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Combination of copanlisib and rituximab significantly prolonged progression-free survival of patients with relapsed indolent non-Hodgkin's Lymphoma

- Phase III study CHRONOS-3 in patients with relapsed indolent non-Hodgkin's Lymphoma (iNHL) who have received one or more lines of prior treatment meets primary endpoint
- Safety and tolerability observed in the trial were generally consistent with previously published data on the individual components of the combination and no new safety signals were identified
- Copanlisib is already approved in the U.S. under accelerated approval based on overall response rate (ORR) of 104 adult patients with relapsed follicular lymphoma (FL) based on the Phase II CHRONOS-1 study

Leverkusen, Germany, October 14, 2020 – Bayer today announced that the Phase III study CHRONOS-3 evaluating copanlisib in combination with rituximab in patients with relapsed indolent non-Hodgkin's Lymphoma (iNHL), which included patients with follicular lymphoma, marginal zone lymphoma, small lymphocytic lymphoma and lymphoplasmacytoid lymphoma/Waldenström macroglobulinemia, has met its primary endpoint of significantly prolonging progression-free survival (PFS). CHRONOS-3 is a Phase III randomized, double-blind, placebo-controlled trial with the objective to evaluate whether copanlisib in combination with rituximab is superior to placebo plus rituximab in extending PFS in patients with relapsed iNHL. The safety and tolerability observed in the trial were generally consistent with previously published data on the individual components of the combination and no new safety signals were identified.

“Indolent forms of non-Hodgkin’s lymphoma are a heterogenous group of malignancies characterized by a chronic pattern of remissions and recurrences. For iNHL patients with disease progression who are in need of treatment, there are few approved treatment options,” said Dr. Scott Z. Fields, Senior Vice President and Head of Oncology

Development at Bayer. “The positive results from CHRONOS-3 demonstrate the potential clinical benefit of copanlisib in combination with rituximab, to address the unmet medical need in these patients.”

Results from CHRONOS-3 will be presented at a scientific congress. Bayer plans to discuss the data from CHRONOS-3 with health authorities worldwide.

Copanlisib is an intravenous pan class I phosphatidylinositol-3-kinase (PI3K) inhibitor with activity against all four isoforms including the PI3K-alpha and PI3K-delta isoforms expressed in malignant B cells. Copanlisib is approved in the U.S. under the accelerated approval pathway for the treatment of adult patients with relapsed follicular lymphoma (FL) who have received at least two prior systemic therapies. Accelerated approval was granted for this indication based on an overall response rate (ORR) of 59% including 14% of complete responses (CRs) from the open-label, single-arm Phase II CHRONOS-1 (NCT01660451) trial of copanlisib monotherapy in 104 adult patients with follicular B-cell NHL who had relapsed or refractory disease following at least two prior systemic therapies. Updated data for CHRONOS-1, published in the American Journal of Hematology 2020, showed an ORR of 59% in the FL population including 20% of CRs. Continued approval for this indication is contingent upon verification and description of clinical benefit in a confirmatory trial.

About CHRONOS-3

CHRONOS-3 is a Phase III randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of copanlisib in combination with rituximab versus placebo in combination with rituximab in patients with relapsed indolent NHL who have received at least one or more lines of prior treatment. Patients were randomized at a 2:1 ratio. Histological subtypes included in the trial were follicular lymphoma (FL), small lymphocytic lymphoma (SLL), lymphoplasmacytoid lymphoma/Waldenström macroglobulinemia (LPL/WM), and marginal zone lymphoma (MZL). Patients must have relapsed after the last rituximab-, rituximab biosimilars-, or anti-CD20 monoclonal antibody (e.g. obinutuzumab)-containing therapy (other previous treatment lines after rituximab were allowed) and either had a treatment-free interval of ≥ 12 months after completion of the last rituximab-containing treatment, or are unwilling to receive chemotherapy or for whom chemotherapy is contraindicated on reason of age, comorbidities, and/or residual toxicity (NCT02367040). The study enrolled 458 participants. Copanlisib is administered on days

1, 8 and 15 of each 28-day cycle in addition to rituximab given weekly during Cycle 1 on days 1, 8, 15 and 22, and then on Day 1 of Cycles 3, 5, 7 and 9.

About non-Hodgkin's Lymphoma

Non-Hodgkin's lymphoma (NHL) comprises a highly heterogeneous group of chronic diseases with poor prognosis. NHL is the most common hematologic malignancy and the tenth most common cancer worldwide, with nearly 510,000 new cases diagnosed in 2018. It also accounted for nearly 249,000 deaths worldwide in 2018.

Indolent NHL consists of multiple subtypes, including follicular lymphoma (FL), marginal zone lymphoma (MZL), small lymphocytic lymphoma (SLL), lymphoplasmacytoid lymphoma/Waldenström macroglobulinemia (LPL/WM). While the disease is typically slowly growing, it can become more aggressive over time. Despite treatment advances, there remains a need for improved treatment options for the relapsed or refractory stage of the disease. After response to initial therapy, response rates and duration of response decline with subsequent lines of therapy, underscoring the need for patients whose disease has already progressed.

About Copanlisib (Aliqopa™)

Developed by Bayer, copanlisib is a pan class I PI3K inhibitor with inhibitory activity against all four isoforms including the PI3K-alpha and PI3K-delta isoforms expressed in malignant B cells. The PI3K pathway is involved in cell growth, survival and metabolism, and its dysregulation plays an important role in the development of lymphoma. Copanlisib is also the only PI3K inhibitor administered intravenously on an intermittent schedule: on days 1, 8, and 15 of a 28-day treatment cycle. Treatment should be continued until disease progression or unacceptable toxicity.

Copanlisib is currently approved in the U.S. and Taiwan under the brand name Aliqopa™.

About Oncology at Bayer

Bayer is committed to delivering science for a better life by advancing a portfolio of innovative treatments. The company has the passion and determination to develop innovative medicines that help improve and extend the lives of people living with cancer. The oncology franchise at Bayer includes six marketed products across various indications and several compounds in different stages of clinical development. Bayer focuses its research activities on first-in-class innovations across the following scientific

platforms: Oncogenic Signaling, Targeted Alpha Therapies, and Immuno-Oncology. Across the areas of focus, we have several prostate cancer treatments on the market or in development, with the goal of extending survival while limiting side effects of treatment throughout the different stages of the disease. Another key focus at Bayer is on innovative precision oncology treatments, with an approved TRK inhibitor exclusively designed to treat tumors that have an *NTRK* gene fusion, the oncogenic driver of tumor growth and spread, and another TRK inhibitor advancing through the pipeline. The company's approach to research prioritizes targets and pathways with the potential to impact the way that cancer is treated.

About Bayer

Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. Its products and services are designed to benefit people by supporting efforts to overcome the major challenges presented by a growing and aging global population. At the same time, the Group aims to increase its earning power and create value through innovation and growth. Bayer is committed to the principles of sustainable development, and the Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2019, the Group employed around 104,000 people and had sales of 43.5 billion euros. Capital expenditures amounted to 2.9 billion euros, R&D expenses to 5.3 billion euros. For more information, go to www.bayer.com.

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Forward-Looking Statements

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