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(74) Agent: **EINHORN, Gregory, P.**; Gavrilovich, Dodd & Lindsey Llp, 4660 La Jolla Village Drive, Suite 750, San Diego, CA 92122 (US).

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(71) Applicants (for all designated States except US): **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** [US/US]; 1111 Franklin Street, 5th Floor, Oakland, CA 94607-5200 (US). **ROSALIND FRANKLIN UNIVERSITY OF MEDICINE AND SCIENCE** [US/US]; 3333 Green Bay Road, North Chicago, IL 60064 (US).

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(72) Inventors; and

(75) Inventors/Applicants (for US only): **MASLIAH, Eliezer** [US/US]; 4661 Corte Mar Del Corazon, San Diego, CA 92130 (US). **SPENCER, Brian** [US/US]; 2912 Kalmia Street, San Diego, CA 92104 (US). **ROCKENSTEIN, Edward** [US/US]; 2026 Terrakappa Avenue, Spring Valley, CA 91977 (US). **MARR, Robert** [US/US]; 3333 Green Bay Road, North Chicago, IL 60064 (US).

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- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

[Continued on next page]

(54) Title: COMPOUNDS FOR REVERSING AND INHIBITING PROTEIN AGGREGATION, AND METHODS FOR MAKING AND USING THEM

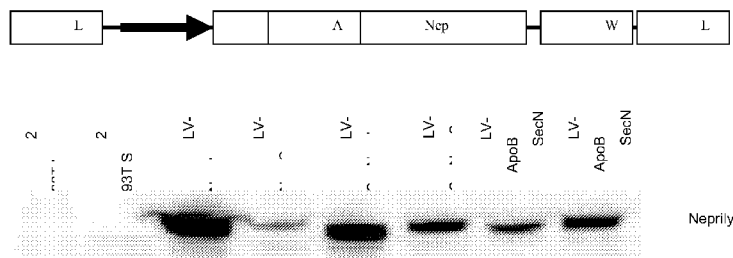


Figure 2

(57) Abstract: The invention provides compositions for increasing the clearance of protein aggregates, and pharmaceutical compositions comprising them, and methods for making and using them, including methods for accelerating protein aggregate clearance in the CNS, e.g., for treating diseases that are characterized by protein aggregation - including some degenerative neurological diseases such as Parkinson's disease. In one aspect, the compositions of the invention specifically target synuclein, beta-amyloid and/or tau protein aggregates, and the methods of the invention can be used to specifically prevent, reverse, slow or inhibit synuclein, beta-amyloid and/or tau protein aggregation. In alternative embodiments, the compositions and methods of the invention, are used to treat, prevent, reverse (partially or completely) or ameliorate (including slowing the progression of) degenerative neurological diseases related to or caused by protein aggregation, e.g., synuclein, beta-amyloid and/or tau protein aggregation. In one aspect, compositions and methods of this invention are used to treat, prevent or ameliorate (including slowing the progression of) Parkinson's disease, fronto-temporal dementia (FTD), Alzheimer's Disease (AD), Lewy body disease (LBD) and Multiple system atrophy (MSA).



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A. CLASSIFICATION OF SUBJECT MATTER*C07K 19/00(2006.01)i, C07K 14/47(2006.01)i, A61K 38/00(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)

IPC 8: C07K 19/00, C12Q 1/68, G01N 33/53, A61K 38/00

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 practicable, search terms used)

eKOMPASS(KIPO internal)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2005/0170359 A1 (Berislav Zlokovic) 4 August 2005 See the whole document.	1-7, 11, 13, 14
A	US 2005/0239062 A1 (Berislav Zlokovic) 27 October 2005 See the whole document.	1-7, 11, 13, 14
A	US 2004/0038302 A1 (Roger Nitsch et al.) 26 February 2004 See the whole document.	1-7, 11, 13, 14
A	William E. Klunk et al., Imaging Brain Amyloid in Alzheimer' s Disease with Pittsburgh Compound-B, Annals of Neurology, 2004, Vol. 55, p306-319 See the whole document.	1-7, 11, 13, 14
A	Angela R. Jones ¹ and Eric V. Shusta, Blood-Brain Barrier Transport of Therapeutics via Receptor-Mediation, Pharmaceutical Research, 2007, Vol. 24, No. 9, p1759-1771 See the whole document.	1-7, 11, 13, 14

 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 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

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Facsimile No. 82-42-472-7140

Authorized officer

CHANG, BONG HO

Telephone No. 82-42-481-8289



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.: 8-10, 12
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 8-10 and 12 pertain to methods for treatment of the human body by therapy, and thus relate to a subject matter which the International Searching Authority is not required to search, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT.
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. 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 fee, this Authority did not invite payment of any additional fee.
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/US2009/058883

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Shingo Ito et al., Cerebral Clearance of Human Amyloid-beta Peptide (1-40) Across the Blood-brain Barrier is Reduced by Self-aggregation and Formation of Low-density Lipoprotein Receptor-related Protein-1 Ligand Complexes, Journal of Neurochemistry, 2007, Vol.103, p2482-2490 See the whole document.	1-7, 11, 13, 14
A	Laura Morelli et al., The Degradation of Amyloid b As a Therapeutic Strategy in Alzheimer's Disease and Cerebrovascular Amyloidoses, Neurochemical Research, 2002, Vol. 27, No. 11, p1387-1399 See the whole document.	1-7, 11, 13, 14
A	Vincenzo Giordan et al., Systemic and Brain Metabolic Dysfunction As a New Paradigm for Approaching Alzheimer's Dementia, Neurochemical Research, 2007, Vol. 32, p555-567 See the whole document.	1-7, 11, 13, 14

INTERNATIONAL SEARCH REPORT

Information on patent family members

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