ADOCIA

innovative medicine
for everyone, everywhere

PRESS RELEASE

# Adocia announces positive topline results of the exploratory Phase 1b study of ADO09 (M1Pram) in people with type 1 diabetes

- M1Pram is a unique co-formulation of pramlintide and a human insulin analog
- In a meal test administered in-clinic at day 24, treatment with M1Pram resulted in a reduction of the post-meal glycemic excursion[1] vs. Novolog® superior to 100% over the first two hours after the meal (*p=0.0001*), resulting in an overall decrease of 39% over the first four hours after the meal (n.s.)
- Over the three-week outpatient period, M1Pram treatment resulted in
  - A 70 min increase in average daily time spent in "tight" glycemic range[2] (*p=0.001*) vs. Novolog®
  - A 0.7 kg average weight loss vs. weight at baseline (*p=0.012*)
- All these results are in line with established pharmacological effects of pramlintide
- Both treatments were well tolerated, and no serious adverse events were reported during the 24 days of treatment

**A conference call in French is scheduled**
**for Monday April 27, 2020 at 6:00 pm (CET) to present these results**
Call number: 0033 (0)172 727 443

**Lyon, April 23rd, 2020-** 6:00 pm CET - 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 of a Phase 1b study of M1Pram ("ADO09"), a ready-to-use, fixed ratio co-

[1] "Glycemic excursion" is the increase in blood glucose ("glycemia") observed after a meal. In a person with type 1 diabetes, the treatment aims to minimize this excursion, as chronic hyperglycemia is associated with long term complications of the disease.

[2] "Tight" target glycemic range defined as 80-140 mg/dL, tight TIR

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 also the main circulating metabolite of insulin glargine. M1Pram is intended as a replacement to prandial insulin therapy; in enabling the combination of two complementary hormones, it aims to improve post-meal glucose control and long-term outcomes.

"*Remarkably, after only three weeks of treatment with M1Pram, all known pharmacological effects of pramlintide were observed in this clinical trial in people with type 1 diabetes*," said Prof. Thomas Pieber, Professor of Medicine at the Medical University of Graz, Austria. "*This trial confirmed the strong reduction of the postprandial glucose excursion previously observed in a clinical trial with M1Pram. Furthermore, the outpatient period showed improvement in time in target glycemic range without increasing the risk of hypoglycemia, as well as an improvement in weight control, two key medical benefits for people with type 1 diabetes.*"

"*We are pleased to be able to share the impressive results of this exploratory study, which confirm the strong potential of M1Pram to improve the lives of people with type 1 diabetes, by delivering a significant benefit over the standard of care in insulin therapy while also removing the burden of additional injections,*" commented Olivier Soula, Director of R&D and Deputy CEO. "*The positive results obtained across multiple endpoints motivated us to rapidly advance this program to a three- month, Phase 2 study. Additionally, the US patent for M1Pram was recently granted, which protects our pioneering position in the field in this territory.*"

This randomized, double-blind, active-controlled, 2 period cross-over clinical trial aimed to assess the safety and efficacy of M1Pram. 24 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. Subjects received an open continuous glucose monitoring (CGM) system which was used for safety and efficacy assessment throughout trial participation. 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 compare 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 39% decrease of the glycemic excursion vs. Novolog over the first 4 hours after the meal (primary endpoint, DeltaAUC-PG0-4h, 24±139 mg.h/dL vs 49±145 mg.h/dL, LSMratio 0.61, *p=0.5*). This effect and its amplitude are consistent with a significant decrease of the same parameter observed in a previous meal test of M1Pram[3], as well as during the meal test administered on Day 1 of the present study (DeltaAUC-PG0-4h, -25±179 mg.h/dL vs 60±164 mg.h/dL, LSMratio -0.48, *p=0.021*). Additionally, the pharmacological effect of M1Pram is further

[3] In a previous meal test comparing M1Pram to Humalog® (insulin lispro) in 24 subjects with type 1 diabetes (NCT03916640), a reduction of -41% of DeltaAUC-BG0-4h was observed (p=0.0052). Detailed results of this study were published during the 13th International Advanced Technologies and Treatment for Diabetes Conference (Madrid, Spain, February 2020).

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, -11±48 mg.h/dL vs 71±69 mg.h/dL, LSMratio -0,14, *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 5% (+51 min, *p=0.013*). 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 14% (+70 min, *p=0.002*).

At the end of the treatment period, a statistically significant average weight loss of 0.7 kg compared to baseline was observed in people treated with M1Pram (*p=0.012*). No weight loss was observed in people treated with Novolog.

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. In line with the known effects of pramlintide, gastro-intestinal side-effects were observed with M1Pram. Most of them were mild and tended to decrease after 10 days. Incidence of inpatient and outpatient hypoglycemic episodes were numerically higher, but not statistically different, in M1Pram arm compared to the Novolog arm. No severe hypoglycemic event was observed in either arm throughout the trial.

All other secondary endpoints relative 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 3 weeks of treatment with M1Pram. Detailed results of this trial have been accepted for publication at a major diabetes conference later this year.

Of note, this study has recently been amended to include 12 additional subjects with type 1 diabetes, whose prandial insulin needs are between 40 and 75 U per day. The purpose of this extension is to document the safety and efficacy of higher doses of M1Pram in a larger population, including one which may benefit the most from improved weight control management. The results of this extension are expected at the end of Q3 2020. Adocia is the sponsor of the study, which is being performed by Profil Neuss in Germany.

The next study is planned as a Phase 2 clinical trial in type 1 diabetes over a period of three months.

## 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 five 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 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) and a combination of a prandial insulin with amylin analog pramlintide (ADO09 or M1Pram). It also includes an aqueous formulation of human glucagon (BioChaperone® Glucagon) for the treatment of hypoglycemia. Adocia preclinical pipeline includes 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. Adocia is also exploring in preclinic the potential of its M1Pram combination to treat people with type 2 diabetes suffering from neurological comorbidities, including Alzheimer's disease.

In 2018, Adocia and Chinese insulin leader Tonghua Dongbao entered 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 agreements included USD 50 million upfront and up to USD 85 million 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 and commercialization.

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

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

ENTERNEXT | TECH40 | LABEL | 2015

ELIGIBLE PEA PME

ADOC LISTED EURONEXT

## For more information please contact:


| Adocia | Adocia Press Relations Europe | Adocia Investor Relations USA |
|---|---|---|
| Gérard Soula | **MC Services AG** | **The Ruth Group** |
| Chairman and CEO | Raimund Gabriel | Tram Bui |
| contactinvestisseurs@adocia.com | adocia@mc-services.eu | tbui@theruthgroup.com |
| Ph.: +33 4 72 610 610 | Ph.: +49 89 210 228 0 | Ph.: +1 646 536 7035 |


## 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 filed with the French Autorité des marchés financiers on April 22, 2020 (a copy of which is available at 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.*