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Cytos Biotechnology updates on the development of the hypertension vaccine CYT006-AngQb

Schlieren (Zurich), Switzerland, November 10, 2009 – Cytos Biotechnology Ltd (SIX:CYTN) today gave an update on the development of its hypertension vaccine CYT006-AngQb. In a first phase IIa study (study 01) the vaccine was safe, well tolerated and efficacious in lowering the mean ambulatory blood pressure by -9/-4 mmHg (systolic/diastolic) vs. placebo (Lancet 371:821 (2008)). In this study the vaccine was administered in a conventional treatment regimen with injections at weeks 0, 4, and 12.

In a second study (study 02), the vaccine was administered more frequently and in shorter intervals than in study 01 with injections at weeks 0, 2, 4, 6 and 10. The intention of the altered regimen was to achieve higher antibody titers and a stronger reduction of the blood pressure. While, as expected, titers were higher in study 02 than in study 01, the decrease in blood pressure was less than reported for study 01, and the antibodies induced by vaccination had a significantly lower affinity towards angiotensin II, i.e. they bound angiotensin II less tightly, which could explain the lower blood pressure reduction.

Study 03 had an identical design as study 02 and was initiated shortly after the start of study 02. The goal of study 03 was to investigate safety, tolerability and efficacy of a higher dose of the vaccine (2.7 mg total for study 03 vs. 1.5 mg total for study 02). Study 03 used the same dosing schedule as study 02. Following the observation of significantly lower affinities induced by the altered treatment regimen in study 02, study 03 should clarify whether lower antibody affinities induced by the altered regimen are a reproducible finding which could explain the lower treatment effect.

Study 03, which included 83 patients suffering from mild to moderate hypertension, essentially reproduced the findings of study 02. While antibody titers were again higher than in study 01, the affinities, which were determined by two independent methods, were in both assays significantly lower than in study 01 and comparable to study 02. Accordingly, blood pressure reduction was also lower than in study 01 and did not achieve significance level vs. placebo.

A plausible explanation for the lower affinities in the accelerated treatment regimens in study 02 and 03 may lie in a natural process called affinity maturation which may be disturbed by too frequent injections of the vaccine. The immune system generates over time antibody responses of increased affinities by selectively expanding those B-cells which get best access to the antigen through binding via surface-bound high affinity antibodies. Those B-cell clones that bind the antigens best are selectively expanded at the expense of those clones that bind them weakly. If too much antigen is delivered too quickly, predominantly weakly binding antibodies may be expanded at the expense of those binding well. This could have happened in studies 02 and 03.

The conclusions drawn from the results of the three studies are that the altered treatment regimen of studies 02 and 03 reproducibly leads to qualitatively different antibody responses with a significantly lower affinity than the conventional treatment regimen of study 01. Therefore studies 02 and 03 do not invalidate the positive outcome of study 01, where the vaccine was efficacious. Furthermore, antibody affinity, which is of critical importance in cases where small target molecules like angiotensin II (8 aminoacids) are to be neutralized, can potentially be controlled by adjusting

treatment parameters like the timing of booster injections. Cytos Biotechnology has therefore decided to continue its R&D program in hypertension.

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.

Phase IIa: clinical trial that examines a new drug candidate's safety, tolerability and preliminary efficacy in a small number of patients.

Renin-angiotensin system (RAS): Important system in the body that regulates blood pressure.

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 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). Currently, the Company has 86 full-time employees. Cytos Biotechnology Ltd is listed on the SIX Swiss Exchange (SIX:CYTN).

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