PRESS RELEASE

# *Onxeo Confirms in Preclinical Studies the Profile of OX401, a Potent PARP Agonist with Strong Anti-Tumor Activity and Immunological Properties*

**Paris (France), June 25, 2020 – 7.00 am CEST - Onxeo S.A.** (Euronext Paris, NASDAQ Copenhagen: ONXEO), ("**Onxeo**" or "the **Company**"), a clinical-stage biotechnology company specializing in the development of innovative drugs targeting tumor DNA Damage response (DDR), in particular against rare or resistant cancers, today announced the confirmation of the preclinical profile of OX401, the second candidate from its platON™ platform. OX401 is a potent PARP[1] agonist and represents a new generation of molecules showing strong anti-tumor activity associated with high immunological activity.

Through its action on PARP and the activation of an antitumor immune response via the cGAS-STING pathway, OX401 has shown in vivo a higher potency of activity than current PARP inhibitors, as evidenced by complete control of tumor growth.

The preclinical program already completed has confirmed the key properties of this new compound. OX401 exhibits potent antitumor activity, demonstrated in an animal model of breast cancer, related to PARP hyperactivation and diversion of its DNA repair function in specific tumor cells. PARP is a major component in the DNA repair mechanism, and the clinical benefit of acting on this protein has already been abundantly demonstrated by PARP inhibitors.

In addition, this activity on PARP induces a strong engagement of the cGAS-STING pathway[2], as shown by the increase in key biomarkers of the tumor immune response. Activation of this pathway is now a very promising new approach in immuno-oncology.

Benefiting from an original mechanism of action of decoy agonist like all candidates sourced from platON™, OX401 does not induce tumor resistance to treatment, which represents a clear differentiation from targeted therapies such as PARP inhibitors. Finally, like AsiDNA™, OX401 has no activity on healthy cells, which should provide a favorable safety profile in the clinic.

**Françoise Bono, Chief Scientific Officer of Onxeo, commented**: *"OX401 is the first representative of the OX400 family from our platON™ platform. Based on our expertise in oligonucleotides and our understanding of the decoy agonist mechanism, we have designed this candidate to be a potent inhibitor of DNA repair via the diversion (decoy effect) and hyperactivation of PARP (agonist effect) which, as a result, activates the cGAS-STING pathway. This is what we have just demonstrated: OX401 has a more potent action, in all areas, than that found with the PARP inhibitors available today, without the emergence of acquired resistance. As OX401 triggers robust local anti-tumor immunity, the next key preclinical step will be to study its association with immune checkpoint inhibitors. For this development, we have benefited from all the expertise accumulated during the development of AsiDNA™ and have thus obtained in the span of a few months an optimized compound, ready to enter the final stages of preclinical validation. These translational studies will allow us to best prepare for entry into the clinic, which could take place within 18 to 24 months*".

Immunotherapy has recently shown the potential to transform the treatment of cancer by triggering anti-tumor T cell responses via immune checkpoint blockade. This approach has led to outstanding clinical responses in previously untreatable tumors, although in limited patient subsets. Stimulator of interferon genes (STING) has been identified as having a key role in the field as a critical mediator of the innate immune-sensing of cancer.

In these in vivo proof of efficacy studies, the therapeutic value of OX401 was further demonstrated, as it has now been shown that OX401 triggers robust local anti-tumor immunity involving both adaptive and

[1] **PARP** is a key protein in the tumor DNA repair process

[2] The **cGAS-STING pathway** is a component of the innate immune system, which detects cytosolic DNA (involved in particular in carcinogenesis) and induces an immune response accordingly

innate immune responses, in mice bearing syngenic breast tumors. This activity led to complete control of tumor growth with OX401 treatment. These results suggest that OX401 could also increase the effectiveness of the traditional immune checkpoint blockade by overcoming the local immunosuppressive environments seen in cancer.

## 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 assessing the safety and efficacy of a 600 mg dose of AsiDNA™ in combination with carboplatin and then with carboplatin and paclitaxel, in patients with solid tumors who are eligible for such treatments. Preliminary results from the first cohort with carboplatin alone showed good tolerability, stabilization of the disease and an increase in the duration of treatment compared to previous treatments.

**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, 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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