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MEDIA UPDATE

Novartis receives priority review by US FDA and filing acceptance by EMA for Kymriah® to treat patients with relapsed or refractory follicular lymphoma

- *Filings supported by pivotal ELARA trial, where treatment with Kymriah showed robust response rates and remarkable safety profile in adult patients with relapsed or refractory (r/r) follicular lymphoma (FL)[1]*

- *Kymriah also received orphan drug designation from the European Commission (EC) for patients with FL earlier this year*

- *Patients with FL who are refractory to treatment or relapse after two prior lines are in need of durable alternatives to traditional therapies as the efficacy of treatments decreases in later lines[2]*

- *Kymriah, the first-ever FDA-approved CAR-T cell therapy, is currently available in 30 countries in one or more indications, with more than 345 certified treatment centers worldwide*

Basel, October 27, 2021 — Novartis today announced that the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have accepted the company's Supplemental Biologics License Application (sBLA) and Type II Variation, respectively, for Kymriah® (tisagenlecleucel) in adult patients with relapsed or refractory (r/r) follicular lymphoma (FL) after two prior lines of treatment. The FDA has also granted priority review to the company's sBLA for Kymriah in adult patients with r/r FL. Kymriah was previously granted orphan medicinal product designation by the European Commission (EC) for FL. If approved in this potential third indication, Kymriah would have the opportunity to present an important treatment option for those patients with r/r FL in need of potentially definitive outcomes.

The regulatory submissions are based on positive data from the pivotal Phase II ELARA trial, which investigated the efficacy and safety of Kymriah in adult patients with r/r FL. The trial met the primary endpoint with robust responses observed in heavily pretreated patients. The safety profile was remarkable, with no patients experiencing grade 3 or higher cytokine release syndrome (CRS) related to Kymriah within the first 8 weeks following infusion[1]. Data from the trial was presented earlier this year as an oral presentation during the 2021 Annual American Society of Clinical Oncology (ASCO) Virtual Scientific Meeting.

"This is an important milestone in our mission to bring Kymriah to adult patients with relapsed or refractory follicular lymphoma. Receiving orphan drug designation from the EC as well as

priority review from the FDA underscores the unmet need and urgency for these patients. With Kymriah demonstrating impressive results in the ELARA trial, we are hopeful that we can offer a unique and potentially definitive treatment that minimizes the burden," said Jeff Legos, Executive Vice President, Global Head of Oncology & Hematology Development, Novartis.

Orphan drug designation is reserved for medicines that treat, prevent or diagnose a life-threatening or chronically debilitating rare disease with a prevalence in the EU of below 5 in 10,000 and with either no currently approved method of diagnosis, prevention or treatment or with significant benefit to those affected by the disease[3]. The decision follows a positive opinion from the Committee for Orphan Medicinal Products (COMP) of the EMA. Kymriah also has Orphan Drug designation from the FDA and the Japan Ministry of Health, Labour and Welfare (MHLW) for this disease.

Priority Review is granted to therapies that have the potential to provide significant improvements in the treatment, diagnosis or prevention of serious conditions, as determined by the FDA[4].

Kymriah is currently approved by the FDA, EMA and other regulatory authorities for the treatment of r/r pediatric and young adult (up to and including 25 years of age) acute lymphoblastic leukemia (ALL), and r/r adult diffuse large B-cell lymphoma (DLBCL).

About follicular lymphoma
Follicular lymphoma (FL), the second most common form of non-Hodgkin lymphoma (NHL), is an indolent lymphoma, and represents approximately 22% of NHL cases[5,6]. It is often an unrelenting malignancy with a relapsing and remitting pattern[7,2]. Throughout the lifetime of a patient with relapsing FL, he or she may be exposed to a median of five lines of prior treatment, with an upper range of 13 lines[8,9]. Although patients in in third or later line treatment for FL have multiple systemic therapies available, the efficacy of these regimens drops off rapidly in later lines[2]. Additionally, because of this relapsing and remitting pattern, patients who are refractory to treatment or relapse may exhaust available treatment options[2].

About the ELARA trial
ELARA is a Phase II, single-arm, multicenter, open-label trial investigating the efficacy and safety of Kymriah in adult patients with r/r FL after at least two prior therapies. This international trial has enrolled patients from over 30 sites in 12 countries worldwide. The primary endpoint is complete response rate (CRR) based on best response by central review (Lugano 2014 criteria). Patients evaluable for efficacy had measurable disease at infusion and more than six months of follow-up from infusion or discontinued early. After infusion, disease assessments were performed every three months. Secondary endpoints include overall response rate, duration of response, progression-free survival, overall survival and safety. Primary analysis data announced at ASCO 2021 showed Kymriah led to responses for the majority of patients treated, with 66% achieving a complete response (95% CI, 56-75). The overall response rate was 86% (95% CI, 78-92)[1]. Importantly, no patients in ELARA trial experienced grade 3 or higher cytokine release syndrome related to Kymriah within the first 8 weeks following infusion, the most common side effect associated with CAR-T therapy[1].

About Novartis Commitment to Oncology Cell & Gene
Novartis has a mission to reimagine medicine by bringing curative cell & gene therapies to patients worldwide. Novartis has a deep CAR-T pipeline and ongoing investment in manufacturing and supply chain process improvements. With active research underway to broaden the impact of cell and gene therapy in oncology, Novartis is going deeper in hematological malignancies, reaching patients with other cancer types and evaluating next-generation CAR-T cell therapies that focus on new targets and utilize new technologies.

Novartis was the first pharmaceutical company to significantly invest in pioneering CAR-T research and initiate global CAR-T trials. Kymriah, the first approved CAR-T cell therapy, developed in collaboration with the Perelman School of Medicine at the University of Pennsylvania, is the foundation of Novartis' commitment to CAR-T cell therapy.

Kymriah is currently approved for use in at least one indication in 30 countries and at more than 345 certified treatment centers, with the ambition for further expansion to help fulfill the ultimate goal of bringing CAR-T cell therapy to every patient in need.

Novartis has an expansive global CAR-T manufacturing footprint that includes both Novartis-owned and contract manufacturing sites. This comprehensive, integrated footprint strengthens the flexibility, resilience and sustainability of the Novartis manufacturing and supply chain.

Important Safety information from the Kymriah SmPC
Kymriah (tisagenlecleucel) is an autologous, immunocellular cancer therapy which involves reprogramming a patient's own T-cells with a transgene encoding a chimeric antigen receptor (CAR) to identify and eliminate CD19-expressing cells. It is administered as intravenous infusion.

Kymriah is indicated for the treatment of pediatric and young adult patients up to and including 25 years of age with B-cell acute lymphoblastic leukemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse as well as for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy.

Kymriah must not be administered in case of hypersensitivity to the active substance or to any of the excipients of the product. In addition, contraindications of the lymphodepleting chemotherapy that is usually preceding the Kymriah infusion to prepare the patient's body, must be considered.

For details, please see the Summary of Product Characteristics (SmPC).

Reasons to delay Kymriah treatment
Kymriah treatment should be delayed, if a patient has any of the following conditions:

- Unresolved serious adverse reactions (especially pulmonary reactions, cardiac reactions or hypotension) from preceding chemotherapies.
- Active uncontrolled infection.
- Active graft-versus-host disease (GVHD).
- Significant clinical worsening of leukemia burden or lymphoma following lymphodepleting chemotherapy.

Monitoring after Kymriah infusion
Kymriah may cause side effects that could be severe, life-threatening or fatal. Therefore, patients should be monitored daily for the first 10 days following infusion for signs and symptoms of potential cytokine release syndrome, neurological events and other toxicities. Physicians should consider hospitalization for the first 10 days post infusion or at the first signs/symptoms of cytokine release syndrome and/or neurological events. After the first 10 days following the infusion, the patient should be monitored at the physician's discretion.

Patients should be instructed to remain within proximity (i.e., 2 hours of travel) of a qualified clinical facility for at least 4 weeks following infusion. They should be advised to contact their healthcare provider right away, if they experience any of signs and symptoms of cytokine release syndrome, neurological events, infections and tumor lysis syndrome or if other severe or serious side effects occur.

Patients are advised to take their body temperature twice a day for 3-4 weeks after treatment with Kymriah, and if the temperature is high to contact their doctor immediately.

Important side effects
Kymriah may cause side effects that could be severe, life-threatening or fatal. They usually happen in the first eight weeks after the infusion, but can also develop later. The following main side effects can occur after Kymriah infusion:

Cytokine release syndrome has been frequently observed and almost always occurred within the first 10 days after Kymriah infusion. Patients may experience high fever, chills, difficulty breathing, nausea, vomiting, diarrhea, muscle pain, joint pain, low blood pressure, dizziness/light headedness, and issues with blood coagulation. Adverse reactions of multiple body organs, such as the heart, the liver or kidney, may occur.

Neurological events, in particular encephalopathy, confusional state or delirium, can occur frequently with Kymriah. Other manifestations can also include altered or decreased consciousness, agitation, seizures, difficulty speaking, understanding speech, or loss of balance. The majority of neurological events occurred within eight weeks following Kymriah infusion and were transient. Because of the risk of neurological side effects, patients should not drive, operate heavy machinery, or do other activities that require alertness for eight weeks after receiving Kymriah.

Infections can occur frequently after Kymriah infusion. As appropriate, prophylactic antibiotics should be administered and surveillance testing should be employed prior to and during treatment with Kymriah. Infections are known to complicate the course and management of concurrent cytokine release syndrome. Vaccination with live virus vaccines is not recommended at least six weeks prior to the start of lymphodepleting chemotherapy, during Kymriah treatment, and until immune recovery following treatment with Kymriah.

Febrile neutropenia was frequently observed in patients after Kymriah infusion. In the event of febrile neutropenia, infection should be evaluated and managed appropriately with broad-spectrum antibiotics, fluids and other supportive care, as medically indicated.

Tumor lysis syndrome is a rapid breakdown of tumor cells and release of their contents into the bloodstream. This can interfere with the workings of various body organs, especially the kidneys, heart and nervous system. To minimize risk of tumor lysis syndrome, patients with elevated uric acid or high tumor burden should receive allopurinol, or an alternative prophylaxis, prior to Kymriah infusion.

Prolonged cytopenias, which is a low count of one or more types of blood cells such as red blood cells, white blood cells, or platelets, can persist for several weeks following Kymriah. The majority of patients who had cytopenias at day 28 following Kymriah treatment improved or resolved within three months after treatment. Prolonged neutropenia has been associated with increased risk of infection.

Hypogammaglobulinemia or Agammaglobulinemia, a condition in which the level of immunoglobulins (antibodies) in the blood is low and the risk of infections is increased, can occur in patients treated with Kymriah. Infection precautions, antibiotic prophylaxis and immunoglobulin replacement should be managed per age and standard guidelines.

Secondary malignancies: After treatment with Kymriah, patients will be monitored life-long by their healthcare provider, as they may develop secondary cancers.

Pregnancy and breast-feeding: It is not known, whether Kymriah has the potential to be transferred to the fetus via the placenta and could cause fetal toxicity, including B-cell lymphocytopenia. Kymriah is not recommended during pregnancy and in women of childbearing potential not using contraception. It is unknown, whether Kymriah is excreted in human milk. A risk to the breast-fed infant cannot be excluded. Women, who are breast-feeding, should be advised of the potential risk to the breast-fed infant.

Blood, organ, tissue and cell donation: Patients treated with Kymriah should not donate blood, organs, tissues and cells for transplantation.

Please see the full Summary of Product Characteristics (SmPC) for KYMRIAH, www.Kymriah.com

Disclaimer

This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “potential,” “can,” “will,” “plan,” “may,” “could,” “would,” “expect,” “anticipate,” “seek,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

Novartis is reimagining medicine to improve and extend people’s lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world’s top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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