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Chordia Therapeutics

This press release is an English translation of a Japanese-language press release. The official language of this press release is Japanese, and the Japanese version takes precedence over the English version in terms of content and interpretation.

<Press Release>
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Notice of Publication of a Joint Research Paper with Kyoto University on CDK12 Inhibitor CTX-439

Chordia Therapeutics Inc (Head Office: Fujisawa City, Kanagawa Prefecture; CEO: Hiroshi Miyake, "Chordia") announces that the results of its joint research with Kyoto University on the identification of tumor types suitable for treatment based on the mechanism of action of CTX-439, the Company's preclinical CDK12 inhibitor, have been published in *Molecular Cancer Therapeutics* on Mar. 12, 2026.

Summary

CTX-439 is an orally available, small-molecule kinase inhibitor with high selectivity for CDK12 and CDK13, which belong to the cyclin-dependent kinase (CDK) family of serine/threonine protein kinases. CDK12/13 phosphorylate the C-terminal domain of RNA polymerase II, thereby regulating mRNA transcriptional elongation and termination. By inhibiting the process of mRNA generation essential for the survival of cancer cells and suppressing the production of proteins required for cell proliferation, CTX-439 imposes lethal stress on cancer cells and induces cell death through a novel mechanism of action.

In this study, the antitumor activity of CTX-439 was analyzed in detail in uterine serous carcinoma, a subtype of endometrial cancer. The research suggests that CDK12 amplification is present in a subset of uterine serous carcinoma and may contribute to reduced responsiveness to existing therapies. Using uterine serous carcinoma cell lines and patient-derived tumor models, the study demonstrated that CTX-439 decreases the mRNA expression of DNA repair–related gene sets through inhibition of CDK12/13, thereby weakening the ability of cancer cells to repair damaged DNA and survive. As a consequence of the impaired DNA repair capacity, cancer cells become more vulnerable to therapeutic agents, and CTX-439 exhibits antitumor efficacy while also enhancing sensitivity to PARP inhibitors, which are among the standard treatments for endometrial cancer in Japan.

This study represents the first report to demonstrate that the novel CDK12/13 inhibitor CTX-439 targets CDK12 amplification in uterine serous carcinoma and enhances the efficacy of PARP inhibitors via modulation of mRNA transcriptional

regulation. These findings provide an important insight into a new therapeutic approach for uterine serous carcinoma, a disease with limited treatment options.

Publication Details

A novel CDK12 inhibitor induces homologous recombination deficiency to enhance PARP inhibitor efficacy in uterine serous carcinoma.
Molecular Cancer Therapeutics, Mar. 12, 2026
URL：https://doi.org/10.1158/1535-7163.MCT-25-0954

About the Journal

Molecular Cancer Therapeutics is an international peer-reviewed journal published by the American Association for Cancer Research (AACR). The journal focuses on translational research in oncology, particularly the discovery and preclinical development of therapeutic agents for cancer. It emphasizes studies on novel anticancer drug candidates, mechanisms of action of existing therapeutics, mechanisms of drug resistance, biomarkers of treatment response, innovative experimental models and technologies, and data-driven approaches in drug discovery. Through these areas, the journal highlights research findings that are essential for advancing cancer therapeutics.

Glossary of Terms

Term	Explanation
Kinase	A general term for enzymes (proteins) that transfer a phosphate group to substrate proteins.
Phosphorylation	The addition of a phosphate group to a substrate protein, which modulates the protein's activity (on/off regulation).
RNA	A molecule required to generate proteins based on genetic information in DNA; includes messenger RNA (mRNA) transcribed from genomic DNA and transfer RNA (tRNA) used during protein synthesis.
mRNA Transcription	The process by which genetic information encoded in DNA is read and transcribed into mRNA—an essential, initiating step that enables cells to synthesize proteins.
CDK12 Amplification	A molecular alteration in which the CDK12 gene is present at increased copy number, potentially enhancing its activity. Observed in a subset of uterine serous carcinoma, this change may affect response to existing therapies; the present study confirmed robust activity of the CDK12 inhibitor CTX-439 in tumors with CDK12 amplification.
DNA Repair	Cellular pathways that detect and correct damage or alterations in DNA. Cancer cells often harbor defects or biases in these pathways, which can be therapeutically exploited when tumors become dependent on specific repair mechanisms.

PARP Inhibitors	Agents that impede DNA repair in cancer cells, showing heightened efficacy in tumors with compromised DNA repair capacity.

This study was conducted as a joint research project with Professor Masaki Mandai of the Department of Gynecology and Obstetrics, Kyoto University Graduate School of Medicine. Furthermore, Chordia's collaborative research with Kyoto University was carried out under the leadership of Professor Kosuke Yusa of the Institute for Life and Medical Sciences, Kyoto University, and was supported by the Japan Agency for Medical Research and Development (AMED) under the "Practical Research for Innovative Cancer Control" program.

About Chordia Therapeutics

Chordia's lead asset, rogocekib (CLK inhibitor CTX-712), is under Phase 1/2 clinical study in the US. Rogocekib potentially targets the vulnerability of cancer and is expected to deliver benefits to patients of various types of cancer. In addition to rogocekib, Chordia is engaged in the research and development of several assets, including CTX-177, a MALT1 inhibitor, CTX-439, a CDK12 inhibitor, and GCN2 inhibitors. For more information, please visit our website https://www.chordiatherapeutics.com/en/.