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(71) Applicant *(for all designated States except US)*: **VITAE PHARMACEUTICALS, INC.** [US/US]; 502 West Office Center Drive, Fort Washington, PA 19034 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CLAREMON, David, A.** [US/US]; 1508 Aidenn Lair Road, Maple Glen, PA 19002 (US). **ZHUANG, Linghang** [CN/US]; 3135 Fox Drive, Chalfont, PA 18914 (US). **YE, Yuanjie** [CN/US]; 835 Meetinghouse Road, Ambler, PA 19002 (US). **SINGH, Suresh, B.** [US/US]; 4 Adams Road, Kendall Park, NJ 08824 (US). **TICE, Colin, M.** [US/US]; 1325 Pinebrook Court, Ambler, PA 19002 (US). **SIMPSON, Robert, D.** [US/US]; 2001 N. Van Buren Street, Wilmington, DE 19802 (US).

(74) Agents: **DAVIS, Steven, G.** et al.; Hamilton, Brook, Smith & Reynolds, P.C., 530 Virginia Road, P.O. Box 9133, Concord, MA 01742-9133 (US).

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

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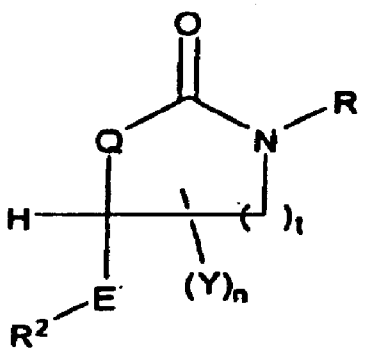
(88) Date of publication of the international search report:
5 November 2009

(54) Title: CYCLOALKYL LACTAME DERIVATIVES AS INHIBITORS OF 11-BETA-HYDROXYSTEROID DEHYDROGENASE 1



(I)

(57) Abstract: This invention relates to novel compounds of the Formula (I), any of the formulas I_1-I_{26} la_{1-3}-lj_{1-3} or pharmaceutically acceptable salts thereof, and pharmaceutical compositions thereof, which are useful for the therapeutic treatment of diseases associated with the modulation or inhibition of 11β-HSD1 in mammals. The invention further relates to pharmaceutical compositions of the novel compounds and methods for their use in the reduction or control of the production of cortisol in a cell or the inhibition of the conversion of cortisone to cortisol in a cell.

WO 2009/102460 A3

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D211/76 C07D243/04 C07D265/10 A61K31/4402 A61P3/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

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 practical, search terms used)
EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/049952 A (LILLY CO ELI [US]; AICHER THOMAS D [US]; CHICARELLI MARK JOSEPH [US];) 11 May 2006 (2006-05-11) page 178, line 1 - page 183, line 20; claims; examples 28,29	1-3,6, 52-65, 90,93, 96,99, 101-110
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; FUKUSHIMA, HIROSHI ET AL: "Preparation of imidazolidinone derivatives as 11.beta.-HSD1 inhibitors" XP002531878 retrieved from STN Database accession no. 2007:1110441 abstract -/--	1-3,6, 52-65, 90,93, 96,99, 101-110

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 June 2009	17/09/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Gavriliu, Daniela

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	-& JP 2007 254409 A (TAISHO PHARMACEUTICAL CO., LTD., JAPAN) 4 October 2007 (2007-10-04)	
X	WO 2007/081570 A (MERCK & CO INC [US]; ALI AMJAD [US]; SINCLAIR PETER J [US]; TAYLOR GAY) 19 July 2007 (2007-07-19) page 11, line 34 - page 12, line 15; claims; examples	1-3,6, 52-65, 90,93, 96,99, 101-110
X	WO 2004/094375 A (MEMORY PHARM CORP [US]; HOFFMANN LA ROCHE [US]; TEHIM ASHOK [US]; HOPP) 4 November 2004 (2004-11-04) claims; examples	1-3,6, 52-65, 90,93, 96,99, 101-110
X	WO 2006/014357 A (MERCK & CO INC [US]; ALI AMJAD [US]; NAPOLITANO JOANN M [US]; DENG QIA) 9 February 2006 (2006-02-09) page 15, line 30 - page 19, line 35; claims; examples	1-3,6, 52-65, 90,93, 96,99, 101-110
P,X	WO 2008/106128 A (VITAE PHARMACEUTICALS INC [US]; CLAREMON DAVID A [US]; MCGEEHAN GERARD) 4 September 2008 (2008-09-04) the whole document	1-3,6, 52-65, 90,93, 96,99, 101-110

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/000908

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 4-5, 7-89, 100,
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-3(part), 6, 50-65(part), 90(part), 93(part), 96(part), 99 (part)
101-110(part)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 4-5, 7-89, 100,

Present Claims 1, 6 and 93 relate to an extremely large number of possible compounds. In fact, Claim 1 contains so many options, variables, possible permutations that a lack of clarity (and conciseness) within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT arises to such an extent as to render a meaningful search of the Claim 1 impossible. The claim 1 can in no way be considered to be a reasonable generalisation of the actual examples since it include numerous possibilities which cannot be considered as equivalents, homologues or analogues of the examples. Consequently, the search was carried out for those parts of the application which do appear to be clear, namely for the compounds as defined in Claim 93. Exactly the same objections arise for substantive examination.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.2), should the problems which led to the Article 17(2)PCT declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-3(part), 6, 50-65(part), 90(part), 93(part), 96(part), 99 (part), 101-110(part)

Compounds of formula (I), wherein Q=CH2, t=1, R=-C(R1aR1b)-A, their pharmaceutical compositions and uses.

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2. claims: 1(part), 15-16(part), 19, 28-51(part), 66(part), 69(part), 72(part), 75(part), 78(part), 81(part), 84(part), 87(part), 96(part), 99(part), 101-109(part), 111(part)

Compounds of formula (I), wherein Q=CH2, t=1, R=-A1R1-Cy1-A2-Cy2, their pharmaceutical compositions and uses.

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3. claims: 1-3(part), 7, 50-65(part), 90(part), 93(part), 98(part), 99(part), 101-110(part)

Compounds of formula (I), wherein Q=NR5, t=1, R=-C(R1aR1b)-A, their pharmaceutical compositions and uses.

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4. claims: 1(part), 15-16(part), 20, 28-51(part), 66(part), 69(part), 72(part), 75(part), 78(part), 81(part), 84(part), 87(part), 98-99(part), 101-109(part), 111(part)

Compounds of formula (I), wherein Q=NR5, t=1, R=-A1R1-Cy1-A2-Cy2, their pharmaceutical compositions and uses.

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5. claims: 1-3(part), 8, 50-65(part), 90(part), 93(part), 97(part), 99(part), 101-110(part)

Compounds of formula (I), wherein Q=O, t=1, R=-C(R1aR1b)-A, their pharmaceutical compositions and uses.

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6. claims: 1(part), 15-16(part), 21, 28-51(part), 66(part), 69(part), 72(part), 75(part), 78(part), 81(part), 84(part), 87(part), 97(part), 99(part), 101-109(part), 111(part)

Compounds of formula (I), wherein Q=O, t=1, R=-A1R1-Cy1-A2-Cy2, their pharmaceutical compositions and uses.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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7. claims: 1-2(part), 4(part), 9, 50-65(part), 91(part), 94(part), 96(part), 99(part), 101-110(part)

Compounds of formula (I), wherein Q=CH2, t=2, R=-C(R1aR1b)-A, their pharmaceutical compositions and uses.

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8. claims: 1(part), 15(part), 17(part), 22, 28-51(part), 67(part), 70(part), 73(part), 76(part), 79(part), 82(part), 85(part), 87(part), 88(part), 96(part), 99-109(part), 111(part)

Compounds of formula (I), wherein Q=CH2, t=2, R=-A1R1-Cy1-A2-Cy2, their pharmaceutical compositions and uses.

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9. claims: 1-2(part), 4(part), 10, 50-65(part), 91(part), 94(part), 98(part), 99(part), 101-110(part)

Compounds of formula (I), wherein Q=NR5, t=2, R=-C(R1aR1b)-A, their pharmaceutical compositions and uses.

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10. claims: 1(part), 15(part), 17(part), 23, 28-51(part), 67(part), 70(part), 73(part), 76(part), 79(part), 82(part), 85(part), 87(part), 88(part), 98-99(part), 101-109(part), 111(part)

Compounds of formula (I), wherein Q=NR5, t=2, R=-A1R1-Cy1-A2-Cy2, their pharmaceutical compositions and uses.

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11. claims: 1-2(part), 4(part), 11, 50-65(part), 91(part), 94(part), 97(part), 99-110(part)

Compounds of formula (I), wherein Q=O, t=2, R=-C(R1aR1b)-A, their pharmaceutical compositions and uses.

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12. claims: 1(part), 15(part), 17(part), 24, 28-51(part), 67(part), 70(part), 73(part), 76(part), 79(part), 82(part), 85(part), 87(part), 88(part), 97(part), 99(part), 101-109(part), 111(part)

Compounds of formula (I), wherein Q=O, t=2, R=-A1R1-Cy1-A2-Cy2, their pharmaceutical compositions and uses.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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13. claims: 1-2(part), 5(part), 12, 50-65(part), 90(part), 92(part), 95-96(part), 99(part), 101-110(part)

Compounds of formula (I), wherein Q=CH2, t=3, R=-C(R1aR1b)-A, their pharmaceutical compositions and uses.

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14. claims: 1(part), 15(part), 18(part), 25, 28-51(part), 68(part), 71(part), 74(part), 75(part), 77(part), 80(part), 83(part), 86-87(part), 89(part), 96(part), 99(part), 101-109(part), 111(part)

Compounds of formula (I), wherein Q=CH2, t=3, R=-A1R1-Cy1-A2-Cy2, their pharmaceutical compositions and uses.

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15. claims: 1-2(part), 5(part), 13, 50-65(part), 92(part), 95(part), 98(part), 99-110(part)

Compounds of formula (I), wherein Q=NR5, t=3, R=-C(R1aR1b)-A, their pharmaceutical compositions and uses.

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16. claims: 1(part), 15(part), 18(part), 26, 28-51(part), 68(part), 71(part), 74(part), 77(part), 80(part), 83(part), 86(part), 89(part), 98-109(part), 111part)

Compounds of formula (I), wherein Q=NR5, t=3, R=-A1R1-Cy1-A2-Cy2, their pharmaceutical compositions and uses.

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17. claims: 1-2(part), 5(part), 14, 50-65(part), 92(part), 95(part), 97(part), 99(part), 101-110(part)

Compounds of formula (I), wherein Q=O, t=3, R=-C(R1aR1b)-A, their pharmaceutical compositions and uses.

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18. claims: 1(part), 15(part), 18(part), 27, 28-51(part), 68(part), 71(part), 74(part), 77(part), 80(part), 83(part), 86(part), 89(part), 92(part), 95(part), 97(part), 99(part), 101-109(part), 111(part)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Compounds of formula (I), wherein Q=O, t=3, R=-A1R1-Cy1-A2-Cy2, their pharmaceutical compositions and uses.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2009/000908

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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