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CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM,
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KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY,
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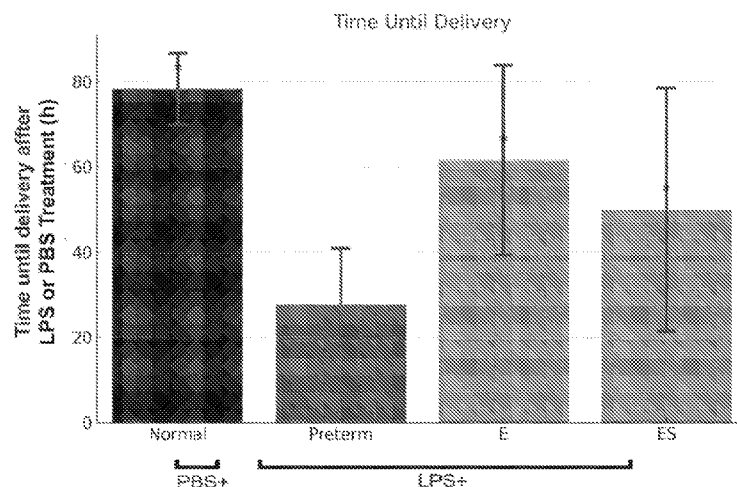
- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))

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13 March 2025 (13.03.2025)

(54) Title: ESTROGENIC COMPOUNDS AND FORMULATIONS FOR GESTATION-RELATED COMPLICATIONS

Fig. 2B



(57) Abstract: Formulations, compounds, and methods to prolong gestation and for treatment of gestational complications are described. Treatments include administration of an estrogenic compound to mitigate uterine contractions.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2024/034368

A. CLASSIFICATION OF SUBJECT MATTERIPC: **A61K 31/565** (2024.01); **A61K 31/56** (2024.01); **A61P 15/00** (2024.01); **A61P 15/06** (2024.01)CPC: **A61K31/565; A61K31/56; A61P15/00; A61P15/06**

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)

See Search History Document

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

See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 2011/0118224 A1 (LOUMAYE, E et al.) 19 May 2011 (19.05.2011) paragraphs [0012], [0078], [0083], [0100]-[0102], [0130]	77, 112/77, 113/77 1-3, 39-41, 78-79, 112/78-79, 113/78-79
A	US 2022/0339176 A1 (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY) 27 October 2022 (27.10.2022) entire document	1-3, 39-41, 77-79, 112-113
Y	GARFIELD, RE et al. "Use of progesterone and progestin analogs for inhibition of preterm birth and other uterine contractility disorders", Facts, Views and Vision in ObGyn 4(4), pages 237-244, 2012; Retrieved on 07 August 2024 from the Internet: [URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3987481/pdf/FVVinObGyn-4-237-244.pdf]; abstract; page 237, column 1, first paragraph; page 239, column 1, first paragraph Entire Document	1-2, 112/77-79



Further documents are listed in the continuation of Box C.



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

"D" document cited by the applicant in the international application

"E" earlier application or patent 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

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Date of mailing of the international search report

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Name and mailing address of the ISA/US

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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.:
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:
3. ☒ Claims Nos.: **4-38, 42-76**
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:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Groups I+, claims 1-3, 39-41, 77-113, formula of claim 78 wherein R1=OH, R2=OH, R3=OH, R4=H (estrogenic compound), are directed to methods for treating recurrent preterm birth, recurrent early term birth, recurrent pregnancy loss, a short cervix, early term birth, spontaneous preterm birth, or spontaneous abortion, and a medicament for use in said methods and for mitigating uterine contractions in an individual, the medicament comprising an estrogenic compound.

The methods and medicaments of Claims 1-3, 39-41, 77, 78 (in-part), 79, and 112-113 are believed to encompass the first named invention of Groups I+ and are the claims that will be searched to the extent that they comprise an estrogenic compound encompassing the formula in claim 78 wherein R1=OH, R2=OH, R3=OH, R4=H (first exemplary estrogenic compound). This first named invention of Group I+ has been selected to encompass the first species of the genus found in claim 78 based on the guidance set forth in section 10.54 of the PCT International Search and Preliminary Examination Guidelines.

Applicant is invited to elect additional compounds, with fully specified functional groups for each variable, and where available as an option within at least one searchable claim, to be searched. Additional compound(s) will be searched upon the payment of additional fees. Applicants must specify the searchable claims that encompass any additionally elected compound(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be formula of claim 78 wherein R1=OH, R2=OH, R3=phosphonic acid, R4=H (antibody estrogenic compound).

Groups I+ share the technical features including: a method of treating a pregnant individual for recurrent preterm birth, recurrent early term birth, recurrent pregnancy loss, or a short cervix, comprising administering an estrogenic compound to an individual, wherein the individual is pregnant and has a medical history indicating recurrent preterm birth, recurrent early term birth, recurrent pregnancy loss, or a short cervix; a method of treating a pregnant individual for early term birth, spontaneous preterm birth or spontaneous abortion, comprising determining that a pregnant individual is experiencing uterine contractions related to early term birth, spontaneous preterm birth or spontaneous abortion; and administering an estrogenic compound to an individual; and a medicament for use in mitigating uterine contractions in an individual, the medicament comprising an estrogenic compound.

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

However, these shared technical features are previously disclosed by US 2011/0118224 A1 to Loumaye, et al. (hereinafter "Loumaye").

Loumaye discloses a method of treating a pregnant individual for recurrent preterm birth (prevention of preterm labor in a patient with a history of preterm labor which leads to preterm birth; paragraphs [0002], [0099]-[0103]), recurrent early term birth, recurrent pregnancy loss, or a short cervix, comprising administering an estrogenic compound to an individual (preventing and/or treating premature uterine contraction disorders in a patient, by administering a steroid sulfatase inhibitor, such as the compound as shown, which is intrinsically an estrogenic compound; paragraphs [0007], [0012], [0132]), wherein the individual is pregnant and has a medical history indicating recurrent preterm birth (prevention of preterm labor in a patient with a history of preterm labor which leads to preterm birth; paragraphs [0002], [0099]-[0103]), recurrent early term birth, recurrent pregnancy loss, or a short cervix; a method of treating a pregnant individual for early term birth, spontaneous preterm birth (prevention of preterm labor which leads to preterm birth in a patient in need thereof; paragraphs [0002], [0099]-[0103]), or spontaneous abortion, comprising determining that a pregnant individual is experiencing uterine contractions (preventing and/or treating premature uterine contraction disorders in a patient in need thereof; paragraph [0012]) related to early term birth, spontaneous preterm birth (prevention of preterm labor which leads to preterm birth in a patient in need thereof; paragraphs [0002], [0099]-[0103]), or spontaneous abortion, and administering an estrogenic compound to an individual (preventing and/or treating premature uterine contraction disorders in a patient, by administering a steroid sulfatase inhibitor, such as the compound as shown in paragraph [0132] of the Loumaye reference, which is intrinsically an estrogenic compound; paragraphs [0007], [0012], [0132]), and a medicament for use in mitigating uterine contractions in an individual (medicament for the prevention or treatment of pre-mature uterine contractions; paragraph [0083]), the medicament comprising an estrogenic compound (medicament comprising a steroid sulfatase inhibitor, such as the compound as shown in paragraph [0132] of the Loumaye reference, which is intrinsically an estrogenic compound; paragraphs [0007], [0012], [0083], [0132]).

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Loumaye reference, unity of invention is lacking.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying 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 report covers 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, 39-41, 77, 78 (in-part), 79, 112-113; formula of claim 78 wherein R1=OH, R2=OH, R3=OH, R4=H (estrogenic compound)**

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.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2024/034368

C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TAYLOR, J et al. "Nanomedicine strategies to improve therapeutic agents for the prevention and treatment of preterm birth and future directions", Nanoscale Advances 5, pages 1870-1889, Published online: 04 March 2023; Retrieved on 07 August 2024 from the Internet: [URL: https://pubs.rsc.org/en/content/articlepdf/2023/na/d2na00834c]; page 1871, column 1, second-third paragraphs; column 2, second-third paragraphs; page 1872, Figure 1 Entire Document	39-41, 113/77-79
Y	National Center for Biotechnology Information "13-Methyl-6,7,8,9,11,12,14,15, 6,17-decahyd rocyclopenta[a]phenanthrene-3,16,17-triol: PUBCHEM CID 3269" Pubchem entry (online), pages 1-24, 25 March 2005; Retrieved on 06 August 2024 from the Internet: [URL: https://pubchem.ncbi.nlm.nih.gov/compound/3269]; page 3, see 2D structure Entire Document	78-79, 112/78-79, 113/78-79
Y	AKINWUNMI, B et al. "Evaluating Vaginal Progesterone in Preventing Recurrent Preterm Birth: A Call to Action", JAMA Network Open online article, pages 1-3, 2022; Retrieved on 08 August 2024 from the Internet: [URL: https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2797994]; page 1, first paragraph Entire Document	1-3