

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>P41704058PCT</b>	<b>FOR FURTHER ACTION</b>	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. <b>PCT/SE2018/050893</b>	International filing date ( <i>day/month/year</i> ) <b>06-09-2018</b>	(Earliest) Priority Date ( <i>day/month/year</i> ) <b>08-09-2017</b>
Applicant <b>DIAMYD MEDICAL AB</b>		

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 7 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. \_\_\_\_\_

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.

**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.: **18-32**  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Claims 18-32 relate to a method for treatment of the human or animal body by surgery or therapy, see PCT Rule 39.1(iv). Nevertheless, a search has been conducted for these claims. The search has been directed to the technical content of the claims.
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).

**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: Claims 2-19, 20(partially), 22-34(p.) directed to a method for assessing the efficacy of an immunotherapy comprising administration of GAD. Furthermore, administration regimens of GAD in treatment or prevention of type 1 diabetes, comprising an assessment of efficacy followed by an adjustment of dosage and/or administration route based on said assessment.

2: Claims 21, 20(p.), 22-34(p.) directed to administration regimens of GAD in treatment or prevention of type 1 diabetes comprising four administrations into a lymph node.

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.:

**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.

**Box No. IV** Text of the abstract (Continuation of item 5 of the first sheet)

The invention relates to a method for assessing the efficacy of an immunotherapy comprising administration of GAD to a patient, comprising the following steps: measuring at least one of GADA IgG subclass distribution; GADA levels; distribution of cytokines secreted from lymphocytes; and lymphocyte proliferation in presence of GAD or CD3/CD28 beads; in a first blood, plasma or serum sample obtained from said patient at a first point in time and in a second blood, plasma or serum sample obtained from said patient at a later point in time; and comparing the so obtained measurements. The invention also relates to novel administration regimens of GAD in treatment or prevention of type 1 diabetes, that may include administration by injection into a lymph node, oral administration of vitamin D and/or an assessment of efficacy according to the above methodology followed by an adjustment of dosage and/or administration route based on said assessment.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/SE2018/050893

A. CLASSIFICATION OF SUBJECT MATTER		
IPC: see extra sheet		
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)		
IPC: A61K, A61P, G01N		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
SE, DK, FI, NO classes as above		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)		
EPO-Internal, PAJ, WPI data, BIOSIS, EMBASE, MEDLINE		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Chéramy M et al. "GAD-alum treatment in patients with type 1 diabetes and the subsequent effect on GADA IgG subclass distribution, GAD65 enzyme activity and humoral response", Clinical Immunology, 2010, 137(1):31-40; abstract; page 32, column 1, paragraph [0003]; pages 33, 36; page 38, column 1, paragraph [0001]; figure 1	2-12, 17, 22-34
Y	--	7-8, 13-16, 28
X	US 20030017509 A1 (KAUFMAN DANIEL L ET AL), 23 January 2003 (2003-01-23); paragraphs [0010], [0025], [0028], [0058]-[0059]	33-34
Y	--	16
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> 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 26-11-2018		Date of mailing of the international search report 26-11-2018
Name and mailing address of the ISA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. + 46 8 666 02 86		Authorized officer Carolina Palmcrantz Telephone No. + 46 8 782 28 00

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/SE2018/050893

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Ludvigsson J et al. "Intralymphatic Injection of Autoantigen in Type 1 Diabetes", N Engl J Med, 2017, 376(7):697-699. publ. 20170216; page 697	33-34
Y	--	7-8, 13-15
X	US 20050250691 A1 (ROBERTSON JOHN ET AL), 10 November 2005 (2005-11-10); paragraphs [0056], [0063], [0058]-[0059]	2, 4-8, 12, 17-18, 22-34
Y	--	19-20, 22-31
X	WO 2015187087 A2 (DIAMYD MEDICAL AB), 10 December 2015 (2015-12-10); page 57; page 58, line 30 - page 59, line 8; claims 2,5-6,15,17; Example 2	21-27, 29-34
Y	-- -----	7-8, 13-15, 19-20, 22-31

**Continuation of:** second sheet

**International Patent Classification (IPC)**

**G01N 33/564** (2006.01)

**A61K 31/592** (2006.01)

**A61K 31/593** (2006.01)

**A61K 39/00** (2006.01)

**A61P 3/10** (2006.01)

A61K 38/51 (2006.01)

G01N 33/15 (2006.01)

G01N 33/569 (2006.01)

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/SE2018/050893

US	20030017509 A1	23/01/2003	AU	7411398 A	22/06/1998
			US	6022697 A	08/02/2000
			US	6207159 B1	27/03/2001
			WO	9823959 A3	06/08/1998
US	20050250691 A1	10/11/2005	NONE		
WO	2015187087 A2	10/12/2015	AU	2015268960 A1	15/12/2016
			CA	2950893 A1	10/12/2015
			CN	106535926 A	22/03/2017
			EP	3151853 A4	25/04/2018
			JP	2017516870 A	22/06/2017
			RU	2016150656 A	10/07/2018
			US	20170196949 A1	13/07/2017