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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
1 July 2004 (01.07.2004)

PCT

(10) International Publication Number
WO 2004/054498 A2

(51) International Patent Classification[7]: A61K

(21) International Application Number:
PCT/US2003/024232

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

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/401,074	2 August 2002 (02.08.2002)	US
60/411,128	16 September 2002 (16.09.2002)	US
60/450,063	24 February 2003 (24.02.2003)	US

(71) Applicant: **NEREUS PHARMACEUTICALS, INC.** [US/US]; 10480 Wateridge Circle, San Diego, CA 92121 (US).

(72) Inventors: **HAYASHI, Yoshio**; 3-9-18-301 Heso, Ritto-shi, Shiga 520-3031 (JP). **GRODBERG, Jennifer**; 3459 Calle del Sur, Carlsbad, CA 92009 (US). **PALLADINO, Michael**; 3357 Fortuna Ranch Road, Olivenhain, CA 92024 (US).

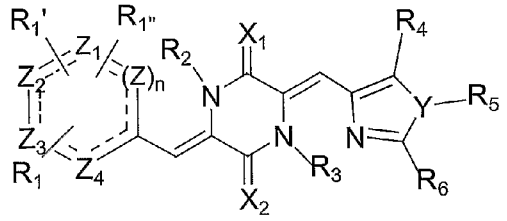
(74) Agent: **MALLON, Joseph, J.**; KNOBBE, MARTENS, OLSON & BEAR, LLP, 2040 Main Street, 14th Floor, Irvine, CA 92614 (US).

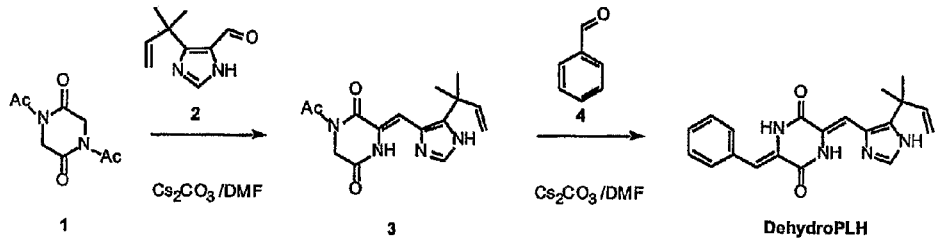
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ (utility model), CZ, DE (utility model), DE, DK (utility model), DK, DM, DZ, EC, EE (utility model), EE, ES, FI (utility model), FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, 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 (utility model), 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,

[Continued on next page]

(54) Title: DEHYDROPHENYLAHISTINS AND ANALOGS THEREOF AND THE SYNTHESIS OF DEHYDROPHENYLAHISTINS AND ANALOGS THEREOF





(57) Abstract: Compounds represented by structure (I) are disclosed, as are methods for making such compounds, wherein said methods comprise reacting a diacyldiketopiperazine with a first aldehyde to produce an intermediate compound; and reacting the intermediate compound with a second aldehyde to produce the class of compounds with the generic structure, where the first aldehyde and the second aldehydes are selected from the group consisting of an oxazolecarboxaldeyhyde, imidazolecarboxaldehyde, a benzaldehyde, imidazolecarboxaldehyde derivatives, and benzaldehyde derivatives, thereby forming the above compound wherein R_1, R_1', R_1'', R_2, R_3, R_4, R_5, and R_6, X_1 and X_2, Y, Z, Z_1, Z_2, Z_3, and Z_4 may each be separately defined in a manner consistent with the accompanying description. Compositions and methods for treating cancer and fungal infection are also disclosed.

WO 2004/054498 A2

SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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.