Novel therapies to treat lung cancer are urgently required and will most likely arise from an improved understanding of the disease biology. Multiple growth factors have been implicated in driving both small and non-small cell lung cancer cell proliferation. Consequently, identifying an intracellular molecule(s) that serves as a point of convergence downstream of multiple growth factor receptors could provide an attractive therapeutic target. Western blot comparison of multiple signaling proteins in normal versus malignant lung cells revealed that mTOR, S6K1 and S6K2 are over-expressed in all tumours examined. Our prior work indicated that mTOR controls S6K1 but not S6K2 in lung cancer cells. Indeed, S6K2 but not S6K1 mediates a novel FGF-2 triggered chemoresistance mechanism in these cells. However, both rapamycin and the clinical relevant rapalogue, RAD001, block basal and multiple growth factor-induced proliferation in vitro, and RAD001 inhibits SCLC xenograft growth in vivo. So are these in vitro and in vivo findings clinically relevant? Immunohistochemical studies in biopsies and tumour resection specimens from patient with lung cancer show over-expression of mTOR in about 50% of all lung cancer. Crucially, enhanced expression of mTOR was a significant predictor of poor outcome in early stage resected non-small cell lung cancer, both on univariate and multivariate analysis. Collectively, our results suggest that inhibitors of mTOR may be of therapeutic value in lung cancer.