PRESS RELEASE

Onxeo to Present New Preclinical Data at AACR 2021

- ***Confirming the effect of AsiDNA™ on resistance to KRAS inhibitors***
- ***Introducing OX400, a new generation of PARP interfering cancer drug candidates***

Paris (France), April 8, 2021 – 6:00 pm CEST - Onxeo S.A. (Euronext Growth Paris: ALONX, First North Copenhagen: ONXEO), ("**Onxeo**" or "the **Company**"), a clinical-stage biotechnology company specializing in the development of innovative drugs targeting tumor DNA Damage response (DDR), today announced the presentation of preclinical data confirming the differentiated antitumoral properties of the drug candidates generated by platON™, its patent-protected platform of decoy-agonists of the DNA Damage Response, in e-poster sessions during the American Association for Cancer Research (AACR 2021) virtual annual meeting on April 10, 2021.

The first e-poster supports the ability of AsiDNA™, the Company's first-in-class DNA Damage Response (DDR) inhibitor, to prevent resistance to KRAS inhibitors (KRASi) emerging from drug-tolerant persister cells (DTC). Novel therapies targeting the inhibition of KRAS, an oncogenic protein present in a third of cancers, have shown very promising clinical results especially in non-small cell lung cancer. However, acquired resistance hinders their efficacy. Combining AsiDNA™ to KRASi could be an additional development opportunity for AsiDNA™, in the context of its use to prevent acquired resistance to targeted therapies.

The second e-poster describes the mechanism of action of the molecules of the new OX400 family, specifically designed to interfere with PARP signaling and display immunomodulatory properties and metabolic effects.

***Judith Greciet, Chief Executive Officer of Onxeo, commented**: "Pharmaco-tolerant cells are a well-established cause of resistance to TKIs, and, as we already demonstrated last year, to PARP inhibitors. We have generated new data demonstrating that these cells are also involved in resistance to KRAS inhibitors and confirmed the efficacy of AsiDNA™ on these cells thus preventing or even reversing tumor regrowth. These results open the door for another potential combination with these innovative compounds which show high efficiency but struggle with resistance issues. In parallel, we continue to optimize the efficacy profile of the next candidates from the OX400 family, while keeping the established benefits shared by all our platON™-sourced compounds in terms of safety and absence of resistance. Our new results confirm that, by trapping and exhausting specifically PARP, OX400 compounds have the potential to modulate the immune response and wear out the tumor cell metabolism. We will continue to explore these original properties."*

Session: PO.ET03.05 - Reversal of Drug Resistance **E-poster**: 1433

Date/ Time: April 10, 2021 – 8:30 AM - 11:59 PM (U.S. Eastern Daylight Time -EDT)

To read the abstract: **Acquired resistance to KRAS^{G12C} inhibitors evolves from drug-tolerant persister cells vulnerable to AsiDNA™.**

Recent progress has been made in the development of therapeutics against KRAS^{G12C} mutated tumors, which represent approximately 15% of lung adenocarcinoma. However, therapeutic resistance to KRASG12C inhibition is still a clinical hurdle. As we have previously shown with PARP inhibitors, we describe in these new data that resistance to KRAS^{G12C} inhibitors could also emerge, at least in part, from drug-tolerant persister cells, a specific cell population that undergo "dormancy" during treatment and accumulate mutations enabling the development of resistance to KRASG12C inhibitors. AsiDNA™ can target specifically this source of resistance and therefore prevents the emergence of acquired resistance to KRAS^{G12C} inhibitors, pointing to the therapeutic opportunity of combining AsiDNA and KRAS^{G12C} to overcome tumor progression or relapse.

Session: PO.CL06.07 - Immunomodulatory Agents and Interventions **E-poster**: 527

Date/ Time: April 10, 2021 - 8:30 AM – 11:59 PM (U.S. Eastern Daylight Time -EDT)

To read the abstract: **A new generation of PARP interfering drug candidates for cancer treatment.**

Onxeo pioneered a new approach of anti-cancer treatment to tackle acquired drug resistance: the decoy agonist mechanism of action. Drugs based on this mechanism hijack and hyperactivate therapeutic targets leading to an impairment of their

physiological function. Our first compound using this breakthrough decoy agonist action, AsiDNA™, has already shown target engagement, excellent safety profile in humans and importantly, lack of acquired resistance. We now describe the mechanism of action of our OX400 molecules, designed to trap PARP proteins. We show that these molecules, by interfering with PARP signaling, display immunomodulatory properties and metabolic effects. Our results provide a preclinical rationale for using OX400 molecules as immunomodulatory and "metabolic exhauster" agents, especially in appropriately molecularly selected patients with tumors showing metabolic deficiencies.

About Onxeo

Onxeo (Euronext Paris, NASDAQ Copenhagen: ONXEO) is a clinical-stage biotechnology company developing innovative oncology drugs targeting tumor DNA-binding functions through unique mechanisms of action in the sought-after field of DNA Damage Response (DDR). The Company is focused on bringing early-stage first-in-class or disruptive compounds from translational research to clinical proof-of-concept, a value-creating inflection point appealing to potential partners.

platON™ is Onxeo's proprietary chemistry platform of oligonucleotides acting as decoy agonists, which generates new innovative compounds and broaden the Company's product pipeline.

AsiDNA™, the first compound from platON™, is a first-in-class, highly differentiated DNA Damage Response (DDR) inhibitor based on a decoy and agonist mechanism acting upstream of multiple DDR pathways. Translational research has highlighted the distinctive properties of AsiDNA™, notably its ability to abrogate tumor resistance to PARP inhibitors regardless of the genetic mutation status. AsiDNA™ has also shown a strong synergy with other tumor DNA-damaging agents such as chemotherapy and PARP inhibitors. The DRIIV-1 (DNA Repair Inhibitor-administered IntraVenously) phase I study has evaluated AsiDNA™ by systemic administration (IV) in advanced solid tumors and confirmed the active doses as well as a favorable human safety profile. The ongoing DRIIV-1b extension study is evaluating the safety and efficacy of AsiDNA™ at a dose of 600 mg in combination with the reference chemotherapy, carboplatin -/+ paclitaxel, in advanced metastatic tumors. Preliminary results from both cohorts showed good tolerability, stabilization of the disease and an increase in treatment duration compared to previous treatments. The ongoing REVOCAN phase 1b/2 study evaluates the effect of AsiDNA™ on the acquired resistance to PARP inhibitor niraparib in relapsed ovarian cancer (sponsored by Gustave Roussy). A phase 1b/2 study, AsiDNA™ Children, will be initiated in 2021 to evaluate the association of AsiDNA™ with radiotherapy in children with relapsed high-grade glioma (sponsored by Institut Curie).

OX401 is a new drug candidate from platON™, optimized to be a next-generation PARP inhibitor acting on both the DNA Damage Response and the activation of immune response, without inducing resistance. OX401 is undergoing preclinical proof-of-concept studies, alone and in combination with immunotherapies.

For further information, please visit www.onxeo.com.

Forward looking statements

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 chapter 3 "Risk Factors" ("*Facteurs de Risque*") of the Company's universal registration document filed with the *Autorité des marchés financiers* on April 27, 2020 under number D.20-0362 and to section 2 of the Amendment to the Universal Registration Document, filed with the AMF on March 9, 2021 under number D.20-0362-A01, which is available on the websites of the *Autorité des marchés financiers* (www.amf-france.org) an the Company (www.onxeo.com).

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