# *Onxeo Final Data from Mechanistic Livatag® Study Show Preferential Affinity for Liver, Support Use as Advanced HCC Treatment*

*Full results presented at AACR Annual Meeting 2016*
*Support continued evaluation of Livatag® in ongoing Phase III ReLive Trial*

**Paris (France), Copenhagen (Denmark), April 18, 2016** – Onxeo S.A. (Euronext Paris, Nasdaq Copenhagen: ONXEO), an innovative company specializing in the development of orphan oncology therapeutics, today reported the final data from a study aiming to confirm the mechanism of action of Livatag®, a doxorubicin loaded nanoparticle formulation based on Onxeo's Transdrug™ technology in overcoming cellular resistance in hepatocellular carcinoma (HCC). Livatag® is currently being evaluated in a Phase III trial (ReLive) in patients with advanced HCC, or primary liver cancer.

Results, presented today in a poster (Abstract #2143 / Poster #13) by Dr. Graham Dixon, PhD, Onxeo's Chief Scientific Officer, at the American Association for Cancer Research (AACR) Annual Meeting, demonstrated that the bio-distribution of doxorubicin Transdrug™ (Livatag®) nanoparticles showed a preferential affinity for the liver and an increased exposure in plasma compared to free doxorubicin, together supporting the use of Livatag® in the treatment of patients suffering from advanced HCC.

While evaluating the mechanism of action the study showed that the nanoparticle formulation of doxorubicin Transdrug™ (Livatag®) entered into HCC cell lines via passive diffusion and avoided recognition by certain multi-drug resistance (MDR) proteins, (P glycoprotein 1, or Pgp) leading to major accumulation of the drug in the cells and a dramatic increase in cytotoxicity in HCC cell lines compared to free doxorubicin.

Further investigations will be performed to test if doxorubicin Transdrug™ (Livatag®) also overcomes resistance induced by other MDR-related proteins expressed by HCC cells as well as the involvement of the Livatag® nanoparticle "ion pair" in overcoming the efflux-mediated resistance.

Graham Dixon, PhD, Chief Scientific Officer of Onxeo, commented, "These are important findings as they confirm that the underlying mechanism of action of Livatag®'s nanoformulation effectively accumulates doxorubicin specifically in the liver and evades tumor cell resistance mediated by multiple drug resistance MDR efflux pumps, enabling an efficacious and safe approach to cancer treatment. These results further support our ongoing Phase 3 ReLive study of Livatag® for the treatment of patients with advanced HCC, for which we anticipate preliminary data readout mid-2017."

###

**Reference**

Dixon, G. et al. "Mechanistic study of the relative cytotoxicity of doxorubicin loaded nanoparticle formulation compared to free doxorubicin in hepatocellular carcinoma (HCC) cell lines." Abstract #2143 / Poster #13. Presented in a poster session at the American Association for Cancer Research (AACR) Annual Meeting. 18 April 2016. New Orleans, Louisiana, USA.

**About hepatocellular carcinoma**

Hepatocellular carcinoma (HCC) or hepatocarcinoma is the most common of the primary liver cancers (85% to 90%). According to Globocan (2012 data), liver cancer is the sixth most common cancer in terms of incidence (782,000 new cases worldwide each year, 5.6% of all new cancer cases) with the second highest mortality rate (746,000 deaths, 9.1% of the total) after lung cancer. The risk factors are well known: infection by hepatitis viruses (B and C), overconsumption of alcohol (another major cause of cirrhosis) and metabolic diseases, especially obesity, a growing cause of cirrhosis and HCC.

**About ReLive**

ReLive is an international Phase III trial designed to assess Livatag®'s efficacy on survival in 400 patients with advanced hepatocellular carcinoma (HCC) following treatment after failure or intolerance to Sorafenib. The trial is ongoing in 11 countries (Europe, US, MENA region). The recruitment rate is in line with expected timelines of issuing preliminary outcomes of the Phase III study by mid-2017.

**About Livatag® (doxorubicin Transdrug™)**

Livatag® (Doxorubicin Transdrug™) is a doxorubicin formulation in the form of lyophilized nanoparticles of polyisohexylcyanoacrylate (PIHCA).This new therapeutic approach allows drug resistance to be avoided by short-circuiting the mechanisms of multi-drug resistance developed by tumor cells through the masking of the anticancer agent. Acting as a 'Trojan horse,' the nanoparticle formulation avoids rejection of doxorubicin outside the cell so that it can exert its cytotoxic action. By specifically targeting tumor cells in the liver and overcoming resistance to doxorubicin, Livatag® represents a significant breakthrough in the treatment of this cancer. The first indication of this product is hepatocellular carcinoma; the sixth most widespread cancer in the world and the second cause of cancer-related death. Livatag® is also being evaluated within a comprehensive preclinical evaluation program, to explore potential combinations with immuno-oncology agents (such as checkpoint inhibitors), cytotoxic agents and targeted therapies and expand product potential, with a primary focus on solid tumors.

**About Onxeo**

Onxeo is a leading developer of orphan oncology drugs. The Company is focused on developing innovative therapeutics for rare cancers, one of the fastest growing markets in the healthcare industry with high, unmet medical needs. Onxeo's comprehensive portfolio features a broad orphan oncology pipeline, with three independent programs in advanced clinical development, including Onxeo's first approved orphan oncology drug, Beleodaq®. In addition, Onxeo has successfully developed and registered two non-cancer products which are currently being commercialized in the U.S. and Europe. Onxeo's vision is to become a global leader and pioneer in oncology, with a focus on orphan or rare cancers, by developing advanced, effective, and safe therapeutics designed to improve the lives of patients. The Company is headquartered in Paris, France and has approximately 50 employees. Onxeo is listed on Euronext in Paris, France (Ticker: ONXEO, ISIN Code: FR0010095596) and Nasdaq Copenhagen, Denmark (Ticker: ONXEO).

***Onxeo orphan oncology products at the advanced development stage are:***

- **Livatag®** (Doxorubicin Transdrug™): Currently being evaluated in a Phase III trial (ReLive) in patients with hepatocellular carcinoma (primary liver cancer); and in combination with other cancer agents in first-line HCC
- **Beleodaq®** (belinostat): FDA-approved in the U.S. in 2014 under the agency's accelerated approval program as a second-line treatment for patients with peripheral T-cell lymphoma (PTCL) and currently marketed by Onxeo's partner in the U.S., Spectrum Pharmaceuticals; belinostat in combination with other cancer agents is currently in development in first-line treatment for patients with PTCL (BelCHOP) and in other solid tumors
- **AsiDNA**: the first-in-class siDNA (signal interfering DNA) which has successfully undergone a proof-of-concept Phase 1/2a trial in metastatic melanoma
- **Validive®** (Clonidine Lauriad®): Positive final results from a Phase II trial in head and neck cancer patients with severe oral mucositis;

Learn more by visiting www.onxeo.com.

To receive our press releases and newsletters, please register on: http://www.onxeo.com/en/newsletter/

Follow us on Twitter: @Onxeo_

**Disclaimer**

This communication expressly or implicitly contains certain forward-looking statements concerning Onxeo and its business. Such statements involve certain known and unknown risks, uncertainties and other factors, which could cause the actual results, financial condition, performance or achievements of Onxeo to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Onxeo is providing this communication as of this date and does not undertake to update any forward-looking statements contained herein as a result of new information, future events or otherwise. For a discussion of risks and uncertainties which could cause actual results, financial condition, performance or achievements of Onxeo to differ from those contained in the forward-looking statements, please refer to the Risk Factors ("Facteurs de Risque") section of the 2014 Reference Document filed with the AMF on April 14, 2015, which is available on the AMF website (http://www.amf-france.org) or on the company's website (www.onxeo.com).

**Contact:**
Nathalie Delair-Trepo
Investor Relations, Onxeo
investors@onxeo.com
+ 33 1 45 58 76 00

Caroline Carmagnol and Florence Portejoie – Alize RP (France)
onxeo@alizerp.com
+33 6 64 18 99 59 / +33 6 47 38 90 04

Kirsten Thomas / Lee Roth – The Ruth Group (U.S.)
kthomas@theruthgroup.com / lroth@theruthgroup.com
+1 508 280 6592 / +1 646 536 7012