SECOND HALF FEBRUARY 2023

ADVANCED THERAPIES CLINICAL & COMMERCIAL NEWS

REACH OUT TO BRYAN KENNEDY AT BK@PROJECTEVOLUTION.ORG WITH ANY QUESTIONS

- 02.28.23 - Sarepta's DMD gene therapy inches closer to market as FDA declines to hold advisory meeting (fiercebiotech)
  - The FDA won't be holding an advisory panel meeting for Sarepta Therapeutics' SRP-9001, which is now that much closer to becoming the first gene therapy for Duchenne muscular dystrophy (DMD). In November, the FDA accepted Sarepta's biologics license application seeking accelerated approval for SRP-9001. The agency has now set May 29 as the expected decision date. A midcycle review related to the process has already occurred, Ingram said, and the FDA did not flag any significant safety issues associated with SRP-9001. The gene therapy is designed to deliver the microdystrophin-encoding gene into muscle tissue to prompt production of the microdystrophin protein. Patients with DMD have a mutation in the DMD gene and can't make the protein on their own, leading to a progressive loss of muscle strength. During the midcycle review, the FDA said it would not require an advisory committee, which is used to provide the agency with independent recommendations for drug products about to enter the market. Beyond that, Ingram said he doesn't have any additional color to provide as questions started pouring in on the earnings Q&A about the regulatory activity.
- 02.28.23 - TransCode Therapeutics, an RNA Oncology Company Announces Orphan Drug Designation Status for TTX-MC138 for Treatment of Pancreatic Cancer (PR)
  - TransCode Therapeutics recently received approval for a first-in-human clinical trial with TTX-MC138 in patients with advanced solid cancers. In this clinical trial, up to 12 patients will be given a single dose of radiolabeled TTX-MC138 followed by noninvasive positron emission tomography-magnetic resonance imaging (PET-MRI). The trial is intended to quantify the amount of TTX-MC138 delivered to metastatic lesions and the pharmacokinetics of the therapeutic candidate in cancer patients. The trial could yield critical data regarding therapeutic dose, timing, and potential safety that could inform later stage clinical trials and further advance TTX-MC138 as a therapeutic candidate against pancreatic cancer and other advanced malignancies. This trial is not intended to demonstrate any therapeutic effect.
- 02.28.23 - Arrowhead Announces Interim Results from Ongoing Phase 1/2 Study of ARO-C3 for Treatment of Complement Mediated Diseases (PR)
  - Arrowhead Pharmaceuticals develops medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep, and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Arrowhead's RNAi-based therapeutics leverage this natural pathway of gene silencing.AROC3-1001 (NCT05083364) is a Phase 1/2, placebo controlled, dose-escalating study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of ARO-C3 in up to 42 adult healthy volunteers (Part 1), and up to 42 adult patients with paroxysmal nocturnal hemoglobinuria (PNH) or with complement-mediated renal disease (Part 2).
- 02.27.23 - OTL-201 gene therapy leads to cognitive gains in Phase 1/2 trial (sanfilipponnews)
  - 'These early results are very encouraging — but there's still a long way to go'. Four out of the five children with Sanfilippo syndrome type A in a Phase 1/2 clinical trial have continued to gain cognitive skills — which in three were similar to healthy children — after being given OTL-201, an experimental gene therapy being developed by Orchard Therapeutics. The children were 6-24 months when they were treated and have been followed up for a median of two years, ranging from nine to 30 months. Researchers are cautious about the findings, however, as most children aren't yet 4-5 years old, which is when the disease usually begins to worsen more rapidly. Follow-up will continue for up to 36 months (three years), with more data becoming available in future reports.
- 02.23.23 - Nektar Therapeutics Announces Phase 2 Topline Data for Rezpegaldesleukin in Patients with Systemic Lupus Erythematosus (PR)
  - REZPEG is an investigational, potential first-in-class selective regulatory T-cell inducing IL-2 conjugate designed to treat select autoimmune diseases. The Phase 2 ISLAND study (NCT04433585) enrolled 291 adults with moderate-to-severe SLE. The study consisted of three arms evaluating rezpegaldesleukin administered subcutaneously at different doses (low-dose of 300mcg Q2W, mid-dose of 900mcg Q2W, high-dose of 1800mcg Q2W) compared to placebo. The primary endpoint of the study was a 4-point reduction in the SLEDAI-2K score in pre-defined study populations. Although the mid-dose level demonstrated a numeric improvement in SLEDAI-2K score as compared to placebo (with a placebo-adjusted response of 8.8% for the modified intent-to-treat (mITT) population [p=0.309] and 13.9% for the per protocol population [p=0.06]), the primary endpoint was not met. The placebo-adjusted responses for the low- and high-doses were less than those of the mid-dose for both populations.
- 02.23.23 - Astellas Presents Update on Recently Cleared Pompe Gene Therapy Trial (biospace)
  - After overcoming a clinical hold, Astellas presented preliminary safety and efficacy data from the Phase I/II FORTIS trial of AT845 in late-onset Pompe disease (LOPD) at the 19th Annual WORLDSymposium 2023. Today, a diagnosis of Pompe disease ties people to twice-monthly infusions of enzyme replacement therapy (ERT). Astellas is trying to change that with AT845, a gene therapy that would serve as a one-time treatment for patients with LOPD. As of September 15, 2022, four participants were treated with a one-time intravenous infusion of AT845. Two patients received 3x1013 vg/kg dose, while two were dosed at 6x1013 vg/kg. At the data cut-off, three of the four participants were free of those ties to ERT. These individuals have shown continued stability in functional endpoints, including forced vital capacity and the 6-minute walk test, while off ERT for 19, 44 and 51 weeks, respectively.
- 02.22.23 - Sangamo Therapeutics Announces Evidence of Clinical Benefit in Phase 1/2 STAAR Study in Fabry Disease (PR)
  - Sustained, elevated expression of alpha-galactosidase A (α-Gal A) activity observed in 13 patients for over two years for the longest treated patient as of cutoff date.Achieved 78% globotriaosylceramide (Gb3) substrate clearance at 6-months and 77% reduction in urine podocyte loss in one of the first kidney biopsies. All dose escalation patients had been withdrawn from enzyme replacement therapy (ERT) and remain off ERT today. Reported a clinically meaningful and statistically significant increase in mean general health scores, as measured by the SF-36 General Health survey. Since the cutoff date, four additional patients have been dosed in the expansion phase, and a further two patients have been withdrawn from ERT. The Phase 1/2 STAAR study expansion phase is ongoing and preparations for a potential Phase 3 trial actively progress, with a trial start anticipated by the end of 2023.

- 02.22.23 - Immunocore announces initial Phase 1 safety and pharmacodynamic activity data with first soluble TCR therapy for people living with HIV (PR)
  - Data from the single ascending dose part of the Phase 1 trial shows IMC-M113V is well tolerated. Expected markers of T cell activation observed in half of participants at 15-mcg dose; plasma viral load remained suppressed throughout dosing and follow-up. The multiple ascending dose part of the trial is enrolling participants to identify safety and anti-viral activity
- 02.21.23 - Third patient free of HIV after receiving virus-resistant cells (nature)
  - A 53-year-old man in Germany has become at least the third person with HIV to be declared clear of the virus after a procedure that replaced his bone marrow cells with HIV-resistant stem cells from a donor. For years, antiretroviral therapy (ART) has been given to people with HIV with the aim of lowering the virus to almost undetectable levels and preventing it from being transmitted to other people. But the immune system keeps the virus locked up in reservoirs in the body, and if an individual stops taking ART, the virus can begin replicating and spreading. A true cure would eliminate this reservoir, and this is what seems to have happened for the latest patient, whose name has not been released. The man, who is being referred to as the 'Düsseldorf patient', stopped taking ART in 2018 and has remained HIV-free since. The stem-cell technique involved was first used to treat Timothy Ray Brown, often referred to as the Berlin patient. In 2007, he had a bone marrow transplant, in which those cells were destroyed and replaced with stem cells from a healthy donor, to treat acute myeloid leukaemia. After the procedure, Brown was able to stop taking ART and remained HIV-free until his death in 2020.
- 02.20.23 - First Gene Therapy for Hemophilia B, CSL's HEMGENIX®, Approved by the European Commission (PR)
  - The European Commission's decision follows the CHMP's positive opinion in December 2022, based on findings from the pivotal HOPE-B trial, the largest gene therapy trial in hemophilia B to date.4,5 These findings showed that hemophilia B patients treated with HEMGENIX® demonstrated stable and durable increases in mean Factor IX activity levels (with a mean Factor IX activity of 36.9%) which led to an adjusted annualized bleed rate (ABR) reduction of 64%.1 Following infusion of HEMGENIX®, 96% of patients discontinued routine Factor IX prophylaxis and mean Factor IX consumption was reduced by 97% at 18 months post-treatment, compared to the lead-in period.The multi-year clinical development of HEMGENIX® was led by uniQure (Nasdaq: QURE) and sponsorship of the clinical trials transitioned to CSL after it licensed global rights to commercialize the treatment. In the United Kingdom, The Medicines and Healthcare products Regulatory Agency (MHRA) is currently reviewing CSL's submission for HEMGENIX®. HEMGENIX® was approved by the U.S. Food and Drug Administration in November 2022.
- 02.19.23 - Travere Snags Accelerated Approval for First Non-Immunosuppressive IgAN Therapy (geneonline)
  - After over a decade of development, Travere Therapeutics, formerly known as Retrophin, announced that the FDA approved its non-immunosuppressive IgAN therapy, Filspari, as the first of its kind under the accelerated approval program. Under its current approval status, the FDA recognized that the drug decreases proteinuria (protein in the urine), but the company plans to submit data at the end of the year demonstrating the drug's ability to slow kidney disease.
- 02.17.23 - Sarepta Therapeutics Announces Initiation of VOYAGENE, a Clinical Study of SRP-9003 for the Treatment of Limb-Girdle Muscular Dystrophy Type 2E/R4 (PR)
  - SRP-9003 (bidridistrogene xeboparvovec) is an investigational gene therapy that uses the AAVrh74 vector, which is designed to be systemically and robustly delivered to skeletal, diaphragm and cardiac muscle, making it an ideal candidate to treat peripheral neuromuscular diseases. SRP-9003 also uses the MHCK7 promoter, chosen for its ability to robustly express in the heart, which is critically important for patients with limb-girdle muscular dystrophy Type 2E (LGMD2E), also known as beta-sarcoglycanopathy and LGMDR4, many of whom die from pulmonary or cardiac complications.
- 02.17.23 - Biosyngen has obtained FDA IND clearance of BRG01 for Phase I/II clinical trials against Nasopharyngeal Cancer (PR)
  - Prior to this approval from the US FDA, Biosyngen's BRG01 was granted IND by China CDE on December 14th, 2022. In addition, China CDE has acknowledged the company's IND submission for another indication, targeting EBV+ Lymphoma. Following this milestone, other products in Biosyngen's portfolio are projected to enter IIT/Phase I in 2023, across Singapore, China and the US. The indications targeted are hepatocellular cancer, colorectal cancer, gastric cancer, esophageal cancer and pancreatic cancer. Biosyngen is founded in Singapore with an ambition to be a global leader in cell and gene therapy, to address unmet needs and bring superior treatment to patients.
- 02.16.23 - Orca Bio Presents Positive Data Reinforcing Clinical Profile of Orca-T and Orca-Q at 2023 Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR (PR)
  - Orca Bio, a late-stage biotechnology company developing high-precision cell therapies for the treatment of cancer, genetic blood disorders and autoimmune diseases, today announced data from the company's investigational high-precision cell therapy programs. Positive data on Orca-T was presented from the single-center Phase 2 and multi-center Phase 1b trials of patients with acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), myelodysplastic syndromes (MDS) and other hematological malignancies. Outcomes with Orca-T appeared to be further enhanced in patients who received a conditioning regimen of busulfan, fludarabine and thiotepa (BFT). At 12 months, the 71 patients in the Orca-T BFT subgroup reported no non-relapse mortality (0%), and high rates of relapse-free survival (87%), graft-versus-host disease-free, relapse-free survival (GRFS) (81%) and overall survival (94%).