DEVELOPMENT OF MODERN BIOLOGICS AND CELL THERAPY PRODUCTS THROUGH GLOBAL CDMOs

Vadim Klyushnichenko
Calibr at Scripps Research, La Jolla CA 92037, USA

The majority of innovative ideas and disruptive technologies are nucleated at academic and educational institutions. However, these organizations have limited budgets and lack the process development and manufacturing infrastructure, particularly if their advanced products belong to different technological platforms. This gap can be closed by contract development and manufacturing organizations (CDMOs), which remain crucial to new drug process development, manufacturing and commercialization.

Calibr at Scripps Research is a translational research institution developed to bring innovative research ideas from bench to clinic. The project portfolio of Calibr includes traditional synthetic small molecules, nucleosides, modified conjugated peptides, proteins, engineered monoclonal antibodies, vaccines, as well as cell and gene therapy products [1-3]. Our chemistry manufacturing and control (CMC) team works with multiple CDMOs located in the US, EU, India and China developing clinical drug candidates.

Some of Calibr's programs like switchable chimeric antigen receptor T-cells (sCAR-T) present the new paradigm in biopharmaceutical manufacturing. This type of controllable cell therapy presents higher persistency, memory, control, efficacy, and safety, while providing lower manufacturing cost compared to traditional CAR-T technology (Fig.1).

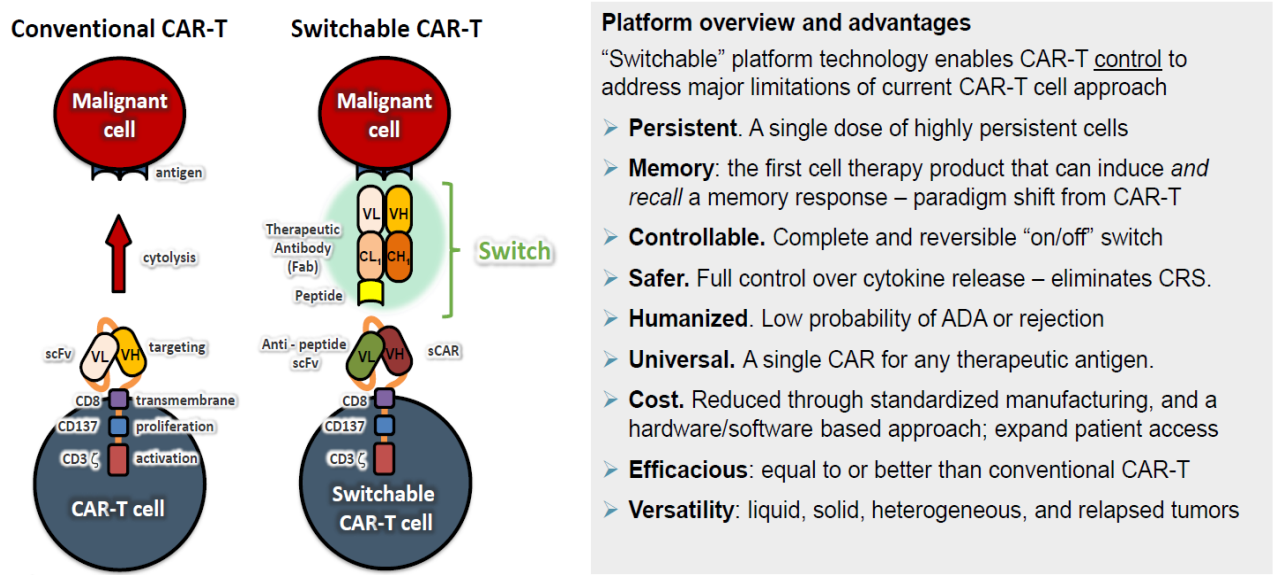

Fig. 1. Switchable CAR-T cell target platform

The first sCAR-T cell product developed at Calibr is currently undergoing clinical trials in the immuno-oncology field. The CMC programs required the involvement of five different CDMOs located in different parts of the world due to the unique nature of product components, CDMO expertise and cost (Fig.2).

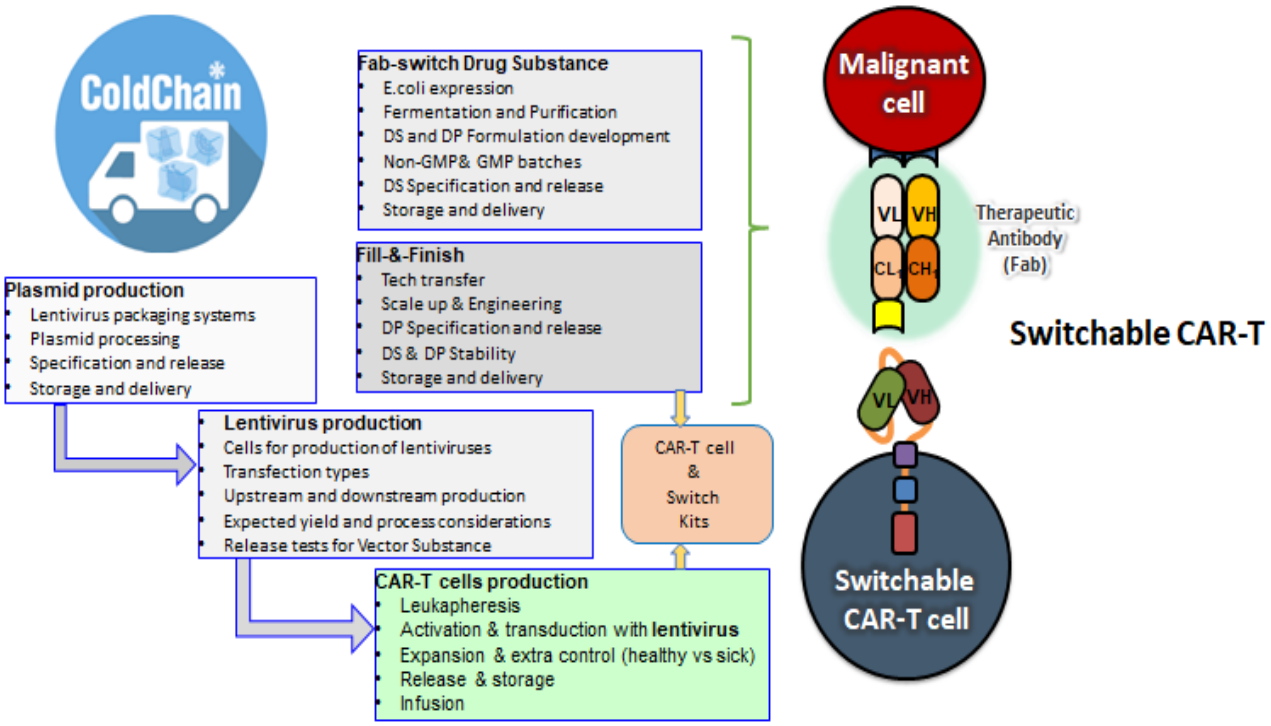

Fig.2. Process Development and GMP manufacturing of sCAR-T cell at five CDMOs

The CDMO selection process includes business documentation, GMP/Quality due diligence process, CDMO structure analysis, communication, technical expertise, as well as establishing the project timeline, and budget (Fig.3).

The scoring of following criteria from one to five units were used for the selection of CDMOs: technical capabilities, quality system, proposed project timeline, facility availability, project price, communication, history of prior collaboration. As the results five primary and several secondary companies the US, EU and China were selected based on the combined scoring. We have developed the analytical system for each of in-process tests, intermediate materials, reference standard, release of final drug substance and formulated drug product, as well as for the stability, comparability, and compatibility studies. The analytical data were used for the development of specifications and certificates of analyses based on the quality attributes required by the US Food and Drug Administration (FDA): appearance, identity, strength, purity/impurities, and safety.

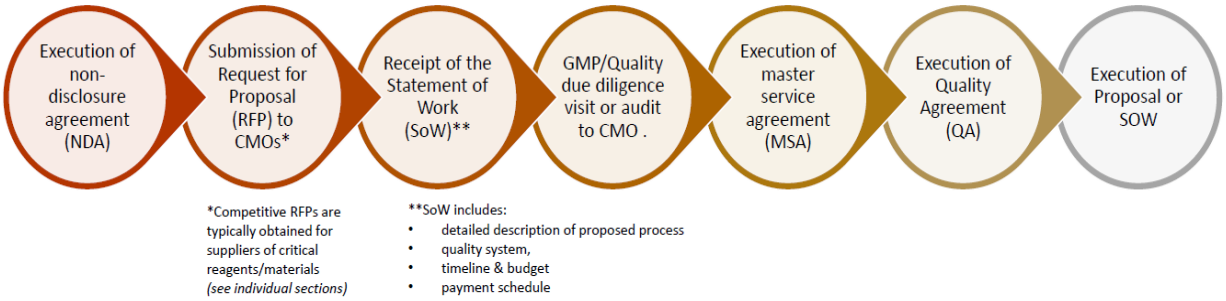

Fig.3. Business documentation and GMP/Quality due diligence activities required for the CDMO selection process

As a result, the sCAR-T cell product was manufactured and tested in Phase I clinical trials designed for patients with relapsed refractory leukemia and resulted in the high level of recovery even at late stages of the disease. This principle is currently used for the development of sCAR-T cell platform for the treatment of other oncological and autoimmune diseases.

References:

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