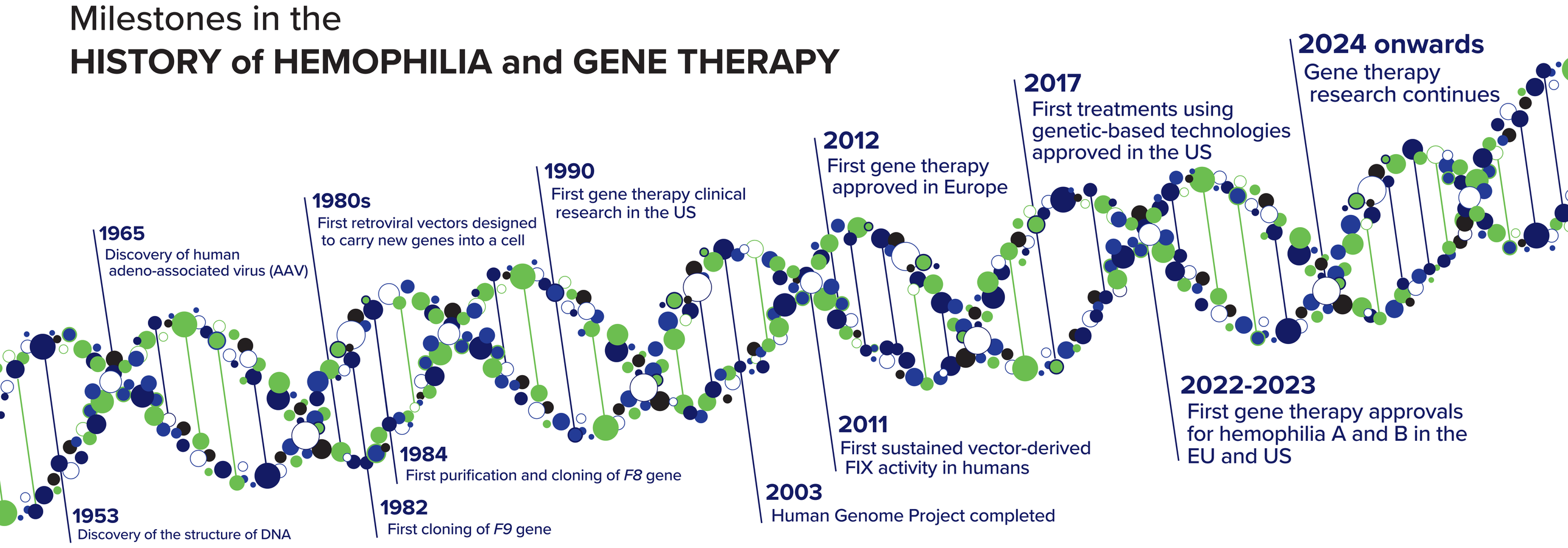
Spark THERAPEUTICS

Milestones in the **HISTORY of HEMOPHILIA and GENE THERAPY**



1953
In 1953, scientists James D. Watson and Francis H.C. Crick determined the chemical structure of DNA. This discovery laid the groundwork for the development of future DNA-based technologies, including gene therapy.

1965
In 1965, human adeno-associated virus (AAV) was discovered as a contaminant of adenovirus preparations. It has recently risen to prominence as a vector for gene therapy. AAV vectors are predominately episomal and rarely integrate into the host genome.

1980s
Constance L. Cepko and colleagues reported the development of a murine retrovirus vector system that could be used to carry new genes into mammalian cells. Retroviral vectors insert genetic material into the host cell genome.

1982
In 1982, the *F9* gene was cloned. This paved the way for the development of new recombinant factor IX products for the treatment of hemophilia B, the first of which was approved by the US FDA in 1997.

1984
In 1984, the *F8* gene was cloned. This paved the way for the development of new recombinant factor VIII products for the treatment of hemophilia A, the first of which was approved by the US FDA in 1992.

1990
In 1990, the first gene therapy clinical trial in the US was started under the direction of Dr. W. French Anderson. Two young girls, ages 4 and 9, with adenosine deaminase (ADA) deficiency, which causes a form of severe combined immunodeficiency (SCID), received investigational gene therapy designed to insert a corrected ADA gene into their white blood cells.

2003
In 2003, the Human Genome Project was completed. The sequencing of the human genome has led to the identification of the gene location for many diseases, which could be potential targets for future gene therapies.

2011
In 2011, the first sustained vector-derived factor IX activity in humans was reported by Amit C. Nathwani and colleagues. In the clinical trial, 6 patients with hemophilia B received investigational AAV-based gene therapy.

2012
In 2012, the first gene therapy was approved by the European Medicines Agency (EMA).

2017
In 2017, the first treatments using genetic-based techonologies received FDA approval in the US, including an AAV-based gene therapy and two Chimeric Antigen Receptor T-cell (CAR-T) therapies.

2022-2023
The EMA and FDA granted the first approvals for hemophilia A and hemophilia B gene therapies.

2024 onwards
A number of life sciences companies and organizations are continuing research into gene therapy applications to treat a variety of diseases, including Spark Therapeutics. Visit **Sparktx.com** to learn more about Spark's pipeline.

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