



PRESS RELEASE

Adocia announces positive Phase 1b results of BioChaperone® Combo in patients with type 2 diabetes

- **BioChaperone Combo demonstrated significantly superior early prandial action and late metabolic effect compared to Humalog® Mix75/25™, consistent with a previous clinical study on patients with type 1 diabetes**
- **This study established the “proof-of-concept” that BioChaperone Combo has a similar effect to the separate injections of Lantus® and Humalog®, based on these two parameters, in patient with type 2 diabetes**
- **BioChaperone Combo, a unique combination of insulin analogs glargine and lispro, represents a two-fold market opportunity, addressing both the established premixed insulin market and a significant portion of the basal insulin market**

Lyon, France, November 25, 2015 – Adocia (Euronext Paris: FR0011184241 – ADOC) announced today positive topline results from a Phase 1b randomized double-blind crossover trial of BioChaperone Combo in 24 subjects with type 2 diabetes under euglycemic clamp. The study was designed to compare the pharmacodynamic profile of BioChaperone Combo (single dose of 0.8 U/kg) to that of Humalog Mix75/25 (Eli Lilly, single dose of 0.8 U/kg) and of the separate and simultaneous injections of Lantus (insulin glargine, Sanofi, single dose of 0.6 U/kg) and Humalog (insulin lispro, Eli Lilly, single dose of 0.2 U/kg). The two key parameters for this comparison were the early prandial effect ($AUC_{GIR}(0-2h)$) and the late basal effect ($AUC_{GIR}(24-30h)$) of the three treatments. Based on these two parameters, BioChaperone Combo was found to be significantly superior to Humalog Mix75/25 and exhibited no difference compared to the separate injections of Lantus and Humalog.

“It is remarkable to establish the proof of concept that a single product, BioChaperone Combo, could offer type 2 diabetes patients the same level of glucose control as a basal plus one bolus regimen.” said Simon Bruce, MD, Adocia’s Chief Medical Officer. “Importantly, the duration of action up to 30h should enable its use both as a once-a-day and a twice-a-day treatment. BioChaperone Combo could become a natural intensification step over basal insulin alone and may deliver a clear advantage over premix in terms of efficacy.”

Type 2 diabetes is a progressive disease requiring treatment intensification as the duration of disease increases. Basal insulin is the standard insulin initiation treatment and insulin glargine (Lantus, Sanofi) delivered in a single daily injection is currently the most used basal insulin worldwide. However, 50% of patients on basal insulin remain uncontrolled¹ and require prandial coverage to counter balance the glucose intake from one or more meals. Today, patients requiring intensified insulin therapy have two main treatment options: a premixed insulin, which is a formulation of a single insulin with both rapid and long actions, or two distinct insulins injected separately, a long-acting and a rapid-acting.

Premixed insulins (human or analog) are a standard treatment option for patients who require simple treatment regimens, such as the elderly, and generate almost \$5 billion in combined annual revenue worldwide². But premixed insulins do not offer ideal medical performance because of a delayed prandial action with increased risk of hypoglycemia, and a basal action profile shorter than 24 hours requiring two administrations per day.

The second option, a basal-bolus regimen, is not always considered a viable option for a large number of patients because of the need for two different insulins at different doses and a higher daily injection burden.

BioChaperone Combo is a unique formulation combining, in a 75/25 ratio, insulin glargine for the basal action and insulin lispro for the prandial action. BioChaperone Combo aims to deliver intensified insulin therapy that would be both as effective as the basal plus one bolus regimen and as simple to use as the premix products. In a previous study in patients with type 1 diabetes, BioChaperone Combo demonstrated a faster prandial effect and a longer basal action compared to premix.³

The first objective of the current study was to confirm these conclusions in type 2 diabetic patients. In the study, BioChaperone Combo was found to have a significantly higher metabolic effect in the first two hours vs. Humalog Mix75/25 ($AUC_{GIR}(0-2h)$ 294 ± 227 mg/kg for BioChaperone Combo vs. 174 ± 126 mg/kg for Humalog Mix75/25, $p = 0.0001$) and a longer basal action ($AUC_{GIR}(24-30h)$ 186 ± 133 mg/kg for BioChaperone Combo vs. 99 ± 102 mg/kg for Humalog Mix75/25, $p = 0.0105$). In a previous study in type 1 diabetes patients, the faster prandial effect of BioChaperone Combo was shown to lead to better glucose control after a standardized meal.⁴

The second objective was to compare BioChaperone Combo to separate injections of Lantus and Humalog. BioChaperone Combo was found to have a similar metabolic effect in the first two hours vs. the separate injections of Lantus and Humalog ($AUC_{GIR}(0-2h)$ 294 ± 227 mg/kg for BioChaperone Combo vs. 277 ± 184 mg/kg for Lantus and Humalog, $p = 0.5227$) and a similar basal action ($AUC_{GIR}(24-30h)$ 186 ± 133 mg/kg for BioChaperone Combo vs. 174 ± 140 mg/kg for Lantus and Humalog, $p = 0.6747$). This confirms the potential of BioChaperone Combo to be administered only once daily.

¹ Sanofi's presentation, JP Morgan Healthcare Conference, January 12, 2015

² Adocia's estimates based on Sanofi, Eli Lilly and Novo Nordisk annual reports, 2014

³ "Adocia Announces Preliminary Positive Clinical Results for its Combination of Long-Acting Insulin Glargine and Fast-acting Insulin Analog Lispro, BioChaperone® Combo", Press Release, February 27, 2014

⁴ "Adocia announces positive Phase 1b results on the post-meal effect of BioChaperone® Combo in patients with type 1 diabetes" Press release, November 4, 2015

No new or unexpected safety findings for BioChaperone Combo, Lantus, Humalog and Humalog Mix75/25 were observed in the study. No local reactions were seen at the site of administration for the three arms.

“These very promising results in patients with type 2 diabetes strengthen our strategy to position BioChaperone Combo as a simple and optimal option for insulin treatment intensification,” said Gérard Soula, CEO of Adocia. “We are aiming at a double opportunity: the large and established premix market, as well as a significant part of the basal insulin market. BioChaperone Combo is also designed to be competitively priced, which would be a key facilitator for market penetration in the current cost-focused healthcare environment.”

The results of the present study strongly support further clinical development of BioChaperone Combo. Additional clinical studies are planned in 2016 to confirm and extend the potential clinical benefit of BioChaperone Combo in the type 2 diabetic population relative to both basal insulin only and premixed insulin therapies. These studies will form the basis for designing a planned phase 3 clinical program.

Detailed results of the present trial, conducted by Profil GmbH in Germany, will be submitted for publication at the American Diabetes Association's 76th Scientific Sessions in June 2016.

About ADOCIA

Adocia is a clinical-stage biotechnology company that specializes in the development of innovative formulations of already-approved therapeutic proteins. Adocia's insulin formulation portfolio, featuring four clinical-stage programs and one preclinical program, is among the largest and most differentiated in the industry.

The proprietary BioChaperone® technological platform is designed to enhance the effectiveness and/or safety of therapeutic proteins while making them easier for patients to use. Adocia customizes BioChaperone to each protein for a given application in order to address specific patient needs.

Adocia's clinical pipeline includes a unique formulation of PDGF-BB for the treatment of diabetic foot ulcer and four novel insulin formulations for the treatment of diabetes: two ultra-rapid formulations of insulin analogs (BioChaperone Lispro U100 and U200), a rapid-acting formulation of human insulin (HinsBet U100) and a combination of insulin glargine and a rapid-acting insulin analog (BioChaperone Combo). Adocia is also developing a concentrated, rapid-acting formulation of human insulin (HinsBet U500).

In December 2014, Adocia signed a partnership with Eli Lilly for the development and commercialization of the BioChaperone Lispro programs.

Adocia's extended, early-stage programs include innovative monoclonal antibody formulations, featuring two ongoing collaborations programs with major pharmaceutical companies in the field, and the delivery of anticancer drugs using the proprietary DriveIn® nanotechnology platform.

Adocia aims to deliver "Innovative medicine for everyone, everywhere."

To learn more about Adocia, please visit us at www.adocia.com



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