



## GENE THERAPY APPROVALS & QPS MILESTONES

### QPS

|             |  |
|-------------|--|
| <b>2003</b> | Oligo PK via LC-MS/MS  |
| <b>2006</b> | CLIA Assay - Inclusion/Exclusion Criteria<br>Biomarkers - Primary End-point                                |
| <b>2007</b> | Oligo PK via hybridization-ELISA   |
| <b>2009</b> | Oligo PK via hybridization-LC-FLD<br>Oligo PK via LC-UV  |
| <b>2010</b> | Oligo Biodistribution via Autoradiography<br>Oligo <i>in vitro</i> Metabolic Stability                     |
| <b>2011</b> | Oligo Biodistribution via QWBA<br>Oligo Mass Balance/Excretion   |
| <b>2012</b> | Oligo Biodistribution via Microautoradiography   |
| <b>2013</b> | Oligo ADA<br>Oligo <i>in vitro</i> CYP Induction   |
| <b>2014</b> | Oligo PK via LC-HRMS<br>Oligo <i>in vitro</i> Protein Binding<br>mRNA PK/Biodistribution/Shedding via QPCR |
| <b>2015</b> | Vector PK/Biodistribution/Shedding via QPCR<br>Oligo <i>in vitro</i> Reaction Phenotyping                  |
| <b>2016</b> | mRNA ADA<br>Vector ADA<br>Oligo <i>in vitro</i> Drug Transport   |
| <b>2021</b> | AOC/POC PK via hybrid LC-MS/MS   |
| <b>2022</b> | ddPCR  |
| <b>2023</b> | dPCR   |

### GENE THERAPY

| YEAR        | TECHNIQUE   | APPLICATION                          | PRODUCT |
|-------------|---|--------------------------------------|---------|
| <b>1998</b> | Gene Interference via ASO                                   | Vitravene/fomivirsen                 |         |
| <b>2004</b> | Gene Interference via Aptamer                               | Macugen®/pegaptanib                  |         |
| <b>2012</b> | <i>In vivo</i> Gene Insertion via AAV1                      | Glybera/alipogene tiparvovec         |         |
| <b>2013</b> | Gene Interference via ASO                                   | Kynamro®/ mipomersen                 |         |
| <b>2015</b> | <i>In vivo</i> Gene Insertion via HSV-1                     | Imlrylic®/ talimogene laherparepvec  |         |
| <b>2016</b> | Gene Interference via polydisperse natural oligonucleotides | Defitelio®/ defibrotide              |         |
| <b>2017</b> | <i>Ex vivo</i> Gene Insertion via CAR-T                     | Yescarta®/ axicabtagene ciloleucel   |         |
| <b>2018</b> | <i>Ex vivo</i> Gene Insertion via CAR-T                     | Kymriah®/ tisagenlecleucel           |         |
| <b>2019</b> | <i>Ex vivo</i> Gene Insertion via LVV                       | Zynteglo®/ betibeglogene autotemcel  |         |
| <b>2020</b> | <i>Ex vivo</i> Gene Insertion via siRNA                     | Givlaari®/ givosiran                 |         |
| <b>2021</b> | <i>Ex vivo</i> Gene Insertion via CAR-T                     | Tecartus™/ brexucabtagene autoleucel |         |
| <b>2022</b> | <i>Ex vivo</i> Gene Insertion via siRNA                     | Vyvesta®/ volanesorsen               |         |
| <b>2023</b> | <i>Ex vivo</i> Gene Insertion via siRNA                     | Amlygen 45™/ casimersen              |         |
| <b>2022</b> | Gene Interference via ASO                                   | Viltepso®/ viltolarsen               |         |
| <b>2023</b> | Gene Interference via siRNA                                 | Oxlumo™/ lumisiran                   |         |
| <b>2022</b> | Gene Interference via siRNA                                 | Amvuttra®/ vutrisiran                |         |
| <b>2023</b> | Gene Interference via ASO                                   | Qalsody®/ tofersen                   |         |
| <b>2022</b> | Aptamer   | Izervay™/ avacincaptad pegol         |         |
| <b>2023</b> | Gene Interference via siRNA                                 | Rivflorza™/ nedosiran                |         |
| <b>2023</b> | Gene Interference via ASO                                   | Wainua™/ eplontersen                 |         |

### KEY

BIOANALYSIS      ADME      GENE THERAPY APPROVALS

