INNOVATIVE MEDICINE FOR EVERYONE EVERYWHERE
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LETTER FROM THE CHAIRMAN
2018, the comeback...

Year 2018 was marked by a comeback on three fronts: first, in commercial terms, with the signature of a partnership with the Chinese company Tonghua Dongbao for our two major projects, BioChaperone Lispro and BioChaperone Combo; then legally, with a favorable decision in the first phase of our arbitration with Eli Lilly for an award of $11.6 million; and finally, scientifically, with the establishment of the “proof of concept” for our BioChaperone pramlintide insulin combinations to treat insulin dependent type 1 diabetes; this in addition to the progress made in the rest of our pipeline on our different projects.

The partnership with Tonghua Dongbao covered our two flagship products, BioChaperone Lispro and BioChaperone Combo, and is the result of our strategic decision to identify a local partner in China while maintaining rights to both projects in the rest of the world, particularly in the United States, Europe, and Japan. In signing supply agreements for insulins lispro and glargine, the two hormones used in BioChaperone Lispro and BioChaperone Combo, we have strengthened our alliance with Tonghua Dongbao. Moreover, we have opened up to new opportunities to collaborate, especially with biopharmaceutical companies operating in the diabetes space that lack capacity to produce insulin. Both companies have now committed to an alliance that takes advantage of their complementary expertise. I’d like to emphasize just how exceptional this partnership is, both in terms of the structure of the collaboration and the investment that Tonghua has made.

The Chinese market, unlike Western markets, is growing fast. In addition, the vast majority of the 115 million people with diabetes in China do not receive treatment. Importantly, our agreement with Tonghua Dongbao has helped us to end 2018 with a net profit. This means we can continue to develop our portfolio of innovative products.

Another great source of satisfaction has been the very promising first clinical results of combining pramlintide with human insulin: BioChaperone Pram Insulin. Once again, Adocia has achieved a great first by successfully combining two incompatible hormones in a single formulation.

Coming off this initial success, we have pursued additional candidates for his combination by developing an original formulation, ADO09, that combines pramlintide with an insulin analog that is the major metabolite of insulin glargine. Note that this is the first combination in our portfolio that does not use our BioChaperone technology. ADO09 was clinically tested in early 2019 in a study which showed that the combination produces the same results as the separate injections of pramlintide and insulin in terms of postprandial blood glucose control in people with type 1 diabetes. Based on this clinically established “proof of concept”, we believe our combination ought to provide people with type 1 or type 2 diabetes with the remarkable therapeutic effects of pramlintide, which is currently underutilized because of the number of additional injections it requires.

Finally, the other notable event this year was the positive decision made by the Tribunal in the first phase of the arbitration proceedings initiated with Eli Lilly to enforce one of the clauses of the contract signed in 2014. The Tribunal awarded Adocia with $11.6 million plus interest, to be paid after the end of the second phase of the procedure. The second phase of the arbitration is complete. It concerns Eli Lilly’s improper use of Adocia’s discoveries and confidential information. As part of this arbitration, Eli Lilly has made counterclaims for a total of $188 million. We believe these claims are unfounded and we are resolutely taking action to defend our rights. The arbitration decision for the second phase is expected to be handed down by the third quarter of 2019. During that same year 2018, Eli Lilly also brought proceedings before an Indianapolis court to enforce its property rights over its own patents for which some employees of Adocia might be acknowledged as inventors. Once again, in these proceedings, we will vigorously defend the interests of the company, our shareholders, and our employees.

On behalf of the board of Directors, I would like to thank all Adocia employees, who over the past two years have shown so much talent and enthusiasm in the face of adversity. I would also like to warmly thank our shareholders, who continue to support us in our plans to develop more effective products for people living with type 1 and type 2 diabetes.

Gérard Soula
Chairman and Chief Executive Officer
Adocia’s mission is to improve everyday life for people with diabetes and other metabolic diseases by developing innovative, more physiologic, and easy-to-use treatments.

To this end, Adocia has developed BioChaperone®, a proprietary technology platform enabling the development of high-performance medical products based on previously approved therapeutic proteins and peptides. This reformulation approach builds on the accumulated safety and efficacy data of these approved proteins. It also fits Adocia’s vision to make its innovations accessible to as many people as possible, by limiting the time and costs of development and avoiding expensive investments in new manufacturing facilities. BioChaperone molecules are easy to manufacture and relatively inexpensive.

To date, Adocia’s research team has developed more than 500 BioChaperone molecules which can be selected to suit specific therapeutic proteins and the targeted medical need. BioChaperone molecules interact physically with proteins and peptides to form reversible complexes which retain the biological activity of the active product.

BIOCHAPERONE® TECHNOLOGY
DEMONSTRATING THE POTENTIAL OF THERAPEUTIC BIOMOLECULES

Three potential properties of these complexes have been demonstrated:
- Increased solubility of proteins that are insoluble at physiological pH
- Stabilization of proteins during storage
- Faster sub-cutaneous absorption.

BioChaperone technology therefore makes it possible to improve the performance of active products, or make them easier to use, or even combine together several synergetic therapeutic agents considered physically incompatible.
In 2018, Adocia’s proprietary portfolio included six clinical and three preclinical programs. The company’s strategy is to license, based on proof of concept in humans, these innovations to pharmaceutical companies which will oversee late-stage development and commercialization. This business model, which focuses on the early stages of development, is less capital-intensive than full development to commercialization and can provide a faster return on investment.

In addition to its own portfolio of products, Adocia offers its partners the opportunity to use BioChaperone technology to co-develop new treatments for patients on the basis of their proprietary compounds:

- Improved performance of existing products
- Combinations of complementary therapeutic agents
- Development of “ready-to-use” products.
OUR “INNOVATIVE FORMULATION” DEVELOPMENT STRATEGY IS ALIGNED WITH THREE KEY TRENDS IN THE CURRENT HEALTHCARE ENVIRONMENT.

AN APPROACH THAT MEETS CURRENT HEALTHCARE CHALLENGES

Large pharmaceutical companies looking for innovation
Increased development of biosimilars and generics is compelling pharmaceutical companies to quickly replace their flagship products that have fallen into the public domain. Together with cost pressures in healthcare, this explains why roughly 50% of products sold by large pharmaceutical companies now come from external research. Adocia’s model fits with this approach, with the added advantage of improving existing products. This approach also helps manage the medicinal product lifecycle by generating more efficient, patent-protected “second generation” agents for the companies that sell them.

Constrained global pharmaco-economic context
The growth and aging of the population, as well as increasing control of healthcare expenditure, adds to the pressure on the cost of treatments, especially for the so-called “mass” indications such as diabetes. BioChaperone technology was designed to address these economic constraints by bringing therapeutic advances while controlling development and production costs of finished products. In this way BioChaperone provides an opportunity to achieve competitive and sustainable prices in the long term for healthcare systems.

Demand from emerging countries
Demand for pharmaceutical products in emerging markets is growing rapidly. For example, more than 100 million of the 425 million people living worldwide with diabetes live in China. Faced with this exponential growth, particularly in mass indications, these countries must rationalize healthcare costs.
By developing potential “best-in-class” products based on already available proteins, our strategy is particularly suitable for meeting the massive demand from emerging countries. This aligns with Adocia’s vision in developing “innovative medicine for everyone, everywhere.”
Since its inception, Adocia has built a unique expertise in the diabetes field with the development of a large portfolio of injectable BioChaperone based treatments for type 1 and type 2 diabetes. Today, Adocia is recognized as a leader in the formulation of injectable products.
Two types of diabetes
Diabetes is a chronic disease in which patients suffer from high levels of sugar in the blood (hyperglycemia). With time, chronic hyperglycemia is responsible for serious long-term micro and macrovascular complications: heart disease, strokes, kidney failure, retinopathy, neuropathy, and more.

Women with diabetes
4 to 5 times more at risk of cardiovascular complications

Men with diabetes
2 to 3 times more at risk of cardiovascular complications

There are two main types of diabetes:

**Type 1:**
Auto-immune disease, most often diagnosed early. People with type 1 diabetes make antibodies which attack the insulin-secreting beta-cells of the pancreas. When approximately 90% of these beta-cells have been destroyed, treatment with insulin is necessary for survival.

**Type 2:**
Progressive disease characterized by cellular resistance to insulin and the slow but relentless deterioration of beta cells, which eventually leads to a decrease in insulin production.

10% Type 1 / 90% Type 2
Breakdown of the two types of diabetes within the population affected by the disease

Source: International Diabetes Federation, 2017

In 2045, the proportion of people with diabetes is expected to exceed 8% in all regions of the world except Africa.
A complex hormonal imbalance

In a person without diabetes, glycemia is regulated by an array of metabolic hormones acting in synergy to keep glycemia levels within a very precise range.

Four hormones, in particular, play a key role:

- **Insulin and amylin** are co-secreted by the beta cells with a peak during meals and act in synergy. Insulin helps cells capture glucides while amylin induces satiety, inhibits glucagon production, and slows down gastric emptying towards normal.

- **GLP-1** is produced after a meal and works in synergy with insulin and amylin by stimulating insulin secretion, inhibiting glucagon secretion, promoting satiety and slowing gastric emptying.

- **Glucagon** is a hyperglycemic agent. It promotes the release of glucose into the bloodstream, particularly between meals and during physical or mental exertion.

### Insulin therapy

For all people with type 1 diabetes and around 25% of people with type 2 diabetes, insulin is a necessary treatment. There are three main types of insulin-based treatment products:

- **Basal insulins** (once a day) to manage glycemia throughout the day.
- **Prandial insulins** (taken before each meal) to prevent glycemic excursions occurring after meals.
- **Premixed insulins** (twice a day), which combine a basal component and a prandial component to reduce the number of injections per day.

Over time, insulin therapy has moved towards increasingly effective treatments, from purified animal insulin, to recombinant human insulin, to insulin analogs. These different "generations" co-exist on the global market. Insulin now represents 50% of the value of the global diabetes treatment market.

**Insulin therapy is required for all people with type 1 diabetes and 25% of those with type 2.**

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**SCHEMATIC REPRESENTATION OF THE SECRETION PATTERNS OF FOUR KEY METABOLIC HORMONES AT MEAL TIME**

IN 2018, ADOCIA AND TONGHUA DONGBAO ENTERED INTO A STRATEGIC ALLIANCE THAT COVERS BOTH DEVELOPMENT AND SALES LICENSES FOR TWO ADOCIA PRODUCTS, AND SUPPLY AGREEMENTS FOR INSULIN LISPRO AND INSULIN GLARGINE.

STRATEGIC ALLIANCE WITH TONGHUA DONGBAO

For Adocia, this alliance is, firstly, an opportunity to develop BioChaperone Lispro and BioChaperone Combo in the Chinese market and other markets Tonghua Dongbao covers. Secondly, it allows Adocia to expand the pool of potential partners for these products on the key American, European and Japanese markets by accessing the manufacturing infrastructure required to sell the products on a large scale.

Who is Tonghua Dongbao?

Tonghua Dongbao Pharmaceutical Co. Ltd (Tonghua Dongbao) is a company based in China, trading on the Shanghai Stock Exchange. It operates on local and international markets, mostly in research and development, production, and distribution of pharmaceutical products. Tonghua Dongbao was the first Chinese company to produce recombinant human insulin, with a production capacity of several metric tons per year. In 2017, Tonghua Dongbao earned 78% of its revenue through insulin therapy, with a market share of 26% in China for products derived from recombinant human insulin.

Of particular note, the company sells the premixed insulins Gansulin 30R and Gansulin 50R: Gansulin R, a prandial insulin, and Gansulin N, a basal insulin. Tonghua Dongbao is also developing several biosimilar insulin analogs (insulin glargine, aspart, and lispro) and an analog of the GLP-1 receptor (liraglutide).

Now, thanks to its alliance with Adocia, Tonghua Dongbao is demonstrating its ambition to compete with international insulin actors with new-generation products that are reaching unprecedented levels of efficacy.

TESTIMONIAL
RÉMI SOULA, BUSINESS DEVELOPMENT AND LEGAL DIRECTOR AT ADOCIA
“The growth of Tonghua Dongbao on the Chinese insulin market has been very rapid. In line with a market transitioning to modern insulins, Tonghua Dongbao has now added capacity for cutting-edge analog insulin production. His strongly motivated our decision to collaborate with this very dynamic company.”

25%1
annual growth of Tonghua Dongbao

26%1
Tonghua Dongbao’s share of the Chinese human insulin market

1. Data provided by Tonghua Dongbao
The Chinese market
China has the highest population of any country and is also the country with the most people with diabetes: an estimated 115 million people there live with the condition1. Though only 30 million patients were treated in 2018, that number is expected to double by 2025² due to better diagnostics, greater access to medicines, and an improvement in treatment reimbursement, which will support an annual growth of over 12% for diabetes therapeutics product³. Premixed insulins currently account for 65% of the Chinese insulin market³.

Licensing and supply agreements
In 2018, Adocia and the leading Chinese insulin company Tonghua Dongbao signed a strategic alliance.

Adocia granted Tonghua Dongbao two licenses to develop and commercialize BioChaperone Lispro and BioChaperone Combo in China and other regions of Asia and the Middle East. The licenses included an upfront payment of $50 million, development milestone payments which could reach $85 million, and double-digit royalties on sales.

In June 2018, Tonghua Dongbao agreed to manufacture and supply Adocia with the pharmaceutical ingredients insulin lispro and insulin glargine globally, except for China, to support the development of Adocia’s portfolio in those regions.

The supply agreements signed with Tonghua Dongbao open new partnering opportunities for Adocia with companies that lack insulin production infrastructure but do have a strong presence in the diabetes therapeutic area.

>100 million
people with diabetes in China¹

60 million
people expected to receive treatment in 2025²

65 %
Volume of premixed insulin in China³

1. IDF 2017
2. Novo Nordisk Market Capital Days 2017 Presentation
3. IQVIA Data, volume, 2018
**PROJECTS IN CLINICAL DEVELOPMENT**

**ADOCIA’S PORTFOLIO OF INJECTABLE PRODUCTS FOR THE TREATMENT OF DIABETES IS ONE OF THE LARGEST AND MOST DIFFERENTIATED IN THE INDUSTRY INCLUDING SIX PRODUCTS IN CLINICAL STAGE.**

**BioChaperone® Lispro U100 & U200**

*More physiologic ultra-rapid insulins*

*9 phase 1/2 clinical trials*

An ultra-rapid insulin is an insulin that has a more rapid action profile than that of insulin analogs currently on the market. This faster action is desirable because, in a healthy person, eating a meal triggers the immediate secretion of insulin to metabolize carbohydrates.

To mimic this “physiologic” action profile, injected prandial insulins must act very rapidly and for a duration limited to a few hours. Currently, human recombinant insulin and prandial insulin analogs must be injected 5-15 minutes (insulin analogs) to 30 minutes (human insulin) before meals. An injection at mealtime, or just after, would make it possible to better determine the appropriate insulin dose as the exact contents of the meal would be known, and also to avoid early or delayed dosing, which can lead to hypo- or hyperglycemia, both of which can cause severe short and long-term consequences.

It would also give patients some flexibility regarding the time of administration, thereby improving quality of life.
Adocia business report 2018 PAGE 18

Next steps for BioChaperone Lispro

Based on the strong clinical performance of BioChaperone Lispro, Adocia is looking for a partner to enter Phase 3 clinical trials and to commercialize the product, mainly on the American, European, and Japanese markets. In 2019, Adocia plans to conduct a so-called “bridging” study to show the comparability of Tonghua Dongbao’s API lispro and the lispro used in previous BioChaperone formulations (Humalog® lispro). This will make it possible to transfer all the clinical results obtained for BioChaperone Lispro to date into the Phase 3 dossier.

Adocia has developed two ultra-rapid insulin lispro formulations:
• BioChaperone Lispro U100 (standard insulin concentration, 100 U1/mL)
• BioChaperone Lispro U200 (twice as concentrated).

The BioChaperone Lispro insulins could provide significant medical benefit to all users of prandial insulin. In particular, they could respond to the specific needs of:
• People requiring high doses of insulin:
  BioChaperone Lispro U200, a concentrated ultra-rapid insulin, may also improve glycemic control for these people whilst also limiting the volume required at each injection.

Testimonial

Dr. Bruce Bode, M.D., FACE, Associate Professor at Emory University (United States of America)

“Insulin pumps are used by around 40% of people with type 1 diabetes in the United States. For these people, the emergence of hybrid closed-loop administration systems is a huge step forward towards better glycemic control and better quality of life. In addition to its rapid onset of action, the “faster-off” effect observed with BioChaperone Lispro [vs. Fiasp & Novolog] could be critical to optimizing the effects of the algorithms used in these systems. That is why this product is bringing so much hope for better solutions for managing this condition.”

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• Children with diabetes: it is very difficult to predict precisely when and how a child will eat. To avoid risk of severe hypoglycemia, children with diabetes are often injected before or after meals, but that can lead to hyperglycemia. Over time, chronic hyperglycemia is correlated with serious complications.
• Insulin pump users: the development of ultrarapid insulin is a key element to facilitate the development of fully automated insulin pumps (also called “artificial pancreas” or “automated insulin delivery systems”) that would deliver insulin in real time depending on the patient’s blood glucose levels. Concentrated ultrarapid insulin (U200) could also facilitate the miniaturization of these devices and increase patient autonomy.
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Ongoing study of BC Lispro in the iLet™ system from Beta Bionics

In January 2019, Adocia announced the beginning of a trial to test the ultra-rapid insulin BioChaperone Lispro in an autonomous insulin delivery system, the iLetTM from BetaBionics. The iLet, when used in an insulin-only mode, is a so-called “hybrid closed-loop” system, made up of an insulin pump controlled by a clinically tested algorithm, that calculates the necessary dose of insulin based on blood glucose level measured in real time, and administers it automatically. The use of an ultra-rapid insulin in a semiautonomous system is expected to improve the system’s responsiveness and therefore its performance in terms of glycemic control. The results for this trial are expected in 2019.

To date, BioChaperone Lispro insulins have been tested in nine clinical studies (phase 1/2) with positive results for people with type 1 or type 2 diabetes and healthy volunteers, using syringes or pumps. They have systemically shown a faster profile than the analog insulins Humalog® and Novolog®, and, in a recent Phase 1 trial in people with diabetes using pumps, a profile at least as fast as the first ultra-rapid insulin Fiasp®. The acceleration of the end of the pharmacokinetic curve, in particular, is considered key to “closing the loop” in the context of an artificial pancreas.

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BioChaperone® Combo

Alternative to premixed insulin for simple, effective insulin therapy

Five phase 1/2 clinical trials

Type 2 diabetes is a progressive disease that requires treatment to be intensified gradually. To reach the target blood glucose level, it may be recommended to add a prandial insulin to a patient’s treatment regimen, or to replace the basal insulin with a premixed insulin. Premixed insulins are a fixed combination of a soluble portion and a precipitated portion of a rapid-acting prandial insulin analog, usually injected twice a day. It is therefore a simpler regimen than the multiple insulin injections: a single product, twice a day at a fixed dose (rather than two products, four times a day at variable doses), but it suffers from a delayed but prolonged prandial action, with a higher risk of hypoglycemia, and a basal action profile that is too short.

To meet the medical need for a regimen as simple as that of premixed insulin but as effective as a multiple-injection regimen, Adocia has developed BioChaperone® Combo, a combination of insulin glargine (basal, Lantus®, Sanofi) and insulin lispro (prandial, Humalog®, Eli Lilly). Indeed, BioChaperone technology makes it possible to solubilize insulin glargine at neutral pH thus enabling its combination with a prandial insulin.

BioChaperone Combo represents an opportunity to significantly improve treatment for patients, especially in countries where premixed insulins dominate, such as China.

To date, BioChaperone Combo has been tested in five positive clinical studies (phase 1/2), in people with type 1 or type 2 diabetes. They systematically demonstrated a more rapid profile than that of Humalog® Mix 75/25TM and a similar profile to that of the separate injections of Lantus® basal insulin and Humalog® prandial insulin.

Next steps for BioChaperone Combo

Adocia is actively looking for a partner to complete late-stage development and commercialization of BioChaperone Combo in regions not licensed to Tonghua Dongbao.

TESTIMONIAL:
GÉRARD SOULA, CEO OF ADOCIA

“We are very pleased and excited to enter into this strategic partnership with Tonghua Dongbao, the second-leading premixed human insulin provider in China. BioChaperone Combo is the most important project in this collaboration as premixed insulins remain the most popular insulin therapy in China.”

POST-PRANDIAL BLOOD GLUCOSE LEVEL AFTER ADMINISTRATION OF BIOCHAPERONE COMBO

Study in 28 subjects with type 1 diabetes (NCT#02514954)

These results were presented by Dr. Steve Edelman (UCSD) at the 76th Scientific Sessions of the American Diabetes Association (June 2016).
HinsBet®

More affordable rapid-acting insulin
2 phase 1/2 clinical trials

Human insulin, still predominantly used in many emerging countries because of its lower price, acts more slowly than analog prandial insulin. HinsBet® is a human insulin formulation incorporating BioChaperone to accelerate its action profile while benefiting from the lower price of human insulin.

HinsBet achieved positive clinical results in two phase 1/2 studies in people with type 1 diabetes, demonstrating that its onset of action was similar to that of a prandial analog insulin (Humalog).

Next steps for HinsBet

Based on the positive results of phase 1b and in light of HinsBet’s particular potential in emerging countries, where human insulin is more commonly used, Adocia intends to seek one or more partners to continue developing HinsBet on these markets.

BioChaperone® Glucagon

Ready-to-use formulation of human glucagon
1 phase 1 clinical trial

In a person without diabetes, glucagon is secreted in the event of hypoglycemia or exertion to keep blood glucose in a normal range. In a diabetic person, glucagon production is imbalanced and does not allow the body to react effectively to hypoglycemia (see, p. 12.)

Human glucagon for injection is therefore the only approved treatment for severe hypoglycemia, which can sometimes be fatal if not managed. Currently available products are unfortunately very difficult to use in emergency situations, as they come in the form of lyophilized human glucagon requiring reconstitution just before the injection. Recent studies assessing the ease of use of these kits show that 80% of the time, users are unable to correctly reconstitute and/or administer the recommended dose.

BioChaperone Glucagon is a ready-to-use, stable, human glucagon aqueous solution to treat severe hypoglycemia, but it could also be used in chronic applications, like the artificial bi-hormonal pancreas (insulin and glucagon).

BioChaperone Glucagon has been successfully tested in a phase 1 study in people with type 1 diabetes, and showed a pharmacokinetic and pharmacodynamic profile similar to that of the freshly reconstituted product.

Next steps for BioChaperone Glucagon

Adocia plans to initiate a second phase 1/2 study in the fourth quarter of 2019. This study could be the last before entry into phase 3. In parallel, Adocia is selecting a high-quality, easy-to-use auto-injector for use in delivering BioChaperone Glucagon.

77 %

of people with diabetes live in a low- or middle-income country

80 %

failure rate when using currently available glucagon kits

1. International Diabetes Federation, 2016
2. Locemia 2015
ADO09 (Pramlintide Insulin)

**Combination of two synergistic hormones for optimal prandial treatment**

**1 phase 1 clinical trial**

Combining two synergistic agents, pramlintide and insulin, ADO09 is designed to achieve better postprandial glycemic control for people with diabetes, without the additional burden associated with the injection of two different products.

Pramlintide is the only analog of the hormone amylin approved in the United States to treat type 1 and type 2 diabetes, as a supplement to mealtime insulin therapy. Like amylin (see p. 12), pramlintide delays the entry and reduces the quantity of glucose circulating in the blood.

Pramlintide used as an adjunct to insulin therapy greatly improves postprandial control by flattening postprandial glycemic excursions. After six months of use, adding pramlintide to insulin therapy is correlated with improved HbA1c, reduced prandial insulin consumption, and weight loss, compared with insulin therapy used alone in patients with type 11 or type 2 diabetes2. However, to the extent that intensive insulin therapy requires multiple injections per day and frequent monitoring of blood glucose levels, the addition of three pramlintide injections per day has proved problematic in terms of patient acceptance, compliance, and persistence.

Adocia’s proprietary formulation ADO09 is for a fixed-ratio combination, in a single product, of pramlintide and the human insulin analog A21G (“A21G human insulin”) at pH4. A21G human insulin is the main metabolite of the insulin analog glargine3, approved by the FDA.

Human insulin A21G has pharmacokinetic and pharmacodynamic profiles similar to those of human insulin and is stable at pH4. By using insulin glargine, millions of people with diabetes have been exposed to A21G human insulin, which is therefore considered safe4.

In a first-in-human clinical trial of ADO09 with people with type 1 diabetes, ADO09 showed a significant 85% reduction in glycemic excursions in the two hours following a meal compared with Humalog®, and a glycemic control similar to separate injections of Symlin® (pramlintide) and Humulin® (human insulin) during the two hours following a meal. All treatments were well tolerated.

**Next steps for ADO09 Pramlintide Insulin**

Adocia plans to initiate a second phase 1/2 study in the first half of 2019.

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**TESTIMONIAL**

**PROF. ROBERT RATNER,**
**PROFESSOR OF MEDICINE AT GEORGETOWN UNIVERSITY, WASHINGTON, D.C. (UNITED STATES OF AMERICA)**

“I believe this combination [ADO09] has the potential to finally deliver on the promise of pramlintide for a large number of patients, by addressing the significant unmet need for tighter postprandial control and lower glycemic variability without the burden associated with another product and a higher number of injections.”

---

4. Lantus® label, Section 12.3.
5. Conway et al, Diabetes Med 2010

…of type 1 diabetes patients in the United States are overweight5
BioChaperone® Glargine GLP-1 for the treatment of diabetes

Agonists of the GLP-1 receptor ("GLP-1s") act in a complementary manner with insulin to improve glycemic control while reducing adverse effects. To intensify treatment without increasing the number of injections, combinations of basal insulin and GLP-1 have recently been approved to treat type 2 diabetes. (Xultophy® from Novo Nordisk and Soliqua® from Sanofi).

BioChaperone Glargine GLP-1 leverages our expertise in solubilizing glargine at neutral pH, to combine it with liraglutide (Victoza®, Novo Nordisk) or dulaglutide (Trulicity®, Eli Lilly).

BioChaperone Glargine GLP-1 is currently in preclinical development.
In January 2018, Adocia announced it would expand its portfolio to include new therapeutic indications that could benefit from BioChaperone technology.

**BioChaperone® Glucagon GLP-1 for the treatment of obesity**

Recent studies have shown that a multi-hormonal approach that targets GLP-1 receptors and other receptors like those of glucagon and GIP could increase energy expenditure and promote major weight loss in people with obesity.

Based on the BioChaperone Glucagon formulation, Adocia is developing a combination of human glucagon and a GLP-1 analog, currently in preclinical development.

**BioChaperone® Teduglutide for the treatment of short bowel syndrome**

In people with short bowel syndrome (SBS), the intestine is too short to absorb enough food. In some severe cases, patients need parenteral or enteral nutrition, which has a highly negative effect on their quality of life.

Revestive® (teduglutide, Shire), an agonist of GLP-2 that promotes growth of intestinal villi and therefore reduces the rate of flow through the intestine, reduces the frequency of parenteral nutrition. Unfortunately, this treatment only exists as a lyophilized powder that must be reconstituted before each daily injection (22 steps). BioChaperone technology makes it possible to develop a liquid formulation that is stable and ready-to-use, aiming to improve quality of life for patients suffering from this severe disease.

**PRECLINICAL PIPELINE**

<table>
<thead>
<tr>
<th>BC</th>
<th>BioChaperone</th>
<th>Gla: insulin glargine</th>
<th>GLP-1: GLP-1 receptor agonist</th>
<th>GLP-2: GLP-2 receptor agonist</th>
<th>GCG: Glucagon</th>
<th>SBS: short bowel syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In Vitro</strong></td>
<td><strong>PC</strong></td>
<td><strong>Phase I/II</strong></td>
<td></td>
<td></td>
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<tr>
<td>BC Gla GLP-1</td>
<td></td>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BC GLP-2</td>
<td>SBS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BC GCG GLP-1</td>
<td></td>
<td>Obesity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

37% of American adults are obese¹

---

2. In the United States and Europe Jeppesen PB, J Parenter Enteral Nutr. 2014 May;38(1 Suppl):85-13S.
Revenue in 2018 was €47.4 million, €37.1 million of which came from licensing agreements signed with Tonghua Dongbao at the end of April. The non-refundable upfront payment of $50 million (€41.1 million) paid at the signature of the contract is recorded partially as revenue (€37.1 million) for year 2018 based on the progress of research and development services provided by Adocia as part of the transfer and development of the products.

As at the end of December, licensing revenue also included a total of €10.3 million from a contractual installment contested by Eli Lilly and for which Adocia obtained a favorable arbitration judgment in August 2018.

Operating expenses in 2018 were €44.2 million and were affected by additional costs related to the arbitration proceedings brought against Eli Lilly. Activity in 2018 was focused on preparing and conducting clinical trials and supporting our Chinese partner Tonghua Dongbao.

Net earnings in 2018 were €7.6 million.

---

### REVENUE UP BY €28 MILLION

#### ALLOCATION OF OPERATING INCOME

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research agreements and Licensing revenues</td>
<td>47.4</td>
<td>19.5</td>
</tr>
<tr>
<td>Grants, research tax credit, and others</td>
<td>6.5</td>
<td>7.7</td>
</tr>
<tr>
<td>TOTAL (M€)</td>
<td>53.9</td>
<td>27.2</td>
</tr>
</tbody>
</table>

#### ALLOCATION OF OPERATING EXPENSES

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purchased used in operations</td>
<td>2.2</td>
<td>1.7</td>
</tr>
<tr>
<td>Payroll expenses</td>
<td>14.9</td>
<td>13.3</td>
</tr>
<tr>
<td>External expenses</td>
<td>16.3</td>
<td>17.0</td>
</tr>
<tr>
<td>Legal fees</td>
<td>9.2</td>
<td>2.0</td>
</tr>
<tr>
<td>Taxes and contribution</td>
<td>0.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Depreciation, amortization and provisions</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>TOTAL (M€)</td>
<td>44.2</td>
<td>35.3</td>
</tr>
</tbody>
</table>
### A STRONGER CASH POSITION

Receiving the upfront payment of $45 million (€37.2 million) net of withheld tax from Tonghua Dongbao, as well as a stable level of expenses (aside from arbitration costs), means the company was able to reach a **cash position** of nearly €40 million at the end of December 2018.

In addition, the Arbitration Tribunal ordered Eli Lilly to make the contested installment payment of $11.6 million, plus interest. In December 2018, the amount due was €11.9 million, and is to be paid in 2019 upon closure of the last stage of arbitration.

### BALANCE SHEET (€M) 2018 2017

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-current assets</strong></td>
<td>9.1</td>
<td>9.1</td>
</tr>
<tr>
<td><strong>Current assets</strong></td>
<td>21.1</td>
<td>9.9</td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>39.8</td>
<td>34.8</td>
</tr>
<tr>
<td><strong>TOTAL ACTIF</strong></td>
<td>70.0</td>
<td>53.8</td>
</tr>
<tr>
<td><strong>Equity</strong></td>
<td>45.8</td>
<td>36.9</td>
</tr>
<tr>
<td><strong>Long-term provisions</strong></td>
<td>4.9</td>
<td>2.2</td>
</tr>
<tr>
<td><strong>Financial debt</strong></td>
<td>7.2</td>
<td>7.6</td>
</tr>
<tr>
<td><strong>Other current liabilities</strong></td>
<td>9.7</td>
<td>7.1</td>
</tr>
<tr>
<td><strong>Deferred revenue</strong></td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL LIABILITIES</strong></td>
<td>70.0</td>
<td>53.8</td>
</tr>
</tbody>
</table>

### 2018-2019 stock market results

**FROM 01/01/2018 TO 04/29/2019**

The share price in 2018 was affected in April 2018 by the signature of the Tonghua Dongbao contract: over 780,000 shares were traded over two days, bringing the share price from €16.30 to €19.72 for an increase of over 20%.

The second half of 2018 was characterized by low share activity (an average of 13,661 shares traded per day during the second half of the year); the share price was €16.54 at the end of 2018. During the first few months of 2019, the volumes traded were higher, and the share price rose to €18.04 on April 30, 2019.

**IPO on February 20, 2012 at share price of €15.88**
2018 PERFORMANCE AND GOVERNANCE

Board of directors

Gérard Soula has been Chairman of the Board of Directors and Chairman-Chief Executive Officer of Adocia since 2005. A PhD in organic chemistry, he graduated from IAD d'Aix-Marseille before receiving his MBA from IAE de Marseille. Co-author of over 120 patents.

Olivier Soula
Deputy General Manager, PhD in physical chemistry of polymers, ENSIC Mulhouse graduate and MBA graduate of IAE de Lyon. Co-author of 40 patents.

Rémi Soula
Director of Business Development and Legal, received his doctorate in polymer science and did his post-doctorate at the Max Planck Institute in Potsdam. He holds an MBA from HEC Paris. Co-author of over 30 patents and six scientific publications.

Valérie Danaguezian
Chief Financial Officer, ISC graduate. She worked as a financial manager before moving into leadership positions in the healthcare and biotechnology industry.

Board of directors

Gérard Soula
Chairman of the Board of Directors

Olivier Soula
Director

Olivier Martinez
Director, member of the Audit Committee, Investment Director at Bpifrance Investissement

Laurent Arthaud
Director, Bpifrance Investissement representative, Head of the Salary Committee, Deputy CEO of Bpifrance Investissement

Dominique Takizawa
Independent Director, Head of the Audit Committee, CFO of Institut Mérieux

Ekaterina Smirnyagina
Independent Director, Member of the Salary Committee, Investment Director at Capricorn Venture Partners (Belgium)

From left to right:
Rémi Soula,
Valérie Danaguezian,
Dominique Takizawa,
Olivier Martinez,
Gérard Soula,
Laurent Arthaud,
Ekaterina Smirnyagina,
Olivier Soula.

FINANCIAL CALENDAR 2019

April 15
Publication of revenue from Q1

May 16
Annual General Meeting, Paris, France

July 17
Publication of half-year results as at June 30

October 22
Publication of revenue from Q3
HUMAN RESOURCES

The Adocia team has remained stable in terms of numbers in 2018: turnover remains very low. New hires were mostly in key roles to advance Adocia towards late stage development, and this trend in the team is continuing in 2019.

The Adocia team is notable for its gender equality (number of employees, pay, training, etc.) and its youth.

<table>
<thead>
<tr>
<th></th>
<th>Phds</th>
<th>All Employees</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>52</td>
<td>39%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>49%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>51%</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Average age 35

Everyone has a future at Adocia

Training and development of all employees is a central priority in Adocia’s HR policy: the goal is to encourage everyone to participate in scientific conferences; seminars; professional development; team building activities; coaching sessions; in-house trainings led by Adocia experts; and an annual lecture with a scientist, philosopher, historian, or doctor, etc. famous in his or her field in order to help employees develop and expand their skills.

USA Subsidiary

In March 2015, Adocia created a subsidiary in the USA, which is managed by Stephen Daly, US General Manager. In 2018, Mike Nguyen joined the US team as Head of Business Development, New Therapeutic Areas. Opening a United States subsidiary has been essential to increase the visibility of Adocia in this key market. This has enabled close contact with opinion leaders in the diabetes field and has helped foster relations with the American financial community.

TESTIMONIAL

ÉLODIE, PHYSICAL CHEMISTRY TECHNICIAN AT A REFLECTION DAY WITH ALL ADOCIA EMPLOYEES

“Adocia is built like a big family that shares a common goal. Recruitment is based on understanding people as human beings. That is why there is good inter-department rapport and true team spirit. Also, the spaces promote communication and dialog. Everyone is brought together by passion for their work, expertise, the desire to advance, and curiosity.”

TESTIMONIAL

ÉMILE, THIRD-YEAR ENGINEERING STUDENT AT ESPCI PARIS

“During my six-month internship in the biology department at Adocia, I have made so much progress! I have learned to be a self-starter on an interesting, innovative project. I have developed my communication skills with my mentor and tutor, and also with the technicians who have supported me. I have gained tons of theoretical and technical knowledge, like how to use cells to test therapeutic proteins. I have explored a great working environment and met some of the nicest colleagues. What a terrific experience!”
A stimulating Chinese collaboration

China, as a nation, is betting on strategic development of the latest biotechnologies. Tonghua Dongbao aligns with this trend.

TESTIMONIAL

VALENTIN, YOHANN, MARC, AND PERAN, TECHNICIANS AND ANALYTIC RESEARCHERS

“Going to visit our partner Tonghua Dongbao let us explore a Chinese pharmaceutical company that has very high standards and meticulous people who know their field well. It was a really good experience.”

TESTIMONIAL

KAI, ALLIANCE MANAGER

“Tonghua Dongbao’s 27 years of experience in insulin production combined with Adocia’s 13 years of experience in innovation makes for a strong alliance that will respond to the challenges of diabetes in China and rest of the world. Adocia’s teams are fully committed to this partnership.”

Alone you go faster, together you go further

The HR Club of Listed Biotechnology Companies (Cellectis, Erytech, Innate Pharma, Onxéo, Poxel, Transgènè, DBV, and more) created by Géraldine Favre Soula, HR Director at Adocia, creates a space for regular sharing of best HR practices regarding issues specific to biotech companies. The club met in 2018 in Paris at Cellectis, and in Marseille at Innate Pharma.

Sharing is caring

TESTIMONIAL

DIANE, PHYSICAL CHEMISTRY TECHNICIAN

“The idea of a company compost bin was instantly popular with Adocia employees and the department, which supported me by buying a compost bin. A team of a dozen volunteers quickly formed to work together to compost peels gathered from meeting rooms or brought from home by employees. Over the years, the volume of organic waste has increased a lot, which shows that Adocia employees are gradually buying into the project. We are now producing so much compost that we were able to give some to a local community garden. Very soon, we will also use it in the Adocia community garden, which I’m sure will be a successful, fulfilling adventure to share with our colleagues.”
Forthcoming Events 2019 – 2020

**June 3-6**
BIO, Philadelphia, USA

**June 7-11**
ADA, San Francisco, USA

**September 16-20**
EASD, Barcelona, Spain

**October 7-8**
Partnership in Drug Delivery, Boston, USA

**November 11-13**
Bio Europe, Hamburg, Germany

**November 21-22**
Salon Actionaria, Paris, France

**December 5-7**
World Congress on Insulin Resistance, Los Angeles, USA

**January 2020**
JP Morgan, New York, USA

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The forward-looking statements contained in this document 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 document and the information it contains does not constitute an offer to sell or the solicitation of an offer to purchase or subscribe for Adocia shares in any country.

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Adocia
115 avenue Lacassagne
69003 Lyon
France
Tél. +33 4 72 610 610
www.adocia.com