



(12) Translation of
European patent specification

(11) NO/EP 3339323 B1

NORWAY

(19) NO
(51) Int Cl.
C07K 16/18 (2006.01)
A61K 39/395 (2006.01)
A61P 25/28 (2006.01)
G01N 33/577 (2006.01)

Norwegian Industrial Property Office

(45)	Translation Published	2020.02.03
(80)	Date of The European Patent Office Publication of the Granted Patent	2019.11.13
(86)	European Application Nr.	18150424.2
(86)	European Filing Date	2011.08.09
(87)	The European Application's Publication Date	2018.06.27
(30)	Priority	2010.08.12, US, 373026 P
(84)	Designated Contracting States:	AL ; AT ; BE ; BG ; CH ; CY ; CZ ; DE ; DK ; EE ; ES ; FI ; FR ; GB ; GR ; HR ; HU ; IE ; IS ; IT ; LI ; LT ; LU ; LV ; MC ; MK ; MT ; NL ; NO ; PL ; PT ; RO ; RS ; SE ; SI ; SK ; SM ; TR
	Designated Extension States:	BA ; ME
(62)	Divided application	EP3042917, 2011.08.09
(73)	Proprietor	ELI LILLY AND COMPANY, Lilly Corporate Center, Indianapolis, IN 46285, USA
(72)	Inventor	Demattos, Ronald Bradley, c/o Eli Lilly and CompanyP.O. Box 6288, Indianapolis, Indiana 46206-6288, USA Lu, Jirong, c/o Eli Lilly and CompanyP.O. Box 6288, Indianapolis, Indiana 46206- 6288, USA Tang, Ying, c/o Eli Lilly and CompanyP.O. Box 6288, Indianapolis, Indiana 46206- 6288, USA
(74)	Agent or Attorney	ZACCO NORWAY AS, Postboks 2003 Vika, 0125 OSLO, Norge

(54)	Title	ANTI-N3PGLU AMYLOID BETA PEPTIDE ANTIBODIES AND USES THEREOF
(56)	References Cited:	WO-A2-2006/036291 US-B1- 7 122 374 US-A1- 2010 021 478 RACKE MARGARET M ET AL: "Exacerbation of cerebral amyloid angiopathy-associated microhemorrhage in amyloid precursor protein transgenic mice by immunotherapy is dependent on antibody recognition of deposited forms of amyloid beta.", THE JOURNAL OF NEUROSCIENCE : THE OFFICIAL JOURNAL OF THE SOCIETY FOR NEUROSCIENCE 19 JAN 2005 LNKD- PUBMED:15659599, vol. 25, no. 3, 19 January 2005 (2005-01-19), pages 629-

636, XP002660549, ISSN: 1529-2401

OLIVER WIRTHS ET AL: "Identification of low molecular weight pyroglutamate A β oligomers in Alzheimer disease: a novel tool for therapy and diagnosis", JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, INC, BETHESDA, MD, USA, vol. 285, no. 53, 31 December 2010 (2010-12-31), pages 41517-41524, XP002658320, ISSN: 1083-351X, DOI: 10.1074/JBC.M110.178707 [retrieved on 2010-10-22]

BAYER T A ET AL: "Intraneuronal A β as a trigger for neuron loss: Can this be translated into human pathology?", BIOCHEMICAL SOCIETY TRANSACTIONS, PORTLAND PRESS LTD, GB, [Online] vol. 39, no. 4, 1 January 2011 (2011-01-01), pages 857-861, XP008142494, ISSN: 0300-5127, DOI: DOI:10.1042/BST0390857

OLIVER WIRTHS ET AL: "Pyroglutamate Abeta pathology in APP/PS1KI mice, sporadic and familial Alzheimer's disease cases", JOURNAL OF NEURAL TRANSMISSION ; BASIC NEUROSCIENCES, GENETICS AND IMMUNOLOGY, PARKINSON'S DISEASE AND ALLIED CONDITIONS, ALZHEIMER'S DISEASE AND ADOLESCENT PSYCHIATRY RELATED DISORDERS, BIOLOGICAL PSYCHIATRY, BIOLOGICAL CHILD AND ADOLESCENT PSYCHIAT, vol. 117, no. 1, 13 October 2009 (2009-10-13), pages 85-96, XP019783126, ISSN: 1435-1463

BRODY DAVID L ET AL: "Active and passive immunotherapy for neurodegenerative disorders.", ANNUAL REVIEW OF NEUROSCIENCE 2008 LNKD- PUBMED:18352830, vol. 31, 2008, pages 175-193, XP002660548, ISSN: 0147-006X

LUO F ET AL: "P2-304: MRI detection and time course of cerebral microhemorrhages during Abeta antibody treatment in living APP transgenic mice", ALZHEIMER'S & DEMENTIA: THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION, ELSEVIER, NEW YORK, NY, US, vol. 4, no. 4, 1 July 2008 (2008-07-01), page T461, XP023174303, ISSN: 1552-5260, DOI: 10.1016/J.JALZ.2008.05.1381 [retrieved on 2008-07-01]

WILCOCK DONNA M ET AL: "Passive immunotherapy against A β in aged APP-transgenic mice reverses cognitive deficits and depletes parenchymal amyloid deposits in spite of increased vascular amyloid and microhemorrhage", JOURNAL OF NEUROINFLAMMATION, BIOMED CENTRAL LTD., LONDON, GB, vol. 1, no. 1, 8 December 2004 (2004-12-08), page 24, XP021010076, ISSN: 1742-2094, DOI: 10.1186/1742-2094-1-24

FRÉDÉRIQUE BARD ET AL: "Epitope and isotype specificities of antibodies to β -amyloid peptide for protection against Alzheimer's disease-like neuropathology", PROC NATL ACAD SCI (US), WASHINGTON, DC; US, vol. 100, no. 4, 18 February 2003 (2003-02-18), pages 2023-2028, XP002630662, ISSN: 0027-8424, DOI: 10.1073/PNAS.0436286100

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (<http://worldwide.espacenet.com>) or via the search engine on our website here: <https://search.patentstyret.no/>

Patentkrav

1. Anti-N3pGlu A β -antistoff omfattende en variabel region i lettkjeden (LCVR) og en variabel region i tungkjeden (HCVR), hvori LCDRI er KSX1X2SLLYSRX3KTYLN (SEQ ID NO: 51), LCDR2 er AVSKLX4S (SEQ ID NO:52), LCDR3 er VQGTHYPFT (SEQ ID NO: 5) og HCDRI er GYX5FTX6YYIN (SEQ ID NO: 53), HCDR2 er WINPGSGNTKYNEKFKG (SEQ ID NO: 8), og HCDR3 er EGX7TVY (SEQ ID NO: 54), hvori XI er S eller T; X2 er Q eller R, X3 er G eller S, X4 er D eller G, X5 er D eller T, X6 er R eller D, og X7 er I, T, E eller V, for anvendelse i forebygging av Alzheimers sykdom.

2. Anti-N3pGluA β -antistoff omfattende en variabel region i lettkjeden (LCVR) og en variabel region i tungkjeden (HCVR), hvori LCDRI er KSX1X2SLLYSRX3KTYLN (SEQ ID NO: 51), LCDR2 er AVSKLX4S (SEQ ID NO:52), LCDR3 er VQGTHYPFT (SEQ ID NO: 5), og HCDRI er GYX5FTX6YYIN (SEQ ID NO: 53), HCDR2 er WINPGSGNTKYNEKFKG (SEQ ID NO: 8), og HCDR3 er EGX7TVY (SEQ ID NO: 54), hvori XI er S eller T; X2 er Q eller R, X3 er G eller S, X4 er D eller G, X5 er D eller T, X6 er R eller D, og X7 er I, T, E, eller V, for anvendelse i forebygging av en tilstand valgt fra klinisk eller preklinisk Alzheimers sykdom, prodromal Alzheimers sykdom og klinisk eller preklinisk CAA.

3. Anti-N3pGluA β -antistoff eller antigenbindende fragment derav for anvendelse ifølge krav 1 eller for anvendelse ifølge krav 2, hvori antistoffet eller det antigenbindende fragmentet derav omfatter en variabel region i lettkjeden (LCVR) og en variabel region i tungkjeden (HCVR), hvori LCVR-en omfatter LCDR1-, LCDR2- og LCDR3-polypeptider, og HCVR omfatter HCDR1-, HCDR2- og HCDR3-polypeptider, som er valgt fra gruppen bestående av:

a) LCDR1 er KSSQSLLYSRGKTYLN (SEQ ID NO: 3), LCDR2 er AVSKLDS (SEQ ID NO: 4), LCDR3 er VQGTHYPFT (SEQ ID NO: 5), HCDR1 er GYDFTRYIN (SEQ ID NO: 6), HCDR2 er WINPGSGNTKYNEKFKG (SEQ ID NO: 8), og HCDR3 er EGITVY (SEQ ID NO: 9);

b) LCDR1 er KSSQSLLYSRGKTYLN (SEQ ID NO: 3), LCDR2 er AVSKLDS (SEQ ID NO: 4), LCDR3 er VQGTHYPFT (SEQ ID NO: 5), HCDR1 er GYTFTRYIN (SEQ ID NO: 7), HCDR2 er WINPGSGNTKYNEKFKG (SEQ ID NO: 8), og HCDR3 er EGTTVY (SEQ ID NO: 10);

c) LCDR1 er KSSQSLLYSRGKTYLN (SEQ ID NO: 3), LCDR2 er AVSKLDS (SEQ ID NO: 4), LCDR3 er VQGTHYPFT (SEQ ID NO: 5), HCDR1 er GYTFTDYIN (SEQ ID

NO: 40), HCDR2 er WINPGSGNTKYNEKFKG (SEQ ID NO: 8), og HCDR3 er EGETVY (SEQ ID NO: 41);

5 d) LCDR1 er KSSQSLLYSRGKTYLN (SEQ ID NO: 3), LCDR2 er AVSKLGS (SEQ ID NO: 35), LCDR3 er VQGTHYPFT (SEQ ID NO: 5), HCDR1 er GYTFTRYIN (SEQ ID NO: 7), HCDR2 er WINPGSGNTKYNEKFKG (SEQ ID NO: 8), og HCDR3 er EGTTVY (SEQ ID NO: 10); eller

10 e) LCDR1 er KSTRSLLYSRSKTYLN (SEQ ID NO: 45), LCDR2 er AVSKLDS (SEQ ID NO: 4), LCDR3 er VQGTHYPFT (SEQ ID NO: 5), HCDR1 er GYTFTDYIN (SEQ ID NO: 40), HCDR2 er WINPGSGNTKYNEKFKG (SEQ ID NO: 8), og HCDR3 er EGVTVY (SEQ ID NO: 46).