



GENE THERAPY APPROVALS & QPS MILESTONES

KEY

BIOANALYSIS ● **ADME** ● **GENE THERAPY APPROVALS** ●

QPS

- 2003**
Oligonucleotides PK via LC-MS/MS
- 2006**
CLIA Assay - Inclusion/Exclusion Criteria
Biomarkers - Primary End-point
- 2007**
Oligonucleotides PK via hybridization-ELISA

- 2009**
Oligonucleotides PK via hybridization-LC-FLD
Oligonucleotides PK via LC-UV
- 2010**
Oligonucleotides Biodistribution via Autoradiography
Oligonucleotides *in vitro* Metabolic Stability
Oligonucleotides Metabolite Identification
Oligonucleotides *in vitro* CYP Inhibition

- 2011**
Oligonucleotides Biodistribution via QWBA
Oligonucleotides Mass Balance/Excretion
- 2012**
Oligonucleotides Biodistribution via Microautoradiography
- 2013**
Oligonucleotides (ASO, siRNA, miRNA) ADA
Oligonucleotides *in vitro* CYP Induction

- 2014**
Oligonucleotides PK via LC-HRMS
Oligonucleotides *in vitro* Protein Binding
mRNA PK/ Biodistribution via RT-qPCR
Vector PK/ Biodistribution/ Shedding via qPCR
- 2015**
Oligonucleotides *in vitro* Reaction Phenotyping

- 2016**
ADA for Gene Therapy Vectors (LNP and Viral Vectors)
ADA from mRNA Expressed Proteins
Oligonucleotides *in vitro* Drug Transport

- 2018**
CRISPR guide and CAS9 mRNA PK via RT-qPCR

- 2021**
AOC/POC PK via Immunocapture LC-MS/MS
AOC/POC PK via LBA
ADA via LBA

- 2022**
ddPCR for Insertion Copy Number/Biodistribution
- 2023**
dPCR and RT-dPCR

- 1998**
Gene Interference via ASO
Vitravene (fomivirsen)
- 2004**
Gene Interference via Aptamer
Macugen® (pegaptanib)

- 2012**
In vivo Gene Insertion via AAV1
Glybera (alipogene tiparvovec)
- 2013**
Gene Interference via ASO
Kynamro® (mipomersen)
- 2015**
In vivo Gene Insertion via HSV-1
Imlygic® (talimogene laherparepvec)

- 2016**
Gene Interference via Polydisperse Natural Oligonucleotides
Defitelio® (defibrotide)
Gene Interference via ASO
Spinraza® (nusinersen)
Gene Interference via ASO
Exondys 51® (eteplirsen)
Ex vivo Gene Insertion via Gammaretrovirus
Strimvelis® (autologous CD34+ enriched cell fraction)

- 2017**
Ex vivo Gene Insertion via CAR-T
Yescarta® (axicabtagene ciloleucel)
Ex vivo Gene Insertion via CAR-T
Kymriah® (tisagenlecleucel)
In vivo Gene Insertion via AAV2
Luxturna® (voretigene neparvovec)
- 2018**
Gene Interference via siRNA
Onpattro® (patisiran)
Gene Interference via ASO
Tegsedi® (inotersen)

- 2019**
Gene Interference via siRNA
Givlaari® (givosiran)
Ex vivo Gene Insertion via LVV
Zynteglo® (betibeglogene autotemcel)
Gene Interference via ASO
Waylivra® (volanesorsen)
In vivo Gene Insertion via AAV9
Zolgensma® (onasemnogene abeparvovec-xioi)
Gene Interference via ASO
Vyondys 53™ (golodirsen)

- 2020**
Gene Interference via ASO
Viltepso® (viltolarsen)
Gene Interference via siRNA
Oxlumo™ (lumisiran)
Ex vivo Gene Insertion via CAR-T
Tecartus™ (brexucabtagene autoleucel)
- 2021**
Gene Interference via ASO
Amondys 45™ (casimersen)
Gene Interference via siRNA
Leqvio® (inclisiran)

- 2022**
Gene Interference via siRNA
Amvuttra® (vutrisiran)
- 2023**
Gene Interference via ASO
Qalsody™ (tofersen)
Aptamer
Izervay™ (avacincaptad pegol)
Gene Interference via siRNA
Rivfloza™ (nedosiran)
Gene Interference via ASO
Wainua™ (eplontersen)

- 2023**
Gene Interference via ASO
Tryngolza™ (olezarsen)
- 2024**
Gene Editing via CRISPR
Casgevy® (exagamglogene autotemcel)

GENE THERAPY