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## **I-Mab and ABL Bio Report Preclinical Data of 4-1BB-targeting Bispecific Antibodies at 2021 SITC**

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- *Preclinical data of TJ-CD4B/ABL111 and TJ-L14B/ABL503 demonstrate targeted safety profile and enhanced anti-tumor activity*
- *Both studies are undergoing phase 1 clinical trials in the United States*

SHANGHAI and GAITHERSBURG, Md. and SEONGNAM, South Korea, Nov. 9, 2021 /PRNewswire/ -- I-Mab (Nasdaq: IMAB), a clinical-stage biopharmaceutical company committed to the discovery, development, and commercialization of novel biologics, and ABL Bio, Inc. (Kosdaq:298380, hereafter "ABL"), a clinical-stage biotech developing bispecific antibody technology for immune-oncology and neurodegenerative diseases, today jointly announced preclinical data of their 4-1BB bispecific antibodies at the 2021 Society for Immunotherapy of Cancer (SITC) Annual Meeting. The new data demonstrate the unique mechanisms of action of TJ-CD4B/ABL111 and TJ-L14B/ABL503 which have resulted in localized drug action and reduced systemic toxicity, as well as sustained anti-tumor efficacy.



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Stimulation of 4-1BB is a promising therapeutic strategy for improving the current immunotherapy for multiple cancers. TJ-CD4B/ABL111 and TJ-L14B/ABL503, both jointly developed by I-Mab and ABL, are undergoing phase 1 clinical studies in the United States.

"Bispecific antibodies are rapidly recognized for their transformative potential, and our pipeline of highly-differentiated 4-1BB bispecific therapies are key components of our biologics pipeline development strategy," said Dr. Taylor Guo, Chief Scientific Officer of I-Mab. "Dose-limiting toxicities have hampered clinical development of 4-1BB targeting molecules as a drug class. The studies being presented at SITC suggested that both our bispecific assets could have the ability to overcome this common problem, and we are confident that this differentiation places TJ-CD4B/ABL111 and TJ-L14B/ABL503 at the forefront of 4-1BB bispecific development."

"The preclinical data from this pair of bispecific molecules prove that our 'Grabody-T' platform effectively reduces peripheral toxicity by allowing the activation of T cells only in the tumor microenvironment," said Dr. Sang Hoon Lee, CEO of ABL Bio. "We look forward to further validating its therapeutic potential in the ongoing clinical studies and as we continue to develop 4-1BB bispecific antibodies in various cancer indications."

Key data highlights:

### **TJ-CD4B/ABL111**

Poster title (#702): TJ-CD4B (ABL111), a Claudin18.2-targeted 4-1BB tumor engager induces potent tumor-dependent immune response without dose-limiting toxicity in preclinical studies

The preclinical studies confirmed the unique pharmacodynamic data and safety of TJ-CD4B/ABL111 in animal models and cell cultures. Analysis of the data found:

- Potent, anti-tumor activity was observed with the proliferation of immune cells in the tumor microenvironment (TME) as well as an increase in memory T cells in the peripheral blood, suggesting long-term immunity against the tumor.
- TJ-CD4B/ABL111 was well tolerated in non-human primates and did not induce a systemic immune response or liver toxicity up to levels of 100mg/kg.
- Activation of immune pathways by TJ-CD4B/ABL111 was demonstrated by a pro-inflammatory profile and increased gamma interferon-regulated gene expression in primary human CD8+ T cells co-cultured with CLDN18.2 expressing cells.

## **TJ-L14B/ABL503**

Poster title (#892): ABL503 (TJ-L14B), PD-L1x4-1BB bispecific antibody induces superior anti-tumor activity by PD-L1-dependent 4-1BB activation with the increase of 4-1BB+CD8+ T cells in tumor microenvironment

The preclinical study data confirms the unique mechanism of action of TJ-L14B/ABL503 and its potential to treat resistance to PD-L1 therapies. Analysis of the data found:

- PD-L1-dependent stimulation of the 4-1BB signaling pathway was demonstrated in 4-1BB bioassays with PD-L1 expressing tumor cells
- More potent 4-1BB activation by TJ-L14B/ABL503 was observed at higher PD-L1 expression confirming the requirement of PD-L1 on both tumor and immune cells for optimal activity. Cytokine release assays have also demonstrated minimal peripheral toxicity with TJ-L14B/ABL503
- The *in vivo* efficacy of TJ-L14B/ABL503 was demonstrated in animal models with tumors expressing different levels of PD-L1. TJ-L14B/ABL503 showed anti-tumor efficacy across the PD-L1 levels. In particular, TJ-L14B/ABL503 demonstrated superior anti-tumor efficacy than atezolizumab in tumors with low PD-L1 expression
- *In vitro* tumor-killing activity of TJ-L14B/ABL503 was superior compared to atezolizumab when tested in organoid system, even in organoids from atezolizumab non-responders
- Pharmacodynamic changes in TILs and blood were evaluated in animal models. An increase in 4-1BB+ cells, CD8+ T cells, and effector memory T cells was observed in the TME and blood, indicating a strong and long-lasting anti-tumor immune response
- Treatment with TJ-L14B/ABL503 increased MIG/CXCL9, MIP-1b/CCL4, and s4-1BB in the serum, and can potentially be used as pharmacodynamic markers in clinical trials

## **About TJ-CD4B/ABL111**

TJ-CD4B, also known as ABL111, is a Claudin 18.2 and 4-1BB bispecific antibody capable of binding to tumor cells expressing Claudin 18.2, i.e., gastric cancer and pancreatic cancer cells, and stimulating intra-tumoral T cells by the 4-1BB arm designed to be activated only upon tumor engagement while silent elsewhere. TJ-CD4B/ABL111 effectively maintains a strong tumor binding property and anti-tumor activity attributable to a synergistic effect of both Claudin 18.2 antibody and 4-1BB antibody while it avoids or minimizes liver toxicity and systemic immunotoxicity commonly seen with 4-1BB antibodies as a drug class. Being developed under collaboration between I-Mab and ABL, TJ-CD4B/ABL111 is currently being investigated in a phase 1 clinical study in the U.S.

## **About TJ-L14B/ABL503**

Being developed jointly with ABL, TJ-L14B/ABL503 is a differentiated PD-L1-based bispecific antibody with the PD-L1 arm as the tumor-dependent T-cell activator and the 4-1BB arm as the conditional T cell activator upon tumor engagement. Using ABL's "Grabody-T" bispecific antibody platform technology, TJ-L14B/ABL503 stimulates 4-1BB activation only in the presence of PD-L1 expressing tumor cells to minimize the risk of off-tumor toxicity. Preclinical studies have demonstrated that the bispecific antibody shows better anti-tumor activity than equimolar doses of single agents alone or in combination. Phase 1 study is currently being conducted in the U.S.

## **About I-Mab**

I-Mab (Nasdaq: IMAB) is an innovation-driven global biopharma company focused on the discovery, development and commercialization of novel and highly differentiated biologics for immuno-oncology and autoimmune diseases. The Company's mission is to bring transformational medicines to patients around the world through innovation. I-Mab's globally competitive pipeline of more than 15 clinical and preclinical-stage drug candidates is driven by its internal discovery and global partnerships for in-licensing, based on the Company's Fast-to-Proof-of-Concept and Fast-to-Market development strategies. The Company is progressing from a clinical-stage biotech company into a fully integrated global biopharmaceutical company with cutting-edge R&D capabilities, a world-class GMP manufacturing facility, and commercial capability. I-Mab has established its global footprint in Shanghai (headquarters), Beijing, Hangzhou, Guangzhou, Lishui and Hong Kong in China, and Maryland and San Diego in the United States. For more information, please visit <http://ir.i-mabbiopharma.com> and follow I-Mab on [LinkedIn](#), [Twitter](#), and [WeChat](#).

## **About ABL Bio**

ABL Bio, Inc. (Kosdaq: 298380) is a clinical-stage South Korean biotechnology company developing antibody therapeutics for immuno-oncology and neurodegenerative diseases. With internal R&D and global partnerships, ABL has developed multiple BsAb platforms, such as "Grabody-T," "Grabody-I" and "Grabody-B" and built an innovative pipeline of multiple clinical and pre-clinical stage drug candidates. In the oncology area, ABL has developed Grabody-T, a modular 4-1BB engaging platform that has demonstrated superior efficacy and safety. In the neurodegenerative disorder space, ABL has developed Grabody-B platform, which is designed to maximize blood-brain barrier (BBB) penetration. Grabody-B is applicable to various CNS targets across a plethora of neurological disorders, potentially providing a breakthrough to address the high unmet medical needs in neurodegeneration. For more information, please visit [www.ablbio.com](http://www.ablbio.com).

## **I-Mab Forward-Looking Statements**

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws, including statements regarding data from the TJ-CD4B and TJ-L14B pre-clinical studies, the potential implications of clinical data for patients, and I-Mab's advancement of, and anticipated clinical development, regulatory milestones, and commercialization of TJ-CD4B and TJ-L14B. Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including but not limited to I-Mab's ability to demonstrate the safety and efficacy of its drug candidates; the clinical results for its drug candidates, which may not support further development or NDA/BLA approval; the content and timing of decisions made by the relevant regulatory authorities regarding regulatory approval of I-Mab's drug candidates; I-Mab's ability to achieve commercial success for its drug candidates, if approved; I-Mab's ability to obtain and

maintain protection of intellectual property for its technology and drugs; I-Mab's reliance on third parties to conduct drug development, manufacturing and other services; I-Mab's limited operating history and I-Mab's ability to obtain additional funding for operations and to complete the development and commercialization of its drug candidates; and the impact of the COVID-19 pandemic on the Company's clinical development, commercial and other operations, as well as those risks more fully discussed in the "Risk Factors" section in I-Mab's most recent annual report on Form 20-F, as well as discussions of potential risks, uncertainties, and other important factors in I-Mab's subsequent filings with the US Securities and Exchange Commission. All forward-looking statements are based on information currently available to I-Mab, and I-Mab undertakes no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required by law.

#### **ABL Forward Looking Statements**

Statements in this press release contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform act of 1995. Words such as "will," "could," "hope," "expect," "plan" and similar expressions that are based on ABL's current expectations and assumptions are subject to risks and uncertainties that are difficult to predict. The risks and uncertainties include but are not limited to, potential delays in clinical trial recruitment and participation; ABL and I-Mab's ability to demonstrate the safety and efficacy of ABL-111 and ABL-503; adverse results in the clinical development process; changes in expected or existing competition; changes in the biopharmaceutical landscape; ABL's ability to obtain and maintain protection of intellectual property for its technology and drugs; ABL's reliance on third parties to conduct drug development; the company's financial position; future decisions by the FDA or other regulatory authorities; volatile global economic conditions; and the impact of the global COVID-19 pandemic. The reader is cautioned not to place undue reliance on these forward-looking statements. All forward-looking statements are based on information currently available to ABL and the company assumes no obligation to provide public updates to these forward-looking statements that are only as of the date of this press release, even if new information is available in the future.

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