Zai Lab-Supported Study Published in Cell Provides New Insights with Potential to Improve Treatment of HRD-Positive Ovarian Cancers, Including Through Combination PARP Inhibitor and CCR8 Therapy

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Manuscript represents the first publication from China's gynecology oncology field to be published in Cell

Publication highlights first-time learnings about the landscape of ovarian cancer microenvironment stratified by HRD and how a PARP inhibitor perturbs it

Data suggest combination of niraparib and ZL-1218, an investigational CCR8 antibody, may decrease tumor burden, offering synergistic potential for improving efficacy in treatment of HRD tumors

SHANGHAI & CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jul. 15, 2024-- Zai Lab Limited (NASDAQ: ZLAB; HKEX: 9688) today announced that data published in the journal *Cell* demonstrate that neoadjuvant monotherapy with the poly (ADP-ribose) polymerase (PARP) inhibitor niraparib results in a high response rate and reshapes the tumor microenvironment (TME), providing new targets for immunotherapy and combination regimens in patients with homologous recombination deficiency (HRD) positive ovarian cancer. The study revealed niraparib preferentially suppresses certain immune cells that support the growth of HRD-positive ovarian tumors.

This Zai Lab-supported study also showed that targeted clearance of infiltrating regulatory T cells (eTregs) using Zai Lab's investigational CCR8 antibody, ZL-1218, significantly sensitized niraparib against HRD tumors, resulting in decreased tumor burden in pre-clinical models.

"Given the prevalence of HRD in cancer and its role in rendering tumors vulnerable to PARP inhibition, this study fills the knowledge gap regarding the impact of HRD and related therapies on the tumor microenvironment," said Professor Qinglei Gao, Chief of Gynecologic Oncology Department, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology. "By decoding the tumor-reactive T cells in the HRD-positive TME that are regulated by eTregs, these findings have profound implications for future oncology research and therapeutic development for HRD-positive ovarian cancer and other HRD-related cancers."

To investigate the effects of HRD, neoadjuvant therapies, and their interactions on the TME, investigators utilized tumor tissues from a clinical study (NCT04507841) evaluating niraparib for the neoadjuvant treatment of unresectable ovarian cancer. In parallel, tissue samples from patients receiving neoadjuvant chemotherapy (NACT) were also collected.

Profiling of these samples yielded valuable data delineating the divergence in TME between HRD-positive vs. homologous recombination-proficient (HRP) tumors, as well as their respective phenotypic evolution following the introduction of neoadjuvant therapies.

Key findings of the study included:

- Patients receiving neoadjuvant monotherapy with niraparib achieved 62.5% and 73.6% response rates per RECIST v.1.1 and GCIG CA125, respectively.
- Overall, the safety profile of NANT was manageable, and no new safety signal was observed, with hematologic toxicities as the most common treatment-related adverse events.
- The results indicate that NANT is an effective neoadjuvant treatment option for controlling disease progression in patients with HRD-positive high-grade serous ovarian cancer (HGSOC).
- eTregs were identified as key responders to HRD and neoadjuvant therapies, co-occurring with other tumor-reactive T cells, particularly terminally exhausted CD8+ T cells.
- The addition of the CCR8 antibody, ZL-1218, to niraparib showed a significantly pronounced inhibitory effect on eTregs in pre-clinical models, suppressing tumor growth without observable toxicities, underscoring the potential of eTreg-focused therapeutics for HGSOC and other HRD-related tumors.

"Zai Lab is pleased to support this important translational research which breaks new ground in our understanding of the tumor microenvironment in HRD-positive ovarian cancer," said Rafael G. Amado, M.D., President, Head of Global Research and Development, Zai Lab. "By identifying new immunotherapeutic targets in the TME, these findings could bolster efforts to improve outcomes for patients with HRD+ tumors."

About Zai Lab

Zai Lab (NASDAQ: ZLAB; HKEX: 9688) is an innovative, research-based, commercial-stage biopharmaceutical company based in China and the United States. We are focused on discovering, developing, and commercializing innovative products that address medical conditions with significant unmet needs in the areas of oncology, autoimmune disorders, infectious diseases and neuroscience. Our goal is to leverage our competencies and resources to positively impact human health in China and worldwide.

For additional information about Zai Lab, please visit www.zailaboratory.com or follow us at www.twitter.com/ZaiLab_Global.

Zai Lab Forward-Looking Statements

This press release contains forward-looking statements relating to our future expectations, plans, and prospects, including, without limitation, statements regarding the possible benefits, safety, and efficacy of niraparib and ZL-1218; the potential treatment of certain ovarian cancers and other solid tumors; and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may contain words such as “aim,” “anticipate,” “believe,” “could,” “estimate,” “expect,” “forecast,” “goal,” “intend,” “may,” “plan,” “possible,” “potential,” “will,” “would,” and other similar expressions. Such statements constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are not statements of historical fact or guarantees or assurances of future performance. Forward-looking statements are based on our expectations and assumptions as of the date of this press release and are subject to inherent uncertainties, risks, and changes in circumstances that may differ materially from those contemplated by the forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including but not limited to (1) our ability to successfully commercialize and generate revenue from our approved products, (2) our ability to obtain funding for our operations and business initiatives, (3) the results of our clinical and pre-clinical development of our product candidates, (4) the content and timing of decisions made by the relevant regulatory authorities regarding regulatory approvals of our product candidates, (5) risks related to doing business in China, and (6) other factors identified in our most recent annual and quarterly reports and in other reports we have filed with the U.S. Securities and Exchange Commission (SEC). We anticipate that subsequent events and developments will cause our expectations and assumptions to change, and we undertake no obligation to 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. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

Our SEC filings can be found on our website at www.zailaboratory.com and on the SEC’s website at www.sec.gov.

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For more information, please contact:
Investor Relations:
Christine Chiou / Lina Zhang
+1 (917) 886-6929 / +86 136 8257 6943
christine.chiou1@zailaboratory.com / lina.zhang@zailaboratory.com

Media:
Shaun Maccoun/ Xiaoyu Chen
+1 (857) 270-8854 / +86 185 0015 5011
shaun.maccoun@zailaboratory.com / xiaoyu.chen@zailaboratory.com

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