

## Phase I/IIa clinical trial with obese individuals shows no effect of CYT009-GhrQb on weight loss

Schlieren (Zurich), Switzerland, November 7, 2006 - Cytos Biotechnology AG (SWX:CYTN) reported today results from its combined phase I/IIa study with CYT009-GhrQb, a therapeutic vaccine candidate for the treatment of obesity. The study was a double-blind, placebo-controlled clinical trial with 111 obese individuals with a body mass index (BMI) between 30 and 35. It was designed to investigate safety, tolerability and exploratory efficacy of the vaccine candidate.

Treatment with CYT009-GhrQb was safe and well tolerated. All patients who received the vaccine mounted a strong antibody response against ghrelin, which was boosted by the subsequent injections. The treatment, however, had no effect on weight loss, the primary efficacy outcome of the study. The median weight loss was 3.6 kilogram after a six months period in both, the vaccine-treated group and the placebo group.

Dr. Wolfgang Renner, CEO of Cytos Biotechnology, commented: "We will be evaluating the data in detail to understand potential reasons why the vaccine candidate did not add a clinical benefit in this trial. Unexpectedly, the only prognostic factor that correlated with high weight loss in this study were high circulating levels of ghrelin at baseline ( $p=0.04$ ). This finding is in stark contrast to previous reports describing ghrelin as a key appetite-inducing hormone and thus questions its validity as a target. Based on the available data, a further development of this particular vaccine candidate in obesity is not warranted, but we are convinced that new treatments for obesity are urgently needed and we will continue to explore novel therapeutic approaches in this important medical area."

Cytos Biotechnology will host a conference call and Q&A session on Tuesday, November 7, 2006 at 10 am CET to discuss the study findings.

To access the conference call, please dial the following numbers:

|        |                   |
|--------|-------------------|
| Europe | +41 91 610 56 00  |
| U.S.   | +1 866 291 41 66  |
| U.K.   | +44 207 107 06 11 |

Cytos Biotechnology will webcast the conference call, which will be held in English. On the internet, you may follow the call live or have it replayed later on demand. To access the webcast and the presentation, please follow the link provided on our homepage [www.cytos.com](http://www.cytos.com). The presentation slides will be available for download 30 minutes prior to the conference call.

### **About the phase I/IIa clinical study and the analysis**

This study, the first clinical trial performed with a ghrelin antagonist, was a randomized, double-blind and placebo-controlled trial with 111 obese patients. It was conducted in 5 clinical centres in Switzerland and included male and female individuals, aged 18-55, with a body mass index (BMI) between 30 and 35. After an initial dose-ranging part of the study with 24 participants, a larger study group designed to evaluate exploratory efficacy of the vaccine followed and included 87 participants. Those participants received 4 injections of 300 µg each of the vaccine or placebo at weeks 0, 4, 8 and 16. All study participants took part in a professional dietary counselling in order to achieve a change in eating habits and improve physical activity. Measurement of body weight was

performed at baseline and biweekly up to week 12, thereafter monthly up to week 24. For the analysis, all 87 study participants who received the 300 µg dose of the vaccine or placebo were included. Non-completers among those were included into the analysis as “last observation carried forward” (LOCF).

### **About CYT009-GhrQb**

CYT009-GhrQb is a therapeutic vaccine candidate for the treatment of obesity. It is designed to instruct the patient’s immune system to produce specific anti-ghrelin antibodies that bind circulating ghrelin in order to inhibit its activity. Ghrelin is a peptide hormone, which has been proposed as a regulator of appetite. It is mainly produced in the stomach and travels via the blood stream and the blood-brain barrier into the brain where it is believed to exert its appetite-stimulating action. Peripheral administration of ghrelin in humans enhanced both appetite and food intake (J Clin Endocrinol Metab, 2001, 86:5992). In addition, the level of ghrelin in obese individuals is increased after diet-induced weight loss and seems to be implicated in the frequently observed rapid regain of weight after diet cessation (Yo-Yo effect). The success of gastric bypass surgery in weight control has, at least in part, been attributed to reduced ghrelin levels (N Engl J Med, 2002, 346:1623). These observations suggested that ghrelin may be an important regulator of food intake and body weight in humans.

### **About obesity**

Obesity is a chronic disease that has become a global pandemic affecting the lives and health of millions of people. According to the World Health Organization, more than 1 billion people worldwide are overweight and of these at least 300 million are clinically obese. Although the underlying causes for obesity are manifold, increased consumption of energy-dense food with high levels of sugar and saturated fats in combination to reduced physical activity are important factors for development of obesity. Consequently, obesity rates have tripled in many countries since the 1980s. Obesity and overweight pose a major risk factor for chronic diseases, including cardiovascular disease, type 2 diabetes, hypertension, stroke, and certain forms of cancer. Today, only few prescription drugs are approved for long-term weight loss therapy and surgical intervention (e.g. gastric bypass surgery) is an effective but also risky undertaken. Thus, there remains a high unmet medical need for new and effective therapies to treat obesity and overweight.

### **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 7 are currently in clinical development. The Immunodrug™ candidates are developed both in-house and together with Novartis Pharma 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 131 employees. Cytos Biotechnology AG has been listed on the SWX Swiss Exchange (SWX:CYTN) since October 2002.*

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## Glossary

**Antagonist:** a substance that inhibits the function of a specific target molecule (e.g. ghrelin).

**Antibody:** class of blood proteins generated by the immune system to bind and neutralize foreign material such as bacteria, viruses or toxins (i.e. antigens). Antibodies can also be induced against self-antigens (i.e. molecules of the organism itself) with the goal to modulate a certain disease process.

**Blood-brain barrier:** physical barrier between the blood vessels in the central nervous system, and the central nervous system itself. The barrier stops many substances from travelling across it.

**BMI:** body mass index. Term used to assess the prevalence of obesity. It is defined as the weight in kilograms divided by the square of the height in meters (kg/m<sup>2</sup>).

**Double-blind:** a set-up often used in clinical trials where neither the doctor nor the patients know if placebo or the active drug substance is applied.

**Efficacy:** strength, effectiveness; the ability of a drug to control or cure an illness.

**Median:** a term used in the statistical analysis of a set of numbers; it relates to or constitutes the middle value in a distribution. 50% of the values are above and 50% below the median.

**Peptide hormone:** belongs to a class of peptides that are secreted into the blood stream and have distinct functions in living organisms.

**Peripheral:** at the periphery (outer boundary).

**Phase I/IIa:** a combined clinical trial that examines a new drug candidate's safety, tolerability and exploratory efficacy in the targeted population.

**Placebo:** dummy medical treatment.

**Prognostic:** a term used in medicine; relates to the prognosis of a disease.

**Randomized:** random assignation of clinical trial volunteers to different treatment groups.

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

This foregoing press release may contain forward-looking statements that include words or phrases such as "designed", "will", "suggest", "propose", "believe", "seem", "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 further 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.