Agreement for Global Strategic Collaboration with Kura Oncology to Develop and Commercialize Ziftomenib

協和キリン株式会社

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Agenda

Agreement for Global Strategic Collaboration with Kura Oncology to Develop and Commercialize Ziftomenib

Managing Executive Officer, Chief Strategy Officer **Yasuo Fujii**

Q&A

Director of the Board, Senior Managing Executive officer and Chief Medical Officer **Takeyoshi Yamashita, Ph.D.**

Managing Executive Officer, Head of Finance **Motohiko Kawaguchi**

Managing Executive Officer, Chief Strategy Officer **Yasuo Fujii**

Managing Executive Officer, Chief International Business officer **Abdul Mullick, Ph.D.**

License agreement for ziftomenib

To strengthen our pipeline in the intractable hematological diseases/hemato oncology and rare diseases, Kyowa Kirin has entered into a license agreement with Kura Oncology for the development and commercialization of ziftomenib

- Strategic partnership agreement signed for global development and commercialization of ziftomenib, an oral menin inhibitor targeting acute myeloid leukemia (AML)
- Upfront payment of $330M, with potential for up to $1,161M in development, regulatory, and commercial milestones

Ziftomenib

- An oral selective small molecule menin inhibitor under development by Kura Oncology
- Target disease: Menin-dependent AML (NPM1 gene mutations and KMT2A gene rearrangements)
  - Up to 50% of AML cases are estimated to be menin-dependent (including those with NPM1 gene mutations and KMT2A gene rearrangements)
  - NPM1 gene mutation is one of the most common AML mutations and a driver mutation that uses the menin pathway. It is observed in 30%-35% of cases.
  - AML with NPM1 gene mutations is a poor prognostic factor in relapsed/refractory AML and is attracting attention as a target for new therapies
- Mechanism of Action: Promotion of leukemic blast differentiation by inhibiting the binding of menin and KMT2A

New Drug Application (NDA) anticipated for R/R NPM1-mutant AML in 2025

Story for Vision 2030

Strategies for creating and delivering life-changing value

Disease Science

Focus disease areas: bone & mineral, intractable hematological diseases/hemato oncology, and rare diseases

- Explore UMN, causes and mechanisms of disease in depth
- Pursuit of molecular and cellular regulatory mechanisms for therapeutic realization

Drug Discovery Technology

Strengthening Innovative Modalities: Advanced Antibody Technologies, Hematopoietic stem cell gene therapy

- Application of optimal modalities for therapeutic realization
- Evolution of drug discovery methods through AI and data science

External Collaboration

- Open Innovation
- Partnering

Life-changing Value Creation

Assets in focus disease areas

Strategic Partnering Assets *

Value delivery on our own

Global deployment of products developed by taking full advantage of the company's strengths

Collaborative value delivery

Aim to maximize value by combining the strengths of the company and its partners

Full-licensing

Maximize the value of developed products and deliver them to patients faster by out-licensing to the most appropriate partners

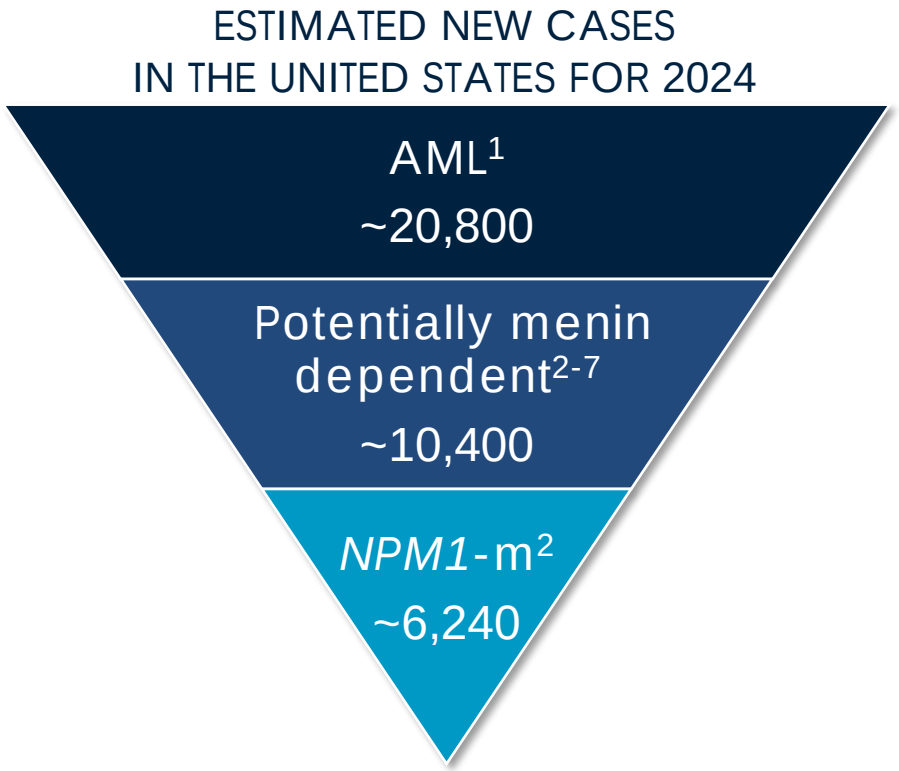
***Assets outside of the disease areas of focus are designated as strategic partnering assets, and value maximization is achieved through collaboration with partners.**

Ziftomenib - Collaboration with Kura -

	US	ex- US
Development	• Kura leads development • Share global development cost • Kura funds development costs (~2028)	• Kyowa Kirin leads development
Commercialization	• Kura books sales • 50/50 profit share	• Kyowa Kirin commercializes and books sales
Sales Royalties		• Double-digit royalty to Kura
Commercial supply	• Kura supplies	• Kura supplies

Kyowa Kirin makes a $330 million up-front payment and future contingent milestone payments potentially worth up to $1,161 million in total, including $420 million in near-term milestone payments and $228M opt-in right for solid tumors, as well as royalty payments on future global sales to Kura.

OVERVIEW

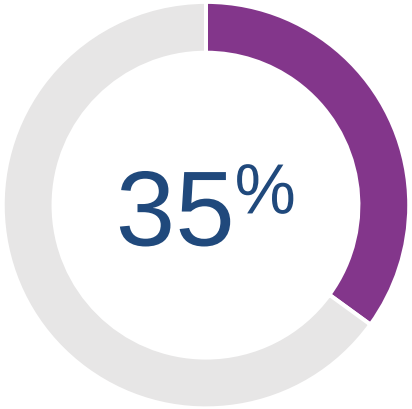


- There are an estimated 20,800 new cases of AML in the United States in 2024[1]
- AML continues to carry a poor prognosis, where there remains a significant unmet need for additional treatments with durable efficacy and greater tolerability[13,14]
- AML is characterized by significant genetic heterogeneity due to the possible presence of multiple driver mutations, such as *NPM1*m and *KMT2A*r[8,9]
- Up to 50% of AML cases may be menin dependent, including those driven by *NPM1*m and *KMT2A*r[2-7]
- *NPM1*-m is one of the most common AML mutations, found in 30% to 35% of cases, and is an important upstream driver mutation that uses the menin pathway[7,10]
- *NPM1*-m AML is associated with poor outcomes in R/R AML,[11,12] making it a potential target for novel therapies

AML, acute myeloid leukemia; *KMT2A*r, lysine methyltransferase 2A rearrangement; *NPM1*-m, mutated nucleophosmin 1; *NPM1*m, nucleophosmin 1 mutation.

1. American Cancer Society. Updated January 17, 2024. Accessed October 16, 2024. https://www.cancer.org/cancer/types/acute-myeloid-leukemia/about/key-statistics.html 2. Issa GC et al. *Leukemia.* 2021;35(9):2482-2495. doi:10.1038/s41375-021-01309-y 3. Candoni A, Coppola G. *Hematol Rep.* 2024;16(2):244-254. doi:10.3390/hematolrep16020024 4. Bertrums EJM et al. *Haematologica.* 2023;108(8):2044-2058. doi:10.3324/haematol.2022.281653 5. National Cancer Institute. Accessed October 16, 2024. https://seer.cancer.gov/seertools/hemelymph/51f6cf59e3e27c3994bd547d/ 6. National Cancer Institute. Accessed October 16, 2024. https://seer.cancer.gov/seertools/hemelymph/5a7e288d1ef557f9c8636d31/ 7. Burrows F et al. Poster presented at: AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics: Discovery, Biology, and Clinical Applications; October 26-30, 2017; Philadelphia, PA. 8. Papaemmanuil E et al. *N Engl J Med*. 2016;374(23):2209-2221. doi:10.1056/NEJMoa1516192 9. The Cancer Genome Atlas Research Network. *N Engl J Med*. 2013;368(22):2059-2074. doi:10.1056/NEJMoa1301689 10. Falini B, Dillon R. *Blood Cancer Discov*. 2024;5(1):8-20. doi:10.1158/2643-3230.BCD-23-0144 11. Issa GC et al. *Blood Adv*. 2023;7(6):933-942. doi:10.1182/bloodadvances.2022008316 12. Ostronoff F et al. *J Clin Oncol*. 2015;33(10):1157-1164. doi:10.1200/JCO.2014.58.0571 13. Kumar CC. *Genes Cancer*. 2011;2(2):95-107. doi:10.1177/1947601911408076 14. Bhansali RS et al. *J Hematol Oncol*. 2023;16(1):29. doi:10.1186/s13045-023-01424-6

*NPM1*m: ONE OF THE MOST COMMON AML MUTATIONS AND AN IMPORTANT DRIVER MUTATION IN THE MENIN COMPLEX



*NPM1*m is present in up to 35% of AML cases, making it one of the most common genetic alterations in AML[1]

- Approximately two-thirds of patients with *NPM1*m carry a co-mutation[2]

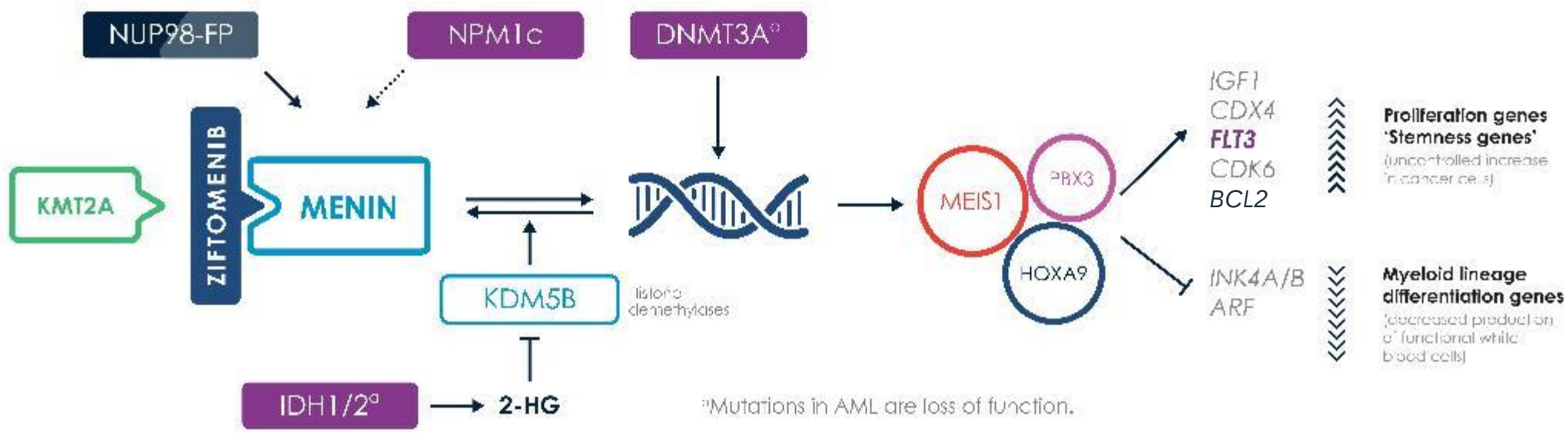
- NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend expedited testing for *NPM1*m at diagnosis to inform prognosis and guide treatment decisions[3]
- Most patients (~97%) retain *NPM1*m after first-line therapy[4,5]
  - Suggests that detection of *NPM1*m, as early as at diagnosis, can be referred back to when making treatment decisions during initial therapy and beyond

AML, acute myeloid leukemia; NCCN, National Comprehensive Cancer Network® (NCCN®); *NPM1*m, nucleophosmin 1 mutation.

1. Falini B, Dillon R. *Blood Cancer Discov*. 2024;5(1):8-20. doi:10.1158/2643-3230.BCD-23-0144 2. Sharma N, Liesveld JL. *Cancers (Basel).* 2023;15(4):1177. doi:10.3390/cancers15041177 3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V.3.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed August 27, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use, or application, and disclaims any responsibility for their application or use in any way. 4. Issa GC et al. *Blood Adv*. 2023;7(6):933-942. doi:10.1182/bloodadvances.2022008316 5. Falini B et al. *Blood*. 2011;117(4):1109-1120. doi:10.1182/blood-2010-08-299990

Ziftomenib Targets the Menin-KMT2A Pathway, A Foundational Target in AML

- *NPM1*-m and *KMT2A*-r drive overexpression of *HOXA9/MEIS1* genes, critical for transformation to AML
- KMT2A(MLL) sits upstream from major AML targets (*i.e.*, *FLT3*, *BCL2*, *IDH1/2*, *DNMT3A*)
- KMT2A(MLL)-dependent genes contribute to therapeutic resistance and relapse to current therapies
- Menin inhibition downregulates HOXA9/MEIS1, leading to differentiation of leukemic blasts



1. Lu et al. Cancer Cell 2016;30(1):92–107; 2. Ferreira et al. Oncogene 2016;35(23):3079-82; 3. Jeong et al. Nat. Genet 2014;46(1):17-23; 4. Wang et al. Blood 2005;106(1):254–64; 5. Chowdhury et al. EMBO Rep 2011;12(5):463-9; 6. Schmidt et al. Leukemia 2019;33(7):1608-19; 7. Xu et al. Cancer Cell 2016;30(6):863-78; 8. Collins & Hess. Curr Opin Hematol 2016;23(4):354-61; 9. Brunetti et al. Cancer Cell 2018; 34(3):499–512.

Ziftomenib Demonstrates Potential to Become a Cornerstone of AML Therapy

Targets foundational mutations in up to 50% of AML cases

- Compelling clinical data support frontline opportunity
  - Good tolerability profile, enabling continuous administration in combination with SOC
  - Combinations appear to mitigate the risk of differentiation syndrome
  - No observed or predicted drug-drug interactions
  - Encouraging preliminary evidence of clinical activity
- Strong investigator enthusiasm as evidenced by rapid enrollment across studies
  - First 20 patients enrolled in KOMET-007 combination trial in less than four months
  - Now dosing patients in KOMET-008 combination trial with SOCs, including FLT3 inhibitor
  - Enrollment in KOMET-001 monotherapy registrational trial completed in < 16 months

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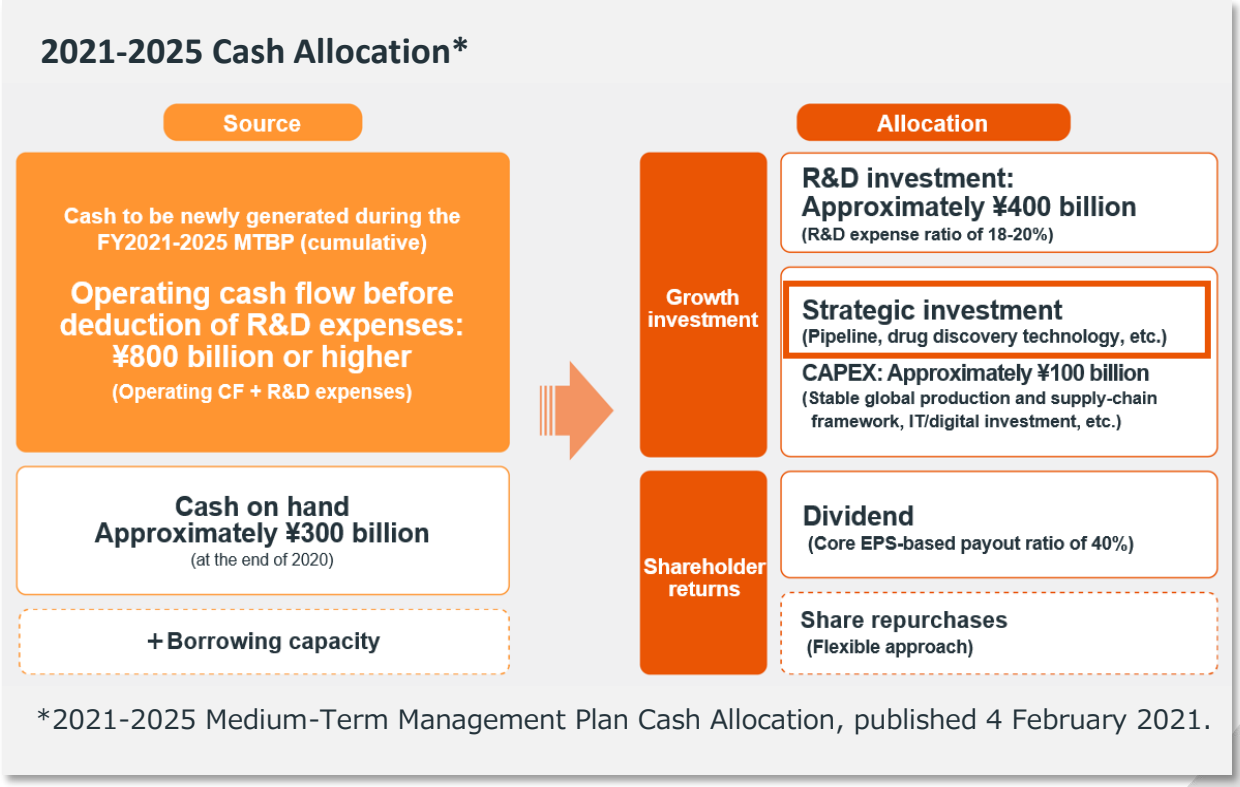
Strategic Investment ～For successful creation and delivery of life-changing value

Licensing-in and M&A investments to strengthen the portfolio

- Development pipeline with synergies with Crysvita and Poteligeo
  - ◆Bone, Mineral ◆Hematologic oncology
- Implementing the strengths of each region
  - ◆Nephrology ◆Hematology / Oncology
  - ◆Immunology

Investment in science and technology to create new strengths

- Investments aimed at acquiring new drug discovery technologies and early pipelines and accelerating cooperation and collaborations
- VC investment and CVC activities for exploring and accessing information.



*2021-2025 Medium-Term Management Plan Cash Allocation, published 4 February 2021.