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Pfizer Bets On Gene Therapy For Rare Diseases In China

by Brian Yang

After excluding China from its early development plans for domagrozumab, Pfizer's rare disease R&D team is now gearing to commence a clinical study of the investigational compound on Duchenne muscular dystrophy patients soon.

Despite its potentially large patient pool, China was not initially included in the development plan for PF-06252616 (domagrozumab), a monoclonal antibody that blocks muscular growth inhibiting protein myostatin, when the rare disease team of *Pfizer Inc.* sat down to plan the study for the investigational compound.

Pfizer's initial plan was to conduct an assessment for the therapy to treat Becker muscular dystrophy (BMD), a milder type of the two muscular dystrophies that includes Duchenne muscular dystrophy (DMD).

The team had expected the patient recruitment process, with a little over 100 patients in enrollment to be a quick process. However, it took the company two and half years to complete.

Pfizer's project head who came to China this September wished they had included China as part of the development plan earlier, disclosed Sun Feifei, researcher at Pfizer China R&D Center, located in Shanghai.

Since 2014, the New York-based drug maker has divided its business into innovative medicines and established products, and prioritized rare disease treatment as one area of focus for its innovative drug development activities. These include rare diseases such as hematology disorders, neuromuscular diseases, idiopathic pulmonary fibrosis and metabolic conditions, Sun told attendees at the 5th DMD Patients and Physicians Exchange Forum, held Nov. 11-12 in Beijing.

Pfizer hopes to leverage its large cash reserve to gain access to innovative new therapies, improve the current treatment, control and maintain conditions, and eventually provide a cure.

One of small biotechs Pfizer acquired is *Bamboo Therapeutics Inc.* Based in Research Triangle, NC, Bamboo uses its core recombinant adeno-associated virus (rAAV) technology to develop gene therapies for rare diseases such as DMD. With over $600m investment, Pfizer also acquired Bamboo's cell manufacturing facility.

DMD Studies In China

DMD is a progressive disease that impacts the whole body and primarily affects boys. The incidence rate is roughly one in 5,000 newborn boys, putting the total patient population at 60,000 to 100,000.

Pfizer's most advanced investigational compound is domagrozumab (PF-06252616), a myostatin inhibitor that is under Phase II clinical study. The multi-regional clinical trial is being studied in 28 centers across the US and in Canada, Japan and the UK.

The anti-GDF8 treatment, is being studied on 6-16 year-old DMD patients. The 96-week study is divided into four stages, and the first stage will be complete in early 2018. The investigative study is not gene-specific so DMD patients with any mutations can participate.

Preparing to start its first clinical study in China for the gene therapy, Sun said Pfizer wants to understand the disease better, and seek collaboration with patients.

DMD is still new in China, and a complete disease history study is lacking. Pfizer expects to start a natural history study soon in collaboration with patients and advocacy groups.

The study will be cross-disciplinary as DMD impacts the nerve system, orthopedics, cardiovascular and rehabilitation. The goal is to start the clinical study in China soon, Sun added.

"Now we are progressing on all three fronts: AAV source study, expansion of manufacturing capability and regulatory filing," said Sun.

"We hope to enter into clinical study soon."

Other promising gene therapies using rAAV as a carrier to deliver transgenic dystrophins to target are also on the horizon. Pfizer's other gene therapy, PF-06939926, using mini-dystrophin for DMD, will enter clinical stage by the year-end, ahead of the planned early 2018 timeline.

The Phase 1/2 study will enroll six patients for each group, and patients will go through one treatment and each patient will get treated every three months, with follow-up visits for four

years, said Sun.

Study Plans And Uncertainties

Responding to questions from parents of DMD patients, Sun said the enrollment of Chinese patients in the domagrozumab study could start as early as 2019.

But she also listed several uncertainties including areas like intellectual property, legal, safety and efficacy, and the investment environment.

China has prioritized rare diseases as an area for policy incentives such as clinical trial waiver/reduction, and the China FDA has recently allowed foreign study data to be used towards a new drug approval in the country. Additionally, quicker patient enrollment could provide benefits to international drug makers eyeing an entry.

Several companies including *PTC Therapeutics Inc.* are also working with patients and physicians and preparing to start clinical studies for their innovative therapies in the coming year (Also see "*PTC Readies China Plan Amid US FDA Translarna Setback*" - Pink Sheet, 13 Nov, 2017.).

For the time being, though, Pfizer is focusing on the disease natural history study, and priming for the clinical study. DMD remains largely unknown in China, and few physicians are familiar with standard care. It remains unclear whether top hospitals in the country such as the Beijing Union Hospital are ready for the gene therapy study.

From the editors of PharmAsia News