CLOSER LOOK

MEMORANDUM

Adocia 3Q19 - No updates on M1Pram (fka ADO09) phase 1b trial; Cash equivalents at $43 million after tranche; Few pipeline updates - October 22, 2019

Executive Highlights

- **Adocia gave its 3Q19 update via press release and accompanying slide deck today.** The company closed the quarter with €39 million (~$43 million) in cash and cash equivalents, following the first €7.5 million tranche of a €15 million debt/warrant financing agreement with IPF Partners.
- **There were no further updates on the phase 1b trial for safety/efficacy of M1Pram (ADO09) given in 2Q19.** Adocia announced a new plan to investigate the compound in Alzheimer's Disease, which is slated to begin sometime in 2020.
- **Adocia provided a few updates on the BC Lispro development pipeline, including intended phase 3 trial initiation in China and an EU/US phase 3 filing planned for some time in 2020.** Trials for BC Lispro, BC Glucagon GLP-1, and BC Combo are set to begin in 2020, but no milestones have been disclosed for any of these ventures. No further updates on BC Pramlintide Insulin and the BC Lispro closed-loop system trials were shared.

See more on our top three highlights below, along with Adocia's expected upcoming milestones.

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Top Three Highlights

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3. As of September 30, Adocia held €32.5 million (~$36.2 million) in cash and cash equivalents, up from €20.7 million (~$23 million)

Diabetes/Obesity Pipeline Summary

Top Three Highlights

1. No Further Updates on Adocia's Pramlintide Insulin Candidate M1Pram (ADO09) Phase 1b Study; Phase 1 Study in Alzheimer's Disease Planned for 2020

Adocia emphasized M1Pram's (fka ADO09) proof-of-concept topline results initially announced in April and announced plans to investigate the compound in Alzheimer's Disease. As a reminder, phase 1 results shared in 1Q19 use of M1Pram conferred a significant 85% decrease in postprandial blood glucose vs. Humalog ($p<0.0001$) with safety and tolerability. The phase 1b trial was initiated in June 2019, and the primary outcome is the comparison between post-meal glucose profiles after bolus of ADO09 versus Novo Nordisk's rapid acting insulin NovoLog. All participants will be given standardized mixed meals at the end of a 24-day long multiple daily injection of either compound. As mentioned in 2Q19, results from this second phase 1b trial are expected in 4Q19. No further details were given on its status other than Adocia's current search for global partners in the venture.

- **Due to pramlintide's potential neuroprotective effects, Adocia will also be investigating M1Pram in patients with type 1 diabetes and Alzheimer's Disease.** Specifically, pramlintide has been associated with removing amyloid plaques linked to Alzheimer's Disease, so treatment with M1Pram may contribute to restoring brain activity hindered by plaques. Adocia did announce that a phase 1 study is slated to begin in 2020.

2. Next Steps for BioChaperone Lispro Development Include Phase 3 Filing in the US/EU in 2020, Start of Phase 3 Study in China Slated for 2020

Adocia provided a few updates on the BC Lispro development pipeline, including intended phase 3 trial initiation in China sometime in 2020. Though no update was given on whether Adocia and partner Tonghua Dongbao (THDB) received qualification requirements to begin a phase 3 study in China, the companies have targeted to begin this trial in 2020. They also shared that undisclosed milestones are attached to the study, which makes us wary on when, if in 2020, the trial will initiate - especially following the initial 1Q19 delay announcement. However, Adocia did offer more updates on US/EU trials, stating that a bridging study comparing BC Lispro to Humalog is planned for 1H2020. Adocia is also planning to file a phase 3 application in the US/Eu sometime in 2020, again, without a detailed timeline.

- **Adocia brought back their obesity pipeline, stating that the first-in-human study for BC Glucagon GLP-1 is planned to initiate in 2020.** Though no other timeline-specific details were shared, we are happy to have learned about this compound after being in the dark since the intial announcement of its entering phase 1 in 1Q19. We also learned of the company's plans for initiating BC Glucagon's phase 1/2 trial in 1H2020.
- **THDB plans to begin their BC Combo (75/25 basal insulin glargine/prandial insulin lispro) bridging study in China in 2020.** While we initially learned in 1Q19 that THDB was planning to begin this study sometime in 2019 to enable use of data from previous BC Combo development, there was no mention of this venture in the 2Q19 report. While we did not gain much clarity from this announcement, we are hoping that future updates in 2020 will include timelines for all BC products.
- **No update on BC Pramlintide Insulin (7.5 U human insulin/45 µg pramlintide) was given, as it appears that the candidate's studies have halted to prioritize development**

of ADO09. Adocia's 4Q18 update revealed that despite positive PD and safety results in phase 1, plans to begin a second, repeated administration trial for BC Pramlintide Insulin were pushed from 1Q19 to 2Q19. The only mention of the candidate in today's update was to reaffirm messaging from 1Q19 that its development has been somewhat deprioritized in an effort to push development of ADO09 forward.

- **After a phase 1 trial began in 1Q19, there were no further updates on BC Lispro in a closed-loop system (Beta Bionics' iLet pump and algorithm and Dexcom CGM).** According to the 1H19 report, the randomized, cross-over study will recruit up to 30 patients with type 1 to compare the PK/PD profiles of insulins lispro, aspart and BC Lispro in the iLet bionic pancreas, on an inter- and intrasubject basis. Just like in 1Q19 and 2Q19, we were unable to find any such trial on ClinicalTrials.gov, so it's unclear whether this study has recruited enough participants to begin or how prioritized it is in Adocia's pipeline.

3. As of September 30, Adocia held €32.5 million (~$36.2 million) in cash and cash equivalents, up from €20.7 million (~$23 million)

Total cash holdings further jumped to €39 million following the first tranche of a debt financing agreement with IPF partners, penned in October 2019. The first tranche of €7.5 million was subscribed immediately upon signing the deal, and a second tranche of equal value is available to Adocia until December 31, 2019. Notably, dilution is limited to 1.89% of the company's share capital for each tranche. The first three quarters of 2019 saw $2 million in revenue, mainly due to licensing agreements with Tonghua Dongbao from April 2018 to develop, manufacture, and commercialize BC Lispro and BC Combo in China, Asia, and the Middle East. Financial debt came in at €8 million compared to €7.1 million in 4Q18.

- **3Q19 also concluded arbitrations between Lilly and Adocia over Lilly's termination of the licensing agreement for BC Lispro.** The €14.3 million in damages awarded to Adocia from first round arbitrations was received in September 2019, but second round claims were dropped in August 2019.

Diabetes/Obesity Pipeline Summary

The table below reflects the latest status, as far as we are aware, of Adocia's diabetes/obesity-related pipeline products. Items highlighted in yellow indicate notable changes to the pipeline in recent months.

Product	Indication	Status	Timeline/Notes
BioChaperone Lispro (ultra-rapid-acting insulin)	Type 1 and type 2 diabetes	Phase 3-ready	▪ Phase 1 closed-loop trial began 1H19 ▪ Phase 2 bridging study to begin in 3Q19, added new APIs (lispro and glargine); phase 3 study filing (US/EU) planned for 1Q20; Phase 3 initiation in China expected in 2019 ▪ Secured Tonghua Dongbao as development and commercialization partner in China, retained rights to US, EU, Japan

			▪ Positive topline phase 1b results released in December 2017; Candidate showed significantly faster offset vs. Novo Nordisk's Fiasp in first-ever head-to-head comparison of ultra-rapid-acting insulins
HinsBet (rapid-acting human insulin)	Type 1 and type 2 diabetes	Phase 3-ready	▪ Adocia plans to license to a "regional player" in emerging markets for phase 3 ▪ Preclinical U500 formulation in development ▪ Positive phase 2a results reported in 4Q16
M1Pram (fka ADO09) (pramlintide/A21G human insulin)	Type 1 diabetes	Phase 1b	▪ Positive phase 1 results released April 2019 ▪ Phase 1/2 planned to begin 2H19 ▪ Promising first-in-human results show ~85% reduction in glycemic excursion first two hours after meal vs. Humalog ▪ Phase 1 trial in patients with type 2 and Alzheimer's planned for 2020
BioChaperone Pramlintide Insulin (pramlintide/ human insulin)	Type 1 diabetes	Phase 1/2	▪ Deprioritized in favor of ADO09 ▪ Second Phase 1/2 trial scheduled to begin in 2Q19 ▪ Positive phase 1 results released in September 2018; Second Phase 1/2 trial scheduled to begin in 2Q19 ▪ Positive phase 1 results released in September 2018; Candidate conferred significant 97% reduction in postprandial excursions compared to Humalog

BioChaperone Combo (75/25 insulin glargine/insulin lispro premix)	Type 1 and type 2 diabetes	Phase 1	▪ Secured Tonghua Dongbao as development and commercialization partner in China, retained rights to US, EU, Japan ▪ Positive phase 1b results reported in 1Q18
BioChaperone Glucagon (liquid-stable glucagon)	Ready-to-inject hypoglycemia rescue treatment (type 1 and type 2 diabetes); also in development for dual hormone AP (type 1 diabetes)	Phase 1	▪ Final phase 1/2 trial initiation delayed to 2H19 ▪ Positive topline phase 1 results reported in 4Q17
BioChaperone Insulin Lispro/Pramlintide	Type 1 diabetes	Preclinical	▪ Apparently de-prioritized in favor of human insulin/pramlintide combo ▪ Phase 1 initiation delayed from "end of 2017" timeline ▪ Added to pipeline in January 2017
BioChaperone Insulin Lispro/Exenatide	Type 2 diabetes	Preclinical	▪ Added to pipeline in January 2017
BioChaperone Insulin Glargine/Liraglutide	Type 2 diabetes	Preclinical	▪ Phase 1 initiation delayed from "end of 2017" timeline ▪ Added to pipeline in September 2016
BioChaperone Insulin Glargine/Dulaglutide	Type 2 diabetes	Preclinical	▪ Added to pipeline in September 2016
BioChaperone Glucagon GLP-1	Obesity	Preclinical	▪ Phase 1 trials delayed to 2H19; adjacent with GLP-2 agonist teduglutide for SBS ▪ Added to pipeline in January 2018 as one of Adocia's first non-diabetes candidates ▪ First-in-human study planned for 2020

--by Ursula Biba, Rhea Teng, Terry Vance, and Kelly Close