Briefing on Cell and Gene Therapy Innovation Center of Tsinghua Industrial Technology Research Institute

In the past half year, Cell and Gene Therapy Innovation Center of Tsinghua Industrial Technology Research Institute (hereinafter referred to as the innovation center) has relied on the coordination and support of Tsinghua Industrial Technology Research Institute in terms of capital, engineering, and technical resources, as well as its first-class talent reserve and technical advantages, to build a complete industry development chain in the cell and gene therapy field. Taking the advantage of its multi-disciplinary and industry-leading technical resources, the innovation center has achieved platform-based development and multiple fundamental breakthroughs in underlying technologies. Besides, the center also has introduced and participated in international advanced innovation projects in the cell and gene therapy field, to incubate highly competitive high-tech innovative enterprises in the cell and gene therapy field and provide end-to-end production and technical services for more and more those enterprises. The following describes the recent development progress and technical achievements of the innovation center from three aspects: engineering construction, production technology breakthrough, and industry chain support and incubation.

In terms of engineering construction, more than CNY100 million has been invested by the center in Building 1, the medical science and technology center of Zhongguancun Life Science Park. It has completed the construction of a cell and gene therapy R&D and pilot test platform and a level-B clean environment cell therapy R&D and production lab that both comply with the China's NMPA standards, US FDA standards, and EU EMA standards, covering key technology research, core process development, and trial production. Having worked with Beijing Drug Inspection Research Institute, the center completed the verification and acceptance of most facilities and equipment. The facilities can provide CDMO production services such as DNA/mRNA, multiple virus vectors, cell therapy products, and enzyme preparations for the cell and gene therapy industry chain. Breakthroughs have been made in the construction of the designed automatic clean logistics system designed. The design prototype of the AGV automatic carrier has entered the scenario commissioning phase. Also, the full-coverage 5G network in the clean environment has been deployed, and equipment networking is in progress. To achieve advanced, efficient, and intelligent smart manufacturing, the innovation center invested capital and manpower to preliminarily build the data and algorithm platform, material innovation platform, device innovation platform, and smart factory system. The factory informatization system architecture has been built, the theoretical design phase of the high-throughput formula screening platform and automatic quality detection platform has been completed, and the hardware and software platform deployment phase will be entered recently.

In terms of production technology breakthroughs, the innovation center has built a complete industry development chain in the cell and gene therapy field based on the first-class discipline strength, talent, and technical advantages of Tsinghua University, related universities, and top research institutes, and supported a number of innovative drug R&D projects, including mRNA COVID-19 enhanced vaccine, mRNA drug trial for rare diseases, iPSC stem cell innovative drug R&D and clinical transformation projects. Breakthroughs have been made in the industrial production field of virus vectors and mRNA. The general platform technology for the suspension culture system of adenoviruses and adenoviruses related virus vectors has been formed, with the purification yield being continuously improved. At the same time, the development and identification of absolute quantitative methods for viruses based on imaging have entered the stage of patent application. For the synthesis of mRNA primary liquid, the Innovation Center creatively proposed the concept of "enzyme-free" environment and adopted a series of technical means to achieve a clean environment of "sterile & enzyme-free" throughout the production process of mRNA primary liquid, to ensure reliable quality of mRNA raw liquid. In the in vitro transcription phase of mRNA, the excellent supply chain system and high-throughput screening system of the innovation center are used to quickly determine the optimal feeding ratio for different sequences, greatly improving the IVT production efficiency while effectively reducing the production cost. Based on the preceding technical breakthroughs, the annual output mRNA of the innovation platform can reach 1 to 1.5 kg. Recently, the innovation platform has successfully delivered mRNA raw fluid in the 2g GMP environment for clinical declaration and clinical research.

In terms of industry chain support and incubation, the innovation center has incorporated and coordinated top R&D enterprises and technical teams in the industry in the form of incubation, share participation, and strategic collaboration based on open, cutting-edge, and large-scale production scenarios. It has worked with a batch of innovative enterprises, including data algorithms, engineering construction, production process development, production raw materials, and key enzymes, to achieve advanced, efficient, and stable supply and fast technology recursion at the supply chain end, and preliminarily built a production support system and all-round production solutions for the entire industry chain. Meanwhile, the center has incubated several high-tech innovative enterprises in the entire industry chain to enhance the innovation ecosystem.