GENES AND TEHRAPY – 18th August 2021

FDA lifts two-year-long hold on Novartis' OAV-101 clinical trials for spinal muscular atrophy

Novartis, on 3rd August, announced that the US FDA has lifted its two-year-long temporary hold on the company's OAV-101 intrathecal (IT) clinical program. The trials had been suspended because of an inflammatory response observed in a small animal study. *B*ased on data from nonclinical toxicology study, the new Phase 3 STEER study will evaluate efficacy, safety, and tolerability of OAV-101 IT (Zolgensma®) in treatment-naïve patients with spinal muscular atrophy (SMA) Type 2 aged between 2 and 18 years old, the first to study gene therapy in this patient population. SMA is a rare, genetic neuromuscular disease caused by a lack of a functional *SMN1* gene. Zolgensma® is a one-time, single-dose, treatment option for older patients with SMA.

Trial to test stem cell therapy for heart disease in babies

A multi-center randomized trial, known as the Autologous Cardiac Stem Cell Injection in Patients with Hypoplastic Left Heart Syndrome (CHILD), will compare outcomes between babies with heart condition who receive stem cell therapy and those who don't. The trial specifically includes children with hypoplastic left heart syndrome, a defect in which the heart's left ventricle is underdeveloped and can't effectively pump blood to the body. It is one of the most complex and common forms of congenital heart disease. Tissue will be extracted from heart muscle of babies for stem cell isolation and expansion. The stem cells will them be injected into infants' hearts and followed up for at least a year with blood tests, echocardiograms and MRIs to reinforce safety and efficacy.

FDA lifts clinical hold on Rocket Pharmaceuticals' Danon Disease Trial of RP-A501

FDA had put Rocket Pharmaceuticals' gene therapy trial RP-A501 on hold in May of 2021 to modify the study protocol and other supporting documents with revised guidelines for patient selection and safety management. On 16th August, the company announced that FDA had lifted the hold following submission of required documents allowing patient enrollment to resume. RP-A501 is an investigational gene therapy product with a functional *LAMP2B* transgene in an AAV9 capsid. It is potentially the first gene therapy for monogenic heart failure. Danon Disease is a rare X-linked inherited disorder caused by mutations in the gene encoding lysosome-associated membrane protein 2 (LAMP-2), an important mediator of autophagy.

FDA halts bluebird bio's ALD-104 gene therapy over cancer risk

On 9th August, the FDA put a hold on bluebird bio's Phase 3 ALD-104 study. This is after a participant in the study developed a bone marrow disorder that can lead to leukemia. The company received a reported Suspected Unexpected Serious Adverse Reaction (SUSAR) of myelodysplastic syndrome (MDS) that is likely mediated by Lenti-D lentiviral vector insertion. The patient was treated with

elivaldogene autotemcel (eli-cel, Lenti-D™) gene therapy (licensed as SKYSONA™ in Europe) for cerebral adrenoleukodystrophy (CALD). Following hardships over gene therapy, the company is also shutting down business in Europe.

Sarepta Therapeutics adds limb-girdle muscular dystrophy type 2A gene therapy to its pipeline

On 4th August, Sarepta Therapeutics announced that it is taking onboard an experimental gene therapy developed by scientists at Nationwide Children's Hospital in Ohio. The gene therapy candidate, calpain 3 (CAPN-3) will be the target for treating the most common type of muscular dystrophy namely, limb-girdle muscular dystrophy type 2A (LGMD2A). CAPN-3 is the most commonly mutated gene in LGMD2A. The LGMD2A program uses the AAVrh74 vector, designed to systematically and robustly deliver treatment to skeletal muscle, including the diaphragm, making it an ideal candidate to treat muscle disease.

HEALIOS K.K. completes patient enrollment for MultiStem® cell therapy treatment for ischemic stroke

Athersys, Inc. announced on 10th August that its partner, HEALIOS K.K. has completed enrollment in its TREASURE study in Japan, evaluating MultiStem® (invimestrocel) cell therapy treatment in patients who have suffered an ischemic stroke. The TREASURE study is a placebo-controlled, double-blind, phase 2/3 trial designed to confirm the efficacy and safety of MultiStem (HLCM051) in treating patients with ischemic stroke. Invimestrocel is a patented regenerative medicine product candidate in clinical development that has shown the ability to promote tissue repair and healing in a variety of ways, such as through the production of therapeutic factors in response to signals of inflammation and tissue damage.