COMPOUNDS FOR TREATING PROLIFERATIVE DISORDERS

The present invention relates to the use of substituted \((E) (styrylsulfonylmethyl)heteroaryl\) and \((E) (styrylsulfanyl)methyl)heteroaryl\) compounds that have broad therapeutic applications as anti-proliferative agents. The invention also provides processes for preparing compounds, pharmaceutically acceptable compositions comprising the compounds, and the use of the compounds and methods of using the compounds and compositions in the treatment of proliferative disorders.

BACKGROUND

The search for novel therapeutic agents has been advanced in recent years by a better understanding of the structure of enzymes associated with diseases. One important class of enzymes that has been the subject of extensive study is protein kinases. Protein kinases constitute a large family of structurally related enzymes that are responsible for the control of a wide variety of signal transduction processes within the cell. Many diseases are associated with abnormal cellular responses triggered by protein-kinase mediated events. These diseases include but are not limited to neurodegenerative diseases, autoimmune diseases, cancer, inflammatory diseases, and metabolic diseases. Therefore a substantial effort has been made in medicinal chemistry to discover protein kinase inhibitors as effective therapeutics.

The demonstration of clinical activity of a number of kinase inhibitors including cancer drugs such as Gleevec and Iressa has generated considerable interest in the search for kinase inhibitors with novel pharmacophores. Non-ATP competitive inhibitors for cancer therapy are of interest in order to overcome the problems associated with ATP-analogues having poor selectivity and drug resistance. Compound ON01910 (which is described in Bioorg. Med. Chem. Lett. 2011 May 15; 21 (10), 3066-9, WO 02/072062 and WO 2008/088803) has recently demonstrated excellent anti-tumor activity and safety profiles in clinical trials.

The present invention provides compounds with similar biological profiles but improved pharmaceutical properties.

The object of the present invention is to provide compositions of substituted \(3\)-\((styrylsulfonylmethyl)heteroaryl\) and \(3\)-\((styrylsulfanyl)methyl)heteroaryl\) compounds, and methods for the treatment of cancer and other proliferative diseases.