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Cytos Biotechnology reports biochemical findings from phase IIa study with hypertension vaccine CYT006-AngQb

Schlieren (Zurich), Switzerland, June 24, 2009 – Cytos Biotechnology Ltd (SIX:CYTN) announced today results from a biochemical analysis from a phase IIa study (study 02) with the vaccine candidate CYT006-AngQb for the treatment of hypertension. CYT006-AngQb has demonstrated in a first phase IIa study (study 01) a significant reduction of the day-time ambulatory blood pressure of -9 / -4 mmHg (systolic/diastolic) vs. placebo (The Lancet 2008, 371:821). In study 02 an accelerated treatment regimen with injections at weeks 0, 2, 4, 6, and 10 was tested, while in study 01 the vaccine was given at weeks 0, 4, and 12. This modification was anticipated to induce higher antibody titers and, thereby, a stronger blood pressure reduction. While first study results which were communicated on March 17, 2009 showed on average a 5-fold higher antibody titer in study 02 than in study 01, the blood pressure reductions in study 02 were much lower than in study 01; they amounted to -2.3 / -0.4 mmHg. In order to understand this discrepancy, the biochemical properties of the induced antibody responses were analyzed in detail. The main findings are as follows:

- Antibody affinities (i.e. the strength by which the antibodies bind angiotensin II) determined by different biochemical methods were significantly lower in study 02 than in study 01 ($p < 0.001$).
- The amount of angiotensin II sequestered in the blood of vaccinated individuals was on average 33% lower in study 02 than in study 01.
- The individual changes in daytime ambulatory blood pressure correlated with the individual antibody affinities ($p = 0.10$) and, in particular, with measures for the off-rates, describing how long angiotensin II is bound to the antibodies ($p = 0.006$). This means that patients whose antibodies had a higher affinity and which bound angiotensin II for a longer period of time showed a larger blood pressure reduction. No such correlation was detected between individual antibody titers and blood pressure reductions ($p = 0.47$).

A hypothesis which would be compatible with the above findings is that an accelerated treatment regimen like in study 02 leads to the induction of antibody responses with higher titers but lower affinities, thereby creating a lower capacity for sequestering angiotensin II in the blood, and ultimately leading to a smaller blood pressure reduction. Cytos Biotechnology will prospectively test this hypothesis in study 03 which is currently ongoing and which will be un-blinded in Q3, 2009. Study 03 uses the same treatment regimen as study 02, but higher doses of the vaccine.

Understanding of how the treatment parameters dose and regimen are affecting pharmacodynamic responses like antibody titers, affinities and effects on blood pressure is crucial for the development of a novel therapy like CYT006-AngQb. A positive validation of the above hypothesis in study 03 would therefore guide the next development step of this vaccine candidate which would then focus on the induction and subsequent boosting of high affinity antibodies.

About the hypertension vaccine CYT006-AngQb

CYT006-AngQb is a therapeutic vaccine in development for the treatment of hypertension^{1,2}. It is designed to instruct the patient's immune system to produce an antibody response against angiotensin II. Angiotensin II is a small peptide in the body and part of the renin-angiotensin system (RAS), which is an important regulator of blood pressure. Angiotensin II causes blood vessels to narrow, resulting in increased blood pressure. In a phase IIa study with hypertensive patients,

vaccination with CYT006-AngQb has been shown to significantly reduce the mean ambulatory day-time blood pressure by induction of antibodies that bind angiotensin II (The Lancet 2008, 371:821). A particularly strong blood pressure reduction has been observed in the early morning hours – a crucial time of day when adverse cardiovascular events are more likely to occur than during other times of the day.

CYT006-AngQb is a first-in-class product candidate in this important indication and represents a completely novel approach to hypertension treatment. Treatment with CYT006-AngQb should allow for convenient dosing schedules and a smooth control of blood pressure due to a sustained antibody response induced by vaccination.

About hypertension

Hypertension, also termed high blood pressure, is a medical condition where the blood pressure is chronically elevated. Although symptomless in nature and in itself rarely an acute problem, persistent hypertension is one of the most important preventable causes of premature death worldwide and contributes to around half of all cardiovascular diseases³. It is one of the major risk factors for stroke, myocardial infarction, heart failure, and vascular disease, and is a leading cause of chronic renal failure. Genetic predisposition and lifestyle habits such as inadequate physical activity, high fat diet, and high salt intake promote high blood pressure. Up to 30% of adults in most countries suffer from hypertension. Despite effective and relatively inexpensive treatment available, less than one out of four hypertensive individuals have their blood pressure controlled successfully^{4,5}. This poor overall treatment success is mainly attributed to the symptomless nature of hypertension and the necessity for long-term treatment with currently available medications that require at least once daily self-administration.

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Glossary

Affinity: A measure which describes how strong an antibody binds to its target molecule.

Ambulatory blood pressure: Blood pressure measured by numerous readings over a 24-hour period or longer. Provides accurate and reliable information about a person's blood pressure.

Angiotensin II: A small peptide that is part of the renin-angiotensin system (RAS). Induces narrowing of blood vessels and other effects to raise blood pressure.

Antibody: Class of blood proteins generated by the immune system to neutralize foreign materials such as bacteria or viruses. Can also be directed against the body's own disease-associated molecules.

Diastolic blood pressure: Lowest pressure within the arterial blood stream occurring with each heart beat.

Off-Rate: Describes the rate at which an antibody-target complex dissociates.

Systolic blood pressure: The highest pressure within the arterial blood stream occurring with each heart beat.

Titer: A relative measure for the amount of antibodies that bind to a target molecule.

References

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2. The Lancet; Effect of immunization against angiotensin II with CYT006-AngQb on ambulatory blood pressure: a double-blind, randomized, placebo-controlled phase IIa study; 2008, 371:821
3. Centres for Disease Control and Prevention (CDC); The Atlas of Heart Disease and Stroke, 2004
4. Journal of the American Medical Association (JAMA); The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; 2003, 289:2560
5. National Institute for Health and Clinical Excellence (NICE), Centre for Health Services Research, UK; Essential Hypertension: managing adult patients in primary care; August 2004

About Cytos Biotechnology

Cytos Biotechnology Ltd 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 diversified pipeline of different Immunodrug™ candidates in various disease areas, of which six are currently in clinical development. The Immunodrug™ candidates are developed both in-house and together with Novartis, Pfizer, and Pfizer Animal Health. Founded in 1995 as a spinoff from the Swiss Federal Institute of Technology (ETH) in Zurich, the company is located in Schlieren (Zurich). Cytos Biotechnology Ltd is listed on the SIX Swiss Exchange (SIX:CYTN).

This foregoing press release may contain forward-looking statements that include words or phrases such as “may”, “will”, “would”, “can”, “could”, “anticipate”, “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 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 Ltd.