Press Release

Astellas Doses First Patient in Phase 3 Study of *setidegrasib* (ASP3082) for KRAS G12D-mutated Metastatic Pancreatic Ductal Adenocarcinoma

- Setidegrasib is an investigational, novel KRAS G12D-targeted protein degrader -
- KRAS G12D mutations occur in approximately 40% of pancreatic ductal adenocarcinomas, with no approved targeted therapies -
- Setidegrasib is the first protein degrader targeting a KRAS mutation to enter a Phase 3 study and marks progression of Astellas' Targeted Protein Degradation research into late-stage development -

TOKYO, April 15, 2026 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, "Astellas") today announced that the first patient has been successfully dosed in the Phase 3 registrational study evaluating *setidegrasib* (ASP3082) in combination with mFOLFIRINOX or NALIRIFOX as first-line treatment for patients with KRAS G12D-mutated metastatic pancreatic ductal adenocarcinoma (PDAC).

KRAS G12D mutations occur in approximately 40% of people with PDAC and remain associated with poor outcomes.[1] There are currently no approved therapies that specifically target the KRAS G12D mutation.

Setidegrasib is an investigational KRAS G12D-targeted protein degrader, discovered through Astellas' in-house research and development capabilities.[2] It is designed to selectively bind mutant KRAS G12D proteins and an E3 ligase to trigger degradation of the disease-driving protein.[3] Phase 1 data demonstrated KRAS G12D target degradation consistent with the proposed mechanism of action.[4] Results from the open-label, two-part Phase 1 study have been published in *The New England Journal of Medicine* and can be accessed here.[5]

Tadaaki Taniguchi, M.D., Ph.D., Chief Research and Development Officer, Astellas:
"KRAS has been recognized for decades as a challenging oncogenic driver, with KRAS G12D representing an area of significant unmet need across multiple cancers. Successfully advancing a KRAS G12D-directed protein degrader into a Phase 3 study is an important milestone for Astellas, underscoring the value of strategic

Date of Preparation: April 2026

investment in our in-house expertise and capabilities to discover and develop our targeted protein degradation platform."

The Phase 3, randomized, double-blind, placebo-controlled study is designed to evaluate the efficacy and safety of *setidegrasib* in combination with mFOLFIRINOX or NALIRIFOX as first-line treatment in participants with confirmed KRAS G12D-mutated metastatic PDAC.[6] The primary endpoint is overall survival in this biomarker-defined population, with key secondary endpoints including progression-free survival and safety.[6] The study plans to enroll more than 600 participants across multiple countries.[6]

###

About setidegrasib

Setidegrasib (ASP3082) is a selective protein degrader discovered through Astellas' in-house research and development capabilities that targets mutated KRAS G12D, which is one of the most common KRAS mutation subtypes across tumors.[7] *Setidegrasib* has been evaluated in a first-in-human, open label Phase 1 study in patients with metastatic or locally advanced unresectable solid tumors harboring a KRAS G12D mutation, including advanced pancreatic and non-small cell lung cancers.[4,8] For more information about the Phase 1 study, visit clinicaltrials.gov with identifier NCT05382559. For more information about the Phase 3 study in PDAC, visit clinicaltrials.gov with identifier NCT07409272**.**

The safety and efficacy of *setidegrasib* is not 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

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.

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

[1] Buscail, L., Bournet, B. & Cordelier, P. Role of oncogenic KRAS in the diagnosis, prognosis and treatment of pancreatic cancer. *Nat Rev Gastroenterol Hepatol* 17, 153–168 (2020). https://pubmed.ncbi.nlm.nih.gov/32005945/
[2] Astellas Pharma Inc. Primary focus: targeted protein degradation. Astellas. Available at: https://www.astellas.com/en/science/research-and-development/primary-focuses/targeted-protein-degradation. Accessed March 2026.
[3] Yoshinari T, Nagashima T, Ishioka H, et al. Discovery of KRAS(G12D) selective degrader ASP3082. *Commun Chem*. 2025;8:254. https://doi.org/10.1038/s42004-025-01662-4
[4] Park W, Kasi A, Goldman JW, et al. Phase 1 evaluation of ASP3082, a first-in-class selective protein degrader, in patients with KRAS G12D-mutant pancreatic ductal adenocarcinoma (PDAC): pharmacokinetics (PK) and biomarker insights [Abstract 775]. *J Clin Oncol*. 2026;44(2_suppl):775. https://doi.org/10.1200/JCO.2026.44.2_suppl.775
[5] Park W, Kasi A, Spira AI, et al. Setidegrasib in advanced non–small-cell lung cancer and pancreatic cancer. N Engl J Med. Published online March 25, 2026. doi:10.1056/NEJMoa2600752
[6] A phase 3, double-blind, placebo-controlled, randomized study to assess the efficacy and safety of ASP3082 in combination with mFOLFIRINOX or NALIRIFOX as first-line treatment in participants with KRAS G12D mutated metastatic pancreatic adenocarcinoma. ClinicalTrials.gov. Identifier: NCT07409272. U.S. National Library of Medicine. Available at: https://clinicaltrials.gov/study/NCT07409272
[7] Lee JK, Sivakumar S, Schrock AB, et al. Comprehensive pan-cancer genomic landscape of KRAS-altered cancers and real-world outcomes in solid tumors. *npj Precision Oncology*. 2022;6:91.
[8] Park W, Kasi A, Spira AI, et al. 608O Preliminary safety and clinical activity of ASP3082, a first-in-class, KRAS G12D selective protein degrader in adults with advanced pancreatic (PC), colorectal (CRC), and non-small cell lung cancer (NSCLC). *Ann Oncol.* 2024;35(suppl 2):S486-S487. doi:10.1016/j.annonc.2024.08.675.