

# PRESS RELEASE

# Adocia Announces Preliminary Positive Clinical Results for its Combination of Long-Acting Insulin Glargine and Fast-acting Insulin Analog Lispro, BioChaperone<sup>®</sup> Combo

Adocia's BioChaperone Combo is the first product combining insulin Glargine with a fast-acting insulin analog

# Phase I/II clinical trial demonstrates proof of concept in patients with type 1 diabetes, showing that BioChaperone Combo acts faster and longer than Humalog Mix

**Lyon, France, February 27 2014 -** Adocia (Euronext Paris : FR0011184241 - ADOC) announces today positive preliminary results for the first clinical trial on an innovative formulation combining insulin analog Glargine (Lantus<sup>®</sup>, Sanofi), the gold standard basal insulin, with a rapid-acting insulin analog, Lispro (Humalog<sup>®</sup>, Eli Lilly) using Adocia's BioChaperone<sup>®</sup> technology.

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

The objective of this trial was to show that this combination of the most widely used basal insulin (Lantus<sup>®</sup>) and one of the best commercial prandial insulins (Humalog<sup>®</sup>) formulated with the BioChaperone<sup>®</sup> technology has the potential to help patients improve their blood glucose control more effectively than with a Premix formulation of insulin analog (Humalog Mix<sup>®</sup>, Lispro and Protamine).

"The preliminary clinical efficacy results show how the BioChaperone Combo could offer patients both the long-lasting effect of Glargine, which is the gold-standard in basal insulin and the fast action of a prandial insulin analog. This confirms the product's strong market potential," said Olivier Soula, Deputy General Manager of Adocia. "From a regulatory point of view, we should benefit from a simplified clinical development path. Development could be short and less costly as Glargine and Lispro have both been on the market for many years and share a proven track record of clinical safety."

### **Trial Design**

This clinical trial, conducted by Profil (CRO,Germany) was a double blind, two-way crossover study that enrolled 20 patients with type 1 diabetes under euglycemic clamp conditions. As part of the crossover design, all patients were treated with BioChaperone Combo and Humalog Mix 25 at the same dose of 0.8 IU/kg. The composition of BioChaperone Combo is based on 75/25 basal prandial ratio like in Humalog Mix 25. Pharmacokinetic (PK) and pharmacodynamic (PD) measurements were taken as patients were monitored for 30 hours after administration. The objective of the study was a comparison of PD and PK profiles of BioChaperone Combo to those of Humalog Mix 25. Safety and tolerability of the two products were also evaluated.

## Efficacy Results Demonstrate Proof of Concept

The study demonstrated that BioChaperone Combo has the ability to deliver insulin with a faster onset and longer duration of action compared to Humalog Mix:

- BioChaperone Combo had a greater than 30% faster onset of action as compared to Humalog Mix.
- Almost all patients treated with BioChaperone Combo experienced a minimal duration of action in excess of 30 hours (end of monitoring).
- Both formulations of insulins (BioChaperone Combo and Humalog Mix) were well tolerated.

The onset of action is the time when glucose level decreases by at least 5% from the starting level and glucose infusion is started. Minimal duration of action is defined by the time when blood glucose concentration exceeds 6.5 mmol/L (118 mg/dL).

The PK profiles confirm these major conclusions based on PD profiles.

The minimal duration of action in excess of 30 hours, support the use of the BioChaperone Combo as a once-a-day insulin treatment. This may provide patients with advantages over Premix formulations that usually require injection two or three times a day. BioChaperone Combo could also be used twice-a-day to support treatment intensification.

"Our ambition is to offer diabetic patients a unique combination of insulins to simplify their lives while giving them access to the best care options. This clinical study is a key step towards this objective. BioChaperone Combo could replace Premix formulations, (which represent a market exceeding \$2.4 billion). They could also capture part of the Lantus market, which is greater than \$7 billion," said Gérard Soula, CEO of Adocia. "We believe that BioChaperone Combo also represents a great commercial opportunity for potential partners."

Adocia intends to publish a detailed analysis when the data become available in a few weeks. Adocia also intends to present the complete results at a major medical conference this year.

### About Lantus and Premix products:

Type I and Type II diabetic patients under insulin therapy currently have two treatment options, either a Premix, which is a formulation of insulin with both a fast and long action, or

the association of two different insulin injections, one basal and one prandial insulin. Lantus is the current gold-standard in basal insulin, generating \$7.8 billion in 2013 (growth exceeding 15%, Sanofi's 2013 Results). Several companies currently develop biosimilars of Lantus, which falls in the public domain in 2015.

Premix products, such as NovoMix<sup>®</sup> (Novo Nordisk) and Humalog Mix<sup>®</sup> (Eli Lilly), help to ease the diabetic patients' life by allowing them to regulate their glycaemia level with only one product, administrated twice-a-day. Premix products have been commercialized for more than 10 years and represented a global market of \$2.4 billion in 2013 (Companies sales figures). Although they are widely used in emerging countries (e.g. 65% of Chinese patients under insulin treatment use Premixes), they do not provide an optimal control of glycaemia.

#### About Adocia:

#### To be a global leader for the formulation of therapeutic proteins

Adocia is a biotech company specialized in the development of best-in-class drugs from the innovative formulation of certain already-approved therapeutic proteins.

Adocia is specialized in insulin therapy and the treatment of the diabetic foot, one of the main complications of diabetes.

Adocia successfully completed two Phases I and II studies on the formulation of a fast-acting human insulin and obtained promising Phase I/II results on a diabetic foot ulcer-healing product. The results of a new phase I/II clinical trial on ultra-fast acting Lispro should be released by 2Q 2014. Adocia has just released preliminary positive Phase I clinical results on a unique combination of Glargine, the gold-standard of basal insulin and fast-acting insulin analog, for an optimal insulin therapy with one single product.

#### Fight cancer by enhancing oncology treatments targeting

Late in 2013, Adocia acquired an exclusive license on a nanotechnology that improves oncology treatments efficacy by targeting their action to solid tumors. This nanotechnology, called DriveIn®, is remarkably efficient in carrying active molecules and delivering them within solid tumors. This new platform in nanotechnology is an exceptional opportunity to enter the oncology market by improving the efficacy of already approved treatments.

Adocia develops proprietary products based on doxorubicin and docetaxel, two of the most used antitumoral treatments, which could greatly benefit from an enhanced intra-cellular delivery. Adocia will also propose the DriveIn technology to pharmaceutical companies to optimize the efficacy of their own proprietary molecules.

#### "Innovative medicine for everyone, everywhere"

Through its BioChaperone® state-of-the-art technological platform, Adocia intends to enhance the effectiveness and safety of therapeutic proteins and their ease of use for patients, with the aim of making these medicines accessible to the broadest public.

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

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: <u>www.adocia.com</u>

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