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Adocia announces Positive Topline Results of Phase 1b Study for M1Pram in People with type 1 Diabetes

- Primary endpoint met: reduction of 69% of post-meal glycemic excursions (delta AUC-PG) over four hours vs. Novolog® (p=0.03)
- Mean weight loss of 1.6 kg for 24 days with M1Pram treatment versus an increase of 0.4 kg in the control group for this population with a mean BMI > 30 kg/m² (p=0.0065)
- 75% of patients in M1Pram group would recommend this medication, and 87% acknowledged its effects on appetite control
- Both treatments were well tolerated, and no serious adverse events were reported during the 24 days of treatment

7:30 am CEST - ADOCIA (Euronext Paris: FR0011184241 – ADOC, the “Company”), the biopharmaceutical company focused on the treatment of diabetes and other metabolic diseases with innovative formulations of proteins and peptides, announced today positive preliminary results from the extension part of the Phase 1b study of M1Pram (“ADO09”), a ready-to-use, fixed ratio co-formulation of pramlintide (Symlin®, AstraZeneca), the only FDA-approved analog of amylin, and A21G human insulin analog (“M1”), a mealtime insulin with a similar time-action profile to human insulin and the main circulating metabolite of insulin glargine. M1Pram is intended to replace prandial insulin therapy. By enabling the combination of two complementary hormones, it aims to improve post-meal glucose control and long-term outcomes.



“The beta cell secretes two hormones – insulin and amylin. Pramlintide is an amylin receptor agonist that helps decrease post-meal plasma glucose levels. Yet its use as a therapeutic has heretofore been limited by the fact that one has had to take separate pre-meal injections of insulin and pramlintide.”

Adocia has developed a product which combines an insulin analog together with pramlintide in a stable mixture, so that only a single pre-meal injection is needed. The glycemic results with M1Pram to date are quite promising as is the observed weight loss, which is important given the characteristics of the population taking prandial insulin. I look forward to the next series of clinical trials.” Jay S. Skyler, MD, MACP, Professor of Medicine, Pediatrics, & Psychology, in the Division of Endocrinology, Diabetes & Metabolism, Department of Medicine, University of Miami Leonard M. Miller School of Medicine.



"We are pleased to share these promising results of this additional study which confirm the strong potential of M1Pram for people with type 1 diabetes. Based on these results we decided to rapidly advance this program to Phase 2 study. Our Medical Advisory Board insisted on the potential value of this product in type 2 population treated with prandial insulin." Olivier Soula, Director of R&D and Deputy CEO "Additionally, the US patent for M1Pram was recently granted, which protects our pioneering position in the field."

This randomized, double-blind, active-controlled, two periods cross-over clinical trial aimed to assess the safety and efficacy of M1Pram. In this extension part of the initial study, patients requiring more than 40 U/ day prandial insulin were recruited, to document the safety/efficacy of high M1Pram titrations. Sixteen subjects with type 1 diabetes received multiple daily doses of M1Pram and Novolog (insulin aspart, Novo Nordisk) over two periods of 24 days each (including 4 days in the clinic and 20 outpatient days), following a run-in period to optimize basal insulin regimen. Glycemia was monitored using continuous glucose monitoring (CGM) system ensuring safety and efficacy assessments throughout the trial. At day 1 and day 24, pharmacokinetic, pharmacodynamic and gastric emptying profiles were measured after bolus injections of M1Pram or Novolog, administered immediately before a standardized mixed meal. The primary objective was to assess post-meal glucose profiles at day 24. Additionally, the study documented the safety and efficacy of M1Pram in an outpatient setting, as well as plasma glucose control as assessed by CGM over the entire period.

In the standardized meal test in clinics at day 24, treatment with individualized doses of M1Pram resulted in a 69% decrease of the glycemic excursion vs. Novolog over the first 4 hours after the meal (primary endpoint, DeltaAUC-PG0-4h, 47 ± 149 mg.h/dL vs 145 ± 162 mg.h/dL, LSM ratio 0.31 $p=0.0266$). This effect and its amplitude are consistent with the significant decrease of the same parameter observed in a previous meal test of M1Pram (study CT034). The pharmacological effect of M1Pram is further confirmed by a statistically significant decrease of the glycemic excursion by more than 100% vs. Novolog over the first 2 hours after the meal (DeltaAUC-PG0-2h, -4 ± 57 mg.h/dL vs 98 ± 54 mg.h/dL, $p < 0.0001$). The pharmacological effect of M1Pram was similar at Day 1 and Day 24, as assessed by the meal tests, demonstrating a sustained effect over three weeks.

Over the 23 days of treatment, average daily Time-in-Range (TIR, time spent within a range of blood glucose of 70-180 mg/dL), as assessed by CGM, was statistically improved for patients treated with M1Pram vs. Novolog by 6% (+58 min, $p=0.0432$). Average daily "tight" TIR (tighter range of 80-140 mg/dL, similar to the physiological range observed in people without diabetes) was statistically improved by 13% (+63 min, $p=0.0107$).

At the end of the treatment period, a significant average weight loss of 1.6 kg compared to baseline was observed in people treated with M1Pram. This weight loss was a statistically difference from the weight increase of 0.4 kg observed in people treated with Novolog ($p=0.0065$).

In terms of safety, both treatments were well tolerated, and no serious adverse event related to the treatments was reported. M1Pram demonstrated good local tolerance. Gastro-intestinal side-effects were observed with M1Pram, in line with the known effects of pramlintide. Most of them were mild and tended to decrease after 10 days. Incidence of outpatient hypoglycemic episodes were almost identical in the M1Pram arm compared to the Novolog arm. No severe hypoglycemic event was observed in either arm throughout the trial.

All other secondary endpoints related to the efficacy of M1Pram were achieved. Consequently, all the expected pharmacological benefits of pramlintide used as an adjunct of insulin were observed in this exploratory study after three weeks of treatment with M1Pram.

Additionally, a treatment satisfaction questionnaire was submitted to all patients after each treatment period. The results reflect the beneficial impact of M1Pram on individuals, since 87% of them reported an improved appetite control through the M1Pram study medication, and 75% of the patients would recommend it to other people with diabetes.

The extension part of this Phase 1b clinical study, performed in 16 additional subjects with type 1 diabetes, whose prandial insulin needs were between 40 and 75 U per day confirm the safety and efficacy of higher doses of M1Pram in an obese T1D population, which may benefit the most from improved weight control management. Historically described as lean and insulin sensitive subjects, T1D patients are now exposed to obesity epidemic with rates of overweight and obesity in T1D of already 65% in US and above 50% in Europe.

Adocia is the sponsor of the study performed by Profil Neuss in Germany.

The next study being planned is a Phase 2 clinical trial.

About Adocia

Adocia is a clinical-stage biotechnology company that specializes in the development of innovative formulations of therapeutic proteins and peptides for the treatment of diabetes and metabolic diseases. In the diabetes field, Adocia's portfolio of injectable treatments is among the largest and most differentiated of the industry, featuring four clinical-stage products. Adocia aims to expand its portfolio towards the treatment of other metabolic diseases and their comorbidities. 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 four novel insulin formulations for prandial 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) and one combination of a prandial insulin with amylin analog pramlintide M1Pram (ADO09). The clinical pipeline also includes an aqueous formulation of human glucagon (BioChaperone® Glucagon) for the treatment of hypoglycemia.

Adocia preclinical pipeline includes three products: a combination of rapid human insulin analogues and Pramlintide (BioChaperone LisPram), a combination of insulin glargine with GLP-1 receptor agonists (BioChaperone® Glargine GLP-1) for the treatment of diabetes and a ready-to-use combination of glucagon and a GLP-1 receptor agonist (BioChaperone® Glucagon GLP1) for the treatment of obesity.

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