Novartis next generation CAR-T cell therapy CTL119 combined with ibrutinib shows high rate of responses in CLL patients

- Eight of nine evaluable patients tested had no signs of CLL in their bone marrow at three months.
- CTL119 is a humanized CD19-directed CAR-T cell therapy being developed in collaboration with the University of Pennsylvania.
- Novartis is committed to advancing a portfolio of next-generation CAR-T cell therapies.

Basel, May 30, 2017 – Novartis announced findings from a pilot study (NCT02640209) of CTL119 in combination with ibrutinib* in patients with relapsed/refractory chronic lymphocytic leukemia (CLL) who had been taking ibrutinib for at least six months and who were not in complete remission. All study patients had to have failed at least one prior regimen before ibrutinib or carried high-risk cytogenetics or mutations. The results, which will be presented at the upcoming 53rd Annual Meeting of the American Society of Clinical Oncology (ASCO; abstract #7509; Monday, June 5, 1:15 PM CDT), that eight of nine evaluable patients had no signs of CLL in their bone marrow at three months. One of those patients had a partial response.

“The data from this pilot study support the potential for CTL119, when combined with the kinase inhibitor ibrutinib, to induce clinically-significant responses in high-risk CLL patients who were unlikely to achieve a complete remission on ibrutinib alone,” said James Bradner, president of the Novartis Institutes for BioMedical Research. “CTL119 represents one of our latest advances in CAR-T cell therapy research and our broader commitment to pioneering breakthrough immuno-oncology treatments.”

The findings will be presented by Saar Gill, MD, PhD, an assistant professor of Hematology-Oncology in the Perelman School of Medicine and the Abramson Cancer Center of the University of Pennsylvania.

CTL119 is a humanized CD19-directed chimeric antigen receptor T cell (CAR-T) cell therapy, which 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 hunt the patient’s cancer cells and other B-cells expressing a particular antigen.

Results from the pilot study also showed that eight of nine patients had no signs of CLL in their bone marrow at three months as tested by flow cytometry and/or analysis for minimal residual disease (MRD). MRD, which measures the presence of residual abnormalities in the blood and bone marrow at the molecular level following treatment, is important because it can be an indicator of potential relapse.

*. ibrutinib is the trade name for Bruton’s tyrosine kinase inhibitor mugosib, approved by the FDA on March 17, 2014. **MRD is a measurement of malignancy cells in the body.
CT scans were performed to measure the inclusion of CLL in the spleens and lymph nodes of study patients. A number of patients showed improvements in the burden of disease in their spleens and lymph nodes at three months, though radiologic responses are less clear cut and they require longer follow-up.

In the study, 10 patients experienced cytokine release syndrome (CRS), two of which were grade 3. However, no patients required treatment with tocilizumab** and all patients recovered from CRS. One patient developed tumor lysis syndrome and two patients had febrile neutropenia.

CLL is one of the most common types of adult leukemia, which typically progresses slowly over time. The majority of patients will relapse after initial therapy4, and newer targeted therapies must be taken continuously for an indefinite period of time5. These are clear indications of the high unmet medical need for new therapies for CLL.

**About the Novartis CAR-T Program**

In 2012, Novartis and the University of Pennsylvania entered into a global collaboration to further research, develop and then commercialize CAR-T cell therapies for the investigational treatment of cancers. In March 2017, Novartis announced that the US Food and Drug Administration (FDA) accepted the company’s Biologics License Application filing and granted priority review for CTL019 in the treatment of relapsed/refractory (r/r) pediatric and young adult patients with B-cell acute lymphoblastic leukemia. In April 2017, FDA granted Breakthrough Therapy designation to CTL019 for relapsed/refractory diffuse large B-cell lymphoma.

During the collaboration between Novartis and the University of Pennsylvania, researchers generated the humanized anti-CD19 CAR, CTL119. CTL119 is in initial clinical development for multiple B-cell malignancies. Because CTL119 and CTL019 are investigational therapies, the safety and efficacy profile has not yet been established. Access to investigational therapies is available only through carefully controlled and monitored clinical trials. These trials are designed to better understand the potential benefits and risks of the therapy. Because of the uncertainty of clinical trials, there is no guarantee that CTL119 or CTL019 will become commercially available.

**Disclaimer**

The foregoing release contains forward-looking statements that can be identified by words such as "next generation," "being developed," "committed," "will," "upcoming," "potential," "commitment," "investigational," "priority review," "Breakthrough Therapy designation," or similar terms, or by express or implied discussions regarding potential marketing approvals for CTL119 and CTL019, or regarding potential future revenues from CTL119 and CTL019. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management 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 CTL119 or CTL019 will be submitted or approved for sale in any market, or at any particular time. Neither can there be any guarantee that the collaboration with the University of Pennsylvania will achieve any or all of its intended goals and objectives or be successful, or at any particular time. Nor can there be any guarantee that CTL119 or CTL019 will receive regulatory approval or be commercially successful in the future. In particular, management’s expectations regarding CTL119, CTL019 and the collaboration with the University of Pennsylvania could be affected by, among other things, the achievement of, or failure to achieve, any or all of the intended goals and objectives of the collaboration with the University of Pennsylvania; 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; the company’s ability to
obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing and reimbursement pressures; 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.

Notes
* Ibrutinib is marketed as IMBRUVICA®, a registered trademark owned by Pharmacycics LLC.
** Tocilizumab is marketed as ACTEMRA®, which is a registered trademark of Chugai Seiyaku Kabushiki Kaisha Corp., a member of the Roche Group.

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 118,000 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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