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Novel Inhibitors of FMS Kinase

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Signal transduction through the mCSF-1/FMS ligand–receptor complex is intimately involved in the differentiation and proliferation of cells of the monocyte/macrophage lineage. Over expression of mCSF-1 and/or FMS has been implicated in a number of disease states including the growth and metastasis of particular cancers, in promoting osteoclast proliferation in bone osteolysis, in inflammatory diseases such as rheumatoid arthritis, atherosclerosis and Crohn's disease and in renal allograft rejection.
Focused screening of compounds from Cytopia's internal small molecule library identified a potent sub 50 nM inhibitor of the FMS enzyme. SAR studies guided by the use of Cytopia's proprietary computer-aided drug design software, ChemaPhore™, have lead to a class of molecules that potently inhibit FMS in both biochemical and functional cellular assays and that have shown efficacy in a mouse model of mesothelioma.
This poster will describe some of the SAR studies undertaken and data from the *in vivo* model.