## GFH375/VS-7375 Program Update: Joint Presentation by GenFleet and Verastem





## **GFH375: Dive in the ESMO Data and More**



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Efficacy and Safety of GFH375 Monotherapy in Previously Treated Advanced *KRAS G12D* Mutant Pancreatic Ductal Adenocarcinoma (PDAC)

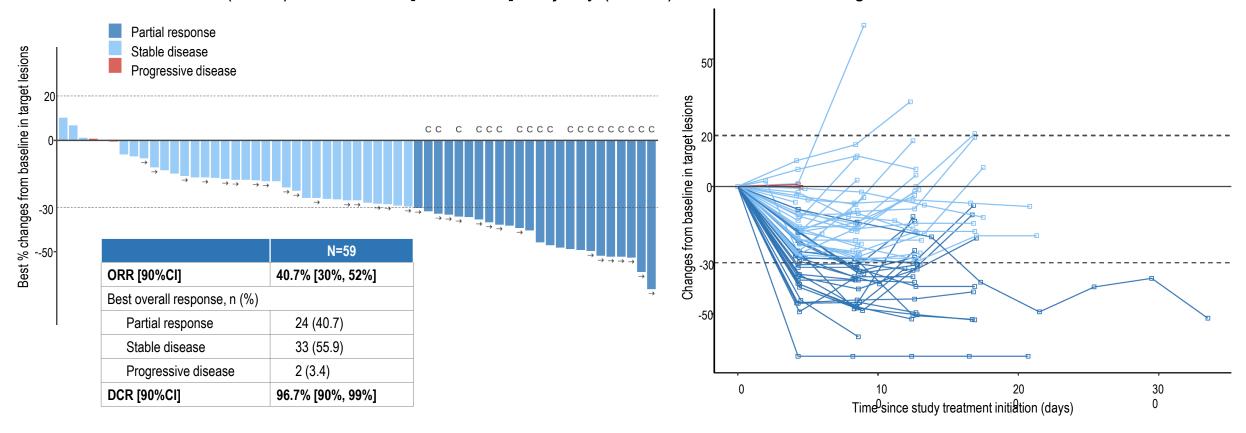
<u>Aiping Zhou<sup>1</sup></u>, Zhihua Li<sup>2</sup>, Yuping Sun<sup>3</sup>, Zuoxing Niu<sup>4</sup>, Heshui Wu<sup>5</sup>, Lingjun Zhu<sup>6</sup>, Hong Zong<sup>7</sup>, Ying Yuan<sup>8</sup>, Zhengbo Song<sup>9</sup>, Ziming Li<sup>10</sup>, Lin Wu<sup>11</sup>, Xiujuan Qu<sup>12</sup>, Jingdong Zhang<sup>13</sup>, Yu Wang<sup>14</sup>, Haige Shen<sup>14</sup>, Huaqiang Zhu<sup>14</sup>, Sharley Zheng<sup>14</sup>, Shuang Wang<sup>14</sup>, Zhao Gui<sup>14</sup>

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#### **Best Overall Response**

- ORR was 40.7% (24/59), 90%Cl was [30%, 52%].
- DCR was 96.7% (57/59), 90%CI was [90%, 99%]. Majority (91.5%) had reduction in target lesions.



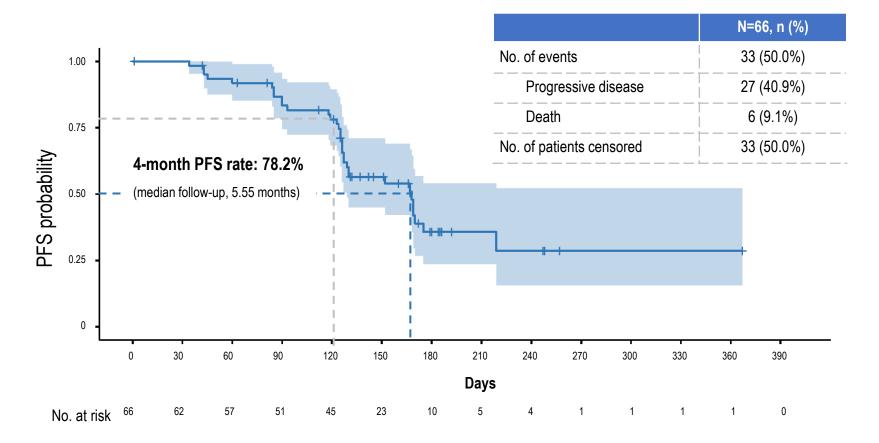
Data cut-off date: September 27, 2025. All patients received first dose of GFH375 for at least 4 months prior to the cut-off date. Seven patients had no post-treatment tumor assessments due to early dropout: 2 due to AEs not related to GFH375 (1 upper gastrointestinal hemorrhage and respiratory failure); 1 started new anticancer therapy; 4 early discontinued due to patient decision. Left figure: "C" represents confirmed responders. Arrows indicate treatment ongoing.

Abbreviations: CI, confidence interval. DCR, disease control rate. ORR, objective response rate.

Aiping Zhou, MD

#### **Progression-Free Survival**

- Median PFS was 5.52 months (90%CI: 4.27, 7.20), with a median follow-up time 5.65 months (90%CI: 4.96, 6.08).
- 4-month PFS rate was **78.2%** (90%CI: 69.8%, 87.5%).

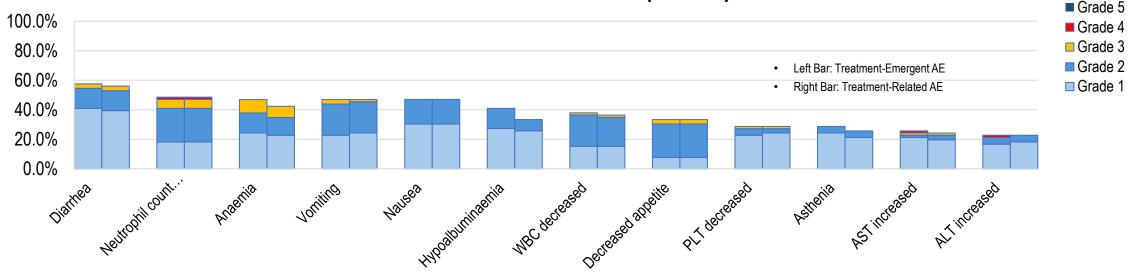




#### **Common Adverse Events**

- The safety profile of GFH375 in KRAS G12D mutant PDAC patients is consistent with previous report. 1,2
  - Common TRAEs were gastrointestinal and hematological AEs; most were grade 1 or 2 and manageable with supportive treatment.
  - Most frequent TRAEs (≥20%) were diarrhea (56.1%), neutrophil count decreased (48.5%), vomiting (47.0%), nausea (47.0%), anaemia (42.4%), white blood cell count decreased (36.4%), decreased appetite (33.3%), hypoalbuminaemia (33.3%), platelet count decreased (28.8%), asthenia (25.8%), aspartate aminotransferase increased (24.2%), and alanine transferase increased (22.7%).













#### **Post ESMO Focus: ORR Fluctuation**



Sample size

**PDAC** baseline

**Prior treatment** 

**Line of patients** 





10:15 - 11:45 Proffered paper session 2: GI tumours, upper digestive

CHAIRS: MAEVE LOWERY, CHRISTOPH BENEDIKT WESTPHALEN

#### LBA84 : GFH375 Monotherapy

Advanced, KRAS G12D mutated, previously treated PDAC, n=66 patients

	GENERAL SECURITY CO. DAYS
Age, median (range), years	60 (35, 74)
≥60, n (%)	35 (53.0%)
Male, n (%)	35 (53.0%)
ECOG PS 1, n (%)	66 (100%)
Histological type, n (%)	
Adenocarcinoma	64 (97.0%)
Adenosquamous carcinoma	2 (3.0%)
Stage IV at study entry, n (%) 6	63 (95.5%)
Baseline metastasis, n (%)	70000
Liver	52 (78.8%)
Lung	19 (28.8%)
Peritoneum	19 (28.8%)
Bone	12 (18.2%)

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		CHACUS EXAMPLED SHIPSE
	Number of prior lines of anticancer therapy, (range)	(1, 5)
	1, n (%)	21 (31.8%)
$\rightarrow$	≥2, n (%)	45 (68.2%)
	Prior anticancer therapy, n (%)	0.0000000000000000000000000000000000000
	Gemcitabine-containing	61 (92.4%)
	Fluorouracil-containing	50 (75.8%)
	Irinotecan-containing	35 (53.0%)
	Immune checkpoint inhibitors	22 (33.3%)

Real world data : < 10% of PDAC patients receive 3<sup>rd</sup> line chemotherapy\*

\*Macarulla et al, ESMO Real World Data & Digital Oncology 2025





Maeve Lowery
Invited Discussant LBA84 and
22150

**BERLIN AUDITORIUM - HUB 27** 



#### **PDAC: Worse Baseline Condition Compared to Competitors**

		GFH375 <sup>1</sup> 600 mg QD	Zoldonrasib <sup>2</sup> 150-1200 mg daily	Daraxonrasib <sup>3</sup> 300 mg daily
		N = 66	N = 104	N = 76
ECOG PS	0	0	29%	34%
ECOG PS	1	100%	71%	66%
Median no. of PLoT (rang	ge)	2 (1-5)	2 (0-6)	2 (1-7)
1L		31.8%	NA	49%
2L+		68.2%	NA	51%
Prior treatment lines per	SoC* , n(%)			
1L		12 (18.2%)	NA	NA
2L+		54 (81.8%)	NA	NA
Prior ICI		33.3%	NA	NA
Liver metastasis at basel	line	78.8%	86%	67%
Peritoneum metastasis a	t baseline	28.8%	NA	NA

Cross-trial comparison. Source: ¹ESMO 2025. ²ASCO GI 2025. ³ASCO GI 2025. \*defined as participants who had received gemcitabine- or 5-Fu-based chemotherapy and without ICI.

Abbreviations: PLoT, prior lines of therapy. 2L+, second line and beyond. NA, not available.



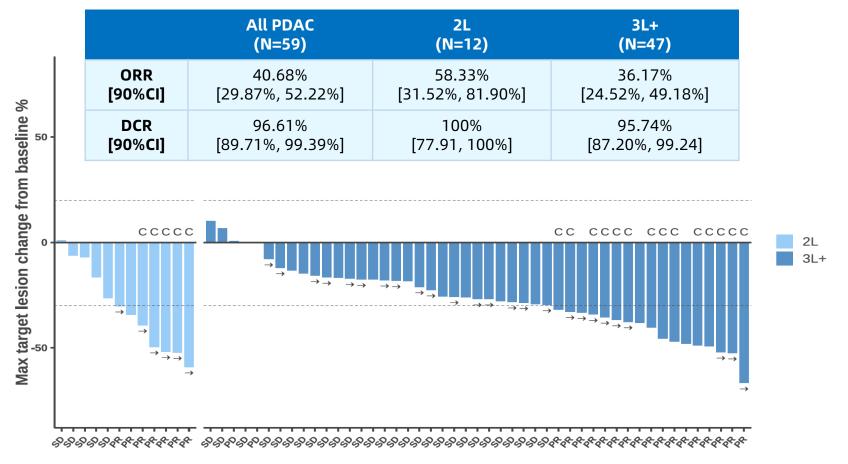
#### **PDAC:** The Non-standard 1st-line Treatments in the Study

Participant	1 <sup>st</sup> line Regimen
1	AG+ <b>S1+Nimotuzumab</b>
2	AG+ <b>S1</b>
3	AG+ <b>S1</b>
4	AG + Sintilimab
5	AG+ Camrelizumab
6	NALIRIFOX+ Cadonilimab
7	GEM + OXA + <b>Avastin + Sintilimab</b>
8	AG + <b>Lenvatinib</b>
9	G <b>S</b>



#### **PDAC: Subgroup Analysis - ORR**

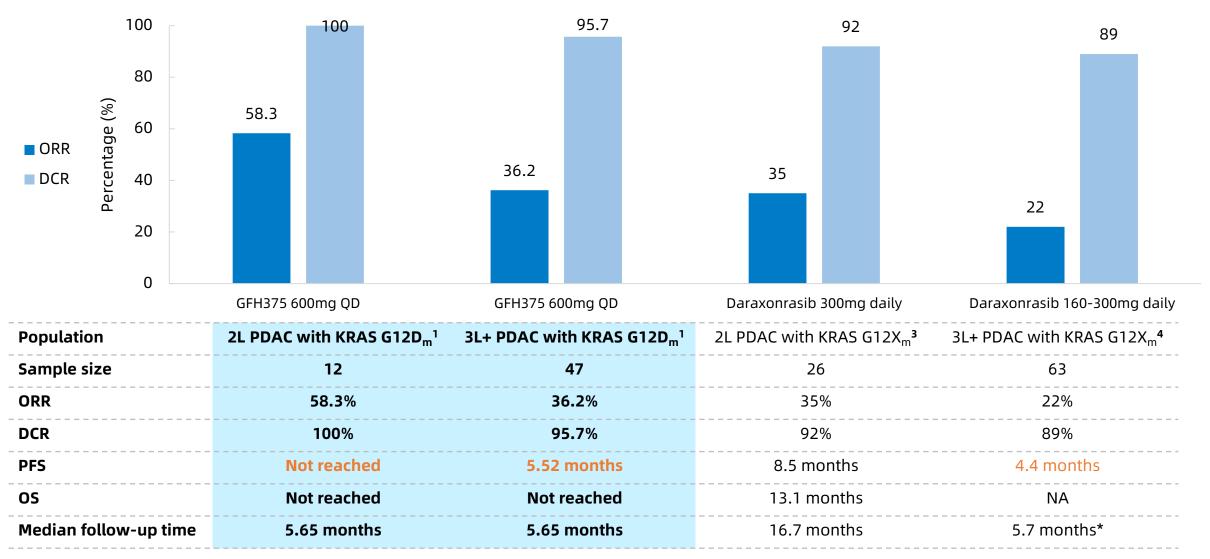
59 participants had measurable disease at baseline and at least one post-baseline tumor assessment



Data cut-off date: September 27, 2025. All participants received first dose of GFH375 for at least 4 months prior to the cut-off date. Seven participants had no post-treatment tumor assessments due to early dropout: 2 due to AEs not related to GFH375 (1 upper gastrointestinal hemorrhage and 1 respiratory failure); 1 started new anticancer therapy; 4 early discontinued due to participant decision. Figure: "C " represents confirmed responders. Arrows indicate treatment ongoing. The bars for 3 participants are not shown in the waterfall plot: a1 had best overall response (BOR) as SD, and the best percentage change from baseline in was 0%. b2 had progressive disease as their BOR: one had a target lesion decrease by 0.4% from baseline with non-target lesion progression; the other had target lesions increase by 0.7% from baseline with non-target lesion progression. Abbreviations: CI, confidence interval. DCR, disease control rate. ORR, objective response rate.

#### GENFLEET THERAPEUTICS

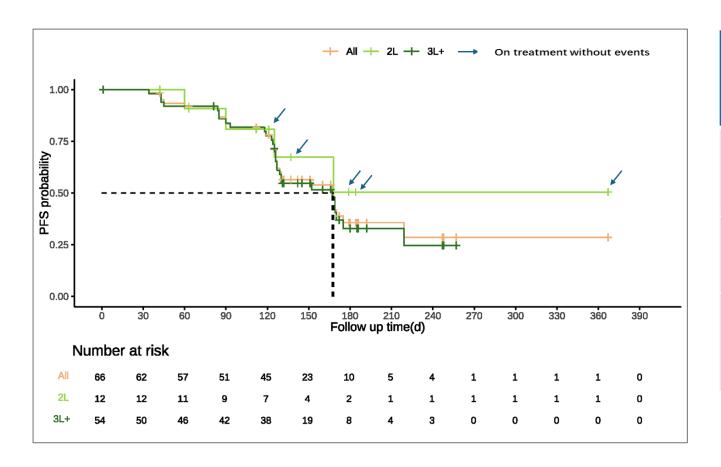
#### **PDAC: Improved Efficacy Compared to Competitors**



Cross-trial comparison. Source: <sup>1</sup>ESMO 2025. <sup>2</sup>ASCO GI 2025. <sup>3</sup>Events & Presentations | Revolution Medicines. <sup>4</sup>ENA 2024. \*For both KRAS G12 and RAS mutant. Abbreviations: 2L+, second line and beyond. ORR, objective response rate. DCR, disease control rate. PFS, progression-free survival. OS, overall survival. NR, not reached. NA, not available.

#### **PDAC: Subgroup Analysis – PFS**





	All PDAC (N=66)	2L (N=12)	3L+ (N=54)
Median PFS (months)	5.52	Not reached	5.52
No. of Events	33	4 (maturity: 33%)	29
On Treatment without Event	25	5	20

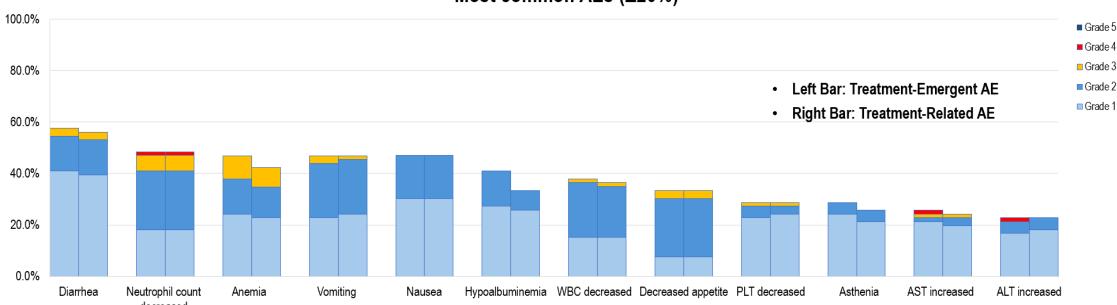
Median follow-up time: 5.65 months





- We reported TEAE in addition to TRAE
- The only case of G4 liver tox was TEAE, not TRAE
  - Billiary tract obstruction due to enlarged lymphode which is not drug-related
- The only case of G4 neutropenia was previously treated with immunotherapy
- No new safety signal has been found
- US patients showed initial better profile than China patients (see VSTM update)

#### Most common AEs (≥20%)







The overall safety/tolerability of GFH375 is better than that of daraxonrasib.

	GFH375 600mg QD <sup>1</sup>	H375 600mg QD¹ Daraxonrasib 300mg daily²	
	2L+ PDAC, N=66	2L+ PDAC, N=83	1L PDAC, N=40
TRAE	100%	96%	95%
G3 or above	31.8%	34%	35%
Leading to discontinuation	3.0%	0	10%
Leading to reduction	6.1%	30%	33%
Leading to interruption	27.3%	43%	53%
Mean dose intensity*	93%	86%	85%

Source: ¹ESMO 2025. ²Events & Presentations | Revolution Medicines. \*Refers to the average amount of a drug administered per unit of time. It is used to assess treatment adherence and drug exposure and directly influences therapeutic efficacy and the risk of adverse events.

Abbreviations: 1L, first line. 2L+, second line and beyond. TRAE, treatment-related adverse event.





- GI Tox: Which one is better?
- Hema Tox: No significant difference in G3 and above
- Liver Tox: lower G3 and above

Source: ¹ESMO 2025. ²Events & Presentations | Revolution Medicines.
Abbreviations: 1L, first line. 2L+, second line and beyond. WBC, white blood cell. PLT, platelet. AST, aspartate transaminase. ALT, alanine transaminase. NA, not available.

	GFH375 600mg QD <sup>1</sup>		Daraxonrasib 300mg daily <sup>2</sup>			
	2L+ PDAC, N=66		2L+ PDAC, N=83		1L PDAC, N=40	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Gastrointestinal disorders						
Diarrhea	56.1%	3.0%	52%	4%	58%	10%
Vomiting	47.0%	1.5%	36%	0	50%	5%
Nausea	47.0%	0	39%	0	50%	3%
Decreased appetite	33.3%	3.0%	NA	NA	15%	0
Hematological toxicities						
Neutrophil count decreased	48.5%	7.6%	6%	4%	0	0
Anemia	42.4%	7.6%	8%	<b>7</b> %	5%	3%
WBC count decreased	36.4%	1.5%	NA	NA	NA	NA
PLT decreased	28.8%	1.5%	10%	4%	8%	0
Liver enzyme abnormalities						
AST increased	24.2%	1.5%	10%	4%	8%	0
ALT increased	22.7%	0	7%	2%	8%	0
Skin toxicities						
Rash	3.0%	0	90%	7%	88%	8%

## ICI Treatment is NOT Approved in PDAC, yet 33% Participants Had Prior ICI Treatment

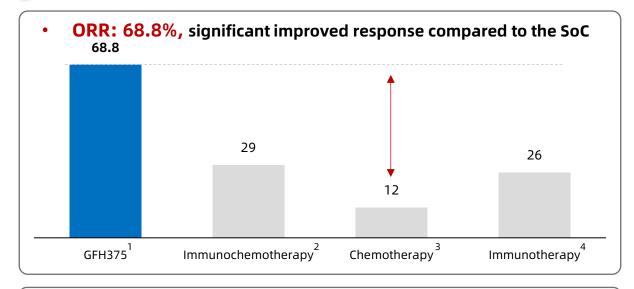


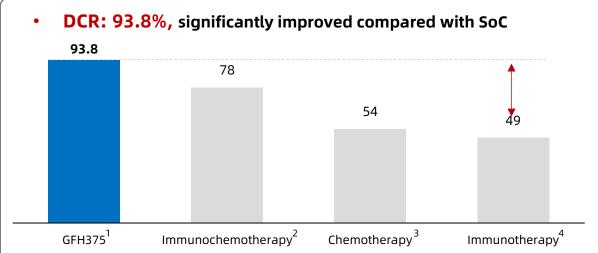
 The incidence of grade ≥3 TEAEs/TRAEs, TEAEs/TRAEs leading to treatment interruption, and SAEs/TRSAEs were higher in participants with prior ICI than in the ICI naïve participants (ESMO2025 data)

AE, n (%)	ICI pretreated (N=22)	ICI naïve (N=44)
At least one ≥Grade 3 TEAE	15(68.2%)	18 (40.9%)
At least one ≥Grade 3 TRAE	10 (45.5%)	11 (25%)
TESAE	9 (40.9%)	8 (18.2%)
TRSAE	5 (22.7%)	4 (9.1%)
Dose modification due to TEAE	11 (50%)	17 (38.6%)
Dose modification due to TRAE	8 (36.4%)	13 (29.5%)
Discontinuation due to TEAE	2 (9.1%)	3 (6.8%)
Discontinuation due to TRAE	1 (4.5%)	1 (2.3%)
Dose reduction due to TEAE	2 (9.1%)	2 (4.5%)
Dose reduction due to TRAE	2 (9.1%)	2 (4.5%)
Dose interruption due to TEAE	9 (40.9%)	16 (36.4%)
Dose interruption due to TRAE	7 (31.8%)	11 (25%)

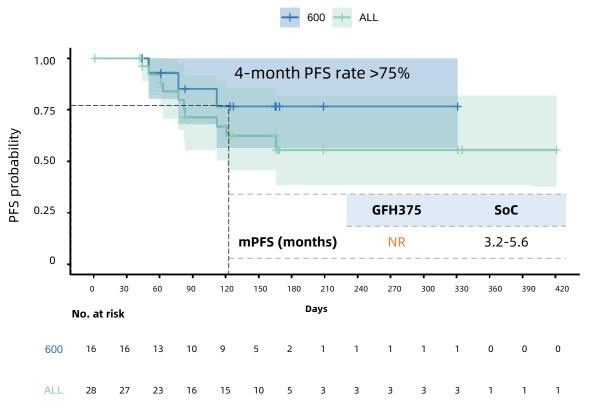
## NSCLC: Better Efficacy in Pretreated Participants Compared to SoC







mPFS was not reached.



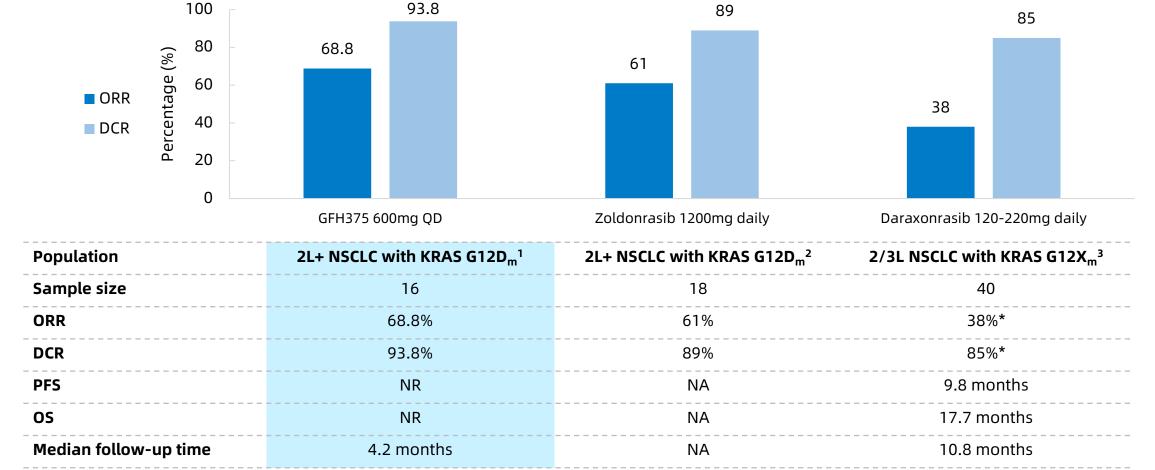
Median follow up times for participants across all dose levels and at 600 mg QD were: 5.5 and 4.2 months, respectively.

Source: <sup>1</sup>WCLC 2025. <sup>2</sup>J Clin Oncol. 2024 Dec;42(34):4029-4039. <sup>3</sup>N Engl J Med. 2015 October 22; 373(17): 1627-1639. <sup>4</sup>Annals of Oncology, Volume 30, Issue 8, 1321 - 1328. Abbreviations: ORR, objective response rate. DCR, disease control rate. PFS, progression free survival. NR, not reached.



#### **NSCLC: Improved Efficacy Compared to Competitors**

- Best-in-class as G12D monotherapy for NSCLC
- Supporting single-arm accelerated approval for 2L+ NSCLC

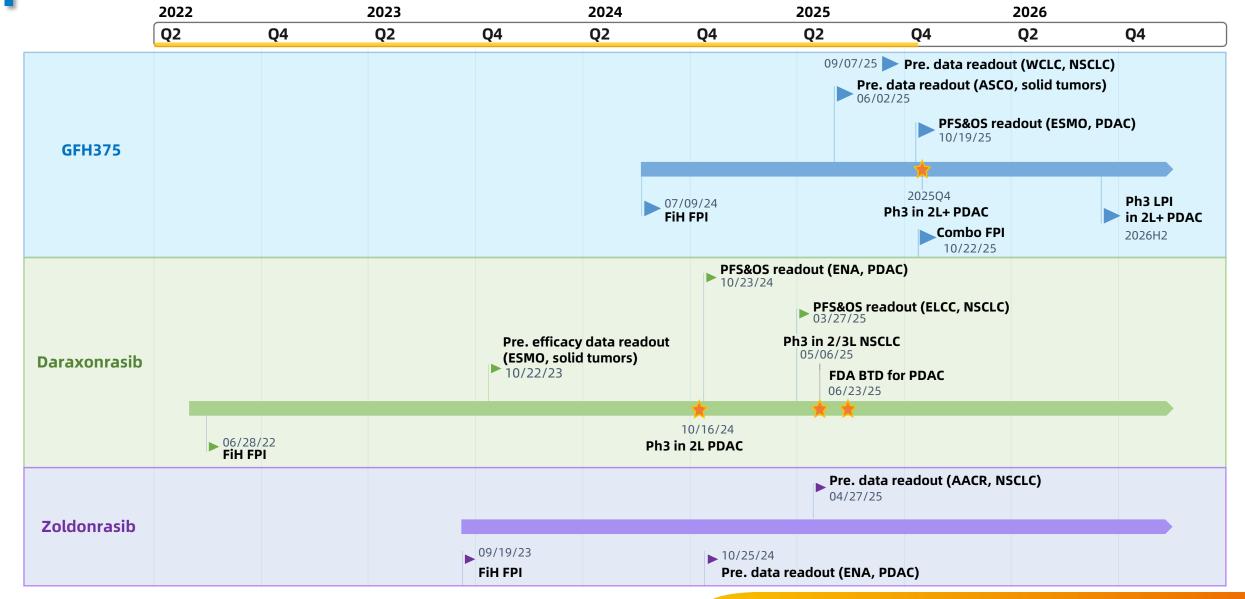


Cross-trial comparison. Source: ¹WCLC 2025. ²AACR 2025. ³ELCC 2025 (participants were required not have received docetaxel previously). \*confirmed.

Abbreviations: 2L+, second line and beyond. ORR, objective response rate. DCR, disease control rate. PFS, progression-free survival. OS, overall survival. NR, not reached. NA, not available.



#### **Clinical Development Status of GFH375 and Competitors**



#### One of Global Leaders in Developing RAS-targeted Therapeutics



#### **Validation**

- Marketed product
- Proven expertise in developing RAS inhibitors

#### **Efficiency**

- First-to-market speed of fulzerasib development
- Rapid enrollment in GFH375 program

**GenFleet's** 

**RAS-targeted** 

**Matrix** 

#### Depth

- Global clinical development
- Diverse targets and modalities

#### Innovation

- First-in-class combo
- Next-generation ADC by FAScon

#### **Fulzerasib**

KRAS G12C

- Mono: First-to-market in China, third globally
- Combo: potential 1st-line NSCLC standard-of-care

**GFH375** 

**KRAS G12D** 

- 1st-tier development of oral G12D inhibitor
- Global clinical development: phase II in China and phase I/IIa in the US

**GFH276** 

**Pan RAS** 

- Differentiated RAS (ON) mechanism: non-degradative molecular glue
- 1st-tier development of pan RAS (ON) inhibitor in China

**GFS784** 

**FAScon** 

- Globally innovative ADC platform: synergy between large and small molecules
- Integrating therapeutic antibody and targeted payload

#### **Marching towards a Leading Pancreatic Cancer Franchise**



#### **Diverse RAS-targeted therapies**

**KRAS G12C** 

**GFH925** 

KRAS G12D

**GFH375** 

Pan RAS (ON)

**GFH276** 

EGFR-Pan RAS ADC

**GFS784** 

2025E

80-90%\*

Pancreatic cancer patients with RAS mutations

\*Source: Seminars in Oncology

**Over 700 thousand** 

Global incidence (2035E)

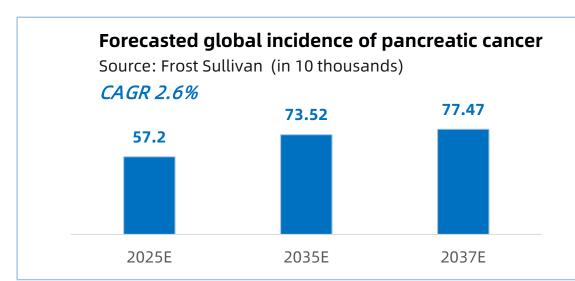
100 Bn-yuan market

Global pancreatic cancer drug sales (2037E)

2037E

#### World's 1st bispecific antibody for cancer cachexia

GDF15/IL-6 GFS202A



## Forecasted global market of pancreatic cancer drugs Source: Research Nester (100 million RMB) CAGR 13.6% 932.24 201.87

Confidential 24

2035E



# Delivering Novel Therapies for RAS/MAPK Pathway Driven Cancers

October 2025





#### **Disclaimers**

#### **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 approval and commercialization of AVMAPKI™ FAKZYNJA™ CO-PACK (avutometinib capsules; defactinib tablets) as a treatment for adult patients with KRAS-mutant 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 with respect to VS-7375, the status of enrollments for and potential of the results of the RAMP 301 Phase 3 trial to confirm the results of the RAMP 201 study specific to KRAS mutation traditions and the structure of our planned and pending clinical trials, the potential clinical value of various of the Company's clinical trials, including the RAMP 201J, RAMP 205, RAMP 301 and VS-7375 trials, the timing of commencing and completing trials, including topline data reports, interactions with regulators, the timing of commencing and completing trials, including topline data reports, interactions with regulators, the timing of commencing and potential for additional development programs involving the Company's lead compound and the potential market opportunities of, and estimated addressable markets for, our drug candidates. The words "anticipate," "estimate," "expect," "may," "plan," "target," "potential," "would," "continue," "can" and similar expressions are intended to identify 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.

Applicable risks and uncertainties include the risks and uncertainties, among other things, regarding: the success in the development and potential commercialization of our product candidates, including avutometinib in combination with other compounds, including defactinib, LUMAKRAS and others; the uncertainties inherent in research and development, such as negative or unexpected results of clinical trials, the occurrence or timing of applications for our product candidates that may be filed with regulatory authorities in any jurisdictions; whether and when regulatory authorities in any jurisdictions may approve any such applications that may be filed for our product candidates, and, if approved, whether our product candidates will be commercially successful in such jurisdictions; our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates; the scope, timing, and outcome of any legal proceedings; 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 testing of our product candidates and preliminary or interim data from clinical trials will be predictive of the results or success 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, which may delay our development programs, including delays in review by the U.S. Food and Drug Administration (FDA); the risk that our RAMP 301 trial may not confirm the results of the RAMP 201 trial specific to the use of AVMAPKI FAKZYNJA CO-PACK in adult patients with KRAS mutant recurrent LGSOC; the risks associated with preliminary and interim data, which may not be representative of more mature data, including with respect to interim duration of therapy data; that our product candidates will 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 be unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so; that the mature RAMP 201 data and associated discussions with the FDA may not support the scope of a new drug application submission for the avutometinib and defactinib combination in LGSOC including with respect to Kirsten rat sarcoma viral oncogene homolog (KRAS) wild-type (KRAS wt); that our product candidates may experience manufacturing or supply interruptions or failures; that any of our third-party contract research organizations, clinical sites, or contractors, among others, who we rely on 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 will 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 will 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 have sufficient cash to fund our contemplated operations, including certain of our product development programs; that we may not attract and retain high quality personnel; that we or Chuqai Pharmaceutical Co., Ltd. may fail to fully perform under the avutometinib license agreement; 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. will fail to fully perform under the asset purchase agreement with Secura Bio, Inc. including in relation to milestone payments; that we will not see a return on investment on the payments we have and may continue to make pursuant to the collaboration and option agreement with GenFleet, or that GenFleet will fail to fully perform under the agreement; that we may not be able to establish new or expand on existing collaborations or partnerships, including with respect to inlicensing 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 will not pursue or submit regulatory filings for our product candidates; that, due to the recent change in presidential administration and the significant reduction in the FDA's workforce and potential reductions to the FDA's budget, we may experience a materially 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, 2024, as filed with the Securities and Exchange Commission (SEC) on March 20, 2025, and in any subsequent filings with the SEC, which are available at <a href="www.sec.gov">www.sec.gov</a> and <a href="www.sec.gov">www.verastem.com</a>. 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.

#### **Use of Non-GAAP Financial Measures**

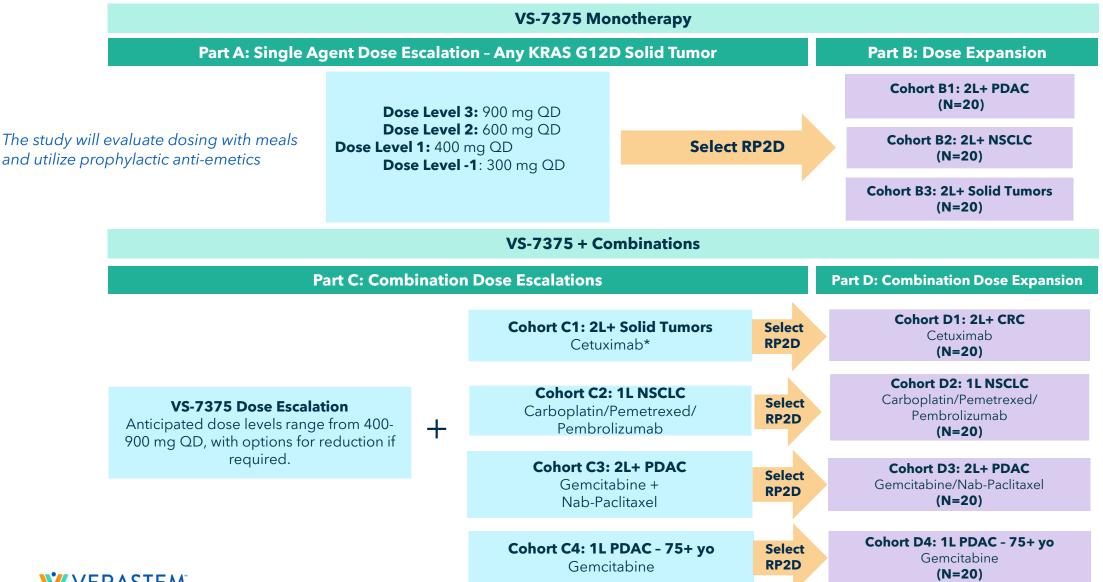
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## VS-7375-101 Study Schema, Efficiently Testing KRAS G12D+ Indications with Monotherapy and SOC Combinations





## **Accelerated Development Approach Builds on Preliminary First-in-Human Study Findings**

#### Multi-Arm Clinical Study Evaluating Monotherapy and Combinations

#### Efficacious starting dose:

- 400 mg starting dose supported by monotherapy efficacy/safety in FIH study
- Evaluating GI side effect mitigations:
  - Use prophylactic anti-emetics
  - Evaluate dosing with and without food
  - Evaluate additional formulation
- Multiple, high-value indication strategy:
  - Monotherapy expansion cohorts in PDAC & NSCLC
  - Combination cohorts with cetuximab for CRC, chemotherapy for PDAC, chemo plus I-O for NSCLC
- Expand to geographies outside of U.S.

#### **FDA Engagement Plans**

- Granted Fast Track Designation for:
  - First-line in patients with KRAS G12D locally advanced or metastatic PDAC and
  - Patients with KRAS G12D locally advanced or mPDAC who received at least one prior line of standard systemic therapy in July 2025
- Plan to pursue Breakthrough Therapy Designation
- Accelerated clinical development with FDA input



#### **VS-7375-101 Study Update as of October 23, 2025**

- First two monotherapy dose levels (400 mg QD and 600 mg QD) cleared,
   with no dose-limiting toxicities (DLT's) reported
- Promising anti-tumor activity observed in patients with various solid tumors, including advanced pancreatic ductal adenocarcinoma
- No nausea, vomiting, or diarrhea greater than Grade 1 was observed
- Enrollment initiated for VS-7375 in combination with cetuximab in patients with advanced KRAS G12D mutant solid tumors, including colorectal cancer
- Plan to report an interim safety and efficacy update on the Phase 1/2a trial in the first half of 2026



#### **Next Steps in VS-7375 Clinical Program**

✓ Reported a preliminary update on the Phase 1 monotherapy dose escalation in Q4 2025

Initiate the dose escalation cohorts in combination with cetuximab, chemotherapy, and chemotherapy with checkpoint-inhibitor for CRC, PDAC, and NSCLC, respectively, in Q4 2025

Subject to the results of the Phase 1 monotherapy dose escalation, **initiate monotherapy expansion cohorts** in PDAC, NSCLC, and other solid tumors Subject to the results of the combination dose escalation cohorts with VS-7375, **initiate combination expansion cohorts** in CRC, PDAC, and NSCLC





