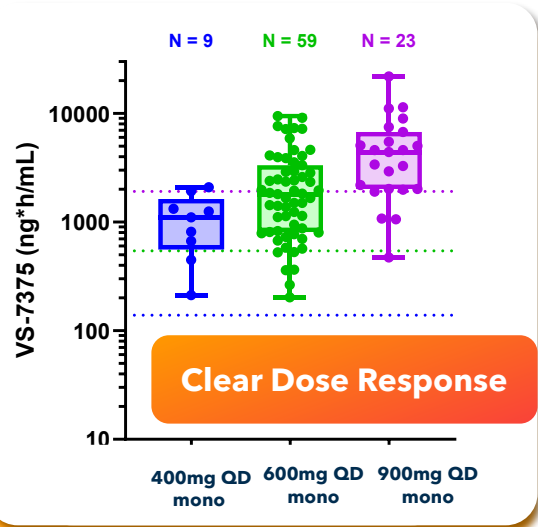
5/6

Patients remain on treatment

VS-7375 900 mg + Cetux Combo Cleared May 2026

VS-7375 900 mg + Cetux Combo Evaluating in Phase 2 TARGET-D 203 trial

3L CRC: VS-7375 900 mg + anti-EGFR Combo Achieves Higher Exposure and Deeper Tumor Reductions Than 600 mg in Early Data



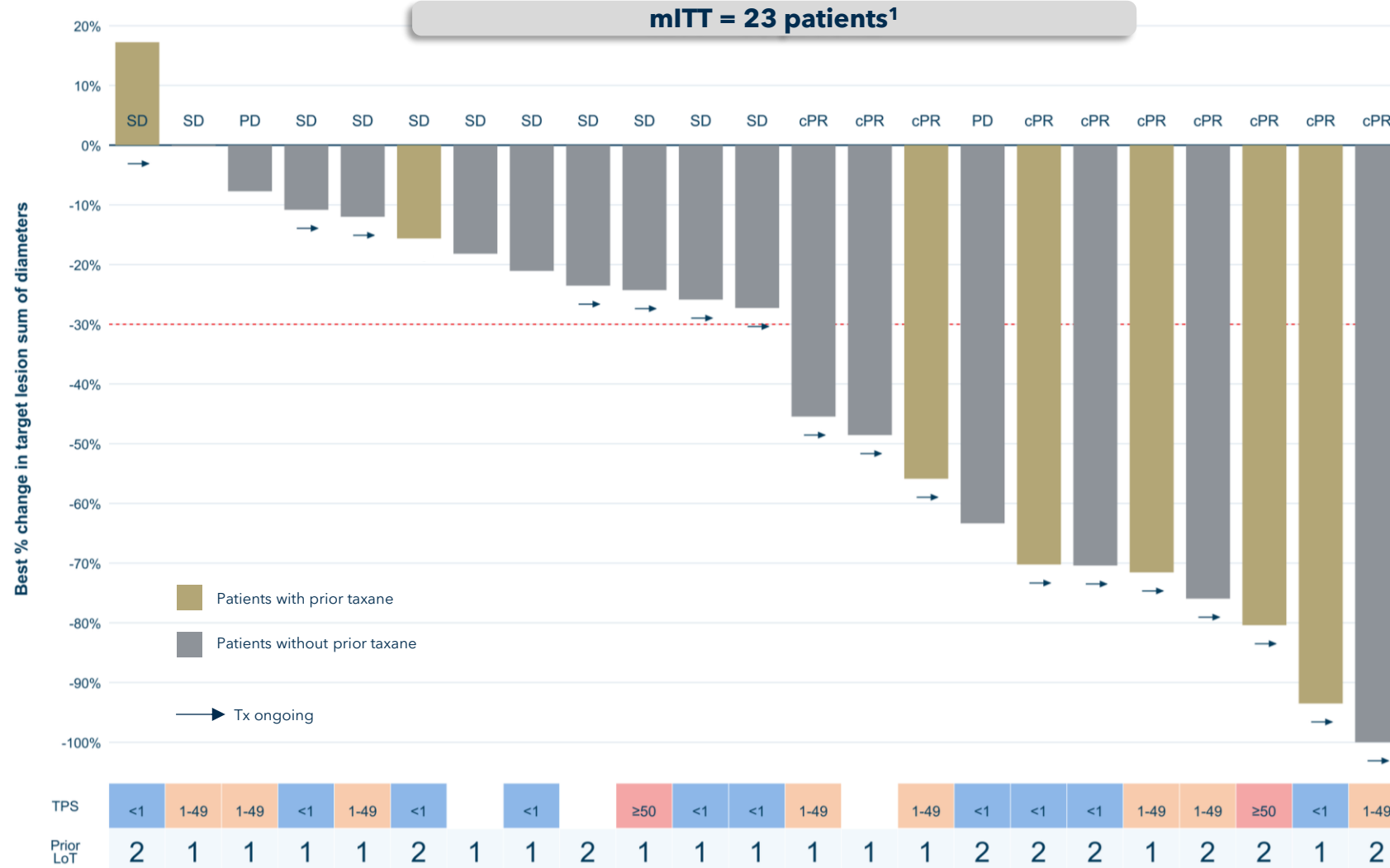
Clinical Activity of **VS-7375**: Non-Small Cell Lung Cancer

Michael G. Kauffman, MD, PhD
President of Development



VS-7375 Demonstrates Confirmed Responses at 600 mg in 2L+ NSCLC

43% cORR (10/23) 2L+ NSCLC, including prior taxane treated



68

Median age (years)

1

Median prior lines of therapy (range 1-3)

17/23

Patients remain on treatment

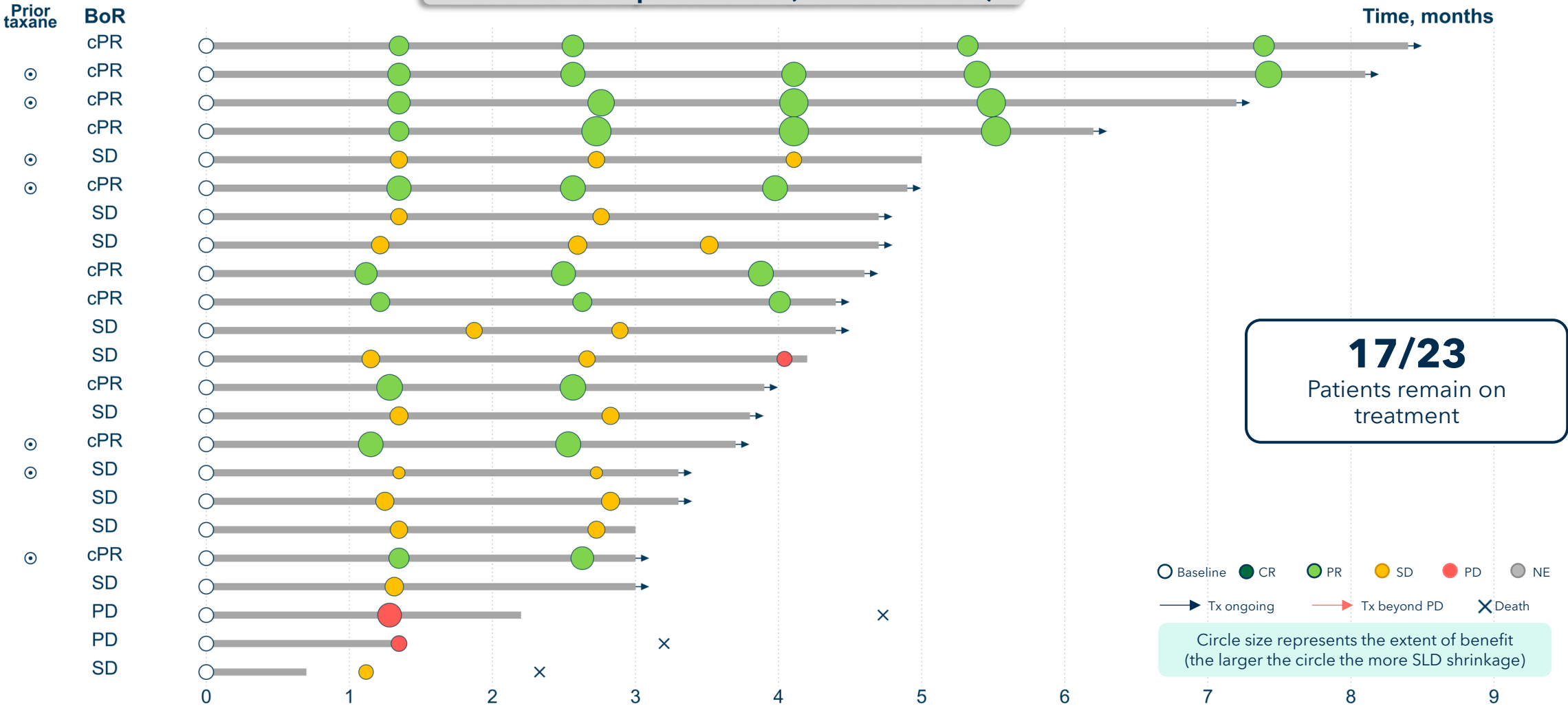
All patients had prior platinum-based chemo Tx, all but 1 patient had prior IO

Enrolling at 900 mg in Phase 2 TARGET-D 202

VS-7375 Shows Encouraging Durability at 600 mg in 2L+ NSCLC

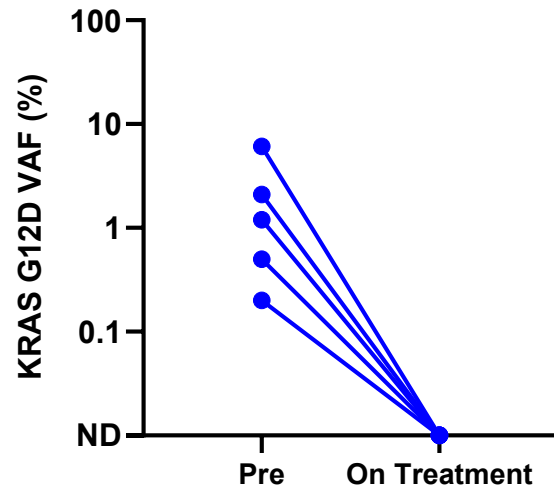
72% landmark PFS rate at 6-months; mPFS not reached

Median Follow-Up: 4.4 months (2.4 – 12.4 months)



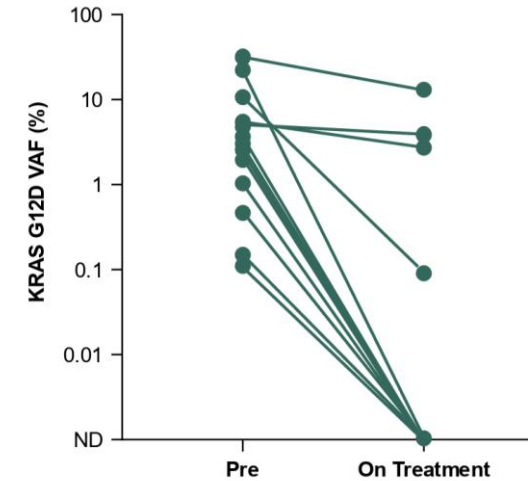
VS-7375 Achieved Complete KRAS G12D VAF Clearance Even at 600 mg in Patients with Advanced NSCLC

**VS-7375 600mg
Monotherapy (N=5)¹**



KRAS G12D VAF Clearance	VS-7375 600mg PO QD
100% Clearance, % (n/N)	100 (5/5)

**Zoldonrasib 1200mg
Monotherapy (N=12)²**

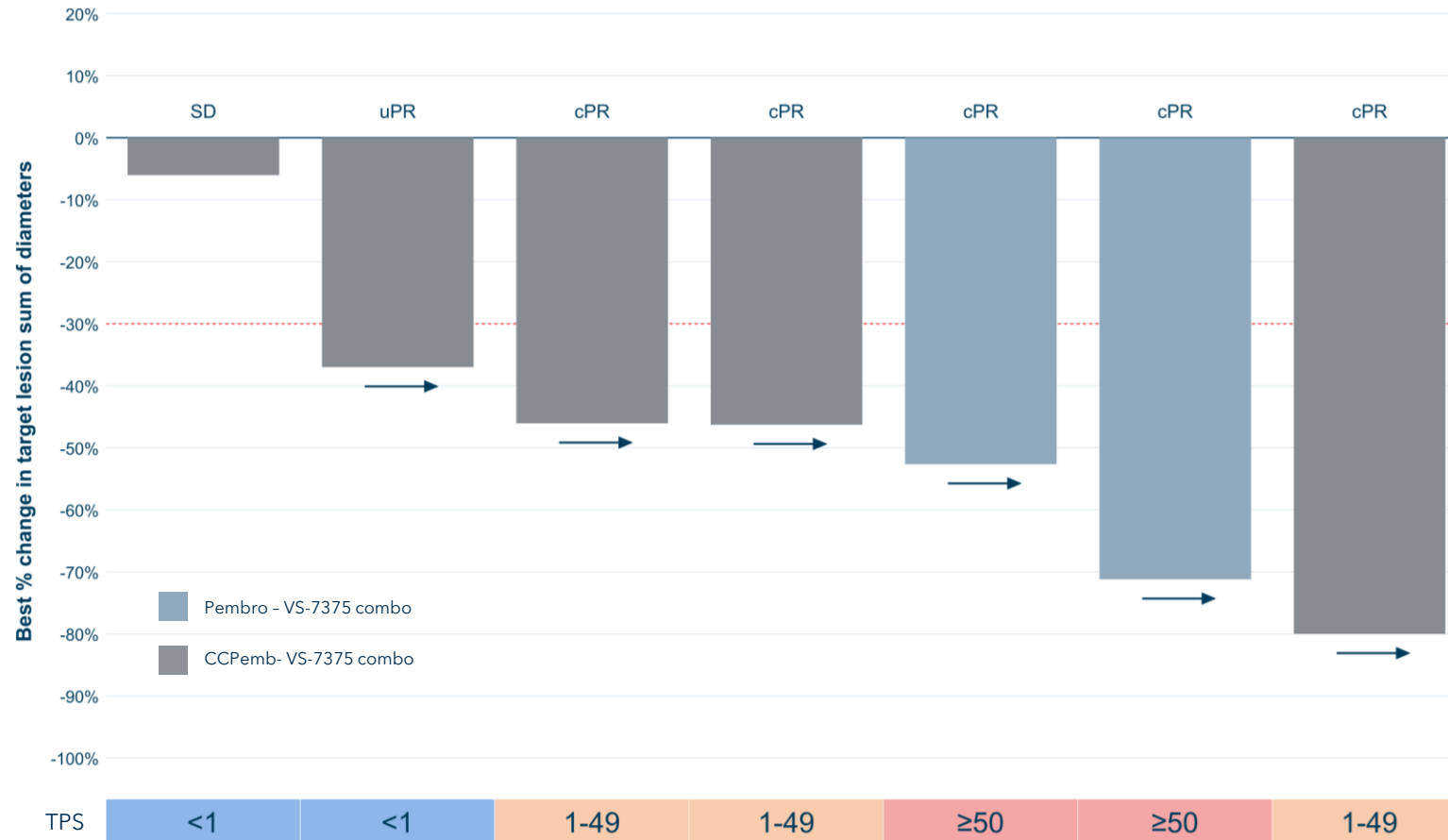


KRAS G12D VAF Clearance	Zoldonrasib 1200 mg PO QD
100% Clearance, % (n/N)	73 (11/15)

VS-7375 at 600 mg Shows Early Antitumor Activity with First-Line Triplet SoC in NSCLC, Supporting Combination Potential

75% ORR* (6/8) in 1L NSCLC combined with SoC

miTT = 8 patients¹ | Median Follow-Up: 4.4 months (0.9–5.8 months)



73

Median age (years)

KRAS G12D

Adenocarcinoma of the Lung

6/8

Patients remain on treatment

VS-7375 600 mg + CPem/Pembro Cleared Sep 2026

VS-7375 900 mg + CPem/Pembro Evaluation ongoing

Expert Perspective: The Evolving RAS Treatment Landscape and the Potential Role of **VS-7375**

Manuel Hidalgo Medina, MD, PHD

Director of the Gastrointestinal Cancer Center at New York University (NYU) Langone Health and as a professor of medicine at NYU Grossman School of Medicine

TARGET-D Investigator

Disclosures

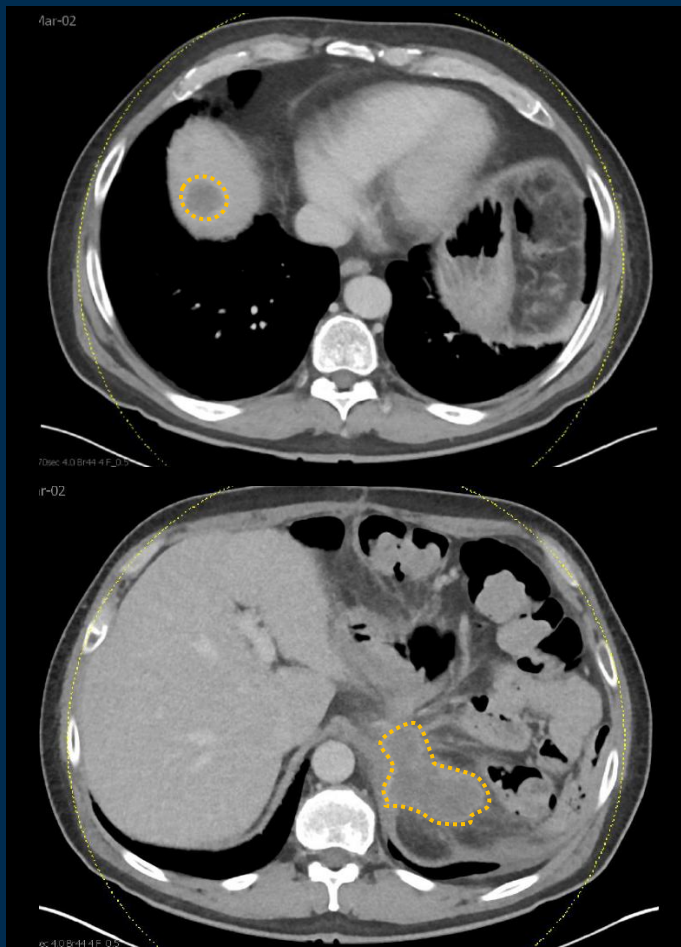
All statements made and opinions expressed are solely my own and do not reflect the views of Verastem. You should not treat any such statement or opinion as a recommendation to make a particular investment or follow a particularly investment strategy.



Confirmed Partial Response at Week 12 with **VS-7375** 900 mg Monotherapy in 55 y/o Male with mPDAC

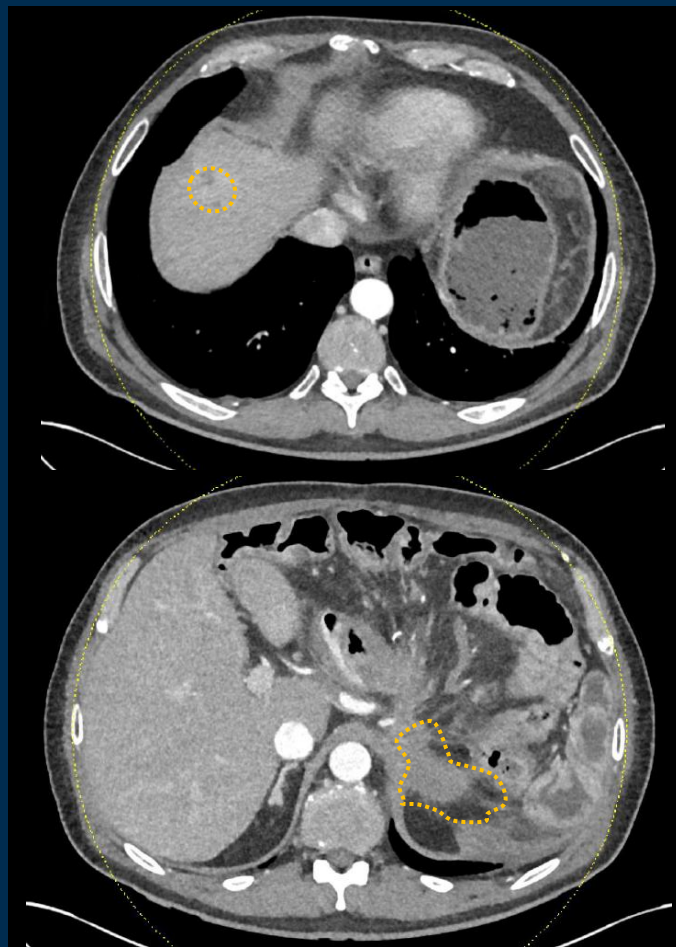
Baseline Lesion:

Liver, surgical bed, peritoneum
(SLD: 151mm)



Week 12:

cPR (-47%) (SLD: 80mm)
Response ongoing



- Prior mFOLFIRINOX (SD for 4 mos) and Gem/NabP (PD after 2 mos)
- Investigator-reported pain resolution within 1 week of treatment (completely off morphine from 100 mg/day)
- No treatment-related AEs reported
- Normal CA-19-9 levels at baseline. (Normal CEA and CA125 at baseline.)
- No KRAS G12D detectable by ctDNA 6 months into the study

Safety, Tolerability, and Combination Potential

Ting-Hui Wu, MD
Vice President of Development



VS-7375 900 mg Monotherapy: High Dose Intensity with Very Low Discontinuations Due to AEs Across Tumor Types

	900 mg (N=48)
Median duration of Tx (range), months	3.0 (0.2 – 10.6)
TRAEs leading to	
Discontinuation	2%
Reduction	6%
Interruption	15%
TEAEs leading to	
Discontinuation	2%
Reduction	6%
Interruption	19%
Relative Dose Intensity Median (IQR)	97% (87–100%)

We believe dose modification rates and dose intensity are favorable compared to any class of targeted therapy

VS-7375 900 mg Tolerability is Characterized by Low Rates of Grade ≥3 and Serious TRAEs, Further Supporting it as the Go-Forward Dose

900 mg (N=48)		
Median duration of Tx (range), months		
3.0 (0.2 – 10.6)		
TRAEs	All Gr.	Gr.3
Patients with Any TRAE	81%	10%
Patients with Any GI TRAE	75%	2%
Patients with Any Serious TRAE	6%	

**Overall low ≥Gr.3
AEs or SAEs**

**Majority of GI adverse
events are low grade,
mostly grade 1**

No Grade 4 or 5 TRAEs.

VS-7375: Predominantly Low-Grade GI Adverse Events Without Evidence of Accumulation Over Time

900 mg
(N=48)

DoT, median (range): 3.0 (0.2 – 10.6) months

Preferred Term	Gr. 1, N(%)	Gr. 2, N(%)	Gr. 3, N(%)	Gr. ≥4, N(%)	All Gr., N(%)
GASTROINTESTINAL DISORDERS					
Nausea	20 (42)	7 (15)	1 (2)	0	28 (58)
Diarrhea	17 (35)	6 (12)	0	0	23 (48)
Vomiting	13 (27)	3 (6)	0	0	16 (33)

25% of patients have not reported a GI AE; By 6 months, ~40% of patients have no GI AEs

No accumulation of GI adverse events

Gr3 nausea in 1 patient that was transient

No Clinically Relevant Differences at 900 mg Since June 2026

VS-7375 900 mg QD is Highly Selective – Without AEs Associated with pan-RAS/KRAS Inhibition

900 mg (N=48)

DoT, median (range): 3.0 (0.2 – 10.6) months

Preferred Term	Gr. 1, N(%)	Gr. 2, N(%)	Gr. 3, N(%)	Gr. ≥4, N(%)	All Gr., N(%)
Rash¹	1 (2)	1 (2)	0	0	2 (4)
Mucositis	0	0	0	0	0
Stomatitis	0	0	0	0	0

Rash is not an inherent effect of targeting KRAS G12D

VS-7375: Low Rates of Hematologic Adverse Events at 900 mg

900 mg (N=48)

DoT, median (range): 3.0 (0.2 – 10.6) months

Preferred Term	Gr. 1, N(%)	Gr. 2, N(%)	Gr. 3, N(%)	Gr. ≥4, N(%)	ALL Gr., N(%)
Blood and lymphatic system disorders					
Anemia	1 (2)	2 (4)	0	0	3 (6)
Neutropenia	0	3 (6)	1 (2)	0	4 (8)
Thrombocytopenia	4 (8)	0	0	0	4 (8)

No Clinically Relevant Differences at 900 mg Since June 2026

VS-7375: Low Rates of Liver Related Adverse Events at 900 mg

900 mg (N=48)

DoT, median (range): 3.0 (0.2 – 10.6) months

Preferred Term	Gr. 1, N(%)	Gr. 2, N(%)	Gr. 3, N(%)	Gr. ≥4, N(%)	All Gr., N(%)
Investigations					
Aspartate aminotransferase increased	3 (6)	1 (2)	1 (2)	0	5 (10)
Alanine aminotransferase increased	3 (6)	1 (2)	0	0	4 (8)

No Clinically Relevant Differences at 900 mg Since June 2026

VS-7375 Demonstrates Combinability with SoC Across Indications to Address a Broad Population

Regimen	VS-7375 Dose		Target Indication(s)
	600 mg QD	900 mg QD	
Cetuximab	✓	✓	1L & 2L PDAC 2L+ (mostly 3L+) CRC
GnP	✓	✓	1L PDAC
CPem / Pembro	✓	✓	1L NSCLC
Cetux-mFOLFOX6	✓		1L CRC

✓ DLT cleared ✓ DLT evaluation ongoing

VS-7375 proven to be combinable with SoC across tumor types

- No overlapping AEs reported with anti-EGFR; similar anti-EGFR associated rash
- GI AE rates are similar to VS-7375 monoTx in GnP and CPem/Pemb combos with proper anti-emetic prophylaxis
- Frequency / severity of LFTs elevation or diarrhea are not meaningfully different to date in CPem/Pemb or pembro combos; overall favorable tolerability and activity

Path Forward: PDAC Phase 3 Trial Design & FDA Feedback, Data Summary

Michael G. Kauffman, MD, PhD
President of Development

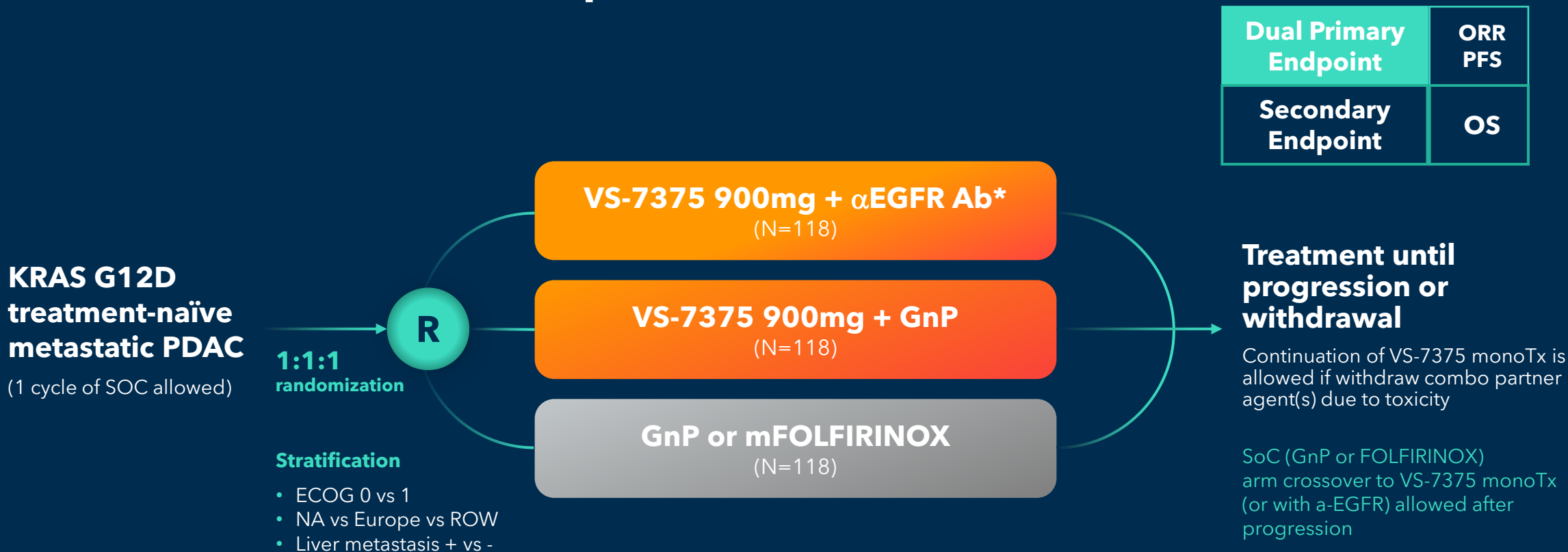


VS-7375: Advancing Potential Best-in-Class Profile to Pursue Parallel Clinical Development Paths



*Subject to discussions with the FDA.
Potential opportunities based on data from ongoing clinical trials; BTD: breakthrough therapy designation

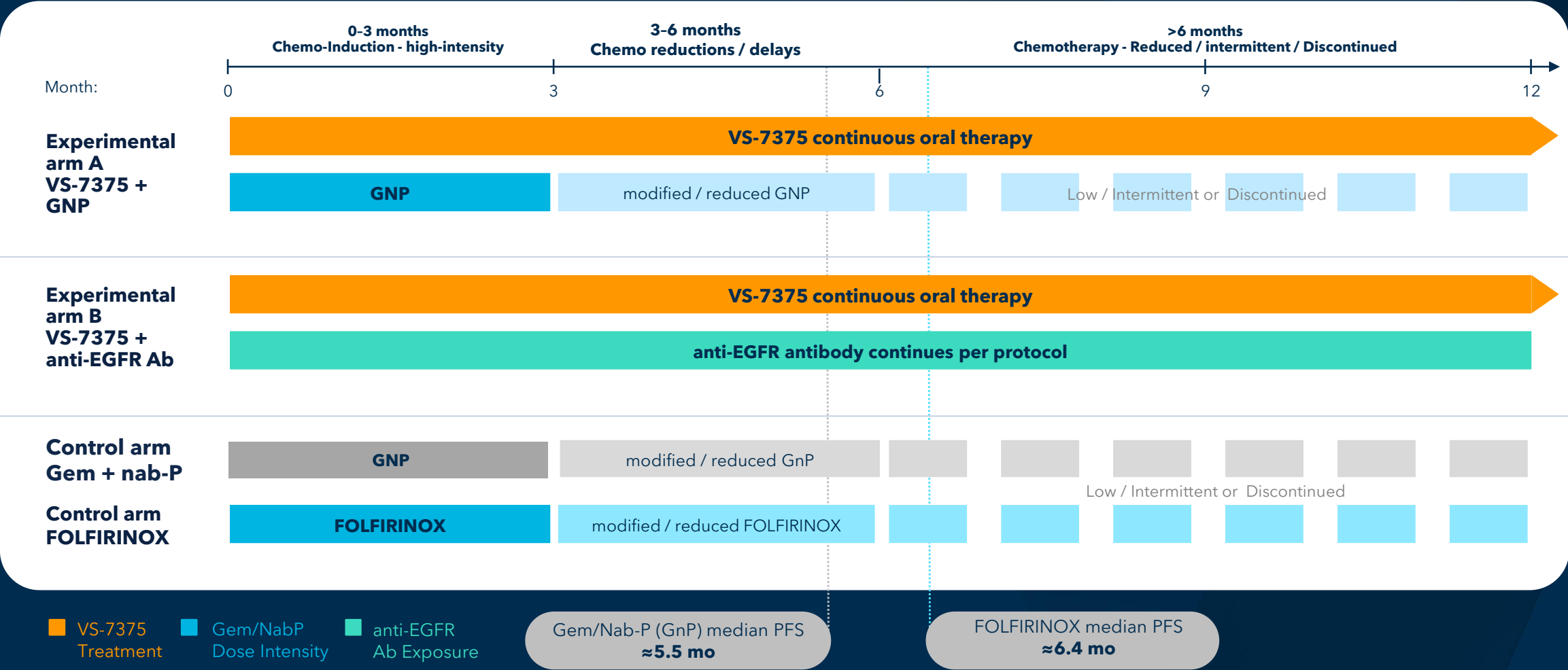
VS-7375 1L PDAC Phase 3: TARGET-D 301 Study Schema - Potential for Chemo Free Option



**REACHED ALIGNMENT ON PROTOCOL WITH FDA -
PLAN TO OPEN PHASE 3, 1L mPDAC TRIAL BY END OF 2026**

Frontline PDAC Phase 3 Protocol – Single Agent Efficacy Matters

Experimental arms maintain continuous VS-7375 exposure as cytotoxic chemotherapy intensity declines over time



Establishing **VS-7375** as Potential Best-in-Class KRAS G12D Inhibitor

1L POTENTIAL

Open 1L mPDAC Phase 3 trial expected by end of 2026;
CRC and NSCLC 1L Phase 3 trials expected to open in 1H 2027



2L ENTRY POINT

Complete enrollment in Phase 2 PDAC & CRC trials expected by end of 2026; NSCLC expected in Q2 2027

Expect to report initial data from Phase 2 2L PDAC trial in Q2 2027; NSCLC and CRC in 2H 2027

Potential Accelerated Approval Pathway

SINGLE-AGENT & COMBO POTENTIAL

Encouraging antitumor activity and tolerability across tumor types

First multi-tumor clinical data update

**PROMISING ANTITUMOR ACTIVITY AND A TOLERABLE, COMBINATION-READY PROFILE
DRIVES MEANINGFUL AND BROAD OPPORTUNITY**

Addendum



Anticipated VS-7375 Milestones

Q4 2026

- Expect to complete enrollment in the Phase 2 TARGET-D 201 (PDAC) and TARGET-D 203 (CRC) trials by end of 2026.
- Expect to report mature data from TARGET-D 101 mCRC 900mg combination cohort and initial data from the mPDAC cetuximab cohort at 600 mg by end of 2026.
- Company plans to open the TARGET-D 301 1L mPDAC trial by end of 2026.
- Company plans to meet with the FDA before the end of the year to review Phase 3 pivotal trial designs in 1L advanced NSCLC (TARGET-D 302) and 1L mCRC (TARGET-D 303).

1H 2027

- Company plans to open the TARGET-D 302 1L NSCLC trial in the first half of 2027.
- Company plans to open the TARGET-D 303 1L mCRC trial in the first half of 2027.
- Expect to report initial data from the 1L combination with Gem/NabP in Q1 2027

Q2 2027

- Expect to report initial data from Phase 2 TARGET-D 201 2L PDAC trial in Q2 2027.
- Expect to complete enrollment in the TARGET-D 202 (NSCLC) in Q2 2027.

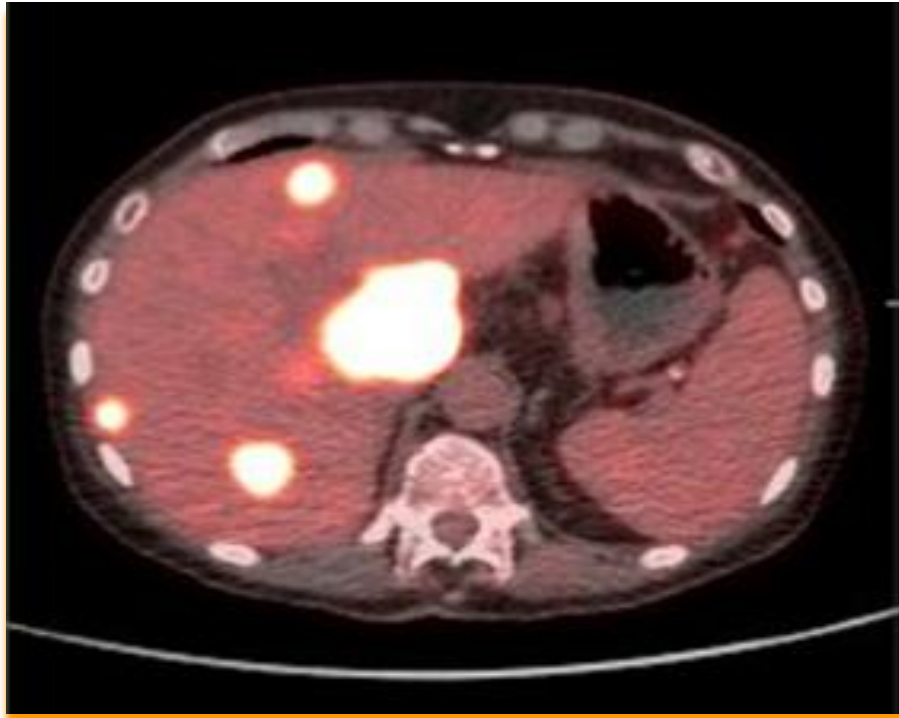
2H 2027

- Expect to report initial data from Phase 2 TARGET-D 202 2L NSCLC trial in 2H of 2027.
- Expect to report initial data from Phase 2 TARGET-D 203 2L CRC trial in 2H of 2027.

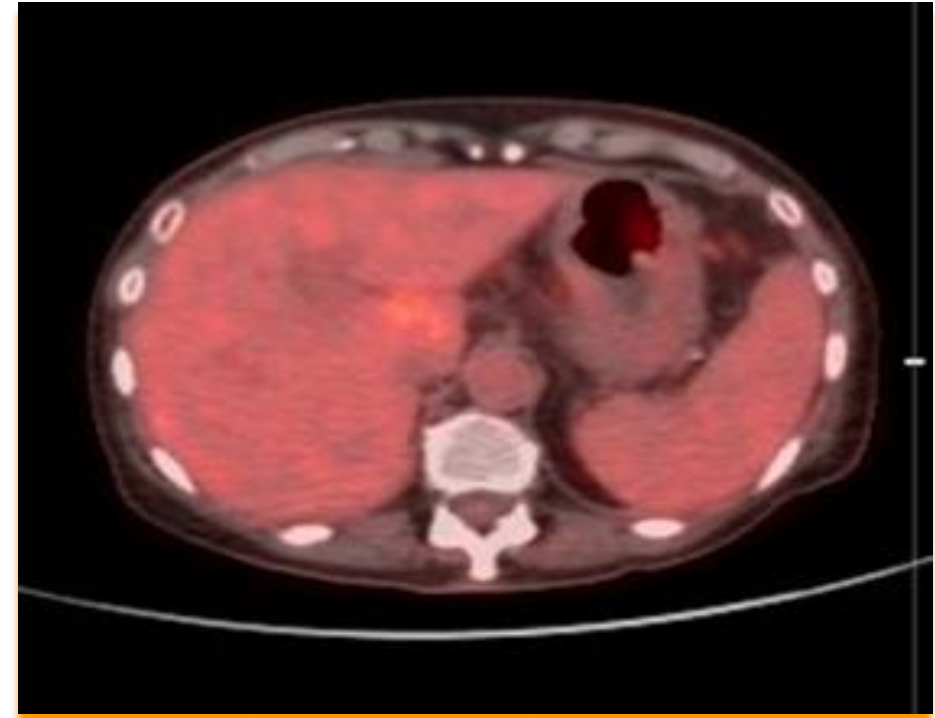
PET Scan Shows Tumor Metabolic Activity Markedly Reduced After 17 Days on **VS-7375** 900 mg Monotherapy in Patient with mPDAC

2L PDAC TARGET-D 201 Phase 2 Study

Baseline



Day 17



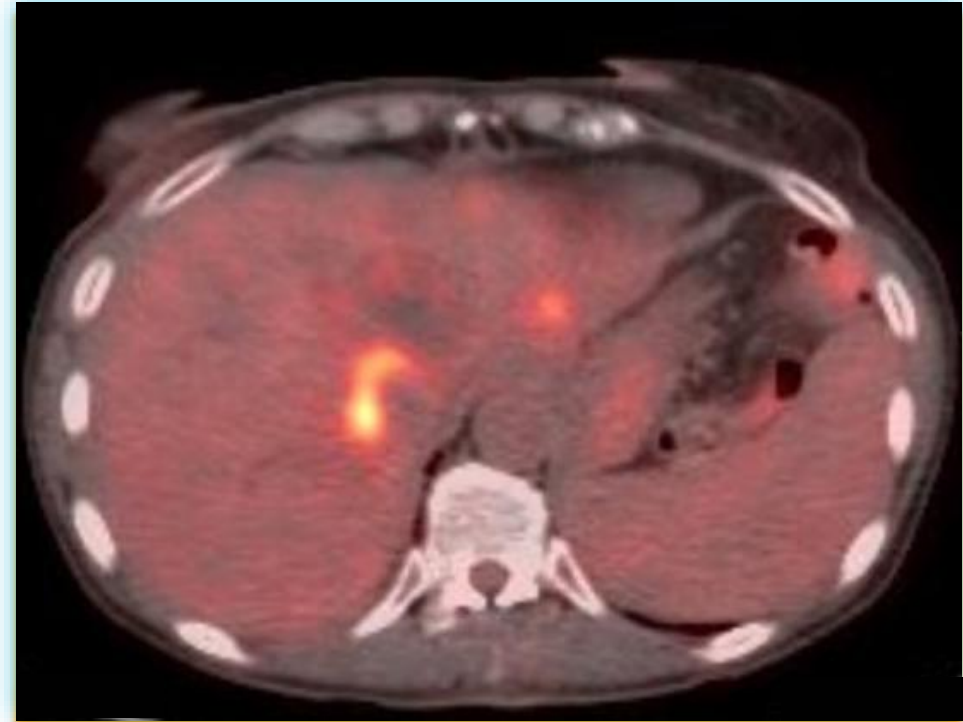
By Day 21, PET Scan Shows Tumor Metabolic Activity Markedly Reduced in Patient with mPDAC Treated with **VS-7375** 900 mg + Cetuximab Combo

2L PDAC TARGET-D 201 Phase 2 Study

SCREENING

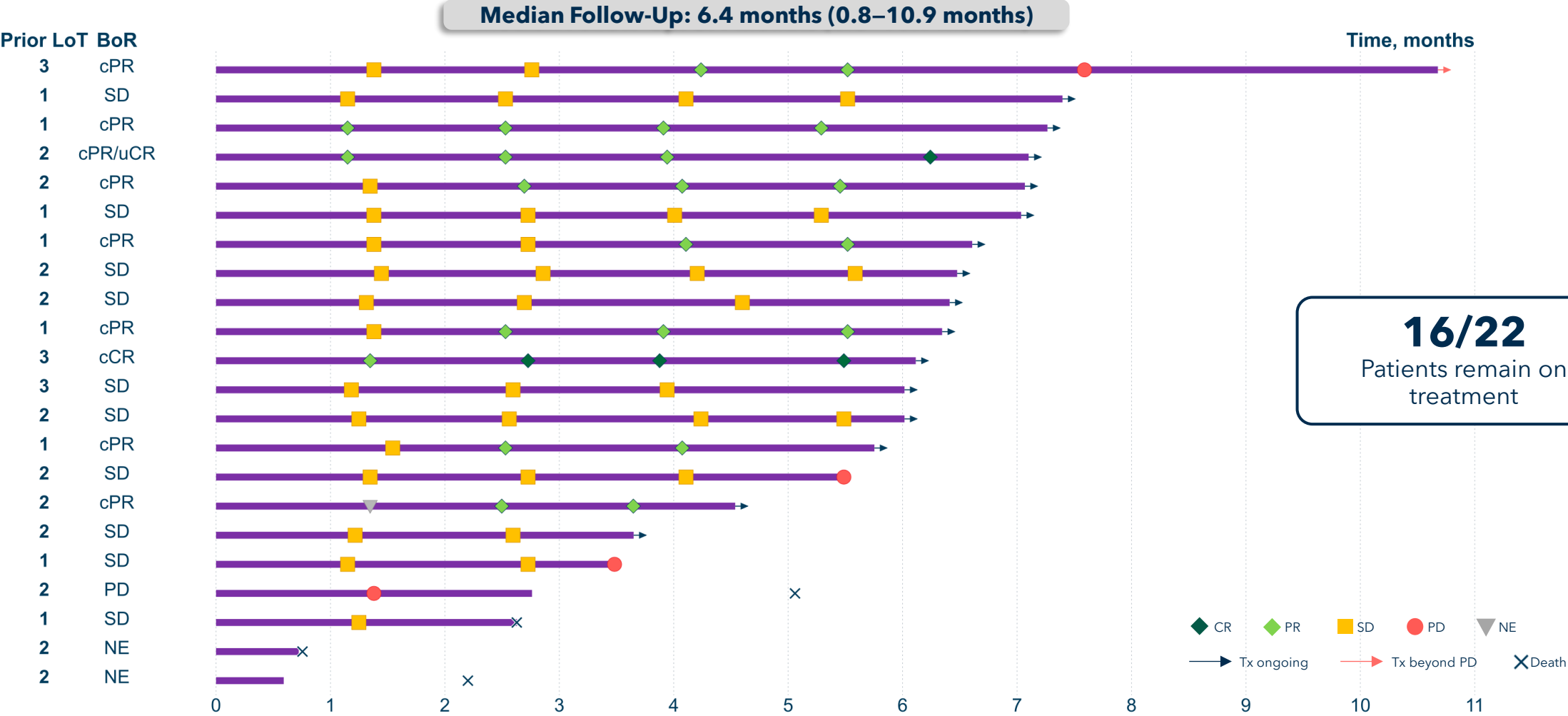


WEEK 3



VS-7375: First KRAS G12D Inhibitor to Demonstrate Favorable Monotherapy Durability in mPDAC

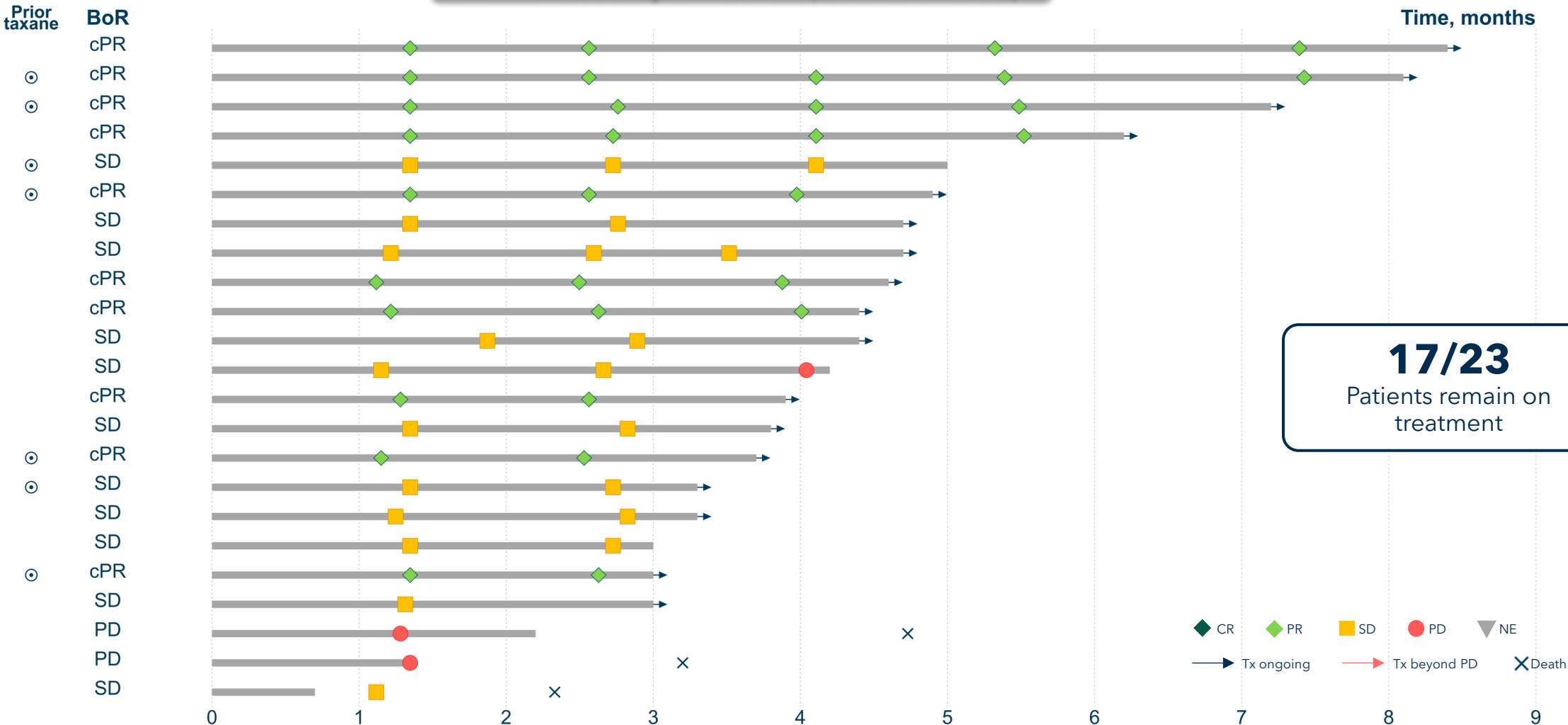
67% Landmark 6-month PFS rate | 80% Landmark 6-month OS in 2L/3L/4L



VS-7375 Shows Encouraging Durability at 600 mg in 2L+ NSCLC

72% landmark PFS rate at 6-months; mPFS not reached

Median Follow-Up: 4.4 months (2.4 – 12.4 months)



VS-7375 is Generally Well Tolerated Without Clear Dose-Dependent Safety Signals (≥5% of Either 600 mg or 900 mg QD); Consistent with June 2026 as Data Continue to Mature

System Organ Class Preferred Term	600 mg (N=73) mDoT (range) = 4.3 (0.5-11.0) mo					900 mg (N=48) mDoT (range) = 3.0 (0.2-10.6) mo				
	Gr. 1 n (%)	Gr. 2 n (%)	Gr. 3 n (%)	Gr. ≥4 n (%)	All Gr. n (%)	Gr. 1 n (%)	Gr. 2 n (%)	Gr. 3 n (%)	Gr. ≥4 n (%)	All Gr. n (%)
Gastrointestinal disorders										
Nausea	29 (40)	10 (14)	4 (5)	0	43 (59)	20 (42)	7 (15)	1 (2)	0	28 (58)
Diarrhoea	28 (38)	11 (15)	4 (5)	0	43 (59)	17 (35)	6 (12)	0	0	23 (48)
Vomiting	18 (25)	8 (11)	1 (1)	0	27 (37)	13 (27)	3 (6)	0	0	16 (33)
Abdominal pain	3 (4)	0	1 (1)	0	4 (5)	0	1 (2)	0	0	1 (2)
Constipation	7 (10)	0	0	0	7 (10)	0	0	0	0	0
Dyspepsia	4 (5)	0	0	0	4 (5)	2 (4)	0	0	0	2 (4)
Abdominal distension	3 (4)	0	0	0	3 (4)	2 (4)	1 (2)	0	0	3 (6)
General disorders and administration site conditions										
Fatigue	17 (23)	5 (7)	1 (1)	0	23 (32)	8 (17)	4 (8)	0	0	12 (25)
Investigations										
Lipase increased	5 (7)	4 (5)	1 (1)	0	10 (14)	0	1 (2)	1 (2)	0	2 (4)
Amylase increased	4 (5)	2 (3)	0	0	6 (8)	1 (2)	0	1 (2)	0	2 (4)
Alanine aminotransferase increased	3 (4)	0	1 (1)	0	4 (5)	3 (6)	1 (2)	0	0	4 (8)
Weight decreased	3 (4)	1 (1)	0	0	4 (5)	0	0	0	0	0
White blood cell count decreased	1 (1)	3 (4)	0	0	4 (5)	0	1 (2)	0	0	1 (2)
Aspartate aminotransferase increased	1 (1)	0	2 (3)	0	3 (4)	3 (6)	1 (2)	1 (2)	0	5 (10)
Blood and lymphatic system disorders										
Anaemia	2 (3)	6 (8)	1 (1)	0	9 (12)	1 (2)	2 (4)	0	0	3 (6)
Neutropenia ¹	4 (5)	3 (4)	1 (1)	0	8 (11)	0	3 (6)	1 (2)	0	4 (8)
Thrombocytopenia ²	2 (3)	0	0	0	2 (3)	4 (8)	0	0	0	4 (8)
Metabolism and nutrition disorders										
Decreased appetite	5 (7)	5 (7)	0	0	10 (14)	9 (19)	1 (2)	0	0	10 (21)
Nervous system disorders										
Dysgeusia	5 (7)	2 (3)	0	0	7 (10)	3 (6)	0	0	0	3 (6)
Skin and subcutaneous tissue disorders										
Pruritus	4 (5)	0	0	0	4 (5)	1 (2)	0	0	0	1 (2)

VS-7375 Cetuximab Combo (TRAE in ≥10% patients) : Consistent Tolerability with the Addition of Cetuximab-associated Rash

System Organ Class Preferred Term	Cetuximab + VS-7375 Dose Level: 600mg (n=41) + 900mg (n=11) 600 mg + 900 mg + Cetuximab (N=52)				
	Gr 1 n (%)	Gr 2 n (%)	Gr 3 n (%)	Gr ≥4 n (%)	All Gr n (%)
Skin and subcutaneous tissue disorders					
Dermatitis acneiform	20 (38)	8 (15)	3 (6)	0	31 (60)
Dry skin	11 (21)	0	1 (2)	0	12 (23)
Pruritus	6 (12)	1 (2)	0	0	7 (13)
Rash maculo-papular	5 (10)	2 (4)	0	0	7 (13)
Gastrointestinal disorders				0	
Diarrhoea	20 (38)	8 (15)	2 (4)	0	30 (58)
Nausea	19 (37)	11 (21)	2 (4)	0	32 (62)
Vomiting	16 (31)	7 (13)	1 (2)	0	24 (46)
Metabolism and nutrition disorders				0	
Decreased appetite	6 (12)	3 (6)	0	0	9 (17)
Hypomagnesaemia	9 (17)	1 (2)	0	0	10 (19)
Hypokalaemia	4 (8)	1 (2)	0	0	5 (10)
Investigations				0	
Weight decreased	6 (12)	1 (2)	0	0	7 (13)
General disorders and administration site conditions				0	
Fatigue	12 (23)	5 (10)	2 (4)	0	19 (37)
Nervous system disorders				0	
Dizziness	6 (12)	0	0	0	6 (12)
Headache	4 (8)	3 (6)	0	0	7 (13)

VS-7375 GnP Combo (TRAE reported in ≥2 patients) : Consistent Tolerability with the Addition of Hematological AEs and Neuropathy (most likely associated with GnP)

System Organ Class Preferred Term	VS-7375 + GnP Dose Level: 600mg (n=13) + 900mg (n=8) 600 mg + 900 mg + GnP (N=21)				
	Gr 1 n (%)	Gr 2 n (%)	Gr 3 n (%)	Gr ≥4 n (%)	All Gr n (%)
Blood and lymphatic system disorders				0	
Neutropenia ¹	1 (5)	2 (10)	10 (48)	0	13 (62)
Thrombocytopenia ²	4 (19)	3 (14)	0	0	7 (33)
Anaemia	0	3 (14)	3 (14)	0	6 (29)
Gastrointestinal disorders					
Nausea	8 (38)	3 (14)	0	0	11 (52)
Diarrhoea	6 (29)	3 (14)	0	0	9 (43)
Vomiting	5 (24)	3 (14)	0	0	8 (38)
Constipation	2 (10)	0	0	0	2 (10)
Stomatitis	1 (5)	1 (5)	0	0	2 (10)
General disorders and administration site conditions					
Fatigue	6 (29)	3 (14)	3 (14)	0	12 (57)
Pyrexia	4 (19)	0	0	0	4 (19)
Influenza like illness	1 (5)	0	1 (5)	0	2 (10)
Skin and subcutaneous tissue disorders					
Alopecia	2 (10)	4 (19)	0	0	6 (29)
Investigations					
White blood cell count decreased	0	4 (19)	2 (10)	0	6 (29)
Alanine aminotransferase increased	1 (5)	1 (5)	0	0	2 (10)
Aspartate aminotransferase increased	1 (5)	0	1 (5)	0	2 (10)
Lymphocyte count decreased	0	1 (5)	2 (10)	0	3 (14)
Weight decreased	2 (10)	1 (5)	0	0	3 (14)
Nervous system disorders					
Neuropathy peripheral	1 (5)	2 (10)	0	0	3 (14)
Peripheral sensory neuropathy	0	2 (10)	0	0	2 (10)
Metabolism and nutrition disorders					
Decreased appetite	1 (5)	1 (5)	0	0	2 (10)
Dehydration	0	2 (10)	0	0	2 (10)
Musculoskeletal and connective tissue disorders					
Myalgia	2 (10)	0	0	0	2 (10)

VS-7375 CPPemb Combo (TRAE reported in ≥2 patients) Outlines Combinability

System Organ Class Preferred Term	VS-7375 + CCPem Dose Level: 600mg (n=9)				
	Gr 1 n (%)	Gr 2 n (%)	Gr 3 n (%)	Gr 4 n (%)	All Gr n (%)
Blood and lymphatic system disorders					
Neutropenia ¹	0	0	1 (11)	1 (11)	2 (22)
Anaemia	0	1 (11)	1 (11)	0	2 (22)
Gastrointestinal disorders					
Nausea	2 (22)	4 (44)	0	0	6 (67)
Diarrhoea	1 (11)	3 (33)	2 (22)	0	6 (67)
Vomiting	2 (22)	2 (22)	0	0	4 (44)
General disorders and administration site conditions					
Fatigue	4 (44)	1 (11)	0	0	5 (56)
Investigations					
Aspartate aminotransferase increased	0	1 (11)	1 (11)	0	2 (22)
Nervous system disorders					
Dysgeusia	1 (11)	1 (11)	0	0	2 (22)
Eye disorders					
Dry eye	1 (11)	1 (11)	0	0	2 (22)

VS-7375: 2L+ mPDAC: Patient Disposition and Baseline Characteristics

Baseline Characteristics

Age, years, median (range)	66.5 (46-79)
Sex, n (%)	
Male	12 (55%)
Female	10 (45%)
Race, n (%)	
White	18 (82%)
Black	1 (5%)
Asian	2 (9%)
Other	1 (5%)
ECOG, n (%)	
0	7 (32%)
1	15 (68%)
Stage at initial diagnosis, n (%)	
I-III	11 (50%)
IV	11 (50%)
Prior LoT, median (range)	2 (1-3)
Liver metastases at enrollment, n (%)	13 (59%)
Baseline SLD, mm, median (range)	61 (13-194)

VS-7375: 2L+ mCRC: Patient Disposition and Baseline Characteristics

Baseline Characteristics

Age, years, median (range)	55 (35-77)
Sex, n (%)	
Male	5 (83%)
Female	1 (17%)
Race, n (%)	
White	5 (83%)
Other	1 (17%)
ECOG, n (%)	
0	4 (67%)
1	2 (33%)
Liver mets at enrollment, n (%)	3 (50%)
Prior LoT, median (range)	2 (2-3)

VS-7375: 2L+ NSCLC: Patient Disposition and Baseline Characteristics

Baseline Characteristics

Age, years, median (range)	68 (30-85)
Sex, n (%)	
Male	14 (61%)
Female	9 (39%)
Race, n (%)	
White	17 (74%)
Asian	4 (17%)
Other	2 (9%)
ECOG, n (%)	
0	6 (26%)
1	17 (74%)
Smoking Status	
Current/Past	8 (35%)
Never	15 (65%)
# of prior herapy	
1	14 (61%)
2	9 (39%)
Prior therapy, n (%)	
Platinum	23 (100%)
Immune checkpoint inhibitor	22 (96%)
Taxane	7 (30%)

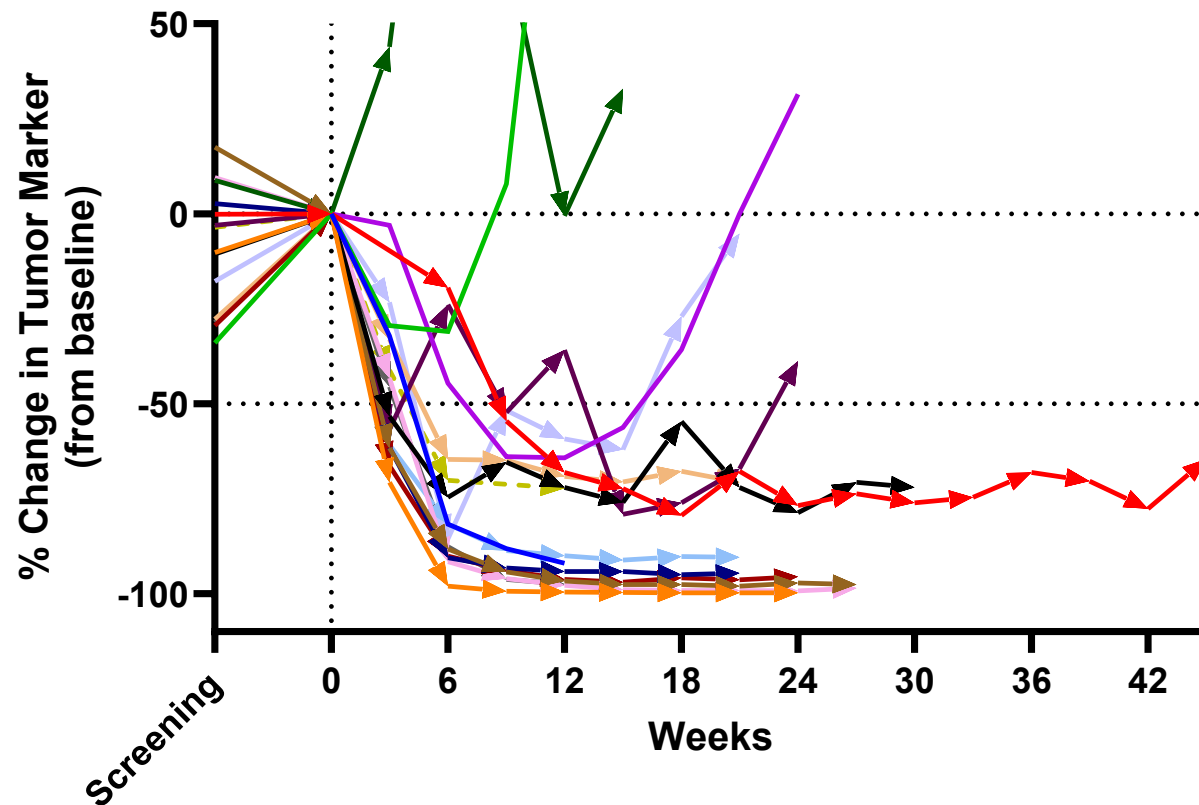
VS-7375 Monotherapy: <5% of Patients Discontinue Due to AEs Across Tumor Types at the 600 mg and 900 mg Dose Levels

	600 mg (n=73)	900 mg (N=48)
Median follow-up (range), months	4.3 (0.5 – 11.0)	3.0 (0.2 – 10.6)
TRAEs Leading to		
Discontinuation	3%	2%
Reduction	10%	6%
Interruption	21%	15%
TEAEs Leading to		
Discontinuation	4%	2%
Reduction	11%	6%
Interruption	38%	19%

VS-7375: Safety Profile Supports 900 mg as Go-Forward Dose

	600 mg (n=73)	900 mg (N=48)		
Median follow-up (range), months	4.3 (0.5 – 11.0)	3.0 (0.2 – 10.6)		
TRAEs	All Gr.	≥Gr.3	All Gr.	≥Gr.3
<i>Patients with Any TRAE</i>	90%	19%	81%	10%
<i>Patients with Any GI TRAE</i>	86%	11%	75%	2%
<i>Patients with Any Serious TRAE</i>	5%		6%	

88% of Patients with PDAC treated with 900mg VS-7375 Monotherapy had a >50% Reduction in CA19-9 or CEA Levels from Baseline



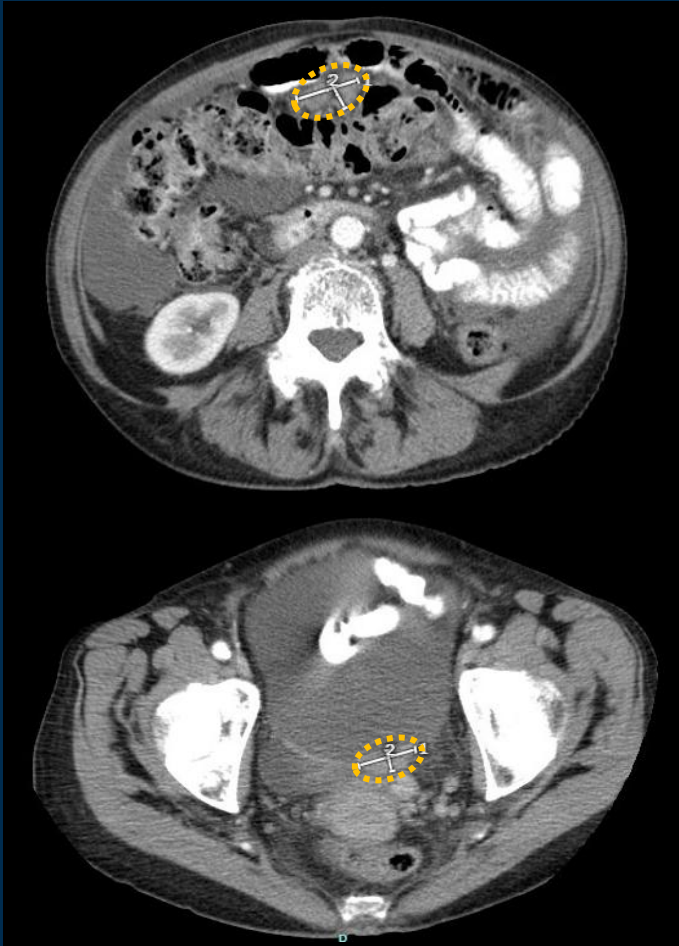
*1 patient (0102-013, gold dashed line) with change in CEA levels shown, max -72.2% decrease from baseline

- **17 PDAC patients** treated with 900mg VS-7375 monotherapy with elevated CA19-9 (>38 U/mL) or CEA levels (>5 ng/mL) at baseline and at least one scheduled on-treatment measurement
 - 16 patients with change in CA19-9 levels, 1 patient with change in CEA levels (normal CA19-9 at baseline)
- **88% (15/17) of patients had >50% reduction in tumor marker levels (either CA19-9 or CEA) from baseline while on treatment**
 - Includes 1 patient with CEA level decrease

Complete Response at Week 12 with VS-7375 900 mg QD Monotherapy in 79 y/o Female with mPDAC

Baseline Lesion:

Mesentery, peritoneum
(SLD: 64mm)



Week 12:

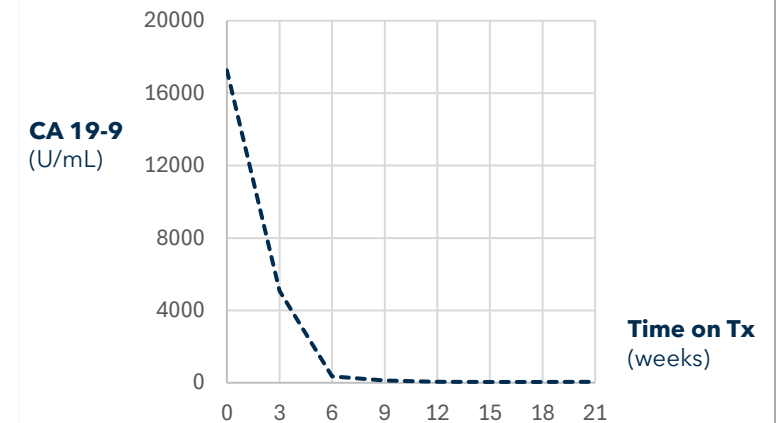
CR -100%

(SLD: 0mm) Response ongoing

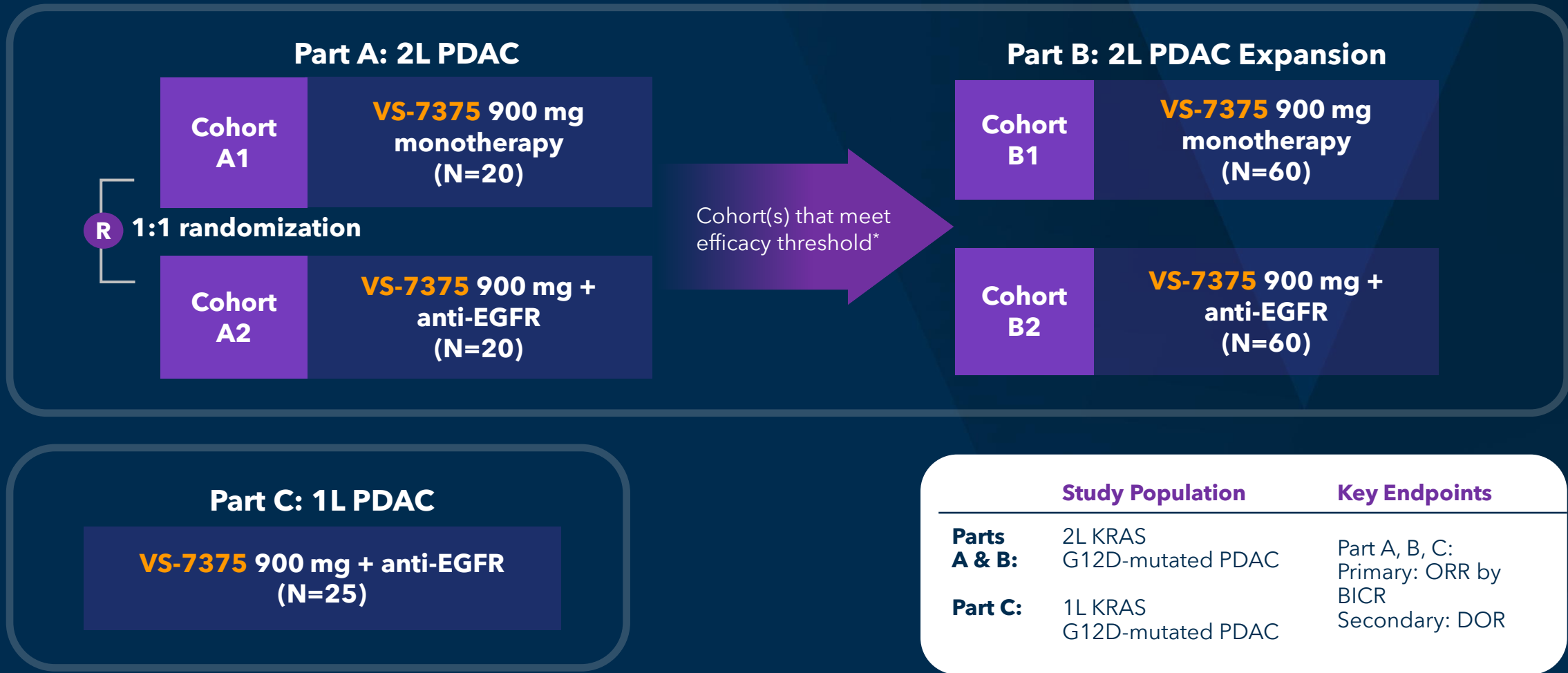


- Prior Gem/NabP (6 mos of Tx) , NALIRI (11 mos of Tx), and FOLFOX (3 mos of Tx)
- Investigator-reported abdominal pain and distention (caused by ascites) resolved in 2 weeks
- Selected AE: G2 diarrhea (resolved), G2 fatigue, G2 anorexia
- Highly elevated CA-19-9 levels at baseline with >60% reduction in 3 weeks and >99% reduction after 6 weeks

>99% reduction of CA 19-9



Maximizing the Opportunity in PDAC Through VS-7375 Monotherapy and EGFR Combination Strategies



Evaluating **VS-7375** Monotherapy in Advanced NSCLC, Including Patients with Brain Metastases

 **TARGET-D 202**

Part A: 2L/3L NSCLC

Cohort A

VS-7375 900 mg QD
(N=20)

Confirm
900 mg QD is the
go-forward dose

Part B: 2L/3L NSCLC

Cohort B

Preferred dose of
VS-7375
(N=60)

Part C: 2L/3L/4L

VS-7375 900 mg QD
with asymptomatic untreated
brain metastasis
(N=25)

Study Population

Key Endpoints

**Parts
A & B:**

- Prior treatment with platinum-based chemo & ICI
- At least 1 and no more than 2 prior systemic lines of therapy

Primary: ORR by BICR

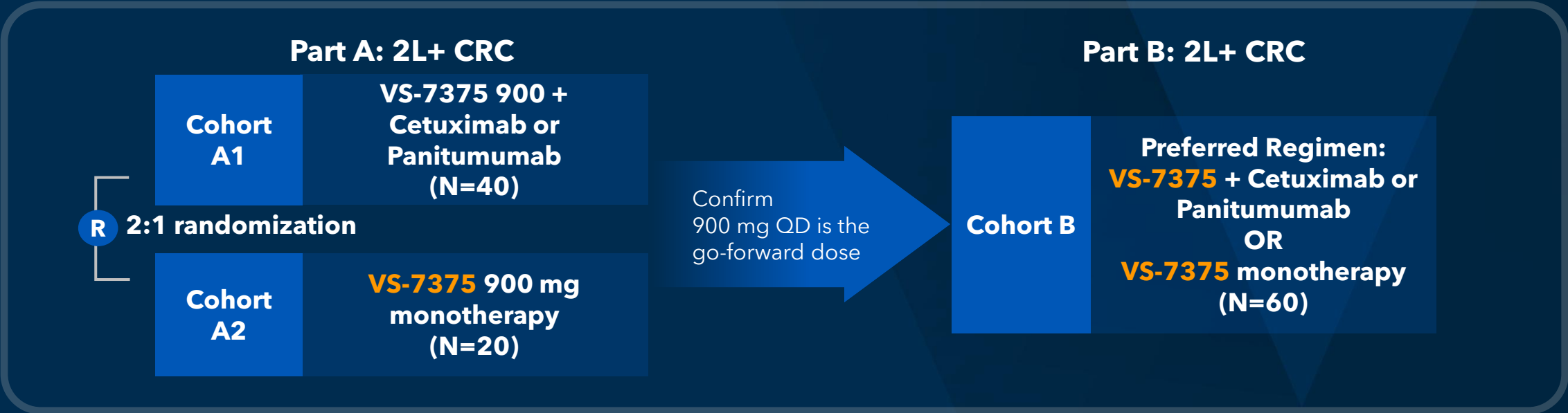
Secondary: DOR

Part C:

Received at least 1 and no more than 3 prior systemic lines of therapy

Intracranial ORR by mRECIST v1.1 by BICR

Advancing a **VS-7375** Combination Strategy with EGFR Inhibitors and Chemotherapy in Metastatic CRC



Part C: 1L CRC

VS-7375 900 mg + Cetuximab + mFOLFOX6 (N=30)

	Study Population	Key Endpoints
Part A, B:	Prior SoC: fluoro-pyrimidine, irinotecan, oxaliplatin, VEGFi [#]	Primary: ORR by BICR Secondary: DOR
Part C:	No prior tx for metastatic disease	Safety/Tolerability

Significant Unmet Need Remains in Previously Treated mCRC*

Study	Regimen	LoT	ORR	DCR	mPFS (months)	mOS (months)
RECOURSE ¹	Trifluridine/tipiracil	3L+	2%	44%	2.0	7.1
SUNLIGHT ²	Trifluridine/tipiracil + bevacizumab	3L	6%	77%	5.6	10.8
CORRECT ³	Regorafenib	2L+	1%	41%	2.0	6.4
FRESCO-2 ⁴	Fruquintinib	3L+	2%	56%	3.7	7.4

6%

Best ORR across trials

5.6 mo

Longest median PFS

