



PRESS RELEASE

Adocia announces positive topline results for the first clinical study of BioChaperone® Pramlintide Insulin in people with type 1 diabetes

- BioChaperone® Pramlintide Insulin (BC Pram Ins) is the first product to clinically demonstrate the feasibility of a fixed-ratio co-formulation of pramlintide and human insulin
- BC Pram Ins showed a significant 97% decrease in blood glucose excursion over the first two hours after the meal compared to Humalog®
- BC Pram Ins showed similar glucose control over the first two hours after the meal compared to separate injections of Symlin® and Humulin®
- All treatments were well tolerated

Lyon, France, September 5th, 2018 – 6:00 pm CET - ADOCIA (Euronext Paris: FR0011184241 – ADOC) the biopharmaceutical company focused on the treatment of diabetes and other metabolic diseases with innovative formulations of approved proteins, announced today positive pharmacodynamic and safety topline results from the Phase 1 study of BioChaperone® Pramlintide Insulin (BC Pram Ins), the ready-to-use co-formulation of pramlintide and human insulin. The proprietary BioChaperone® technology enables the solubilization and stabilization of pramlintide, the only FDA-approved amylin analog for the treatment of diabetes, in aqueous solution at neutral pH. BioChaperone unlocks the development of the first fixed-ratio combination of pramlintide with prandial insulins, aiming at improving post-prandial glucose control.

“These are encouraging results, confirming that a co-formulation of pramlintide with human insulin can reproduce the marked reduction of postprandial glucose shown in previous studies of pramlintide and insulin given separately,” said Dr. Matthew Riddle, Professor of Medicine, Oregon Health & Science University, Division of Endocrinology, Diabetes, & Clinical Nutrition. *“By mimicking the normal co-secretion of amylin and insulin with meals, this 2-in-1 combination has the potential to address the persisting unmet need for mealtime glucose control for people with diabetes.”*

This randomized, double-blind, active comparator-controlled, three-period cross-over study, enrolled 24 participants with type 1 diabetes. Subjects were randomly allocated to a sequence of three treatments, administered at the time of the intake of a standardized mixed meal. This study aimed to investigate the pharmacokinetics, pharmacodynamics, and the safety and tolerability of a single fixed dose of BC Pram Ins (containing 7.5U insulin and 45 µg pramlintide), compared on the one hand to separate and simultaneous injections of human insulin (7.5U, Humulin®, Eli Lilly) and pramlintide (45 µg, Symlin®, AstraZeneca), and on the other hand to an injection of rapid-acting insulin analog lispro (7.5U, Humalog®, Eli Lilly).

Treatment with BC Pram Ins resulted in a statistically significant 97% reduction of blood glucose excursions over the first two hours compared to Humalog (Mean(\pm SD) DeltaAUC_{GIR 0_2h} = 4 (63) mg*h/dL vs. 126 (74) mg*h/dL; $p < 0.0001$) and a comparable postprandial glycemic control to that of the separate injections of Humulin and Symlin (LS- Mean DeltaAUC_{GIR 0_2h} = 21 (66) mg*h/dL, n.s.).

“Our breakthrough consists in enabling the co-formulation of pramlintide and human insulin while preserving their known synergistic benefits in a single product injected at mealtime and intended to be as simple to use as a mealtime insulin.” said Dr. Olivier Soula, Adocia’s Deputy General Manager and Director of R&D, *“Following these convincing first clinical results, we are now eager to move forward with this project and are preparing additional clinical studies.”*

Using acetaminophen absorption as a marker of gastric emptying kinetic, this study further demonstrated that BC Pram Ins and Symlin + Humulin separate injections resulted in similarly slower gastric emptying compared to Humalog. This is a known and expected pharmacological effect of pramlintide, critical for smoothing meal glucose absorption and reducing post prandial blood glucose excursion which is thus preserved with the BC Pram Ins formulation. It is established that gastric emptying is abnormally rapid in people with type 1 diabetes and pramlintide is proven to help restore a slower and more physiologic gastric emptying.

All treatments were well tolerated. Notably, the overall number of hypoglycemia was similar between treatments (BC Pram Ins: n=4; Symlin + Humulin: n=3; Humalog: n=3) and there were no warnings on gastrointestinal side-effects with any of the administered treatments. As a reminder, hypoglycemia and gastrointestinal side effects have been previously associated with Symlin® clinical use.

Comparison of pharmacokinetic profiles of pramlintide and human insulin after a single dose administration of BC Pram Ins with that observed after simultaneous injections of pramlintide and human insulin was an additional objective of this study. These results will be published separately.

Adocia was the sponsor of this study, which was performed by Profil Neuss in Germany.

About BioChaperone® Pramlintide Insulin

BioChaperone Pramlintide Insulin is a fixed-ratio combination of the synergistic FDA-approved products pramlintide and human insulin. It is designed to deliver superior postprandial glycemic control for people with diabetes without the burden of separate administration of the two agents. Pramlintide (Symlin®, AstraZeneca) is the only FDA-approved analog of the pancreatic beta cell hormone amylin.

In people without diabetes, insulin and amylin are co-secreted by pancreatic beta cells and act in synergy to control blood glucose. While insulin controls glucose disposal, amylin modulates glucose appearance in the blood by suppressing liver glycogenolysis through glucagon inhibition and by slowing gastric emptying. Amylin also decreases food intake by inducing satiety. As diabetes progresses, and beta cell mass declines, the secretion of both insulin and amylin is diminished and, eventually, absent.

Pramlintide is approved in the USA for both type 1 and type 2 diabetes as an adjunct therapy to mealtime insulin treatment. The Phase 3 trials leading to pramlintide approval showed that, when added to an existing insulin regimen, pramlintide significantly improves post-prandial glucose control by flattening postprandial glucose excursions. After 6 months of use, pramlintide as an adjunct to insulin therapy, resulted in improved HbA1c, reduced prandial insulin consumption, and

resulted in weight loss compared to the use of insulin alone in both people with type 1¹ and with type 2² diabetes. Like amylin, pramlintide delays the timing and reduces the magnitude of postprandial blood glucose spikes. As intensified insulin therapy requires multiple daily injections and frequent glucose monitoring, however, the addition of daily mealtime injections of pramlintide has proved a challenge to patient adherence, compliance, and persistency. Adocia's BioChaperone[®] technology enables the combination of human insulin and pramlintide into a single product, aiming to deliver superior postprandial glycemic control while limiting the injection burden.

About ADOCIA

Adocia is a clinical-stage biotechnology company that specializes in the development of innovative formulations of already-approved therapeutic proteins and peptides for the treatment of diabetes and other metabolic diseases. In the diabetes field, Adocia's portfolio of injectable treatments is among the largest and most differentiated of the industry, featuring six clinical-stage products. Additionally, Adocia recently expanded its portfolio to include the development of treatments of obesity and short bowel syndrome.

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. Adocia's clinical pipeline includes five novel insulin formulations for the treatment of diabetes: two ultra-rapid formulations of insulin analog lispro (BioChaperone[®] Lispro U100 and U200), a combination of basal insulin glargine and rapid-acting insulin lispro (BioChaperone[®] Combo), a rapid-acting formulation of human insulin (HinsBet[®] U100), and a prandial combination of human insulin with amylin analog pramlintide (BioChaperone[®] Pramlintide Insulin). It also includes an aqueous formulation of human glucagon (BioChaperone[®] Glucagon) for the treatment of hypoglycemia. Adocia preclinical pipeline includes combinations of insulin glargine with GLP-1 receptor agonists (BioChaperone[®] Glargine GLP-1) for the treatment of diabetes, a ready-to-use combination of glucagon and a GLP-1 receptor agonist BioChaperone[®] Glucagon GLP1) for the treatment of obesity and a ready-to-use aqueous formulation of teduglutide (BioChaperone[®] Teduglutide) for the treatment of short bowel syndrome.

Adocia and Chinese insulin leader Tonghua Dongbao recently entered into a strategic alliance. In April 2018, Adocia granted Tonghua Dongbao licenses to develop and commercialize BioChaperone Lispro and BioChaperone Combo in China and other Asian and Middle-Eastern territories. The licensing included 50 million dollars upfront and up to 85 million dollars development milestones, plus double-digit royalties on sales. In June 2018, Tonghua Dongbao agreed to manufacture and supply active pharmaceutical ingredients insulin lispro and insulin glargine to Adocia globally, excluding China, to support Adocia's portfolio development in these territories.

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

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



¹ Whitehouse F, et al. Diabetes Care. 2002; 25(4): 724-730; Ratner RE, et al. Diabet Med. 2004; 21(11): 1204-1212.

² Hollander PA, et al. Diabetes Care. 2003; 26(3): 784-790.

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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 filed with the French Autorit  des march s financiers on April 19, 2018 (a copy of which is available on 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.

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