(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 July 2005 (07.07.2005)

PCT

(10) International Publication Number
WO 2005/060456 A2

(51) International Patent Classification: Not classified

(21) International Application Number:
PCT/US2004/037169

(22) International Filing Date:
8 November 2004 (08.11.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/526,883 4 December 2003 (04.12.2003) US

(71) Applicant *(for all designated States except US)*: **WYETH** [US/US]; Five Giralda Farms, Madison, NJ 07940 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **MORRIS, Elisabeth, A.** [US/US]; 15 Apple Street, Sherborn, MA 01770 (US). **GLASSON, Sonya, S.** [US/US]; 98 Shaw Road, Belmont, MA 02478 (US). **XIANG, Jason, Shaoyun** [US/US]; 3 River Street, Winchester, MA 01890 (US).

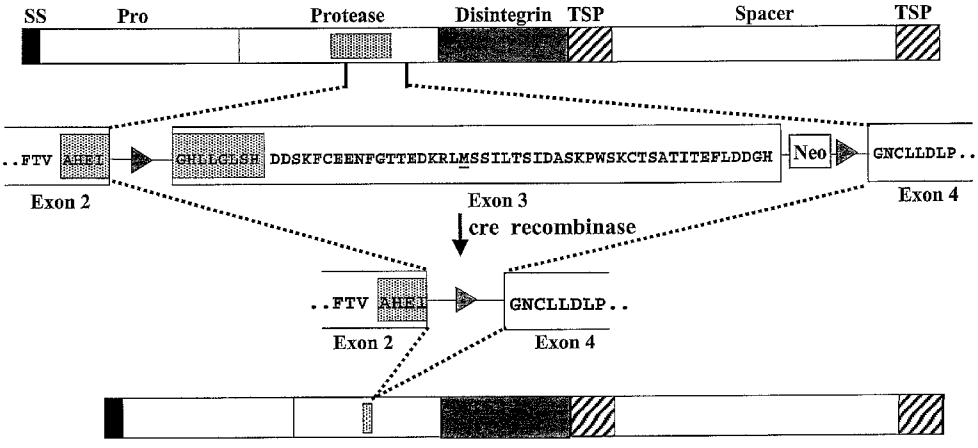
(74) Agents: **PERRY, Lawrence, S.** et al.; Fitzpatrick, Cella, Harper & Scinto, 30 Rockefeller Plaza, New York, NY 10112-3801 (US).

(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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, 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, LU, 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).

[Continued on next page]

(54) Title: METHOD FOR TREATING ADAMTS-5-ASSOCIATED DISEASE



(57) Abstract: The present invention relates to methods of treating ADAMTS-5-associated diseases and particularly osteoarthritis comprising administering an agent capable of modulating ADMATS-5 activity to a subject afflicted with the disease. The agent is preferably a biaryl sulfonamide compound. The invention is based, in part, on the discovery that transgenic animals that do not express functional ADAMTS-5 show a reduction in the degree of osteoarthritis after the induction of osteoarthritis as compared to WT animals. Furthermore, the ADAMTS-5 transgenic animals have reduced aggrecanase activity in articular tissue as compared to WT animals. These animals are good models for ADAMTS-5-associated diseases, and for screening of drugs useful in the treatment and/or prevention of these diseases. There are no other animal models in which the deletion of the activity of a single gene is capable of abrogating the course of osteoarthritis. Accordingly, these animals also show that osteoarthritis can be prevented and/or treated by administering to a subject an ADAMTS-5 inhibitory agent and particularly an agent capable of inhibiting the aggrecanase activity of ADAMTS-5.

WO 2005/060456 A2

Published:

— *without international search report and to be republished upon receipt of that report*

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.