Press Release

Orano Med enters Next Phase of Collaboration with Roche

Paris, December 4th, 2025

Orano Med, a subsidiary of the Orano group specializing in nuclear medicine, announced today that its long-standing collaboration with the multinational pharmaceutical company Roche (SIX: RO, ROG; OTCQX: RHHBY) is entering the next phase. Over the past years, the companies have conducted extensive preclinical research to develop a potential novel cancer treatment approach called "two-step pretargeted radioimmunotherapy" (or PRIT). This innovative technology, which pretargets the tumor with an antibody that is subsequently able to capture chelated lead-212 (^{212}Pb) to target tumor cells, is now ready to advance into clinical development in humans. Orano Med will be responsible for the manufacturing of ^{212}Pb, utilizing its industrial manufacturing platform in France and the US.

Nicolas Maes, Chief Executive Officer of the Orano group, commented: *"We are very pleased about the progress made in collaboration with Roche for the development of a potential new treatment approach for cancer patients. After the licensing agreement signed with Sanofi last year for our most advanced clinical program, AlphaMedix™, the achievement with this potential new drug candidate marks an important milestone that we accomplished jointly with another major player in the pharmaceutical industry. It illustrates our capacity to execute our long-term strategy, aimed at developing a solid pipeline of ^{212}Pb-targeted alpha therapies to treat multiple oncology indications. In addition, thanks to the Orano Group's expertise in the nuclear industry and its access to thorium-232, a scarce raw material required for producing ^{212}Pb, Orano Med is also responsible for the entire production and distribution chain for these isotopes."*

Julien Torgue, Chief Scientific Officer of Orano Med, commented: *"The application of two-step pretargeted radioimmunotherapy represents a potentially game-changing advancement in radioligand therapies and cancer treatment more broadly. Instead of delivering radiation and targeting vector together, the novel technique separates the process into two precise steps: first, allowing time for antibodies to accumulate on the tumor, and then capturing the alpha particle emitting radioactive isotope lead-212, which allows for the precise targeting of cancer cells while sparing healthy tissue. In preclinical studies, we could already demonstrate both strong efficacy and, importantly, a reduction*

About Orano

As a recognized international operator in the field of nuclear materials, Orano delivers solutions to address present and future global energy and health challenges. Its expertise and mastery of cutting-edge technologies enable Orano to offer its customers high value-added products and services throughout the entire fuel cycle. Every day, the Orano group's 18,000 employees draw on their skills, unwavering dedication to safety and constant quest for innovation, with the commitment to develop know-how in the transformation and control of nuclear materials, for the climate and for a healthy and resource-efficient world, now and tomorrow.
Orano, giving nuclear energy its full value.

About Orano Med

Orano Med, a subsidiary of the Orano Group, is a clinical-stage biotechnology company developing a new generation of targeted therapies against cancer using the unique properties of lead-212 (^{212}Pb), a rare alpha-emitting radioisotope and one of the more potent therapeutic payload against cancer cells. This technology is known as targeted alpha therapy (TAT). AlphaMedix™, its most advanced asset in clinical development for GEP-NET tumors, received Breakthrough Designation from the FDA in 2024. The company is advancing several potential treatments using ^{212}Pb combined with various targeting agents through clinical and preclinical studies. Orano Med has ^{212}Pb manufacturing facilities, laboratories, and R&D centers in France and in the US and is currently investing to further expand its GMP-manufacturing capacities for ^{212}Pb radiolabeled pharmaceuticals in North America and Europe.
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in off-target uptake in healthy tissues. If these results translate to the clinic, this could bring us a major step closer to a more effective and for patients also safer form of radioligand therapy. We are looking forward to further continue the development of this innovative approach with Roche."

Under the terms of the agreement, Orano Med and Roche have committed to develop this new therapeutic solution targeting a specific antigen known as carcinoembryonic (CEA), a cell surface glycoprotein overexpressed in several cancers. This antigen serves as a marker for various types of cancer, such as colorectal, pancreatic, and gastric cancers, as well as certain lung cancers. These are cancers for which the current therapeutic options are often limited or insufficient to meet patients' needs. CEA shows restricted expression in normal tissues, making it a very suitable target for antibody-based therapies and radioimmunotherapy.

The Roche sponsored phase 1 clinical trial is expected to start in the first half of 2026, initiating the development of a broader platform dedicated to alpha radioimmunotherapies, underscoring Orano Med's global leading position in the field of targeted alpha therapies.

About ^{212}Pb two-step PRIT

Compared with conventional radioligand therapies (RLT), where the isotope and targeting moiety are co-delivered, pretargeted radioimmunotherapy (PRIT) uses a sequential approach. A tumor-targeting bispecific antibody (bsAb) is first administered, followed by a radioligand carrying the radioactive payload. The delay gives the bsAb the necessary time to accumulate on the tumor cells while unbound radioligand is rapidly cleared. It thus enables highly specific antibody targeting while remaining compatible with the relatively short half-life of ^{212}Pb (10.6 hours). By introducing the cytotoxic radioligand only after the bsAb has largely cleared from circulation, radiation is concentrated in the tumor. This sequential approach is designed to minimize systemic radiation exposure, achieve high tumor-to-nontumor ratios, and thus improve safety and tolerability compared to other RLTs.

One of the main challenges of the PRIT approach has been to ensure fast excretion of the radioactive payload while maintaining high affinity for the slower-clearing pretargeting molecule. An intermediate step to clear or neutralize circulating pretargeting antibodies has often been employed to prevent off-tumor capture of the radioligand, but this adds complexity and safety risks, posing challenges to the clinical implementation of PRIT.

The new approach developed by Roche and Orano Med represents a novel two-step PRIT regimen for CEA-positive tumors that eliminates the need for an intermediate clearance step. This strategy combines a complementary bispecific antibody pair with the chelated ^{212}Pb, demonstrating both high efficacy and improved tolerability in preclinical studies compared with three-step PRIT.

Preclinical studies have confirmed proof of mechanism and therapeutic efficacy of the two-step PRIT, showing a favorable biodistribution with substantial uptake in CEA-positive tumors and rapid clearance of unbound ^{212}Pb-DOTAM, with limited accumulation in kidneys and other organs. This confirms the excellent ^{212}Pb tumor specificity and its high potential to significantly delay tumor growth.