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(54) **Title**: SYNTHETIC APELIN MIMETICS FOR THE TREATMENT OF HEART FAILURE

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

(57) **Abstract**: The invention provides a synthetic polypeptide of Formula 1': 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. The polypeptides are agonist of the APJ receptor. The invention also relates to a method for manufacturing the polypeptides 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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A. CLASSIFICATION OF SUBJECT MATTER
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B. FIELDS SEARCHED

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A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BEILSTEIN Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JURI HAMADA ET AL: "Evaluation of novel cyclic analogues of apelin.", INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE, vol. 22, no. 4, 1 October 2008 (2008-10-01), pages 547-552, XP055072884, ISSN: 1107-3756 Discussion; figure 1; table 1 ----- -/--	1-36

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	N. MACALUSO ET AL.: "Exploring the 'RPRL' Motif of Apelin-13 through Molecular Simulation and Biological Evaluation of Cyclic Peptide Analogues", CHEMMEDCHEM, vol. 5, no. 8, 2 August 2010 (2010-08-02), pages 1247-1253, XP055072887, ISSN: 1860-7179, DOI: 10.1002/cmdc.201000061 figure 1; tables 2,3	1-36
Y	N. MACALUSO ET AL: "Discovery of a Competitive Apelin Receptor (APJ) Antagonist", CHEMMEDCHEM, vol. 6, no. 6, 6 June 2011 (2011-06-06), pages 1017-1023, XP055072896, ISSN: 1860-7179, DOI: 10.1002/cmdc.201100069 figure 2; tables 2,3	1-36
A,P	ALEXANDRE MURZA ET AL: "Elucidation of the Structure-Activity Relationships of Apelin: Influence of Unnatural Amino Acids on Binding, Signaling, and Plasma Stability", CHEMMEDCHEM, vol. 7, no. 2, 6 February 2012 (2012-02-06), pages 318-325, XP55072892, ISSN: 1860-7179, DOI: 10.1002/cmdc.201100492 abstract; tables	1-36
A	SIDOROVA ET AL.: "Synthesis and cardioprotective properties of apelin-12 and its structural analogues", RUSSIAN JOURNAL OF BIOORGANIC CHEMISTRY, vol. 38, no. 1, 1 January 2012 (2012-01-01), pages 40-51, XP002706051, ISSN: 1068-1620, DOI: 10.1134/S1068162012010177 the whole document	1-36

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