

**PATENT COOPERATION TREATY**

**PCT**

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference E5372-17-WO	<b>FOR FURTHER ACTION</b>		See item 4 below
International application No. PCT/IB2017/050754	International filing date ( <i>day/month/year</i> ) 10 February 2017 (10.02.2017)	Priority date ( <i>day/month/year</i> ) 11 February 2016 (11.02.2016)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant FONDAZIONE ISTITUTO ITALIANO DI TECNOLOGIA			

<p>1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.</p>																								
<p>3. This report contains indications relating to the following items:</p> <table border="0"> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> <p>4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).</p>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<p align="center">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 338 82 70</p>	<p>Date of issuance of this report 14 August 2018 (14.08.2018)</p>
	<p>Authorized officer</p> <p align="center"><b>Cécile Chatel</b></p> <p>e-mail: ro.ib@wipo.int</p>

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

# PCT

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)**

To:

see form PCT/ISA/220

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/IB2017/050754

International filing date (day/month/year)  
10.02.2017

Priority date (day/month/year)  
11.02.2016

International Patent Classification (IPC) or both national classification and IPC  
INV. A61K9/51 A61K9/00

Applicant  
FONDAZIONE ISTITUTO ITALIANO DI TECNOLOGIA

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application


2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office  
P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Pays Bas  
Tel. +31 70 340 - 2040  
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Date of completion of this opinion

see form  
PCT/ISA/210

Authorized Officer

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of:
  - the international application in the language in which it was filed.
  - a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2.  This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3.  With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
  - a.  forming part of the international application as filed:
    - in the form of an Annex C/ST.25 text file.
    - on paper or in the form of an image file.
  - b.  furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
  - c.  furnished subsequent to the international filing date for the purposes of international search only:
    - in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
    - on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
4.  In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	<u>4, 7</u>
	No: Claims	<u>1-3, 5, 6, 8-11</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-11</u>
Industrial applicability (IA)	Yes: Claims	<u>1-11</u>
	No: Claims	

2. Citations and explanations

see separate sheet

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Cited Documents**

The following documents are referred to in this communication:

- D1 US 6 663 881 B2 (KUNZ LAWRENCE L [US] ET AL) 16 December 2003 (2003-12-16)
- D2 LÜTFİ GENÇ: "Preparation and characterization of nocodazole-loaded solid lipid nanoparticles",  
PHARMACEUTICAL DEVELOPMENT AND TECHNOLOGY,  
vol. 19, no. 6, 10 September 2014 (2014-09-10), pages 671-676,  
XP055309542,  
US  
ISSN: 1083-7450, DOI: 10.3109/10837450.2013.819017
- D3 ROLANDO E. YANES, DERRICK TARN, NGELA A. HWANG, DANIEL P. FERRIS: "Involvement of lysosomal exocytosis in the excretion of mesoporous silica nanoparticles and enhancement of the drug delivery effect by exocytosis inhibition",  
SMALL,  
vol. 9, no. 5 , pages 697-704,

**2. Clarity**

The expression "inhibitor of exocytosis" used in claim 1 encompasses a large number of compounds which are defined only by reference to a desired functional activity, namely compound being an inhibitor of exocytosis. This functional term does not give a specific technical guidance for the selection of the suitable derivatives, without proven general knowledge, to show which derivatives are suitable "inhibitors" in the particular case of the current problem and thus could be seen as a mere invitation to the skilled person to perform a research program in order to find the suitable variants. Therefore claim 1 lacks clarity, Article 6 PCT.

### **3. Novelty**

D1 discloses (see column 4, line 46 - line 63; column 21, line 30 - line 60 and the claims) a therapeutic method comprising administering to a traumatized mammalian blood vessel a sustained release dosage form comprising biodegradable poly (DL-lactide-co-glycolide) nanoparticles having a size of 5 to 500 nanometers and comprising a cytoskeletal inhibitor, e.g., cytochalasin A,B or D. The sustained release dosage form comprising a cytochalasin is preferably administered via an implantable device which is not a catheter used to perform bloodless angioplasty.

The drug cytochalasin A,B or D is an inhibitor of exocytosis and an active ingredient.

The subject-matter of claims 1-3,5,6,8-11 is therefore not new in view of D1 (Article 33(2) PCT).

D2 discloses (see the abstract; page 671, column 2, line 8 - page 672, column 1, line 4; page 672; table 1; page 676, column 1, line 1 - line 11) Nocodazole-loaded solid lipid nanoparticles. Said nanoparticles are prepared using hot homogenization technique, which consists of:

- i) forming a nanoemulsion comprising: a) 5% w/w nocodazole, b) 1,2% Tween 80, c) 5% Compritol (glyceryl behenate) and d) 90,8% water and
- ii) obtaining solid lipid nanoparticles by recrystallization.

The drug nocodazole is an inhibitor of exocytosis and an active ingredient.

The subject-matter of claims 1-3,5,10,11 is therefore not new in view of D2 (Article 33(2) PCT).

### **4. Inventive Step**

4.1. Not being new the subject-matter of claims 1-3,5,6,8-11 cannot be considered as inventive (Article 33(3) PCT).

4.2. Dependent claims 4 and 7 are not considered inventive in view of D1 and D2, insofar as they do not appear to comprise any technical features which lead to a non-obvious solution of a technical problem (Article 33(3) PCT).

**5. Industrial applicability**

Claims 1-11 satisfy the criterion of industrial applicability (Article 33(4) PCT).