# RESEARCH sparks INVENTION

This journey through milestones in the history of gene therapy illustrates how time and time again, **#ResearchSparksInvention.**

To reflect our research at Spark Therapeutics we have focused on milestones relating to diseases of:

- the retina
- the liver
- central nervous system

## ~1,000 A.D.

Disease resembling hemophilia described in ancient medical encyclopedia by Albucasis, an Arab physician

Hemophilia is a rare genetic bleeding disorder that causes a delay in clot formation as a result of a deficiency in one of several blood-clotting factors.

## 1803

Philadelphia doctor first to identify an inherited bleeding disorder, primarily affecting men

## 1824

Invention of braille

## 1841

First published description of Huntington's disease

Huntington's disease is a fatal genetic disorder that causes the progressive breakdown of nerve cells in the brain.

## 1871

Inherited retinal disease LHON first described

Leber hereditary optic neuropathy (LHON) is a mitochondrial disease that can cause the optic nerve to atrophy, leading to sudden, severe loss of central vision.

## 1903

First published description of Batten disease

Batten disease is a fatal neurological disorder involving mutations in the *TPP1* gene that begins in early childhood.

## 1932

First published description of Pompe disease

Pompe disease is an oftentimes fatal lysosomal storage disorder and neuromuscular disease.

## 1947

First laboratory distinction between hemophilia A and B

## 1953

Discovery of the structure of DNA

## 1965

Discovery of human adeno-associated virus (AAV)

An AAV vector is a virus, with its viral genes removed, that carries genetic material into target cells.

## 1980s

First retroviral vectors designed to carry new genes into a cell

## 1984

First purification and cloning of the Factor VIII gene

Factor VIII is one of the several blood clotting factors, normally produced by cells located in the liver, that interact as part of the blood clotting process.

## 1990

First gene therapy clinical research in the U.S.

Gene therapy uses a transporter or "vector", to replace or inactivate a mutated gene to treat a disease or help the body fight a disease.

## 1990

First cloning of *CHM* gene associated with choroideremia

Choroideremia usually manifests in affected males during childhood as night blindness and a reduction of visual field, followed by progressive constriction of visual field, ultimately leading to complete blindness.

## 1992

First recombinant factor product approved in the U.S.

## 1993

Researchers discover gene mutation that causes Huntington's disease.

Huntington's disease is a fatal genetic disorder that causes the progressive breakdown of nerve cells in the brain. It is characterized by motor, cognitive and behavioral symptoms which usually appear between the ages of 30 to 50, and worsen over a 10- to 25-year period. Ultimately, the weakened individual succumbs to pneumonia, heart failure or other complications.

## 1998

First published map of the *CLN2* gene (causes a form of Batten's disease)

## 2001

First successful use of an investigational gene therapy to treat an inherited blindness in dogs

## 2003

Human Genome Project completed

## 2011 ONWARDS

First successful clinical approach to gene therapy for hemophilia spurs multiple investigational gene therapies now in clinical development

## 2017

Investigational gene therapies for Huntington's disease and Batten's disease in development

Explore **www.sparktx.com** to learn more about the science of gene therapy and our investigational therapies.

Spark THERAPEUTICS

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