## OUR STRATEGIC FOCUS: HIGH-VALUE DISRUPTIVE PRODUCTS

Dear Madam, Dear Sir, Dear Shareholders,

For several years, Onxeo has undertaken a strategic transformation through a diversification of its portfolio towards innovative oncology products based on tumor DNA-targeting mechanisms, a field appealing to the pharmaceutical industry. This model of value creation relies on the strong translational expertise of Onxeo's teams who advance these programs through to the proof of concept in human, an attractive stage for industrial partners.

This forward-thinking strategy has provided Onxeo with a diversified and promising product development portfolio, notably including belinostat, an epigenetics drug already marketed in the United States, and AsiDNA™, a first-in-class compound targeting tumor DNA break repair pathways.

AsiDNA™ has already completed a very encouraging phase I trial via intra-tumoral administration and is currently developed for intravenous administration in order to fully unlock its potential in multiple indications. Furthermore, AsiDNA™ has already demonstrated a clear synergistic effect in preclinical studies when combined with PARP inhibitors and HDAC inhibitors, notably with our belinostat, which opens the way for other potential applications in combination, further strengthening the already substantial potential of AsiDNA™.

Our goal is to efficiently take our programs to the clinical stage, firstly in monotherapy and then in combination (Belinostat + AsiDNA™ and AsiDNA™ + PARPi), in order to reach the proofs of activity and tolerance in man, the two most attractive inflection points for the pharmaceutical industry in the field of oncology.

*Our value creation model relies upon our expertise and know-how to advance our innovative programs through to proof-of-concept in man, an attractive stage for industrial partners.*

In parallel, we have continued to reinforce the value of AsiDNA™ technology through PlatON™, the chemistry platform of 'decoy' oligonucleotides of which AsiDNA™ is the first candidate. This patented technology will enable Onxeo to generate, in the short term, new and innovative compounds targeting various regulation mechanisms of the tumor DNA, and thus to substantially enrich our pipeline.

To strengthen our expertise, we have established a Scientific Advisory Board with international scientific experts in the field of tumor DNA repair and targeting, chaired by Professor Tomas Lindahl, joint recipient of the Nobel Prize in Chemistry in 2015 for his mechanistic studies of DNA repair.

All our teams are focused and determined to create new value as we bring our key assets to their optimal inflection point for the Company and advance towards transactions generating value and funding.

On behalf of Onxeo, I would like to thank you for your continued support and confidence and hope you enjoy reading this Letter.

**Judith Greciet**
*Chief Executive Officer*

### IN THIS LETTER

## OUR STRENGTHS TO TRANSFORM LEADING-EDGE SCIENTIFIC RESEARCH INTO DISRUPTIVE TREATMENTS

**DIFFERENTIATED SCIENCE AND BUSINESS MODEL**
targeting unique mechanisms of action in DNA-targeting with strategy to partner post Proof-of-Concept

**PROPRIETARY platON™ CHEMISTRY PLATFORM**
will be leveraged to generate new breakthrough oncology compounds.


**ROBUST DEVELOPMENT PIPELINE**
with two product candidates entering clinic in 2018 targeting multiple potential indications

**MULTIPLE NEAR-TERM CATALYSTS**
with data from Phase I trials expected within the next 12-18 months

## A DEVELOPMENT MODEL ALIGNED WITH THE NEEDS OF MAJOR ONCOLOGY PLAYERS

*An interview with **Philippe Maître**, EVP Onxeo US Inc., in charge of Corporate Development*

### Onxeo has mostly early stage programs today. Is this a strategic intent?

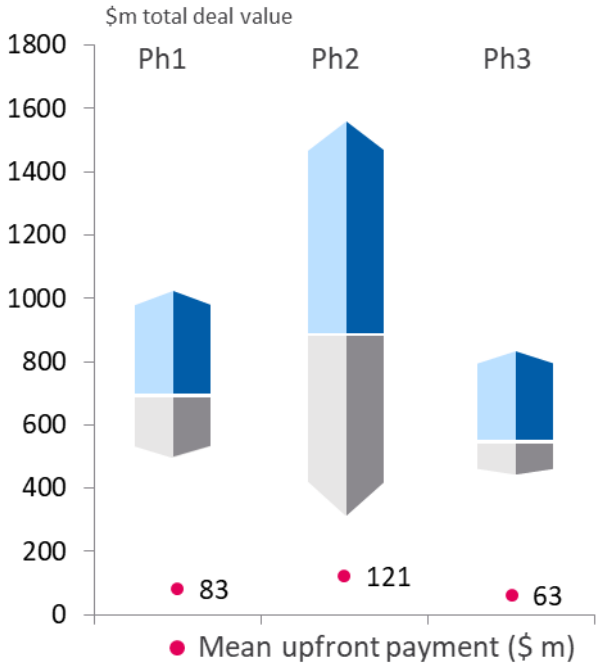
**Philippe Maître:** This is definitely a deliberate strategy, initiated a few years ago, materialized in 2014 via the merger with Topotarget and strongly reinforced in 2016 with the acquisition of DNA Therapeutics. We want to concentrate on innovative and even disruptive compounds, hence the choice of the DNA-targeting field. Our goal is to focus on assets that are one to two years from entry into the clinical stage, and bring them up to the best value inflexion point. This strategy is supported by Onxeo's know-how in what matters most at the early development stages, such as translational expertise, formulation, CMC, etc.

At the preclinical stage, a well-done job can make a huge difference in positioning a product optimally for the fastest and most efficient clinical development. Last but not least, this business model is aligned with Onxeo's human and financial resources: project timelines are shorter than for late clinical phase trials, initial investments are lower. This considerably reduces both the risk and the length of clinical development, and enables the exploration of multiple development pathways, monotherapies or combinations, which also contributes to derisking our developments.

### Doesn't this repositioning considerably delay the clinical milestones that will create value for shareholders?

**PM:** As a matter of fact, there is value creation at each and every step in a drug R&D spectrum of activities, and this is particularly true in oncology. This is clearly illustrated by the value of some recent early-stage transactions. Preclinical or early clinical stage technologies or products do generate substantial transaction prices if they are truly innovative*. In terms of the number of transactions, there is also a recent but quite clear trend: key oncology partners are filling their pipeline at an earlier stage than they used to a few years ago. We therefore believe that this positioning is the best use of Onxeo's resources to create short-term value for its shareholders.

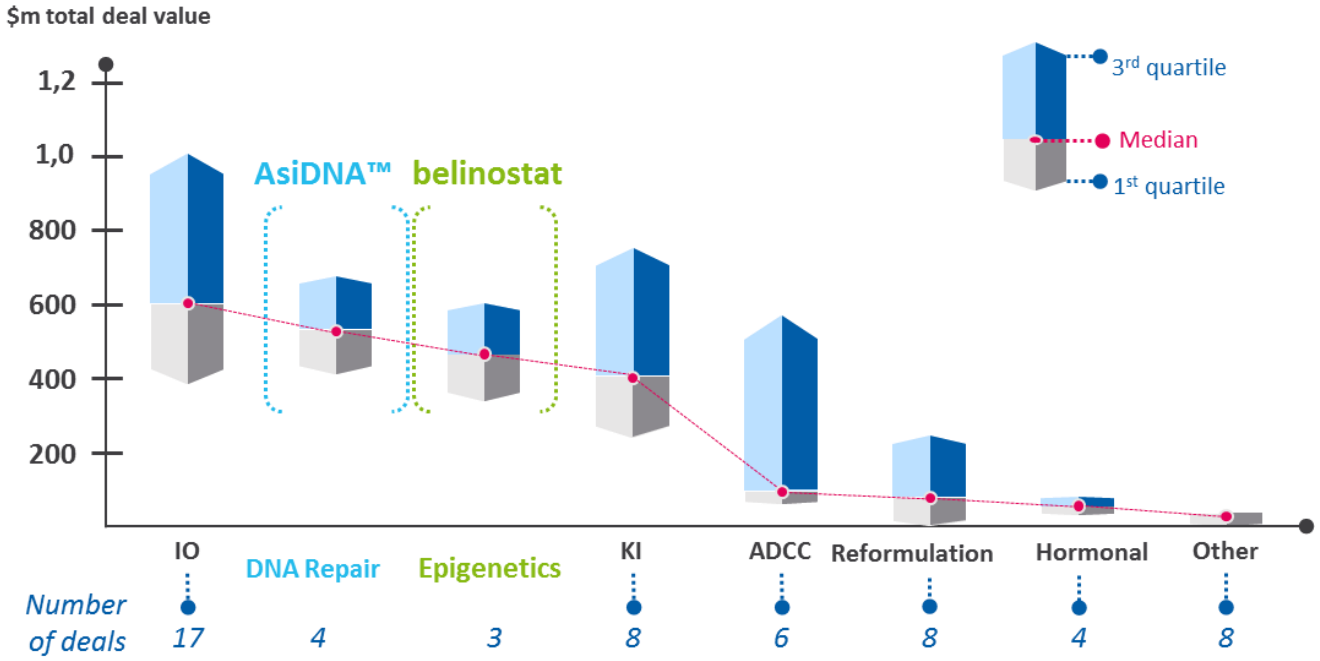
*Preclinical or early clinical stage technologies or products do generate substantial transaction prices if they are truly innovative.*




## Why are epigenetics and DNA repair today amongst the most appealing fields in oncology today?

**PM:** Together with immuno-oncology, DNA-targeting, which includes DNA break repair and epigenetics, is the field that garners the most interest from key oncology players today. The ratio between the large number of companies seeking to supplement their pipeline in this field and the limited number of companies offering truly innovative technologies partly explains the value of the transactions*. From a scientific standpoint, interfering with the tumor response to the damages to its DNA is clearly a way to address the increasing cancer resistance to existing DNA-damaging treatments, opening a new era in cancer treatment.

*DNA break repair and epigenetics garner the most interest from key oncology players today.*




**Graphs from Onxeo's analysis based on Clarivate Cortellis (only licensing deals with publicly available financial information, excluding M&A - 2013-06/2017): https://www.cortellis.com/intelligence/ - for illustration purposes only.*

## SCIENTIFIC AND MEDICAL DEPARTMENTS: A CLOSE DAY-TO-DAY COLLABORATION

### Onxeo points out its translational expertise; what does it mean exactly and when do you expect results?

**Françoise Bono (FB), Chief Scientific Officer:** Translational expertise means that preclinical work is done with the end in mind: to help our colleagues in charge of clinical studies to design the most efficient and targeted protocols for the early clinical phases. For example, we work closely together in determining biomarkers that will help select the right patients and indications, confirm the drug has reached its target or effectively measure the activity. Our objective is to deliver clinical proof of mechanism (phase I) and then proof of concept (phases I/II). Onxeo plans to conduct such studies in 2018 and 2019.

**Olivier de Beaumont,** *Chief Medical Officer*
***Françoise Bono,*** *Chief Scientific Officer*

### In what way is the mechanism used by your AsiDNA™ candidate to inhibit tumor DNA repair unique?

**FB:** The "decoy" mechanism of AsiDNA™, called signal-interfering DNA (siDNA) is genuinely unlike any other: it uses small "broken" DNA molecules to trigger a false DNA damage signal that hides the signal emitted by true DNA lesions on tumor cells, whether induced by spontaneous mutations in genetically unstable cancer cells or by anti-cancer treatments. The repair enzymes are distracted by this false DNA damage signal, and are no longer recruited at the true damage sites. Tumor cells will thus die from continuing to divide with damaged DNA. Another differentiated feature of AsiDNA™ is that - unlike DNA damage response agents that act on a specific repair enzyme, such as PARP inhibitors - AsiDNA™ is not limited to a single DNA repair pathway but impairs multiple pathways, hence bypassing the usual tumors resistance to treatments. In addition, AsiDNA does not seem to be damaging healthy cells or tissues in any of our studies so far, including in its first phase I in combination with radiotherapy in metastatic melanoma. This is another reason why we believe it has real potential, not only alone, in genetically instable cancer types, but also in combination with other treatments in many solid tumors.

*A combination therapy between a product that induces DNA breaks like belinostat and a potent DNA break repair inhibitor such as AsiDNA™ makes a lot of sense.*

### What are the synergies between your two candidates, or in combination with other molecules, and how are they useful?

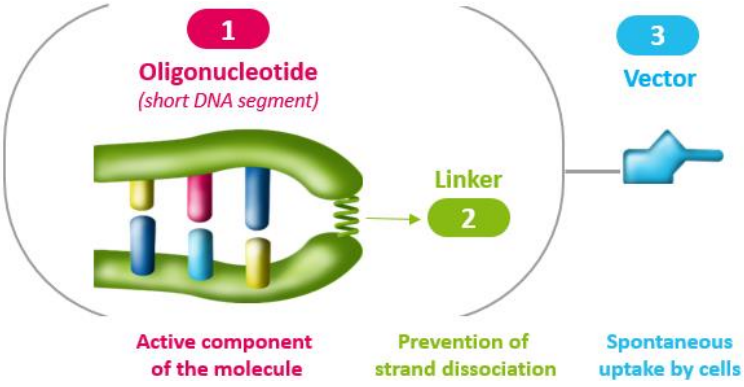
**Olivier de Beaumont (OB):** Cancer cells resist treatments notably by activating DNA damage response pathways. A combination therapy between a product that induces DNA breaks like belinostat and a potent DNA break repair inhibitor such as AsiDNA™ thus makes a lot of sense. Data from our preclinical in-vitro studies has shown a strong synergistic effect between these two drugs in different tumors. AsiDNA™ has also shown a strong synergy with PARP inhibitors in several preclinical studies. PARPi are already approved in some types of ovarian cancer, but their mechanism of action restricts them to mutated tumor types (about 15% in ovarian cancers), while AsiDNA™ has no such restrictions. These combinations, as well as other ones under review, could prevent or reduce resistance to treatment, increase efficacy and thus expand the indications of existing treatments without increased side effects.

### What specific pathologies will you target?

**OB:** Given their mechanisms of action, neither AsiDNA™ nor belinostat are limited to a specific cancer type. AsiDNA™ could be very effective as a monotherapy in genetically instable cancer types, which exist in most major cancers such as breast, ovary, lung, prostate, etc. Refining the indications that we have already explored in our extensive preclinical studies – such as triple negative breast cancer or non-small cell lung cancer – is one purpose of the phase I studies we plan, in monotherapy and in combination. The work we are currently doing to confirm activity biomarkers is also paramount to characterize the tumor types that will respond best and will be carried forward during clinical studies to build robust data sets and choose the most relevant indications going forward.

## You recently presented your platON™ platform. What are its applications?

**FB:** platON™ is Onxeo's patented platform of decoy oligonucleotides, resulting from our acquisition of DNA Therapeutics. AsiDNA™ is actually the first compound based on platON™ technology. Each of the three components of platON™ *(graph below)* is modifiable in its nature and/or position to generate new compounds that will all have different properties or applications. These new compounds may not relate to DNA repair inhibition, but they will all target the regulation of tumor DNA functions through a decoy mechanism. In a way, we could say that platON™ applications are limitless… We are applying our significant knowledge of oligonucleotides and DNA-targeting to generate from platON™ several disruptive compounds that will fuel our pipeline on an ongoing basis starting in 2018. Our teams have already identified the most promising candidates, and we will of course leverage the expertise of our newly-formed Scientific Advisory Board to advance these candidates through our pipeline.




*Components of* **platON™**

## ADVANCING A LEADING-EDGE R&D PIPELINE IN DNA-TARGETING …

| | PROGRAMS | INDICATION | PRECLINICAL | PHASE I | PHASE II | PHASE III |
|---|---|---|---|---|---|---|
| Platform | **platON™** Proprietary chemistry platform of decoy oligonucleotides | GENERATION OF NEW DNA-TARGETING COMPOUNDS | | | | |
| DNA Break repair Inhibition | AsiDNA™ IV | Solid tumors | | | | |
| | AsiDNA™ + PARPi | Solid tumors | | | | |
| | AsiDNA™ + chemo/radio | Solid tumors | | | | |
| | AsiDNA™ + belinostat /HDACi | Solid tumors | | | | |
| Epigenetics | Oral belinostat | Liquid & solid tumors | | | | |
| | Beleodaq® + CHOP | PTCL 1st line | | | | |
| BD | Livatag® | Hepatocellular carcinoma | | | | |

## … WITH NEAR-TERM MILESTONES

- ***End 2017*** – Filing for AsiDNA™ Phase I (IV route) as monotherapy in solid tumors
- ***H1 2018*** – Peer-reviewed publications of AsiDNA™ and belinostat preclinical in-vivo proofs of concept in combinations
  – Initiation of a phase I/II study of belinostat in combination and/or monotherapy
- ***H2 2018*** – Intermediate findings from AsiDNA™ phase I (mono) and belinostat (combo)
  – First new compound from platON™ patented and produced
- *End 2018 – AsiDNA™ (IV) proof-of mechanism in man*

## SHAREHOLDERS QUESTIONS

### Drug development usually takes over 10 years. How can the share price recover quickly when all your products are at an early stage?

Onxeo's strategy is not based on the full development cycle of its innovative assets. We do not intend to conduct phase III trials, as this latest stage is the longest and most expensive one. As discussed in this newsletter *(page 2-3)*, transactions on innovative assets in oncology tend to happen at an earlier stage and generate more value at these earlier stages than post-phase III. We focus on bringing our candidates from preclinical up to the clinical proof-of-concept, and, at that stage, we will proceed to negotiate value-creating partnerships. We are confident that the market will soon recognize the value of our assets as new clinical data become available over the next few months.

### I read, on an internet forum that Onxeo is now an "empty shell"? What does this mean?

An empty shell is a company with no products, projects nor contracts. This is far from the case for Onxeo. The company has multiple strategic assets, such as a diversified pipeline with near to mid-term clinical milestones in the most sought-after areas of oncology, ongoing licensing agreements and a platform set up to generate new best-in-class compounds starting in 2018. Thanks to the strong commitment of our teams and our unique know-how in translational research, Onxeo is well positioned to build on these strong assets in the near term.

### What are your plans for Livatag?

As Validive used to be, Livatag is now dedicated to partnering, and Onxeo intends to actively look for a partner able to develop its potential. While the primary endpoint was not met in the phase III study, the product showed an effect on survival when used as a single agent (vs. polytherapies in the BSC group), as well as a good safety profile. Livatag could be eligible to several development pathways. However, Onxeo will not execute or fund any such development as it would not be the most valuable usage of our capital in the best interest of our shareholders.

## PRESS COVERAGE

Les Echos — **September 19, 2017**

*" Onxeo will bounce back from its failure in liver cancer.*

actulabo — **September 20, 2017**

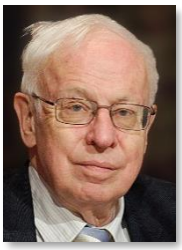
*" Onxeo sells the license of Validive to Monopar Therapeutics. The deal includes milestone payments of up to $108 m and royalties on future sales.*

BOURSIER.COM — **October 2, 2017**

*" Onxeo unveiled a new patented chemical platform of decoy oligonucleotides called "platON" to enhance its portfolio with innovative drug candidates targeting tumor DNA.*

## LATEST NEWS! INTERNATIONAL SCIENTIFIC ADVISORY BOARD OF UNDISPUTED EXPERTS IN DNA-TARGETING

Onxeo is proud and honored to host the inaugural session of its Scientific Advisory Board chaired by Professor Tomas Lindahl, which will be held on December 18, 2017 in Paris.



**Tomas Lindahl, Chair of the Onxeo Scientific Advisory Board**, FRS, FMedSci, Emeritus Professor at the Francis Crick Institute, London, United Kingdom.

Joint recipient of the **2015 Nobel Prize** in chemistry for his pioneering work on DNA repair mechanisms.

**Marie Dutreix,** Ph.D., Director of Research (CNRS – Institut Curie), Paris, France, **co-founder of DNA Therapeutics and inventor of signal-interfering DNA technology.**

**Yves Pommier**, M.D., Ph.D., Chief of the Developmental Therapeutics Branch and Laboratory of Molecular Pharmacology, NHS- NCI, Bethseda, MD, USA.

**Sebastian Amigorena**, Ph.D., Head of the Immunology Department (INSERM U932, "Cancer Immunity") at the Institut Curie.

**Robert Bristow,** M.D., PhD., formerly Professor of the Departments of Radiation Oncology at the University of Toronto, Canada and recently appointed Director of the Manchester Cancer Research Centre, United Kingdom.

**Penny Jeggo**, Ph.D., Professorial Fellow at the Genome Damage and Stability Centre - University of Sussex, Brighton, United Kingdom.

**Josef Jiricny**, Ph.D., Emeritus Professor at the Institute of Biochemistry of the Swiss Federal Institute of Technology (ETH), Zurich, Switzerland.

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