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(54) Title: PLASMIN-RESISTANT PEPTIDES FOR IMPROVED THERAPEUTIC INDEX

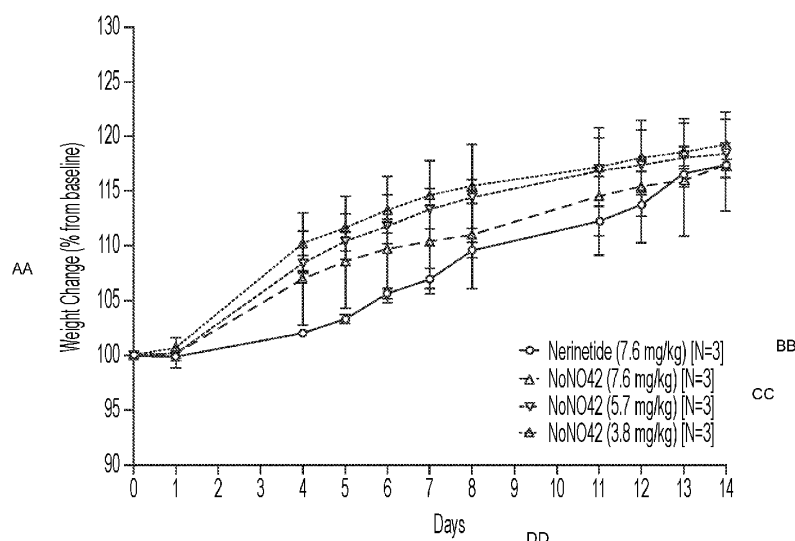


FIG. 34

(57) Abstract: The invention provides variants of a previously described active agent for treating stroke, Tat- NR2B9c, in which target binding characteristics are retained by inclusion of L-amino acids at the C -terminus and plasmin-resistance is conferred by inclusion of D-amino acids. Nephrotoxicity associated with D-amino acids can be reduced by including D-amino acids at a minimal number of positions and/or by co-administration with an inhibitor of D-amino acid oxidase. The resulting active agents have several advantages including administration at the same time as thrombolytic agents without significant loss of activity due to plasmin digestion. The resulting agents are also more suitable for administration by alternative routes to intravenous infusion, such as subcutaneous, intranasal and intramuscular, and for multi-dosing regimes for treatment of chronic conditions.

[Continued on next page]

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