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Podcast: China CEO Interview – Gracell Aims To Enter US CAR-T Sector Through Partnerships, Faster Delivery

Quick Turnaround CAR-Ts

by Brian Yang

With the success of the partnership between J&J and partner Legend, more Chinese cell therapy developers are now looking to enter the US market. But for a complex product like a CAR-T therapy, the journey to the West is not short of challenges. Nasdaq-listed Gracell Bio wants to give it a shot based on quicker delivery and cost-effectiveness advantages.

Founded six years ago, Shanghai-based, US Nasdaq-listed *Gracell Biotechnologies Co. Ltd.* is now aiming to bring its lead asset, the dual-targeting CD19 and B-cell maturation antigen (BCMA) CAR-T cell therapy GC012F for multiple myeloma, to the US market.

Founded with the promise of pushing multiple assets forward, the Chinese company is now keenly focused on this goal, while developing allogenic therapies and investigating Claudin 18.2 antibodies for solid tumors in mainly domestic investigator-initiated studies.

The autologous cell therapy GC012F, having "persistent efficacy and next-generation safety" and being developed for first-line use, will be leading the way for the company to go global, Gracell CEO and founder William Wei Cao told *Scrip* in an exclusive interview on 25 October at the company's office in the Gubei area of Shanghai's Changning district.

CAR-T cell therapies are complex, depending on multiple factors from manufacturing to turnaround time, along with safety and quality, Cao observed. Partly due to these complexities, they are so far indicated mainly for hematological malignancies including B-cell lymphoma/leukemia and multiple myeloma, while studies for solid tumors have stalled.

GC012F is based on the firms's proprietary FastCAR-T platform and now in Phase Ib/II development in the US, and is expected to be “very effective” and “cost-effective for all markets," Cao emphasized.

> *"It can be innovative in China...drug development is more of an engineering job than rocket science." - William Wei Cao, CEO and Founder, Gracell Bio*

Apart from manufacturing issues, cost and affordability play a big role in the consideration of CAR-T therapies, which are routinely priced at more than half a million US dollars outside China.

Within the country, the cost is over CNY1.2m ($164,000) for the two currently approved such therapies, Breyanzi (lisocabtagene maraleucel) from *JW Therapeutics Co., Ltd*, a joint venture between *Juno Therapeutics Inc.* and *WuXi AppTec*, and Yescarta (axicabtagene ciloleucel) from *Fosun Kite Biotechnology Co Ltd*, a JV between *Shanghai Fosun Pharmaceutical (Group) Co., Ltd.* and *Kite Pharma, Inc.*

Quicker Delivery Times

Cao said the company hopes GC012F will be able to cut lengthy turnaround times for CAR-Ts to make it easier for US physicians to prescribe.

Such therapies require deriving, engineering and re-infusing a patient’s white blood cells, a process that can routinely take weeks. The median time is 71 days or two months, during which bridging anticancer therapies must be used. A faster process would help to convince physicians willing to use cell therapies earlier but who want to avoid the lengthy process, suggested Cao.

“It is not so much about costs and side-effects, but faster delivery,” stressed the executive, saying that such times could be shortened to around 12 days. (Also see "*Gracell Revs FasTCar To Catch Big Pharma Rivals In Myeloma*" - Scrip, 14 Jun, 2023.)

Noting Gracell was among the first to publish data, Cao said other leading CAR-T developers globally, including *Novartis AG* and *Bristol Myers Squibb Company*, are also working on faster delivery times. The two firms were pioneers in the field through Kymriah (tisagenlecleucel) and Abecma (idecabtagene vicleucel; developed with *bluebird bio*), respectively.

'Let The Market Speak'

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Asked about the prospects for US approval of a second cell therapy from China after *Legend Biotech Corp.* and partner *Johnson & Johnson*'s Carvykti (ciltalcabtagene autolecel), the executive said the market ultimately will decide.

He noted the efficacy and safety data so far for GC012F are "very competitive." Its dose is also 10 times lower than currently available therapies for multiple myeloma and Cao believes the full set of data should be enough to convince regulators.

Key Takeaways:

- Gracell hopes competitive clinical data, quicker process turnaround, faster delivery and cost-effectiveness will facilitate US market entry
- China can lead cell therapy innovation due to strength in engineering, CEO believes
- Partnerships eyed with MNCs for cell therapy to allow internal focus on autoimmune and lupus trials

While he wouldn't disclose details, the CEO said from gene vectors to manufacturing to scalability, cell therapy development is transforming fast in China. "It can be innovative in China," noted the executive, adding "drug development is more of an engineering job than rocket science."

Cost-effectiveness may be another differentiating factor and Gracell's asset will be the "lowest possible cost" due to automation during the preparation process. Despite the multiple CAR-Ts already in the US more coming in China from domestic developers such as *Innovent Biologics, Inc.* and partner *IASO Biotherapeutics*, the overall market is not yet too crowded, Cao believes.

While not working in NK cell therapies, Gracell is also pushing forward with allogenic cell therapy approaches, along with a combination therapy targeting Claudin 18.2.

First-Line Data At ASH

Entering the cell therapy scene as a latecomer, Cao said his company is effectively "jumping the line" for GC102F in multiple myeloma, studying it in newly diagnosed patients rather than in later-line treatment.

"Encouraging" data will be presented at the American Society of Hematology (ASH) meeting in December, noted the CEO. Updated findings released on 2 November from a Phase I open label, single arm study, show early use in newly diagnosed patients with high-risk multiple myeloma achieved an overall response rate (ORR) of 100% and stringent complete response (sCR) rate of 95.5%, based on all treated patients (100%) across all dose levels.

Only six patients (27%) experienced low-grade cytokine release syndrome (CRS); no treatment-

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related Grade 3 CRS, nor ICANS of any grade or deaths, occurred in the study. The results are prompting others to look at early-line treatment, Cao noted.

GRACELL BIO CEO AND FOUNDER WILLIAM WEI CAO *Source: Courtesy Gracell Bio*

Partnering Strategy

To realize Gracell's strategic goals, it will need to execute its US plan and enter into clinical partnerships. Currently, the Chinese company is looking for multinationals that can complement its assets with their pipelines and with an oncology or cell therapy focus.

"Cell therapy offers a potential cure and there are already over four years of survival data for such therapies to treat myeloma. That has seen increasing interest from multinationals in cell therapies," Cao noted.

A partnership would allow the company to give more focus internally to another of its target areas, autoimmune conditions such as systematic lupus, for which preclinical investigator-initiated studies are underway and IND filing and clearance times in China and the US would be shorter.

> *"Cell therapy offers a potential cure...that has seen increasing interest from multinationals" - Gracell Bio CEO William Wei Cao*

Expansion In US

Multiple Chinese oncology drug developers have made leaps forward in the US market in recent years, starting from *BeiGene, Ltd.* and Nanjing Legend.

Beigene's BTK inhibitor Brukinsa (zanubrutinib) became the first cancer drug from China to be commercialized in the US market, while Legend's BCMA-targeting CAR-T for multiple myeloma became one of the six CAR-T therapies currently marketed in the US.

Inside China, Innovent and Iaso's Fucaso (equecabtagene autoleucel) in July gained a new drug

approval from the National Medical Products Administration for relapsed/refractory multiple myeloma, marking the first nod for a fully domestically developed CAR-T. The therapy also has US regenerative advanced treatment and fast track status.

For Gracell, the goal is to quickly expand its US footprint. When asked what the key factors are for a Chinese biotech to successfully expand overseas, Cao pointed to a strong team stationed locally and an "in China for global" R&D approach, which also provide confidence to US investors. Being patient and good governance are other must-haves, he said.

Meanwhile, with multiple biotechs in China facing ongoing capital raising challenges, they must be smart by conserving cash, prioritizing key products and delivering value in the later development stages, rather than selling short at an early stage, Cao noted.

Audio interview timestamps:

00-0005: cell therapy complexities

0006-0010: first published data on quick turnaround CAR-Ts

0011-0015: scalability, importance of engineering in cell therapy development

0016-0020: allogenic CAR-T development

0021-0025: combination of CAR-Ts with antibodies

0026-0030: jumping the line to newly diagnosed patients

0031-0035: partnerships with MNCs

0036-0040: getting into autoimmune indications

0041-0045: expanding in US and going global

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