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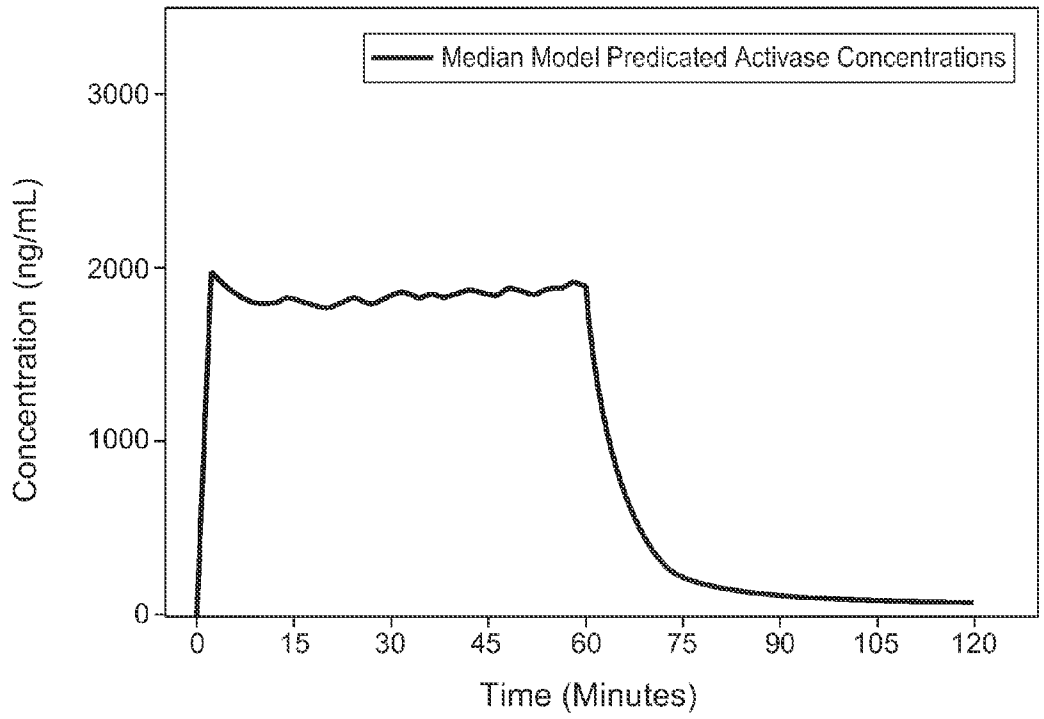
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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— *with international search report*

(88) Date of publication of the international search report:
22 May 2008

(54) Title: USE OF TENECTEPLASE FOR TREATING ACUTE ISCHEMIC STROKE



(57) Abstract: A method for treating acute ischemic stroke in a human comprises administering tenecteplase to the human in a total dose of about 0.05 to 0.5 mg/kg, given as (a) an initial bolus dose of about 0.015 to 0.15 mg/kg, followed by infusion of an amount equaling the total dose minus the initial dose over a period of about 50-90 minutes, or (b) a bolus. Also described are kits for carrying out this method.

WO 2008/027687 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/074997

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K38/16 A61P9/10

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 A61P

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 practical, search terms used)
EPO-Internal, BIOSIS, WPI Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HALEY E CLARKE JR ET AL: "A pilot dose-escalation safety study of tenecteplase in acute ischemic stroke" STROKE, vol. 36, no. 3, March 2005 (2005-03), pages 607-612, XP002463474 ISSN: 0039-2499 the whole document ----- -/--	1-4, 10-14, 17-23

[X] Further documents are listed in the continuation of Box C.

[X] 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 document 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	Date of mailing of the international search report
7 January 2008	14/02/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Allnutt, Sarah

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/074997

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material

   [X] a sequence listing

   [ ] table(s) related to the sequence listing

   b. format of material

   [ ] on paper

   [X] in electronic form

   c. time of filing/furnishing

   [ ] contained in the international application as filed

   [X] filed together with the international application in electronic form

   [ ] furnished subsequently to this Authority for the purpose of search

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/074997

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	THOMAS G ROGER ET AL: "A long-half-life and fibrin-specific form of tissue plasminogen activator inrabbit models of embolic stroke and peripheral bleeding" STROKE, AMERICAN HEART ASSOCIATION, DALLAS TX, US, vol. 25, no. 10, October 1994 (1994-10), pages 2072-2078, XP009094086 ISSN: 0039-2499 cited in the application page 2072, column 2, paragraph 3 page 2073, column 2, paragraph 2 page 2074, column 2, lines 3-5,18-20 page 2075, column 1, lines 14-16 page 2076, column 2, lines 27-36 page 2077, column 1, paragraph 3	1-25
A	US 2003/180282 A1 (SEREBRUANY VICTOR [US] ET AL) 25 September 2003 (2003-09-25) paragraphs [0007], [0010], [0012], [0026], [0033]	1-25
A	CHAPMAN DEBORAH F ET AL: "Incidence of cerebral hemorrhage and thrombolysis following treatment with TNK or tPA in a rabbit model of thromboembolic stroke" NEUROLOGY, vol. 54, no. 7 Supp. 3, 11 April 2000 (2000-04-11), page A261, XP009094130 & 52ND ANNUAL MEETING OF THE AMERICAN ACADEMY OF NEUROLOGY.; SAN DIEGO, CA, USA; APRIL 29-MAY 06, 2000 ISSN: 0028-3878 abstract	1-25
A	LAPCHAK PAUL A ET AL: "Comparison of Tenecteplase with Alteplase on clinical rating scores following small clot embolic strokes in rabbits." EXPERIMENTAL NEUROLOGY, vol. 185, no. 1, January 2004 (2004-01), pages 154-159, XP002463505 ISSN: 0014-4886 cited in the application page 155, column 1, paragraph 1 page 155, column 2, paragraph 2; figure 2	1-25

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/074997

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ZHANG RUI LAN ET AL: "Postischemic intracarotid treatment with TNK-tPA reduces infarct volume and improves neurological deficits in embolic stroke in the unanesthetized rat" BRAIN RESEARCH, vol. 878, no. 1-2, 29 September 2000 (2000-09-29), pages 64-71, XP002463483 ISSN: 0006-8993 abstract	1-25
A	KEYT BRUCE A ET AL: "A faster-acting and more potent form of tissue plasminogen activator" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 91, no. 9, 1994, pages 3670-3674, XP002463508 ISSN: 0027-8424 cited in the application abstract	1-25
A	SEMBA C P ET AL: "Alteplase and tenecteplase: applications in the peripheral circulation." TECHNIQUES IN VASCULAR AND INTERVENTIONAL RADIOLOGY JUN 2001, vol. 4, no. 2, June 2001 (2001-06), pages 99-106, XP002463509 ISSN: 1089-2516 page 104, column 2, lines 7-12, paragraph 2	1-25
P,X	SACCO ET AL: "Experimental treatments for acute ischaemic stroke" LANCET THE, LANCET LIMITED. LONDON, GB, vol. 369, no. 9558, 27 January 2007 (2007-01-27), pages 331-341, XP005858957 ISSN: 0140-6736 page 333, column 1, paragraph 3	1-25
P,A	WO 2006/094120 A (UNIV CALIFORNIA [US]; LAPCHAK PAUL A [US]; ARAUJO DALIA [US]; ZIVIN JU) 8 September 2006 (2006-09-08) paragraphs [0040], [0044], [0078], [0083]	1-25
P,A	US 2007/014779 A1 (SEMBA CHARLES P [US]) 18 January 2007 (2007-01-18)	1-25

Continuation of Box II.1

Although claims 1-16 are directed to a method of treatment of the human, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.1

Claims Nos.: 1-16

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/074997

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. [X] Claims Nos.: 1-16
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

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 allsearchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an 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 reportcovers 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

Information on patent family members

International application No
PCT/US2007/074997

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003180282 A1	25-09-2003	NONE	
WO 2006094120 A	08-09-2006	NONE	
US 2007014779 A1	18-01-2007	NONE	