Technetium and rhenium have radioactive isotopes that are clinically useful for diagnostic (Tc-99m) or therapeutic (Re-186/188) purposes. This makes them attractive candidates for incorporation into pharmaceuticals. One way to incorporate radioactive metals into pharmaceuticals is through the use of a bifunctional chelating agent (BFCA), which inertly traps the metal while also attaching it to a targeting biomolecule.

Technetium-99m is an attractive radionuclide not only because of its diagnostic capabilities, but also because it is a widely available and relatively affordable option. Two Tc-99m radiopharmaceuticals were created that seek to target somatostatin receptors (SSTRs), which are commonly overexpressed on neuroendocrine tumor tissues. Two different histidine-derived BFCAs were used to chelate a technetium-99m tricarbonyl core while simultaneously tethering it to an antagonist peptide with a high affinity for somatostatin receptor subtype two (SSTR2).

Due to the fact that non-radioactive Re is in the same group as Tc, the analogous macroscale Re compounds were synthesized. This helped to determine the identity of the products made on the radiotracer level (nano- to picomolar) as well as determine receptor affinity through competitive binding assays in SSTR2-expressing cells. Both Re compounds, exhibited very good, low nanomolar affinities for SSTR2. The Tc-99m radiotracer products both exhibited high in vitro stability during challenges in cysteine, histidine, and mouse serum. Biodistribution and imaging studies in mice were also performed.

The complexation of Re using a tetradeutate diphosphinedithiol (DPDT) ligand was also explored. Rhenium is more readily oxidized than technetium, which can cause complications when seeking to use Re-186/188 radiopharmaceuticals in the body. Complexation with more reducing ligands (such as DPDT) may help stabilize Re(V) in the body. Thus, the initial chemistry of Re- and Tc-DPDT complexes was explored. This led to the creation of a highly stable Re(V)-DPDT complex, which remained stable in oxidative environments over a period of several months. Macroscale reactions using the DPDT ligand to synthesize the Tc-99 counterpart led to the formation of Tc(III) complexes from Tc(VII), without the need for additional reducing agents.