Novartis highlights research on investigational, personalized T cell therapy CTL019 in patients with forms of acute and chronic leukemia

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- -- Data at ASH show increased scientific understanding of CTL019 and its potential role in the treatment of certain types of lymphocytic leukemia(1,2,3,4)
- -- Presentations include findings that 19 of 22 pediatric patients with acute lymphoblastic leukemia (ALL) (86%) experienced complete remissions(1)
- -- Novartis and Penn exclusive global collaboration to develop chimeric antigen receptor (CAR) technology is moving forward with the goal of expanding clinical trials

EAST HANOVER, N.J., Dec. 7, 2013 /PRNewswire/ -- Novartis is highlighting new research from members of the faculty at the University of Pennsylvania's Perelman School of Medicine (Penn) on the investigational chimeric antigen receptor (CAR) therapy, CTL019. Several studies being presented at the American Society of Hematology (ASH) annual meeting add to the scientific understanding of CTL019 in the treatment of acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL) and build on earlier research findings[1,2,3,4].

"These data reflect a significant advance in our understanding of the novel, investigational CAR therapy, CTL019, which shows potential for advancing the treatment of patients with ALL and CLL," said Herve Hoppenot, President, Novartis Oncology. "We are committed, through our collaboration with Penn, to expand the clinical trials of CTL019 to include as many patients as soon as possible."

Highlights of the presentations include findings that 19 of 22 pediatric patients with ALL (86%) experienced complete remissions. The first pediatric patient treated with the protocol remains in remission 20 months later. Five pediatric patients have relapsed, including one whose tests revealed new tumor cells that do not express the CD19 protein targeted by the reprogrammed cells. Additionally, all five of the first adult ALL patients treated to date have experienced complete remissions, the longest of which continues six months after treatment. One adult patient subsequently underwent a bone marrow transplant and remains in remission. Another adult patient relapsed after three months with disease that also tested negative for the CD19 protein (abstract #67)[1].

In studies of adult patients with CLL, 15 of 32 adult patients (47%) responded to the therapy, with seven of those experiencing a complete remission of their disease (abstract #4162 and #873). These results are derived from a completed pilot study of 14 CLL patients (abstract #4162) and results to date of the first 18 patients in a Phase II, dose-optimization trial (abstract #873)[2,3]. Separately, investigators observed in vivo expansion of CTL019 cells in all patients who achieved a complete response. This was followed by contraction and, in all but one patient, ongoing stable persistence of the reprogrammed T cells (abstract #163)[4].

Novartis and Penn have an exclusive global agreement to research, develop and commercialize personalized CAR T cell therapies for the treatment of cancers. Novartis holds the worldwide rights to CARs developed through the collaboration for all cancer indications, including the lead program CTL019 (also known as

CART19). This innovative collaboration has expanded to include multiple CART programs now in discovery and pre-clinical research phases for both hematological cancers and solid tumors.

"This strong collaboration with Novartis, combined with our exciting new research, has brought us closer to making CTL019 available for children and adults who have no other effective treatment options," said Carl H. June, M.D., director of Translational Research and professor of Pathology and Laboratory Medicine in the University of Pennsylvania's Abramson Cancer Center and Perelman School of Medicine. "These CTL019 data at ASH reinforce that CAR therapy has the potential to change the treatment paradigm for those suffering from various types of leukemia."

CTL019 is an investigational, personalized T cell therapy, which was pioneered by Carl June and his team at Penn. In a CTL019 treatment cycle, immune cells (T cells) are drawn from a patient's blood. Then, using CAR technology, the T cells are reprogrammed to "hunt" cancer cells that express specific proteins, called CD19. When the T cells are re-introduced into the patient's blood, the cells proliferate and bind to the targeted cancer cells and destroy them. CD19 is associated with a number of B-cell malignancies including ALL, CLL, diffuse large B-cell lymphoma, follicular lymphoma and mantle cell lymphoma[5,6].

Additional ASH CTL019 Study Details

In a study evaluating CTL019 for the treatment of children and adults with relapsed/refractory ALL (abstract #67), pediatric patients (n=22) received a targeted T cell dose range of 10^7 to 10^8 cells/kg with a transduction efficiency (TE) of 11-45% and adult patients (n=5) received a target dose of $5x10^9$ total cells split over three days with a TE of 6-31%. The study found that 19 of 22 pediatric patients with ALL (86%) experienced complete remissions and all five of the first adult ALL patients treated have thus far experienced complete remissions. There were no infusional toxicities greater than Grade 2, although five patients developed fevers within 24 hours of infusion and did not receive planned subsequent infusions of CTL019 cells[1].

In studies of adult patients with CLL, 15 of 32 adult patients (47%) responded to the therapy, with seven of those experiencing a complete remission of their disease (abstract #4162 and #873). These results are derived from a completed pilot study of 14 CLL patients (abstract #4162) and results to date of the first 18 patients in a Phase II, dose-optimization trial (abstract #873)[2,3]. In the pilot study of CTL019 for the treatment of adult patients (n=14; median age=67) with relapsed/refractory CLL (abstract #4162), the target dose of cells administered to patients was $5x10^9$ mononuclear cells with an expected TE of 10-40% (total CTL019 dose $5x10^8$ – $2x10^9$ total cells)[2]. The Phase II dose optimization study (abstract #873) of two doses of CTL019 cells in patients with relapsed/refractory CLL (n=27; median age=63 years) was conducted to better define an optimal CTL019 cell dose following results from the initial pilot study. In this ongoing trial, patients were randomly assigned to receive either $5x10^8$ vs. $5x10^7$ transduced CTL019 cells. Results thus far from 18 patients in the study are being presented. A preliminary analysis through July 15, 2013 showed that in 10 adult patients, 20% of patients (n=2) achieved a complete response (CR) and 20% a partial response, for an overall response rate of 40% (n=4)[3].

Finally, a separate study (abstract #163) evaluating functional persistence, trafficking and bioactivity of CTL019 cells in patients treated with CTL019 determined that CTL019 holds the potential to effectively target CD19-positive malignancy. In all patients who achieved CR, in vivo expansion of CTL019 cells was observed followed by contraction and in all but one patient, ongoing stable persistence of engineered cells, elimination of tumor B cells and ongoing B cell aplasia in blood and marrow at all evaluated time points (minimum 3 months, maximum ongoing at 35 months)[4].

About CTL019

Because CTL019 is an investigational therapy, 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 uncertainty of clinical trials, there is no guarantee that CTL019 will ever be commercially available anywhere in the world.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as "investigational," "potential," "to develop," "goal," "is highlighting," "being presented," "committed," "are being," "ongoing," or similar terms, or by express or implied discussions regarding potential marketing approvals for CTL019, or regarding potential future revenues from 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 CTL019 will be submitted or approved for sale in any market, or at any particular time. Nor can there be any guarantee that CTL019 will receive regulatory approval or be commercially successful in the future. In particular, management's expectations regarding CTL019 could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected 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 pressures; unexpected 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.

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