AstraZeneca

news release

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Astrazeneca provides update on RECENTIN™ Clinical development programme

HORIZON Colorectal Cancer Programme Continues Into Phase III;
BR24 Non-Small Cell Lung Cancer Trial Will Not Progress

AstraZeneca today announced that its HORIZON III Phase II/III head-to-head study of RECENTINTM (cediranib, AZD2171) with chemotherapy versus bevacizumab (Avastin™) with chemotherapy in patients with first line metastatic colorectal cancer (CRC) will be progressing directly into Phase III at 20mg. Patients will also continue to be recruited at 20mg into the first line CRC HORIZON II study of RECENTIN with chemotherapy versus chemotherapy alone.

The HORIZON Independent Data Monitoring Committee (IDMC) conducted a planned end of Phase II (EOP II) review of efficacy and tolerability data from HORIZON I, HORIZON II and HORIZON III. Data from HORIZON I, in second line colorectal cancer, would not by itself have contributed to a positive EOP II decision. However, when combined with a review of data from HORIZON II and III by the IDMC, the IDMC confirmed the HORIZON programme in 1st line CRC could continue and HORIZON II and III had met pre-defined EOP II criteria.

AstraZeneca today also announced that the National Cancer Institute of Canada Clinical Trials Group (NCIC-CTG) has informed AstraZeneca that the BR24 Phase II/III study of RECENTIN at 30mg in first line non-small cell lung cancer (NSCLC) will not continue into Phase III following the planned end of Phase II efficacy and tolerability analysis by the study's Data Safety Monitoring Committee. Although evidence of clinical activity was seen, there appeared to be an imbalance in toxicity and therefore the study was considered not to have met the pre-defined criteria for automatic continuation into Phase III.

AstraZeneca is working in close collaboration with the NCIC-CTG to understand the BR24 data further.

In addition to colorectal and non-small cell lung cancer, the RECENTIN development programme includes trials in recurrent glioblastoma and a number of signal search studies in other tumours.

John Patterson, AstraZeneca's Executive Director for Development, said: "Given there is such a high unmet patient need for more effective treatments in cancer, we are pleased that the HORIZON colorectal cancer programme has met its pre-defined criteria to continue recruitment into Phase III. Due to the Phase II/III trial

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design, HORIZON III is able to move directly into Phase III utilising all the Phase II data and this saves valuable time in assessing the potential benefit of RECENTIN in the first line metastatic colorectal cancer setting.

“AstraZeneca supports the NCIC-CTG’s BR24 recommendation and is working with them to understand the data more fully in NSCLC. As evidence of clinical activity was seen in BR24, AstraZenenca remains committed to investigating the potential of RECENTIN in lung cancer and reducing the incidence of serious adverse events.”

RECENTIN™ is a trademark of the AstraZeneca group of companies.

About the National Cancer Institute of Canada Clinical Trials Group
The National Cancer Institute of Canada Clinical Trials Group (NCIC-CTG), funded by the Canadian Cancer Society and based at Queen's University in Kingston, Ontario, Canada, develops, conducts and analyses national and international trials of cancer therapy, including trials for new cancer drugs, cancer prevention and supportive care to improve quality of life for people with cancer. Since its inception in 1971, the NCIC-CTG has enrolled more than 40,000 patients from Canada and around the world in over 300 clinical trials.

BR24 Background
NSCLC accounts for approximately 80 percent of all cases of lung cancer. Lung cancer is the most common cancer in the world with 1.3 million new cases diagnosed every year and nearly 1.2 million people dying as a result of the disease annually.

BR24 is a collaboration between AstraZeneca and the NCIC-CTG, based at Queen’s University in Kingston, Ontario. The study is a randomised, double-blind, placebo-controlled Phase II/III investigation of RECENTIN plus paclitaxel and carboplatin versus the chemotherapy arm alone. In the Phase II part of the study, patients were recruited from countries including: Argentina, Australia, Brazil, Canada, Romania and Singapore.

RECENTIN and Colorectal Cancer
Colorectal cancer is the third most commonly reported cancer worldwide, with around 945,000 new cases and 492,000 deaths annually.

The Horizon Study Programme is evaluating RECENTIN in patients with first line advanced colorectal cancer:

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Study	Phase	Design	Population
Horizon III	II/III	Double blind, randomised trial of cediranib in combination with FOLFOX compared to bevacizumab in combination with FOLFOX	Patients with first line metastatic colorectal cancer
Horizon II	III	Double blind, randomised trial of cediranib plus standard chemotherapy compared to standard chemotherapy alone	Patients with first line metastatic colorectal cancer
Horizon I	II	Double blind, randomised trial of cediranib in combination with FOLFOX compared to bevacizumab in combination with FOLFOX	Patients with second line metastatic colorectal cancer

RECENTIN: a potent and selective VEGF signalling inhibitor.

RECENTIN is a once-daily, orally available, highly potent and selective VEGF signalling inhibitor that inhibits all three VEGF receptors.

VEGF signalling is a key driver of angiogenesis – the formation of new blood vessels that tumours need to grow and spread. RECENTIN inhibits this signal by binding to the intracellular domain of all three VEGF receptors, in particular VEGFR-2, the predominant receptor through which VEGF exerts its effects on angiogenesis, preventing the growth of new blood vessels. This effectively “starves” the tumour of the oxygen and nutrients it needs to grow.

Phase I data indicate that RECENTIN is generally well tolerated, with the most common adverse events being diarrhoea, fatigue, hoarseness, nausea, vomiting, headache, hypertension and hand foot syndrome.

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