ArmaGenÃ,® Re-engineers Erythropoietin for Brain Penetration

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LOS ANGELES, July 16 /PRNewswire/ -- Human erythropoietin (EPO) is a potent neuroprotective agent for multiple brain disorders, including stroke, brain and spinal cord injury, and Parkinson's disease. However, EPO drug development for the brain is limited, because EPO does not cross the blood-brain barrier (BBB). In acute stroke or brain injury, the BBB is intact in the early hours after the insult when neuroprotection is still possible. Therefore, large molecule biopharmaceuticals such as EPO must be re-engineered to enable BBB transport. ArmaGen Technologies has developed the BBB molecular Trojan horse platform technology for solving the BBB drug delivery problem, and has used this technology to create a brain penetrating form of human EPO. ArmaGen® has successfully re-engineered human EPO as an IgG fusion protein that penetrates the brain following intravenous (IV) administration. Human EPO is fused to a genetically engineered monoclonal antibody (MAb) to the human insulin receptor (HIR). The HIRMAb acts as a molecular Trojan horse to ferry the EPO across the BBB via transport on the endogenous BBB insulin receptor. The HIRMAb-EPO fusion protein is a dual receptor specific protein with low nM binding constants for both the human EPO receptor and the human insulin receptor. The HIRMAb part of the HIRMAb-EPO fusion protein cross-reacts with the Rhesus monkey insulin receptor. Therefore, brain penetration of the HIRMAb-EPO fusion protein was demonstrated in vivo in the adult Rhesus monkey following IV administration. EPO alone was shown not to cross the primate BBB. The brain uptake of the HIRMAb-EPO fusion protein in the Rhesus monkey is high, 2% injected dose/brain, and comparable to the brain uptake of small molecules. The plasma pharmacokinetics (PK) of the HIRMAb-EPO fusion protein differs markedly from the PK of EPO, which minimizes any effect of the fusion protei
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