

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
18 December 2003 (18.12.2003)

PCT

(10) International Publication Number
WO 2003/103475 A3

(51) International Patent Classification⁷: **A61K 9/00**,
A61P 7/00

(21) International Application Number:
PCT/US2003/017665

(22) International Filing Date: 6 June 2003 (06.06.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/387,239 7 June 2002 (07.06.2002) US
60/407,003 28 August 2002 (28.08.2002) US

(71) Applicant (for all designated States except US): **DYAX CORP.** [US/US]; 300 Technology Square, Cambridge, MA 02139 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **LADNER, Robert, C.** [US/US]; 3827 Green Valley Road, Ijamsville, MD 21754 (US). **LEY, Arthur, C.** [US/US]; 122 Adena Road, Newton, MA 02465 (US). **HIRANI, Shirish** [US/US]; 19 Maple Road, Arlington, MA 02476 (US). **WILLIAMS, Anthony** [GB/US]; 129 Franklin Street #140, Cambridge, MA 02139 (US).

(74) Agent: **BUTLER, Laurie, Lawrence**; Fish and Richardson, 225 Franklin Street, Boston, MA 02110-2804 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (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:
10 March 2005

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.

(54) Title: PREVENTION AND REDUCTION OF BLOOD LOSS

(57) Abstract: Methods are described for preventing or reducing ischemia and/or systemic inflammatory response in a patient such as perioperative blood loss and/or systemic inflammatory response in a patient subjected to cardiothoracic surgery, *e.g.*, coronary artery bypass grafting and other surgical procedures, especially when such procedures involve extra-corporeal circulation, such as cardiopulmonary bypass.



WO 2003/103475 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/17665

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K9/00; A61P7/00

US CL : 435/6; 514/2

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; 514/2; 514/12

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,786,328 (DENNIS et al) 28 July 1998 (28.07.1998), columns 6-7, column 8, lines 50-61.	1-39
Y	US 5,994,125 (MARKLAND et al) 30 November 1999 (30.11.1999), column 3, lines 39-45, column 11, lines 57-62.	1-39
A	MARKLAND et al., Iterative Optimization of High-Affinity Protease Inhibitors Using Phage Display. 1. Plasmin, 1996, Biochemistry, Vol. 35, pages 8045-8057.	1-39
A	MARKLAND et al. (1996) Iterative Optimization of High-Affinity Protease Inhibitors Using Phage Display. 2. Plasma Kallikrein and Thrombin, Biochemistry, 1996, Vol. 35, pages 8058-8067.	1-39



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	"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
"E " earlier application or patent published on or after the international filing date	"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
"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)	"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
"O " document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P " document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 26 October 2004 (26.10.2004)	Date of mailing of the international search report 06 JAN 2005
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. (703) 305-3230	Authorized officer <i>Marsha M. Tsay</i> Marsha M. Tsay Telephone No. 517-272-2938