Introduction to the Office of Tissues and Advanced Therapies (OTAT)

FDA Small Business Regulatory Education for Industry (REdI)

July 22, 2021

Wilson W. Bryan, MD

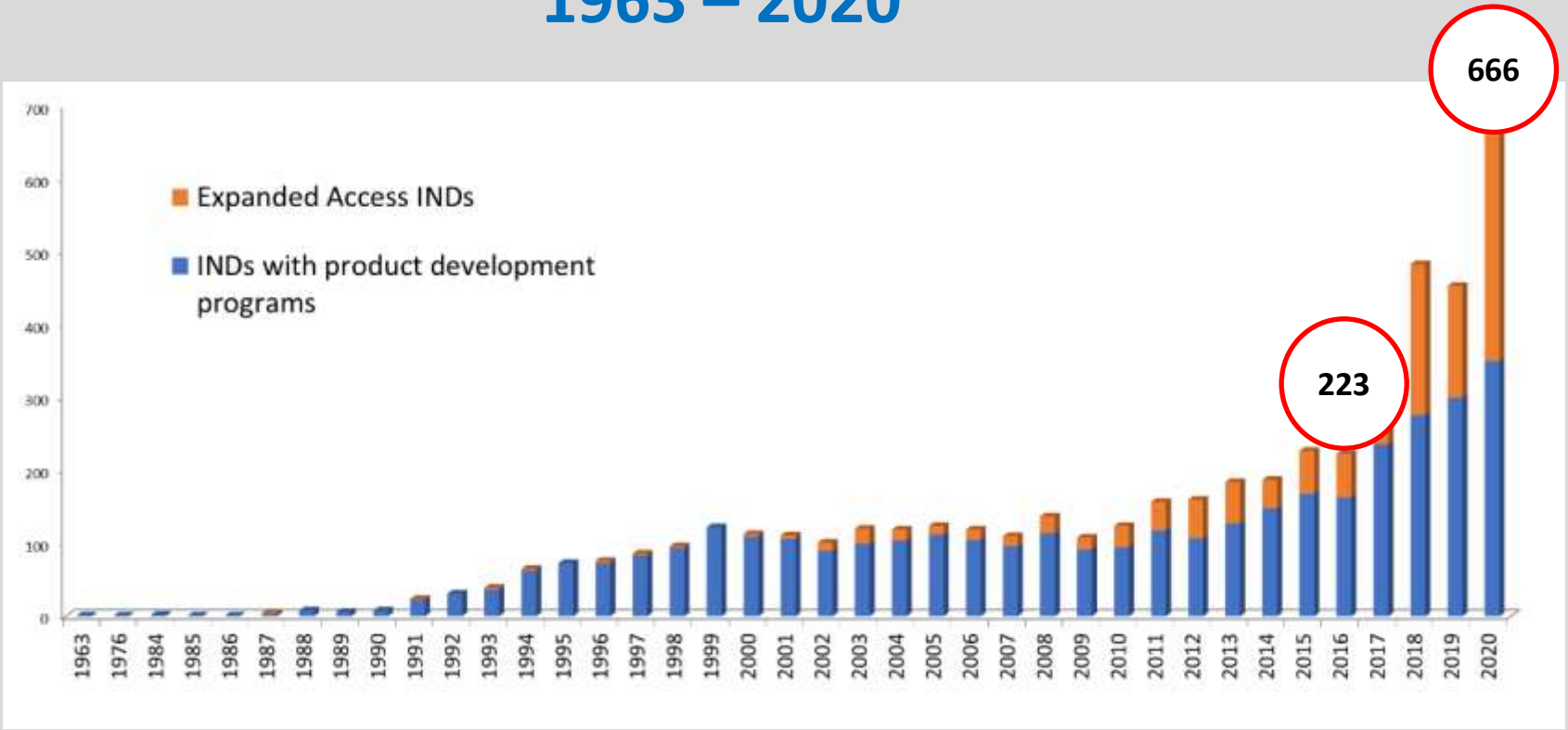
Director

Office of Tissues and Advanced Therapies (OTAT)

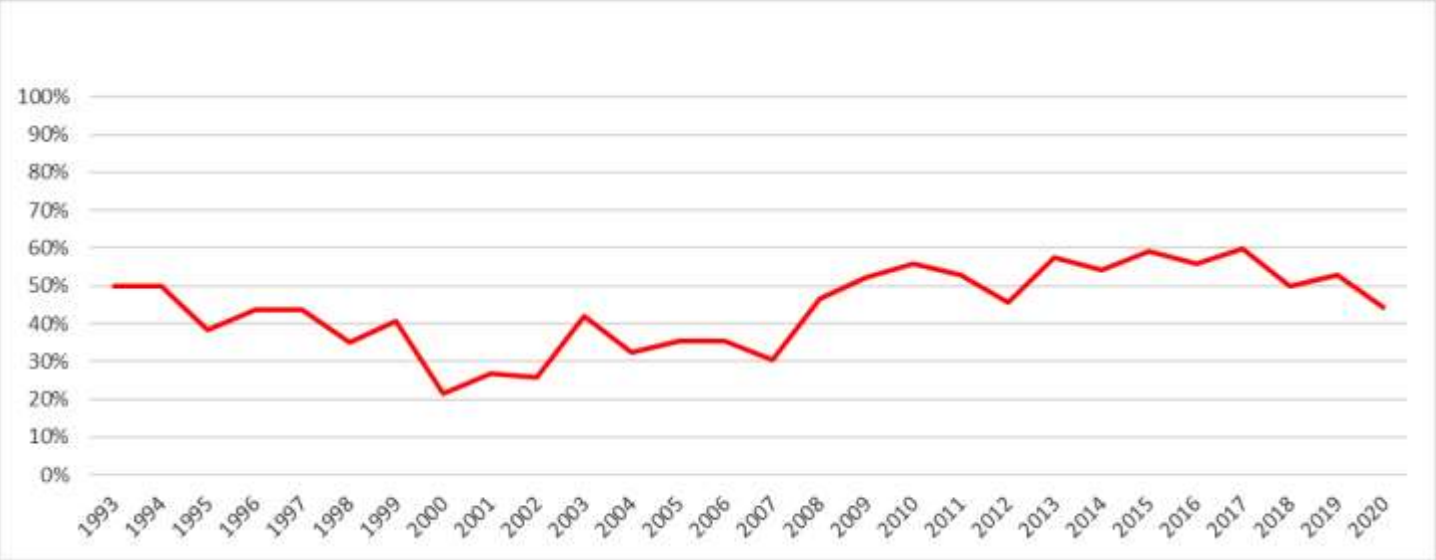
Center for Biologics Evaluation and Research (CBER)

U.S. Food and Drug Administration

OTAT Investigational New Drug Applications (INDs) 1963 – 2020



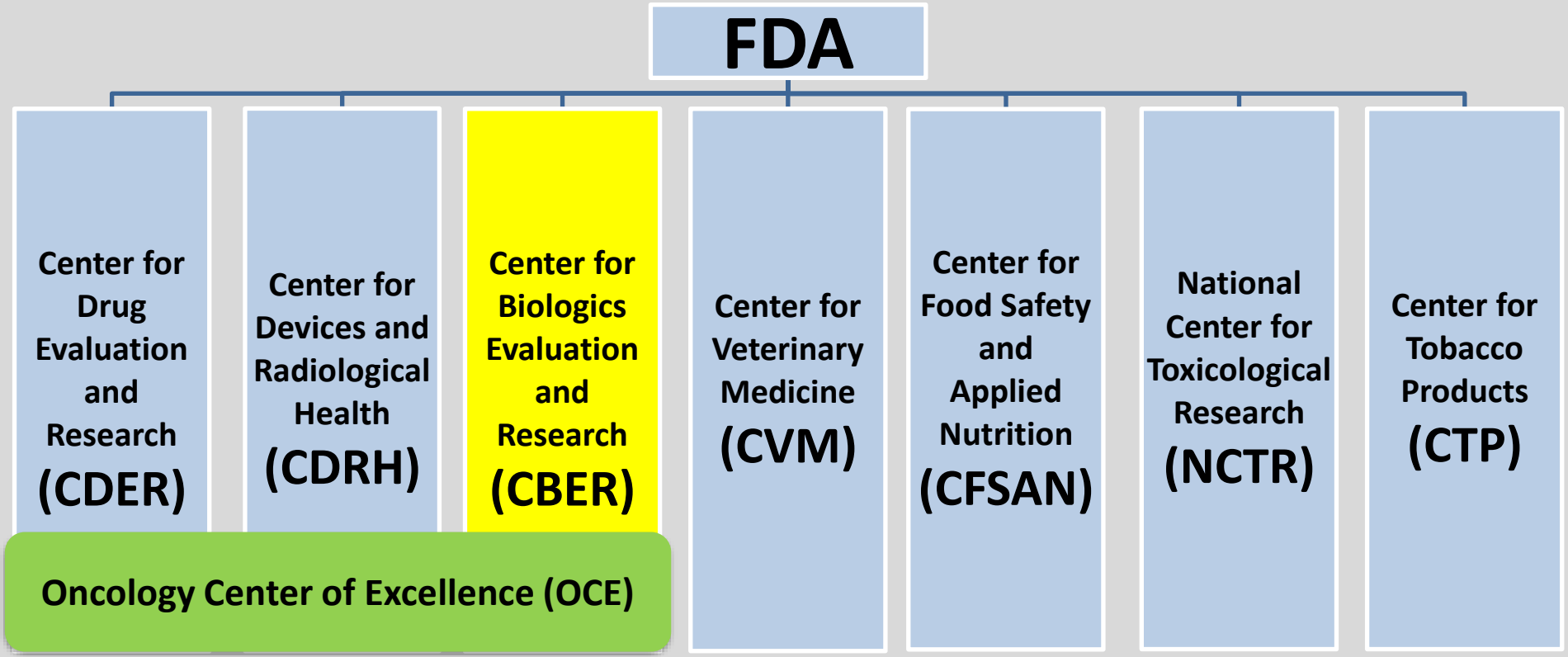
Research INDs for Rare Diseases (percent per year)



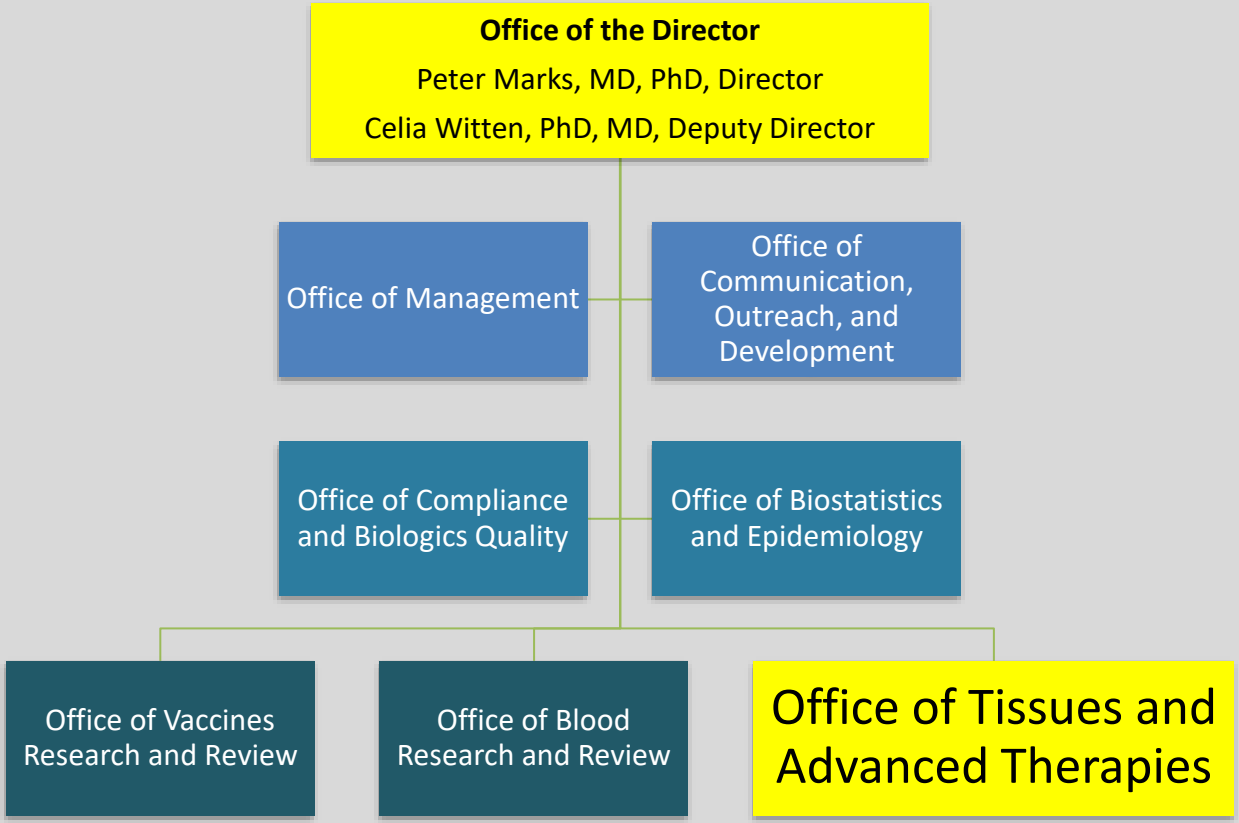
OTAT

FUNDAMENTALS

FDA Organization



Center for Biologics Evaluation and Research (CBER)



OTAT Mission

The Office of Tissues and Advanced Therapies (OTAT) promotes the public health through collaborative, science-based regulation of medical products. This includes facilitating drug development and ensuring safety of individuals. OTAT's regulatory decisions are data-driven, impartial, and compassionate.

OTAT Regulatory Science

- 22 laboratories
- 31 publications in 2020
- 40+ external conference presentations

OTAT Products

- Purified and recombinant proteins for hematology (e.g., coagulation factors, thrombin, botulism antitoxin, diphtheria anti-toxin, fibrin sealants)
- Antivenins

OTAT Products, Cont'd.

- Stem cell and stem cell-derived products
  - Hematopoietic, mesenchymal, cord blood, embryonic, induced pluripotent stem cells (iPSCs)
- Terminally-differentiated cell therapies
  - Pancreatic islets, chondrocytes, myoblasts, keratinocytes, hepatocytes
- Therapeutic vaccines and other antigen-specific active immunotherapies
  - Cancer vaccines and immunotherapies, such as dendritic cells, lymphocyte-based therapies, cancer cell-based therapies, peptides, proteins
  - Non-infectious disease therapeutic vaccines, such as peptides, proteins, small molecules

OTAT Products, Cont'd.

- Gene therapies
  - Genetically modified cells
  - Plasmids, viral vectors, bacterial vectors
- Xenotransplantation products
- Tissues and tissue-based products
- Some devices and combination products
  - Devices with a cellular component
  - Selected devices for the manufacture or delivery of cells
  - Donor screening tests (for use with cadaveric blood samples)

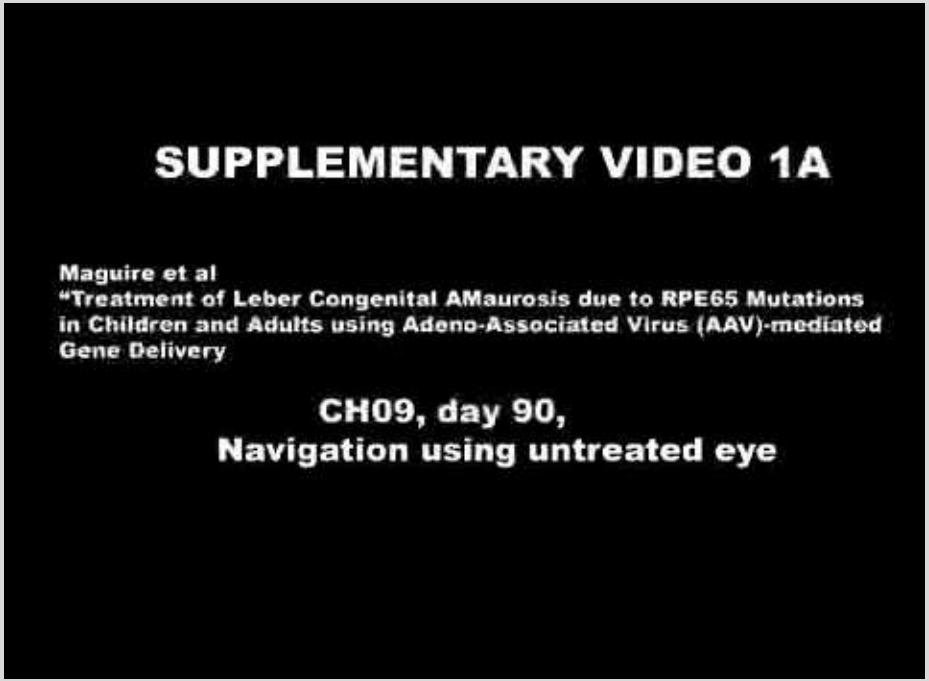
OTAT Products

RECENT APPROVALS

In vivo Gene Therapy

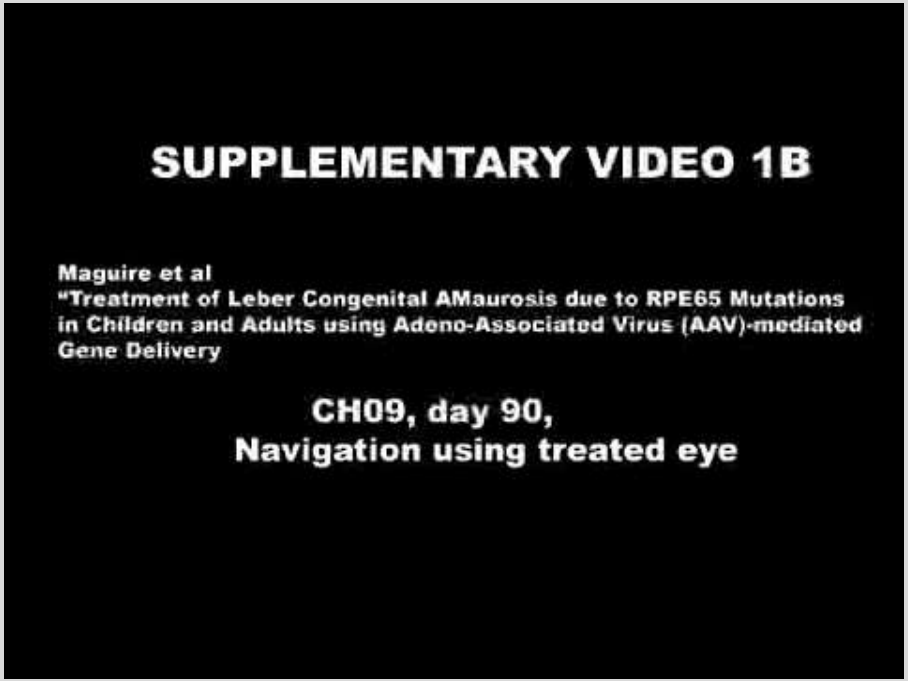
- LUXTURNA (voretigene neparvovec-rzyl)
- Directly administered adeno-associated viral vector-based gene therapy that targets a disease caused by mutations in a specific gene
- Indicated for the treatment of patients with *RPE65* mutation-associated retinal dystrophy
  - Eventual complete blindness in all patients

Multi-luminance Mobility Test – untreated eye



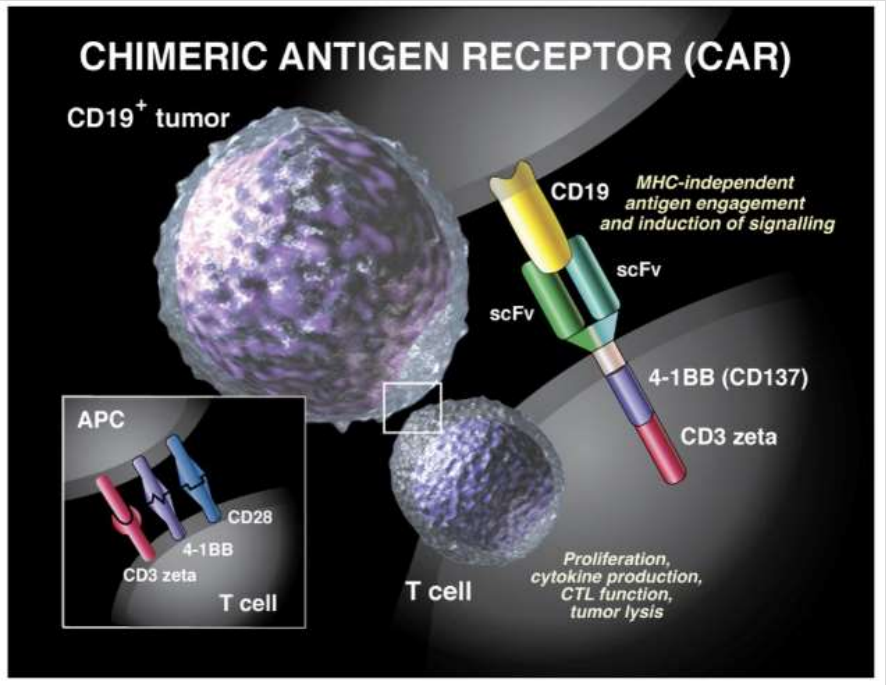
Maguire, Albert M et al. Lancet vol. 374, 9701 (2009): 1579-1605.

Multi-luminance Mobility Test – Luxturna-treated eye



Maguire, Albert M et al. Lancet vol. 374, 9701 (2009): 1579-1605.

CAR T Cells: Ex vivo Gene Therapy



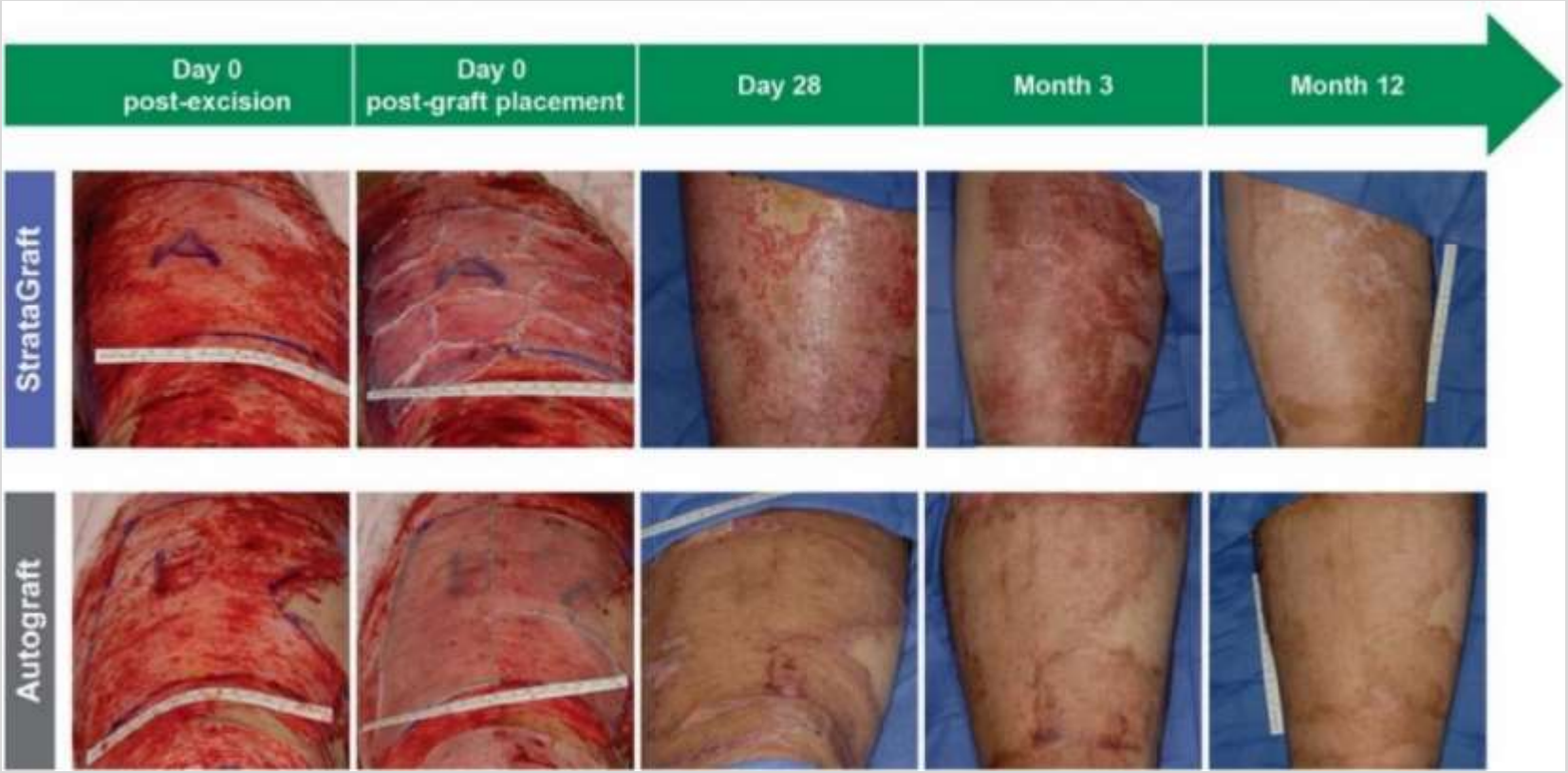
Maude, Shannon L. et al; Blood 2015; 125 (26): 4017–4023.
CTL, cytotoxic T lymphocyte; MHC, major histocompatibility complex

- KYMRIAH (tisagenlecleucel)
- YESCARTA (axicabtagene ciloleucel)
- TECARTUS (brexucabtagene autoleucel)
- BREYANZI (lisocabtagene maraleucel)
- ABECMA (idecabtagene vicleucel)

Allogeneic Cell Therapy

- StrataGraft
- Produced from two kinds of human skin cells (keratinocytes and dermal fibroblasts) grown together to make a bi-layered construct (a cellularized scaffold)
- Treatment of adult patients with thermal burns containing intact dermal elements (remaining deep skin layers) for which surgical intervention is clinically indicated
  - also referred to as deep partial thickness burns

StrataGraft

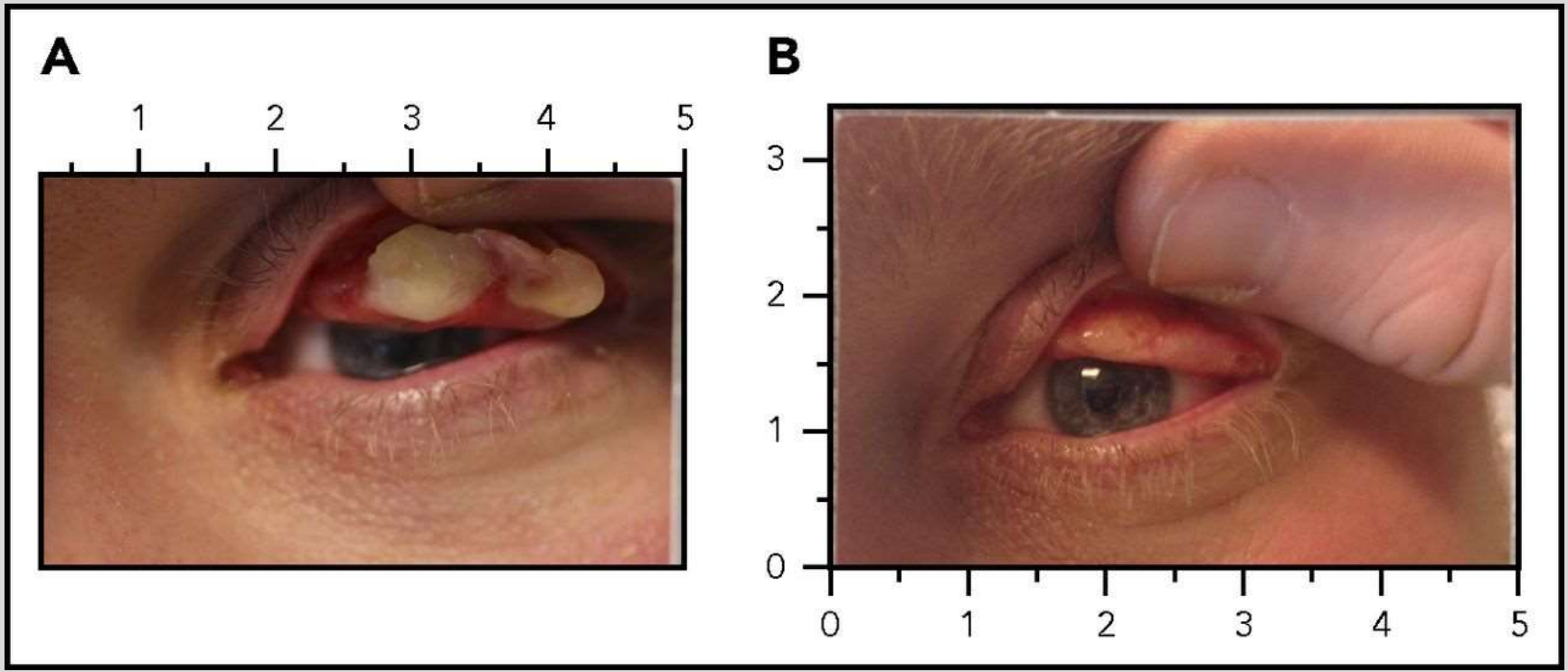


Holmes, James H 4th et al. *Burns : journal of the International Society for Burn Injuries* vol. 45,8 (2019): 1749-1758.

Purified Plasma Protein

- RYPLAZIM (plasminogen, human-tvmh)
- Treatment of plasminogen deficiency type 1 (hypoplasminogenemia)
  - Disorder can impair normal tissue and organ function, may lead to blindness

Effect of RYPLAZIM on Ligneous Lesions

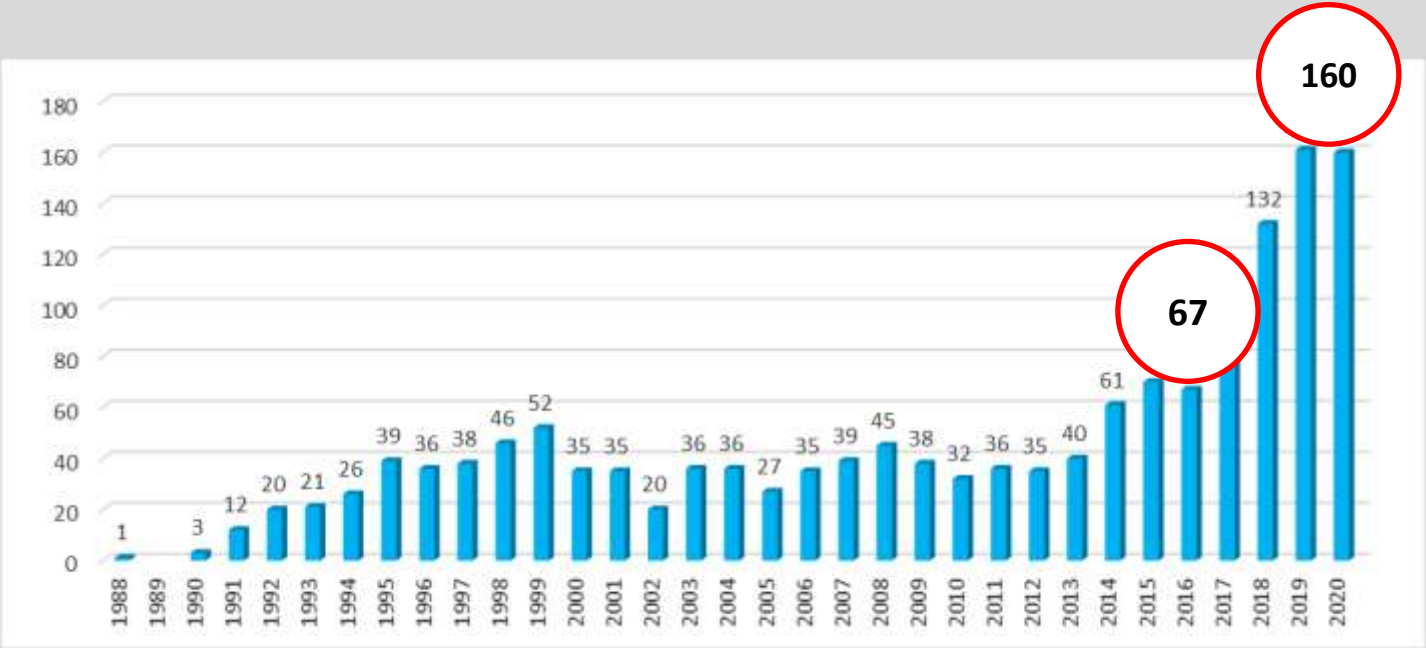


Shapiro, Amy D et al. Blood vol. 131,12 (2018): 1301-1310.

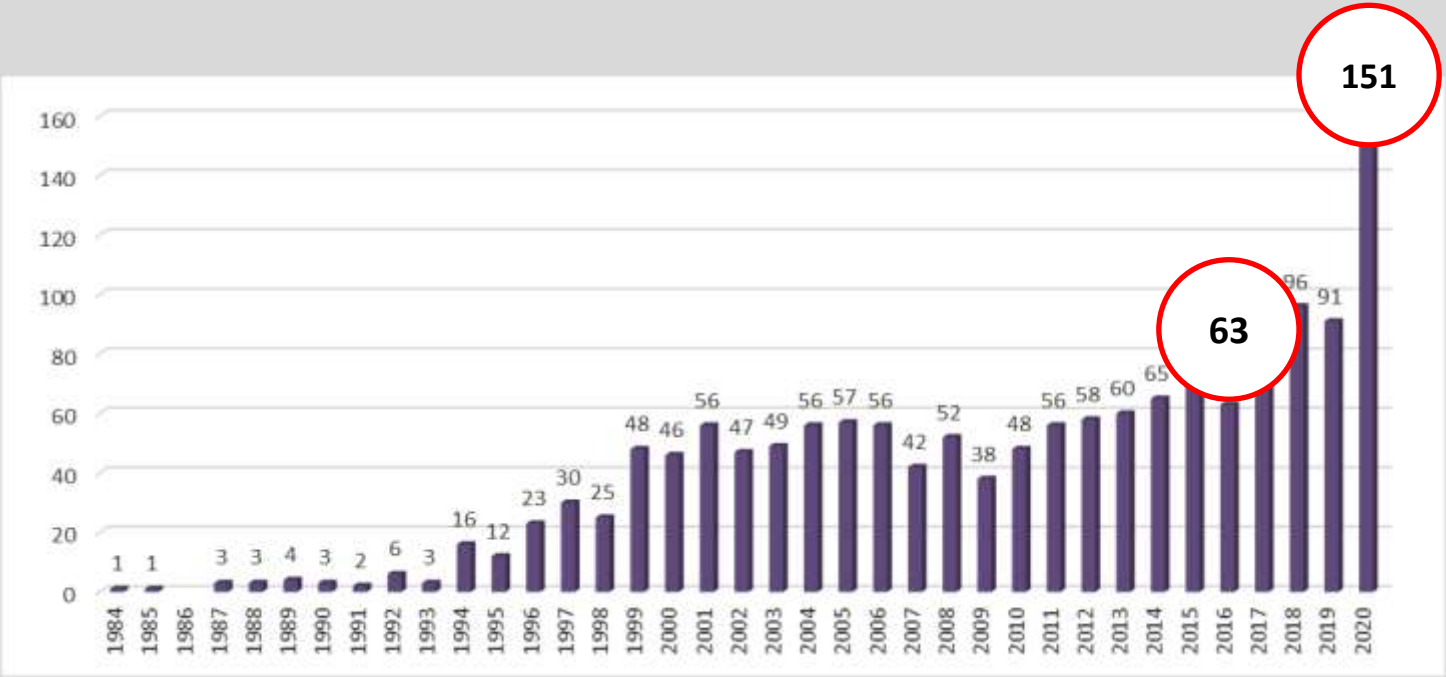
OTAT Products

FACILITATING DEVELOPMENT

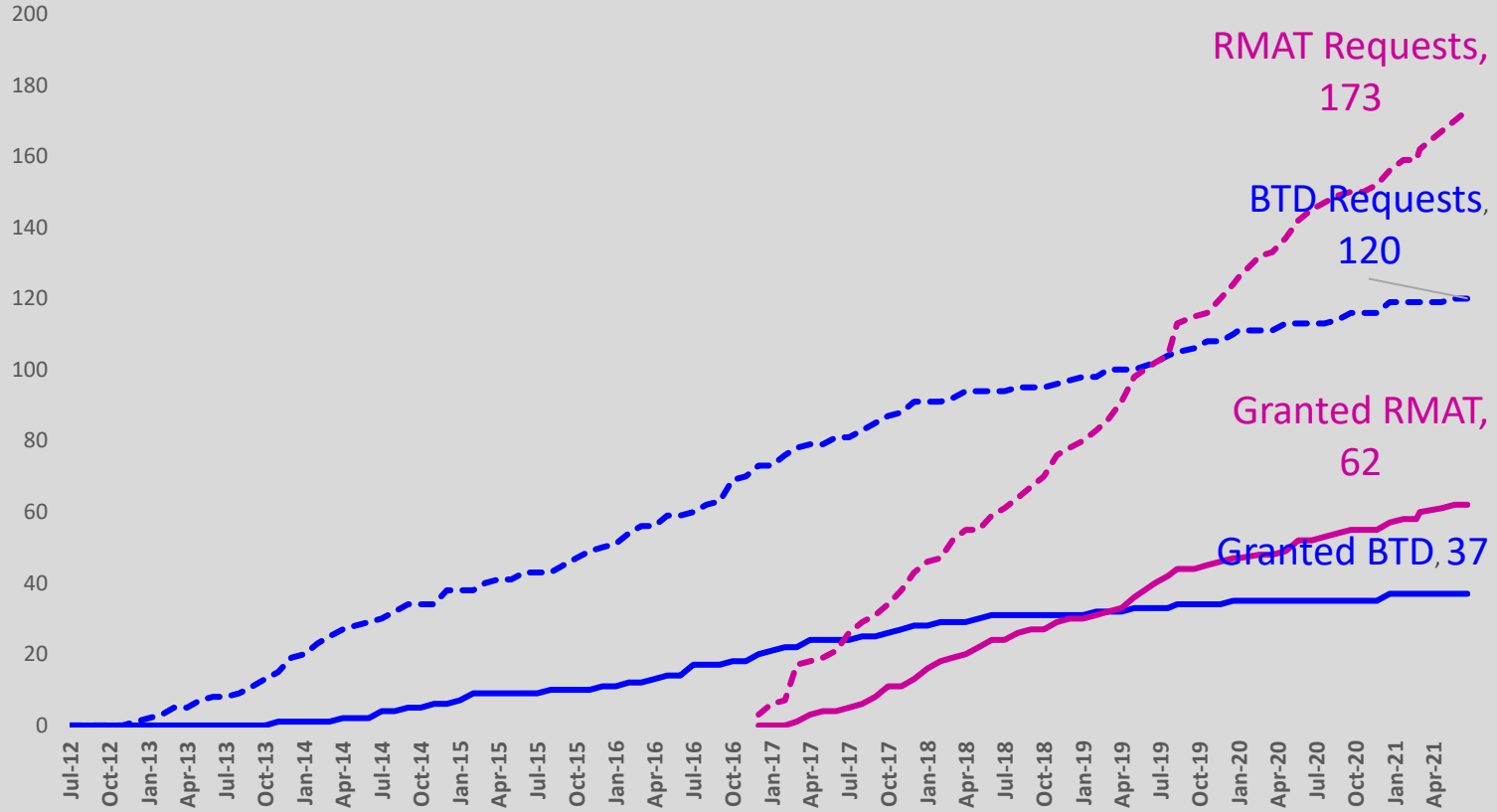
Research INDs: Gene Therapy



Research INDs: Cell Therapy



Breakthrough Designation (BTD) and Regenerative Medicine Advanced Therapy (RMAT) Designation



Summary

- Scientific advances have spurred recent growth in research and development of advanced therapies.

- OTAT is dedicated to facilitating the development of novel products to treat serious and life-threatening diseases.

Acknowledgements

- Division of Cellular and Gene Therapies
  - Thomas Finn, PhD
  - Malcolm Moos, MD, PhD
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  - Anna Kwilas, PhD
  - Andrea Gray, PhD





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- Division of Plasma Protein Therapeutics
  - Basil Golding, MD

- Division of Regulatory Project Management
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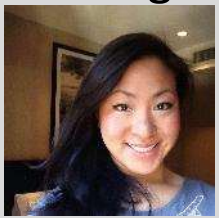
  - Niloofar Kennedy, MS

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  - Ekaterina Allen

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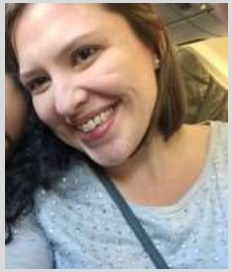
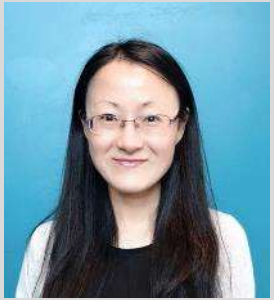
  - Rachael Anatol, PhD
  - Anne Rowzee, PhD
  - Xiaofei Wang, PhD







Contact Information

- **Regulatory Questions:**

  OTAT Main Line – 240 402 8190

  Email: OTATRPMS@fda.hhs.gov and

  Lori.Tull@fda.hhs.gov

- **OTAT Learn Webinar Series:**

  http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/ucm232821.htm

- **CBER website:** www.fda.gov/BiologicsBloodVaccines/default.htm
- **Phone:** 1-800-835-4709 or 240-402-8010
- **Consumer Affairs Branch**: ocod@fda.hhs.gov
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