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Abbisko Cayman Limited
和譽開曼有限責任公司

(Incorporated in the Cayman Islands with limited liability)
(Stock Code: 2256)

VOLUNTARY ANNOUNCEMENT
PRECLINICAL STUDY RESULTS OF
PRMT5*MTA AND PD-L1 PRESENT AT ENA

Abbisko Cayman Limited (the “**Company**”, together with its subsidiaries, the “**Group**”) hereby informs the shareholders and potential investors of the Company of the attached press release that Abbisko Therapeutics Co., Ltd. (“**Abbisko Therapeutics**”), a subsidiary of the Company, announced that the results of its two preclinical studies were published at the 35th International Molecular Targets and Cancer Treatment Conference (EORTC-NCI-AACR conference, hereinafter referred to as the ENA conference) held in Boston, U.S. in October. These two research results respectively demonstrate the latest preclinical research progress of the next generation of PRMT5*MTA inhibitors and small molecule brain penetrant PD-L1 inhibitors in Abbisko Therapeutics’ pipeline. As the world’s highest-quality research conference focusing on molecular targeting and tumor treatment, the ENA conference collects the most cutting-edge researches on innovative drugs and therapies in the field of tumor treatment.

This is a voluntary announcement made by the Company. The Group cannot guarantee that ABK-PRMT5-1 and ABSK044 will ultimately be successfully marketed. Shareholders and potential investors of the Company are advised to exercise caution when dealing in the shares of the Company.

By order of the Board
Abbisko Cayman Limited
Dr. Xu Yao-Chang
Chairman

Shanghai, October 16, 2023

As at the date of this announcement, the board of directors of the Company comprises Dr. Xu Yao-Chang, Dr. Yu Hongping and Dr. Chen Zhui as executive directors; Ms. Tang Yanmin as a non-executive director; and Dr. Sun Piaoyang, Mr. Sun Hongbin and Mr. Wang Lei as independent non-executive directors.

Abbisko Therapeutics Presented Two Preclinical Research Results at the ENA Conference

On October 16, 2023, Abbisko Therapeutics announced that the results of its two preclinical studies were published at the ENA conference held in Boston, U.S. in October. These two research results respectively demonstrate **the latest preclinical research progress of the next generation of PRMT5*MTA inhibitors and small molecule brain penetrant PD-L1 inhibitors in Abbisko Therapeutics' pipeline**. As the world's highest-quality research conference focusing on molecular targeting and tumor treatment, the ENA conference collects the most cutting-edge researches on innovative drugs and therapies in the field of tumor treatment.

Abbisko Therapeutics presented the following posters at the ENA conference:

Title: Discovery and characterization of an MTA-cooperative and brain-penetrant PRMT5 inhibitor

Poster number: C130

Session date and time: Saturday, October 14 | 12:30 pm-4:00 pm

Session location: Exhibit Hall D, Level 2

Background: MTAP gene is homozygous deleted in ~50% in glioblastoma and many other cancers. PRMT5*MTA inhibition has been shown to be synthetic lethal with MTAP gene deletion. The first generation of PRMT5 inhibitors could not distinguish between PRMT5*MTA and PRMT5 alone, thus limited by their shallow therapeutic windows in clinical use. Development of selective PRMT5*MTA inhibitors may improve not only safety but also therapeutic efficacy. Leveraging advanced computation-aided structural analysis and medicinal chemistry design, we have developed a potent and selective MTA-cooperative and brain-penetrable PRMT5 inhibitor ABK-PRMT5-1, which demonstrates strong anti-tumor activity and brain-penetrating activity in various preclinical models.

Conclusion:

ABK-PRMT5-1, presented by Abbisko Therapeutics, strongly inhibits cell proliferation in MTAP-deleted cancer cell lines, with minimal effects on MTAP wildtype cell lines. Furthermore, it significantly reduces SDMA in MTAP-deleted cancer cell lines. Oral administration of ABK-PRMT5-1 strongly inhibits tumor growth in MTAP-deleted xenograft tumor models. In addition, ABK-PRMT5-1 demonstrates strong brain penetration with excellent K_p values in animals. DMPK and safety profiling shows good overall drug-like properties of ABK-PRMT5-1. ABK-PRMT5-1, presented by Abbisko Therapeutics, is a highly selective MTA-cooperative and brain-penetrable PRMT5 inhibitor. Its superior profile supports fast-track preclinical development.

Title: Discovery and characterization of a novel small molecule brain penetrant PD-L1 inhibitor

Poster number: B151

Session date and time: Friday, October 13 | 12:30 pm-4:00 pm

Session location: Exhibit Hall D, Level 2

Background: Immunotherapy has revolutionized cancer treatment in the last decade. Several monoclonal PD-1 and PD-L1 antibodies have been approved for treating various cancers. Small molecule PD-L1 inhibitors with brain-penetrating ability may have potential to overcome the limitations of antibodies and bring benefit for patients with intracranial tumors. Leveraging advanced computation-aided structural analysis and medicinal chemistry design, we have successfully discovered an innovative orally available small molecule PD-L1 inhibitor ABSK044. In preclinical studies, this compound demonstrates robust T-cell activation ability, strong anti-tumor efficacy, and brain-penetrating activity.

Conclusion:

ABSK044 strongly inhibits PD-1-PD-L1 interaction with an IC50 less than 1nM in vitro and very potently rescues PD-L1-induced suppression of T cell activation signaling in cells. Furthermore, it efficiently rescues cytokine production in CD8+ T cells suppressed by PD-L1, reaching a level comparable to that of PD-L1 antibodies. In in vivo studies, oral administration of ABSK044 strongly inhibits tumor growth to an extent similar to therapeutic anti-PD-L1 antibodies. Notably, ABSK044 demonstrates excellent brain penetration with a Kp value exceeding 0.4. DMPK and safety profiling demonstrate excellent drug-like properties of ABSK044.

ABSK044 is a highly potent and orally available small molecule PD-L1 inhibitor with brain-penetrating activity. Its superior profile supports its fast-track preclinical development.

About Abbisko Therapeutics

Founded in April 2016, Abbisko Therapeutics Co., Ltd., a subsidiary of Abbisko Cayman Limited (Stock Code on the Hong Kong Stock Exchange: 2256.HK), is an oncology-focused biopharmaceutical company founded in Shanghai, dedicated to discovering and developing innovative medicines to treat unmet medical needs in China and globally. The Company was established by a group of seasoned drug hunters with rich R&D and managerial expertise from top multinational pharmaceutical companies. Since its founding, Abbisko Therapeutics has built an extensive pipeline of 15 innovative small molecule programs focused on precision oncology and immuno-oncology, including eight clinical stage assets.

Please visit www.abbisko.com for more information.

Forward-Looking Statements

The forward-looking statements made in this article relate only to the events or information as of the date on which the statements are made in this article. Except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise, after the date on which the statements are made or to reflect the occurrence of unanticipated events. You should read this article completely and with the understanding that our actual future results or performance may be materially different from what we expect. In this article, statements of, or references to, our intentions or those of any of our Directors or our Company are made as of the date of this article. Any of these intentions may alter in light of future development.