ONXEO

THE ORPHAN ONCOLOGY INNOVATOR

Letter to Shareholders - May 2015

Dear Sir or Madam, Dear Shareholders

"Onxeo now has all it takes to become a biotech leader in orphan oncology"

2015 began very dynamically, and is a construction year for the future of the company.

2014 was the year of the merger and integration of TopoTarget in terms of products, teams and environment. Everything is now in place, and the teams are working together, creating everyday an increasingly strong Onxeo, with an innovative portfolio of three advanced products and a global organization.

This building period did not slow us down. On the contrary, Onxeo has accelerated its developments , especially in the field of scientific activities.

On the operational side, we are moving forward just as planned and in accordance with the scheduled timeframe. Last year, major steps were accomplished. Indeed, many scientific publications, attesting to the quality and the relevance of the developments carried out, have been released.

Our goal on the short term is to pursue the extension of ReLive (Livatag®) internationally and to prepare the upcoming clinical studies on Beleodaq® and Validive® as efficiently as possible, adding further value to these promising programs.

We are undertaking a very exciting adventure, building an international player; building a leading pioneer in the development of rare cancer treatments, with the overarching aim of making the difference for patients suffering from these severe diseases.

On the behalf of Onxeo teams, I thank you for your loyalty and your ongoing support, which will help us to develop innovative treatments and thus to build the future of Onxeo together.

Judith Greciet
CEO

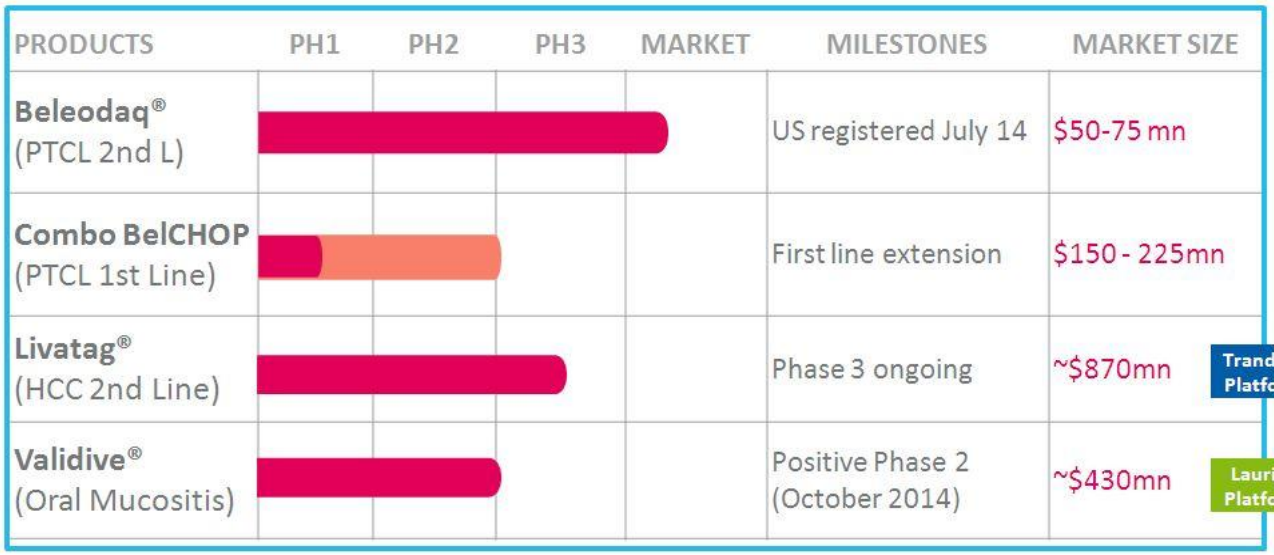
CONTENTS

Pipeline and next steps

With its 3 independant programs adressing severe diseases, Onxeo has a large and innovative pipeline with an optimized risk profile.

Moreover, the 3 programs are in advanced clinical development stage, in phase III or ready to enter phase III.

UNIQUE, STRONG AND DIVERSIFIED PIPELINE



Livatag®, nanoformulated doxorubicin developped for the treatment of primary liver cancer (c.f. following pages).

- Currently in phase III in 8 countries, extension ongoing to 3 additional countries.
- The 7th DMSB is scheduled Q4 2015, major half-year step validating the good safety profile of the product.
- The preliminary phase III results are expected early 2017.

Validive®, clonodine mucoadhesive tablet developped in the prevention of severe oral mucositis in head and neck cancer patients treated by radio-chemotherapy.

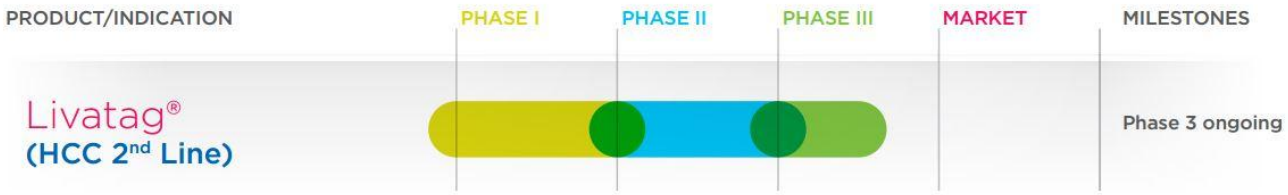
- Based on the positive phase II results, we are preparing the phase III to be initiated by end 2015.
- Discussions ongoing with potential partners. The company will assess the best option: to keep or to license the rights, according to the potential conditions.

Beleodaq®, HDAC inhibitor, registered by FDA in 2nd line treatment of Peripheral T-Cell Lymphoma (PTCL).

- Currently in phase I (BelCHOP) to assess the safety profile of Beleodaq® in combination with CHOP, the standard treatment 1st line treatment of PTCL.
- Results expected Q3 2015.
- Preparation of a phase III to confirm the efficacy of the association BelCHOP in 1st line treatment, expanding the product's potential.
- Pivotal study for the European registration of Beleodaq® in the treatment of PTCL.
- Commercialization initiated since August 2014 by the US sales teams of Spectrum.

FOCUS ON LIVATAG®

We propose to have a specific focus in the coming Newsletters on one of our development programs and on its targeted pathology



Key points:

- **Ongoing international phase III clinical trial**
- **HCC, an highly severe cancer**
- **Fast-track status received from the FDA**
- **Results expected in 2017**
- **Max Sales potential : €800 million at peak**

Hepatocellular carcinoma (HCC)

Hepatocellular carcinoma (HCC) develops from liver cells (hepatocytes) and represents 85% of primary liver cancers. In the great majority of cases (>90%), HCC occurs when the liver is already abnormal (cirrhosis). Risk factors are well established: infection with hepatitis B and C viruses, consumption of large amounts of alcohol, because of its implication in cirrhosis. Metabolic diseases, and in particular obesity, are also a growing cause of cirrhosis and HCC.

Liver cancer is the 6th most common cancer in terms of incidence (782,000 new cases in the world, 5.6% of all new cancer cases) with the 2nd highest mortality rate (746,000 deaths, 9.1% of the total). The incidence of HCC is particularly high in Asia, and notably in China (50% of the patients) due to a high rate of viral hepatitis B.

HCC is often diagnosed at an advanced stage as the tumor progresses with very little visible clinical manifestation in the early stage and the first symptoms or signs are usually not specific to HCC.

A severe prognosis and insufficient treatments

At an early stage, the only possible curative treatment for HCC is surgical resection to remove the whole tumor. However, due to late diagnosis of HCC, the tumors are often too large and numerous and only 15 to 20% of patients can undergo such surgical treatment.

Radiofrequency is an alternative to surgical resection, causing thermal destruction (via electric current) of the tumor. This technique is usually limited to tumors of small size and in limited number.

Beyond the early stage enabling surgery, two treatment options are available: chemoembolization (intra-tumoral infusion of the chemotherapy treatment to "dry" the tumor) and sorafenib (Nexavar®, Onxy/Bayer), the only drug registered that has shown a survival increase by 2.8 months *versus* placebo in patients having undergone chemoembolization.

After failure to sorafenib, palliative systemic chemotherapy may be used.

The 5-year survival rate remains extremely low. For example in the USA, it is 16% for all patients but only 10% for those diagnosed at an advanced stage (stage III, regional invasion) and 3% at metastatic stage (stage IV).

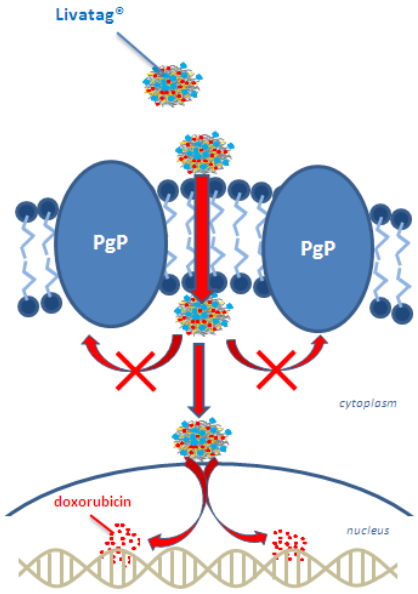
Sources : Globocan, 2012 - Facts & Figures Report 2014 by American Cancer Society

Livatag®: A nanoparticle formulation to fight against tumor resistance

Liver cancer is a particularly resistant cancer. Liver cancerous cells develop a resistance due to a resistance gene (called MDR-1) that activates of transmembrane transport proteins. They act as veritable “pumps” pumping cytotoxic out of the cell, preventing it from exerting its therapeutic action.

As a result of this, conventional chemotherapies are not effective and the need for new treatments of advanced HCC is strong.

Livatag® is based on the innovative « Transdrug ™ » technology designed to formulate a chemotherapy (doxorubicin) with nanoparticles. Interactions between doxorubicin and transmembrane proteins (P-gp) are thus modified, preventing or restricting rejection of doxorubicin outside the tumor cell.



Acting as a Trojan horse, the nanoparticles penetrate and remain in the cell where they release the doxorubicin into the nucleus, its cytotoxic site of action.

In the preclinical studies, Livatag® has demonstrated the capacity to overcome efflux pumps, drug concentrations being higher than those of “traditional” doxorubicin within the tumor cell and nucleus.

The phase II clinical trial in HCC patients has shown particularly encouraging efficacy results with an increase of 17 months in median survival (32 months in patients treated with Livatag® as compared to 15 months in patients treated by chemoembolization, the standard treatment at this stage of the disease).

Nevertheless, the trial had to be suspended due to adverse events (acute respiratory distress syndrom).

These events, related to the presence of nanoparticles at the pulmonary level, are avoided with the use of a slow infusion rate (fast infusion was used in the phase II trial) as demonstrated in animal models.

ReLive: A Phase III clinical trial to confirm the efficacy of Livatag®

Based on these efficacy and safety data, the authorities validated the implementation of a Phase III clinical trial (ReLive) comparing the efficacy and the safety of Livatag® to those of the best standard care (BSC), i.e. the treatment prescribed by the practitioner as the most adequate and in line with the current practice.

ReLive is a randomized (the practioner does not choose which product will be administered between Livatag and BSC), controlled, open study. Two doses of Livatag® are evaluated (20mg/m² and 30 mg/m²) and 400 HCC patients failing or intolerant to sorafenib are planned to be included.

The ReLive study was first initiated in France, then expanded one year later to several European countries and to the USA. This progressive expansion, due to cost control, results in an exponential increase in the recruitment rate of patients as new investigator sites are opened. Indeed, as the number of HCC patients remains limited in Europe and in the USA, implementation of a significant number of sites is necessary to optimize the recruitment rate.

As of March 31, 2015, more than 40% of the patients planned were randomized in about 40 investigation sites. The teams are actively opening additional countries and sites, especially in Egypt, Saudi Arabia and Lebanon. In this purpose, Onxeo has engaged MCT, a contract research organization (CRO) specialized in running clinical trials in the Middle East and in North Africa (MENA region).
The preliminary results of the trial are expected early 2017.

The DSMB on ReLive once more confirms the good safety profile of Livatag®

Since its initiation, a committee of independent experts regularly reviews the tolerance of the treatments administered. Its mission is to identify possible unexpected adverse events in order to ensure patients' safety.

This DSMB meets twice a year and for the 6th time in April 2015, it issued a positive recommendation to pursue the clinical trial without any modification, thus validating the safety profile of Livatag® so far.

FOCUS ON LIVATAG®

Livatag®: An advantageous status

Livatag® enjoys orphan drug status in Europe and the United States. This status is delivered by the health agencies to drugs targeting rare pathologies (< 200.00 cases in Europe and < 250.000 cases in the US) and for which the medical need is strong.

Thanks to this status, Livatag® will benefit from a commercial protection in the US (7 years) and in Europe (10 years) in addition to its patent. Access to health authorities is also facilitated.

As the number of patients is limited, it is accepted to perform a single phase III trial to demonstrate the clinical benefit of a product (whereas 2 trials are usually required), subject to the level of efficacy demonstrated of course. In addition, and for the same reason, the price level negotiated with the "payor authorities" is generally more favourable than in the case of treatments targeting a large population of patients.

Livatag® also received fast-track status (accelerated procedure) in the US, allowing to optimize duration of data review from the Food and Drug Administration. The review of a new drug authorization dossier is thus estimated to be reduced by 3 to 6 months.

The industrial protection of Livatag®

Already patented until 2019 with a first patent family covering the pharmaceutical product's composition, Livatag® enjoys a reinforced and prolonged protection until 2032 with a second patent family covering its specific administration scheme and delivered by the European Patent Office in February 2014.

A sales market potential

With an incidence of 800.000 new cases worldwide each year, the peak sales potential could reach €800 million.

Livatag®: latest scientific news

A ReLive investigators' meeting was held on April 24, 2015, during the 50th EASL (European Association for the Study of the Liver) annual meeting. On this occasion, the clinical team presented the study's advancement to 10 investigators who could share views.

In addition, the ReLive study design was published at the EASL meeting as an e-poster, enhancing the awareness of the scientific community about ReLive and Livatag®.

Consortium NICE (Nano Innovation for Cancer)

NICE (Nano Innovation for Cancer), the first consortium of nanomedicine stakeholders in France focused on aspects of characterization and industrialization of processes specific to nanodrugs. Consisting of five public and private partners and led by Onxeo, the NICE consortium includes partners with deep expertise in the field of nanomedicine. Its mission is to build a platform to accelerate the development and industrialization of nanomedicine in France by capitalizing on the strong and complementary expertise of each partner.

Finally, in July 2013, Onxeo obtained financing from BPI France of nearly €9m of which €4.3m was granted directly to the company via an Industrial Strategic Innovation (ISI) programme, payable over 5 years. In October 2014, the company received the second payment of €1.25m based on the Livatag® programme progressing as per schedule. This financing is aiming to enable the acceleration of the industrial development of Livatag®.

ONXEO IN THE PRESS

DECIDEURS TV

Interview of Judith Greciet about Onxeo 's product porfolio – 03/04/2015

« Phase III trial began 2 and a half years ago, it was firstly launched in France, before being extended to other European countries, and the United States in 2013. This progressive international extension of the Phase III trial will allow us to boost recruitment. Preliminary data from the "ReLive" study are expected to be delivered by early 2017.»

Seeking Alpha α

Onxeo: An Upcoming Mid-Sized Pharma With Ambitions – 12/03/2015

"Onxeo is a French/Danish biotech company building a portfolio of innovative therapies with a focus on orphan oncology indications."

BOURSIER.COM

6th positive DSMB recommendation for Livatag® ReLive study in HCC – 14/04/2015

" Onxeo announced that the independent European board of experts, the Data Safety Monitoring Board ("DSMB"), which monitors the safety of the Livatag® phase III trial, "ReLive", has once again unanimously recommended to continue the study without modification."

A STRONG SCIENTIFIC CONSIDERATION

ASCO® American Society of Clinical Oncology

Validive® (clonidine Lauriad®) phase II clinical trial results have been accepted for a poster presentation at the 2015 Annual Meeting of the American Society of Clinical Oncology (ASCO). The event will be taking place in Chicago (USA), from May 29 to June 2, 2015. The phase I/II clinical trial of belinostat in combination with doxorubicin will also be presented by Onxeo.

The ASCO annual meeting is a major event in the field of oncology that brings together 30.000 health professionals and updates on the major latest steps and results achieved in oncology worldwide.

EASL European Association for the Study of the Liver

Onxeo has been selected to present an e-poster on the Livatag® phase III study design, about the design of this international study, at EASL (European Association for the study of the Liver).

The EASL was founded almost 50 years ago to promote and exchange science in the field of liver diseases. Its annual meeting involves the specialists of hepatology and liver cancer and is therefore an ideal opportunity to gather the European and US investigators of the ReLive clinical trial who will attend the congress.

Q & A SESSION

You will find below the questions frequently asked during meetings or received by email.

Are intermediary data planned for Livatag®'s Phase III trial?

The protocol approved by the regulatory agencies did not plan a futility study for phase III Relive trial and no intermediary analysis will be performed until the end of the trial, the regulatory authorities being very strict on this point . The preliminary results of the trial are expected early 2017.

Will the Transdrug ™ technology be used in other indications?

Transdrug™ technology uses nanoparticles to help fight against chemotherapy resistance.
This platform belongs to us and it is possible to extend its use to other compounds and / or use Livatag® to other pathologies.

For now, our priority is our development of Livatag® in HCC, for resource and focus management, but others developments are foreseeable. Of course, the experience already acquired will be a strong asset in the establishment of such an experimental plan.

What is the country of taxation of Onxeo?

Onxeo is taxed in France and Denmark, on the basis of respective revenues received for assets developed in each country. Therefore, the revenues generated by the commercialization of Beleodaq®, which has been developed in Denmark, are subject to Danish tax system.
Onxeo is a French company, and pays its taxes in France on its consolidated income in accordance with the rules in force.

What is your visibility on the company's cash situation ?

The year-end fund raising has enabled the company to obtain a net amount of €37m thanks to the support of the shareholders. Moreover, €25m of milestone payments from Spectrum was added to this total.

The consolidated cash position stood at €49.9 million as of March 31, 2015, which gives us a visibility of about two years to pursue our programs at constant scope.

Could you explain the funding transactions which took place in 2014?

All the answers are available on the website, section « General Assembly » in the file « Written questions ».

This document follows the chronology of events and clarifies the conditions of the loan, contracted with our main shareholder Financière de la Montagne.

AGM

Annual General Meeting: A privileged meeting with our shareholders

The Annual General Meeting originally scheduled for April 15th, could not take place due to unmet quorum.

If this may seem surprising, one should keep in mind that following the merger, about 1/3 of the Capital is now owned by Danish shareholders, a large part of which being retail shareholders. Therefore, the part of Onxeo's capital held by individual shareholders has increased and represents about 60% of the total capital, i.e. several thousands of physical persons. If it is a very good thing for us to have the confidence of individual shareholders, their mobilization to vote at GA is lower and we are not able to contact all of them individually.

Furthermore, some technical difficulties between French and Danish banks appeared during the voting process, which have strongly complicated the procedure.

The next AGM will be held at the company's headquarters in Paris on May 20th, 2.30pm

A new meeting is planned and will be an opportunity to present our strategy, our achievements and outlook, and answer your questions directly. Feel free to participate if you can, in order to continue the dialogue.

The method of participating at the Meeting and exercise your voting rights, by attending personally, voting by mail or voting by proxy is particularly complex. Detailed explanations can be founded on our website:
http://www.onxeo.com

Feel free to contact us if necessary: contact@onxeo.com

2015 FINANCIAL CALENDAR

AGM
20 May 2015

HALF YEAR RESULTS
29 July 2015

INVESTORDAGEN, COPENHAGEN
22 September 2015

ACTIONARIA CONGRESS FOR SHAREHOLDERS
20 – 21 November 2015

KEEP IN TOUCH

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Come & meet us at Actionaria **20 and 21 November 2015** at **Palais des congrès de Paris** !

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