

TB: this is revised version for the US which includes several new sections that were not included in the original Japanese version.

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Oncolys BioPharma Inc.

## Oncolys BioPharma announces the initiation of Investigator-Sponsored Clinical Trial exploring Telomelysin (OBP-301)-Pembrolizumab Combination Therapy in Advanced Esophagogastric Adenocarcinoma

Oncolys BioPharma (“Oncolys”) today announced the initiation of a Phase II Clinical Trial to study the efficacy and safety of a combination therapy, with Telomelysin (OBP-301), oncolytic viral immunotherapy, and pembrolizumab, an anti-PD-1 therapy. This Phase II clinical trial will be conducted in patients with advanced gastric cancer and gastro-esophageal junction (GEJ) who have disease progression following treatments on at least two lines of prior therapy for advanced disease. Pembrolizumab was approved by the FDA in September 2017 and is indicated for the treatment of patients with PD-L1–positive recurrent or advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received two or more lines of systemic therapy for advanced disease. The study is being led by Dr. Manish Shah, Division of Hematology and Medical Oncology, Department of Medicine, Weill Cornell Medical College, Cornell University. The study will be open across the US in multiple centers.

“The Oncolys clinical development strategy for Telomelysin in esophageal cancer is designed to rationally exploit the compound’s unique activity profile in combination with other therapies,” said Mr. Yasuo Urata, president and chief executive officer of Oncolys BioPharma. One of the research concepts of Telomelysin is a “cure without surgery”, and Oncolys is determined to continue to make a contribution to the development of effective cancer therapy by discovering the potential of Telomelysin combining it with another anti- tumor treatment” .

“This investigator-sponsored trial is designed to provide important insight into the potential clinical utility of a combination of Telomelysin and Pembrolizumab as a 3<sup>rd</sup> or 4<sup>th</sup> line therapy. “Based on the extensive preclinical and clinical data generated to date for both compounds, we believe that a combination regimen of Telomelysin and Pembrolizumab may provide patients with esophageal cancer improved outcomes” .

This Phase II clinical trial is scheduled to be conducted in parallel to an investigator- sponsored trial of Telomelysin-pembrolizumab combination therapy led by Dr. Takashi Kojima, at the National Cancer Center Hospital East, Japan. While squamous cell cancer represents the majority of Japanese esophageal cancer,

adenocarcinomas represent majority esophageal cancer in the US and Europe. Both clinical trials will enable to characterize efficacy of Telomelysin in both patient populations.

Currently, clinical trials of radiation combined esophageal cancer Phase I in Japan are in the final stage, and Investigator-sponsored trials at the National Cancer Center Hospital East are proceeding to the Phase Ib clinical trial. In addition, Oncolys has a Phase II clinical trial for melanoma in the US, and a Phase I/II trial for hepatocellular cancer in Taiwan and Korea where the safety of the highest single-dose level administration was confirmed and multi-dose administration on Cohort 5 is in progress.

### **Rationale for the combination approach:**

Immunotherapy for gastroesophageal adenocarcinoma has primarily been examined as monotherapy, with response rates ranging from 10-15%, and patient selection only marginally improved by PD-L1 status. A novel concept in immuno-oncology is the use of cancer specific oncolytic viral therapy to induce an immunogenic cell death in the tumor to augment the immune activation driven by PD-1 inhibition. This involves selective replication within neoplastic cells, and induction of systemic antitumor immunity.

Telomelysin (OBP-301) is a telomerase-specific, replication-selective adenovirus in which the human telomerase reverse transcriptase (hTERT) promoter drives viral replication efficiently killing only cancer cells. Preclinical data show that OBP-301 is synergistic with anti-PD-1 therapy with a projected improved response rate of 30% or greater providing the rationale for the proposed use of Telomelysin (OBP-301) in patients with PD-L1-positive, advanced gastric and gastroesophageal junction cancers.

“Although the recent approval of several new agents for the treatment of gastroesophageal adenocarcinoma has helped to improve the treatment and outcomes for patients with this disease, this is an indication that still has significant unmet medical need,” said Manish Shah, M.D, Chief, Solid Tumor Service, Director, Gastrointestinal Oncology Program, Co-Director, Center for Advanced Digestive Care, Bartlett Family Associate Professor of Gastrointestinal Oncology at Weill Cornell Medical College, and the principal investigator of this trial. “The combination of Telomelysin (OBP-301) and Pembrolizumab may improve the control of this disease. Data from this study will provide a foundation on which to explore the clinical benefit this combination regimen may provide to patients with esophageal cancer in a larger registration study” .

### **Trial Design**

This phase II study will enroll patients with advanced gastric and gastroesophageal junction adenocarcinoma that has progressed on at least 2 lines of prior therapy for advanced disease and will examine the addition of the oncolytic virus, OBP-301, administered prior to pembrolizumab in this patient population. Patients will receive

OBP-301 at  $1 \times 10^{12}$  viral particles (VP)/ tumor injection administered every two weeks x 4 injections as well as standard dose pembrolizumab 200 mg IV every 3 weeks. The primary endpoint is the objective response rate (RR), as measured by iRECIST criteria. The secondary endpoints include the disease control rate, duration of response, progression-free survival (PFS), and overall survival (OS).

Exploratory analysis includes changes in certain biomarkers.

#### **Additional comment from Mr. Yasuo Urata, President & CEO**

We have already obtained very promising clinical results showing high regional-CR (Complete Response) around 60% in stage II and III of esophageal squamous cell carcinoma from Japanese clinical study. I am confident that this Phase II study clinical study at Cornell University would be very important for further development of our oncolytic virotherapy, OBP-301. Once we obtain synergistic effect of OBP-301 in combination with Pembrolizumab for esophagogastric adenocarcinoma in terms of response rate and overall survival rate, the potential market value of OBP-301 would become tremendously high and OBP-301 could potentially change the treatment strategy for esophagogastric cancer globally .

#### **About Telomelysin (OBP-301)**

Telomelysin (OBP-301) is a novel, condition-restricted, replication-competent adenovirus derived from human adenovirus type 5 (Ad-5). The normal transcriptional regulatory element of the Ad5 E1A gene is replaced by the human Telomerase Reverse Transcriptase gene (hTERT) promoter. The hTERT promoter encodes for the catalytic protein subunit of telomerase, a polymerase that acts to stabilize telomere lengths and is highly expressed in tumors but not in normal, differentiated adult cells. Additional modifications to enhance specificity of the OBP-301 construct include the replacement of the normal transcriptional element of viral E1B gene by an internal ribosomal entry site (IRES) sequence to minimize “leakiness”). Furthermore, OBP-301 is the first replication-competent adenovirus that retains a fully functional viral E3 region, which codes for proteins that regulate the immune response to the virally infected cell

#### **About Oncolys BioPharma Inc.**

*Oncolys BioPharma is a TSE Mothers-listed biopharmaceutical company which focuses on the development of novel biologics for the treatment of cancer and infectious diseases. The company's lead product for the treatment of cancer, Telomelysin (OBP-301), is based on replication-competent oncolytic virus, and is being tested in Phase I/II clinical trial in Asia and Phase II in the USA, for various solid tumors. A novel cancer diagnostic product, TelomeScan® (OBP-401/1101), is expected to be effective in detecting various types of cancer and inflammatory diseases and*

*adopted in several private practices. The company also has a major program OBP-601 (Censavudine) for infectious diseases, for which it completed Phase II clinical trial in the U.S. for HIV/AIDS therapy, supported by BMS.*

*For more information, please visit <http://www.oncolys.com/en/>*

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The announcement above will not affect Oncolys' earnings for the fiscal year.

**Ends**

TRANSLATION