Delivering Novel Therapies for RAS/MAPK Pathway Driven Cancers

VERASTEM ONCOLOGY

At Verastem Oncology, we are advancing breakthroughs in oncology to address some of the toughest challenges in RAS/MAPK-pathway driven cancers - aggressive cancers that, despite advances in drug development, lack effective therapies targeting these critical mutations.

We developed and commercialized the first-ever FDA approved treatment for KRAS-mutated recurrent low-grade serous ovarian cancer (LGSOC), a rare ovarian cancer, and are continuing to advance a clinical pipeline of novel small molecule drugs that inhibit critical signaling pathways in cancers that promote cancer cell survival and tumor growth, including RAF/MEK inhibition, FAK inhibition, and KRAS G12D inhibition.

> *RAS/MAPK pathway-driven cancers are difficult to treat and often resistant to current therapies. With deep expertise and a novel scientific approach, we are committed to staying one step ahead of cancer, blocking not just a single pathway but the multiple escape routes tumors use to grow, spread, and develop resistance mechanisms.*

We are committed to addressing RAS/MAPK-pathway-driven cancers with novel and innovative treatment approaches that provide a more complete blockade of the signaling that drives the growth of RAS/MAPK pathway-dependent tumors.

> *30% of all cancers have KRAS, HRAS, or NRAS mutations, with mutant KRAS found in 90% of pancreatic cancers, 30% in LGSOC, and 25% in solid tumors.*

Pioneers for Low-Grade Serous Ovarian Cancer
Not all ovarian cancers are the same. LGSOC is a distinct and different disease from other types of ovarian cancers, such as high-grade serous ovarian cancer, and as such, it requires a different clinical approach to treatment.

> *An estimated 6,000-8,000 women in the U.S. and 80,000 worldwide are living with LGSOC.*

Maximizing the Synergistic Potential of Avutometinib plus Defactinib for Advanced Solid Tumors
Verastem is currently conducting clinical trials with avutometinib plus defactinib in RAS/MAPK-driven tumors as part of its **R**af **A**nd **M**ek **P**rogram or **RAMP**.

> *70% of LGSOC tumors have RAS/MAPK pathway mutations.*

RAMP 301 (GOG-3097/ENGOT-ov81/NCRI/NCT06072781): RAMP 301 is an international Phase 3 trial, which will serve as a confirmatory study for the initial indication and has the potential to support an expanded indication regardless of KRAS mutation status.

For more information, email media@verastem.com or visit www.verastem.com. Follow us on LinkedIn.

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More than 90% of pancreatic cancers have a KRAS mutation.

RAMP 205 (NCT05669482): Verastem is conducting an open-label Phase 1b/2a clinical trial designed to evaluate the safety, tolerability, and efficacy of avutometinib and defactinib in combination with standard-of-care chemotherapy (gemcitabine and Nab-paclitaxel) in patients with previously untreated metastatic pancreatic ductal adenocarcinoma. RAMP 205 is supported by a PanCAN Therapeutic Accelerator Award.

KRAS mutations occur in approximately 25% of NSCLC. One of the most common types of KRAS mutations is G12C, which occurs in approximately 13% of patients with NSCLC.

VS-7375-101 as Monotherapy and in Combination (NCT07020221): Verastem is conducting a Phase 1/2 clinical trial in the U.S., with the potential to expand globally, evaluating the safety and efficacy of VS-7375, a potential best-in-class selective oral KRAS G12D (ON/OFF) inhibitor, in patients with advanced KRAS G12D-mutated solid tumors such as pancreatic, colorectal, and non-small cell lung cancers.

Company History at a Glance:

- **2010**: Founded to target cancer stem cells
- **2012**: IPO; NASDAQ listing (VSTM)
- **2017**: Focus shifts to RAS/MAPK pathway-driven cancers; supports FRAME, an investigator-sponsored Phase 1/2 study of avutometinib and defactinib in LGSOC, NSCLC, and other solid tumors
- **2021**: Breakthrough Therapy designation from FDA for avutometinib and defactinib in LGSOC
- **2022:** PanCan Therapeutic Accelerator Award for pancreatic cancer research
- **2024:** Orphan Drug Designation for avutometinib alone or in combination with defactinib for recurrent LGSOC
- **2024:** Orphan Drug Designation for avutometinib plus defactinib for the treatment of pancreatic cancer
- **2024**: NDA acceptance under accelerated approval and priority review for avutometinib plus defactinib
- **2025**: IND clearance for VS-7375 to initiate a Phase 1/2a study in advanced KRAS G12D mutant solid tumors
- **2025**: FDA approval of avutometinib plus defactinib combination therapy in KRAS-mutated recurrent LGSOC

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