
Press Release

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CD Communications

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First pivotal trials begin for Boehringer Ingelheim's novel triple angiokinase inhibitor Vargatef™ (BIBF 1120)

Progress continues across expanding oncology pipeline with two compounds now in phase III clinical development and a potential first-in-class polo-like kinase 1 inhibitor soon to enter phase II

Ingelheim, Germany. Monday 17 November 2008 - Boehringer Ingelheim has marked a new milestone within its rapidly expanding oncology portfolio with the announcement today that the company has progressed another of its oncology compounds into pivotal phase III clinical development. The two studies, known as LUME-Lung 1 and LUME-Lung 2, for Vargatef™ (BIBF 1120), a triple angiokinase inhibitor¹, will evaluate the molecule as a second-line therapy in combination with standard chemotherapy agents in patients with advanced non-small-cell lung cancer (NSCLC), a patient population with limited treatment choices. This significant advance represents encouraging progress for the company across a portfolio that spans three key areas of focus: angiokinase inhibition, signal transduction inhibition and cell cycle kinase inhibition and further confirms its continued commitment to the field of oncology.

In addition, Boehringer Ingelheim's most advanced compound Tovok™ (BIBW 2992) will soon enter its second pivotal trial, LUX-Lung 3 in first-line NSCLC. Furthermore, a new compound and potentially first-in class-molecule, polo-like kinase 1 (Plk1) inhibitor, BI 6727, has demonstrated such positive phase I results that it will be progressed to phase II.

According to Dr Nasser Hanna, Associate Professor of Medicine in the Division of Oncology at Indiana University and principal investigator of one of the LUME-Lung studies, the commencement of these trials heralds another stepping stone in the quest to combat the world's most common fatal malignancy.

“While our battle to conquer cancer continues, lung cancer remains the leading cause of worldwide cancer deaths despite the availability of numerous therapeutic

options. The need to develop newer, smarter therapies has never been so urgent,” said Dr Hanna.

“The fact remains that one in two non-small cell lung cancer patients who receive treatment fail their initial therapies and remain well enough to receive additional options. The LUME-Lung studies will look at whether the addition of Vargatef™ (BIBF 1120) to standard second-line treatment regimes will improve the outcome for these patients, and with 2,600 patients, is one of the largest clinical trial programmes in this indication. There remains a great need for new treatments for cancer patients to prevent suffering and prolong life,” he added.

Vargatef™ (BIBF 1120), works by simultaneously inhibiting vascular endothelial growth factor receptors (VEGFRs), platelet-derived growth factor receptors (PDGFRs) and fibroblast growth factor receptors (FGFRs)¹ – all crucially involved in the formation of blood vessels and is administered as a capsule taken twice daily. As angiogenesis plays a pivotal role in the growth of all solid tumours, Vargatef™ (BIBF 1120) is currently being investigated in a number of indications including advanced NSCLC, prostate cancer, ovarian cancer and colorectal cancer.

The decision to progress this molecule into phase III trials in NSCLC was based on phase I and II results which showed the agent to be both efficacious and well tolerated when administered as both monotherapy and in combination.

In a phase II Vargatef™ (BIBF 1120) study², which included 74 patients with relapsed, advanced NSCLC, notable results were reported for patients with good performance status (ECOG* 0 or 1) (n=57): these patients experienced longer overall survival (OS) (median OS was 9.5 months), longer Progression Free Survival (PFS) (median PFS was 2.9 months) and a higher rate of disease control (59%) compared to the overall study population. Stable disease rate was 48%. The majority of adverse events reported in the study were mild to moderate in nature.

In phase I studies, Vargatef™ (BIBF 1120) was observed to be well tolerated at a dose of 200mg twice daily when given in combination with pemetrexed³ or paclitaxel/carboplatin⁴ in NSCLC patients and when given in combination with docetaxel in hormone refractory prostate cancer patients. In addition, initial signs of clinical efficacy were observed.⁵

According to Dr Manfred Haehl, Corporate Senior Vice President Medicine, Boehringer Ingelheim, the latest developments across the company’s oncology portfolio are testament to its continued commitment to research and development in oncology and indicative of the continual progress being made.

“The commencement of our second pivotal phase III trial programme within the oncology portfolio, a potential first-in-class within our cell cycle kinase family and an additional phase III trial planned for Tovok™ (BIBW 2992) reinforce the fact

* **ECOG Definition:** The Eastern Cooperative Oncology Group performance status are scales and criteria used by doctors and researchers to assess how a patient's disease is progressing, assess how the disease affects the daily living activities of the patient, and determine appropriate treatment and prognosis.

that our pipeline continues to move closer to our goal – to develop innovative treatment options that we hope will ultimately offer patients with cancer better treatment options,” said Dr Haehl.

– *Ends* –

About ECOG

Grade	Eastern Cooperative Oncology Group (ECOG) performance status
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead

About Boehringer Ingelheim in Oncology

Building on scientific expertise and excellence in the fields of pulmonary and cardiovascular medicine, metabolic disease, neurology, virology and immunology, Boehringer Ingelheim has embarked on a major research programme to develop innovative cancer drugs.

Working in close collaboration with the international scientific community and a number of the world’s leading cancer centres, Boehringer Ingelheim is committed to discovering and developing novel cancer treatments that have the potential to provide significant clinical and quality of life benefits for patients. This commitment is underpinned by using advances in science to develop a range of targeted therapies in areas of medical need, including various solid tumours and haematological cancers.

The current focus of research includes compounds in three areas: angiogenesis inhibition, signal transduction inhibition and cell-cycle kinase inhibition. Tovok™ (BIBW 2992), a novel representative of the new generation of tyrosine kinase inhibitors, entered phase IIb/III clinical development in NSCLC earlier in 2008 and was granted Fast Track designation by the FDA. Its second pivotal trial LUX-Lung 3, will commence soon.

In the area of cell-cycle kinase inhibition, Boehringer Ingelheim is developing novel, potent and highly selective inhibitors of polo-like kinase 1 (Plk1), a protein that is involved in the processes of cell division. These molecules are in the early stages of clinical development.

The clinical trial programme for Boehringer Ingelheim’s oncology portfolio is themed around the concept of light, and the notion that the company is committed to illuminating research and development within the field of oncology. All trials are named accordingly, as variations on this overall theme.

Boehringer Ingelheim

The Boehringer Ingelheim group is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, it operates globally with 135 affiliates in 47 countries and 39,800 employees. Since it was founded in 1885, the family-owned company has been committed to researching, developing, manufacturing and marketing novel products of high therapeutic value for human and veterinary medicine.

In 2007, Boehringer Ingelheim posted net sales of 10.9 billion euro while spending one fifth of net sales in its largest business segment Prescription Medicines on research and development.

For more information please visit www.boehringer-ingelheim.com

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