

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	15208537
				Filing Date	07-12-2016
				First Named Inventor	OSTROW; Gregory I.
				Art Unit	1621
				Examiner Name	Zohreh A Fay
Sheet	1	of	1	Attorney Docket Number	46682-701.301

U. S. PATENT DOCUMENTS					
Examiner Initials*	Cite No.	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	001	US-20120028910	02-02-2012	COMBAL; Jean-Philippe et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No.	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	001	WO-2011019940-A2	02-17-2011	SEROS MEDICAL LLC [US], et al.		<input type="checkbox"/>
	002	WO-2016172712-A2	10-27-2016	SYDNEXIS INC [US]		<input type="checkbox"/>

NON-PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	001	PCT/US2016/029222 International Search Report and Written Opinion dated October 21, 2016.	<input type="checkbox"/>
	002	U.S. Serial No. 14/859,042 Office Action dated October 25, 2016.	<input type="checkbox"/>

Examiner Signature		Date Considered	
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
YANG, XIAOFAN

WILSON SONSINI GOODRICH & ROS 650 PAGE MILL
ROAD PALO ALTO CA 94304 USA

PCT

**NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION**

(PCT Rule 44.1)

Date of mailing
(day/month/year) 21 October 2016 (21.10.2016)

Applicant's or agent's file reference
46682-701602

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/US2016/029222

International filing date
(day/month/year) **25 April 2016 (25.04.2016)**

Applicant
SYDNEXIS, INC.

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

How? Directly to the International Bureau of WIPO preferably through ePCT or on paper to, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 338 82 70

For more detailed instructions, see *PCT Applicant's Guide*, International Phase, paragraphs 9.004 . 9-011.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
☐ the protest together with the decision thereon has been transmitted to the International Bureau together with any request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. Following the expiration of 30 months from the priority date, these comments will also be made available to the public.

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90bis.1 and 90bis.3).

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices. In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months. For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

Within **19 months** from the priority date, the applicant may request that a supplementary international search be carried out by an International Searching Authority, that offers this service (Rule 45bis.1). The procedure for requesting supplementary international search is described in the *PCT Applicant's Guide*, International Phase, paragraphs 8.006-8.032.

Name and mailing address of the ISA/KR
International Application Division
Korean Intellectual Property Office
189 Cheongsa-ro, Seo-gu, Daejeon, 35208, Republic of Korea
Facsimile No. 82-42-481-8578

Authorized officer

COMMISSIONER

Telephone No. 82-42-481-5875



* Attention

Copies of the documents cited in the international search report can be searched in the following Korean Intellectual Property Office English website for six months(expire date : **2017.04.21**) from the date of mailing of the international search report.

<http://www.kipo.go.kr/en/> => PCT Services => PCT Services

ID : PCT international application number

PW : **VD73HPDY**

Inquiries related to PCT International Search Report or Written Opinion prepared by KIPO as an International Searching Authority can be answered not only by KIPO but also through IPKC (Intellectual Property Korea Center), located in Vienna, VA, which functions as a PCT Help Desk for PCT applicants.

Homepage: <http://www.ipkcenter.com>

Email: ipkc@ipkcenter.com

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 46682-701602	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2016/029222	International filing date (<i>day/month/year</i>) 25 April 2016 (25.04.2016)	(Earliest) Priority Date (<i>day/month/year</i>) 23 April 2015 (23.04.2015)
Applicant SYDNEXIS, INC.		

This International search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out 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))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box No. II)

3. ☐ **Unity of invention is lacking** (See Box No. III)

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant.
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant.
☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 4
☒ as suggested by the applicant.
☐ as selected by this Authority, because the applicant failed to suggest a figure.
☐ as selected by this Authority, because this figure better characterizes the invention.
- b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/029222

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.: 19, 20
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 19 and 20 pertain to methods for treatment of the human body by surgery or therapy, and thus relate to a subject matter which this International Searching Authority is not required, under PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv), to search.
2. ☒ Claims Nos.: 14
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:
Claim 14 is unclear since it refers to multiple dependent claim 13 which does not comply with PCT Rule 6.4(a).
3. ☒ Claims Nos.: 4-13, 15-20
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:

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 any 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.:

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/US2016/029222**A. CLASSIFICATION OF SUBJECT MATTER****A61K 31/46(2006.01)i, A61K 9/08(2006.01)i, A61P 27/02(2006.01)i**

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 31/46; A61K 31/135; A61K 31/55; A61K 31/505; A61K 9/50; A61K 47/32; A61K 47/38; A61K 47/42; A61K 47/00; A61K 9/08; C07D 401/14; A61P 27/02

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

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) & Keywords: ophthalmic, muscarinic antagonist, deuterated water

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0332826 A1 (TEVA PHARMACEUTICAL INDUSTRIES LIMITED) 20 September 1989 See abstract; column 2, lines 10-26; column 4, lines 1-7; column 5, lines 44-55; column 6, lines 35-40; column 7, lines 29-31; and claims 1, 13-15.	1-3
A	US 5716952 A (WOLDEMUSSIE, E. et al.) 10 February 1998 See abstract; and claims 1, 8.	1-3
A	WO 97-16192 A1 (MERCK & CO., INC.) 9 May 1997 See abstract; and claims 5-9, 17.	1-3
A	US 2012-0015035 A1 (WILDSOET, C. F. et al.) 19 January 2012 See abstract; paragraphs [0030], [0031]; and claim 1.	1-3
A	WO 2011-019940 A2 (SEROS MEDICAL, LLC) 17 February 2011 See abstract; paragraph [0020]; and claims 1, 3.	1-3



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

"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

21 October 2016 (21.10.2016)

Date of mailing of the international search report

21 October 2016 (21.10.2016)

Name and mailing address of the ISA/KR

International Application Division

Korean Intellectual Property Office

189 Cheongsu-ro, Seo-gu, Daejeon, 35208, Republic of Korea

Facsimile No. +82-42-481-8578

Authorized officer

CHO, KI YUN

Telephone No. +82-42-481-5655



INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2016/029222

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0332826 A1	20/09/1989	AU 1989-51489 A	03/08/1989
		IL 85312 A	16/08/1991
		JP 02-022220 A	25/01/1990
		KR 10-1989-0012634 A	18/09/1989
US 5716952 A	10/02/1998	AU 1993-10993 A	21/10/1993
		AU 666536 B2	15/02/1996
		CA 2132007 C	18/07/2006
		DE 69332048 T2	23/01/2003
		EP 0634932 A1	25/01/1995
		EP 0634932 B1	19/06/2002
		ES 2177543 T3	16/12/2002
		JP 07-504915 A	01/06/1995
		WO 93-18772 A1	30/09/1993
WO 97-16192 A1	09/05/1997	AU 1997-28696 A	22/05/1997
US 2012-0015035 A1	19/01/2012	US 8883214 B2	11/11/2014
		WO 2010-083129 A2	22/07/2010
		WO 2010-083129 A9	09/12/2010
WO 2011-019940 A2	17/02/2011	EP 2464387 A2	20/06/2012
		EP 2464387 A4	15/05/2013
		US 2012-0203161 A1	09/08/2012
		WO 2011-019940 A3	16/06/2011

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To: YANG, XIAOFAN WILSON SONSINI GOODRICH & ROS 650 PAGE MILL ROAD PALO ALTO CA 94304 USA
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Date of mailing (day/month/year)	21 October 2016 (21.10.2016)
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Applicant's or agent's file reference 46682-701602

FOR FURTHER ACTION

See paragraph 2 below

International application No. PCT/US2016/029222	International filing date (day/month/year) 25 April 2016 (25.04.2016)	Priority date(day/month/year) 23 April 2015 (23.04.2015)
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International Patent Classification (IPC) or both national classification and IPC

A61K 31/46(2006.01)i, A61K 9/08(2006.01)i, A61P 27/02(2006.01)i

Applicant SYDNEXIS, INC.

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

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" 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 Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input checked="" type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will 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/KR International Application Division Korean Intellectual Property Office 189 Cheongsu-ro, Seo-gu, Daejeon, 35208, Republic of Korea Facsimile No. +82-42-481-8578	Date of completion of this opinion 21 October 2016 (21.10.2016)	Authorized officer CHO, KI YUN Telephone No. +82-42-481-5655
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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2016/029222

Box No. I Basis of this opinion

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:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2016/029222

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 4-20

because:

☒ the said international application, or the said claims Nos. 19, 20

relate to the following subject matter which does not require an international search (*specify*):

Claims 19 and 20 pertain to a method for treatment of the human body by therapy (PCT Rule 43bis2.1(b) and Rule 67.1(iv)).

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 14

are so unclear that no meaningful opinion could be formed (*specify*):

Claim 14 is unclear since it refers to multiple dependent claim 13 which does not comply with PCT Rule 6.4(a).

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for said claims Nos. 4-20

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b).

☐ See Supplemental Box for further details.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US2016/029222

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

1. Statement

Novelty (N)	Claims	1-3	YES
	Claims	NONE	NO
Inventive step (IS)	Claims	NONE	YES
	Claims	1-3	NO
Industrial applicability (IA)	Claims	1-3	YES
	Claims	NONE	NO

2. Citations and explanations :

Reference is made to the following document:

D1: EP 0332826 A1 (TEVA PHARMACEUTICAL INDUSTRIES LIMITED) 20 September 1989

1. Novelty and Inventive Step

1.1. Claim 1

The subject matter of claim 1 relates to an ophthalmic composition, comprising about 0.001- 0.005 wt% of a muscarinic antagonist and deuterated water, at a pD of about 4.2-7.9, wherein the muscarinic antagonist does not extend singlet oxygen lifetime.

D1, which is considered to be the closest prior art to the subject matter of claim 1, discloses an injectable pharmaceutical composition having a long term shelf life, which composition comprises, at least one pharmacologically active ingredient; a solvent medium containing an aqueous component, said aqueous component comprising at least a major proportion by volume of deuterium oxide; and additionally at least one further pharmacologically active ingredient such as atropine (See claims 1, 13-15). Moreover, D1 discloses that benactyzine hydrochloride (40 mg), atropine sulfate (10 mg) and trimedoxime bromide (400 mg) are dissolved in 18 ml of deuterium oxide (See column 7, lines 29-31).

The subject matter of claim 1 differs from the injectable pharmaceutical composition of D1 in three aspects: (1) the composition used for ophthalmology, (2) a range of the amount of muscarinic antagonist, and (3) a range of pD.

However, the difference (1) comes within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Regarding the difference (2), it would have been readily modified or optimized by a person skilled in the art from D1 and no unexpected effects or properties are

Continued on Supplemental Box

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2016/029222

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Claims 4-13 and 15-20 do not comply with PCT Rule 6.4(a) because multiple dependent claims should not serve as a basis for any other multiple dependent claim.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2016/029222

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The expression "about" used in claims 1 and 6-11 is technically vague and unclear, thus leaving the reader in doubt as to the scope of the technical feature to which they refer (PCT Article 6).

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of : Box No. V

indicated in the application. Regarding the difference (3), it can be predicted from D1 by a person skilled in the art considering that the pharmaceutical composition comprises atropine in deuterium oxide (See claims 1, 13-15).

Accordingly, claim 1 would have been obvious over D1. Therefore, claim 1 is novel under PCT Article 33(2) but lacks an inventive step under PCT Article 33(3).

1.2. Claims 2, 3

The additional feature of claim 2 dependent on claim 1, relating to a kind of the muscarinic antagonist, is disclosed in D1 in atropine used as the sulfate salt (See column 5, lines 51-52).

The additional feature of claim 3 dependent on claim 1 or 2, relating to the muscarinic antagonist quenching photogenerated singlet oxygen species in the composition, is not disclosed in D1. However, said difference can be predicted from D1 by a person skilled in the art considering that the injectable pharmaceutical composition comprises atropine used as the sulfate salt (See column 5, lines 51-52).

Accordingly, claims 2 and 3 would have been obvious over D1. Therefore, claims 2 and 3 are novel under PCT Article 33(2) but lack an inventive step under PCT Article 33(3).

2. Industrial Applicability

Claims 1-3 are industrially applicable under PCT Article 33(4).