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[54] **QUINOLINE COMPOUNDS**

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[51] **Int. Cl.**[6] **C07D 213/80**; A61K 31/44

[52] **U.S. Cl.** **514/312**; 514/313; 546/153; 546/159

[58] **Field of Search** 546/153, 159; 514/312, 313

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,470,186	9/1969	Hanifin et al.	546/160
4,343,804	8/1982	Munson, Jr. et al.	514/313
4,806,550	2/1989	Ife et al.	514/313
4,966,849	10/1990	Vallee et al. .	
5,089,498	2/1992	Ife et al.	514/235.2
5,143,920	9/1992	Ife et al.	514/313
5,217,999	6/1993	Levitzki et al.	514/613
5,302,606	4/1994	Spada et al.	514/357
5,330,992	7/1994	Eissenstat et al.	514/312

FOREIGN PATENT DOCUMENTS

566 266	10/1993	European Pat. Off. .
WO 91/15495	10/1991	WIPO .
WO 92/20642	11/1992	WIPO .
WO 92/21660	12/1992	WIPO .
WO 94/03427	2/1994	WIPO .
WO 94/10202	5/1994	WIPO .
WO 94/14808	7/1994	WIPO .

OTHER PUBLICATIONS

Mirek, J.; Urbanek, Z. H.;Burzynski, L.;Chojnacka-Wojcik, E.; Wiczynska, B. Synthesis and Pharmacological Properties of sone 7H-[1] Benzothiopyrano-[3,2-c] Quinolin-7-ones. Pol. J. Pharmacol. Pharm. 1983, 35, 139–149 1992.

Marecki, P. E.; Bambury, R. E. Synthesis of 4-Substituted Aminoquinoline-3-carboxylates as Potential Antimicrobial Agents. J. Phar. Sci., 1984, 73 (8), 1141–1143 1984.

Ife, R. J.; Brown, T. H.; Keeling, D. J.; Leach, C. A.; Meeson, M. L.; Parsons, M. E.; Reavill, D. R.; Theobald, C. J.; Wiggall, K. J. Reversible Inhibitors of the Gastric (H+/K+)-ATPase. 3. 3-Substituted-4-(phenylamino)quinolines. J. Med. Chem., 199 1992.

Savine, L.; Massarelli, P.; Pellerano, C. New Quinoline Derivatives: Synthesis and Evaluation for Antiinflammatory and Analgesic Properties-Note II. Il Farmaco, 1993, 48(6), 805–825 1993.

Aaronson, S. A. (1991). Growth factors and cancer. Science 254, 1146–1153.

Arvidsson, A.-K., et al. (1994). Tyr-716 in the platelet-derived growth factor b-receptor kinase insert is involved in GRB2 binding and ras activation. Molecular and Cellular Biology 14, 6715–6726.

Baserga, R. (1995). The insulin-like growth factor I receptor: a key to tumor growth? Cancer Research 55, 249–252.

Bisbee, C. (1995). Scatter factor/hepatocyte growth factor gene deletion leads to death in knockout mice. BioWorld Today 24 Feb. 1995, 2.

Carraway, L. K., et al. (1994). The erbB3 Gene Product Is a Receptor for Heregulin. The Journal of Biological Chemistry 269, 14303–14306.

Carraway, K. L., and Cantley, L. C. (1994). A Neu Acquaintance for ErbB3 and ErbB4: A role for receptor heterodimerization in growth signaling. Cell 78, 5–8.

Claesson-Welsh, L. (1994). Signal transduction by the PDGF receptors. Progress in Growth Factor Research 5, 37–54.

Cullen, K. J., Yee, D., and Rosen, N. (1991). Insulinlike Growth Factors in Human Malignancy. Cancer Investigation 9, 443–454.

Dati, C., Antoniotti, S., Taverna, D., Perroteau, I., and De Bortoli, M. (1990). Inhibition of c-erB-2 oncogene expression by estrogens in human breast cancer cells. Oncogene 5, 1001–1006.

(List continued on next page.)

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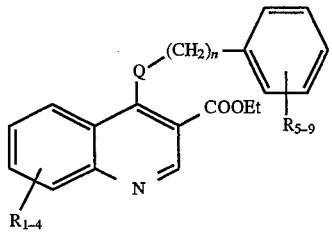
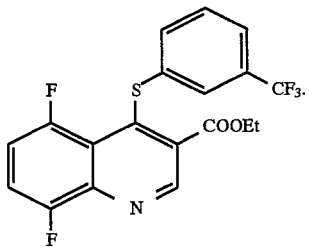
[57] **ABSTRACT**

A method of inhibiting cell proliferation or differentiation by exposing a cell to a compound of the formula



or a pharmaceutically acceptable salt thereof. Q is selected from the group consisting of NH and S, n is 0 or 1; and R_{1-9} are independently selected from the group consisting of halo, trihalomethyl, alkyl, nitro, hydroxy, alkoxy, sulphoxy, sulphonyl, amide, sulfonamide, carboxamide, amino, and hydrogen. Also provided is a compound of the structure



14 Claims, No Drawings