

Roche's divarasib demonstrated best-in-class efficacy, advancing the standard of care in previously treated KRAS G12C-mutated lung cancer

- **Divarasib monotherapy demonstrated superior efficacy over first-generation KRAS G12C inhibitors, lowering the risk of disease progression or death by 42% and the overall risk of death by 44%, in the phase III Krascendo 1 study^{1,2}**
- **At the time of primary analysis, divarasib achieved a median overall survival of approximately 18 months, compared to 12 months for sotorasib or adagrasib^{1,2}**
- **No new safety signals were observed with divarasib; the most common treatment-related adverse events were mainly low grade and manageable^{1,2}**
- **Data presented as a late-breaking abstract during a Presidential Symposium at the 2026 ESMO Congress and simultaneously published in The New England Journal of Medicine^{1,2}**

Basel, 25 October 2026 - Roche (SIX: RO, ROP; OTCQX: RHHBY) announced today pivotal results from the phase III Krascendo 1 study, which demonstrated the superior efficacy of investigational divarasib, a next-generation KRAS G12C inhibitor, compared with current standard of care KRAS G12C inhibitors in people with previously treated KRAS G12C-mutated non-small cell lung cancer (NSCLC).^{1,2} Participants treated with divarasib monotherapy lived significantly longer, lowering the risk of death by 44% compared with sotorasib or adagrasib (overall survival, OS, HR 0.56, [95% CI: 0.41-0.78], p=0.0005).^{1,2} Median OS for divarasib is currently approximately 18 months, compared to 12 months for the control arm (see table below).^{1,2} No new safety findings were observed with divarasib and the most common treatment-related adverse events (TRAEs) were mainly low grade and manageable.^{1,2} These data were presented as a late-breaking abstract during a Presidential Symposium at the 2026 European Society for Medical Oncology (ESMO) Congress and simultaneously [published](#) in The New England Journal of Medicine.^{1,2}

"The phase III Krascendo 1 results demonstrate the potential for divarasib to become a new standard of care for people with previously treated KRAS G12C-mutated lung cancer," said Levi Garraway, MD, PhD, Roche's Chief Medical Officer and Head of Global Product Development. "The superior efficacy against the current standard of care demonstrated in this head-to-head trial reinforces divarasib's best-in-class profile. We are working closely with health authorities to bring this new treatment option to the people who need it."

The G12C mutation is one of the most common KRAS mutations, found in approximately one in eight people with NSCLC.^{3,4} Accumulating evidence suggests that people with NSCLC who have the KRAS G12C mutation may have poorer outcomes than those who have the

unmutated KRAS gene (wild-type disease).^{5,6} Despite the approval of current, first-generation KRAS G12C-targeted treatments, there remains a significant unmet need for more effective therapy options.

“New life-extending treatments are greatly needed, as most patients with this type of cancer will eventually relapse after initial therapy, and there are limited effective treatments for recurrent disease,” said study lead author Ferdinandos Skoulidis, MD, PhD, Professor of Thoracic/Head and Neck Medical Oncology at The University of Texas MD Anderson Cancer Center. “The Krascendo 1 results highlight divarasil’s practice-changing potential, as the first KRAS inhibitor to meaningfully improve overall survival for people with previously treated KRAS G12C-mutated lung cancer, compared with current treatment options.”

The Krascendo 1 study is the only global head-to-head study to evaluate a next-generation KRAS G12C inhibitor versus approved first-generation KRAS G12C inhibitors.^{1,2} The study met primary and key secondary endpoints, and divarasil demonstrated statistically significant and clinically meaningful improvements in OS and progression-free survival (PFS) over sotorasib or adagrasib.^{1,2} In addition to the OS benefit, divarasil reduced the risk of disease progression or death by 42% (PFS HR 0.58, [95% CI: 0.44-0.76], $p < 0.0001$).^{1,2} The OS and PFS benefit was consistent across clinically relevant subgroups, and was observed regardless of PD-L1 expression or KEAP1 mutation status.^{1,2} The objective response rate (ORR) with divarasil was nearly double that of sotorasib or adagrasib.^{1,2}

Key efficacy results from the phase III Krascendo 1 study:^{1,2}

Primary and key secondary endpoints	Divarasil arm (n=167)*	Control arm (adagrasib, sotorasib) (n=171)*	Hazard Ratio / (95% CI)	p-value
Median OS (months)	17.7	12.0	HR 0.56 (0.41-0.78)	$p = 0.0005$
Median PFS (months)	9.8	5.7	HR 0.58 (0.44-0.76)	$p < 0.0001$
12-month PFS rate (%)	44%	24%	-	-
Confirmed ORR (%)*	58%	32%	-	-

Median DOR (months)*	11.9	6.9	-	-
----------------------	------	-----	---	---

**Assessed in response-evaluable population (n=328; ten patients [divarasil arm, n=6; control arm, n=4] did not have measurable disease at baseline and were excluded from the response-evaluable set). Duration of Response (DOR) evaluated in those who responded to treatment (divarasil arm, n=94; control arm, n=54).*

The safety profile of divarasil monotherapy was consistent with the known class effects of KRAS G12C inhibitors.^{1,2} The most common TRAEs comprised GI toxicity (most commonly, diarrhoea, nausea, and vomiting) and hepatotoxicity.^{1,2} Fewer participants discontinued treatment due to TRAEs with divarasil (4.8% versus 11.7%) and the rate of serious TRAEs was approximately half that of sotorasil or adagrasib (7.8% versus 15.2% respectively), despite patients remaining on treatment for more than twice as long (11.3 months compared with 5.0 months).^{1,2}

Roche is advancing a comprehensive phase III clinical development programme in NSCLC, investigating divarasil as both a monotherapy and as a chemotherapy-free combination, across different disease settings and lines of therapy. The US Food and Drug Administration granted Breakthrough Therapy Designation to divarasil in 2022, and in 2026, Orphan Drug Designation for KRAS G12C-mutated NSCLC.

About Krascendo 1^{1,2}

The Krascendo 1 study [[NCT06497556](#)] is the only global head-to-head study evaluating a Kirsten rat sarcoma virus (KRAS) G12C inhibitor in direct comparison with first-generation approved KRAS G12C inhibitors. This phase III, randomised, open-label, multicentre study evaluates the efficacy and safety of divarasil monotherapy versus sotorasil or adagrasib in people with previously treated KRAS G12C-mutated advanced or metastatic non-small cell lung cancer. The study includes 338 adults, randomised to receive either divarasil once daily (n=167) or, either sotorasil once daily or adagrasib twice daily (n=171). The primary endpoint is blinded independent central review (BICR)-assessed progression-free survival. Secondary endpoint measures include overall survival, confirmed objective response, duration of response, as well as other efficacy and safety measures.

About divarasil

Divarasil is an investigational, best-in-class, next-generation, oral, KRAS G12C inhibitor, discovered and developed by researchers within Roche and Genentech. It has shown greater potency and selectivity in preclinical studies compared with first-generation KRAS G12C-targeting treatments, sotorasil or adagrasib, with superior efficacy demonstrated in people with previously treated KRAS G12C-mutated NSCLC.^{1,2,7} Divarasil is designed to selectively bind to the KRAS G12C protein, locking the protein in an inactive (off) state, thereby turning off its tumour-driving signalling.^{7,8,9}

Divarasib's comprehensive clinical development programme is anchored by three phase III studies:

Study	Intervention	Patient population
Krascendo 1 [NCT06497556]	Divarasib monotherapy vs sotorasib or adagrasib	Previously treated KRAS G12C-mutated advanced or metastatic NSCLC (second-line)
Krascendo 2 [NCT06793215]	Divarasib plus pembrolizumab (chemotherapy-free combination) vs chemotherapy plus pembrolizumab	Previously untreated KRAS G12C-mutated advanced NSCLC (first-line)
Krascendo 3 [NCT07541170]	Adjuvant divarasib monotherapy vs immunotherapy or observation	Resected stage II–IIIB KRAS G12C-mutated NSCLC after standard of care chemoimmunotherapy (early-stage)

Divarasib underpins Roche's diversified pipeline targeting the RAS signalling pathway, including other mutant-selective inhibitors and a pan-RAS inhibitor, designed to extend the benefits of RAS inhibition strategies to more patients.

About KRAS G12C-mutated non-small cell lung cancer

Despite advances in treatment, lung cancer remains the leading cause of cancer-related deaths worldwide, surpassing the combined mortality rates of breast, prostate, and stomach cancers.^{10,11} Each year, it claims the lives of 1.8 million people, with non-small cell lung cancer (NSCLC) accounting for approximately 85% of cases.^{10,12} KRAS is one of the most frequently mutated genes in lung cancer, occurring in approximately 25% of newly diagnosed lung cancers, and is associated with poor prognosis for patients.⁹ The G12C mutation is one of the most common KRAS mutations, found in approximately 12-14% of NSCLC cases.^{3,4}

The KRAS gene produces the KRAS protein, which acts as a cellular control switch, cycling between an active (on) and inactive (off) state to regulate cell growth and proliferation, making it a critical target for new therapeutic strategies.⁹ G12C mutation locks the KRAS protein in its active (on) state, leading to continuous, unregulated signalling for cell growth, driving tumour proliferation.^{8,9}

About Roche in lung cancer

Roche is committed to advancing the field of lung cancer treatments, leveraging more than 20 years of deep scientific expertise to improve patient outcomes and their overall experience. Roche's strong commitment to investment in research and development has built

a robust portfolio of approved medicines and companion diagnostics, which empowers physicians to better understand a patient's disease and optimise care.

Roche's broad portfolio includes approved medicines such as Alecensa® (alectinib), Tecentriq® (atezolizumab), and Rozlytrek® (entrectinib). Its extensive pipeline includes investigational treatments across three key focus areas: small cell lung cancer, non-small cell lung cancer (NSCLC) with actionable genomic alterations (AGA), and NSCLC without AGA. Utilising diverse approaches, ranging from cancer-cell-killing 'cytotoxics' and immunotherapies to treatments targeting specific characteristics of cancer cells, we aim to translate scientific discoveries into meaningful progress in patient care.

About Roche

Roche (SIX: RO, ROP; OTCQX: RHHBY) is a healthcare company uniquely placed to prevent, stop and cure diseases by uniting leading science and technology across diagnostics, medicines and digital solutions.

Roche was founded in Basel, Switzerland in 1896 and today is a leading provider of transformative medicines and diagnostics for millions of people in over 150 countries around the world. It is dedicated to tackling healthcare challenges that place the greatest strain on patients, families, communities and healthcare systems. Across its Diagnostics and Pharmaceutical divisions, Roche focuses on areas including oncology, neurology, cardiovascular and metabolic diseases, ophthalmology, infectious diseases and immunology with the aim of providing real and positive change for patients, the people they love and the professionals who care for them.

Genentech in the United States is a fully owned subsidiary in the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, a major innovator in the Japanese therapeutic antibody market.

For more information, please visit www.roche.com.

All trademarks used or mentioned in this release are protected by law.

References

- [1] Skoulidis F, et al. Krascendo 1: efficacy and safety of divarasib vs sotorasib or adagrasib in previously treated locally advanced or metastatic KRAS G12C-mutated NSCLC. Presented at: ESMO Congress; 2026 October 23-27; Madrid, Spain. #LBA5.
- [2] Skoulidis F, et al. Divarasib as compared with sotorasib or adagrasib in KRAS G12C-mutated NSCLC. N Engl J Med 2026; DOI: 10.1056/NEJMoa2605703
- [3] Nassar AH, et al. Distribution of KRAS (G12C) Somatic Mutations across Race, Sex, and Cancer Type. N Engl J Med. 2021; 384 (2): 185-187.
- [4] Lee JK, et al. Comprehensive pan-cancer genomic landscape of KRAS altered cancers and real-world outcomes in solid tumors. NPJ Precis Oncol. 2022;9;6(1):91.

- [5] Wankhede D, et al. Prognostic role of KRAS G12C mutation in non-small cell lung cancer: a systematic review and meta-analysis. *Diagnostics*. 2023; 25;13(19): 3043.
- [6] Isaksson J, et al. KRAS G12C Mutant Non-Small Cell Lung Cancer Linked to Female Sex and High Risk of CNS Metastasis: Population-based Demographics and Survival Data From the National Swedish Lung Cancer Registry. *Clin Lung Cancer*. 2023; 24(6):507-518.
- [7] Endres NF, et al. Discovery and Characterization of Divarasib (GDC-6036), a Potent Covalent Inhibitor of KRAS G12C. *J Med Chem*. 2026; 69 (5): 5147-5165.
- [8] Friedlaender A, et al. KRAS as a druggable target in NSCLC: rising like a phoenix after decades of development failures. *Cancer Treat Rev*. 2020;85:101978.
- [9] Pakkala S, et al. Personalized therapy for lung cancer: striking a moving target. *JCI Insight*. 2018; 3 (15).
- [10] World Health Organization. Global cancer burden growing, amidst mounting need for services [Internet; cited 2026 September]. Available from: <https://www.who.int/news/item/01-02-2024-global-cancer-burden-growing--amidst-mounting-need-for-services>.
- [11] American Lung Association. Lung Cancer Statistics [Internet; cited 2026 September]. Available from: <https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/resource-library/lung-cancer-fact-sheet>.
- [12] World Health Organization. Lung cancer [Internet; cited 2026 September]. Available from: <https://www.who.int/news-room/fact-sheets/detail/lung-cancer>.

Roche Global Media Relations

Phone: +41 61 688 88 88 / e-mail: media.relations@roche.com

Tristan Schmitz

Phone: +41 79 529 70 35

Nathalie Altermatt

Phone: +41 79 771 05 25

Lorena Corfas

Phone: +41 79 568 24 95

Simon Goldsborough

Phone: +44 797 32 72 915

Karsten Kleine

Phone: +41 79 461 86 83

Kirti Pandey

Phone: +41 79 398 38 53

Yvette Petillon

Phone: +41 79 961 92 50

Irène Stephan

Phone: +41 79 377 83 75

Albert Thottiyil

Phone: +41 79 775 66 12

Roche Investor Relations

Dr Bruno Eschli

Phone: +41 61 68-75284

e-mail: bruno.eschli@roche.com

Dr Sabine Borngräber

Phone: +41 61 68-88027

e-mail: sabine.borngraeber@roche.com

Dr Birgit Masjost

Phone: +41 61 68-84814

e-mail: birgit.masjost@roche.com

Investor Relations North America

Loren Kalm

Phone: +1 650 225 3217

e-mail: kalm.loren@gene.com