Innovative medicine for everyone, everywhere

Annual report 2013

ADOCIA
The year 2013 was paved with both good and bad news. The major news, which promoted the value of ADOCIA, came from our clinical results on our projects of innovative formulations of insulin. We are very happy and very proud of the results obtained in our clinical trials of Phase I/II on our product “Ultra-fast-lispro” and on the “Insulin Combo” which brought the “proof of concept” of the efficacy of our insulin-based formulations thanks to the BioChaperone® technology. With these studies, ADOCIA has reached a major step. Based on the results obtained with type 1 diabetic patients, the probability of success of these products being brought to market has increased very significantly. The reactions of interest shown by certain pharmaceutical companies committed to diabetes, further to the publication of our results, are concrete signs of this.

In 2013, we had the opportunity to acquire a technology, DriveIn®, which shows great potential to treat solid cancerous tumors more effectively. We are actively working on the development of this nanotechnology in order to start clinical development as quickly as possible.

Finally, our innovative formulations of monoclonal antibodies gave rise to several feasibility studies by big pharmaceutical laboratories.

The other important event of 2013 was the decision, by mutual agreement, to terminate our collaboration with the company Eli Lilly on the project “Ultra-fast-lispro”. This difficult, even painful, decision allowed us to regain control of the development of this product and to accelerate its clinical development in order to establish the proof of concept among type 1 diabetic patients, which we carried out in record time. Naturally, we had to bear the costs generated by this clinical study as well as the costs of the development of the product.

But this risk-taking today allows ADOCIA to own the proof of concept of this product which arouses the interest of numerous actors in the field of diabetes.

Finally concerning our project to launch a Phase III clinical study in India, at the time of publication, we have not yet obtained the license to start this study due to a complete reorganization of the Indian regulatory authorities. However, the authorization request should receive approval as soon as the agency resumes business as usual. We therefore hope to be in a position to announce the launch in the coming weeks.

Our cash position is solid and will allow us to finance our development plan as well as the scheduled clinical studies over the next eighteen months (end of 2015). During the year we strengthened our technical teams as well as the intellectual property department to support our international development.

I would like to thank all the ADOCIA team whose talent and perseverance were the keys to our fast and effective development.

I would also like to thank our shareholders who support us in our relentless efforts to supply more effective medicines to the largest number of sick patients.

Gérard SOULA
Chairman of the Board of Directors and Chief Executive Officer
The Company and its strategy

**INNOVATION FIRST!**

ADOCIA’s mission is to develop “best-in-class” medicines for mass pathologies. As a biotechnology company, ADOCIA develops innovative formulations with already approved therapeutic proteins. These proteins have proven their practical advantages, however they also demonstrate some significant weaknesses. Due to its technological platform of innovative polymers, BioChaperone, ADOCIA develops products that help improve the efficacy and the safety of the therapeutic proteins as well as their ease of use for patients. Moreover, ADOCIA’s ambition is to make its products accessible to the greatest number of people.

**Creating and developing inventions which will then be licensed...**

ADOCIA’s business model is founded upon the signing of sustained partnership agreements with the largest players of the pharmaceutical industry, biotechnologies or medical devices, based on results of feasibility and clinical studies that it is conducting. ADOCIA is neither considering producing nor commercializing its products.

Its strategy is to license innovations as soon as the proof of concept in humans or in animals is demonstrated. This business model is less capital-intensive as the development costs are supported by ADOCIA over a limited period (4 years instead of more than 10 years), which is the least costly period during the development of a pharmaceutical product. Proposed formulations with polymers that do not have biological activity of their own reduces risk of failure and facilitates registration in terms of regulatory authorities, due to their status as excipients*.

ADOCIA has chosen to remain firmly focused on innovation, which represents the greatest added value for a drug development process. The signing of license agreements should permit the company to keep focalizing on its competitive advantages within the polymer chemistry and drug delivery, based on its own expertise and of its partners who will be in charge of the clinical development, regulatory issues, production, marketing and commercialization of products.

**... to contribute to treatments for mass pathologies**

ADOCIA’s strategy relies on taking into account three key elements from its environment.

1. **The world’s big pharmaceutical groups’ needs for innovation**

   The pharmaceutical laboratories must face the expiration of a large number of patents that are protecting their leading products as well as the rise of many companies that are proposing generic drugs. ADOCIA can propose pharmaceutical products that are more efficient and more reliable, with competitive production costs and prices. The development of these products made from therapeutic proteins, having already proven their practical advantages, in most cases, and benefiting from marketing authorizations worldwide, does limit risks of failure. Its solutions thus provide a response to the leading pharmaceutical corporations’ needs for innovation and to the management of their products’ lifecycle.

2. **The world pharmaco-economic context**

   Population growth and aging, within a political context of control over public health expenses in the western countries and the fast-growing demand from emerging countries will not permit the development for treatments without taking into account the dimension of costs. The products developed by ADOCIA are perfectly in line with these economic issues. They improve the efficacy of the proteins and allow dosage reduction, the number of applications and/or the duration of treatment as well as a reduced production cost through a manufacturing process that can easily be produced industrially.

3. **The demand of emerging countries**

   If demand for pharmaceutical products in emerging countries is increasing, access to healthcare as well as to drugs remains however very problematic and even critical in some areas. The World Health Organization considers that more than 80% of deaths resulting from chronic pathologies occur in countries with low and middle income. Through the introduction of pharmaceutical products likely to become “Best-in-Class Products” with much lower costs than those existing, the strategy developed by ADOCIA is particularly well suited to meet the mass demand of these emerging countries. Moreover, this strategy could be much more developed with the support of a fast growing local pharmaceutical industry and through potential license agreements with local players.

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*An excipient refers to any substance other than the active principle contained in a drug, cosmetic or food, its addition is designed to grant new properties of delivery to the active principle, or other physical or gustative characteristics, to the final product while at the same time avoiding interaction, particularly chemical, with the active principle.*
Innovative solutions in a very sensitive global pharmaco-economic context

ADOCIA chooses to focus on mass markets. The aim is to provide, via innovative reformulation, treatments at the cutting edge of performance which remain affordable to patients. ADOCIA’s strategy takes into account needs of public health while responding to the global pharmaco-economic context. Indeed, a combination of population growth and aging population as well as the increase in prevalence\(^1\) and in incidence\(^2\) of pathologies targeted by ADOCIA lead all countries, western and emerging countries, to consider improving the management of the medical care of their populations in the context of control of public spending.

A unique technological platform: BioChaperone

ADOCIA has designed and developed a technological platform made from innovative polymers, named BioChaperone. These polymers, which do not have a biological activity of their own, possess the ability to spontaneously link with certain therapeutic proteins\(^3\). This association helps improve performances of numerous therapeutic proteins. To date, ADOCIA’s team of researchers have developed more than 300 BioChaperone polymers and thus assembled a true collection destined to evolve over time. ADOCIA’s clinical portfolio includes four innovative products formulated with BioChaperone: three insulin formulations for diabetes treatment and one growth factor formulation for wound healing.

A new nanotechnology for targeted delivery in oncology: DriveIn

While chemotherapies have remained a standard in cancer treatment, its side effects, as a result of its distribution throughout the patient’s body, remain a major limitation to its best use. Recently, treatment in oncology evolved towards more targeted approaches seeking to limit the action to tumor treatment, or even certain cancer cells. In December 2013, ADOCIA acquired the rights to develop and commercialize DriveIn, a nanotechnology developed in a French academic laboratory. DriveIn is remarkably efficient in delivering active molecules into solid tumors. This new platform is an exceptional opportunity to enter the oncology market by improving the efficacy of already approved treatments and of proprietary molecules.

WHAT IS DIABETES?

Diabetes results from a high level of blood glucose. It is a chronic disease due to the inability of the pancreas to produce insulin (type 1) or the inability of cells to respond to insulin (type 2).

WHAT IS DIABETES WORLDWIDE

Diabetes is a worldwide pandemic. Type 2 diabetes incidence increases with urbanization and population aging, and is especially on the rise in emerging countries.

MAIN COMPICATIONS OF DIABETES

- Retinopathy
- Stroke
- Heart disease
- Nephropathy
- Neuropathy
- Diabetic foot ulcer

**Source:** Diabetes Atlas 6th edition (2013), International Diabetes Foundation

**Source:** Diabetes Atlas 3rd edition (2006), International Diabetes Foundation
DIABETES TREATMENTS

Insulin is the ultimate therapy for diabetic patients

Maintaining glycaemia within a specific range is critical in order to delay complications of diabetes. Diabetic patients have multiple treatment options to control their glycaemia, depending on the intensity of their disease. Insulin has to be the ultimate therapy as it is about 25% of diabetic patients use insulin. Insulin is essential to treating type 1 diabetes and represents the last stop in treatment intensification for type 2 diabetic patients.

INSULIN THERAPY

Insulin-based treatment aims to replicate in diabetic patients the insulin secretion pattern observed in healthy individuals.

Two types of treatments are needed:

1. Prandial insulins are used to regulate glycaemia after a meal. In a healthy individual, meal consumption immediately triggers insulin secretion for metabolizing carbohydrates. This secretion decreases when blood glucose level goes down again. Consequently, injected prandial insulins must act very rapidly and for only a few hours. This has led to prandial insulin treatment evolving towards faster-acting insulins. Currently marketed insulin analogs need to be injected 15 minutes before a meal (vs. 30 minutes for older treatments such as recombinant human insulin).

2. Basal insulins are used to regulate glycaemia throughout the day. Healthy individuals continuously produce a low, so-called “basal”, quantity of insulin. Injected basal insulins have a long duration of action, and are thus said to be “long-acting.” The best currently available basal insulins have a duration of action of 24 hours.

A demanding treatment: a diabetic patient may require up to four injections a day of basal and prandial insulins. Blood glucose level must be monitored very frequently and insulin dosage needs to be adapted to meals and daily activities, which can make disease management very demanding for patients.

Premixed insulins (“premix”) offer a simple alternative to using both basal and prandial insulins by combining a fast and prolonged (18 hour) effect. They may also reduce the daily injections number to twice a day (instead of three if patients need one basal and two prandial shots). However, their performance is second-rate to that obtained by using two insulins. On this topic, patients’ expectations in terms of quality of life and doctors’ expectations in terms of diabetes treatment may go against each other. Choosing a premix is often the result of a compromise between these two aspects.

Only Novo Nordisk has recently introduced a real Combo, i.e. a real “two-in-one” product that combines a basal insulin with a prandial insulin: Ryzodeg® is based on Novo Nordisk’s new basal insulin, Tresiba®, combined with its fast-acting insulin, NovoLog®.

The market for insulin therapy is worth more than $22 bn today

(Source: Novo Nordisk)

Disease progression

Insulin

Glucose level

Oral anti-diabetic treatments

GLP-1

TOWARDS MORE PHYSIOLOGICAL PRANDIAL INSULINS

In a healthy individual, insulin secretion immediately increases after the beginning of a meal, to control the sudden input of glucose.

In a diabetic patient, controlling glycaemia may require using exogenous insulin. Currently marketed insulins are injected subcutaneously. This administration mode means that there is a delay between insulin injection and its entry in the blood stream: injected insulins do not act immediately. To anticipate the input in sugar due to the meal and avoid a peak in blood glucose, patients must inject their insulin dose 30 minutes (recombinant human insulin) to 15 minutes (prandial insulin analogs) before a meal. This creates dosage accuracy issues, as it is hard to anticipate both the exact timing and the exact food types and quantities that will actually be consumed.

The BioChaperone technology significantly improves prandial insulin absorption and accelerates its action so that it is quasi-immediate and much more closely mimics the insulin secretion pattern observed in a healthy individual. Indeed, the main challenge is to make injected prandial insulins act as fast as naturally secreted insulin.

ADOCIA’s BioChaperone technology overcomes several challenges:

• Allowing insulin injection at the time of the meal, with ultra-rapid formulations BC Lispro U100 and BC Lispro U300.

• Maintaining optimal prandial insulin performance for patients who require high insulin doses: the concentrated ultra-fast formulation BC Lispro U300 is adapted to patient populations requiring important daily insulin doses.

• Improving recombinant human insulin performance to allow more patients to access a fast-acting treatment. HinsBet (BioChaperone recombinant human insulin) acts as fast as an insulin analog, but at a lower cost.

Our mission: pursue the improvement of insulin treatment
PRODUCTS AND MARKETS

BioChaperone for prandial insulins: accelerating subcutaneous absorption

BC Lispro U100: the ultra-fast insulin

Although they start acting faster than recombinant human insulin, analog insulins must still be injected 15 minutes before a meal. ADOCIA innovates by applying the BioChaperone technology to the formulation of insulin analogs, in order to inject insulin at the time of the meal. An ultra-fast insulin would improve glycemic control. This is a key advantage for all patients and is of critical importance for treating children, whose meal behavior is extremely hard for parents to predict, and for the development of "intelligent" insulin pumps (also called "artificial pancreas", of which there are prototypes under study) that could adjust insulin dosage to blood glucose in real time.

ADOCIA’s innovation

Phase I (2013) and Phase IIa (2014) clinical studies showed that BioChaperone Lispro acts faster and for a shorter duration than Humalog®, with a “fast-on/fast-off” profile. A complementary, dose-response Phase IIa study is ongoing and results are expected during Q3 2014.

BC Lispro U300: the ultra-fast insulin for severely insulin-resistant patients

Type 2 diabetes is characterized by insulin resistance that may ultimately lead to injecting daily insulin doses superior to 100 IU. Consequently, there is a need for more concentrated insulin formulations than those currently available, in order to maintain sustainable injection volumes and decrease the related injection pain. Moreover, the increasing success of insulin pumps and their miniaturization also contribute to the need for more concentrated insulins. In both cases, concentrating insulin should not compromise the rapidity of action of insulins, which has generally been observed so far.

ADOCIA’s innovation

BioChaperone Lispro U300 is a concentrated ultra-fast formulation of insulin lispro. Preclinical studies showed that this formulation accelerated the action of insulin lispro (compared to standard dosage or to a concentrated dosage of insulin lispro). ADOCIA is actively pursuing the development of this product, which is expected to enter clinical studies in 2015.

THE REAL CHALLENGE OF DIABETES TREATMENT

Today, while 75% of insulin is sold in developed countries, 80% of diabetic patients live in so-called “emerging” countries. China, India, as well as Latin America, the Middle East and North Africa face dramatic increases in diabetes prevalence, mainly due to changes in ways of life and population aging. China is expected to become the first market for one diabetes; in 2035, the International Diabetes Foundation forecasts that the diabetic patients population in China will reach 142 million people.

Although all diabetic patients share the same medical needs, three main factors limit access to appropriate treatment in these countries: treatment prices, the size of the population to treat and the level of patients’ health education.

Human insulin market

HinsBet: fast-acting human insulin

Human insulin has been used for several decades. It is extremely safe and its production is less costly than that of insulin analogs. However, it starts acting slower than insulin analogs, and thus needs to be injected 30 minutes before a meal. This potentially exposes the patients to hypoglycemia if the dosage is not accurate enough, or the meal is taken later than expected.

This major drawback has led to human insulin being replaced in developed countries by insulin analogs, which act faster and can be injected 15 minutes before a meal.

ADOCIA’s innovation

ADOCIA developed HinsBet, a formulation of human insulin using BioChaperone, which accelerates human insulin action to reach insulin analogs performance. In a Phase I clinical study, HinsBet was as fast-acting and as well tolerated as insulin lispro.

A complementary, dose-response Phase IIa clinical study confirmed this good performance in type 1 diabetic patients. ADOCIA recently developed an improved formulation of HinsBet, which showed superior performance in preclinical testing. This formulation will be tested in a Phase IIa clinical study starting in July 2014.

This product received the support of OSEO and FEDER funding.
BioChaperone for insulins Combo: solubilizing basal insulin

#### BioChaperone Combo: a real two-in-one product combining basal and prandial insulins

Today, the basal insulin market is largely dominated by Lantus® (Sanofi), which has been proven to be safe and efficient for millions of patients. However, this insulin cannot be formulated with available prandial insulin analogs, due to incompatible formulation pHs. A real basal-prandial combination would allow good glyemic control while facilitating treatment observance, in particular for elderly patients and in emerging countries, where premix products are mostly prescribed.

**ADOCIA’s innovation**

To this day, BioChaperone is the only technology that succeeds in formulating a homogeneous solution of Lantus with any marketed prandial insulin, in different proportions and at neutral pH. This innovation was confirmed by preclinical and clinical results. In 2013, a Phase IIa clinical study of BioChaperone Combo Glargin Lispro showed that the product acted faster than Humalog® Mix™ (Insulin lispro premixed) and for longer, with a duration of action superior to 24 hours. A complementary, dose-response Phase IIa study should be launched in Q4 2014.

#### Premixed market: $2.4 bn

Lantus market: $7.8 bn

**BioChaperone PDGF-BB: an efficient treatment for a poorly managed disease**

**Diabetic foot ulcer (DFU)**

In diabetic patients, chronic hyperglycemia may lead to nerve and blood vessel degeneration (respectively called neuropathy and ischemia). Diabetic foot ulcers are a serious consequence of both complications. If infected, these chronic wounds can lead to limb amputation. The only approved treatment for neuropathic DFU is Regranex®, a gel formulation of Platelet-derived growth factor BB (PDGF-BB), but it is difficult to use, limiting its actual efficacy. Other treatments exist, but are either poorly efficient (dressings) or very costly (cellular substitutes). No treatment is currently approved for neuroischemic DFU, which is the most severe form of the disease. ADOCIA aims to develop an efficient, easy-to-use and affordable treatment for this largely prevalent disease, including its most severe form.

**ADOCIA’s innovative solution:**

**BioChaperone PDGF-BB**

BioChaperone PDGF-BB is an innovative formulation of the PDGF-BB growth factor used in Regranex, the standard treatment for DFU. Using BioChaperone confers important properties to the resulting formulation:
- **Efficient dose is decreased by 3x, for a more affordable treatment.**
- **Product is applied once every two days, instead of daily, which significantly decreases associated nurse and dressing costs.**
- **Product is stable at room temperature as a sterile solution in a spray, making the product easy-to-use and avoiding product degradation.**

In 2012, ADOCIA completed a first Phase I-II clinical study in India. ADOCIA is currently preparing a Phase III clinical study in India, which is expected to start in 2014. At the same time, ADOCIA is also preparing a clinical study in Europe, expected to start in 2015. The EMA (European Medical Agency) previously confirmed that only one Phase III study conducted in Europe would be required for the marketing authorization dossier, as clinical data from the Phase III study conducted in India would be admissible to support the European NDA’s application.

**China and India: 65% of patients use premix products**

**ADOCIA’s innovative solutions**

ADOCIA has developed several technological innovations for mAb formulation:
- **BioChaperone** improves mAbs solubility, their bioavailability and stabilizes them at high concentration.
- **ADOCIA Viscosity Reducers** decrease mAb viscosity at high concentration.
- **ADOCIA Stabilizers** limit mAbs aggregation, hence improving their stability upon storage in solution.

ADOCIA is currently conducting collaborative development programs with major pharmaceutical and biotechnology companies, using one or several of the above technologies to improve the formulation of our partners’ proprietary products. Beyond assessing the proof-of-concept for these technologies, these collaborative agreements may be the first step towards license agreements.
A team of highly qualified staff

As an innovative company in the health sector and listed on the Euronext stock market, ADOCIA aims not only for scientific and technical excellence, but also social innovation to contribute to the development of each employee. In 8 years, ADOCIA has developed a team of high-level innovation. The ADOCIA team consists mainly of scientists (lab technicians, engineers and doctors in chemistry, biology, biochemistry, physical chemistry, analytical chemistry, patent engineers, veterinarians...).

The management of the company consists of a team with extensive experience in the management of technological innovation and partnerships with large industrial groups both in pharmacy and in biotechnology.

Career development through ambitious training and by encouraging internal mobility

ADOCIA’s sustainability is related to its ability to attract, motivate and retain talents. This is all the more important given ADOCIA’s young population.

Average age of 34 years

ADOCIA offers each employee the opportunity to expand their skills and expertise through professional training and participation in scientific conferences, to grow, to learn, to improve their level of qualification to specialize or perfect to evolve.

26 hours of training a year and per employee

Between 3 and 4 training courses a year per employee

ADOCIA participates in the training of young people and contributes to their employability. Every year, it hosts a dozen interns and 4-5 youth apprenticeships. Special relationships have been developed with universities and higher education institutions as the University Claude Bernard Lyon I, School CPE Lyon, ESPCI in Paris, the ECPSM Strasbourg, ITU Chemistry Villeurbanne and different schools of pharmacy.

AN OPEN AND COLLABORATIVE GOVERNANCE

The management committee

Rémi Soula
Director of Business Development and Intellectual Property
Doctor in Chemistry of Polymers, graduate of CPE Lyon, he is co-author of 30 patents and of 6 scientific publications.

Valérie Danaguezian
Administrative and financial Director
Graduate of ESC, she has gained significant experience in terms of controlling, international standards rules and internal control.

Gérard Soula
Chairman of the Board of Directors and Chief Executive Officer
Doctor in Organic Chemistry, graduate of IAE (Aix-Marseille), he is the founder of Flamel Technologies. Gérard Soula has a strong track record regarding negotiation of licensing agreements for technological innovations with major biopharmaceutical companies.

Olivier Soula
Deputy General Manager, R&D Director
Doctor in Physical chemistry of Polymers, graduate of ENSIC Mulhouse and holder of a MBA from IAE of Lyon, he is co-author of 40 patents.

The management board

The company’s management board is composed of 6 members: Gérard Soula, Olivier Soula, Olivier Martinez, BPI France (represented by Laurent Arthaud), Dominique Takizawa (independent administrator) and Dr Ekaterina Smirnyagina (independent administrator).

Until October 24th 2011, the company was set up as a SAS (société anonyme simplifiée). On October 24th 2011, the General Shareholders’ Meeting approved the conversion of the company into a public limited company (SA) which includes a board of directors, and to adopt new rules of governance.

In 2013, members of the audit committee are:
• Ms. Dominique Takizawa, an independent member with financial and accounting skills,
• Mr. Olivier Martinez.

The compensation committee

The compensation committee was established on June 6th 2008. It is composed of three members of the management board designated by the management board.

In 2013, members of the compensation committee are:
• Mr. Laurent Arthaud,
• Dr Ekaterina Smirnyagina (independent administrator).

6 members of management board among which two independent members (33%) and two women (33%)
Finances and stock exchange

KEY FINANCIAL ELEMENTS

Income statement

<table>
<thead>
<tr>
<th>INCOME STATEMENT (in thousands Euros)</th>
<th>2013</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenue</td>
<td>5,586</td>
<td>3,995</td>
</tr>
<tr>
<td>Other operating income</td>
<td>3,253</td>
<td>3,241</td>
</tr>
<tr>
<td><strong>Total operating income</strong></td>
<td>8,839</td>
<td>7,236</td>
</tr>
<tr>
<td>R&amp;D expenses</td>
<td>(11,475)</td>
<td>(11,784)</td>
</tr>
<tr>
<td>SG&amp;A</td>
<td>(1,649)</td>
<td>(1,522)</td>
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<tr>
<td><strong>Total operating expenses</strong></td>
<td>(13,124)</td>
<td>(13,306)</td>
</tr>
<tr>
<td><strong>OPERATING INCOME (LOSS)</strong></td>
<td>(4,302)</td>
<td>(6,070)</td>
</tr>
<tr>
<td><strong>NET INCOME (LOSS)</strong></td>
<td>(4,293)</td>
<td>(6,070)</td>
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Balance sheet

<table>
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<tr>
<th></th>
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<tbody>
<tr>
<td><strong>TOTAL ASSETS</strong></td>
<td>24,729</td>
<td>36,827</td>
</tr>
<tr>
<td>including</td>
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<td></td>
</tr>
<tr>
<td>Labs equipment</td>
<td>528</td>
<td>550</td>
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<tr>
<td>Other tangible assets</td>
<td>416</td>
<td>284</td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>19,415</td>
<td>30,462</td>
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<tr>
<td><strong>TOTAL LIABILITIES</strong></td>
<td>24,729</td>
<td>36,827</td>
</tr>
<tr>
<td>including</td>
<td></td>
<td></td>
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<tr>
<td>Shareholders’ equity</td>
<td>19,130</td>
<td>23,028</td>
</tr>
<tr>
<td>Long term debt</td>
<td>1,814</td>
<td>2,040</td>
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</table>

Operating income

Revenue for 2013 amounts to EUR 5.6 million compared to EUR 4 million in 2012, that is to say an increase by EUR 1.6 million. The increase is essentially due to the termination of the licensing contract with Eli Lilly that occurred in July 2013 which had two effects: on one hand, the amortization of the licensing contract for EUR 4.7 million which corresponds to the remaining non-amortized part of the initial up-front payment received in 2011, and, on the other hand, the lack of revenue from research and collaborative development contracts which represented the majority of revenue recorded in 2012 under this line.

2013 stock-exchange

In 2013, ADOCIA stock was impacted by the announcement of the termination of the licensing agreement with Eli Lilly, which lead to a decrease by nearly 40% of the stock (from 9.35 euro per share to 5.50 euro per share). In the second semester of 2013, the stock market price knew few variations and the exchanged volumes were restricted.

At the end of 2013 and at the beginning of 2014, the company published several press releases regarding the development of its product pipeline, in particular its insulin combo product (combination of a glargine and an ultra-fast-acting analog) pushing the stock upward. This internal situation was associated with a very favorable global environment for the biotech sector, the Next Biotech Index progressing by more than 20% over this period.

As a consequence the stock increased to 15.28 euros per share in March 2014, the average shares exchanged per day in 2014 being 10 times over the average in 2013 (an average of 50,000 shares exchanged per day).

Shareholding at December 31st, 2013

<table>
<thead>
<tr>
<th>Shareholder</th>
<th>Shares (%)</th>
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<td>Deléage, Familly</td>
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<tr>
<td>Muñoz</td>
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<td>Amundi</td>
<td>2.90%</td>
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<td>IdInvest</td>
<td>26.65%</td>
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<td>Bpi France</td>
<td>5.87%</td>
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<td>Viveris</td>
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<td>Soula Family</td>
<td>2.02%</td>
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<tr>
<td>Life Sci Advisors, Deléage Family</td>
<td>1.10%</td>
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</table>

EUR 19.4 million of cash and cash equivalents at the end December 2013

EUR 11 million burn rate in 2013

Close to 87% of the operating expenses are dedicated to R&D

Long term debt: EUR 1.8 million of loan from OSEO

ADOCIA share value over the past year

Financial memo

<table>
<thead>
<tr>
<th>Stock market</th>
<th>NYSE Euronext Paris</th>
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<tr>
<td>First trading day of the company’s shares</td>
<td>February 20th, 2012</td>
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<tr>
<td>ISIN Code</td>
<td>FR0011184241</td>
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<td>Mémento/Reuters/Bloomberg</td>
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<tr>
<td>Total number of shares in circulation</td>
<td>6,211,876</td>
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<td>Sector</td>
<td>Pharmacy and biotechnology</td>
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<td>Index</td>
<td>Next Biotech - CAC PME</td>
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<td>OSEO Label</td>
<td>Eligible to investment in FCPI</td>
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ADR Program (American Deposit Receipt)

<table>
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<tr>
<th>Type of ADR program</th>
<th>Sponsorisés - Niveau 1</th>
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<td>Exchange</td>
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<td>Symbol</td>
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<td>CUSIP</td>
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<td>Ratio</td>
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</tbody>
</table>

Financial analyst on the basis of value

Kapler Chevreux L. LABOURDETTE
Invest Securities D. ANIZON
Life Sci Advisors A. I. MC DONALD
A MAJOR TECHNOLOGICAL BREAKTHROUGH
- BioChaperone, molecular delivery system for therapeutic proteins
- Drivelin, nanoparticles technology for drug delivery

VERY SUBSTANTIAL POTENTIAL FOR DEVELOPMENT
Promising clinical results in two therapeutic areas amounting to billions of dollars: treatment of chronic wounds and insulin therapy for diabetes

LOW CAPITAL-INTENSIVE BUSINESS MODEL
License agreements as soon as the proof of concept is established: clinical studies, commercialization and product marketing delegated to partners

PROTECTED KNOW-HOW
Close to 100 patents and patent applications worldwide

INNOVATIVE COMPANY
73 employees including 27 holding a doctorate degree
More than 85% of the staff allocated to R&D

MAIN SHAREHOLDERS
Soula Family, BPI France Investissement (Innobio, BioAmri), Idlnvest, Sham, Viveris, Oréo Finance, Delage Family

EXPERIENCED MANAGEMENT TEAM
- Specialized and familial oriented entrepreneurship
- Experience of Flamel Technologies (founded by Gérard Soula):
  - 2nd French company listed on Nasdaq (1996)

RECOGNIZED EXPERTISE
2 ongoing collaborative development programs with leading names in the pharmaceutical industry in monoclonal antibodies

DISCLAIMER
“Any document 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 may be no assurance that the estimates contained in such forward-looking statements will be realized, which estimates are subject to numerous risks and uncertainties, including the risks set forth in the “Risk Factors” section of the Reference Document registered by the Autorité des Marchés Financiers on April 25th, 2012 under number R13-017 (a copy of which is available on 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 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 neither an offer to sell nor an offer of subscription, nor the solicitation of a purchase order or of ADOCIA’s share subscriptions in any one country.”

ADOCIA’S 8 ASSETS

STRIKING EVENTS

IN 2013

MARCH
Treatment of Diabetic foot ulcers: EMA (European Medicines Agency) validation of the clinical development plan in Europe. The EMA agreed that only one Phase III study conducted in Europe would be required for the MAA (Marketing Authorization Application).

AUGUST
Rupture, by mutual agreement, of the license agreement signed with Eli Lily concerning the development of ultra-fast insulin analog. Recovery of rights and decision to accelerate the clinical development of the project.

NOVEMBER
Launch of clinical trial for BioChaperone Combo, a combination of long-acting insulin Glargine and a fast-acting insulin analog. This Phase III clinical trial on type I diabetics seeks to compare the performance of this combo based on insulin Glargine to Humalog Mix.

DECEMBER
Acquisition of a new technology DriveIn, improving the efficacy of anti-tumoral agents by targeting their action into tumors.

IN 2014

JANUARY
Strengthening of its diabetic foot ulcer patent portfolio: delivery of two of major patents, one in Japan (BioPSG Composition) and the other in United States (Polymer BioChaperone)

MARCH
Launch of Phase IIa clinical trial for its ultra-fast-acting formulation of insulin analog Lispro.

APRIL
Confirmation of positive clinical results for BioChaperone Combo, combination based on long-acting insulin Glargine and a fast-acting insulin analog.

JUNE
Eligibility PEA-PME and integration of ADOCIA in the CAC PME index.

SEPTMBER
Phase IIa positive results for ultra-fast insulin for BioChaperone Lispro.

OCTOBER
Launch of clinical trial for BioChaperone Combo, a combination of long-acting insulin Glargine and a fast-acting insulin analog. This Phase III clinical trial on type I diabetics seeks to compare the performance of this combo based on insulin Glargine to Humalog Mix.

FUTURE EVENTS