CLOSER LOOK

MEMORANDUM

Adocia 1Q17 - Evaluation continues for new licensing partner for BioChaperone Insulin Lispro; Several pipeline candidates to advance to clinical trials in 2017; Strong €52 million (~$55.4 million) cash position - April 18, 2017

Executive Highlights

- Adocia's 1Q17 update highlighted the advancement of BioChaperone Insulin Lispro into phase 3 as the company's main priority. The product's licensing partnership with Lilly was terminated in late January, and Adocia intends to continue preparations for phase 3 while seeking a new clinical partner.
- In-human studies of BioChaperone Glucagon are slated for 2Q17 and the first clinical trials for BioChaperone basal insulin/GLP-1 agonist formulations and BioChaperone multi-hormonal rapid-acting insulin co-formulations are slated for 4Q17.

Adocia provided its 1Q17 update via press release today. Reported below are our top five highlights from the update:

1. Adocia underscored that its main priority is to advance its ultra-rapid-acting insulin candidate BioChaperone Insulin Lispro into phase 3 trials, despite the January termination of its licensing agreement with Lilly for the candidate.

2. Results from Adocia's phase 1/2 trial for BioChaperone Combo (insulin glargine/insulin lispro) in people with type 2 diabetes are expected in 2Q17.

3. Adocia announced its intention to license phase 3-ready HinsBet to a "regional player" in emerging markets to support the continued development and hopeful launch of this rapid-acting formulation of human insulin.

4. Adocia additionally highlighted its extensive pipeline of preclinical programs, including several recently-announced BioChaperone-based projects expected to enter clinical trials in 2017: in-human studies of BioChaperone Glucagon are slated for 2Q17 and the first clinical trials for BioChaperone basal insulin/ GLP-1 agonist formulations and BioChaperone multi-hormonal rapid-acting insulin co-formulations are slated for 4Q17.

5. Adocia had cash and cash equivalents of €52 million (~$55.4 million) as of March 31, down from €58 million (~$64 million) in 4Q16 and €64.2 million (~$73.1 million) in 1Q16.

Top Five Highlights

1. Adocia underscored that its main priority is to advance its ultra-rapid acting insulin candidate BioChaperone Insulin Lispro into phase 3 trials. As a reminder, BioChaperone Lispro was previously under development in partnership with Lilly until, in an unexpected announcement at the end of January, Lilly terminated the licensing agreement in favor of the development of its own internal ultra-rapid insulin lispro candidate. The rights for BioChaperone Lispro have now reverted back to Adocia, and the company has reaffirmed its intention to continue preparations for phase 3 while seeking a new clinical partner. Adocia management emphasized in a conference call recently after the announcement of the partnership termination that Lilly's decision was grounded purely in economics and should not reflect negatively on the clinical profile of the BioChaperone candidate, which has undergone six positive phase 1/2 studies, including a particularly promising one presented at ADA 2016. Indeed there is plenty of room for

innovation in the currently ~$6 billion rapid-acting insulin market, which continues to face intense competitive pressure from the increased uptake of GLP-1 agonist and SGLT-2 inhibitor therapy to address postprandial excursions. We especially see upside for faster-acting insulins in pumps and closed-loop systems, and also to reduce hypoglycemia through faster-onset, faster-offset. Adocia noted that it will be closely observing how Novo Nordisk's Fiasp (faster-acting insulin aspart) will fare in this challenging climate, as the only ultra-rapid acting insulin currently on the market. (Fiasp has launched in Canada, the UK, and Germany and recently resubmitted its NDA for FDA approval.) Refer to our full coverage of the termination of this licensing partnership for more information on Lilly's decision, and how this may impact the greater rapid-acting insulin market.

2. Results from Adocia's phase 1/2 trial for BioChaperone Combo (insulin glargine/insulin lispro) in people with type 2 diabetes are expected in 2Q17, slightly behind the 1Q17 timeline reported in Adocia's most recent 4Q16 and full year update. This trial is expected to complement existing positive results in people with type 1 diabetes presented at ADA 2016. Adocia has two more studies of BioChaperone Combo planned - a dose-response study (slated for 2Q17) and a brief two-week outpatient study (slated for 4Q17) - all intended to prepare for entry into phase 3. We assume that Adocia will also look to partner for phase 3 development of BioChaperone Combo - it'll be interesting to see if perhaps a single partner may look to scoop up Adocia's BioChaperone portfolio.

3. Adocia announced its intention to license phase 3-ready HinsBet to a "regional player" in emerging markets to support the continued development and hopeful launch of this rapid-acting formulation of human insulin. Adocia recently reported positive phase 2a results for HinsBet in October 2016. The study (n=36) was a randomized, double-blind, three-treatment, three-period cross-over trial comparing the effectiveness of HinsBet (BioChaperone human insulin) on post-meal glycemic control versus Lilly's Humulin (human insulin) and Humalog (insulin lispro). During the first hour after a meal, HinsBet significantly reduced glucose excursion vs Humulin (p-0.0002) and was not significantly different from Humalog (p=0.5373).

4. Adocia additionally highlighted its extensive pipeline of preclinical programs, including several recently-announced BioChaperone-based projects expected to enter clinical trials in 2017: (i) co-formulation of insulin glargine with liraglutide (Novo Nordisk's GLP-1 agonist Victoza); (ii) co-formulation of insulin glargine with dulaglutide (Lilly's GLP-1 agonist Trulicity); (iii) co-formulation of insulin lispro with pramlintide (AZ's amylin analogue Symlin); (iv) co-formulation of insulin lispro with exenatide (AZ's GLP-1 agonist Byetta); and (v) liquid-stable glucagon.

- **At least one of Adocia's BioChaperone basal insulin/GLP-1 agonist products is expected to enter phase 1 studies by 4Q17.** With these new candidates - co-formulations of insulin glargine with liraglutide (Novo Nordisk's Victoza) and dulaglutide (Lilly's Trulicity), both of which were first announced in September 2016 - Adocia will enter the competitive landscape for basal insulin/GLP-1 agonist combinations, which currently features Novo Nordisk (Xultophy, once-daily), Sanofi (Soliqua, once-daily), Lilly, PhaseBio, and AntriaBio (all with once-weekly formulations in their preclinical pipelines). It's unclear what the dose timing for Adocia's combinations will be. Given that the "next-generation" of these combos is shaping up to emphasize once-weekly dosing, we're curious how Adocia might position its own product - given that insulin glargine and liraglutide at least will likely be off-patent by the time these candidates arrive on the market, perhaps Adocia will offer its combinations at a discount as a kind of biosimilar combination.
- **At least one of Adocia's BioChaperone multi-hormonal rapid-acting insulin combination products is expected to enter phase 1 studies in 4Q17.** First announced in January 2016, the insulin lispro/pramlintide (AZ's amylin analogue Symlin) product is intended for people with type 1 diabetes and the insulin lispro/exenatide (AZ's GLP-1 agonist Byetta) product is intended for people with type 2 diabetes. To date, Adocia's candidates represent the only rapid-acting insulin/pramlintide and rapid-acting insulin/GLP-1 co-formulations currently in development, and the only rapid-acting insulin co-formulation products in general for that matter (both the recently-approved Xultophy [Tresiba/Victoza] from Novo Nordisk and Soliqua [Lantus/

lixisenatide] from Sanofi are basal insulin combinations). Given that the non-insulin biologics in these combinations are noted for their postprandial glucose lowering effect, we're curious if these combination products could serve as "next-generation" prandial insulins in a sense by providing greater postprandial control than is currently offered by standalone rapid-acting insulins. We're especially curious as to the effect of these agents on hypoglycemia - presumably, combination with gut peptides allows for a smaller dose of insulin lispro which could reduce hypoglycemia risk.

- **BioChaperone human glucagon is expected to enter phase 1 studies in 2Q17.** First announced in June, this project aims to develop an aqueous formulation of human glucagon for the rescue treatment of severe hypoglycemia and for use in a dual hormone closed-loop system. Several other soluble glucagon formulations are in more advanced stages of development, including Zealand's dasiglucagon (recently completed phase 2), Xeris' line of G-Pen glucagon autoinjectors (phase 3), and Lilly's soluble glucagon candidate (phase 1). See our glucagon competitive landscape for a complete overview.

5. Adocia had cash and cash equivalents of €52 million (~$55.4 million) as of March 31, down from €58 million (~$64 million) in 4Q16 and €64.2 million (~$73.1 million) in 1Q16. Management noted that it expects to receive reimbursement of research activities and tax credit for 2016 in the next few months, which should increase Adocia's cash position by €7.8 million (~$8.3 million). Overall the company expressed optimism regarding its strong cash position, which will enable it to finance its entirely diabetes-focused portfolio.

-- by Abigail Dove, Helen Gao, and Kelly Close