PRESS RELEASE

SAPPHIRE
AP 12009-G005

April 27, 2009

Antisense Pharma begins pivotal Phase III clinical trial with trabedersen in aggressive brain tumors

First patients enrolled in international SAPPHIRE study of recurrent or refractory anaplastic astrocytoma

REGENSBURG – April 27, 2009 – The biopharmaceutical company Antisense Pharma GmbH has announced today that the first patients with recurrent or refractory anaplastic astrocytoma have been enrolled in the pivotal Phase III clinical trial SAPPHIRE.
The SAPPHIRE study is a randomized, active-controlled, clinical trial designed to confirm the efficacy and safety of the investigational drug trabedersen (AP 12009), observed in the previous clinical studies. Trabedersen is being investigated as monotherapy compared to current standard therapy with temozolomide (alternatively BCNU). The results of the previous randomized, active-controlled Phase IIb study show that the novel, targeted therapy holds much promise.

International Phase III study design

The SAPPHIRE study will be carried out in Europe, America and Asia. Approximately 70 hospital centers will participate. The Phase III study is designed as a randomized, active-controlled, open-label clinical trial with two treatment arms: Trabedersen in a dose of 10 µM will be compared to current standard therapy with either temozolomide or BCNU. Clinical centers conducting the SAPPHIRE study aim to enroll a total of approximately 130 adult patients with recurrent or refractory anaplastic astrocytoma. Trabedersen will be administered intratumorally via one single catheter using convection-enhanced delivery (CED) on an outpatient treatment basis. The treatment period lasts up to 6 months consisting of 7-day cycles every other week.

Study objectives

The primary efficacy endpoint is the survival rate at 24 months. Further efficacy endpoints include overall survival and time to death. The 14-month progression rate is the surrogate endpoint for an interim analysis. Safety parameters will include adverse events, serious adverse events, ECG parameters, neurological examination and vital signs. Also the patient's quality of life is an important parameter of the study.

Great need for new approaches in cancer therapy

"The diagnosis of recurrent or refractory anaplastic astrocytoma is still devastating even today, since the therapeutic possibilities available to treat such patients are indeed quite inadequate. Most patients die within a few months after their diagnosis. Hospitals worldwide are committed to improve his situation in the framework of the SAPPHIRE study. The results of the previous studies show that the new, targeted therapy holds much promise," remarked Dr. Rolando Del Maestro, Director of Brain Tumor Research at the Montreal Neurological Institute and Hospital. Dr. Del Maestro is the coordinating investigator of the SAPPHIRE study.

Targeted therapies drive market growth

Trabedersen is a first-in-class targeted therapy. This novel compound acts multimodally via inhibition of transforming growth factor-beta 2 (TGF-β2). Unlike non-specific therapies, e. g. chemotherapy or radiotherapy, targeted therapies act much more specifically at the molecular roots of the disease. Commanding up to 80% of the growing oncology market, the targeted therapies like trabedersen substantially drive the growth of the pharmaceutical market (Source: IMS Health). A successful marketing authorization would make trabedersen the first TGF-beta targeting drug for the treatment of cancer.

Combating cancer at its roots

"We have taken trabedersen all the way from drug discovery to the pivotal Phase III clinical trial. The enrollment of the first patients in the SAPPHIRE study is a key milestone in our drug development program for trabedersen. It is also in Phase I/II clinical development for advanced pancreatic carcinoma, malignant melanoma and colorectal carcinoma. Trabedersen with its unique mode of action can lead to a paradigm shift towards tackling malignant tumors at their roots while providing a better quality of life for patients," commented Dr. Karl-Hermann Schlingensiepen, Chief Executive Officer of Antisense Pharma.

For more information on the SAPPHIRE trial please visit the website www.anticancer.de.

PRESS RELEASE

Additional information

Original title Phase III SAPPHIRE study

Efficacy and Safety of AP 12009 in Adult Patients with Recurrent or Refractory Anaplastic Astrocytoma (WHO grade III) as Compared to Standard Treatment with Temozolomide or BCNU: A Randomized, Actively Controlled, Open-label Clinical Phase III Study.
Principal Investigator: Professor Rolando Del Maestro, MD, PhD, Director Brain Tumour Research Centre, Montreal Neurological Institute and Hospital, Canada

Trabedersen (AP 12009) and TGF-beta 2

Trabedersen is a first-in-class gene silencing antisense compound – a phosphorothioate oligodeoxynucleotide – designed to selectively downregulate the production of transforming growth factor-beta 2 (TGF-β2) at the translational level. TGF-β2 plays a pivotal role as a multimodal cytokine by regulating key mechanisms of tumor progression. Immunosuppression, invasion and metastasis, proliferation and angiogenesis are simultaneously promoted by TGF-β2 in a variety of malignant tumors. Trabedersen is a targeted multimodal therapy, therefore.

Results of the Phase IIb study with trabedersen

The completed clinical Phase IIb study AP 12009-G004 was an open-label, randomized, active-controlled, parallel-group dose-finding study to evaluate the efficacy and safety of two doses of trabedersen (AP 12009) in adult patients with recurrent or refractory high-grade glioma. At 29 international clinical centers, 134 evaluable patients (39 with recurrent or refractory anaplastic astrocytoma, AA, WHO grade III and 95 with recurrent or refractory glioblastoma, GBM, WHO grade IV) were randomized to three arms: 10 µM trabedersen, 80 µM trabedersen or standard chemotherapy (temozolomide or PCV) as active control. Analysis of the core phase revealed long-lasting tumor responses and life extension in AA and GBM patients, by far exceeding the active treatment period with trabedersen. For recurrent or refractory anaplastic astrocytoma patients, median survival times in the 10 µM trabedersen group were 39.1 months compared to 21.7 months in the standard chemotherapy control arm, translating to a survival benefit of 17.4 months for patients receiving the antisense treatment over standard chemotherapy. 83.3% of the patients with recurrent anaplastic astrocytoma who received 10 µM trabedersen survived two years or more, whereas only 41.7% survived two years in the control arm with standard chemotherapy. Both efficacy and safety results have demonstrated, that the 10 µM concentration of trabedersen was superior to the 80 µM concentration. This further underlines the specificity of this targeted therapy since for optimally targeted therapies maximum tolerated dose is not necessarily the most efficant dose.

High-Grade Glioma

Anaplastic astrocytoma (AA) and glioblastoma multiforma (GBM) are the two most common forms of primary brain tumors and are diseases with high unmet medical need. Adults as well as children may be affected, although the peak age is 45-65 years. Current therapies comprise surgery, radiation and/or chemotherapy. Despite recent advances, the prognosis for these patients is still poor, with a high proportion dying within two years after initial diagnosis. Antisense Pharma is the sponsor of the SAPPHIRE clinical Phase III study, investigating the efficacy and safety of trabedersen (AP 12009) in adult patients with recurrent or refractory anaplastic astrocytoma. A further clinical trial with trabedersen to treat glioblastoma patients is in preparation.

About Antisense Pharma GmbH

Antisense Pharma is a biopharmaceutical company located in Regensburg, Germany. The company focuses on targeted therapies for malignant tumors and is dedicated to discovering and developing drugs based on antisense technology for worldwide commercialization. The medications specifically block the synthesis of key cancer proteins. Antisense Pharma has clinical trials running that involve patients with brain tumors, advanced pancreatic carcinoma, malignant melanoma and colorectal carcinoma. Therapies for other indications are under preclinical development. The company has been honored with the Bavarian Innovation Award and the German Founder‘s Award.

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