DRUG FUSIONS AND CONJUGATES

The present invention relates to drug fusions that have improved serum half lives. These fusions and conjugates comprise polypeptides, immunoglobulin (antibody) single variable domains and GLP and/or exendin molecules. The invention further relates to uses, formulations, compositions and devices comprising such drug fusions and conjugates.

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(54) Title: DRUG FUSIONS AND CONJUGATES

(57) Abstract: The present invention relates to drug fusions that have improved serum half lives. These fusions and conjugates comprise polypeptides, immunoglobulin (antibody) single variable domains and GLP and/or exendin molecules. The invention further relates to uses, formulations, compositions and devices comprising such drug fusions and conjugates.

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Declarations under Rule 4.17:
— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(h))
— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(h))
— of inventorship (Rule 4.1.7(iv))

Published:
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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K47/48 C07K16/18
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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)
A61K C07K A61P

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, BIOSIS, EMBASE, WPI Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<td>WO 2006/059106 A2 (DOMANTIS LIMITED) 8 June 2006 (2006-06-08) examples 10-18 claims</td>
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Further documents are listed in the continuation of Box C

See patent family annex

Date of the actual completion of the international search
13 July 2010

Date of mailing of the international search report
08/10/2010

Name and mailing address of the ISA
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Authorized officer
Nooij, Frans
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<td>WO 2008/149143 A2 (DOMANTIS LIMITED) 11 December 2008 (2008-12-11) example 16 sequence 99 figure 51a</td>
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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. because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a):

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 all searchable 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 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 1-32.

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

1. claims: 1-32

A fusion or conjugate composition comprising or consisting of (a) an insulinoactive agent or an incretin drug present as a fusion or a conjugate with (b) a dAb which binds serum albumin selected from (i) the DOM 7h-14 domain antibody (dAb), (ii) the DOM 7h-14-10 dAb), or a dAb which has up to 4 amino acid differences from the sequences of the DOM7h-14-10 dAb, and (iii) the DOM7h-ll-15 dAb, or (iv) the DOM7h-14-10 R108C dAb. (Pharmaceutical) composition and formulations, and (therapeutic) uses thereof. Encoding nucleic acids. Vector. Host cell. Method of production.

2. claims: 33-37

A modified leader sequence which has at its C terminal end the amino acid sequence AMA or AWA, wherein the leader sequence is not the wild type sequence. Use of said sequence.

3. claims: 38, 39

A process of producing a mixture of (i) an insulinoactive agent or an incretin drug; and (ii) an insulinoactive agent or an incretin drug minus two amino acids at the N-terminus of the insulinoactive agent or incretin drug, the process comprising the step of expressing (i) in a host cell using a leader sequence which results in cleavage before position 1 and cleavage before position 3 of said insulinoactive agent or incretin drug.
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