Spark THERAPEUTICS™

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 investigate treatments that go to an inherited disease at its root by augmenting, replacing or suppressing the function of a mutated gene. We engineer investigational gene therapy vectors using a cutting-edge, proprietary adeno-associated viral (AAV) vector platform, developed through vigorous preclinical and clinical testing.

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.

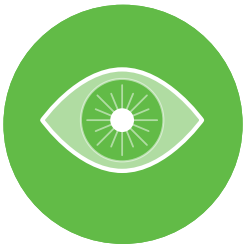
The Spark Therapeutics team includes more than 300 industry professionals with deep experience in research and development activities, manufacturing and commercializing complex and novel biotechnology products. We are headquartered in Philadelphia in a 48,000-square foot facility that includes a state-of-the-art 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 participants in more than a dozen clinical trials.

Since our founding, we have secured $1 billion in financing to support the growth of our clinical programs and platform. Our company has been named to *MIT Technology Review*'s list of the world's "50 Smartest Companies" in the top 10 for two years in a row (2016, 2017).

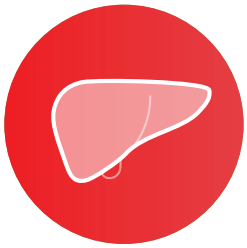
We don't follow footsteps. We create the path.

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 – LUXTURNA™ (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.



INHERITED RETINAL DISEASES (IRDs)



LIVER-MEDIATED DISEASES

NEURODEGENERATIVE DISEASES

Our most advanced investigational candidate, LUXTURNA™, is being developed to potentially treat biallelic *RPE65*-mediated inherited retinal disease (IRD). With LUXTURNA™, 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 United States and the five major European markets LUXTURNA™ has orphan and breakthrough therapy designations in the United States. Investigational voretigene neparvovec also has orphan designation in the European Union. The U.S. FDA accepted our Biologics License Application (BLA) for filing in July 2017. If approved, LUXTURNA™ would become the first approved gene therapy for a genetic disease in the United States.

We are leveraging our development experience with LUXTURNA™ to potentially address other IRDs caused by mutations in other genes. Our first such 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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Spark Therapeutics, Inc.
3737 Market Street
Philadelphia, PA 19104
Phone: 1-855-SPARKTX / +1 215-220-9300

communications@sparktx.com

sparktx.com