PRESS RELEASE

Gracell Announces Progressive Outcomes from Multiple Human Clinical Trials to Investigate FasTCAR and Dual CAR Cell Platform Technologies

- FasTCAR-19 (GC007F) shows a high response rate, with 34 of 35 evaluable r/r B-ALL patients achieving CR on Day 28, where 32 patients achieving MRD negative CR
- Dual CAR-19-22 (GC022) shows sound safety profile and effectiveness, with 15/16 evaluable r/r B-ALL patients achieving MRD-CR on Day 28
- Dual CAR-BCMA-19 (GC012) demonstrates excellent tumor eliminating capabilities in preclinical study aligned with encouraging safety and efficacy data for r/r MM treatment

SUZHOU and SHANGHAI, China, 9 December 2019 -- Gracell Biotechnologies Co., Ltd ("Gracell"), a clinical-stage immune cell therapy company, today announced the progressive clinical outcomes for leading product candidates FasTCAR-19, Dual CAR-19-22, and Dual CAR-BCMA-19 at the American Society of Hematology (ASH) Annual Meeting in Orlando, Florida, held from December 7-10. Multiple pilot studies intend to evaluate the safety and efficacy of Gracell's first-in-class FasTCAR-19 (GC007F), Dual CAR-19-22 (GC012F) and Dual CAR-BCMA-19 (GC022F) cell therapy.

FasTCAR-19

FasTCAR-19 or GC007F uses Gracell's patented FasTCAR^{TM} solution, which genetically modifies a patient's T-cells to express CD19-specific chimeric antigen receptor (CAR) for the treatment of B-cell acute lymphoblastic leukemia (B-ALL).

Utilizing the unique bioprocessing, FasTCAR-19 cells can be produced overnight through viral transfection in use of Gracell's proprietary fully-closed manufacturing system (from apheresis to filling). These cells are considered far more potent and durable in comparison to current market alternatives. To date, all 37 patient samples have been successfully manufactured. The process has been proven efficient, stable and duplicable, with a median 36.8% (range 13.1%-70.3%) transfection success and a median copies of 0.95 (range 0.2-4.21).

As of November, this investigational study enrolled 37 adult and adolescent patients aged from 14 to 70 years, who suffered from r/r B-ALL and had failed to respond to multiple prior lines of therapy, from eight clinical centers. All patients received a single infusion of FasTCAR-19 at one of the three-dose level (low: 0.6*10^5/kg; mid: 1.0*10^5/kg, and high: 1.6*10^5/kg), followed by prior conditioning regimen of fludarabine-cyclophosphamide (FC).

The treatment efficacy was assessed in 35 patients over 28 days of follow-up, of which:

- 34 (97.1%) achieved a complete remission with or without complete blood count recovery (CR/CRi) on Day 28;
- 32 (91.4%) achieved minimum residual disease negative complete remission (MRD-CR);

During the over six month-durable remission period, FasTCAR-19 demonstrated a good level of persistence in line with previous clinical trials. In terms of safety, all 37 patients tolerated the single infusion of FasTCAR-19 at different dose levels, with no dose-limiting toxicities observed. The most common safety concerns were cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) where mild to moderate side effects were observed. Across 30 patients in the low to mid doses group, only 5 (16.7%) manageable Grade 3 CRS and 5 (16.7%) manageable Grade 3 ICANS were reported; while the remaining 23 (76.7%) had Grade 1-2 CRS. The low to mid doses group will likely be selected for extensive study in future clinical trials.

Beyond single-antigen CAR, Dual CAR-T cells can deliver promising clinical outcomes

Single-antigen CAR-T cells have demonstrated considerable efficacy; however, antigen loss and high relapse rate have been observed in a significant number of patients. To combat this, treatments containing two separate CARs and dual transduction (GC022 targeting CD19 and CD22, GC012 targeting BCMA and CD19) were developed. Following positive results from *in vitro* and *in vivo* studies, human clinical trials have commenced testing the safety and feasibility of Dual CAR-19-22 and Dual CAR-BCMA-19 to treat B-ALL and MM, respectively.

Dual CAR-19-22

Dual CAR-19-22 or GC022 has achieved a manufacturing success rate of 20/20, without any patient loss due to manufacturing failure. Enrolled patients aged from 4-45 years old who has B-ALL, received a single infusion of Dual CAR-19-22 at one of the three-dose levels (low: 0.5*10^6/kg; mid: 2.0*10^6/kg, and high: 3.0*10^6/kg), under conventional bioprocessing. The study demonstrated a very good safety profile and high efficacy at mid to high doses.

The treatment efficacy was assessed in 20 patients with a 28-day follow-up, of which:

- 4 in the low dose group reported no response;
- 15 of 16 (93.8%) in mid and high dose groups achieved complete remission, and confirmed with MRD-CR, with or without complete blood count recovery (CR/CRi) on Day 28.

Dual CAR-19-22 proved effective on patients who had previously been treated with CD19 CAR-T cells and/or received allogeneic hematopoietic stem cell transplantation (allo-HSCT) for r/r B-ALL but failed to benefit from prior treatments. Among these five patients, four (80%) patients achieved MRD-CR with a 28-day follow-up. Surpassing the 3-month durable remission period, fifteen patients still retain ongoing response.

Furthermore, Dual CAR-19-22 demonstrated an excellent safety profile, with 6/20 (30%) patients indicating no CRS, 14/20 (70%) reporting Grade 1 CRS. No ICANS events were reported.

Dual CAR-BCMA-19

Dual CAR-BCMA-19 or GC012 has been demonstrated effective in eliminating multiple myeloma (MM) tumor cells both *in vitro* and *in vivo*. The first-in-human study showed a good safety profile and

effectiveness. Beyond, FasTCAR™ has successfully been applied to Dual CAR-BCMA-19, expected to enhance proliferation, potency, and migration in the human body.

“We are delighted to see that patients with relapsed/refractory B-ALL continue to gain substantial clinical benefit from FasTCAR-19. Furthermore, Dual CAR-19-22 with conventional bioprocess can generate promising clinical data. This marks our confidence to utilize FasTCAR technology to both Dual CAR programs for various indications,” said Dr. William Cao, CEO of Gracell. “The results from our latest clinical trials reveal the immense potential of FasTCAR technology, and we are eager to see Gracell’s highly efficacious, yet affordable therapies benefit more patients in China and worldwide.”

About B-ALL

Acute lymphoblastic leukemia (ALL), although rare, is one of the most common forms of cancer in children between the ages of two and five and adults over the age of 50[1]. In 2015, ALL affected around 837,000 people globally and resulted in 110,000 deaths worldwide[2]. It is also the most common cause of cancer and death from cancer among children. ALL is typically treated initially with chemotherapy aimed at bringing about remission. This is then followed by further chemotherapy carried out over several years.

About MM

Multiple myeloma (MM) is a cancer that forms in a type of white blood cell known as a plasma cell. MM cells are abnormal plasma cells (a type of white blood cell) that build up in the bone marrow and form tumors in many bones of the body. Healthy plasma cells make antibodies to help the body fight infection and disease. As the number of MM cells increases, more antibodies are produced. This can cause the blood to thicken and keep the bone marrow from making enough healthy blood cells. MM cells can also damage and weaken the bone. In 2018, MM affected around 160,000 people globally and resulted in 106,000 deaths worldwide[3]. Different types of treatments are available for patients with plasma cell neoplasms. Chemotherapy and targeted therapy are typical treatments; while stem cell transplant, biologic therapy, and radiation therapy, even surgery are also adopted.

About Gracell

Gracell Biotechnologies Co., Ltd. ("Gracell") is a clinical-stage biopharma company, committed to developing highly reliable and affordable cell gene therapies for cancer. Gracell is dedicated to resolving the remaining challenges in CAR-T, such as high production costs, lengthy manufacturing process, lack of off-the-shelf products, and inefficacy against solid tumors. Led by a group of world-class scientists, Gracell is advancing FasTCAR™, TruUCAR™ (off-the-shelf CAR), Dual CAR and Enhanced CAR-T cell therapies for leukemia, lymphoma, myeloma, and solid tumors.

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[1] https://www.cancer.org/cancer/acute-lymphocytic-leukemia/about/key-statistics.html
[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5055577/
[3] https://gco.iarc.fr/today/fact-sheets-cancers