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(54) Title: BIOCONJUGATES OF SYNTHETIC APELIN POLYPEPTIDES

X1-X2-X3-X4-X5-X6-X7-X8-X9-X10-X11-X12-X13

(I)

(57) Abstract: The invention provides a bioconjugates comprising a synthetic polypeptide of Formula I': I' or an amide, an ester or a salt thereof, wherein X1, X2, X3, X4, X5, X6, X7, X8, X9, X10, X11, X12 and X13 are defined herein and a half-life extending moiety wherein the peptide and the half-life extending moiety are covalently linked or fuse, optionally via a linker. The polypeptides are agonist of the APJ receptor. The invention also relates to a method for manufacturing the bioconjugates of the invention, and its therapeutic uses such as treatment or prevention of acute decompensated heart failure (ADHF), chronic heart failure, pulmonary hypertension, atrial fibrillation, Brugada syndrome, ventricular tachycardia, atherosclerosis, hypertension, restenosis, ischemic cardiovascular diseases, cardiomyopathy, cardiac fibrosis, arrhythmia, water retention, diabetes (including gestational diabetes), obesity, peripheral arterial disease, cerebrovascular accidents, transient ischemic attacks, traumatic brain injuries, amyotrophic lateral sclerosis, burn injuries (including sunburn) and preeclampsia. The present invention further provides a combination of pharmacologically active agents and a pharmaceutical composition.

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