

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
08 December 2022 (08.12.2022)



(10) International Publication Number
WO 2022/253941 A1

(51) International Patent Classification:
A61K 31/4468 (2006.01) *A61P 9/10* (2006.01)
A61P 9/04 (2006.01)

(21) International Application Number:
PCT/EP2022/065013

(22) International Filing Date:
02 June 2022 (02.06.2022)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
21177292.6 02 June 2021 (02.06.2021) EP

(71) Applicants: **HELSINN HEALTHCARE SA** [CH/CH];
Via Pian Scairolo 9, 6912 Lugano / Pazzallo (CH). **ANAC-**
ARDIO AB [SE/SE]; Nanna Svartz Väg 4, 171 65 Solna
(SE).

(72) Inventors: **LUND, Lars**; Skeppargatan 58, 11459 Stock-
holm (SE). **BERNAREGGI, Alberto**; Via Ortigara 21,
22012 Cernobbio (CO) (IT). **LOVATI, Emanuela**; Via del-
la Selva 18, 6850 Mendrisio (CH). **GIULIANO, Claudio**;
Via Prudeniziana 28A, 22100 Como (IT). **PIETRA, Clau-**
dio; Via Antonio Gramsci 7, 27028 San Martino Siccomario
(PV) (IT).

(74) Agent: **M. ZARDI & CO S.A.**; Via G. B. Pioda, 6, 6900
Lugano (CH).

(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, DJ, DK, DM, DO,
DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,
HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH,
KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA,
MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,

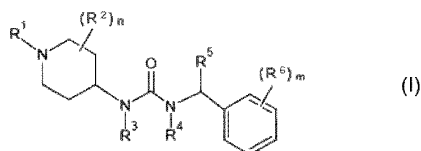
NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU,
RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM,
ZW.

(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).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))

(54) Title: PIPERIDINE UREA DERIVATIVES FOR USE AS INOTROPIC AGENTS



(57) **Abstract:** The invention concerns the use of com-
pounds represented by formula (I) as inotropic agents. The
compounds of formula (I), which include, as preferred, 1-
[(1S)-1- (2,3-dichloro-4-methoxyphenyl)ethyl]-3-methyl-3-[(4R)-1-
methyl-3,3-dimethyl-4-piperidyl]-urea and its hydrochloride salt, are
herein reported to have a significant inotropic activity on cardiomy-
ocytes from both normal and myocardial infarction-induced heart fail-
ure animal models, which makes them useful for treating cardiovascu-
lar patients in need thereof. Differently from known inotropic agents,
the present compounds are effective on cardiomyocyte contractility
without influencing calcium mobilization. Accordingly, they are ad-
vantageously free from adverse effects caused by increased calcium
concentrations, such as increased oxygen demand, tachycardia, ar-
rhythmia, ischemia, etc. Overall, a new, safe and effective inotropic
treatment is thus made available.

WO 2022/253941 A1