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(54) **Title**: TRAIL R2-SPECIFIC MULTIMERIC SCAFFOLDS

(57) **Abstract**: The present invention provides Tenascin-3 FnIII domain-based multimeric scaffolds that specifically bind to TRAIL Receptor 2 (TRAIL R2), a cell membrane receptor involved in apoptosis. The invention further provides engineered variants with increased affinity for the target, increase stability, and reduced immunogenicity. Furthermore, the present invention is related to engineered multivalent scaffolds as prophylactic, diagnostic, or therapeutic agents, and their uses against diseases caused by cells expressing TRAIL R2, in particular to a therapeutic use against cancer.