A Phase 1/2 Open-Label Study of IOV-GM-1-201 of TALEN®-Mediated PD-1 Inactivated Autologous Tumor-Infiltrating Lymphocytes (TIL; IOV-4001) in Patients with Advanced Melanoma and NSCLC

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Background

• Adjuvant cell therapy using autologous tumor-infiltrating lymphocytes (TIL; i.e., ILN-145) has demonstrated excellent efficacy in patients with advanced solid tumors, including melanoma and non-small-cell lung cancer (NSCLC).

• One-time transgenic TIL cell therapy achieved durable responses in the post-immune checkpoint inhibitor (ICI) setting in patients with advanced (unresectable or metastatic) melanoma, with an investigator-assessed objective response rate (IRR) of 88% for 36% and median duration of response (DOR) not reached after 13.1 months of follow-up. However, low TIL persistence, toxicity, and high costs have limited its clinical application.

• In-ICI patients with advanced melanoma, combination of bilateral plus pembrolizumab resulted in 100% objective response rate, 100% durable response rate (DOR), and 100% overall survival at 2 years. The median duration of response was not reached, and the estimated 3-year overall survival was 21%.

• Among patients with advanced metastatic NSCLC, ILN-145 monotherapy resulted in a 21.4% ORR after a median of 2 prior lines of therapy, including ICI and chemotherapy (in most patients). Hence, there is a need for systemic anti-PD-1 therapy, while avoiding short- and long-term systemic adverse events (AEs) associated with ICIs.

Objectives

• Here, we describe the IOV-GM-1-201 study investigating IOV-4001 for treatment of patients with advanced melanoma and NSCLC.

Study Design and Treatment Regimen

Objectives

• Phase 1: Confirm safety of IOV-4001 during safety run-in and determine recommended phase 2 dose (RP2D) of IOV-4001

• Phase 2: Assessment of efficacy of IOV-4001 (per RECIST v1.1 as assessed by the investigator) using RP2D determined in phase 1

Study Endpoints

Primary Endpoints

• Safety as assessed by DLTs and AEs

Secondary Endpoints

• OR rate, DOR safety, TIL persistence, OS, safety, tolerability, feasibility

Exploratory Endpoints

• IOV-4001 persistence, relationship between IOV-4001 persistence and efficacy, relationship between IOV-4001 persistence and correlative immune biomarkers

Inclusion Criteria

• Cohort 1: Confirmed histopathologic or radiologic stage IIIC, IIID, or IV unresectable or metastatic melanoma that has progressed during or ≤12 weeks after last anti–PD-1/PD-L1 line of therapy

• Patients must have also received a BRAF and/or MEK inhibitor or BRAF V600 mutation-positive

• Cohort 2: Stage III or IV NSCLC with ≤12 months of therapy and disease progression after first line of therapy

• No other primary malignancy within prior 3 years

• Any form of primary immunodeficiency

• ECOG performance status ≤1

Exclusion Criteria

• Unresectable melanoma

• Symptomatic untreated brain metastases

• Organ allograft or prior cell therapy

• Systemic steroid therapy ≤10 days of prednisone or another steroid equivalent

• Any form of prior immunotherapy

• No other malignancy within prior 3 years

• Live or attenuated vaccination within 28 days prior to the start of NMA-LD

• DLT: Dose-limiting toxicity

• AEs: Adverse events

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