

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
30 March 2006 (30.03.2006)

PCT

(10) International Publication Number
WO 2006/033854 A3

(51) International Patent Classification:

C12Q 1/68 (2006.01) *C07H 21/02* (2006.01)
C12P 19/34 (2006.01) *C07H 21/04* (2006.01)
A61K 38/00 (2006.01) *C12N 15/88* (2006.01)

US 60/678,427 (CIP)
Filed on 6 May 2005 (06.05.2005)
US 60/690,231 (CIP)
Filed on 13 June 2005 (13.06.2005)

(21) International Application Number:

PCT/US2005/032134

(71) Applicant (for all designated States except US): **AR-CHEMIX CORP.** [US/US]; One Hampshire Street, 5th Floor, Cambridge, MA 02139 (US).

(22) International Filing Date:

7 September 2005 (07.09.2005)

(72) Inventors; and

(75) Inventors/Applicants (for US only): **DIENER, John, L.** [US/US]; 87 Bristol Street, Unit 1B, Cambridge, MA 02139 (US). **LAGASSÉ, Daniel, H., A.** [US/US]; 112 Highland Avenue, Apt. F, Somerville, MA 02143 (US).

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/608,047 7 September 2004 (07.09.2004) US
60/661,950 11 March 2005 (11.03.2005) US
60/678,427 6 May 2005 (06.05.2005) US
60/690,231 13 June 2005 (13.06.2005) US

(74) Agent: **ELRIFI, Ivor, R.**; Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., One Financial Center, Boston, MA 02111 (US).

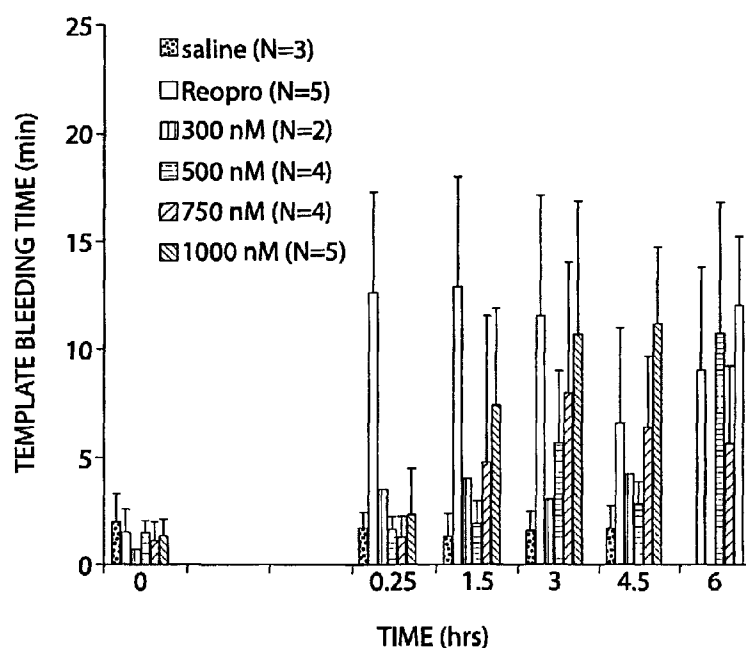
(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier applications:

US 60/608,047 (CIP)
Filed on 7 September 2004 (07.09.2004)
US 60/661,950 (CIP)
Filed on 11 March 2005 (11.03.2005)

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,

[Continued on next page]

(54) Title: APTAMERS TO VON WILLEBRAND FACTOR AND THEIR USE AS THROMBOTIC DISEASE THERAPEUTICS



(57) Abstract: The invention relates generally to the field of nucleic acids and more particularly to aptamers capable of binding to von Willebrand Factor useful as therapeutics in and diagnostics of thrombotic diseases and/or other diseases or disorders in which von Willebrand Factor mediated platelet aggregation has been implicated. The invention further relates to materials and methods for the administration of aptamers capable of binding to von Willebrand Factor.

WO 2006/033854 A3



SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US (patent),
UZ, VC, VN, YU, ZA, ZM, ZW.

- (84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) **Date of publication of the international search report:**

31 May 2007

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/32134

A. CLASSIFICATION OF SUBJECT MATTER

IPC: C12Q 1/68(2006.01);C12P 19/34(2006.01);A61K 38/00(2006.01);C07H 21/02(2006.01);21/04(2006.01);C12N 15/88(2006.01)

USPC: 435/6,91.1,455,458;514/44;536/23.1,24.5

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)

U.S. : 435/6, 91.1, 455,458; 514/44; 536/23.1, 24.5

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)
West, Dialog, Seq Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HWANG et al. Inhibition of gene expression in human cells through small molecule-RNA interactions, Proc. Nat'l. Acad. Sci. 9 November 1999, Vol. 96, No. 23, pages 12997-13002, see entire document.	1-7, 9-11, 18-26 and 37-42

☐ 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 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
19 March 2007 (19.03.2007)

Date of mailing of the international search report

10 APR 2007

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (571) 273-3201

Authorized officer

Jane Zara

Telephone No. (703) 308-0196

Felicia D. Roberts
for

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/32134

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.:
because they relate to subject matter not required to be searched by this Authority, namely:
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:
Please See Continuation Sheet

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 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.: 1-7,9-11,18-26 and 37-42
- Remark on Protest**
- | | |
|--------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input type="checkbox"/> | The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee. |
| <input type="checkbox"/> | 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. |
| <input type="checkbox"/> | No protest accompanied the payment of additional search fees. |

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

The inventions listed as Groups 1-213 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: because.

This international searching authority has found 213 inventions claimed in the International Application covered by the claim(s) indicated below:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid. Each sequence listed in the claims is a distinct invention for the reasons cited below.

Claims 1-42 are generic, and include 213 different sequences among SEQ ID NOs. 31 through 323. Each sequence comprises a separate invention. SEQ ID NO: 214, listed in claims 1-3 and in generic claims 4-7, 9-11, 18-26, and 37-42 comprise the first invention.

Nucleotide sequences among the SEQ ID NOs. 31-323, listed in claims 1, 44 comprise the second through the 213th invention.

This international searching authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2, and 13.3) for the reasons indicated below:

According to the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markush-group are of similar nature. For chemical alternatives, such as the claimed nucleotide and polypeptide sequences, the Markush group shall be regarded as being of similar nature when

(A) all alternatives have a common property or activity and

(B)(1) a common structure is present, i.e., a significant structure is shared by all of the alternatives or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant sequences are considered to be each separate inventions for the following reasons:

The various nucleotide or polypeptide sequences do not meet the criteria of (A), common property or activity or (B)(2), art recognized class of compounds. Each sequence behaves in a different way in the context of the claimed invention. Each member of the class cannot be substituted, one for the other, with the expectation that the same intended result would be achieved.

Further, the sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure.

Accordingly, unity of invention between the different sequences is lacking and each sequence claimed is considered to constitute a special technical feature.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/32134

For PCTs: If the sequences are recited in the first claimed invention, Applicants will obtain a search of the first sequence listed in the claim. For every other sequence applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.

If the sequences are recited in the second or subsequent claimed invention, Applicants will need to elect the group and pay the fee to obtain a search of the first sequence listed in the claims encompassed by the second or subsequent group. For every other sequence in the second/subsequent group that applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.