



Europäisches Patentamt
European Patent Office
Office européen des brevets



(11)

EP 0 988 059 B8

(12)

CORRECTED EUROPEAN PATENT SPECIFICATION

Note: Bibliography reflects the latest situation

(15) Correction information:

Corrected version no 1 (W1 B1)
INID code(s) 73

(51) Int Cl.:

A61K 47/48 ^(1990.01) **A61P 35/00** ^(2000.01)
A61K 38/44 ^(1995.01) **A61K 31/4422** ^(2000.01)

(48) Corrigendum issued on:

01.03.2006 Bulletin 2006/09

(86) International application number:

PCT/GB1998/001731

(45) Date of publication and mention
of the grant of the patent:

07.12.2005 Bulletin 2005/49

(87) International publication number:

WO 1998/057662 (23.12.1998 Gazette 1998/51)

(21) Application number: **98929555.5**

(22) Date of filing: **15.06.1998**

(54) **HUMAN QUINONE REDUCTASE 2 CONJUGATES FOR ADEPT AND GDEPT**

MENSCHLICHE CHINON REDUKTASE KONJUGATE FÜR ADEPT UND GDEPT

CONJUGES DE QUINONE-REDUCTASE HUMAIN POUR ADEPT ET GDEPT

(84) Designated Contracting States:

AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE

(56) References cited:

WO-A-93/08288 **WO-A-95/12678**
WO-A-97/07097 **WO-A-97/24143**
WO-A-98/22577

(30) Priority: **14.06.1997 GB 9712370**

(43) Date of publication of application:

29.03.2000 Bulletin 2000/13

(60) Divisional application:

04076964.8 / 1 468 698

(73) Proprietor: **Protherics Molecular Design Limited**

Runcorn
Cheshire WA7 4QF (GB)

(72) Inventors:

- **BURKE, Philip, John**
London SE7 7PF (GB)
- **KNOX, Richard, John**
Sutton,
Surrey SM1 2SU (GB)

(74) Representative: **Miles, John Stephen**

Eric Potter Clarkson LLP
Park View House
58 The Ropewalk
Nottingham NG1 5DD (GB)

- **KNOX R J ET AL: "THE BIOACTIVATION OF CB 1954 AND ITS USE AS A PRODRUG IN ANTIBODY-DIRECTED ENZYME PRODRUG THERAPY (ADEPT)" CANCER AND METASTASIS REVIEWS, vol. 12, no. 2, 1993, pages 195-212, XP000618513 cited in the application**
- **FRIEDLOS F ET AL: "METABOLISM OF NADPH BY BLOOD COMPONENTS RELEVANCE TO BIOREDUCTIVELY ACTIVATED PRODRUGS IN A TARGETED ENZYME THERAPY SYSTEM" BIOCHEM PHARMACOL, vol. 44, no. 4, 1992, pages 631-635, XP000618526 cited in the application**
- **WU K ET AL: "Catalytic properties of NAD(P)H:quinone oxidoreductase-2 (NQO2), a dihydronicotinamide riboside dependent oxidoreductase." ARCH BIOCHEM BIOPHYS, NOV 15 1997, 347 (2) P221-8, XP002080156 UNITED STATES**
- **MELTON, R. G. ET AL: "Antibody-directed enzyme prodrug therapy (ADEPT). Review article" DRUGS OF THE FUTURE, vol. 21, no. 2, 1996, pages 167-184, XP002080157**

Note: Within nine months from the publication of the mention of the grant of the European patent, any person may give notice to the European Patent Office of opposition to the European patent granted. Notice of opposition shall be filed in a written reasoned statement. It shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

EP 0 988 059 B8

- SHERWOOD R F: "ADVANCED DRUG DELIVERY REVIEWS: ENZYME PRODRUG THERAPY" ADVANCED DRUG DELIVERY REVIEWS, vol. 22, 1996, pages 269-288, XP002064128
- GREEN N. K. ET AL: "Sensitization of colorectal and pancreatic cancer cell lines to the prodrug 5-(aziridin-1-yl)-2,4-dinitrobenzamide (CB1954) by retroviral transduction and expression of the E. coli nitroreductase gene" CANCER GENE THERAPY, vol. 4, no. 4, August 1997, pages 229-238, XP002092056
- DRABEK D. ET AL: "The expression of bacterial nitroreductase in transgenic mice results in specific cell killing by the prodrug CB1954" GENE THERAPY, vol. 4, no. 2, February 1997, pages 93-100, XP002092057