

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
12 February 2004 (12.02.2004)

PCT

(10) International Publication Number  
**WO 2004/012672 A3**

(51) International Patent Classification<sup>7</sup>: **A61K 9/12**, 9/14

(21) International Application Number:

PCT/US2003/024323

(22) International Filing Date: 1 August 2003 (01.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

|            |                               |    |
|------------|-------------------------------|----|
| 60/400,159 | 1 August 2002 (01.08.2002)    | US |
| 60/406,525 | 28 August 2002 (28.08.2002)   | US |
| 60/427,388 | 18 November 2002 (18.11.2002) | US |
| 60/489,191 | 22 July 2003 (22.07.2003)     | US |

(71) Applicant: **MANNKIND CORPORATION** [US/US]; 1 Casper Street, Danbury, CT 06810 (US).

(72) Inventors: **GELBER, Cohava**; 11 Clubway, Hartsdale, NY 10530 (US). **ROUSSEAU, Kathleen**; 9 Van Wyck Street, Ossining, NY 10562 (US).

(74) Agents: **PABST, Patrea, L.** et al.; One Atlantic Center, Suite 2000, 1201 West Peachtree Street, Atlanta, GA 30309-3400 (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, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, 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:  
5 August 2004

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: CELL TRANSPORT COMPOSITIONS AND USES THEREOF

(57) Abstract: Compositions and methods have been developed for transporting compounds across membranes with little or no toxicity and, when targeted through the appropriate routes of administration (i.e., lung, gastrointestinal (GI) tract), little or no immune stimulation. The compositions can mediate cellular delivery of compounds that would otherwise not enter cells and enhance the intracellular delivery of compounds that would otherwise enter cells inefficiently. The methods are carried out by contacting a proximal face of a lipid bilayer or membrane (e.g. the surface of an intact cell) with a complex containing a compound (e.g., a therapeutic agent) and a diketopiperazine (DKP). DKP and the compound are non-covalently associated with each other or covalently bound to each other.



WO 2004/012672 A3

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/24323

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 9/12, 14  
US CL : 424/45, 46, 489

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. : 424/45, 46, 489

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)  
EAST, Dialog

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|------------|--|-----------------------|
| X          | US 6,071,497 A (STEINER et al) 06 June 2000 (06.06.2000), see entire document.       | 1-37                  |
| P, X       | US 6,428,771 B1 (STEINER et al.) 06 August 2002 (06.08.2002), see entire document.   | 1-37                  |
| T, X       | US 6,652,885 B2 (STEINER et al.) 25 November 2003 (25.11.2003), see entire document. | 1-37                  |



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  |  |
| "F" document published prior to the international filing date but later than the priority date claimed  | "Z" document member of the same patent family  |

Date of the actual completion of the international search

26 April 2004 (26.04.2004)

Date of mailing of the international search report

29 JUN 2004

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) 872-9305

Authorized officer

Karen Cochrane Carlson, Ph.D.

Telephone No. (571) 272-1600