We don't follow footsteps. We create the path.

Company Overview*

Spark Therapeutics, a fully integrated company, strives to challenge the inevitability of genetic disease by working to discover, develop and deliver gene therapies that address inherited retinal diseases (IRDs), neurodegenerative diseases, as well as diseases that can be addressed by targeting the liver. We aim to reawaken healthy biologic processes through the potential one-time administration of gene therapies, and **spark** a transformation for people affected by rare genetic diseases where no, or only palliative, therapies exist.

Our approach to gene therapy is to treat an inherited disease at its root by augmenting, replacing or suppressing the function of a mutated gene. We engineer gene therapy vectors using a cutting-edge, proprietary adeno-associated viral (AAV) vector platform, developed through vigorous preclinical testing and evaluated in several clinical trials.

Spark Therapeutics was founded in March 2013 as a result of the technology and know-how developed at Children's Hospital of Philadelphia (CHOP). Members of our scientific team have been at the forefront of gene therapy research for more than two decades. They are responsible for numerous development milestones, including the first clinical trials of AAV vectors in skeletal muscle tissue and the liver, the first clinical studies to evaluate AAV administration to the second eye, and the first gene therapy trial for a non-lethal disorder that included pediatric participants.

The Spark Therapeutics team includes more than 200 industry professionals with deep experience in research and development activities, manufacturing and commercializing complex and novel biotechnology products. We are headquartered in Philadelphia in a 48,000-square foot facility that includes a state-of-the-art cGMP manufacturing facility. With AAV vector GMP manufacturing capabilities in-house, investigational clinical-grade vectors developed and manufactured by our team have been delivered through six routes of administration to hundreds of patients in more than a dozen clinical trials.

Since our founding, we have secured more than $500 million in financing to support the growth of our clinical programs and platform. Spark Therapeutics has also been recognized for its groundbreaking science and leadership in gene therapy: In 2016, our company was ranked #9 on the *MIT Technology Review* list of the world's "50 Smartest Companies."

Our Clinical Programs*

We have a growing pipeline of eight investigational gene therapies, including four gene therapies currently in clinical trials. Two of our investigational therapies (voretigene neparvovec and *SPK-9001*) hold breakthrough therapy designations from the U.S. Food and Drug Administration

(FDA). Breakthrough status indicates that the investigational therapy, if approved, may offer substantial treatment advantages over existing treatment options for patients with serious or life-threatening diseases.

Our most advanced investigational candidate, voretigene neparvovec, is being developed to potentially treat biallelic *RPE65*-mediated inherited retinal disease (IRD). With voretigene neparvovec, Spark Therapeutics has completed the first-ever randomized, controlled, pivotal Phase 3 trial in gene therapy for a genetic disease. There are approximately 3,500 individuals with *RPE65*-mediated IRD in the U.S. and the five major European markets. Voretigene neparvovec has orphan designations in the U.S. and European Union, and breakthrough therapy designation in the U.S. We anticipate completing the Biologics Licensing Application (BLA) submission to the U.S. FDA in early 2017. If approved, voretigene neparvovec would become the first approved gene therapy for a genetic disease in the U.S.

We are leveraging our development experience with voretigene neparvovec to potentially address other IRDs caused by mutations in other genes. Our first such follow-on investigational candidate is *SPK-7001* for the potential treatment of choroideremia, a rare IRD that usually manifests in affected males during childhood as night blindness and a reduction of visual field, ultimately leading to complete blindness. An open-label, dose-escalating Phase 1/2 trial is designed to assess the safety and preliminary efficacy of subretinal administration of investigational *SPK-7001* for choroideremia.

Spark Therapeutics reported initial data from our open-label Phase 1/2 trial of investigational *SPK-9001* in hemophilia B in mid-2016. Hemophilia B is a serious and rare inherited hematologic disorder, characterized by mutations in the factor IX, or *FIX* gene, which lead to deficient blood coagulation and an increased risk of bleeding or hemorrhaging. *SPK-9001* has received both breakthrough therapy and orphan product designations from the U.S. FDA, and has been granted access to the European Medicines Agency (EMA) PRIority MEdicines (PRIME) program. *SPK-9001* is being developed in collaboration with Pfizer.

We also have initiated the Phase 1/2 trial for *SPK-8011*, an investigational gene therapy for hemophilia A, or factor VIII deficiency. Hemophilia A is a serious and rare inherited hematologic disorder, characterized by mutations in the factor VIII, or *FVIII* gene, which lead to deficient blood coagulation and an increased risk of bleeding or hemorrhaging. Spark Therapeutics retains global commercialization rights to its *SPK-8011* program for hemophilia A.

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