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PRESS RELEASE

# Adocia confirms positive clinical results for its BioChaperone® Combo, a combination of long-acting insulin glargine and fast-acting insulin lispro

- **BioChaperone Combo is the first combination based on insulin glargine to show a fast and long action in type I diabetic patients**
- **Phase I/II clinical trial establishes proof-of-concept with a statistically improved short- and long-term blood glucose control with the BioChaperone Combo versus Humalog® Mix**
- **Market opportunity is estimated to exceed $3 Billion. BioChaperone Combo has the potential to serve both the premix insulin analogs market plus a portion of the insulin glargine market**

**Lyon, France, March 20th 2014** - Adocia (Euronext Paris : FR0011184241 - ADOC) announced today positive final results for the first clinical trial on its innovative formulation combining insulin analog glargine (Lantus®, Sanofi), the gold standard basal insulin, with a rapid-acting insulin analog, lispro (Humalog®, Eli Lilly) using Adocia's BioChaperone® technology.

BioChaperone technology enables the solubilization of insulin glargine at physiological pH, which allows its combination in solution with prandial insulins analogs such as lispro. Eight patent applications have been filed to protect this innovation until 2032.

The objective of this trial was to compare the Pharmacodynamics (PD) and Pharmacokinetics (PK) of the BioChaperone Combo with a premix formulation of an insulin analog (Humalog® Mix, lispro and protamine, Eli Lilly).

## Clinical results

In this double-blind crossover study, the PK/PD characteristics of BioChaperone Combo (insulin glargine 75% and insulin lispro 25%) were investigated. Twenty people with type 1 diabetes received single 0.8 U/kg doses of BioChaperone Combo and Humalog Mix25 under automated euglycemic clamp conditions (ClampArt®, target blood glucose (BG) 100 mg/dL, clamp duration 30 h post-dosing).

Both formulations were well tolerated and did not induce any local reaction.

BioChaperone Combo had a faster onset of action (25±11 vs. 40±13 min; p=0.002) and a higher early metabolic effect (AUC_GIR[0-2h] 504±210 vs. 325±183 mg/kg; p=0.001). The study also demonstrates a stronger late metabolic effect (AUC_GIR[12-30h] 1480±900 vs. 961±553 mg/kg; p=0.026) and a longer duration of action. Indeed, 30 hours after administration, 17 of the 19 patients treated with BioChaperone Combo were still under glucose control vs. only 6 of the 20 with Humalog Mix (p=0.0002). In summary, significant difference was observed for all these comparisons (p<0.05).

PK parameters are consistent with PD and will be submitted for communication to the 74th scientific sessions of the American Diabetes Association (ADA) and the 50th European Association for the Study of Diabetes (EASD) annual meeting.

In conclusion, the clinical results demonstrate faster prandial phase and longer basal action for BioChaperone Combo vs. Humalog Mix, indicating a better control of blood glucose.

“We are very pleased with the final analysis of the performance of our BioChaperone Combo. There is strong evidence of the superiority of this innovative formulation to Humalog Mix, with a statistical difference for all key parameters. What is remarkable in these results is not only that the action of our Combo lasts more than 30 hours, but also, it acts more rapidly,” says Olivier Soula, Deputy General Manager of Adocia.

“Based on these results, BioChaperone Combo could be a single daily injection treatment. This treatment simplification would be an important advantage for patients who currently require at least two injections per day of premix or one of Lantus plus at least one of a fast-acting insulin,” adds Dr Tim Heise, medical doctor, CEO of Profil.

## BioChaperone Combo, combining simplicity and medical performance

Today, diabetic patients who cannot control their glycemia with basal insulin alone need to add prandial insulin to their treatment. They have two options: to use either one insulin analog premix product or two insulin products, one basal and one prandial.

Premix consists in protamine precipitated (basal fraction) and soluble (prandial fraction) insulin. It eases patient life with a single product to use but it requires two injections per day to cover the patient’s basal insulin needs. The market for insulin analog premixes was worth approximately $2.4 billion in 2013, with $1.8 billion sales of NovoLog® Mix (Novo Nordisk) and estimated $0.6 billion sales of Humalog Mix (Eli Lilly).

Nevertheless, the use of both Lantus and fast-acting insulin remains the preferred physicians’ choice because it offers a basal plateau effect and a fast prandial action. It is estimated that the market share of Lantus used in association with fast-acting insulin exceeds $2 billion.

“BioChaperone Combo combines the efficacy of both insulin glargine and insulin lispro in a single product,” says Gerard Soula, President & CEO of Adocia. “Our objective is to serve patients and BioChaperone Combo offers the simplicity of the premix treatment with the medical efficacy of insulin glargine. The potential market for this combination could be worth the $2.4 billion of the premix market plus a significant part of the $7.8 billion insulin glargine market”.

The development of BioChaperone Combo is in line with the ongoing trend of treating diabetes with combination products. Notably, 2 long-acting insulins combined with GLP-1 agonists are currently in phase 3 clinical trials: insulin glargine with lixisenatide (Lixilan®, Sanofi) and insulin degludec with liraglutide (IDegLira, Novo Nordisk). In addition, a combination of long-acting and fast-acting insulin analogs is ready for commercialization (insulin degludec and insulin aspart 70/30, Ryzodeg®, Novo Nordisk).

BioChaperone Combo is the only combination of the gold-standard basal insulin glargine with a fast-acting insulin analog with an established clinical proof-of-concept.

## Clinical Development Plan

Adocia intends to launch a phase 2a clinical trial on type 1 diabetic patients in order to document the dose-response and dose-exposure of the BioChaperone Combo. This clinical trial is to be conducted by the same CRO in Germany, Profil GmbH, during the third quarter of this year. It should enroll 20 type 1 diabetic patients under automated euglycemic clamp conditions with 3 doses of BioChaperone Combo, insulin glargine (75%) and insulin lispro (25%) and one dose of Humalog Mix. Results are expected at the end of 2014.

### About Adocia:

***To be a global leader for delivery of insulins and therapeutic proteins***

Adocia is a biotech company specialized in the development of innovative formulations of already-approved therapeutic proteins with a strong expertise on insulins. The proprietary BioChaperone® technological platform is designed to enhance the effectiveness and safety of therapeutic proteins and their ease of use for patients.

Adocia successfully completed two Phases I and II studies on the formulation of a fast-acting human insulin, one Phase I of an ultra-fast acting insulin lispro and one Phase I/II on a unique combination of Glargine, the gold-standard of basal insulin and fast-acting insulin analog, lispro. The results of a new phase I/II clinical trial on ultra-fast acting lispro should be released by 2Q 2014.

Adocia has also obtained positive results on a Phase I/II on a diabetic foot ulcer healing product based on PDGF-BB.

Adocia has extended its activities to the formulation of monoclonal antibodies, which are gold standard molecules for the treatment of various chronic pathologies (oncology, inflammation, etc.). In this field, Adocia is engaged in collaborative programs with two major pharmaceutical companies.

***To fight cancer by targeting oncology treatments***

DriveIn® is a nanotechnology which is remarkably efficient in carrying active molecules and delivering them into solid tumors. This new platform is an exceptional opportunity to enter the oncology market by improving the efficacy of already approved treatments and of proprietary molecules.

***"Innovative medicine for everyone, everywhere"***

Adocia's therapeutic innovations aim at bringing solutions in a profoundly changing global pharmaceutical and economic context, characterized in particular by the increased prevalence and impact of the targeted pathologies, population growth and ageing, the need to control public health expenditures and increasing demand from emerging countries.

Adocia is listed on the regulated market of Euronext in Paris (ISIN: FR0011184241, mnemo / Reuters / Bloomberg: ADOC, ADOC.PA, ADOC.FP) and its share included in the Next Biotech index.
For more information: www.adocia.com

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