Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

http://www.novartis.com

MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG

Novartis announces NEJM publication of updated analysis from ELIANA trial showing longer-term durable remissions with Kymriah™ in children, young adults with r/r ALL

- *Analysis of 75 patients with median follow-up of more than a year demonstrated an overall remission rate of 81%*
- *Event-free survival and overall survival at six months were 73% and 90%, with median duration of remission not reached*
- *Kymriah was detected in patients up to 20 months, demonstrating long-term persistence*
- *Novartis is committed to bringing Kymriah to more patients with a regulatory application currently under review by the EMA for r/r ALL and r/r DLBCL based on Novartis global clinical trial program, including ELIANA*

Basel, January 31, 2018 – Novartis today announced updated results from the pivotal ELIANA clinical trial of Kymriah™ (tisagenlecleucel), formerly CTL019, in relapsed or refractory (r/r) pediatric and young adult patients with B-cell acute lymphoblastic leukemia (ALL) have been published in *The New England Journal of Medicine* (NEJM). New data include longer-term follow-up and efficacy in 75 infused patients, analysis of expansion and persistence of Kymriah, and longer-term safety. Kymriah became the first chimeric antigen receptor T (CAR-T) cell therapy to receive regulatory approval in August 2017, when it was approved by the US Food and Drug Administration (FDA) 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, based on previous results from the ELIANA study, which was conducted in collaboration with the University of Pennsylvania (Penn) and Children's Hospital of Philadelphia (CHOP).

In the analysis of 75 infused patients with three or more months of follow-up, Kymriah demonstrated an overall remission rate of 81% (95% CI: 71% - 89%). Sixty percent of patients achieved complete remission (CR) and 21% of patients achieved CR with incomplete blood count recovery (CRi), with no minimal residual disease (MRD) detected among all responding patients (95% [58/61] by day 28). Median follow-up was 13.1 months.

"Kymriah, the first FDA-approved CAR-T cell therapy, has shown the potential to be a definitive therapy, providing early, deep and durable remissions for children and young adults with relapsed or refractory ALL," said Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. "These data are a testament to our commitment at Novartis for continued CAR-T cell therapy research to bring this therapy to as many patients as possible."

Among patients who achieved CR/CRi, median duration of response was not reached. Remissions were durable with six-month relapse-free survival of 80%. Event-free survival was 73% at six months (95% CI: 60%-82%) and 50% at 12 months (95% CI: 35%-64%), with median event-free survival not reached. Overall survival in the 75 infused patients was 90% (95% CI: 81%-95%) at six months, and 76% (95% CI: 63%-86%) at 12 months. Kymriah was

detected in patients up to 20 months. Median persistence of Kymriah was 168 days (range: 20-617; n=60 patients with CR/CRi) at data cutoff. All responding patients demonstrated B-cell aplasia (a low number of or absent B-cells), an on-target effect of treatment with Kymriah, and most received immunoglobulin replacement per local practice. Evaluable patients with a response at day 28 had a median time to maximum expansion of 10 days (5.7-28 days; n=60), whereas six patients with no response had a median time to maximum expansion of 20 days (13-63 days). Kymriah uses the 4-1BB costimulatory domain in its chimeric antigen receptor, which has shown to enhance early cellular expansion and long-term endurance of CAR-T cells.

“We continue to be encouraged by the results demonstrated with Kymriah in a patient population who previously had limited treatment options, and now have the potential for durable remissions translating into longer-term survival,” said lead study author Shannon L. Maude, MD, PhD, Assistant Professor of Pediatrics, at Children’s Hospital of Philadelphia and Perelman School of Medicine at the University of Pennsylvania. “Not only does this longer-term follow-up from the ELIANA study reinforce that this is a potentially paradigm-changing treatment, but it also contributes to the growing body of evidence which shows the critical role of cell function, expansion and ongoing persistence of Kymriah associated with the durability of clinical response.”

Any grade treatment-related adverse events (AE) occurred in 95% of patients, with the most common non-hematologic AEs being cytokine release syndrome (CRS; 77%), pyrexia (40%), decreased appetite (39%), febrile neutropenia (36%) and headache (36%). Seventy-three percent of patients experienced a grade 3/4 treatment-related AE. CRS, a known complication of Kymriah that may occur when engineered cells become activated in the patient’s body, occurred in 77% of patients. Forty-six percent of patients experienced grade 3/4 CRS (grade 3: 21%; grade 4: 25%), using the Penn Grading Scale, a rigorous scale for grading CRS. CRS was managed globally using prior site education on implementation of the CRS treatment algorithm. Thirty-five of 75 infused patients (47%) were admitted to the intensive care unit for management of CRS. Neurological events occurred in 40% of patients within eight weeks of infusion, and 13% (n=10) of patients had grade 3, which were managed with best supportive care. No incidence of grade 4 neurological events or cerebral edema was reported. Eighteen patients (24%) received Kymriah in the outpatient setting. To support safe patient access, Kymriah is only available through a network for certified treatment centers throughout the country which are fully trained on the use of Kymriah and appropriate patient care.

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, demonstrating effective distribution of CTL019 across four continents using a global supply chain. In 2012, Novartis and Penn entered into a global collaboration to further research, develop and commercialize CAR-T cell therapies, including Kymriah, for the investigational treatment of cancers.

A Marketing Authorization Application for Kymriah for the treatment of children and young adults with r/r B-cell ALL and adult patients with r/r diffuse large B-cell lymphoma (DLBCL) who are ineligible for autologous stem cell transplant (ASCT) is currently under review by the European Medicines Agency (EMA). A supplemental Biologics License Application is also under review by the FDA for Kymriah for the treatment of adult patients with r/r DLBCL who are ineligible for or relapse after ASCT. Additional filings beyond the US and EU are anticipated in 2018.

About Kymriah
In August 2017, Kymriah became the first available chimeric antigen receptor T cell (CAR-T) therapy when it received FDA approval for children and young adults with B-cell acute lymphoblastic leukemia (ALL) that is refractory or has relapsed at least twice. Kymriah is a

novel immunocellular therapy and a one-time treatment that uses a patient's own T cells to fight cancer.

About Kymriah Manufacturing
Kymriah will be 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 high-quality and reproducible product. Novartis continues to advance its CAR-T manufacturing expertise and make investments to support the anticipated demand to meet the needs of patients. 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.

Kymriah™ (tisagenlecleucel) Important Safety information
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 Kymriah, regarding our ability to scale and sustain commercial manufacturing for Kymriah, or regarding potential future revenues from Kymriah. 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 Kymriah 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 scale and sustain commercial manufacturing for Kymriah, or successfully sustain a network of treatment centers to offer Kymriah. Nor can there be any guarantee that Kymriah will be commercially successful in the future. In particular, our expectations regarding Kymriah could be affected by, among other things, our ability to successfully scale and sustain commercial manufacturing 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 2017, the Group achieved net sales of USD 49.1 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 122,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

Novartis is on Twitter. Sign up to follow @Novartis at http://twitter.com/novartis
For Novartis multimedia content, please visit www.novartis.com/news/media-library
For questions about the site or required registration, please contact media.relations@novartis.com

# # #

Novartis Media Relations
Central media line: +41 61 324 2200
E-mail: media.relations@novartis.com

Eric Althoff
Novartis Global Media Relations
+41 61 324 7999 (direct)
+41 79 593 4202 (mobile)
eric.althoff@novartis.com

Fiona Phillips
Novartis Oncology Communications
+1 862-778-7705 (direct)
+1 862-217-9396 (mobile)
fiona.phillips@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central		North America	
Samir Shah	+41 61 324 7944	Richard Pulik	+1 212 830 2448
Pierre-Michel Bringer	+41 61 324 1065	Cory Twining	+1 212 830 2417
Thomas Hungerbuehler	+41 61 324 8425		
Isabella Zinck	+41 61 324 7188		