

## R&D IN ONCOLOGY: Clinical Trial Overview

The current focus of Boehringer Ingelheim's cancer research includes compounds in three areas: angiogenesis inhibition, signal transduction inhibition and cell-cycle kinase inhibition, that are relevant across a variety of cancers including lung cancer. New compounds are being investigated to evaluate their potential to be effective in patients who are resistant to existing treatments, to improve the efficacy of established drugs in combination regimens, and to provide targeted therapies with more favourable tolerability profiles.

Compound	Mode of Action	Indications Investigated	Clinical Status	Results to Date
<b>BIBF 1120 (Vargatef™)*</b>	A novel triple angiokinase inhibitor: inhibits VEGFR, PDGFR and FGFR simultaneously. All are involved in blood vessel formation.	Solid tumours: NSCLC, RCC, HCC, ovarian cancer, colorectal cancer and prostate cancer.	<b>Phase III</b> Now in phase III development in NSCLC with the LUME-Lung 1 and LUME-Lung 2 trials: efficacy in patients with advanced NSCLC (2nd line).	Results from a Phase II study suggest that BIBF 1120 (Vargatef™) monotherapy is well tolerated and may offer promising efficacy in patients with relapsed advanced NSCLC.  BIBF 1120 is already in phase III development in patients suffering from advanced lung cancer. Trials have recently started.  As angiogenesis plays a pivotal role in the growth of all solid tumours, BIBF 1120 is being investigated in a number of indications including advanced NSCLC, RCC, HCC, ovarian cancer, colorectal cancer and prostate cancer. Indeed, new phase II data presented for the first time at ASCO 2009 show BIBF 1120 may have a role in delaying disease progression in ovarian cancer patients who had previously responded to chemotherapy.
<b>BIBW 2992 (Tovok™)*</b>	A novel, potent and irreversible tyrosine kinase inhibitor of both EGFR and HER2 kinases.	Solid tumours: NSCLC, breast cancer, colorectal cancer, head and neck cancers.	<b>Phase IIb/III</b> Entered Phase IIb/III clinical development: efficacy in patients with NSCLC progressing after erlotinib or gefitinib (LUX-LUNG I).	New data presented at ASCO 2009 from the ongoing phase II clinical study (LUX-Lung 2) showed patients with activating epidermal growth factor receptor (EGFR) mutations experienced a high overall response rate – one in two patients (64%; 43/67 patients) had a partial response – and a high rate of disease control (96%; 64/67 patients).  The LUX-Lung phase III trial programme is investigating BIBW 2992 in a number of patient populations. LUX-Lung 1 is a phase IIb/III randomised, double-blind study evaluating BIBW 2992 as monotherapy in NSCLC patients who have previously failed first generation EGFR Tyrosine Kinase Inhibitors (TKIs). Preliminary safety data from LUX-Lung 1 were presented at ASCO.
<b>BI 6727*</b>	Cell cycle kinase inhibitor. BI 6727 inhibits a key regulator in the process of cell division (mitosis), called polo-like kinase 1 (Plk1).	Solid tumours and haematological cancers.	<b>Phase II</b> BI 6727 will advance further in clinical development. The phase II programme will assess the efficacy and safety of BI 6727 in several tumour types.	Results from phase I indicate promising anti-tumour activity. Due to its unique mode of action typical side effects induced by established anti-mitotic agents such as neuropathy have not occurred.

\*BIBF 1120 (Vargatef™), BIBW 2992 (Tovok™) and BI 6727 are investigational compounds. Their safety and efficacy have not yet been fully established.