

FDA and EMEA grant orphan drug designation for Antisense Pharma's investigational drug trabedersen in pancreatic carcinoma

Orphan drug designation ensures market exclusivity for seven to ten years following market approval

Regensburg, Germany – September 14, 2009. The biopharmaceutical company Antisense Pharma GmbH has announced today that it has received orphan drug designation from both the European Medicines Agency EMEA and the US Food and Drug Administration FDA for its investigational drug trabedersen in the treatment of pancreatic carcinoma. Trabedersen has already been granted orphan drug designation by both authorities in the treatment of high-grade gliomas in 2002. This underlines the high potential of trabedersen to treat various aggressive tumors.

Orphan drug designation can be applied for if the disease is life-threatening or chronically debilitating and affects not more than five in 10,000 persons in the European Community (equals around 250,000 people) and fewer than 200,000 people in the United States, respectively, in case that no other satisfactory therapy exists or the medicinal product is expected to provide significant benefit over existing therapies.

The orphan drug designation is meant to encourage pharmaceutical companies to develop drugs for diseases that meet the above criteria by providing them scientific advice, reduction or waiver of registration fees and market exclusivity in addition to patent protection.

This is another important milestone in the development of trabedersen, a first-in-class, targeted compound based on antisense technology for the treatment of various aggressive tumors.

Highly promising preliminary efficacy data

In an ongoing clinical Phase I/II study, trabedersen has shown a good safety and tolerability profile and encouraging survival data in patients with advanced pancreatic carcinoma. "The preliminary clinical data are quite impressive" states the Committee on Orphan Medicinal Products (COMP) of the EMEA in its report.

33 patients received single agent trabedersen intravenously as second-, third-, or fourth-line treatment either in a 7-day on/7-day off or 4-day on/10-day off schedule.

Median overall survival (mOS) for patients in the first schedule was 6.8 months (status Aug 2009). Moreover, one patient with recurrent advanced pancreatic cancer (after surgical resection and three chemotherapies) and liver metastases had a complete response and is still alive 49 months after receiving trabedersen therapy (as of June 2009).

The current mOS for pancreatic carcinoma patients in the first cohort of five patients in the second schedule is 13.4 months (as of Aug 2009). One patient is still alive 19 months after start of study treatment (as of April 2009).

In the same study good safety, tolerability and encouraging first efficacy data for trabedersen was observed also in patients with advanced malignant melanoma or colorectal carcinoma. Of five malignant melanoma patients treated with trabedersen, one from the first schedule showed stable disease and lived for 13.8 months.

Incentives for development and competitive advantages

Orphan drugs generally follow the same regulatory development path as any other pharmaceutical product. However, incentives such as scientific advice and reduction or waiver of registration fees may be given in an effort to maintain development momentum. In addition, Antisense Pharma may sell trabedersen without competition for seven years in the US and for ten years in the EU following market approval, in respect of a medicinal product containing a similar active substance for the same indication; unless a similar product would demonstrate superior therapeutic benefit.

"We are delighted to have received the orphan drug status from the EMEA and FDA for the treatment of pancreatic carcinoma. This further accelerates our efforts to make trabedersen available to those who need it as quickly as possible" says Dr. Karl-Hermann Schlingensiepen, Chief Executive Officer of Antisense Pharma. "Pancreatic carcinoma is one of the most aggressive and devastating cancers. Despite various therapeutic approaches including surgery, radio- and chemotherapy, the prognosis for the patients remains poor. Based on the results of several clinical studies, we expect trabedersen to significantly improve the therapeutic outcome not only of patients with pancreatic carcinoma but also of patients suffering from high-grade gliomas, malignant melanoma or colorectal carcinoma. Indeed, with its unique mode of action, we believe that trabedersen has the potential to lead to a paradigm shift towards tackling malignant tumors at their roots while providing a better quality of life for patients."

Additional Information

About pancreatic carcinoma

Pancreatic carcinoma is one of the most aggressive cancers with high unmet medical need. It has a dismal prognosis, with one of the highest mortality rates:

Worldwide, pancreatic cancer causes 227,000 deaths annually and is the eighth most common cause of death from cancer.

In Europe, cancer of the pancreas is the 10th most frequent cancer, accounting for about 65,000 deaths each year.² European data show that the incidence rate of pancreatic cancer is approximately 5 to 9 (female/male) per 100,000 of the population per year.²

The American Cancer Society estimated for the US that of about 1.5 million new cases of cancer diagnosed in 2009, 44,380 people of both men and women will have pancreatic cancer and that 33,740 would die of the disease, making this type of cancer the fourth leading cause of cancer death in the US.³

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 one year after initial diagnosis.

How trabedersen works

Trabedersen is a first-in-class, targeted, antisense compound (a phosphorothioate oligodeoxynucleotide) designed to selectively downregulate the production of a protein known as transforming growth factor-beta 2 (TGF- β 2) at the translational level.^{4,5} Various aggressive tumors such as high-grade gliomas, advanced pancreatic cancer, malignant melanoma and advanced colorectal cancer cells produce an excessive amount of TGF- β 2, which plays a critical role in tumor progression (proliferation, angiogenesis and metastasis) and acts as a shield that protects the tumor from the body's immune system.^{4,5,6} By inhibiting TGF- β 2, trabedersen has multiple antitumoral effects: it hinders tumor progression, angiogenesis and metastasis.^{4,7} In addition, trabedersen restores the body's immune system, by breaking down the protective shield so that the immune system can recognize and destroy the tumor cells.

Targeted therapies drive market growth

Unlike non-specific therapies, e.g. chemotherapy or radiotherapy, targeted therapies act 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 market⁸. A marketing authorization would make trabedersen the first TGF-beta targeting drug for the treatment of cancer.

Clinical studies

For more information on the clinical Phase I/II study in advanced pancreatic carcinoma, malignant melanoma or colorectal carcinoma please visit the website www.krebsstudien.info (only in German).

For more information on the clinical Phase III SAPHIRE trial in recurrent or refractory anaplastic astrocytoma please visit the website www.anticancer.de.

About Antisense Pharma GmbH

Antisense Pharma is a biopharmaceutical company located in Regensburg, Germany. The company focuses on targeted gene silencing 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 currently 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 and was awarded one of the 100 most innovative medium-sized companies in Germany in 2009.

References

1. Parkin DM (2005) CA Cancer. J Clin 55(2):74-108
2. Cascinu S et al. (2009) Pancreatic Cancer ESMO Clinical Recommendations. Ann Oncol 20 (Suppl. 4): iv37-iv40
3. American Cancer Society. <http://www.cancer.org> last accessed 08/2009.
4. Schlingensiepen KH et al. (2006) Cytokine Growth Factor Rev 17(1-2):129-139
5. Tsamandas, AC, Kardamakis, D et al. (2004) The potential role of TGFbeta1, TGFbeta2 and TGFbeta3 protein expression in colorectal carcinomas. Correlation with classic histopathologic factors and patient survival. Strahlenther Onkol 180(4):201-8
6. Kouvidou, C, Latoufis, C et al. (2006) Expression of Smad4 and TGF-beta2 in colorectal carcinoma. Anticancer Res 26(4B):2901-7
7. Schlingensiepen R et al. (2005) Oligonucleotides 15(2):94-104
8. IMS Health



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