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(54) Title: ANTI-TUMOR NECROSIS FACTOR-ALPHA AGENTS AND USES THEREOF

(57) Abstract: The present invention relates to polypeptides comprising one or more antibody single domains, or antigen-binding fragments thereof, directed against Tumor Necrosis Factor-alpha, in particular, two light chain variable domains in dimeric form, where the dimer has high solubility. It also relates to methods of using anti-Tumor Necrosis Factor-alpha polypeptides in treating inflammatory disorders, including rheumatoid arthritis. Compositions and methods for enhancing therapeutic potential of anti-Tumor Necrosis Factor-alpha polypeptides are provided, including linking the polypeptide to an albumin-binding domain and/or de-immunizing the polypeptide, to provide therapeutic agents with good solubility, enhanced serum half-life, and/or reduced immunogenicity, while substantially maintaining the specific binding properties of the anti-Tumor Necrosis Factor-alpha polypeptides.

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