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## Press Release

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### **Boehringer Ingelheim to Present New Phase II Clinical Data on two Lead Oncology Compounds at ASCO 2009**

- *Boehringer Ingelheim's LUX-Lung programme moves forward with new studies revealing the potential of BIBW 2992 in personalising lung cancer care –*
- *The first presentation of data from BIBF 1120 in Ovarian Cancer -*

**Ingelheim, Germany, 15 May 2009 –** **Boehringer Ingelheim will present new data on the company's two lead oncology compounds, BIBW 2992<sup>1</sup> and BIBF 1120<sup>2</sup> at the 2009 Annual Meeting of the American Society of Clinical Oncology (ASCO), the company announced today. Two studies in the LUX-Lung clinical development programme for BIBW 2992 and a Phase II study of BIBF 1120 in ovarian cancer patients will be presented.**

#### ***LUX Lung 2 interim results***

Interim Phase II data from the LUX-Lung 2 study suggest BIBW 2992 has anti-tumour activity in advanced second-line non-small cell lung cancer (NSCLC) patients who have epidermal growth factor receptor (EGFR) mutations.<sup>1</sup>

“Lung cancer kills more people than any other cancer.<sup>3</sup> The LUX-Lung 1 and 2 studies represent an opportunity to investigate BIBW 2992 across a range of different patient populations,” said Dr Manfred Haehl, Corporate Senior Vice President Medicine at Boehringer Ingelheim. “The preliminary data from the LUX-Lung 2 study suggests that BIBW 2992 may have activity in the second-line setting among NSCLC patients with EGFR mutations, which is encouraging news.”<sup>1</sup> BIBW 2992 is an orally administered irreversible dual inhibitor of the epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor 2 (HER2) tyrosine kinases.<sup>4</sup> It is the first irreversible EGFR-TKI (tyrosine kinase inhibitor) to reach Phase III for third/fourth-line NSCLC.<sup>5</sup>

In the emerging era of personalised cancer medicine, Boehringer Ingelheim is one of the first companies to prospectively identify appropriate patients for clinical trials based on biomarkers. As part of the LUX-Lung clinical development programme, Boehringer Ingelheim is evaluating BIBW 2992 in NSCLC patients who test positive for EGFR activating mutations.

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<sup>1</sup> (planned trade name Tovok™)  
<sup>2</sup> (planned trade name Vargatef™)

“It is well documented that ‘activating’ mutations that arise in the tyrosine kinase (TK) domain of the EGFR gene are associated with an increased sensitivity to first generation EGFR TKIs.<sup>6,7,8</sup> The majority of patients who initially respond to EGFR TKIs such as gefitinib or erlotinib will eventually develop resistance, often through gaining another mutation, such as the so-called T790M resistance mutation,”<sup>9,10</sup> said Dr Haehl.

### ***Detailed Findings from LUX-Lung 2:***<sup>1</sup>

To date, 409 NSCLC patients have been screened in the LUX-Lung 2 study and 104 patients with EGFR mutations have started treatment with BIBW 2992 once daily. Preliminary data will be presented at ASCO for the first 73 second line patients, all of whom had previously received one regimen of chemotherapy. 67 patients are evaluable for response.

Interim data show:<sup>1</sup>

- 64% of patients (43/67) taking BIBW 2992 in the 2<sup>nd</sup> line setting experienced a partial response (75% among patients with deletion 19 and 66% in patients with L858R mutations)
- 31% (21/67) of patients taking BIBW 2992 in the 2<sup>nd</sup> line setting experienced stable disease
- Median progression-free survival (PFS) in 2nd line setting is 10.2 months
- The most common related adverse events were diarrhea and skin-related disorders in 86% and 89% of patients respectively [16% and 18% being grade 3 respectively]
- 37 patients had dose reduction and 4 patient discontinued treatment due to adverse events

### ***Findings from LUX Lung 1***

In addition, preliminary data on the demographic and blinded safety data from the ongoing Phase III study, the LUX-Lung 1 trial, will be presented at ASCO for the first time.<sup>11</sup>

The LUX-Lung 1 study addresses a critical need for treatment options for NSCLC patients after failure with a second-line or third-line reversible EGFR inhibitor (i.e. erlotinib or gefitinib). This study recently moved from Phase IIb into Phase III.<sup>11</sup>

“The LUX-Lung 1 study is important as it investigates BIBW 2992 in a group of patients for whom there are no other approved treatment options. These are patients who have already been through standard first-line or second-line chemotherapy and then received treatment with an EGFR TKI. The LUX-Lung 1 study will evaluate whether BIBW 2992 will extend the lives of these cancer patients.”<sup>11</sup> said Dr Haehl.

***First presentation of Phase II data for BIBF 1120 in ovarian cancer***

Data from a Phase II study of BIBF 1120 in patients with ovarian cancer who responded to at least second-line chemotherapy will be presented at ASCO in Orlando. The study showed a potential delay in disease progression: with BIBF 1120 the median time to RECIST progression was 4.8, and 2.8 for placebo.<sup>2</sup> BIBF 1120 is an oral compound that works by simultaneously inhibiting vascular endothelial growth factor receptors (VEGFRs), platelet-derived growth factor receptors (PDGFRs) and fibroblast growth factor receptors (FGFRs) – all factors which are crucially involved in the formation of blood vessels, a process known as angiogenesis.<sup>12,13.</sup>

"There is a great need for more effective and well tolerated treatment options for women with ovarian cancer. We have a growing body of evidence that anti-angiogenic agents may represent an important treatment approach for this disease," commented Prof. Jonathan A Ledermann, MD, Professor of Medical Oncology & Director at the Cancer Research UK & UCL Cancer Trials Centre, University College London. "These data indicate BIBF 1120 may have a potential role in delaying disease progression in patients with ovarian cancer who had previously responded to chemotherapy."

Because angiogenesis plays a pivotal role in the growth of solid tumours,<sup>13</sup> BIBF 1120 is currently being investigated in a number of cancer types including advanced NSCLC. The LUME-Lung Phase III clinical trial programme is investigating BIBF 1120 in combination with standard second-line chemotherapy treatments for patients with advanced NSCLC. Approximately 2,600 patients will be enrolled, making this one of the largest Phase III study programmes in this NSCLC patient population to date.

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Boehringer Ingelheim Oncology: A podcast update from ASCO 2009  
Available from **Saturday 16th May 2009**

Visit [www.personalisingcancercare.com](http://www.personalisingcancercare.com) to find out more about Boehringer Ingelheim's compounds and watch experts Dr. James Spicer and Dr. Rolf Kaiser discuss the significance of these exciting trial results.

**--- Ends ---**

**Notes to editors**

Lung cancer is the world's most common cancer and kills more people than any other cancer.<sup>3,14</sup> In 2008, approximately 1.52 million new cases of lung cancer were diagnosed worldwide, with 1.31 million people dying from the disease.<sup>14</sup> In the United States, an estimated 161,840 deaths, accounting for 29 percent of all cancer deaths, occurred in 2008, according to the American Cancer Society (ACS).<sup>15</sup>

According to the 2008 World Health Organization *World Cancer Report*, as of 2002, ovarian cancer was ranked as the 6th most common cancer in women. Additionally, approximately 204,000 new cases were diagnosed worldwide and 125,000 women died from the disease in 2002.<sup>14</sup> The ACS estimates that about 21,650 new cases of ovarian cancer were diagnosed in the United States (U.S.) during 2008. Only forty-five percent of women with ovarian cancer are still alive at least five years after diagnosis in the U.S.<sup>16</sup>

### **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. 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. BIBW 2992 entered Phase IIb/III clinical development in NSCLC earlier in 2008 and was granted Fast Track designation for a third/fourth line treatment indication in NSCLC by the US Food & Drug Administration. In addition, the LUME-Lung Phase III clinical trial programme, which is investigating BIBF 1120 in combination with standard second-line chemotherapy treatments for patients with advanced NSCLC, is currently ongoing. In the area of cell-cycle kinase inhibition, Boehringer Ingelheim is developing 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 Boehringer Ingelheim group is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, it operates globally with 138 affiliates in 47 countries and 41,300 employees. Since it was founded in 1885, the independent, family-owned company has been committed to researching, developing, manufacturing and marketing novel products of high therapeutic value for human and veterinary medicine.

In 2008, Boehringer Ingelheim posted net sales of \$17 billion (11.6 billion euro) while spending one-fifth of net sales in its largest business segment, Prescription Medicines, on research and development.

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## References

1. Shih J-Y et al. "A Phase II study of BIBW 2992, a novel irreversible dual EGFR and HER2 tyrosine kinase inhibitor (TKI), in patients with adenocarcinoma of the lung and activating EGFR mutations after failure of 1 line of chemotherapy (LUX-Lung 2)." Poster Discussion Presentation. 1 June 2009, Session Time: 8:00AM - 12:00PM. #8013
2. Ledermann, J. A. "A randomised Phase II placebo-controlled trial using maintenance therapy to evaluate the vascular targeting agent BIBF 1120 following treatment of relapsed ovarian cancer (OC)." Oral presentation, Clinical Science Symposium. Monday, 1 June 2009, Session Time 9:45AM – 11:15AM. # 5501
3. "Ask the Expert Online Q&A: Are the number of cancer cases increasing or decreasing in the world?" 1 April 2008. World Health Organization. 5 May 2009. <http://www.who.int/features/qa/15/en/print.html>.
4. Li D et al. "BIBW2992, an irreversible EGFR/HER2 inhibitor highly effective in preclinical lung cancer models." *Oncogene* 2008;27:4702-4711
5. Boehringer Ingelheim Pharmaceuticals. "BIBW 2992 and BSC Versus Placebo and BSC in Non-Small Cell Lung Cancer Patients Failing Erlotinib or Gefitinib (LUX-LUNG 1)" 23 April 2009. ClinicalTrials.gov. 5 May 2009. <http://clinicaltrials.gov/ct2/show/NCT00656136?term=BIBW+2992+and+Phase+III&rank=1>.
6. Lynch, T. J. et al. "Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib." *N. Engl. J. Med.* 350, 2129-2139 (2004). Available at: <http://content.nejm.org/cgi/reprint/350/21/2129.pdf>. Accessed on 5 May 2009.
7. Paez, J. G. et al. "EGFR mutations in lung cancer: correlation with clinical response to gefitinib therapy." *Science* 304, 1497-1500 (2004). Available at: <http://www.sciencemag.org/cgi/reprint/1099314v1.pdf?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=egfr&searchid=1&FIRSTINDEX=0&fdate=//&tda te=//&resourcetype=HWCIT>. Accessed on 5 May 2009.
8. Pao, W. et al. "EGF receptor gene mutations are common in lung cancers from 'never smokers' and are associated with sensitivity of tumors to gefitinib and erlotinib." *Proc. Natl Acad. Sci. USA* 101, 13306-13311 (2004). Available at: [www.pnas.org/cgi/doi/10.1073/pnas.0405220101](http://www.pnas.org/cgi/doi/10.1073/pnas.0405220101). Accessed on 5 May 2009.
9. Riely G. J. et al. "Clinical Course of Patients with Non -Small Cell Lung Cancer and Epidermal Growth Factor Receptor Exon19 and Exon 21 Mutations Treated with Gefitinib or Erlotinib." *Clin. Cancer Res*, 12, 839-844(2006). Available at: <http://clincancerres.aacrjournals.org/cgi/reprint/12/3/839>. Accessed on 5 May 2009.
10. Balak, M. N. et al. "Novel D761Y and common secondary T790M mutations in epidermal growth factor receptor-mutant lung adenocarcinomas with acquired resistance to kinase inhibitors." *Clin. Cancer Res*, 12, 6494-6500 (2006). Available at: <http://clincancerres.aacrjournals.org/cgi/reprint/12/21/6494>. Accessed on 5 May 2009.
11. Yang C-H et al. "Phase IIb/III double-blind randomized trial of BIBW 2992, an irreversible, dual inhibitor of EGFR and HER2 plus best supportive care (BSC) versus placebo plus BSC in patients with NSCLC failing 1–2 lines of chemotherapy (CT) and erlotinib or gefitinib (LUX-Lung1): a preliminary report. General Poster Session: Lung

Cancer – Metastatic.” Saturday 30 May 2009, Session Time: 2:00PM - 6:00PM. # 8062

12. Hilberg F. et al. “BIBF1120 a novel, small molecule triple angiokinase inhibitor: profiling as a clinical candidate for cancer therapy.” *European Journal of Cancer Supplements*. 2004; 2:50.
13. Lewis J. Kleinsmith. “Understanding Cancer and Related Topics: Understanding Angiogenesis.” Rockville: National Cancer Institute, 2006. Available at: <http://cancer.gov/cancertopics/understandingcancer>. Accessed on 5 May 2009.
14. P Boyle and B Levin (eds). “World Cancer Report 2008.”, World Health Organization: International Agency for Research on Cancer. Lyon: 2008.
15. American Cancer Society. “Cancer Facts and Figures 2008.” Atlanta: 2008. Available at: <http://www.cancer.org/downloads/STT/2008CAFFfinalsecured.pdf>. Accessed on 5 May 2009.
16. American Cancer Society. “Ovarian Cancer Detailed Guide.” Atlanta: 2008. Available at: <http://documents.cancer.org/114.00/114.00.pdf>. Accessed on 5 May 2009.