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PRESS RELEASE

Adocia reports positive results from phase IIa clinical study of ultra-fast acting BioChaperone® Lispro

- **BioChaperone Lispro is significantly faster than Humalog in type I diabetic patients; onset of action is 30 per cent earlier and early metabolic effect is 69 per cent stronger**
- **The ultra-fast action of BioChaperone Lispro should make a positive impact on short and long-term glycemic control, improving the medical benefit for patients**
- **BioChaperone Lispro is the third insulin product in Adocia's portfolio to demonstrate clinical proof of concept in diabetic patients. Adocia plans to launch a dose-response phase IIa clinical trial in the second quarter of 2014**

Lyon, France, April 9, 2014 - Adocia (Euronext Paris: FR0011184241 - ADOC) announces positive results from a Phase IIa clinical trial evaluating its innovative ultra-fast formulation of insulin lispro in comparison to Eli Lilly's Humalog® commercial insulin. Adocia's formulation incorporates proprietary BioChaperone® technology which enables accelerated absorption of prandial insulins. Humalog, which is now off-patent, has annual sales of USD 2.6B[1].

The present study met its primary endpoint, showing a significant increase in BioChaperone Lispro bioavailability in the first half-hour compared to Humalog. This parameter is critical as the ultimate goal for prandial insulins is an immediate absorption in the blood following subcutaneous injections. This result demonstrates that BioChaperone Lispro more closely mimics the endogenous insulin secretion observed in healthy individuals in response to a meal.

"We are excited by the performance of BioChaperone Lispro in diabetic patients, as it confirms the positive results obtained in healthy volunteers. Adocia now has three insulin products with an established proof-of-concept in diabetic patients, including BioChaperone Combo, our combination of the insulins glargine and lispro, and HinsBet, our fast-acting human insulin," said Gerard Soula, chairman and CEO of Adocia. "We think our insulin pipeline positions us to become an important player in the insulin field. Our priority is to bring, as rapidly and as efficiently as possible, these innovative treatments to patients. Adocia is now focused on finding the right partners to achieve this."

[1] 2013 annual report, Eli Lilly

Clinical results support the ultra-fast action of BioChaperone Lispro

In this double-blind crossover study, the pharmacokinetic (PK) and pharmacodynamic (PD) characteristics of BioChaperone Lispro were compared to those of Humalog. Thirty-six patients with type I diabetes received single 0.2 U/kg doses of BioChaperone Lispro and Humalog under automated euglycemic clamp conditions (ClampArt®, target blood glucose (BG) 100 mg/dL, clamp duration six hours post-dosing).

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

BioChaperone Lispro has a significantly faster rate of absorption than Humalog with an increase in the early insulin exposure of 170% (primary endpoint, $AUC_{lispro\_0\text{-}30min}$ 23.7 ± 11.4 vs. 9.5 ± 6.2 h*mU/L; $p<0.0001$). The time to peak insulin concentration was reduced by more than 35% (T_{max} 42 ± 11 vs. 69 ± 22 min; $p<0.0001$). BioChaperone Lispro was cleared from the blood significantly earlier than Humalog, reflected in the time to half-maximum insulin levels after T_{max} (late $T_{50\%max}$ = 141 ± 43 vs. 173 ± 41 min, $p<0.0001$).

The acceleration of insulin lispro absorption translated into a significant acceleration of insulin action. The metabolic effect is triggered significantly earlier for BioChaperone Lispro than for Humalog with 30% faster onset of action (T_{onset} = 23.1 ± 7.0 vs. 34.4 ± 15.3 min; $p<0.0001$). The early metabolic effect is increased by 69% relative to Humalog during the first hour after administration ($AUC_{GIR\_0\text{-}1h}$ = 218 ± 88 vs. 129 ± 63 mg/kg; $p<0.0001$). The time to reach the maximal observed hypoglycemic effect is significantly shorter relative to Humalog (T_{GIR_max} = 99 ± 42 vs. 133 ± 45 min; $p=0.0002$).

Finally, the total insulin exposure and potency of insulin lispro was similar for both formulations.

“It is an outstanding result to improve by more than 35% the pharmacokinetics of insulin lispro. Strikingly, BioChaperone triggers an immediate entry of insulin lispro into the blood stream, which closely mimics the kinetics of physiological insulin release. This is particularly meaningful as this translates into a faster insulin action”, said Olivier Soula R&D director and deputy general manager. “Our last clinical results confirm the high value and versatility of the BioChaperone technology for insulin formulation to reach unique performances.”

The clinical data has been 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.

BioChaperone Lispro more closely mimics physiologic prandial insulin action

The main objective of prandial insulins is to control the rapid rise in glycaemia associated with digesting a meal. Ideally, the insulin release in the blood stream should begin immediately after the start of the meal as this is the case in physiological conditions. However, even with modern fast-acting insulin analogs, there is a lag time between the injection and presence of active insulin in the bloodstream. This results in the need to inject prandial insulin analogs around 15 minutes before the meal.

The ultra-fast action of insulin is key to reducing the risk of both hyper- and hypoglycemia. Hyperglycemia results from a delay in insulin response compared to glucose entry in the blood flow following a meal. Chronic hyperglycemia is correlated with cardiovascular complications in diabetic patients and represents a major health issue. The earlier onset and higher early bioavailability of BioChaperone Lispro compared to Humalog has the potential to reduce the incidence of hyperglycemic events. Conversely, hypoglycemia results from an excess of insulin relative to blood glucose concentration. The shorter exposure of BioChaperone Lispro compared to Humalog may also limit the incidence of hypoglycemic events.

“These clinical results demonstrate that BioChaperone Lispro is an ultra-fast-acting insulin that could be used at meal times or even after a meal. Moreover, as a result of its fast-in and fast-out profile, this ultra-fast-acting formulation of insulin lispro could reduce hyperglycemic and hypoglycemic events, which would be a key benefit for patients with diabetes”, said Dr. Tim Heise, medical doctor, CEO of Profil Neuss. “Ultra-fast acting insulin may also facilitate the development of an artificial pancreas, since today the ability of closed-loop algorithms to control glucose is severely limited by the slow onset of action of available prandial acting insulin analogs.” added Dr. Tim Heise.

Clinical Development Plan for Adocia’s prandial insulins

BioChaperone Lispro now has a complete clinical data package ready to support the next clinical trial, a dose-response study which will be launched this quarter. This trial will be conducted in Germany by the same CRO, Profil Neuss. According to the current design, the primary goal of the study is to examine the dose-response and dose-exposure of BioChaperone Lispro. The trial is expected to enroll 36 type I diabetic patients under automated euglycemic clamp conditions with three doses of BioChaperone Lispro and one dose of Humalog. Results are expected before the end of 2014.

Adocia plans to follow a similar development plan for HinsBet, the prandial fast-acting human insulin formulated using BioChaperone. HinsBet is on track to enter a phase IIa dose-response clinical trial expected to start in the third quarter of 2014.

In parallel, Adocia intends to meet both the FDA for a pre-IND meeting in 2014 and the EMA for a scientific advice to validate its clinical development plans for both prandial insulins.

These two insulin products fulfill all the FDA and EMA requirements in terms of chemical and physical stability. The BioChaperone technology for prandial insulin is protected by six patent families running until 2033.

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 of the formulation of a fast-acting human insulin, two Phases I and II studies of an ultra-fast acting insulin lispro and one Phase I/II on a unique combination of insulin glargine, the gold-standard of basal insulin and insulin lispro, a fast-acting insulin analog. Dose-escalating Phase IIa studies are planned for these three products in 2014.

Adocia has also obtained positive results on a Phase I/II study of 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 by an increased prevalence and impact of targeted pathologies, a growing and ageing population, a need to control public health expenditures and an increasing demand from emerging countries.

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

For more information: http://www.adocia.com

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registered by the Autorite des Marches Financiers on April 25, 2013 under number R13-017 (a copy of which is available on hhtp://www.adocia.com) and to the development of economic conditions, financial markets and the markets in which Adocia operates. The forward-looking statements contained in this press release are also subject to risks not yet known to Adocia or not currently considered material by Adocia. The occurrence of all or part of such risks could cause actual results, financial conditions, performance or achievements of Adocia to be materially different from such forward-looking statements.