Antisense Pharma unveils its corporate strategy for 2013

- Trabedersen clinical development program update
- Advances in ‘Next Generation’ TGF-β oligonucleotide program and expansion of scientific advisory board
- Organization streamlined and senior management strengthened
- Strong, continued support from investors

Regensburg, February 26, 2013. The biopharmaceutical company Antisense Pharma GmbH, today announced its revised corporate and development strategy, receiving full support from its main investors.

The updated corporate strategy focuses on streamlining the organization to meet its current business objectives and strengthen key senior management positions in light of the new direction for trabedersen’s clinical development program and the advancement of Antisense Pharma’s ‘Next Generation’ TGF-β inhibitor oligonucleotide program.

Revised development path for Trabedersen

The data analysis of “SAPPHIRE” (G005), trabedersen’s early terminated phase III study in glioma, is in progress. Due to a need for additional outcome data collection, final results are now expected within the third quarter of 2013.

However, preliminary safety data analyses revealed that the benefit/risk ratio might not be in favor of the trabedersen treatment arm due to serious adverse events (SAE) associated with the local mode of administration of the drug in this trial. The convention-enhanced delivery (CED) of trabedersen via intra-cranial infusion with surgical catheter placement seemed to result in a distinct, clinically relevant imbalance of SAEs observed. In light of this finding, the company decided that the risk to the patient outweighs the potential clinical benefits for this type of administration of the drug. As a consequence, the company will no longer pursue further development of the local administration of trabedersen in glioma.

Future clinical development of TGF-β targeted drugs in glioma is still considered for the ‘Next Generation’ TGF-β oligonucleotide development program based on the encouraging survival data for anaplastic astrocytoma from an earlier glioma trial with trabedersen (G004).¹

From now onwards, trabedersen’s development path will only focus on the systemic intravenous (IV) mode of administration.

This decision is further supported by the findings from the Phase I/II clinical study (P001) presented at ASCO in June 2012.² The data demonstrated that the systemic IV administration of trabedersen treatment is safe...
and well tolerated by patients. First clinical signs of efficacy were observed in this study with encouraging survival outcomes for patients suffering from pancreatic cancer or malignant melanoma when compared to historical controls.

With this intent, Antisense Pharma is currently under way to launch a clinical Phase II study to evaluate systemic, intravenous trabedersen treatment in patients suffering from malignant melanoma, pancreatic cancer and other tumors by the second half of 2013. This clinical trial will be conducted in two stages. The first stage has a dose-confirmatory component and will further define the pharmacodynamic (PD) activity of trabedersen in terms of TGF-β2 target down-regulation as a primary PD parameter and immunomodulation in the selected patient populations. Upon successful completion of the first stage, the second stage of the study is set to demonstrate a survival benefit over standard chemotherapy for one or two key tumor indications in a larger patient population.

Dr. Philippe Calais, Chief Executive Officer of Antisense Pharma commented: “Our revised trabedersen clinical program takes into consideration all learnings from the G005 and P001 studies. We move forward with the systemic intravenous administration of trabedersen in a well-tailored, two stage clinical development program aiming at further optimizing our chances of success in the regulatory path leading to approval and market. This creative development approach minimizes the risk and costs usually associated with larger, less tailored programs. Indeed trabedersen holds a strong value for the company, as it is supported by orphan drug designation for several indications in the US and Europe as well as a fully validated manufacturing process. In parallel, we are also exploring partnership opportunities to further accelerate trabedersen’s development path.”

Progress of ‘Next Generation’ TGF-β oligonucleotide program and expansion of the scientific advisory board (SAB)

Since its foundation in 1998 Antisense Pharma has accumulated a vast amount of expertise and intellectual property by focusing its research and development efforts on the TGF-β pathway and on oligonucleotides in high-medical-need diseases in oncology. This expertise is unique in the world.

The company recently merged its indication-focused advisory boards into a single corporate SAB comprised of 11 established academics, researchers and clinicians who are worldwide leaders in fields of TFG-β, oncology, and oligonucleotides.

Upon strategic considerations from the company’s senior management team supported by recommendations from the SAB, Antisense Pharma started a ‘Next Generation’ TGF-β inhibitor oligonucleotide program that provides the company with a portfolio of additional assets, comprised of compounds specifically designed to down regulate the TGF-β pathway by targeting different TGF-β isoforms or combinations thereof, for the treatment of high unmet medical need cancer indications. These potent compounds have meanwhile shown highly impressive anti-TGF-β activity in initial preclinical evaluations.
Antisense Pharma is committed to aggressively move forward a number of potential lead candidates for further development and to explore development collaborations at an early stage to further accelerate those highly promising assets.

Dr. Michael Weller, Professor of Neurology and Chairman of the Department of Neurology at Zurich University Hospital, and member of the Antisense Pharma SAB, as well as having a strategic research collaboration with Antisense Pharma, commented: “The cytokine TGF-ß has a critical role in several tumors. As a soluble factor it travels through the body and hits immune cells which then are shut off and don’t recognize the tumor anymore. This is one of several ways how TGF-ß promotes tumor growth and invasion. Antisense Pharma pursues an important therapeutic approach to treat cancer by inhibiting TGF-ß. I am excited to test their next generation antisense TGF-ß inhibitors in our animal models and support their further clinical development.”

Organization Streamlined and senior management strengthened

The revised corporate strategy necessitated an organizational streamlining to better suit the current business objectives.

Refocusing Antisense Pharma’s R&D efforts into lean and focused preclinical and clinical development programs did impact the organization. Accordingly, Antisense Pharma decided to outsource non-critical expertise and adjusted its headcount, reducing its workforce by half on February 1st, 2013. The company furthermore announced the addition of new talents in several key senior management positions. Added to the team are Eugen Leo, M.D. Ph.D. M.B.A., a board certified hematologist and medical oncologist and Professor of Medicine with a long-standing international targeted therapy clinical development experience in both academia and industry, and Michel Janicot, Ph.D., a biochemist, scientist and drug-developer with extensive global industry expertise in preclinical development of targeted therapies for oncology.

Dr. Philippe Calais, CEO of Antisense Pharma commented further: “I am convinced that the adoption of our development strategy and our refined corporate strategy is the right way to secure a sustainable portfolio of clinical assets for Antisense Pharma and at the same time reduces the risk for our investors. I am committed to build on our great expertise in the area of TGF-ß and oligonucleotide research. The strength of our refocused trabedersen development, our well defined pipeline, as well as our renewed efforts to shape the organization in a way to fit our new strategy will undoubtedly bring significant opportunities for a bright future for Antisense Pharma.”

The company’s long term main investors are fully supportive of the new corporate strategy of Antisense Pharma.

Dr. Matthias Kromayer of MIG commented: “We are fully supportive of the updated strategy presented by Dr. Calais and his newly appointed team of development experts. Considering the challenging environment, the entire Antisense Pharma team is doing a great job in streamlining the organization and focusing activi-
ties around Antisense Pharma’s core capabilities – the vast experience and skills in the area of TGF-β, oncology, and oligonucleotide research. We are especially encouraged by the recent US FDA approval of the first systemic antisense drug, which further validates the scientific rationale of this drug technology platform. We are convinced that Antisense Pharma will be able to make a significant contribution to the development of innovative oligonucleotide therapies in oncology and expect management to deliver the promised development and corporate milestones.”

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ADDITIONAL INFORMATION

About Antisense Technology
Antisense compounds are biological molecules which consist of fragments of 2 to 20 ribonucleic acid (RNA) or deoxyribonucleic acid (DNA) nucleotides (oligonucleotides). They are designed to bind in a sequence-specific manner to a matching messenger ribonucleic acid (mRNA) known to code for a defined protein. The binding of an oligonucleotide to its matching mRNA sequence results in the degradation of the mRNA through enzyme-mediated pathways or disruption of mRNA function through binding alone. As a consequence the synthesis of a specific protein, which affects the onset and progression of a certain disease, is inhibited without altering the genome of the patient. Using antisense molecules to inhibit the synthesis of pathogenic proteins is an innovative therapeutic approach. It enables to treat the root of the disease and not merely its symptoms.

About the target protein TGF-beta
The cytokine human transforming growth factor beta (TGF-β) plays a key role in the progression of various aggressive tumors. Its overexpression induces a profound state of cellular immunodeficiency and mediates the tumor’s escape from immunosurveillance. In addition, TGF-β plays a significant role in invasive tumor growth and the infiltration into non-affected tissue, in the promotion of tumor angiogenesis, as well as tumor cell migration and metastasis.

About Trabedersen
The antisense molecule trabedersen consists of 18 DNA oligonucleotides and is complementary to the human mRNA encoding for TGF-β2. Trabedersen, specifically designed to target the TGF-β2 mRNA, is believed to reverse its immunosuppressive effects, rendering the tumor visible to the patient’s immune system and resulting in priming and specific activation of the patient’s anti-tumor immune response. Trabedersen has been granted orphan designation for three tumor indications: high grade glioma (US, EU), pancreatic cancer (US, EU) and malignant melanoma (US). Trabedersen has been evaluated extensively in several preclinical and clinical studies across selected oncological indications. The compound has shown encouraging early signs of therapeutic activity in cancer patients.
About Antisense Pharma

Antisense Pharma GmbH is a biopharmaceutical company based in Regensburg and Munich, Germany, developing innovative therapies targeting the TGF-β pathway to treat tumor diseases with high unmet medical need. These therapies are highly specific and antisense technology based as they aim at enabling the body’s own immune system to respond against tumor diseases with a potentially long-lasting effect.

In addition, the company is expanding its pipeline through the development of a “Next Generation” TGF-β inhibitor oligonucleotide program identifying novel proprietary compounds to target cancer.

The private company was founded in 1998 and funded mainly by renowned private equity lead investor MIG and others such as S-Refit and Bayern Kapital.

For further information please visit www.antisense-pharma.com.

References

1. Bogdahn U. et al. (2011): Targeted Therapy for High-Grade Glioma with the TGF-beta2 Inhibitor Trabedersen: Results of a Randomized and Controlled Phase IIb Study; Neuro-Oncology 13, doi: 10.1093/neuonc/noq142
2. Oettle H. et al. (2012): Final results of a Phase I/II study in patients with advanced pancreatic carcinoma, malignant melanoma, or colorectal carcinoma with trabedersen; ASCO American Society of Clinical Oncology #4034, abstract and poster presentation
3. Press Release (Jan-29-2013): Genzyme and Isis Announce FDA Approval of KYNAMRO™ (mipomersen sodium) Injection for the Treatment of Homozygous Familial Hypercholesterolemia

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