



Andarix

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## Arming somatostatin to fight cancer

Andarix Pharmaceuticals is a clinical-stage company that develops highly specific radiolabeled peptides for targeted radiotherapy and diagnostic imaging in cancer. The company's key product is P2045, a proprietary somatostatin (SST) peptide optimized for radioisotope binding. Two lead compounds are in clinical trials for lung cancer—therapeutic candidate  $^{188}\text{Re}$ -P2045 (Tozaride) and imaging agent  $^{99\text{m}}\text{Tc}$ -P2045. Andarix is looking to expand its global partnership network.

### Targeting SST receptors

SST receptors (SSTRs) constitute a superfamily of five G-protein-coupled receptors that are differentially upregulated on a number of solid tumors. For example, in both small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC), SSTR2 is the most widely upregulated subtype of SSTR.

Andarix's P2045 is a synthetic SST analog that contains (1) a 'chelating' sequence that forms stable complexes with metal radioisotopes and (2) an SSTR-binding pharmacophore—the Tyr-D-Trp-Lys-Thr peptide sequence—that binds with high-affinity to SSTRs. In vitro binding affinity studies of P2045 with SSTR-rich tumor membranes and with Chinese hamster ovary (CHO) cells that express human SSTRs have

shown that P2045 has a high affinity for SSTRs, comparable to that of native SST (half-maximal inhibitory concentration ( $\text{IC}_{50}$ ): 0.09–0.2 nM). Among the SSTRs, P2045 shows the highest affinity for SSTR2.

To 'arm' P2045 for therapeutic purposes, Andarix researchers turned to rhenium-188, a readily available metal isotope that decays with the emission of two high-energy  $\beta$ -particles suitable for therapeutic purposes and a  $\gamma$ -photon suitable for imaging. The product,  $^{188}\text{Re}$ -P2045 (Tozaride), delivers its cytotoxic high-energy  $\beta$ -radiation with high specificity to target tumor cells. The team also labeled P2045 with technetium-99, a standard metal isotope tracer for medical applications, to generate a companion imaging compound.

### The Andarix edge

Four clinical trials with P2045 have been completed to date: an exploratory imaging trial using  $^{99\text{m}}\text{Tc}$ -P2045; a biodistribution study comparing  $^{99\text{m}}\text{Tc}$ -P2045 and  $^{188}\text{Re}$ -P2045 that shows similar biodistribution and rapid clearance of both agents; and two dose-escalation trials of  $^{188}\text{Re}$ -P2045 indicating that  $^{188}\text{Re}$ -P2045 is well tolerated and demonstrated early signs of efficacy, with a significant reduction in tumor mass and

an overall median survival that exceeded the current standard of care by 40%.

Andarix has a codevelopment and commercialization agreement in place for Torazide to treat lung and other cancers. The company's business model is to partner with, and license its technology to, leading pharmaceutical marketing and sales organizations in several markets on a worldwide basis. Such deals may include upfront development fees and downstream royalties.

"Our somatostatin-based targeted radiotherapy represents a potential therapeutic breakthrough in lung cancer and is expected to yield significant clinical benefit in other tumors such as pancreatic cancer," said Chris Adams, Andarix's CEO. "We are looking forward to advancing our compounds through the clinical development process with partners around the globe."

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