Our Mission in Oncology

Put Patients' Needs First and Foremost

Bayer is committed to delivering science for a better life by advancing a portfolio of innovative treatments. The oncology franchise at Bayer includes products and compounds in various stages of clinical development. Our approach to oncology research prioritizes targets and pathways with the potential to impact the way cancer is treated.

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for more information about
Bayer's investigational oncology pipeline.

Oncology Pipeline in Clinical Development

Explore our expanding commitment to clinical research and patients

Oncology Pipeline by Phase

Areas of Oncology Research

Tumor Intrinsic Pathways

- Androgen Receptor Signaling
- Oncogenic Signaling
- HER2/mEGFR Signaling

- Immuno-oncology
- Targeted Radionuclide Therapy

CCR8, chemokine receptor 8; DGK, diacylglycerol kinase; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; PSMA, prostate specific membrane antigen.

†**The compounds presented in this brochure are either investigational, have ongoing confirmatory studies, or are being investigated for uses that have not been approved by the FDA, EMA, or other health authorities. This information is presented only for purposes of providing a general overview of clinical trials and should not be construed as a recommendation for use of any product for unapproved uses.**

*In collaboration with Orion Pharma.
‡In collaboration with German Cancer Research Center (DKFZ).
§In collaboration with Broad Institute.

Phase of Development

Investigational Compounds by Tumor Type

Gastric/Gastroesophageal Cancer

● **BAY 2965501***	DGK-zeta inhibitor

Prostate Cancer

● **BAY 3546828**	^{225}Ac-pelgifatamab
● **BAY 3563254**	^{225}Ac-PSMA-Trillium

Melanoma

● **BAY 3375968**	Anti-CCR8 antibody

Head and Neck Cancer

● **BAY 3375968**	Anti-CCR8 antibody

Breast Cancer

● **BAY 3375968**	Anti-CCR8 antibody

Non–Small Cell Lung Cancer

● **BAY 2862789***	DGK-alpha inhibitor
● **BAY 2927088†**	HER2/mEGFR inhibitor
● **BAY 3375968**	Anti-CCR8 antibody
● **BAY 2965501***	DGK-zeta inhibitor

● In Phase I Clinical Trials

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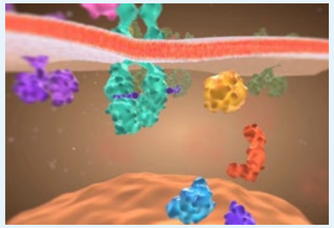
Areas of Oncology Research

Hover over an area of research for an enlarged view.

Tumor Intrinsic Pathways

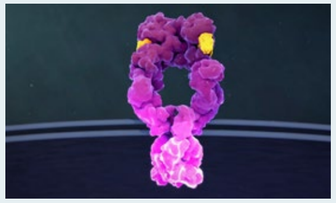
Oncogenic Signaling



References
1. Chappell WH, Steelman LS, Long JM, et al. *Oncotarget*. 2011;2(3):135-164. **2.** Grünwald V, Hidalgo M. *J Natl Cancer Inst*. 2003;95(12):851-867. **3.** Haugsten EM, Wiedlocha A, Olsnes S, et al. *Mol Cancer Res*. 2010;8(11):1439-1452. **4.** Hanahan D, Weinberg RA. *Cell*. 2011;144(5):646-674.

- Activation of many oncogenic signaling pathways (e.g., VEGFR, Akt/mTOR) due to genetic alterations and/or driver mutations plays a critical role in cancer development. Dysregulation of these oncogenic pathways may promote cancer progression through changes in various cellular events, including[1-4]:
  - Uncontrolled cell proliferation
  - Resistance to cell death
  - Increased cell metastasis
  - Development of drug resistance
- Bayer is actively engaged in researching these oncogenic signaling pathways, as well as in exploring the identification of biomarkers for patient-enrichment trials

HER2/mEGFR Signaling



References
1. Clinical Trials.gov: NCT05099172. Accessed February 19, 2022. **2.** Wieduwilt M, Moasser MM. *Cell Mol Life Sci*. 2008;65(10):1566–1584. **3.** Burnett H, et al. PLoS ONE. 2021; 16(3):e0247620. doi: 10.1731/journal.pone.0247620. **4.** Rangachari D, et al. *J Thorac Oncol*. 2019;14(11):1995-2002. **5.** Siegel F, Karsli-Uzunbas G, Kotynkova K, et al, Preclinical activity of BAY 2927088 in HER2 mutant non-small cell lung cancer. [abstract]. In: Proceedings of the American Association for Cancer Research Annual Meeting 2023; Part 1 (Regular and Invited Abstracts); 2023 Apr 14-19; Orlando, FL. Philadelphia (PA): AACR; Cancer Res 2023;83(_Suppl):Abstract nr 4035. **6.** Siegel F, Siegel S, Graham K, et al. BAY 2927088: The first non-covalent, potent, and selective tyrosine kinase inhibitor targeting EGFR exon 20 insertions and C797S resistance mutations in NSCLC. European Journal of Cancer. 2022;174:S9-S10.

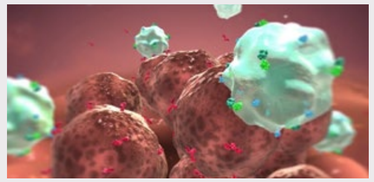
- Epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor 2 (HER2) are proteins that help cells to grow and divide[1,2]
- Patients with non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) or EGFR exon 20 insertion mutations have an unmet medical need
- BAY 2927088 is an oral, reversible tyrosine kinase inhibitor (TKI) that potently inhibits mutant human epidermal growth factor receptors 2 (HER2), including HER2 exon 20 insertions and HER2 point mutations, as well as epidermal growth factor receptors (EGFR), with high selectivity for mutant vs wild-type EGFR.

Androgen Receptor Signaling

References
1. Wong YN, Ferraldeschi R, Attard G, et al. *Nat Rev Clin Oncol*. 2014;11(6):365-376. **2.** Tan MH, Li J, Xu HE, et al. *Acta Pharmacol Sin*. 2015;36(1):3-23.

- Androgen receptor signaling occurs through the binding of androgens or alternative ligands to the receptor, which causes translocation of the receptor complex to the nucleus[1,2]
  - Once inside the nucleus, the receptor complex binds to response elements controlling androgen-responsive genes such as PSA, modulating gene transcription and expression and potentially leading to uncontrolled tumor cell proliferation and increased cell survival[1]

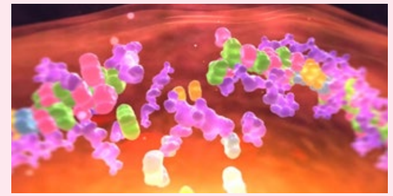
Immuno-oncology



References
1. National Cancer Institute. https://www.cancer.gov/about-cancer/understanding/what-is-cancer#celldifferences. Updated February 9, 2015. Accessed February 18, 2022. **2.** Hütter J, Griztan U, Gutcher I, et al. Presented at: American Association for Cancer Research Annual Meeting; April 14-18, 2018; Chicago, IL. Abstract 2778. **3.** Hecht I, Toporik A, Podojil JR, et al. *J Immunol*. 2018;200(6):2025-2037. **4.** Opitz CA, Litzenburger UM, Sahm F, et al. *Nature*. 2011;478(7368):197-203. **5.** Gutcher I, Kober C, Roehn U, et al. Presented at: American Association for Cancer Research Virtual Annual Meeting I; April 27-28, 2020. Abstract DDT01-02. **6.** Van Damme H, et al. *J Immunother Cancer*. 2021;9:e001749. doi:10.1136/jitc-2020-001749. **7.** Abdel-Magid AF. *ACS Med Chem Lett*. 2020;11(6):1083-1085.

- The immune system plays an important role in recognizing and eliminating cancer cells; however, cancer cells can escape immune-mediated anti-tumor effects through various mechanisms, such as[1]:
  - Expression of immune checkpoint proteins (e.g., PD-1/PD-L1)[2,3]
  - Activation of immunomodulatory pathways (e.g., TDO-Kyn-AhR pathway)[4,5]
  - Tumor-mediated suppression of T and NK cell activity through induction of intratumoral Treg cells or suppression of cytotoxic immunocyte activity[6,7]
- Bayer is now conducting research and development on several investigational compounds targeting different immune-mediated pathways to enhance anti-tumor immune response

Targeted Radionuclide Therapy



References
1. Parker C, et al. *JAMA Oncol*. 2018;4(12):1765-1772. **2.** Tafreshi NK, et al. *Molecules*. 2019;24(23):4314. **3.** Marcu L, et al. *Crit Rev Oncol Hematol*. 2018;123:7-20. **4.** Briechbiel MW. *Dalton Trans*. 2007;21(43):4918-4928. **5.** Suominen MI, et al. *Clin Cancer Res*. 2017;23(15):4335-4346. **6.** Lomax ME, et al. *Clin Oncol*. 2015;25:578-585. **7.** Schatz, C et al. Presented at: Annual Meeting of European Association of Nuclear Medicine; October 2022; Barcelona, Spain. Abstract EP-037. **8.** ClinicalTrials.gov. NCT06052306. Accessed September 26, 2023. https://clinicaltrials.gov/study/NCT06052306. **9.** News Release. Bayer. May 10, 2023. Accessed December 18, 2023. https://www.bayer.com/media/en-us/bayer-and-bicycle-therapeutics-enter-strategic-collaboration-for-development-of-novel-targeted-radionuclide-therapies-in-oncology/. **10.** Bayer. Data on file. **11.** Scheinberg DA, et al. *Curr Radiopharm*. 2011;4(4):306-320.

- Targeted alpha therapy (TAT) is a potent and selective anticancer treatment approach that delivers highly ionizing alpha particle radiation to tumor cells and the tumor microenvironment, leading to antitumor activity while limiting exposure to surrounding normal tissue[1,2]
  - Properties of alpha particles include high linear energy transfer (LET) with short range of penetration, which causes complex cluster double-strand DNA breaks upon decay[3-6]
- Bayer's developing TAT portfolio includes novel targeting approaches combining alpha radionuclides with different targeting moieties, such as antibodies, small molecules, or peptide-based molecules. We are exploring TATs to provide additional treatment modalities for a range of solid tumors[7-10]
  - Current compounds under development utilize actinium-225, an alpha particle–emitting radionuclide with a 9.9-day half-life, which delivers high linear energy capable of inducing DNA damage, cell cycle arrest, and cell death[11]

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Akt, protein kinase b; mTOR, mechanistic target of rapamycin; PD-1, programmed death receptor 1; PD-L1, programmed death-ligand 1; PSA, prostate-specific antigen; TDO-Kyn-AhR, tryptophan 2,3-dioxygenase-kynurenine-aryl hydrocarbon receptor; VEGFR, vascular endothelial growth factor receptor.

Areas of Oncology Research