Regulatory Pathways for Gene Therapies

Peter Marks, MD, PhD
Advancing Gene-Targeting Therapy for CNS Disorders Workshop
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Advanced Therapy Medicinal Products (ATMPs)

Products included

• Gene therapies
• Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) requiring licensure
• Xenotransplantation products

Clinical benefit comes from having a controlled manufacturing process and understanding critical quality attributes for ATMPs because product quality, safety, and efficacy are inextricably linked
Delivering Gene Therapy

Ex vivo

Introduce modified cells back into patient

In vivo

Direct delivery to patient using viral or non-viral delivery vehicle

Deliver targeted nucleases to cells by physical, chemical, or viral methods

DNA
RNA
Protein
Lentivirus

Extract stem or progenitor cells

AAV
Lipid nanoparticle
Recent Product Approvals

- **Tisagenlecleucel (KYMRIAH)**
  - Treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) refractory or in second or later relapse; Relapsed or refractory large B-lymphoma indication subsequently added

- **Axicabtagene ciloleucel (YESCARTA)**
  - Treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy

- **Voretigene neparvovec-rzyl (LUXTURNA)**
  - Treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy in patients with viable retinal cells as determined by the attending physician(s)
Predicted Growth of Gene Therapy

Number of Investigational New Drug (IND) applications to FDA is increasing noticeably.

Correlates with prediction of 40 to 60 product launches and more than 500,000 treated by 2030.
Expedited Development Programs

• Fast Track
• Priority Review
• Accelerated Approval
• Breakthrough Therapy
• Regenerative Medicine Advanced Therapy

These programs may be applicable to drugs or biologics intended to treat serious conditions
Regenerative Medicine Advanced Therapy Designation (RMAT)

• To expedite the development and review of regenerative medicine advanced therapies
  – Applies to certain cell therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products
  – Genetically modified cell therapies and gene therapies producing durable effects included
Regenerative Medicine Advanced Therapy Designation (RMAT)

• Products must be intended for serious or life-threatening diseases or conditions
• Preliminary clinical evidence must indicate potential to address unmet medical needs
• Designated products are eligible as appropriate for priority review and accelerated approval
• Expanded range of options for fulfilling post approval requirements of accelerated approval
RMAT Designations Granted

- 33 products granted designation
- Majority have Orphan Product designation (20/33)
- Most are cellular therapy products or cell-based gene therapy products

Data as of April 1, 2019
Advancing the Development of Cell and Gene Therapy

- Guidance documents
- Reduction of administrative burden
- Clinical development initiatives
- Standards
- Manufacturing initiatives
INTERACT Program

INitial Targeted Engagement for Regulatory Advice on CBER producTs

• To further encourage early interaction with sponsors and replace the pre-pre-IND meeting process across the Center regarding preclinical, manufacturing and, clinical development plans

https://www.fda.gov/BiologicsBloodVaccines/ResourcesforYou/Industry/ucm611501.htm