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Cytos Biotechnology presents encouraging phase IIa study results for its melanoma vaccine CYT004-MelQbG10

Vaccine candidate was safe, well tolerated and demonstrated good T cell immunogenicity

Schlieren (Zurich), Switzerland, November 20, 2007 – Cytos Biotechnology AG (SWX:CYTN) today announced encouraging results from three parallel open-label phase IIa clinical trials with the Immunodrug™ candidate CYT004-MelQbG10, a therapeutic vaccine to treat malignant melanoma. The present studies were first-time-in-man clinical trials and included a total of 22 patients with malignant melanoma at different disease stages (stages II-IV). The studies assessed safety, tolerability and T cell immunogenicity of three different dose regimens of CYT004-MelQbG10 and also compared two different routes of administration.

All dose regimes of CYT004-MelQbG10 tested in the studies were safe and well tolerated and reported adverse events included mostly mild to moderate injection site reactions. Upon vaccination, Melan-A (MART-1)-specific CD8⁺ T cell responses could be detected directly *ex vivo* in 14 of 22 patients, indicating a good T cell immunogenicity of the vaccine candidate. In patients responding to the vaccine, the melanoma-specific CD8⁺ T cells increased by a median factor of 3 (individual increases were 2 to 8 fold).

Seven of 22 patients entered the study without detectable tumor after surgical intervention. Six of these seven patients remained tumor-free throughout the study period, whereas one patient developed new metastases. The remaining 15 participants entered the study with detectable metastases. Of those, 11 patients had progressive disease leading to death of two patients; one patient had stable disease, one patient showed a partial response, one patient was not assessable since the tumor lesion was removed during the trial, and one patient died before the final assessment. At study end, 19 of the 22 patients were alive.

Prof. Daniel Speiser, MD, study investigator, Ludwig Institute for Cancer Research, Lausanne Branch, Switzerland, comments: "There is important medical need for effective and safe therapies to treat malignant melanoma, one of the most aggressive cancers. The favorable safety and tolerability profile of this vaccine candidate indicates that it can be used with the attempt to protect patients from disease recurrence and progression for extended periods of time, which is essential because melanoma relapses often occur after one or even several years. We are delighted to see that the primary objectives of the three studies was met, namely to confirm good T cell immunogenicity of the melanoma vaccine candidate. The achieved increase in Melan-A specific CD8⁺ T cells is superior to what is accomplished by the majority of other immunization strategies, particularly when we consider the fact that an un-adjuvanted formulation was used in these first-time-in-man studies. Furthermore, this is the first time that tumor specific immune responses have been demonstrated in stage II patients *ex vivo*, underlining the potential of the vaccine candidate for treatment of this important patient group. I look forward to the further development of this promising vaccine candidate with a next study planned to begin in 2008."

About malignant melanoma

Malignant melanoma is the most deadly of all skin cancers and more than 130'000 cases occur worldwide each year¹. The disease is strongly related to the frequency of recreational exposure to the

sun and a history of sunburn. The incidence of malignant melanoma continues to increase globally, mainly due to lifestyle habits and to the gradual reduction in the stratospheric ozone that shields people from UV radiation.

Melanoma is a malignant tumor of melanocytes that often starts from harmless-looking moles. Once the tumor has started to metastasize, the survival prognosis is generally poor. The metastases may spread to any organ; however, the lungs and liver are the most common sites. Despite intensive research and numerous therapeutic approaches, no satisfactory treatment is available today. The first treatment of choice is, whenever possible, surgical removal of the tumor.

Active vaccination strategies represent a relatively new discipline in the management of melanoma. Based on evidence that the immune system could play a potent role in tumor regression, there is well-founded hope that the power of the immune system could be enhanced by the use of melanoma vaccines. The key to an effective tumor vaccine lies in the ability to overcome self-tolerance and to specifically activate tumor-specific CD8⁺ T cells (i.e. killer cells) of which it is known that they are able to recognize and destroy tumor cells².

About the Immunodrug™ candidate CYT004-MelQbG10

CYT004-MelQbG10 is a therapeutic vaccine in development for the treatment of malignant melanoma. The vaccine candidate is based on Cytos Biotechnology's second Immunodrug™ platform, which applies immunostimulatory DNA sequences to induce targeted T cell responses³. CYT004-MelQbG10 consists of a modified fragment of the Melan-A protein coupled to the Immunodrug™ carrier QbG10. QbG10 itself encompasses the virus-like particle Qb, which has been filled with the immunostimulatory DNA sequence G10. G10 is a synthetically produced stretch of DNA originally derived from bacteria. This DNA sequence is recognized by so called toll-like receptors, which sound an "alarm signal" to the immune system and this way provide the inflammatory context necessary to promote T cell activation. Melan-A is a melanocyte-differentiation antigen and, although its exact function is not yet known, it has been found to be over-expressed in melanoma cells. This over-expression renders the protein a potentially promising target for tumor therapies. CYT004-MelQbG10 aims at activation of Melan-A-specific CD8⁺ T cells (i.e. killer cells) with the ability to recognize and destroy melanoma cells.

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About Cytos Biotechnology

Cytos Biotechnology AG is a public Swiss biotechnology company that specializes in the discovery, development and commercialization of a new class of biopharmaceutical products – the Immunodrugs™. Immunodrugs™ are intended for use in the treatment and prevention of common chronic diseases, which afflict millions of people worldwide. Immunodrugs™ are designed to instruct the patient's immune system to produce desired therapeutic antibody or T cell responses that modulate chronic disease processes. Taking advantage of the high flexibility of its Immunodrug™ platform, Cytos Biotechnology has built a full pipeline of different Immunodrug™ candidates in various disease areas, of which 6 are currently in clinical development. The Immunodrug™ candidates are developed both in-house and together with Novartis and Pfizer Animal Health. Founded in 1995 as a spin-off from the Swiss Federal Institute of Technology (ETH) in Zurich, the company is located in Schlieren (Zurich). Currently, the company has 130 employees. Cytos Biotechnology AG has been listed on the SWX Swiss Exchange (SWX:CYTN) since October 2002.

References

1. Sunbeds, tanning and UV exposure, WHO Fact Sheet No 287, March 2005.
2. Nonmethylated CG motifs packaged into virus-like particles induce protective cytotoxic T cell responses in the absence of systemic side effects; *Journal of Immunology*, 2004, 172:1777.
3. Efficient homologous prime-boost strategies for T cell vaccination based on virus-like particles; *European Journal of Immunology*, 2005, 35:816.

Glossary

Adjuvant: a pharmaceutical compound that enhances an immune response.

CD8⁺ T cell: subset of T cells playing an important role for direct lysis (killing) of altered body cells (i.e. virus-infected or tumor cells).

Differentiation antigen: a protein, which is not only expressed in tumor cells, but also in normal cells during at least some stage of development. Differentiation antigens may be over-expressed in tumor cells such that they are potentially promising targets for tumor therapies.

Disease stages of malignant melanoma: clinical staging (stage I-IV) of malignant melanoma is defined according to AJCC 2001 (American Joint Committee on Cancer). Stages are defined by different criteria including the size of the primary tumor and the number and site of metastases. Stage IV defines the most severe form of the disease.

Dose regimen: describes the dose and the schedule according to which a drug is administered.

Ex vivo: outside of the living body. Refers in this context to a procedure in which cells or tissue are taken from a living body and are directly applied for biochemical / immunological laboratory analysis without further propagation *in vitro*.

Immunogenicity: the ability of a substance to evoke an immune response.

Malignant melanoma: the most fatal kind of skin cancer. It begins in certain cells in the skin called melanocytes.

Melan-A (MART-1): a melanocyte-differentiation antigen found to be over-expressed in melanoma cells. This over-expression renders the protein a potentially promising target for tumor therapies.

Melanocyte: pigment-producing cell type in the skin, hair and eye that determines their colour.

Metastasis: process by which cancer spreads from the place at which it first arose as a primary tumor to distant locations in the body.

Phase IIa: clinical trial that examines a new drug candidate's safety, tolerability and exploratory efficacy and may involve between 10 and 100 patients.

Open-label: a set-up used in clinical trials where the doctor and the patient know what substance is administered (e.g. placebo or active drug).

Over-expression: enhanced synthesis of certain proteins in tumor cells when compared to normal cells.

Self-tolerance: non-reactivity of the immune system to molecules belonging to the organism itself.

T cell: immune cell playing an important role in cell-mediated immunity. One differentiates various subgroups such as cytotoxic (killer) T cells and T helper cells.

Therapeutic vaccine: a preparation of disease-related molecules (antigens) that is capable of inducing an immune response to such antigens with the aim of modulating the disease process.

This foregoing press release may contain forward-looking statements that include words or phrases such as "will", "indicate", "aim", "potential / potentially", "promising", "designed", "intend" or other similar expressions. These forward-looking statements are subject to a variety of significant uncertainties, including scientific, business, economic and financial factors, and therefore actual results may differ significantly from those presented. There can be no assurance that any other therapeutic entities will enter clinical trials, that clinical trial results will be predictive for future results, that therapeutic entities will be the subject of filings for regulatory approval, that any drug candidates will receive marketing approval from the U.S. Food and Drug Administration or equivalent regulatory authorities, or that drugs will be marketed successfully. Against the background of these uncertainties readers should not rely on forward-looking statements. The company assumes no responsibility to update forward-looking statements or adapt them to future events or developments. This document does not constitute an offer or invitation to subscribe or purchase any securities of Cytos Biotechnology AG.