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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 March 2001 (22.03.2001)

PCT

(10) International Publication Number
WO 01/19320 A2

(51) International Patent Classification[7]: A61K

(21) International Application Number: PCT/IL00/00562

(22) International Filing Date:
13 September 2000 (13.09.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
131887 14 September 1999 (14.09.1999) IL

(71) Applicant *(for all designated States except US)*: **D-PHARM LIMITED** [IL/IL]; Kiryat Weizmann Science Park, P.O. Box 2313, 76123 Rehovot (IL).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **KOZAK, Alexander** [IL/IL]; 8 Naphtali Ben Ephraim Street, 76555 Rehovot (IL). **SHAPIRO, Israel** [IL/IL]; 1 Aharon Bouganium Street, 75122 Ramla (IL). **VINNIKOVA, Marina** [IL/IL]; 1 Aharon Bouganium Street, 75122 Ramla (IL). **ERSHOV, Leonid** [IL/IL]; Ganei Shemesh 64/20, 99510 Beit Shemesh (IL). **SENDERIKHIN, Alexander** [IL/IL]; Eben Ezra 11/32, 77622 Ashdod (IL). **AYALON, Oran** [IL/IL]; Shikun Banim 143, 76922Ganei Yohanan (IL).

(74) Agent: **WALKER, Naomi**; Kiryat Weizmann Science Park, P.O. Box 2313, 76123 Rehovot (IL).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, 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, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, 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.

WO 01/19320 A2

(54) Title: PHOSPHOLIPID PRODRUGS OF ANTI-PROLIFERATIVE DRUGS

(57) Abstract: The invention discloses prodrugs comprising anti-proliferative drugs covalently linked, via a bridging group, to a phospholipid moiety such that the active species is preferentially released, preferably by enzymatic cleavage, at the required site of action. The invention further discloses pharmaceutical compositions comprising said prodrugs and the uses thereof for the treatment of diseases and disorders related to inflammatory, to degenerative or atrophic conditions, and to uncontrolled cell growth.