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MEDIA & INVESTOR RELEASE

Novartis analyses confirm benefit of Kymriah® with clinically meaningful rates of complete response seen in patients with certain advanced lymphomas

- *Interim analysis from the investigational ELARA study shows, 65% of patients with r/r follicular lymphoma evaluated for efficacy achieved a complete response and the overall response rate was 83%*[1]
- *Longer-term median follow-up of 40 months from the JULIET study showed a 33% two-year progression-free survival rate in patients with r/r DLBCL*[2]
- *Both ELARA and JULIET trials reaffirm safety profile of Kymriah with no new short- or long-term safety signals identified*

Basel, December 5, 2020 — Novartis announced analyses from two separate trials with Kymriah® (tisagenlecleucel) in patients with certain advanced lymphomas. In the interim analysis of the investigational Phase II ELARA study, Kymriah led to a complete response (CR) in 65% of patients with relapsed or refractory (r/r) follicular lymphoma (FL) and an overall response rate (ORR) of 83% after at least three months of follow-up. These patients continued to relapse or have refractory disease despite exposure to numerous lines of therapy (median four prior lines of therapy [range 2-13]) prior to Kymriah infusion[1]. The second analysis – a 40-month median follow-up from the Phase II JULIET trial – reported that the two-year progression-free survival (PFS) rate was 33% in patients with r/r diffuse large B-cell lymphoma (DLBCL), an important finding given these patients have limited treatment options that provide durable responses[2]. The JULIET study continued to show the effectiveness and well-characterized safety profile of Kymriah for these patients. These results were presented today during the 62nd American Society of Hematology Annual Meeting & Exposition (ASH).

“For people who have follicular lymphoma that continues to relapse or does not respond after treatment with many lines of therapy, response to therapy becomes less likely with each additional treatment,” said Nathan H. Fowler, MD, Department of Lymphoma and Myeloma, Division of Cancer Medicine at MD Anderson Cancer Center. “We are encouraged by these interim results from the ELARA trial, as there is a great need for potentially definitive options and an alternative to stem cell transplant. We look forward to continuing to learn more about how Kymriah may provide benefit for these patients.”

In the interim analysis of the investigational ELARA clinical trial, in which 52 patients were evaluable for efficacy with a median follow-up of 9.9 months, Kymriah led to responses for the majority of patients treated. Specifically, after at least three months of follow-up, 65% (99.5% CI, 45.1-82.4) of patients achieved a complete response, meeting the primary endpoint. The overall response rate was 83% (95% CI, 69.7-91.8). For those who had a complete response, the vast majority (90%) sustained responses for six months or more.

Safety results from this analysis of the ELARA trial suggest there was no emergence of new safety signals for Kymriah in the 97 patients evaluable for safety. No patients experienced grade 3/4 CRS, as defined by the Lee Scale, and any grade CRS occurred in 49% of patients (29% grade 1; 20% grade 2). To treat CRS, 15% of patients required tocilizumab and 3% required steroids. One percent of patients experienced grade 3/4 NEs and any grade NEs occurred in 9% of patients. Median time to CRS and severe NE onset was four and 8.5 days respectively, with respective median time to resolution of four and two days. All neurological and CRS events resolved with appropriate management. Three patients died from progressive disease and no deaths were treatment-related. Kymriah was administered in the outpatient setting for 18% of patients in the ELARA trial[1].

Results from the primary analysis of the ELARA study, with data from 90 patients followed up for at least 6 months, will be presented at an upcoming medical meeting.

“Novartis is dedicated to continuing to explore the safety and efficacy of Kymriah for patients with advanced blood cancers who do not achieve long-term remissions despite multiple prior lines of therapy,” said John Tsai, MD, Head of Global Drug Development and Chief Medical Officer, Novartis. “As we go deeper with our research in CAR-T cell therapies, these new analyses showcase the potential to rewrite cancer survival in patients with certain advanced lymphomas.”

New updated efficacy results from pivotal JULIET clinical trial

New updated efficacy results from a 40-month median follow-up analysis demonstrated continued durable responses for patients with r/r DLBCL treated with Kymriah in the JULIET trial (n=115). Among the 61 patients who responded to treatment, the relapse-free probability was 60% at 24 and 36 months; median DOR was not reached (95% CI, 10-not estimable [NE])[3]. Two-year progression-free survival rate was 33% [2]. Survival probability at 24 and 36 months was 40% and 36%, respectively. Importantly, no new safety signals were observed after more than three years of long-term follow-up observation[3].

“Before the availability of Kymriah, long-term responses to treatment for those living with relapsed or refractory DLBCL were rare,” said Ulrich Jaeger, MD, Medical University of Vienna, Vienna, Austria. “With these results from the JULIET trial, including biomarker analysis to better define patient subgroups who may benefit the most from CAR-T cell therapy, we are providing further evidence that Kymriah may be a definitive option for some patients. Additionally, with no new safety signals observed, physicians can continue to confidently refer their patients to certified centers to be treated with Kymriah.”

The relationship between biomarkers, such as baseline Myc overexpression in tumors and tumor microenvironment (TME) characteristics, and response to Kymriah was also assessed in this analysis. Outcomes were better for those with negative Myc expression compared to those who had Myc overexpression, which leads to an unfavorable immunosuppressive TME with a restricted T-cell response. These results are consistent with historical outcomes for patients with Myc- and Myc+ expression[4]. Analyses to further identify biomarkers for response to CAR-T cell therapy are ongoing.

More information about Novartis activities at ASH can be found on the Novartis 2020 ASH Annual Meeting **virtual portal**.

About Follicular Lymphoma
Follicular lymphoma, the second most common form of non-Hodgkin lymphoma (NHL), is an indolent lymphoma, and represents approximately 22% of NHL cases[5,6]. Despite new treatments that improve overall survival, FL is regarded as an incurable malignancy with a relapsing and remitting pattern[7,8]. Throughout the lifetime of a patient with relapsing FL, they may be exposed to a median of five lines of prior treatment, with an upper range of 12 lines[9,10]. Although patients in third or later line treatment for FL have multiple systemic

therapies available, the efficacy of these regimens drops off rapidly in later lines[5]. Additionally, because of this relapsing and remitting pattern, patients who are refractory to treatment or quickly relapse may exhaust available treatment options[8].

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. This international trial has enrolled patients from over 30 sites in 12 countries worldwide. The primary endpoint is 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.

In Q2 2020, the FDA granted Regenerative Medicine Advanced Therapy (RMAT) designation to Kymriah in r/r FL, based on preliminary results from the ELARA trial. RMAT designation is intended to expedite the development and review of Kymriah as a regenerative therapy for this underserved patient population. Kymriah also has Orphan Drug designation from the FDA for this indication.

About the JULIET Trial
JULIET was the first multi-center global registration study for Kymriah in adult patients with r/r DLBCL. JULIET, led by researchers at the University of Pennsylvania, enrolled patients from 27 sites in 10 countries across the US, Canada, Australia, Japan and Europe, including Austria, France, Germany, Italy, Norway and the Netherlands.

About Kymriah
Kymriah is the first-ever FDA-approved CAR-T cell therapy, and the first-ever CAR-T to be approved in two distinct indications. It is a one-time treatment designed to empower patients' immune systems to fight their cancer. Kymriah is currently approved for the treatment of r/r pediatric and young adult (up to 25 years of age) acute lymphoblastic leukemia (ALL), and r/r adult DLBCL[11].

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 27 countries and at more than 270 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.

The Novartis global CAR-T manufacturing footprint spans seven facilities, across four continents. This comprehensive, integrated footprint strengthens the flexibility, resilience and sustainability of the Novartis manufacturing and supply chain. Commercial and clinical trial manufacturing is now ongoing at Novartis-owned facilities in Stein, Switzerland, Les Ulis, France and Morris Plains, New Jersey, USA, as well as at the contract manufacturing sites at Fraunhofer-Institut for cell therapy and immunology (Fraunhofer-Institut für Zelltherapie und Immunologie) facility in Leipzig, Germany, and now FBRI in Kobe, Japan. Manufacturing production at Cell Therapies in Australia and Cellular Biomedicine Group in China is forthcoming.

Kymriah® (tisagenlecleucel) US Important Safety information

Kymriah may cause side effects that are severe or life-threatening, such as Cytokine Release Syndrome (CRS) or Neurological Toxicities. Patients with CRS may experience symptoms including difficulty breathing, fever (100.4°F/38°C or higher), chills/shaking chills, severe nausea, vomiting and diarrhea, severe muscle or joint pain, very low blood pressure, or dizziness/lightheadedness. Patients may be admitted to the hospital for CRS and treated with other medications.

Patients with neurological toxicities may experience symptoms such as altered or decreased consciousness, headaches, delirium, confusion, agitation, anxiety, seizures, difficulty speaking and understanding, or loss of balance. Patients should be advised to call their healthcare provider or get emergency help right away if they experience any of these signs and symptoms of CRS or neurological toxicities.

Because of the risk of CRS and neurological toxicities, Kymriah is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called Kymriah REMS.

Serious allergic reactions, including anaphylaxis, may occur after Kymriah infusion. Kymriah can increase the risk of life-threatening infections that may lead to death. Patients should be advised to tell their healthcare provider right away if they develop fever, chills, or any signs or symptoms of an infection.

Patients may experience prolonged low blood cell counts (cytopenia), where one or more types of blood cells (red blood cells, white blood cells, or platelets) are decreased. The patient's healthcare provider will do blood tests to check all of their blood cell counts after treatment with Kymriah. Patients should be advised to tell their healthcare provider right away if they get a fever, are feeling tired, or have bruising or bleeding.

Patients may experience hypogammaglobulinemia, a condition in which the level of immunoglobulins (antibodies) in the blood is low and the risk of infection is increased. It is expected that patients may develop hypogammaglobulinemia with Kymriah, and may need to receive immunoglobulin replacement for an indefinite amount of time following treatment with Kymriah. Patients should tell their healthcare provider about their treatment with Kymriah before receiving a live virus vaccine.

After treatment with Kymriah, patients will be monitored lifelong by their healthcare provider, as they may develop secondary cancers or recurrence of their cancer.

Patients should not drive, operate heavy machinery, or do other dangerous activities for eight weeks after receiving Kymriah because the treatment can cause temporary memory and coordination problems, including sleepiness, confusion, weakness, dizziness, and seizures.

Some of the most common side effects of Kymriah are difficulty breathing, fever (100.4°F/38°C or higher), chills/shaking chills, confusion, severe nausea, vomiting and diarrhea, severe muscle or joint pain, very low blood pressure, dizziness/lightheadedness, and headache. However, these are not all of the possible side effects of Kymriah. Patients should talk to their healthcare provider for medical advice about side effects.

Prior to a female patient starting treatment with Kymriah, their healthcare provider may do a pregnancy test. There is no information available for Kymriah use in pregnant or breast-feeding women. Therefore, Kymriah is not recommended for women who are pregnant or breast feeding. Patients should talk to their healthcare provider about birth control and pregnancy.

Patients should tell their healthcare provider about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

After receiving Kymriah, patients should be advised that some commercial HIV tests may cause a false-positive test result. Patients should also be advised not to donate blood, organs, or tissues and cells for transplantation after receiving Kymriah.

Please see the full Prescribing Information for Kymriah, including Boxed WARNING, and Medication Guide at 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 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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