信達生物製藥

INNOVENT BIOLOGICS, INC.

(Incorporated in the Cayman Islands with Limited Liability)

(Stock Code: 1801)

VOLUNTARY ANNOUNCEMENT
THE NATIONAL MEDICAL PRODUCTS ADMINISTRATION APPROVES TYVYT® (SINTILIMAB INJECTION) IN COMBINATION WITH BEVACIZUMAB AND CHEMOTHERAPY IN PATIENTS WITH EGFR-MUTATED NON-SQUAMOUS NSCLC WHO PROGRESSED AFTER EGFR-TKI THERAPY

This announcement is made by Innovent Biologics, Inc. (the "**Company**", together with its subsidiaries, the "**Group**") on a voluntary basis to inform the shareholders and potential investors of the Company about the latest business updates of the Group.

The board of directors of the Company (the "**Board**") is pleased to announce that the National Medical Products Administration ("**NMPA**") of China has approved the supplemental New Drug Application ("**sNDA**") for innovative PD-1 inhibitor TYVYT® (sintilimab injection) in combination with bevacizumab and chemotherapy (pemetrexed and cisplatin) in patients with epidermal growth factor receptor ("**EGFR**")-mutated non-squamous non-small cell lung cancer ("**NSCLC**") who progressed after EGFR tyrosine kinase inhibitor ("**TKI**") therapy. It makes TYVYT® (sintilimab injection) globally the first PD-1 inhibitor approved for patients with EGFR-mutated non-squamous NSCLC that progressed after EGFR-TKI therapy, which is a breakthrough in the field of immunotherapy.

This is the seventh NMPA-approved indication of TYVYT® (sintilimab injection). The first six indications of TYVYT® (sintilimab injection) are included in the National Reimbursement Drug List ("**NRDL**"), making TYVYT® (sintilimab injection) the only PD-1 inhibitor for the first-line treatment of five high-incidence cancer types in the NRDL – including non-squamous NSCLC, squamous NSCLC, hepatocellular carcinoma, esophageal squamous cell carcinoma, and gastric cancer. TYVYT® (sintilimab injection) is also the first and the only immunotherapy medicine for gastric cancer in the NRDL. This is also the eighth NMPA-approved indication of BYVASDA® (bevacizumab injection).

This new approval in China was based on the results of a randomized, double-blind, multi-center, prospective Phase 3 clinical trial (ORIENT-31, NCT03802240) evaluating TYVYT® (sintilimab injection) ± BYVASDA® (bevacizumab injection) + chemotherapy (pemetrexed and cisplatin) for the treatment of patients with EGFR-mutated non-squamous NSCLC who progressed after EGFR-TKI therapy.

In the second interim analysis (data cutoff date: March 31st, 2022), in the intent-to-treat ("**ITT**") population, based on the assessment by the Independent Radiographic Review Committee ("**IRRC**"), significant and clinically meaningful progression-free survival ("**PFS**") benefit was sustained with sintilimab plus bevacizumab plus chemotherapy compared with chemotherapy alone (median PFS: 7.2 months vs. 4.3 months; HR=0.51, p<0.0001). Additionally, the key secondary endpoints of objective response rate ("**ORR**") and duration of response ("**DOR**") were improved with sintilimab plus bevacizumab plus chemotherapy, compared with chemotherapy alone.

As of data cutoff date July 4th, 2022, a trend towards overall survival ("**OS**") benefit with sintilimab plus bevacizumab and chemotherapy was observed although the OS for chemotherapy was prolonged due to crossover after progression in chemotherapy group. The median OS for sintilimab plus bevacizumab plus chemotherapy and chemotherapy alone were 21.1 months vs 19.2 months, HR=0.98. After adjusting for crossover, the OS HR ranged from 0.79 to 0.84. In the exploratory analyses of quality of life, compared with the chemotherapy alone, sintilimab plus bevacizumab and chemotherapy showed longer median time-to-deterioration of the Global Health Status Dimension Score of EORTC Quality of Life Questionnaire Core 30 (QLQ-C30). The safety profile of this study was consistent with that observed in previously reported studies of sintilimab and bevacizumab, without new or unexpected safety signals.

The first interim analysis results of ORIENT-31 were published in *The Lancet Oncology* on July 28, 2022[i]. The second interim analysis results were published in *The Lancet Respiratory Medicine* on May 5, 2023[ii].

Lung cancer is the leading cause of cancer death worldwide, and the second most commonly diagnosed tumor type[iii]. NSCLC accounts for about 80% to 85% of all lung cancer, in which about 70% of NSCLC patients present with locally advanced or metastatic disease that is not suitable for surgical resection at diagnosis. In China, non-squamous NSCLC accounts for about 70% of NSCLC patients. Different from the western population, about half of the Chinese patients with NSCLC have EGFR mutations. EGFR-TKI targeted therapy is the first line treatment choice in NSCLC patients with EGFR sensitive mutation. However, almost all patients will eventually develop TKI-resistance and progression of disease and there are no good treatment options for EGFR-TKI failed NSCLC population[iv].

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[i] Lu S, Wu L, Jian H, et al. Sintilimab plus bevacizumab biosimilar IBI305 and chemotherapy for patients with EGFR-mutated non-squamous non-small-cell lung cancer who progressed on EGFR tyrosine-kinase inhibitor therapy (ORIENT-31): first interim results from a randomised, double-blind, multicentre, phase 3 trial. Lancet Oncol. 2022;S1470-2045(22)00382-5. doi:10.1016/S1470-2045(22)00382-5.

[ii] Lu S, Lin, Wu, et al. Sintilimab plus chemotherapy for patients with EGFR-mutated non-squamous non-small-cell lung cancer with disease progression after EGFR tyrosine-kinase inhibitor therapy (ORIENT-31): second interim analysis from a double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Respir Med May 5, 2023. doi:10.1016/S2213-2600(23)00135-2.

[iii] Zheng R, Zhang S, Wang S, et al. Lung cancer incidence and mortality in China: updated statistics and an overview of temporal trends from 2000 to 2016[J]. Journal of the National Cancer Center, 2022.

[iv] Chen P, Liu Y, Wen Y, et al. Non-small cell lung cancer in China[J]. Cancer Communications, 2022, 42(10): 937-970.

The ORIENT-31 study is globally the first prospective, randomized and double-blind phase 3 study that demonstrated that PD-1 inhibitor ± bevacizumab combined with chemotherapy can significantly prolong PFS in EGFR-mutated non-squamous NSCLC population who have failed EGFR-TKI treatment. In addition, compared with standard platinum-based chemotherapy, TYVYT® (sintilimab injection) and bevacizumab combined with chemotherapy significantly improved the ORR and DOR, showing survival benefit trend as well as improvement in quality of life. The approval of this indication brings a new treatment option for NSCLC patients who have failed EGFR-TKI treatment, benefiting more Chinese patients. The Company believes that the approval of this new indication will further strengthen the leading position of TYVYT® (sintilimab injection) in the PD-(L)1 market in China and bring safe and efficacious treatment options to more cancer patients.

About the ORIENT-31 Study

ORIENT-31 is a randomized, double-blind, multi-center Phase 3 clinical study conducted in China evaluating sintilimab, with or without bevacizumab, combined with chemotherapy (pemetrexed and cisplatin) in patients with EGFR-mutated locally advanced or metastatic non-squamous NSCLC who have progressed following EGFR TKI treatment (ClinicalTrials.gov, NCT03802240). The primary endpoint is PFS as assessed by IRRC based on RECIST v1.1. The secondary endpoints include OS, PFS as assessed by investigators, ORR and safety.

About Sintilimab

Sintilimab, marketed as TYVYT® (sintilimab injection) in China, is a PD-1 immunoglobulin G4 monoclonal antibody co-developed by the Company and Eli Lilly and Company. Sintilimab is a type of immunoglobulin G4 monoclonal antibody, which binds to PD-1 molecules on the surface of T-cells, blocks the PD-1/PD-Ligand 1 (PD-L1) pathway, and reactivates T-cells to kill cancer cells[v]. The Company is currently conducting more than 20 clinical studies of sintilimab to evaluate its safety and efficacy in a wide variety of cancer indications, including more than 10 registrational or pivotal clinical trials.

In China, sintilimab has been approved for seven indications and included in the NRDL for six indications. The NRDL reimbursement scope of TYVYT® (sintilimab injection) include:

- For the treatment of unresectable locally advanced, recurrent or metastatic gastric or gastroesophageal junction adenocarcinoma;
- For the treatment of unresectable locally advanced, recurrent or metastatic esophageal squamous cell carcinoma;
- For the treatment of unresectable locally advanced or metastatic non-squamous NSCLC lacking EGFR or ALK driver gene mutations;
- For the treatment of unresectable locally advanced or metastatic squamous NSCLC;
- For the treatment of unresectable or metastatic hepatocellular carcinoma with no prior systematic treatment; and

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[v] Wang J, Fei K, Jing H, et al. Durable blockade of PD-1 signaling links preclinical efficacy of sintilimab to its clinical benefit. mAbs 2019;11(8): 1443-1451.

- For the treatment of relapsed or refractory classic Hodgkin's lymphoma after two lines or later of systemic chemotherapy.

Additionally, sintilimab has been approved in combination with bevacizumab and chemotherapy (pemetrexed and cisplatin) for the treatment of patients with EGFR-mutated non-squamous NSCLC who progressed after EGFR-TKI therapy.

Besides, two clinical studies of sintilimab have met their primary endpoints:

- Phase 2 clinical study of sintilimab monotherapy as second-line treatment of esophageal squamous cell carcinoma; and

- Phase 3 clinical study of sintilimab monotherapy as second-line treatment for squamous NSCLC with disease progression following platinum-based chemotherapy.

About BYVASDA® (bevacizumab injection)

BYVASDA® (bevacizumab injection) is a recombinant humanized anti-Vascular endothelial growth factor ("**VEGF**") monoclonal antibody drug. VEGF is an important factor in angiogenesis that is highly expressed by the endothelial cells in most human tumors. An anti-VEGF antibody binds VEGF-A selectively with high affinity and blocks its binding to VEGF-2 receptors on the surface of vascular endothelial cells, thereby inhibiting signaling pathways such as PI3K-Akt/PKB and Ras-Raf-MEK-ERK. BYVASDA®(bevacizumab injection) produces anti-tumor effects by inhibiting the growth, proliferation and migration of vascular endothelial cells, blocking angiogenesis, reducing vascular permeability, blocking blood supply to tumor tissues, inhibiting the proliferation and metastasis of tumor cells and inducing apoptosis in tumor cells[vi]. In China, BYVASDA®(bevacizumab injection) is approved for eight indications including advanced NSCLC, metastatic colorectal cancer, adult recurrent glioblastoma, advanced or unresectable hepatocellular carcinoma, epithelial ovarian, fallopian tube, or primary peritoneal cancer and cervical cancer, seven of which are included in the NRDL.

By Order of the Board
Innovent Biologics, Inc.
Dr. De-Chao Michael Yu
Chairman and Executive Director

Hong Kong, China,
May 9, 2023

As at the date of this announcement, the Board comprises Dr. De-Chao Michael Yu as Chairman and Executive Director and Mr. Ronald Hao Xi Ede as Executive Director, and Dr. Charles Leland Cooney, Ms. Joyce I-Yin Hsu, Dr. Kaixian Chen and Mr. Gary Zieziula as Independent Non-executive Directors.

[vi] International Journal of Nanomedicine 2019:14 7643-7663