Radio-DARPins: Expanding the Target and Indication Space for Targeted Alpha Therapy

The clinical-stage biotech Molecular Partners AG (SIX, NASDAQ: MOLN) is leveraging its novel DARPin miniproteins as isotope-agnostic vectors to develop targeted alpha radiotherapeutics. Molecular Partners designs its radiotherapeutic medicines matching disease and target biology with vector and isotope properties to address unmet medical needs.

DARPins (Designed Ankyrin Repeat Proteins), a novel class of medicines tested in >2500 patients and developed through to the registrational stage, have the potential to unlock a broad range of cancer targets and indications – going beyond PSMA and SSTR.

MP0712 – "Best-in-Class" DLL3 Targeted Radio-Therapy Advances in Phase 1/2a

The Company's lead Radio-DARPin candidate MP0712, co-developed with Orano Med, pairs a DLL3-targeting DARPin with the alpha-emitting isotope lead-212 (^{212}Pb). DLL3 is a tumor target expressed in over 85% of small cell lung cancer (SCLC) and other neuroendocrine carcinomas.

MP0712 is half-life-optimized to leverage DLL3 internalization and continued replenishment at the cell surface – in spite of low DLL3 target density – for optimal uptake and accumulation of MP0712 in tumor lesions.

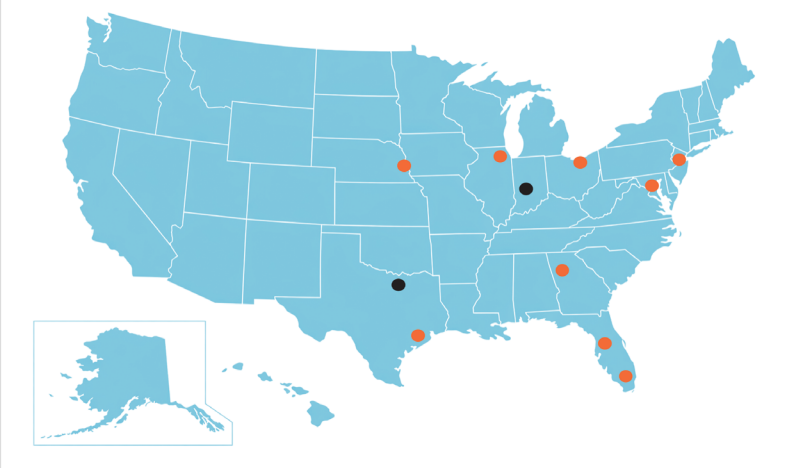
The multicenter US Phase 1/2a study (NCT07278479) is well underway, dosing ongoing in the fully recruited dose level 2 (DL2, 105 MBq). No dose-limiting toxicities and only mild, transient adverse events were reported in DL1 (75 MBq). Blood, kidney, and liver parameters were all within safety bounds by a generous margin. These encouraging initial data provide confidence to escalate to higher dose levels. Initial results will be presented at the North America Conference on Lung Cancer 2026 and efficacy data are anticipated in 2027.

Molecular Partners is mapping several dose expansion cohorts, including tarlatamab-experienced patients,

MP0712 – DLL3 x ^{212}Pb Targeted Radiotherapy

- US multicenter Phase 1/2a study of MP0712 monotherapy (NCT07278479)
- For patients with SCLC and other DLL3-expressing neuroendocrine cancers
- All 9 planned centers to open in 2026 across the US

NCT07278479

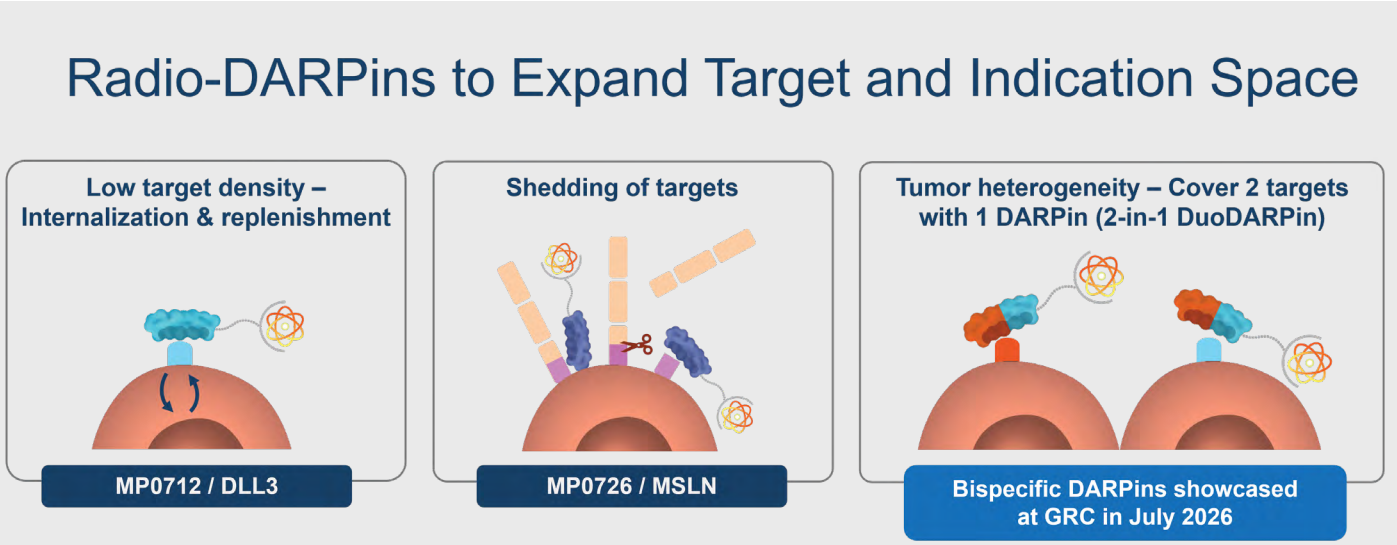


Study centers
- United Theranostics Princeton, NJ
- Nebraska Cancer Specialists, NE
- United Theranostics Maryland, MD
- Emory University School of Medicine, GA
- University Hospital Cleveland, OH
- Moffitt Cancer Center, FL
- MD Anderson, TX
- University of Chicago, IL
- University of Miami, FL

Manufacturing sites
- Plano, TX
- Indianapolis, IN

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tarlatamab-naïve patients, as well as combination settings and additional indications – to be triggered upon reaching RP2D.

Widening the Aperture: MSLN and CD70 for Multiple Cancer Indications

MP0726, the Company's second Radio-DARPin candidate, is designed to selectively bind membrane-bound mesothelin (MSLN) without being impacted by shed MSLN – a feature difficult to achieve with other vectors and which has hampered the development of MSLN-directed therapies. MP0726 could enable targeted alpha therapy for multiple indications, including ovarian cancer. MP0726 is advancing to first-in-human imaging in H2 2026.

The Company's third candidate MP0730 targets CD70, a tumor antigen overexpressed in clear-cell renal cell carcinoma and other indications. This Radio-DARPin has the potential to overcome resistance mechanisms to cytotoxic therapies inherent to kidney cancer. First-in-human program is expected to start mid 2027.

Beyond Monospecific: Showcasing Bispecifics to Tackle Heterogeneous Tumors

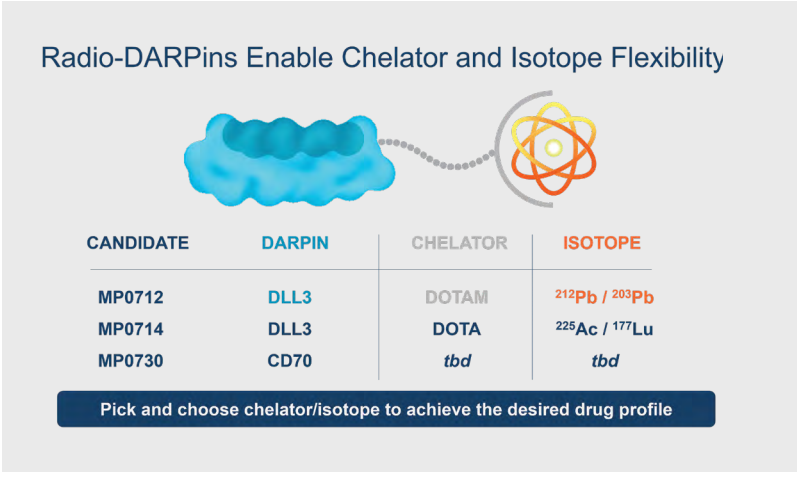
Molecular Partners intends to expand its impact through multispecific DARPins. Most tumors are heterogeneous, and in many cases a single target can't cover every lesion, patient, or stage of disease.

Bispecific Radio-DARPins could offer improved precision and therapeutic efficacy to patients. These can be formatted either as a bispecific – two DARPins, each binding an individual target – or as a 2-in-1 DuoDARPin able to bind one or the other target. First candidate selection is targeted for 2027.

Isotope-Agnostic in Patients

Molecular Partners' isotope-agnostic strategy is enabled by its robust yet versatile DARPins. Preclinical data showed highly comparable biodistribution profiles for two Radio-DARPin candidates, each specific for a different target, labeled with ^{177}Lu or ^{203}Pb – confirming that biodistribution is not impacted by isotope and chelator choice but rather by vector and disease biology. This is a potential competitive advantage for DARPins as vectors, allowing selection of the most suitable therapeutic isotope as late as with initial clinical data at hand, without having to restart development.

In addition, ^{203}Pb-MP0712 human dosimetry data presented at TWC 2026 suggest both ^{212}Pb and ^{225}Ac could work as therapeutic isotopes for the DLL3-targeted alpha therapy.



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Proof will come from experience in patients. Dr. Mike Sathekge from NuMeRI has launched an early-access program using the same DLL3-targeting DARPin as in MP0712, paired instead with ^{177}Lu/^{225}Ac and referred to as MP0714. Imaging and treatment of patients is ongoing under South Africa's compassionate care framework, while Molecular Partners fully focuses on the execution of the US Phase 1/2a study of MP0712 with ^{212}Pb.

Isotope Supply & Development Capabilities Established with Global Leaders

Molecular Partners is future-proofing isotope supply. It has a strategic agreement with Orano Med, a pioneer in targeted alpha therapy, for co-developing up to ten ^{212}Pb-based programs and also has agreements with Eckert & Ziegler, a global leader in radiopharmaceutical manufacturing, and PanTera, a leading ^{225}Ac producer.

Outlook

Molecular Partners' targeted radiotherapeutics engine is based on innovative technology and strong partnerships to develop tailored, impactful medicines for patients. The Radio-DARPin pipeline is expanding, with a presentation on MP0712 initial safety data in December 2026 and efficacy data are expected in 2027.

Pioneering Precision Theranostics. Continued from page 8.

clinical practice an approach used internationally for many years and supported by a substantial body of clinical evidence.

Supporting Access and Implementation in Practice

FDA approval and broader U.S. access are important inflection points in Telix's commitment to patients and the nuclear medicine community. The Pixclara® prescribing information directs imaging centers to acquire images 20 to 30 minutes after administration for a duration of 20 minutes,[1] providing practical guidance for incorporating ^{18}F-FET PET into clinical workflows. As adoption expands, Telix continues to generate evidence aimed at supporting implementation of molecular imaging in routine clinical practice.

Beyond its approved use in glioma, Telix is advancing a Phase 3 registrational study of Pixclara® for potential indication expansion in brain metastases, extending its molecular imaging strategy into another area of significant unmet need in neuro-oncology.

Advancing a Neuro-Oncology Theranostic Platform

FDA approval of Pixclara® represents more than the introduction of a new imaging agent. It also marks an important step in Telix's broader vision for precision medicine in neuro-oncology, where molecular imaging and targeted radionuclide therapy work together to support patients across the continuum of care.

Complementing this imaging program, iodofalan (^{131}I), also known as TLX101-Tx, is an investigational LAT1-targeted radionuclide therapy. The theranostic relationship between LAT1-targeted imaging and therapy is illustrated in a published case report of a patient with recurrent glioblastoma treated with investigational TLX101-Tx in combination with lomustine.[4] Serial MRI and ^{18}F-FET PET images documented the patient's disease before treatment and at follow up, providing complementary structural and molecular views of the reported near-complete treatment response.[4]

TLX101-Tx is currently being evaluated in the global Phase 3 IPAX BrIGHT study (NCT07100730) for recurrent glioblastoma. IPAX BrIGHT represents an important milestone in the clinical development of radionuclide therapy for glioblastoma.

Together, Pixclara® and TLX101-Tx reflect Telix's **"See it. Treat it."** approach and its commitment to advancing a precision theranostic platform for brain cancer, from molecular characterization of disease to the investigation of targeted radionuclide therapy.

REFERENCES

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2. Law I, Albert NL, Arbizu J, et al. Joint EANM/EANO/RANO practice guidelines/SNMMI procedure standards for imaging of gliomas using PET with radiolabelled amino acids and [^{18}F]FDG: version 1.0. *Eur J Nucl Med Mol Imaging*. 2019;46:540–557.
3. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology: Central Nervous System Cancers*. V3.2026.
4. El Ghalbouni A, Snijders TJ, Tolboom N, Braat AJAT. Near complete response recurrent glioblastoma after treatment with [^{131}I]-iodofalan. *Eur J Nucl Med Mol Imaging*. 2026;53:4785–4787.

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