(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
28 July 2016 (28.07.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/116842 A1

(51) International Patent Classification:
*A61K 47/48* (2006.01) *A61P 9/04* (2006.01)
*A61K 45/06* (2006.01)

(21) International Application Number:
PCT/IB2016/050206

(22) International Filing Date:
15 January 2016 (15.01.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/107,040 23 January 2015 (23.01.2015) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

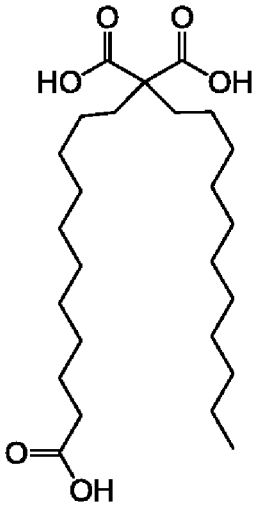
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

**Declarations under Rule 4.17**:

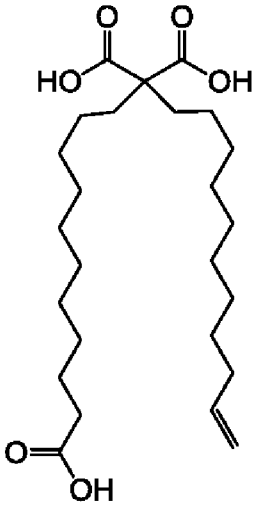
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

*[Continued on next page]*

(54) Title: SYNTHETIC APELIN FATTY ACID CONJUGATES WITH IMPROVED HALF-LIFE



and



(57) Abstract: The invention provides a conjugate, or a pharmaceutically acceptable salt thereof, comprising a synthetic polypeptide of Formula I: Q-R-P-R-L-C*-H-K-G-P-(Nle)-C*-F (I) or a amide or ester thereof; and a fatty acid selected from: wherein said fatty acid is covalently linked to the N-terminus of the peptide via one of its carboxylic acid functionality, optionally via a polyethylene glycol linker; and wherein the two cysteine amino acids labeled with "*" form a disulfide bond between the thiol functionalities of their side chain. The conjugates are agonist of the APJ receptor. The invention also relates to a method for manufacturing the conjugates 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.

WO 2016/116842 A1

**Published**:

— *with international search report (Art. 21(3))*