



## PRESS RELEASE

## Adocia announces positive Phase 1b results on the post-meal effect of BioChaperone® Combo in patients with type 1 diabetes

- **BioChaperone Combo demonstrated significantly superior control of post-meal blood glucose compared to Humalog® Mix75/25™**
- **BioChaperone Combo, a unique combination of insulin analogs glargine and lispro, may prove to be a superior alternative to current premixed insulin products, which are associated with inadequate post-meal and fasting control**

**Lyon, France, November 4, 2015** – Adocia (Euronext Paris: FR0011184241 – ADOC) announced today positive topline results from a Phase Ib randomized double-blind crossover trial of BioChaperone Combo in 28 subjects with type 1 diabetes. The study, comparing the effect on post-meal glycemic control of individualized doses of BioChaperone Combo and Humalog® Mix75/25™ (Eli Lilly) injected at the beginning of standardized meals, met its primary endpoint, demonstrating superiority of BioChaperone Combo in the reduction of post-meal blood glucose over the first two hours (Delta-AUC-BG(0-2h)) compared to Humalog® Mix75/25™.

BioChaperone Combo is a unique formulation of a basal insulin, glargine, and a prandial insulin, lispro, in a 75/25 ratio. In a previous study in patients with type 1 diabetes, BioChaperone Combo demonstrated a basal action lasting over 30 hours. The objective of the current study was to document the post-prandial glucose control with BioChaperone Combo. Mealtime blood glucose control requires on the one hand limiting the early post-prandial blood glucose increase (0-2 hours post-meal) to avoid hyperglycemia and on the other hand preventing blood glucose decrease due to residual insulin (2-6 hours post-meal) to reduce the risk of hypoglycemia.

In this study, BioChaperone Combo has been demonstrated to be superior to Humalog® Mix75/25™ on these two criteria, consistent with tighter blood glucose control:

- BioChaperone Combo was associated with significantly lower blood glucose excursions in the first two hours vs. Humalog® Mix75/25™ (primary endpoint, Delta-AUC-BG(0-2h)=  $89.2 \pm 48.6$  mg\*h/dL vs  $117.7 \pm 47.6$  mg\*h/dL,  $p=0.0078$ ). This result is confirmed by a reduction of the maximum blood glucose level of 23 mg/dL (BGmax: ratio = 0.9;  $p=0.0003$ ).
- The minimum blood glucose level observed during the period with BioChaperone Combo was also significantly better controlled than with Humalog® Mix75/25™ (BGmin: ratio = 1.3;  $p=0.0030$ ). While this study was not designed to measure differences in hypoglycaemia between both treated groups, a lower number of hypoglycaemic events was observed with BioChaperone Combo vs. Humalog® Mix75/25™.

"We are glad to see that BioChaperone Combo achieved a superior performance on mealtime glycemic control over Humalog Mix in this study. Post-prandial glucose control is particularly important for diabetic patients requiring intensified insulin treatment," said Simon Bruce, MD, Adocia's Chief Medical Officer. "These results suggest that BioChaperone Combo could become a simple and more efficient alternative treatment option for people using premixed insulin."

No new or unexpected safety findings for BioChaperone Combo and Humalog® Mix75/25 were observed in the study. No local reactions were seen on the site of administration for either treatment.

Premixed insulins (human or analog) are a standard treatment option for patients who need simpler treatment regimens, such as the elderly, generating almost \$5 billion in combined annual revenue worldwide. Although these products offer an important treatment option for patients who need simpler twice daily injection regimens, versus more complex multi-injection basal-bolus regimens, they are associated with compromised mealtime and fasting glucose control and an increased risk of hypoglycemia.

"In addition to its very promising performance, BioChaperone Combo offers an opportunity for very competitive pricing, thanks to the combination of off-patent insulins." said Olivier Soula, R&D Director and Deputy General Manager of Adocia. "Medical benefit, ease of use and competitive pricing are key product attributes in the current cost-focused healthcare environment."

Additional clinical studies are planned in 2016 to further establish the medical benefit of BioChaperone Combo. A Phase Ib clinical trial is also ongoing in type 2 diabetes patients, to compare the pharmacodynamic profiles of BioChaperone Combo to those of Humalog® Mix™ and of the basal-bolus injection of Lantus® and d'Humalog®. Results for this study are expected before year end.

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 premixed insulin:*

Premixed insulins facilitate glycemic control by allowing the patient to inject only one product, twice daily. However, premixed insulins do not offer ideal medical performance because of a delayed prandial action, a short basal action profile (less than 24 hours) and an elevated risk of hypoglycemia.

Currently marketed premixed insulins are mixture of a protamine suspension providing basal action and a soluble portion for prandial action of the same insulin in variable proportions. They include products based on human insulin (such as Novolin<sup>®</sup>70/30 by Novo Nordisk or Humulin<sup>®</sup>70/30 by Eli Lilly) and products based on fast-acting insulin analogs (such as NovoMix<sup>®</sup> by Novo Nordisk and Humalog<sup>®</sup> Mix<sup>™</sup> by Eli Lilly). These products generate nearly \$5 billion in combined annual revenue worldwide.

### **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<sup>®</sup> 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 fast-acting formulation of human insulin (HinsBet U100) and a combination of insulin glargine and a fast-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<sup>®</sup> nanotechnology platform.

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

To learn more about Adocia, please visit us at [www.adocia.com](http://www.adocia.com)

**For more information please contact:**

<b>Adocia</b> G�rard Soula Chairman and CEO <a href="mailto:contactinvestisseurs@adocia.com">contactinvestisseurs@adocia.com</a> Tel.: +33 4 72 610 610	<b>Adocia Press Relations</b> <b>ALIZE RP</b> Caroline Carmagnol and Florence Portejoie <a href="mailto:caroline@alizerp.com">caroline@alizerp.com</a> <a href="mailto:adocia@alizerp.com">adocia@alizerp.com</a> Tel.: + 33 1 44 54 36 61
---	---

**Disclaimer**

*This press release contains certain forward-looking statements concerning Adocia and its business. Such forward-looking statements are based on assumptions that Adocia considers to be reasonable. However, there can be no assurance that the estimates contained in such forward-looking statements will be verified, which estimates are subject to numerous risks including the risks set forth in the 'Risk Factors' section of the Reference Document registered by the French Autorit  des march s financiers on April 30, 2015 under number R.15-032 (a copy of which is available on [www.adocia.com](http://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. This press release and the information contained herein do not constitute an offer to sell or the solicitation of an offer to buy Adocia shares in any jurisdiction.*