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PRESS RELEASE

Adocia initiates First-in-Human Clinical Study of BioChaperone® Pramlintide Insulin in people with type 1 diabetes

- **BioChaperone Pramlintide Insulin is the first fixed dose combination of pramlintide and human insulin for the prandial treatment of diabetes**
- **This meal test study will document pharmacokinetic and pharmacodynamic profiles of BioChaperone Pramlintide Insulin as well as its safety and tolerability in people with type 1 diabetes**
- **Study is expected to be completed in Q3 2018**

Lyon, France, April 16th, 2018 - 7:45 am 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 the initiation of a Phase 1 study of BioChaperone® Pramlintide Insulin (BC Pram Ins), its ready-to-use co-formulation of pramlintide and human insulin. The BioChaperone® proprietary technology enables the solubilization and stabilization, in aqueous solution at neutral pH, of pramlintide, the only FDA-approved amylin analog for the treatment of diabetes, hence allowing its combination with insulin.

This study aims to investigate the pharmacokinetics, pharmacodynamics, and the safety and tolerability of BC Pram Ins in people with type 1 diabetes compared to separate injections of human insulin (Humulin®, Eli Lilly) and pramlintide (Symlin®, AstraZeneca), and also to an injection of insulin lispro (Humalog®, Eli Lilly).

"*We are very pleased to initiate the clinical evaluation of BioChaperone Pramlintide Insulin as this combination may significantly improve post-prandial glucose control compared to available insulin regimens. Indeed, the co-formulation of insulin and pramlintide mimics the physiologic co-secretion of the synergetic hormones amylin and insulin from pancreatic beta cells."* said Dr. Stan Glezer, Adocia's Chief Medical Officer, *"By removing the adherence barrier presented by additional injections, we hope to fully realize the therapeutic potential of pramlintide for people with type 1 diabetes."*

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 controlling gastric emptying and decreases food intake by inducing a feeling of satiety. As diabetes progresses, neither insulin nor amylin are eventually secreted. While life-saving for people with type 1 diabetes and ultimately required for people with type 2 diabetes, insulin therapy alone is often not sufficient to achieve optimal prandial control, possibly because amylin is also needed. Many people using insulin therapy exhibit profound glycemic variability, especially after a meal, and they frequently fail to reach their treatment goals.

Pramlintide (Symlin®, AstraZeneca), a short-acting amylin analog, is the only molecule in this class approved by FDA for the treatment of diabetes. Pramlintide is approved in the USA for both type 1 and type 2 diabetes as an adjunct therapy to insulin treatment. The Phase 3 trials leading to pramlintide approval showed that, when added to an existing insulin regimen, pramlintide strongly 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 induced weight loss compared to the use of insulin alone in both people with type 1[1] and with type 2[2] diabetes. Like amylin, pramlintide delays the timing and reduces the amount of postprandial blood glucose. Some studies suggest that, because of the resulting delay in glucose appearance, human insulin's slow action profile makes it the most suited agent to combine with pramlintide in order to enable an optimal reduction of postprandial glucose excursion [3].

However, as intensified insulin therapy requires multiple daily injections and frequent glucose monitoring, the addition of three injections of pramlintide a day has proved a challenge to patient adherence, compliance and persistency. Indeed, to achieve optimal long-term effects, new treatment options in diabetes should not only demonstrate superior efficacy, but also avoid increasing the everyday burden of disease management, while remaining affordable. This should be achieved with this novel combination product, BioChaperone Pramlintide Insulin.

"*We are very proud to have achieved, by using our proprietary BioChaperone® technology, the first stable co-formulation of pramlintide and prandial insulin, a combination which we believe could improve the life of many people with diabetes."* said Dr. Olivier Soula, Adocia's Deputy General Manager and Director of R&D *"BioChaperone® Pramlintide Insulin is our second fixed-dose formulation to enter clinical trials, after BioChaperone Glargine Lispro, leveraging the ability of our technology to solubilize and stabilize peptides and proteins at neutral pH to enable innovative new therapeutic options."*

In this randomized, double-blind, active comparator-controlled, three-period cross-over study, 24 participants with type 1 diabetes will be randomly allocated to a sequence of three treatments, administered before the intake of a standardized mixed meal. The main objective is to compare the pharmacokinetic profile of pramlintide after a single dose administration of BC Pram Ins with that observed after simultaneous injections of pramlintide and human

[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.
[3] Weyer C. et al, Diabetes Care 2003; 26 :3074-3079.

insulin. Secondary objectives include the comparison of BC Pram Ins pharmacodynamic profile with those of the two comparators, as well as the assessment of the safety and tolerability of BC Pram Ins.

Adocia is the sponsor of this study, which will be performed by Profil Neuss in Germany. Study is expected to be completed in Q3 2018. This trial is registered and will appear on clinicaltrials.gov.

About ADOCIA

Adocia is a clinical-stage biotechnology company that specializes in the development of innovative formulations of already-approved therapeutic proteins and peptides. Adocia's portfolio of injectable treatments for diabetes, featuring five clinical-stage products and three preclinical products, is among the largest and most differentiated of the industry. Adocia expanded its portfolio to develop treatments for 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 to address specific patient needs.

Adocia's clinical pipeline includes four 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). An aqueous formulation of human glucagon (BioChaperone Human Glucagon) successfully completed a Phase 1 trial. Adocia also develops two combinations of insulin glargine with GLP-1 receptor agonists (BioChaperone Glargine Dulaglutide and BioChaperone Glargine Liraglutide), a ready-to-use aqueous formulation of teduglutide (BioChaperone Teduglutide) and a ready-to-use combination of glucagon and exenatide (BioChaperone Glucagon Exenatide), all of which are in preclinical development.

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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