AACR 2022: Oxford BioTherapeutics to Present Potential Novel Immuno-Oncology Mechanism in Combination with Checkpoint Inhibitors for Experimental ADC Medicine OBT076

- *Initial data from the Phase 1 dose escalation part of the OBT076 trial in adult patients with advanced solid tumors indicated that OBT076 had a favorable tolerability profile; recommended dose was defined at 3.0 mg/kg*
- *OBT076 showed preliminary signs of clinical activity as a single agent and in combination with a checkpoint inhibitor (CPI), including near complete responses after 2-5 cycles of OBT076 and 1-2 cycles of a CPI, in two chemo-refractory patients with low PD-L1 expression*
- *Preliminary analysis of PD markers suggests OBT076 activates the patient's immune response against primary and metastatic tumors through a potentially novel mechanism: drug-induced depletion of CD205+ immuno-suppressive cells and subsequent T-cell activation*
- *Company to advance OBT076 into single agent expansion cohorts and combination trials (with CPIs) in both checkpoint-naïve and resistant patients*
- *Data to be presented at AACR 2022 in the session titled: Immune Response to Therapies / Immune Monitoring and Clinical Correlates, on 11th April 2022 at 13:30:00 PM.*

Oxford, UK and San Jose, California, 7th April 2022 - Oxford BioTherapeutics (OBT), a clinical stage oncology company with a pipeline of immuno-oncology and Antibody Drug Conjugate (ADC)-based therapies, today announced a forthcoming presentation featuring preliminary clinical data from its ongoing Expansion Phase I Trial (NCT04064359) of its experimental CD205-directed ADC, OBT076, at the American Association of Cancer Research (AACR) Annual Meeting 2022, taking place 8th – 13th April in New Orleans, US.

The presentation highlights are below:

- Near complete responses in two chemo-refractory advanced cancer patients with low PD-L1 expression after 2-5 cycles of OBT076 and 1-2 cycles of a CPI indicate preliminary signs of clinical activity, and
- Translational work on patients receiving OBT076, followed by an immune CPI, whose immuno- blood profiling revealed a potential novel immuno-oncology mechanism for immune system reactivation and tumor shrinkage.

“We are pleased to share these data showing promising preliminary signs of clinical activity and a favorable tolerability profile for our experimental CD205-directed ADC, OBT076, in patients with advanced and chemo-refractory cancers,” said **Christian Rohlff, PhD, Chief Executive Officer (CEO) of Oxford BioTherapeutics.** “The results support our excitement around OBT076 as a therapeutic capable of harnessing the immune system to treat patients with advanced, difficult to treat cancers both as monotherapy and in combination with a CPI. Our preliminary data suggest that depletion of CD205+ immuno-suppressive cells and subsequent T-cell activation after OBT076 treatment followed by a single cycle of a CPI coincides with the rapid resolution of the primary tumor, as well as metastases in a chemo-refractory advanced gastric cancer patient.”

Summary of the Data to Be Presented at AACR
The objective of the translational work emerging from the ongoing Phase I OBT076 trial (NCT04064359), presented at AACR, is to evaluate the antitumor activity of OBT076, at a lower test dose of 2.0-2.5 mg/kg, in combination with a CPI in chemo-refractory solid tumor patients.

As of the data cut-off (January 31, 2022), 2 patients with advanced solid tumors with at least 1 metastatic site had been treated with the combination. Patient 1 received OBT076 for 5 cycles; the first cycle at 2.5 mg/kg and subsequent cycles at 2.0 mg/kg, followed by 1 cycle of a CPI at 200 mg approximately 2 weeks later. Clinical response was evaluated and immunological markers (CD45, CD205, CD4, CD8, and PD1) in peripheral blood cells were quantified using flow cytometry.

Patient 1 had a diagnosis of chemo-refractory advanced gastric cancer with 60% CD205 expression in the primary tumor and had previously undergone 2 lines of conventional chemotherapy treatment. After 3 OBT076 cycles at 2.0 mg/kg, there was a ~40% shrinkage in the primary gastric tumor size and resolution of ascites and lymph node metastases.

Following 2 further cycles of OBT076 and 1 cycle of CPI, complete response was achieved for the primary tumor. Flow cytometry showed simultaneously occurring increases in PD1+ T-cells, T-cell induction, and decreases in immuno-suppressive CD4+ CD205+ and CD8+ CD205+ cells; coinciding with rapid resolution of the primary tumor, lymph node metastases and ascites.

Similar findings were reported for Patient 2 after 2 cycles with OBT076 followed by CPI. Both Patients 1 and 2 had near complete response after treatment with OBT076 followed by 1-2 cycles with CPI despite having low PD-L1 expression.

“These findings suggest that OBT076 may activate the patient’s immune response against the tumor through a potentially novel mechanism: drug-induced depletion of CD8+ CD205+ immuno-suppressive cells and subsequent T- cell activation,” said **Rahim Fandi, MD, PhD, Chief Medical Officer (CMO) of Oxford BioTherapeutics**. “The treatment of patients who are resistant to therapy with CPIs is challenging. These data give us hope that OBT076 could achieve favorable clinical outcomes in such patients when used in combination with immune CPIs. Based on these encouraging results, we are advancing OBT076 into the next stage of clinical development as both a single agent and in combination with a CPI, for the treatment of multiple solid tumor indications, with the goal of improving outcomes for patients with difficult-to-treat cancers.”

The e-poster and abstract will be accessible on the AACR conference website. The abstract and presentation details are as follows:

Title: Potential Novel Immuno-oncology Mechanism revealed during Translational Phase I Immuno- blood Profiling of Experimental ADC medicine OBT076 in A Gastric Cancer Patient.

Session: Immune Response to Therapies / Immune Monitoring and Clinical Correlates
Date: 11th April 2022 13:30:00 PM
Location: Poster Section 31
Poster #: 5497
Authors: Christian Rohlff et al.

OBT076 Further Clinical Development Plans

Based on these preliminary results, OBT plans to advance OBT076 as a monotherapy as well as in combination in trials in both checkpoint-naïve and resistant patients. These Phase 1b trials will assess the safety of OBT076 in combination with CPI in patients with solid tumors, and as a monotherapy in patients with solid tumors. Subsequent disease-specific Phase 2a trials are planned in patients with non-small cell lung cancer, ovarian cancer and gastric cancer. OBT is also planning for later-stage trials of OBT076, including in combination with CPI.

About Oxford BioTherapeutics

Oxford BioTherapeutics is a clinical stage oncology company based in Oxford, UK and San Jose and Morristown NJ USA; with a pipeline of first-in-class immuno-oncology (IO) and antibody-drug conjugate (ADC) based therapies designed to fulfill major unmet patient needs in cancer therapeutics. These include bispecific, Chimeric Antigen Receptor T Cell (CAR-T), Antibody Drug Conjugate (ADC) and Antibody Dependent Cell-mediated Cytotoxicity (ADCC) therapeutics.

OBT's first clinical program, OBT076, initiated expansion in a U.S. Clinical Trial in 2021 in patients with advanced or refractory solid tumors, including gastric, bladder, ovarian and lung cancer, where CD205 is overexpressed. Infiltration of tumors by immunosuppressive cells correlates with adverse outcomes (lower progression free and overall survival), suggesting that this process contributes to the progression of several cancers.

OBT's proprietary OGAP® target discovery platform is based on one of the world's largest proprietary cancer membrane proteomic databases, with data on over 5,000 cancer cell proteins providing unique, highly-qualified oncology targets, of which three programs are in clinical development in the USA and Europe. OBT's IO discovery process provides unique insights into the cancer-immune cell synapse and has identified several novel IO monoclonal and bispecific antibody candidates for cancer therapies.

A major differentiator between OBTs discovery platform and other approaches is the retention of the link between individual patient samples through to the design of therapeutic antibodies and diagnostic patient selection tools, increasing the overall successful transition into clinical development.

OBT's pipeline and development capabilities have been validated through multiple strategic partnerships including with Boehringer Ingelheim and our cell therapy research collaboration with Kite Pharma as well as other world leaders in antibody development (such as Amgen, Immunogen, WuXi, Medarex (BMS), Alere (Abbott), BioWa, and Nerviano). OBT has a strong oncology focused management team and board with significant experience in developing IO and antibody-based therapies.

For more information on Oxford BioTherapeutics, please visit www.oxfordbiotherapeutics.com

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