

Press Release

Astellas Doses First Patient in Phase 3 Study of *setidegrasib* in Previously Treated KRAS G12D-Mutated Advanced Non-Small Cell Lung Cancer

- *Study evaluates novel, investigational KRAS G12D-targeted protein degrader setidegrasib versus docetaxel in previously treated patients with advanced NSCLC -*
- *Milestone marks second Phase 3 study of setidegrasib initiated within six months -*

TOKYO, 24 September, 2026 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, “Astellas”) today announced that the first patient has been dosed in a Phase 3 study evaluating *setidegrasib*, a novel, investigational KRAS G12D-targeted protein degrader, versus docetaxel in people with KRAS G12D-mutated locally advanced (unresectable) or metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on or after initial platinum-based chemotherapy and checkpoint inhibitor therapy (CPI).¹

Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer-related death worldwide, with NSCLC accounting for approximately 80% of cases.^{2,3} Around 5% of people with NSCLC have a KRAS G12D mutation.⁴ Despite advances in targeted treatment for other molecularly defined forms of NSCLC, there are currently no therapies approved specifically for people with KRAS G12D-mutated NSCLC.^{3,5} Patients whose disease progresses on or after initial treatment currently rely on standard systemic options, such as chemotherapy.⁵

Setidegrasib is an investigational targeted protein degrader designed to degrade and eliminate the disease-driving KRAS G12D protein. By removing this protein, *setidegrasib* may help disrupt cancer cell signaling and destroy cancer cells.⁴ This Phase 3 study in previously treated NSCLC builds on early clinical evidence published in *The New England Journal of Medicine* in March 2026, which demonstrated antitumor activity and a manageable safety profile in patients with KRAS G12D-mutated solid tumors, supporting the proposed mechanism of action of *setidegrasib*.⁴

Hidegori Kitai, M.D., Ph.D., Department of Respiratory Medicine, Faculty of Medicine, Hokkaido University, Japan:

“For too long, patients with KRAS G12D-mutated non-small cell lung cancer have had limited treatment options after standard therapies. This Phase 3 study represents an important step forward for the field, helping to build the evidence needed to understand whether setidegrasib could offer a potential new approach for this molecularly defined patient population.”

Tadaaki Taniguchi, M.D., Ph.D., Chief Research and Development Officer, Astellas:

“The initiation of this Phase 3 study in NSCLC, our second Phase 3 study of setidegrasib within six months, reflects continued progress in its clinical development. This study will help us understand how setidegrasib’s novel approach to degrading disease-driving KRAS G12D may help address unmet needs for patients with this type of NSCLC. We are grateful to the patients, investigators and study teams making this research possible.”

Setidegrasib is Astellas’ lead investigational targeted protein degrader. Initiation of the Phase 3 study in previously treated patients with NSCLC supports Astellas’ Corporate Strategic Plan, with an ambition to initiate five or more Phase 3 or pivotal studies by fiscal year 2027. It follows the initiation of a Phase 3 study of *setidegrasib* in front-line pancreatic ductal adenocarcinoma (PDAC) in April 2026.⁶

To further inform the scientific understanding of *setidegrasib* and KRAS G12D-driven disease biology, Astellas will also present translational analyses from the Phase 1 study of *setidegrasib* in patients with KRAS G12D-mutated PDAC at the upcoming AACR Conference on Pancreatic Cancer, September 25–28, 2026.^{7,8} The analyses will provide further insight into mechanisms of response, resistance and potential rational combination approaches in pancreatic cancer. The findings will be featured in both a proffered oral presentation and a poster presentation.*

*** Presentation details at AACR Conference on Pancreatic Cancer**

Title: Integrated translational analyses of the first-generation KRAS G12D degrader *setidegrasib* identify mechanisms of response and resistance and offer rational combination strategies

Lead author: Wungki Park, Gastrointestinal Oncology Service, Memorial Sloan Kettering Cancer Center

Details: Poster Presentation: Poster Number: B040, Date: September 27, 2026, 5:00–7:00 p.m. PT;

Oral Presentation (short talk from proffered abstract): Abstract Number: PR014 B040, Date: September 28, 2026, 9:42 a.m. PT.

About the Phase 3 NSCLC Study¹

The randomized, open-label Phase 3 study is evaluating *setidegrasib* compared with docetaxel in people with KRAS G12D-mutated locally advanced (unresectable) or metastatic NSCLC whose disease

has progressed on or after platinum-based chemotherapy and checkpoint inhibitor therapy (CPI). The dual primary endpoints are progression-free survival (PFS), assessed by blinded independent central review, and overall survival (OS). Astellas plans to enroll approximately 356 patients across multiple countries into the study.

About *setidegrasib*^{4,9,10}

Setidegrasib is a novel, investigational targeted protein degrader designed to degrade and eliminate the disease-driving KRAS G12D protein. By removing this protein, *setidegrasib* may help disrupt cancer cell signaling and destroy cancer cells. Discovered and advanced through Astellas' in-house R&D capabilities, *setidegrasib* is designed to work with the cancer cell's own protein degradation machinery to bring together the KRAS G12D protein and an E3 ligase. This triggers selective degradation of the disease-driving protein, providing a distinct approach to targeting this cancer-driving mutation.

For more information on the Phase 3 study of *setidegrasib* in previously treated NSCLC, visit ClinicalTrials.gov and search for identifier [NCT07566052](https://clinicaltrials.gov/ct2/show/study/NCT07566052). For more information about the Phase 3 study of *setidegrasib* in front-line PDAC, visit ClinicalTrials.gov and search for identifier [NCT07409272](https://clinicaltrials.gov/ct2/show/study/NCT07409272).

The safety and efficacy of *setidegrasib* have not been established for the uses being considered. There is no guarantee that *setidegrasib* will receive regulatory approval and become commercially available for the uses being investigated.

About Astellas' Corporate Strategic Plan

Learn more at www.astellas.com/en/about/corporate-strategic-plan.

About Astellas

Astellas is a global life sciences company committed to turning innovative science into value for patients. We provide transformative therapies in disease areas that include oncology, ophthalmology, urology, immunology and women's health. Through our research and development programs, we are pioneering new healthcare solutions for diseases with high unmet medical need. Learn more at www.astellas.com.

Cautionary Notes

In this press release, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions, and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas' intellectual property rights by third parties. Information about pharmaceutical products (including products currently in development) which is included in this press release is not intended to constitute an advertisement or medical advice.

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Contacts for inquiries or additional information:

Rachel Norager
Global Brand Communications
+65 9271 1071
rachel.norager@astellas.com

Astellas Pharma Inc.
Corporate Communications
+81-3-3244-3201

References

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