Press Release

ESMO: AlphaMedix™ phase 2 data support first-in-class potential of new targeted alpha therapy in gastroenteropancreatic neuroendocrine tumors

- New AlphaMedix data showed sustained and clinically meaningful responses across both RLT-naïve and RLT-exposed patients with unresectable or metastatic GEP-NETs
- First phase 2 study to evaluate TAT with lead-212 supporting its potential to address high unmet medical needs in difficult-to-treat, rare cancers
- Phase 2 study met all primary efficacy endpoints and was presented across two oral presentations at the 2025 ESMO Congress in Berlin, Germany

Paris, October 20, 2025. New data from the ALPHAMEDIX-02 phase 2 study (clinical study identifier: NCT05153772) evaluating AlphaMedix (^{212}Pb-DOTAMTATE), an investigational somatostatin receptor (SSTR) targeted alpha therapy (TAT) using the lead-212 isotope, underscore the first-in-class potential of this investigational medicine for the treatment of patients with advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs). Detailed results from the phase 2 study, the first to evaluate a TAT across both radioligand therapy (RLT)-naïve and RLT-exposed patients affected by GEP-NETs, were presented in two oral presentations at the 2025 European Society for Medical Oncology (ESMO) Congress, Berlin, Germany.

> *"Lead-212-based Targeted Alpha Therapy (TAT) could have a transformative impact across a broad range of solid tumors. With AlphaMedix's consistent and clinically meaningful responses across both RLT-naïve and RLT-exposed gastroenteropancreatic neuroendocrine tumor (GEP-NET) patients, the positive results underscore its potential in this rare and difficult-to-treat cancer,"* said **Volker Wagner**, MD, PhD, Chief Medical Officer at Orano Med. *"These data strongly encourage us to further advance the clinical development of AlphaMedix, and jointly with our partner, Sanofi, make this innovative TAT available to patients in need."*

ALPHAMEDIX-02 phase 2 study

ALPHAMEDIX-02 is a phase 2, open-label, multicenter study evaluating the efficacy and safety of AlphaMedix in patients with unresectable or metastatic SSTR+ GEP-NETs. The study included two cohorts evaluating RLT-naïve and RLT-exposed patients. The primary efficacy endpoint across both cohorts was the overall response rate (ORR). Secondary endpoints included progression-free survival (PFS) and overall survival (OS).

The study's efficacy endpoints are based on local investigator assessment, per protocol. In addition, a blinded independent central review (BICR) was conducted subsequently. The key efficacy endpoints were met within both the investigator-assessed and BICR results.

The following results were presented:

RLT-Naïve (n=35)		
	Investigator assessment	***Independent assessment (BICR)***
**DOR is determined only for participants who have achieved a confirmed complete response (CR) or partial response (PR) per RECIST 1.1* ***Defined as the percentage of patients achieving CR or PR or SD per RECIST 1.1* ****OS assessment is independent of RECIST 1.1 criteria, so BICR is n/a*		
ORR	60.0% (95% CI: 42.1-76.1)	57.1% (95% CI: 39.4-73.7)
Duration of Response (DoR) per Kaplan-Meier (KM) estimate (95% CI)*	71.9% for ≥ 24 months (95% CI: 44.6-87.4)	81.7% for ≥ 24 months (95% CI: 53.1-93.8)
Complete Response (CR)	-	2.9%
Partial Response (PR)	60.0%	54.3%
Stable Disease (SD)	34.3%	28.6%
Disease control rate (DCR)**	94.3% (95% CI: 80.8-99.3)	85.7% (95% CI: 69.7-95.2)
PFS	36-month PFS rate of 72.3% (95% CI: 53.3-84.5)	36-month PFS rate of 63.3% (95% CI: 40.3-79.4)
OS	36-month OS rate of 88.2% (95% CI: 71.5-95.4)	Not applicable***

RLT-Exposed (n=26)		
	Investigator assessment	***Independent assessment (BICR)***
**DOR is determined only for participants who have achieved a confirmed complete response (CR) or partial response (PR) per RECIST 1.1* ***Defined as the percentage of patients achieving CR or PR or SD per RECIST 1.1* ****OS assessment is independent of RECIST 1.1 criteria, so BICR is n/a*		
ORR	34.6% (95% CI: 17.2-55.7)	19.2% (95% CI: 6.6-39.4)
Duration of Response (DoR) per Kaplan-Meier (KM) estimate (95% CI)*	100% for ≥ 18 months (95% CI: 100-100)	100% for ≥ 18 months (95% CI: 100-100)
Partial Response (PR)	34.6%	19.2%
Stable Disease (SD)	61.5%	80.8%
Disease control rate (DCR)**	96.2% (95% CI: 80.4-99.9)	100% (95% CI: 86.8-100)
PFS	18-month PFS rate of 82.6% (95% CI: 59.0-93.3)	18-month PFS rate of 88% (95% CI: 67.3-96.0)
OS	18-month OS rate of 85.1% (95% CI: 58.5-95.2)	Not applicable***

AlphaMedix™ had a similar safety profile across both cohorts. Within the RLT-naïve cohort, 85.7% of patients received all four doses of AlphaMedix, and 84.6% of patients within the RLT-exposed cohort. All GEP-NET patients experienced at least one treatment-emergent adverse event (TEAE). Grade ≥3 TEAEs occurred in 42.3% of RLT-exposed patients and 54.3% of RLT-naïve patients. The most common Grade ≥3 TEAEs in both groups was lymphocyte count decrease (25.7% of RLT-naïve patients and 15.4% of RLT-exposed patients).

> *"The future of oncology research will be driven by cutting-edge science and next-generation modalities, such as radioligand therapies. AlphaMedix, a promising targeted alpha therapy, embodies the type of solution Sanofi is working to advance,"* said **Christopher Corsico**, MD, Global Head of Development at Sanofi. *"We are excited to share these robust scientific findings at ESMO as the data could represent a significant advancement in how we treat gastroenteropancreatic neuroendocrine tumors. As we engage with health authorities and advance the clinical program, we remain focused on bringing this innovative modality to patients who need new treatment options"*

Advancing AlphaMedix in GEP-NETs

RLTs, which work by delivering radiation directly to tumor cells, represent an emerging area of oncology research. While current approved beta-emitting RLTs have improved outcomes in patients with GEP-NETs, there remains a critical gap in care, including in those who have progressed following previous RLT.

TAT represents an innovative modality in RLT, harnessing high-energy, short-range alpha emissions to precisely target cancer cells while reducing potential exposure to surrounding tissue.

> *"The results observed in the ALPHAMEDIX-02 trial clearly demonstrate exceptional levels of efficacy for a Targeted Alpha Therapy (TAT), based on current available therapies, in both radioligand therapy (RLT)-naïve and RLT-exposed populations and could potentially set new expectations when treating gastroenteropancreatic neuroendocrine tumor (GEP-NET) patients with RLTs"* said **Ebrahim Delpassand**, MD, Founder and Chairman, CEO of RadioMedix. *"For too long, this patient population has experienced inadequate disease control with current approved therapies. This important work provides hope for a new treatment for GEP-NET patients, their caregivers, and their healthcare providers."*

In February 2024, AlphaMedix™ was designated as a breakthrough therapy by the US Food and Drug Administration in RLT-naïve patients with unresectable or metastatic GEP-NETs, recognizing the potential clinical benefits of lead-212–based TATs. The ALPHAMEDIX-02 results will form the basis for further discussions with health authorities.

An international phase 3 study to further evaluate AlphaMedix in GEP-NETs is actively being planned. AlphaMedix is an investigational medicine and has not been approved by any regulatory authority.

In September 2024, Sanofi entered an exclusive licensing agreement with Orano Med and RadioMedix to globally commercialize AlphaMedix.

About the ALPHAMEDIX-02 study

ALPHAMEDIX-02 is a phase 2, open-label, multicenter study evaluating the efficacy and safety of AlphaMedix (^{212}Pb-DOTAMTATE) in patients with histologically confirmed unresectable or metastatic GEP-NETs, positive somatostatin analogue imaging and at least one site of measurable disease. The study included two cohorts evaluating RLT-naïve (n=35) and RLT-exposed (n=26) GEP-NET patients. RLT-exposed patients had progressive disease after receiving up to four doses of ^{177}Lu-DOTATATE and received their last dose at least six months prior to Day 1. In both cohorts, AlphaMedix was administered at 67.6 µCi/kg every eight weeks for up to four cycles (6 mCi maximum per cycle). The primary efficacy endpoint across both cohorts was ORR per RECIST 1.1. Secondary endpoints included PFS and OS.

About NETs

NETs are a heterogeneous group of cancers that originate from neuroendocrine cells. These cancers occur mostly in the gastrointestinal tract and pancreas but can also occur in other tissues including the thymus, lung, and other uncommon sites such as the ovaries, heart, and prostate. Most NETs strongly express somatostatin receptors. Despite the global prevalence of NETs increasing each year, it is considered a rare cancer that is estimated to affect approximately 35/100,000 individuals worldwide. In the United States, around 12,000 patients annually are expected to be diagnosed with neuroendocrine tumors, with an average five-year survival rate of 60% at a metastatic stage.

About Orano Med

Orano Med is a subsidiary of the Orano Group. Orano Med is a clinical-stage biotechnology company that develops a new generation of targeted therapies against cancer using the unique properties of lead-212 (^{212}Pb), an alpha-emitting radioisotope and one of the more potent therapeutic payloads against cancer cells known as Targeted Alpha Therapy (TAT). Leveraging its unique and secured access to ^{212}Pb, the company is developing several ^{212}Pb-based

radioligand therapies combined with various targeting agents. Orano Med has ^{212}Pb manufacturing facilities, laboratories, and R&D centers in France and in the US and is currently expanding its GMP-manufacturing capacities for ^{212}Pb radiolabeled pharmaceuticals in North America and Europe.

About RadioMedix

RadioMedix, Inc., a clinical-stage biotechnology company and former sponsor of the AlphaMedix trial, is based in Houston and Humble, Texas. The company is focused on innovative targeted radiopharmaceuticals for diagnosis, monitoring, and therapy of cancer. RadioMedix is developing radiopharmaceuticals for PET imaging and therapy (alpha- and beta-labeled agents). The company established contract service facilities for academic and industrial partners. including a cGMP and analytical suite for Phase I-II-III clinical trials and commercial launch. To learn more, visit www.radiomedix.com and LinkedIn.

About Sanofi

Sanofi is an R&D driven, AI-powered biopharma company committed to improving people's lives and delivering compelling growth. We apply our deep understanding of the immune system to invent medicines and vaccines that treat and protect millions of people around the world, with an innovative pipeline that could benefit millions more. Our team is guided by one purpose: we chase the miracles of science to improve people's lives; this inspires us to drive progress and deliver positive impact for our people and the communities we serve, by addressing the most urgent healthcare, environmental, and societal challenges of our time.

Sanofi is listed on EURONEXT: SAN and NASDAQ: SNY

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Sanofi forward-looking statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions, and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that global crises may have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. The risks and uncertainties also include the uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary

Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2024. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

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