Diagnostic imaging platform:

MTTI believes its ^{18}F-TumorVue, which also targets PS on the apoptotic cell surface, will be superior to Annexin-V for monitoring cancer therapy. To construct our novel phosphatidylserine (PS)-targeted PET imaging agent, we used bis-zinc(II)-dipicolylamine (Zn-DPA) coordination complex technology to target bio-membranes, which contain anionic phospholipids. Probes containing two Zn-DPA units were known to selectively stain the anionic membrane surfaces of apoptotic animal cells as opposed to the near neutral membranes of healthy animal cells. It is well known that during apoptosis the surface charge on the plasma membrane becomes increasingly negative due to appearance of anionic PS. The utility of various fluorescent versions of these compounds to detect apoptosis in vitro has been shown using fluorescence microscopy and flow cytometry techniques. Co-staining and blocking experiments with annexin-V-FITC has provided evidence that the PS-affinity group (Zn-DPA) is binding to the same membrane sites as annexin-V. Further, Smith et al have recently shown that a Zn-DPA probe with a Cy7 fluorochrome can target the anionic dead and dying cells within prostrate and mammary xenograft tumor models. It is known that PS becomes exposed on the accessible outer surface of tumor vascular endothelium in response to oxidative stresses present in the tumor microenvironment. Chemotherapy, radiation, and androgen deprivation therapy markedly increase PS exposure on tumor vessels, so that the large majority (70-95%) become positive. Therefore, we believe that anionic phospholipids exposed on apoptotic and living tumor cells may be targeted for the purpose of monitoring the effectiveness of antitumor therapy.

MTTI has also licensed from the Medical College of Wisconsin (MCW) rights to an allowed US composition of matter patent covering the preparation of 99mTc-HYNIC-Duramycin and its use for the non-invasive imaging of phosphatidylethanolamine (PE) residues. The company is currently optimizing the kit vial drug product for use in preclinical research for support of studies in selected potential clinical indications. ^{99m}Tc-Duramycin, which targets PE on the apoptotic cell surface, has also been show to be an effective targeting agent for multiple disease states. MTTI plans to develop these radiopharmaceutical candidates for various clinical indications with the lead indications shown in the table below. The company believes it enjoys a competitive advantage created by the intellectual property and extensive research associated with these potential new entries into the molecular imaging market.

Product Candidate	**Potential indication**	**Development Status**	**Available License Territories**
F-18-TumorVue	Cancer therapy monitoring	Preclinical Research	World-wide
Tc-99m Duramycin	Cardiotoxicity	Completed limited toxicology study	World-wide
Tc-99m Duramycin	Atherosclerotic plaque	Completed limited toxicology study	World-wide
Tc-99m Duramycin	Cancer therapy monitoring	Completed limited toxicology study	World-wide