Abstract: Two-domain MHC polypeptides are useful for modulating activities of antigen-specific T-cells, including for modulating pathogenic potential and effects of antigen-specific T-cells. Exemplary MHC class II-based recombinant T-cell ligands (RTLs) of the invention include covalently linked .beta.1 and .alpha.1 domains, and MHC class I-based molecules that comprise covalently linked .alpha.1 and .alpha.2 domains. These polypeptides may also include covalently linked antigenic determinants, toxic moieties, and/or detectable labels. The disclosed polypeptides can be used to target antigen-specific T-cells, and are useful, among other things, to detect and purify antigen-specific T-cells, to induce or activate T-cells, to modulate T-cell activity, including by regulatory switching of T-cell cytokine and adhesion molecule expression, to treat conditions mediated by antigen-specific T-cells, including treatment and/or prevention of central nervous system damage relating to stroke.