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Novartis granted US FDA Priority Review for Kymriah™ (tisagenlecleucel), formerly CTL019, for adults with r/r DLBCL

- *Filing acceptance marks second Priority Review granted to Kymriah by the FDA for two distinct indications, underscoring the potential of first ever FDA-approved CAR-T therapy*
- *EMA granted accelerated assessment to Kymriah for children, young adults with r/r B-cell ALL and adults with r/r DLBCL who are ineligible for autologous stem cell transplant*
- *Novartis is working closely with the FDA and EMA to make Kymriah available to more patients with critical unmet need*

Basel, January 17, 2018 – Novartis today announced that its supplemental Biologics License Application (sBLA) for Kymriah™ (tisagenlecleucel) suspension for intravenous infusion, formerly CTL019, for the treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) who are ineligible for or relapse after autologous stem cell transplant (ASCT) has been accepted by the US Food and Drug Administration (FDA) for Priority Review. In addition, the European Medicines Agency (EMA) has granted accelerated assessment to the Marketing Authorization Application (MAA) for Kymriah for the treatment of children and young adults with r/r B-cell acute lymphoblastic leukemia (ALL) and for adult patients with r/r DLBCL who are ineligible for ASCT. Priority Review and accelerated assessment are granted to therapies which may provide a significant improvement in the safety and effectiveness of the treatment of a serious disease, and the designations are intended to expedite the standard review time. If approved by the FDA and EMA, Kymriah would represent the first chimeric antigen receptor T cell (CAR-T) therapy available for two distinct indications in non-Hodgkin lymphoma and B-cell ALL.

Kymriah became the first CAR-T cell therapy to receive regulatory approval when it was approved by the FDA in August 2017 for the treatment of patients up to 25 years of age with B-cell precursor ALL that is refractory or in second or later relapse.

“The first approval of a CAR-T therapy truly redefined the future of the cancer treatment landscape, and we are only at the beginning of this new era in cancer care,” said Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. “The Priority Review designation and accelerated assessment signal that the FDA and EMA have recognized the potential of Kymriah to provide a much-needed therapeutic option for these patients with relapsed or refractory B-cell ALL and DLBCL. We are now focused on working with these regulatory agencies to bring this potentially transformative therapy to more patients.”

Kymriah is a novel immunocellular therapy and a one-time treatment that uses a patient’s own T cells to fight cancer. Kymriah uses the 4-1BB costimulatory domain in its chimeric antigen receptor to enhance cellular expansion and persistence. In 2012, Novartis and the University of Pennsylvania (Penn) entered into a global collaboration to further research, develop and commercialize CAR-T cell therapies, including Kymriah, for the investigational treatment of cancers.

The regulatory applications in the US and EU are based on data from the Novartis-sponsored global clinical trial program of Kymriah in children and young adults with r/r B-cell ALL and adult patients with r/r DLBCL demonstrating the efficacy and safety of Kymriah across studies. Results from the pivotal phase II JULIET clinical trial served as the basis of the sBLA and MAA (applications submitted by pharmaceutical companies to health authorities when seeking approval of a new product) for Kymriah in adult patients with r/r DLCBL. Results from the pivotal phase II ELIANA study were submitted as part of the MAA for Kymriah in children and young adults with r/r B-cell ALL.

JULIET is the first multi-center global registration study for Kymriah in adult patients with r/r DLBCL. JULIET is the largest study examining a CAR-T therapy in DLBCL, enrolling patients from 27 sites in 10 countries across the US, Canada, Australia, Japan and Europe, including: Austria, France, Germany, Italy, Norway and the Netherlands. Data from the six-month primary analysis of JULIET were presented at the annual meeting of the American Society of Hematology (ASH) in December 2017.

ELIANA is the first pediatric global CAR-T cell therapy registration trial, examining patients in 25 centers in the US, Canada, Australia, Japan and the EU, including: Austria, Belgium, France, Germany, Italy Norway, and Spain.

Novartis plans additional regulatory submissions for Kymriah in pediatric and young adult patients with r/r B-cell ALL and adult patients with r/r DLBCL beyond the US and EU in 2018.

About CAR-T
CAR-T is different from typical small molecule or biologic therapies because it is manufactured for each individual patient using their own cells. During the treatment process, T cells are drawn from a patient's blood and reprogrammed in the laboratory to create T cells that are genetically coded to recognize and fight the patient's cancer cells and other B cells expressing a particular antigen.

About Kymriah Manufacturing
Kymriah is manufactured for each individual patient using their own cells at the Novartis Morris Plains, New Jersey facility. In the US, the target turnaround time for manufacturing Kymriah in the commercial setting is 22 days. The reliable and integrated manufacturing and supply chain platform for Kymriah allows for an individualized treatment approach on a global scale. The process includes cryopreservation of a patient's harvested (or leukapheresed) cells, giving treating physicians and centers the flexibility to initiate therapy with Kymriah based on the individual patient's condition. Building on the company's experience, having manufactured CAR-T cells for over 300 patients from 11 countries across various indications in clinical trials, it has demonstrated a reproducible product. Novartis continues to advance its CAR-T manufacturing expertise in Morris Plains where we have been supplying CAR-T cells for global clinical trials and where we continue to invest in support of the anticipated demand to meet the needs of patients.

Novartis has also successfully established the CTL019 manufacturing process at the Fraunhofer-Institut for cell therapy and immunology (Fraunhofer-Institut für Zelltherapie and Immunologie) facility in Leipzig, Germany, which currently supports the manufacturing of CTL019 for global clinical trials.

Novartis Leadership in Immuno-Oncology
Novartis is at the forefront of investigational immunocellular therapy as the first pharmaceutical company to initiate global CAR-T trials, and has significantly invested in CAR-T research and worked with pioneers in the field. Kymriah™, the first approved CAR-T cell therapy, is the cornerstone of this strategy. Active research programs are underway targeting other hematologic malignancies and solid tumors, and include efforts focused on next generation CAR-Ts that involve simplified manufacturing schemes and gene edited cells.

Kymriah™ (tisagenlecleucel) US Important Safety information (for patients up to 25 years of age with B-cell precursor ALL that is refractory or in second or later relapse)
The full prescribing information, including Boxed WARNING, for Kymriah can be found at:
https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/kymriah.pdf

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 high fever, difficulty breathing, 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 health care 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) in the US 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 health care 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 health care provider will do blood tests to check all of their blood cell counts after treatment with Kymriah. Patients should be advised to tell their health care 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 health care provider about their treatment with Kymriah before receiving a live virus vaccine.

After treatment with Kymriah, patients will be monitored life-long by their health care provider, as they may develop secondary cancers or recurrence of their leukemia.

Patients should not drive, operate heavy machinery, or do other dangerous activities for 8 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, and dizziness/lightheadedness. However, these are not all of the possible side effects of Kymriah. Patients should talk to their health care provider for medical advice about side effects.

Prior to a female patient starting treatment with Kymriah, their health care 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. If either sex partner has received Kymriah, patients should talk to their health care provider about birth control and pregnancy.

Patients should tell their health care 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.

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,” “expect,” “anticipate,” “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, regarding our ability to implement, scale and sustain commercial manufacturing for the investigational or approved products described in this press release, regarding our ability to build and sustain a network of treatment centers to offer 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. Neither can there be any guarantee that Novartis will successfully implement, scale and sustain commercial manufacturing for the investigational or approved products described in this press release, or successfully build and sustain a network of treatment centers to offer the investigational or approved products described in this press release. 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, our ability to successfully implement, scale and sustain commercial manufacturing and build and sustain a network of treatment centers; 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; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; general economic and industry conditions, including the effects of the persistently weak economic and financial environment in many countries; safety, quality or manufacturing issues, 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 provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 121,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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