



Bayer AG
Communications
51368 Leverkusen
Germany
Phone +49 214 30-1
www.bayer.com/en/media

News Release

Not intended for UK Media

Bayer initiates Phase I study targeting GPC3 with actinium-225 radiopharmaceutical in patients with advanced hepatocellular carcinoma

- ²²⁵Ac-GPC3 (BAY 3547926) is an investigational targeted alpha radiopharmaceutical being developed to treat tumors expressing Glypican-3 (GPC3) in patients with advanced hepatocellular carcinoma (HCC)
 - BAY 3547926 comprises a high affinity antibody radiolabeled with ²²⁵Ac (actinium-225) targeting GPC3
 - Targeted alpha therapy induces lethal DNA double-strand breaks with the potential to cause anti-tumor activity
 - Liver cancer, including HCC, is the third leading cause of cancer-related deaths in the world, with almost 900,000 new cases annually
 - The third targeted alpha therapy in active clinical development by Bayer was presented during the “New Drugs on the Horizon” session at the 2025 American Association for Cancer Research Annual Meeting
-

Berlin, April 29, 2025 – Bayer announced today initiation of a Phase I clinical trial with ²²⁵Ac-GPC3 (BAY 3547926), an investigational targeted alpha radiopharmaceutical being developed to treat tumors expressing Glypican-3 (GPC3) in patients with advanced hepatocellular carcinoma (HCC). Oncofetal protein GPC3 is a membrane-associated proteoglycan which is overexpressed in 70-75% of HCC lesions making it an attractive target for targeted radionuclide therapy.^{1,2} The first-in-human, dose escalation study ([NCT06764316](https://clinicaltrials.gov/ct2/show/study/NCT06764316)) will evaluate the safety, tolerability and preliminary efficacy of BAY 3547926 alone, and as a combination therapy in patients with advanced HCC.

¹ Kolluri A and Ho M (2019), The Role of Glypican-3 in Regulating Wnt, YAP, and Hedgehog in Liver Cancer. *Front. Oncol.* 9:708. doi: 10.3389/fonc.2019.00708.

² Yongle Wu, Hui Liu, Huiguo Ding, GPC-3 in hepatocellular carcinoma: current perspectives, *Journal of Hepatocellular Carcinoma* 2016:3, 63-67.

“Hepatocellular carcinoma continues to be a devastating disease for millions of patients and a pressing unmet need in cancer care. The launch of the Phase I trial using the ²²⁵Ac-GPC3 radionuclide therapy marks an important milestone in our commitment to develop new medicines targeting cancer cells with high effect size and precision to improve the lives of people living with cancer,” said Dominik Ruettinger, M.D., Ph.D., Global Head of Research and Early Development for Oncology at Bayer’s Pharmaceuticals Division. “Through continued research innovation we can unlock the full potential of targeted alpha therapies which is an emerging class of targeted radionuclide therapy and a strategic focus area for Bayer’s precision oncology development portfolio.”

Liver cancer, including hepatocellular carcinoma, is the third leading cause of cancer-related deaths in the world with almost 900,000 new cases annually.³ It is the most rapidly growing cause of cancer deaths in the US accounting for approximately 2% of new cases and 5% of cancer deaths.⁴ Despite recent scientific advancements, most patients do not experience durable therapeutic benefits from the currently available treatments.

Targeted alpha therapy (TAT) has the potential to address high unmet medical need across various cancer types. Bayer’s growing TAT portfolio combines alpha particle-emitting radionuclides with different targeting moieties. ²²⁵Ac-GPC3 is the third TAT program in clinical development and the first investigational targeted radiopharmaceutical for Bayer in HCC. The newly disclosed targeted alpha conjugate joins ²²⁵Ac-Pelgifatamab and ²²⁵Ac-PSMA-Trillium, which are currently in Phase I clinical trials in patients with advanced metastatic castration resistant prostate cancer.

On April 28, 2025 Bayer introduced ²²⁵Ac-GPC3 in an oral presentation during the “New Drugs on the Horizon” session at the AACR (American Association of Cancer Research) Annual Meeting, showcasing preclinical characterization of the asset including the low uptake and fast clearance from normal organs as well as induction of tumor regression in *in vivo* models. Recognition in this special symposium highlights the company’s commitment for precision oncology development portfolio.

About BAY 3547926

³ Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, Freddie Bray BSc, MSc, PhD; Mathieu Laversanne MSc; Hyuna Sung PhD; Jacques Ferlay ME; Rebecca L. Siegel MPH; Isabelle Soerjomataram MD, MSc, PhD; Ahmedin Jemal DVM, PhD.

⁴ SEER Cancer Stat Facts: Liver and Intrahepatic Bile Duct Cancer. National Cancer Institute. Bethesda, MD, <https://seer.cancer.gov/statfacts/html/livibd.html>

BAY 3547926 is an investigational targeted alpha radiopharmaceutical being developed to treat tumors expressing Glypican-3 (GPC3) in patients with advanced hepatocellular carcinoma (HCC). It is composed of a GPC3 targeting high affinity antibody radiolabeled with actinium-225 (^{225}Ac). ^{225}Ac -GPC3 delivers highly potent alpha-particles to the GPC3-expressing cancer cells, with the potential to inducing DNA double-strand breaks, reducing cancer cell viability which may potentially cause anti-tumor activity.

About Targeted Alpha Therapy

Targeted alpha therapy (TAT) is an emerging class of radionuclide therapy that can be used against a variety of tumors. It delivers alpha particle radiation directly to the tumor inside the body, either via its bone-seeking property (radium-223) or by combining alpha radionuclides, such as actinium-225, with specific targeting moieties.

Actinium-225 is an alpha particle—emitting radionuclide with a 9.9-day half-life. Alpha particles deposit highly ionizing radiation over a short range. This localized delivery of the radioactive payload induces irreparable DNA double-strand breaks, often resulting in cell death. At the same time, because the energy travels a short range, damage to nearby normal tissues is much reduced.^{5,6,7}

About Oncology at Bayer

Bayer is committed to delivering science for a better life by advancing a portfolio of innovative treatments. The company has the passion and determination to develop new medicines that help improve and extend the lives of people living with cancer. The oncology franchise at Bayer includes several marketed products across diverse indications and multiple compounds in different stages of clinical development. We have a wealth of expertise in areas including Tumor Cell Intrinsic Pathways, Targeted Radionuclide Therapies, and selective Next-Generation Immuno-Oncology. With our portfolio we are advancing cancer treatments from early to metastatic stage, with the goal of extending survival while limiting side effects for the cancer patients we serve.

About Bayer

Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. In line with its mission, “Health for all, Hunger for none,” the company’s

⁵ Parker C, et al. JAMA Oncol. 2018;4(12):1765-1772. 2. 3.

⁶ Tafreshi NK, et al. Molecules. 2019;24(23):4314.

⁷ Hagemann UB, et al. Cancer Biother Radiopharm. 2020;35(7):497-510.

products and services are designed to help people and the planet thrive by supporting efforts to master the major challenges presented by a growing and aging global population. Bayer is committed to driving sustainable development and generating a positive impact with its businesses. At the same time, the Group aims to increase its earning power and create value through innovation and growth. The Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2024, the Group employed around 93,000 people and had sales of 46.6 billion euros. R&D expenses amounted to 6.2 billion euros. For more information, go to www.bayer.com.

Bayer Media Contact:

Anna Kanmaz, phone +49 1741463541

Email: anna.kanmaz@bayer.com

Contact for media inquiries Bayer U.S.:

Elaine Colon, phone +1 732 236 1587

Email: elaine.colon@bayer.com

Find more information at <https://pharma.bayer.com/>

Follow us on Facebook: <http://www.facebook.com/bayer>

aka (2025-0076)

Forward-Looking Statements

This release may contain forward-looking statements based on current assumptions and forecasts made by Bayer management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at www.bayer.com. The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.