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Sumitomo Pharma Presents New Clinical Data on DSP-5336 at the European Hematology Association 2024 Congress

– DSP-5336, an Investigational Menin and Mixed-lineage Leukemia Inhibitor, is Being Evaluated in Patients with Relapsed or Refractory Acute Leukemia –

MARLBOROUGH, Mass., June 14, 2024 – Sumitomo Pharma America, Inc. (SMPA) today announced the oral presentation of data from the ongoing Phase 1/2 first-in-human study of DSP-5336 in patients with relapsed or refractory acute leukemia at the European Hematology Association (EHA) 2024 Hybrid Congress. DSP-5336 is an investigational small molecule inhibitor of the menin and mixed-lineage leukemia (MLL) protein interaction, which plays key roles in biological pathways, including cell growth regulation, cell cycle control, genomic stability, bone development, and hematopoiesis.[1,2,3]

Building on preliminary data presented at the 2023 American Society of Hematology (ASH) Annual Meeting, authors presented updated data from the open-label, ongoing dose escalation and optimization portion of the Phase 1/2 study. Patients received oral DSP-5336 in repeating 28-day cycles at doses ranging from 40 mg to 300 mg twice-daily.

The oral presentation at EHA included the results of 57 patients. Responses were more consistently observed in patients who received 140 mg twice-daily or higher, particularly in the 21 patients with either Nucleophosmin 1 (NPM1) mutation or KMT2A (MLL) rearrangement documented by local testing. Objective response was observed in both patient populations with 57% of patients (12/21), with complete remission or complete remission with partial hematologic recovery (CR/CRh) observed in 24% (5/21 patients).

To date, DSP-5336 remains well-tolerated with no dose limiting toxicity (DLT) observed and no significant cardiac signal nor treatment-related discontinuations or deaths. No significant drug-drug interactions with azoles have been identified and repeat dosing results in minimal to no pharmacokinetic accumulation. Importantly, no differentiation syndrome (DS) prophylaxis was needed, and the three cases of DS reported (5%) were manageable and did not result in intensive care unit (ICU) stays or discontinuation of DSP-5336.

“The response in patients previously untreated with menin inhibitors is encouraging, and competitive with greater than 50% objective response rate alongside a favorable safety profile in patients with relapsed or refractory acute leukemia,” said Naval Daver, M.D., Director, Leukemia Research Alliance Program and Professor in the Department of Leukemia at The University of

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Texas MD Anderson Cancer Center, and lead author on the DSP-5336 poster at EHA. “Menin inhibitors have tremendous potential to improve the outcomes of certain types of acute leukemia, as they reverse the leukemogenic activity of MLL fusion and mutated NPM1 proteins. In addition to promising clinical activity the safety profile of DSP-5336 has been especially encouraging and may differentiate it from other menin inhibitors with no severe DS, DLTs nor treatment-related discontinuations.”

Leukemia is a type of cancer that forms in blood-forming tissue, characterized by the uncontrolled growth of blood cells, usually white blood cells, in the bone marrow. Acute leukemia, a form of leukemia, requires immediate treatment as blood cells multiply rapidly leading to a sudden onset of symptoms.[4] Approximately 30% of acute myeloid leukemia (AML) patients have NPM1 mutations[7] and 5-10% of AML patients have KMT2A (MLL) rearrangements.[5]

“There remains a high unmet need in relapsed or refractory acute leukemia, as there are no approved targeted treatments for AML with KMT2A (MLL) rearrangements or NPM1 mutations,” said Jatin Shah, M.D., Chief Medical Officer – Oncology at SMPA. “The biology of menin inhibition is clearly important and we are very early in the rapidly evolving field. We’re excited by these early results and aim to provide a needed option that is both efficacious and well-tolerated. We look forward to continuing to progress the study of DSP-5336 in the hopes of improving outcomes in AML and advancing patient care.”

About DSP-5336

DSP-5336 is an investigational small molecule inhibitor of the menin and mixed-lineage leukemia (MLL) protein interaction. Menin is a scaffold nuclear protein that plays various key roles in biological pathways, including cell growth regulation, cell cycle control, genomic stability, bone development, and hematopoiesis.[1,2] In preclinical studies, DSP-5336 has shown selective growth inhibition in human acute leukemia cell lines with KMT2A (MLL) rearrangements or NPM1 mutations.[1,3] DSP-5336 reduced the expression of the leukemia-associated genes HOXA9 and MEIS1, and increased the expression of the differentiation gene CD11b in human acute leukemia cell lines with MLL rearrangements and NPM1 mutation.[9,10] The safety and efficacy of DSP-5336 is currently being clinically evaluated in a Phase 1/2 dose escalation/dose expansion study in patients with relapsed or refractory acute leukemia (NCT04988555). The FDA granted Orphan Drug Designation for DSP-5336 for the indication of acute myeloid leukemia in June 2022.

About Sumitomo Pharma

Sumitomo Pharma Co., Ltd. is a global pharmaceutical company based in Japan with key operations in the U.S. (Sumitomo Pharma America, Inc.), Canada (Sumitomo Pharma Canada, Inc.) and Europe (Sumitomo Pharma Switzerland GmbH) focused on addressing patient needs in oncology, urology, women’s health, rare diseases, psychiatry & neurology, and cell & gene therapies. With several marketed products in the U.S., Canada, and Europe, a diverse pipeline of early- to late-stage assets, and in-house advanced technology capabilities, we aim to

accelerate discovery, research, and development to bring novel therapies to patients sooner. For more information on SMPA, visit our website https://www.us.sumitomo-pharma.com or follow us on LinkedIn.

For a copy of this release, visit Sumitomo Pharma America's website at www.us.sumitomo-pharma.com.

References

1. Cierpicki T, Grembecka J. Challenges and opportunities in targeting the menin-MLL Interaction. *Future Med Chem*. 2014; 6(4):447-462. doi:10.4155/fmc.13.214.
2. Matkar S, Thiel A, Hua X. Menin: a scaffold protein that controls gene expression and cell signaling. *Trends Biochem Sci*. 2013; 38(8):394-402. doi:10.1016/j.tibs.2013.05.005.
3. Kuhn MWM, Song E, Feng Z, et al. Targeting chromatin regulators inhibits leukemogenic gene expression in NPM1 mutant leukemia. *Cancer Discov*. 2016;6(10):1166-1181. doi:10.1158/2159-8290.CD-16-0237.
4. Chennamadhavuni A, Lyengar V, Mukkamalla SKR, et al. Leukemia. [Updated 2023 Jan 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560490/.
5. Borkin D, Klossowski S, Pollock J, et al. Complexity of Blocking Bivalent Protein-Protein Interactions: Development of a Highly Potent Inhibitor of the Menin-Mixed-Lineage Leukemia Interaction. *J Med Chem*. 2018;61(11):4832-4850. doi:10.1021/acs.jmedchem.8b00071.
6. Issa GC, Aldoss I, DiPersio J, et al. The menin inhibitor revumenib in KMT2A-rearranged or NPM1-mutant leukaemia. *Nature*. 2023;615(7954):920-924. doi:10.1038/s41586-023-05812-3
7. Brandi ML, Agarwal SK, Perrier ND, Lines KE, Valk GD, Thakker RV. Multiple Endocrine Neoplasia Type 1: Latest Insights. *Endocr Rev*. 2021;42(2):133-170. doi:10.1210/endrev/bnaa031
8. Borlenghi E, Cattaneo C, Bertoli D, et al. Prognostic Relevance of *NPM1* and *FLT3* Mutations in Acute Myeloid Leukaemia, Longterm Follow-Up-A Single Center Experience. *Cancers (Basel)*. 2022;14(19):4716. Published 2022 Sep 28. doi:10.3390/cancers14194716
9. Eguchi K, Shimizu T, Kato D, et al. Preclinical Evaluation of a Novel Orally Bioavailable Menin-MLL Interaction Inhibitor, DSP-5336, for the Treatment of Acute Leukemia Patients with *MLL*-Rearrangement or *NPM1* Mutation. *Blood* 2021; 138 (Supplement 1): 3339. Available at: https://doi.org/10.1182/blood-2021-152050.

10. Daver N, Zeidner JF, Yuda J, et al. Phase 1/2 First-in-Human Study of the Menin-MLL Inhibitor DSP-5336 in Patients with Relapsed or Refractory Acute Leukemia. *Blood* 2023; 142 (Supplement 1): 2911. Available at: https://doi.org/10.1182/blood-2023-179252.