



(11) **EP 2 269 654 A3**

(12) **EUROPEAN PATENT APPLICATION**

(88) Date of publication A3:  
**13.04.2011 Bulletin 2011/15**

(51) Int Cl.:  
**A61K 47/48 (2006.01)**

(43) Date of publication A2:  
**05.01.2011 Bulletin 2011/01**

(21) Application number: **10011095.6**

(22) Date of filing: **24.08.2000**

(84) Designated Contracting States:  
**AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU  
MC NL PT SE**  
Designated Extension States:  
**AL LT LV MK RO SI**

(30) Priority: **24.08.1999 US 150510 P**

(62) Document number(s) of the earlier application(s) in  
accordance with Art. 76 EPC:  
**00957830.3 / 1 210 121**

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(54) **Enhancing drug delivery across and into epithelial tissues using oligo arginine moieties**

(57) This invention provides compositions and methods for enhancing delivery of drugs and other agents across epithelial tissues, including the skin, gastrointestinal tract, pulmonary epithelium, and the like. The compositions and methods are also useful for delivery across endothelial tissues, including the blood brain barrier. The compositions and methods employ a delivery enhancing

transporter that has sufficient guanidino or amidino sidechain moieties to enhance delivery of a compound conjugated to the reagent across one or more layers of the tissue, compared to the non-conjugated compound. The delivery enhancing polymers include, for example, poly-arginine molecules that are preferably between about 6 and 25 residues in length.

**Figure 5A**

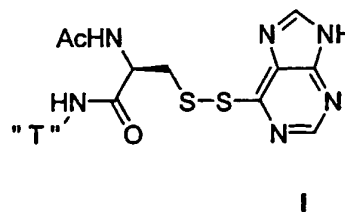


Figure 5B

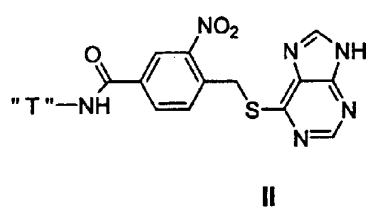


Figure 5C

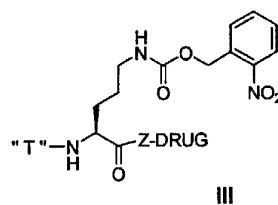


Figure 5D

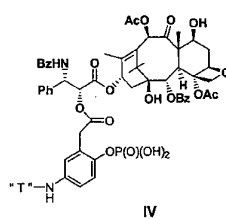


Figure 5E

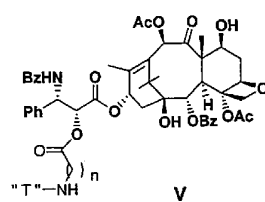


Figure 5F

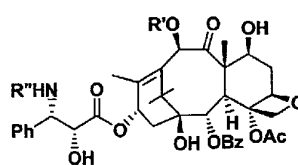


Figure 5G

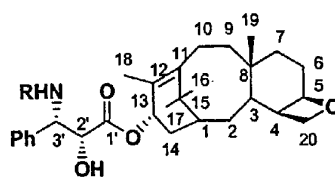
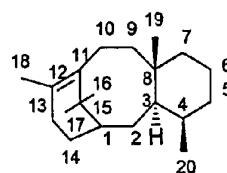


Figure 5H





## EUROPEAN SEARCH REPORT

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EP 10 01 1095

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The present search report has been drawn up for all claims			
Place of search <b>The Hague</b>		Date of completion of the search <b>8 March 2011</b>	Examiner <b>Dullaart, Anwyn</b>
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons % : member of the same patent family, corresponding document	

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EPO FORM 1503 03.02 (P04C001)



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EP 10 01 1095

DOCUMENTS CONSIDERED TO BE RELEVANT			
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The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 8 March 2011	Examiner Dullaart, Anwyn
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

EPO FORM 1503 03/82 (P04C01)



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Application Number  
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The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 8 March 2011	Examiner Dullaart, Anwyn
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

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EPO FORM 1503 03.82 (P04C01)



## EUROPEAN SEARCH REPORT

Application Number  
EP 10 01 1095

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
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The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 8 March 2011	Examiner Dullaart, Anwyn
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ..... &amp; : member of the same patent family, corresponding document</p>			

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EPO FORM 1503 (3.02.02) (P04001)



Application Number

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**CLAIMS INCURRING FEES**

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

**LACK OF UNITY OF INVENTION**

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☒ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

☐ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).



**LACK OF UNITY OF INVENTION  
SHEET B**

Application Number  
EP 10 01 1095

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-9, 12-14(all partially)

Method for enhancing transport of a compound across tissue,  
in which the compound is a diagnostic compound.

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2. claims: 10(completely); 1-9, 12-14(partially)

Method for enhancing transport of a compound across tissue,  
in which the compound is an antibody or an antibody  
fragment.

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3. claims: 11, 15(completely); 1-9, 12-14(partially)

Method for enhancing transport of a compound across tissue,  
in which the compound is a therapeutic agent.

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**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 10 01 1095

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08-03-2011

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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EP 10 01 1095

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