



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

FDA Small Business Regulatory Education for Industry (REdI)

June 9, 2022

Wilson W. Bryan, MD

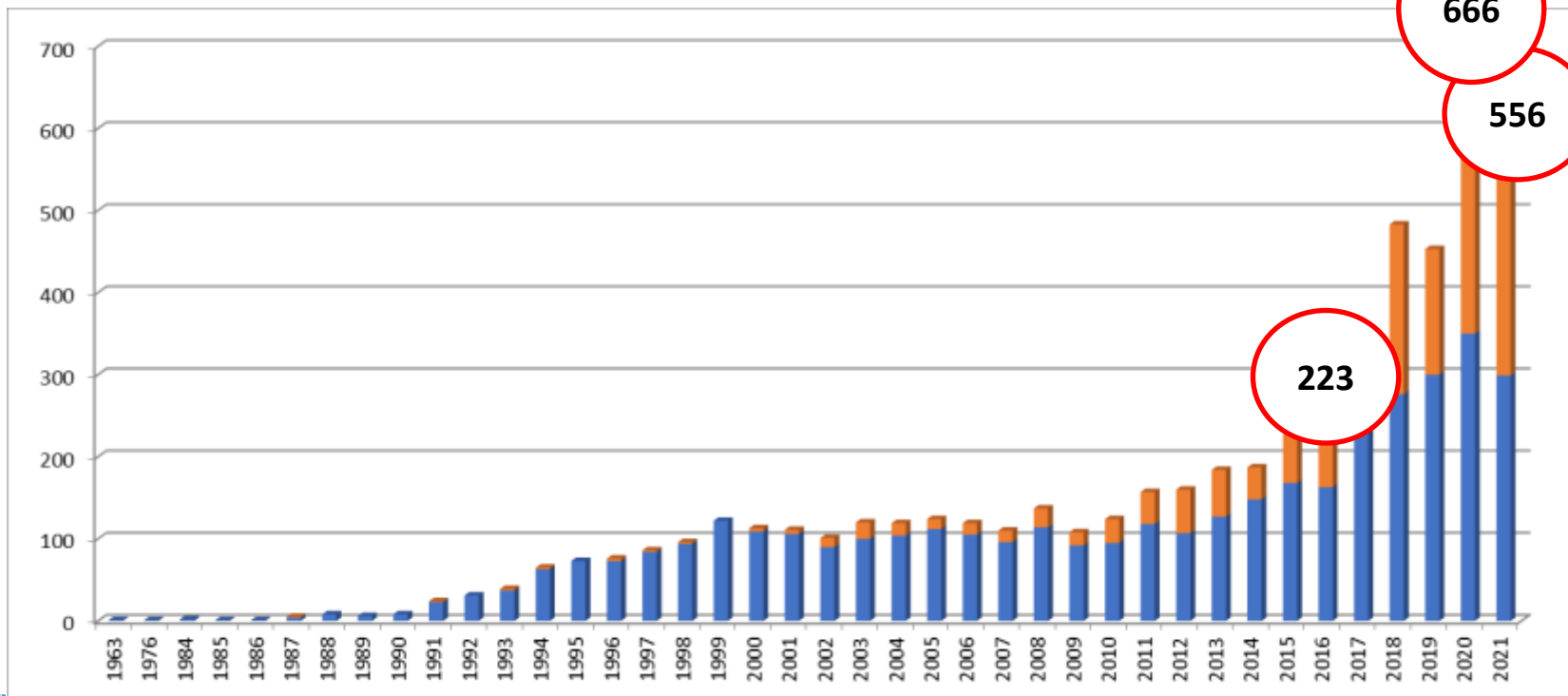
Director

Office of Tissues and Advanced Therapies (OTAT)
Center for Biologics Evaluation and Research (CBER)
U.S. Food and Drug Administration

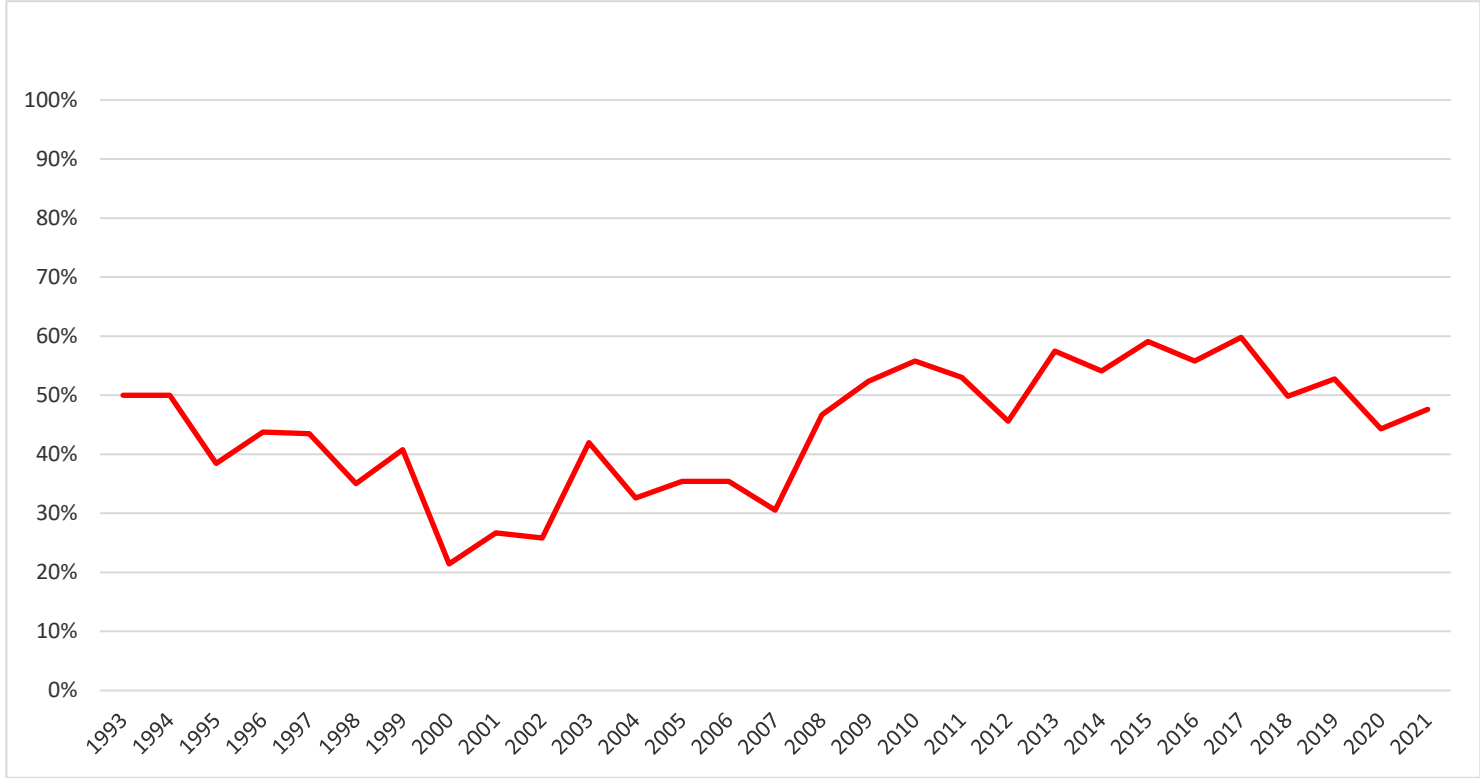
OTAT Investigational New Drug Applications (INDs)



1963 – 2021



Research INDs for Rare Diseases (percent per year)





OTAT

Fundamentals

FDA Organization



FDA

Center for
Drug
Evaluation
and
Research
(CDER)

Center for
Devices and
Radiological
Health
(CDRH)

Center for
Biologics
Evaluation
and
Research
(CBER)

Center for
Veterinary
Medicine
(CVM)

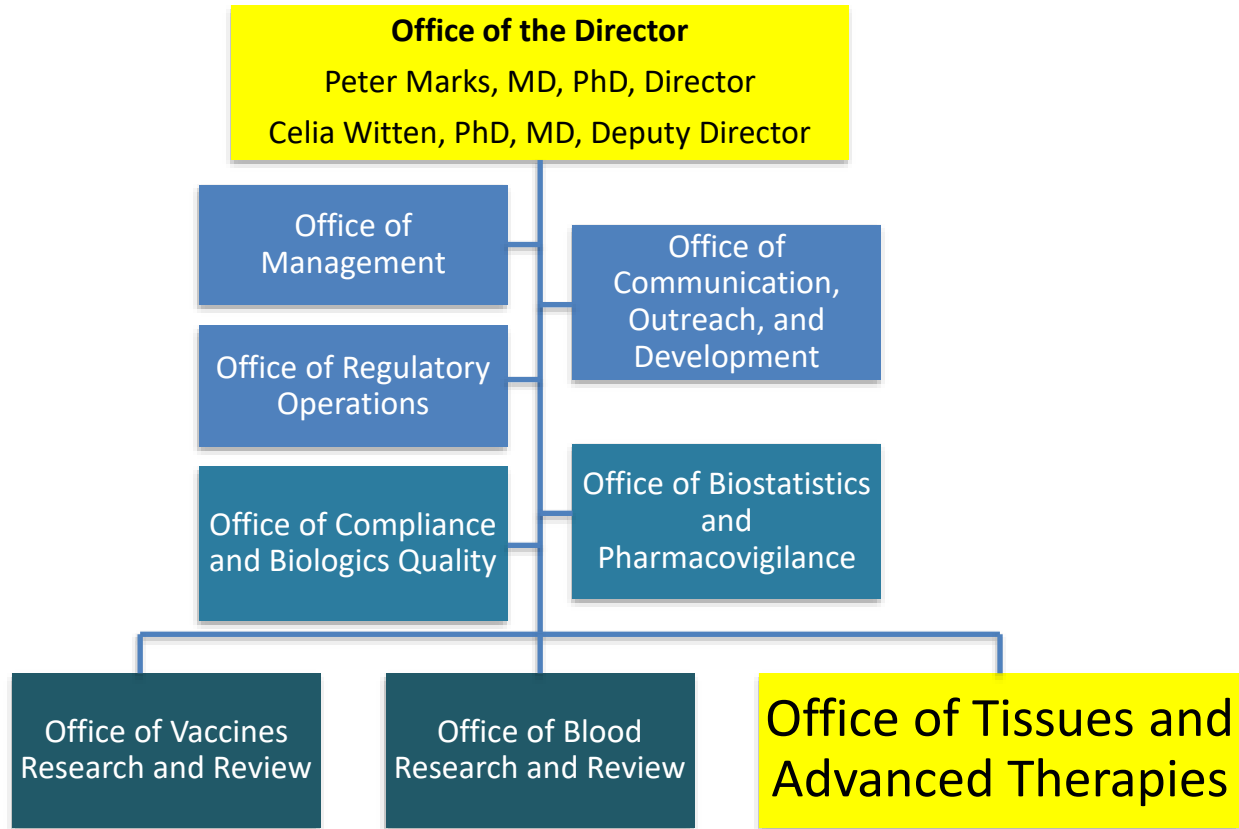
Center for
Food Safety
and
Applied
Nutrition
(CFSAN)

National
Center for
Toxicological
Research
(NCTR)

Center for
Tobacco
Products
(CTP)

Oncology Center of Excellence (OCE)

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



- 21 laboratories
- 51 publications in 2021
- 47 external conference presentations in 2021

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

- LUXTURN A (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



SUPPLEMENTARY VIDEO 1A

Maguire et al
"Treatment of Leber Congenital AMaurosis due to RPE65 Mutations
in Children and Adults using Adeno-Associated Virus (AAV)-mediated
Gene Delivery

CH09, day 90,
Navigation using untreated eye

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

Multi-luminance Mobility Test – Luxturna-treated eye



SUPPLEMENTARY VIDEO 1B

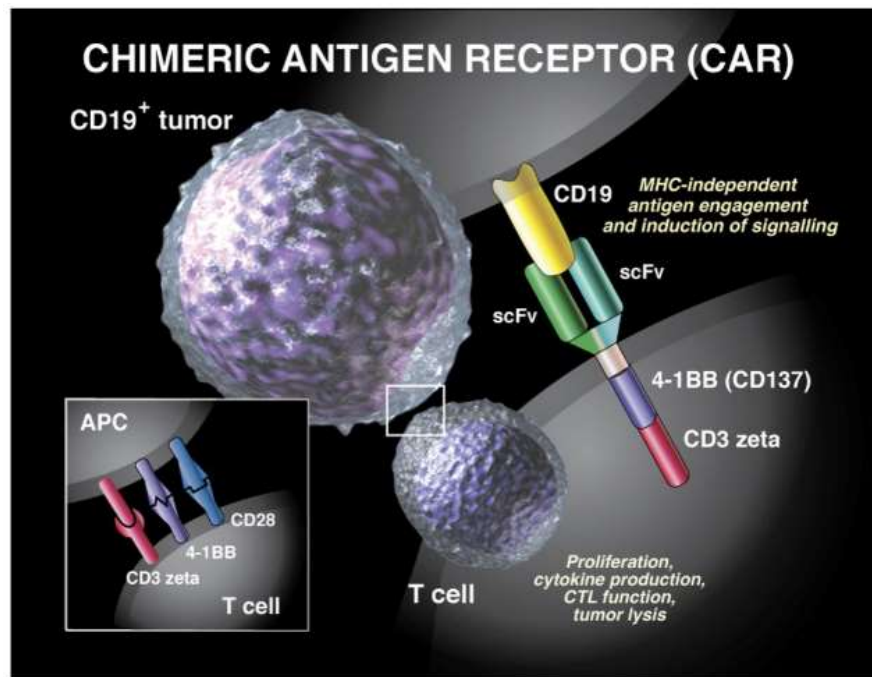
Maguire et al

**"Treatment of Leber Congenital AMAurosis due to RPE65 Mutations
in Children and Adults using Adeno-Associated Virus (AAV)-mediated
Gene Delivery**

**CH09, day 90,
Navigation using treated eye**

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

CAR T Cells: Ex vivo Gene Therapy



- [KYMRIA](#) (tisagenlecleucel)
- [YESCARTA](#) (axicabtagene ciloleucel)
- [TECARTUS](#) (brexucabtagene autoleucel)
- [BREYANZI](#) (lisocabtagene maraleucel)
- [ABECMA](#) (idecabtagene vicleucel)
- [CARVYKTI](#) (ciltacabtagene autoleucel)

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

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



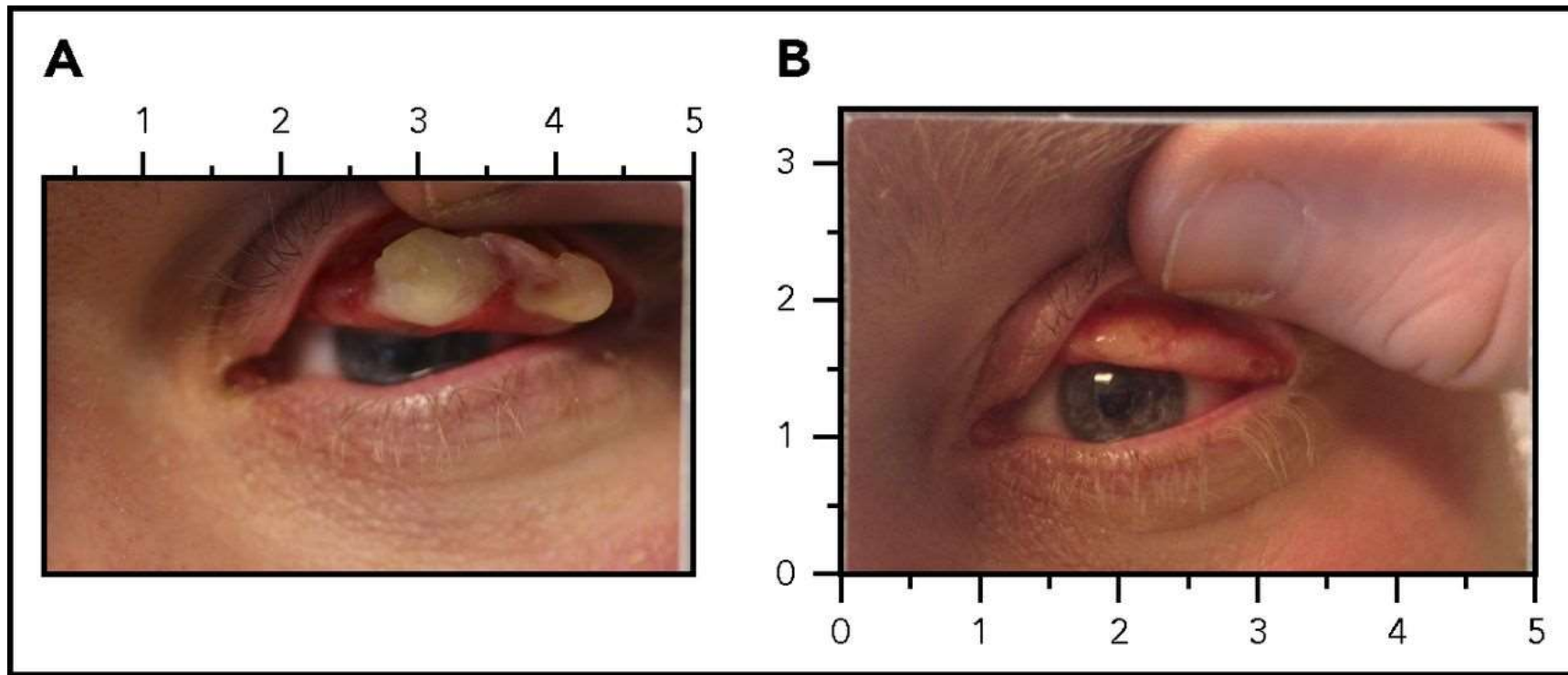
Holmes, James H 4th et al. *Burns : journal of the International Society for Burn Injuries* vol. 45,8 (2019): 1749-1758.

Purified Plasma Protein



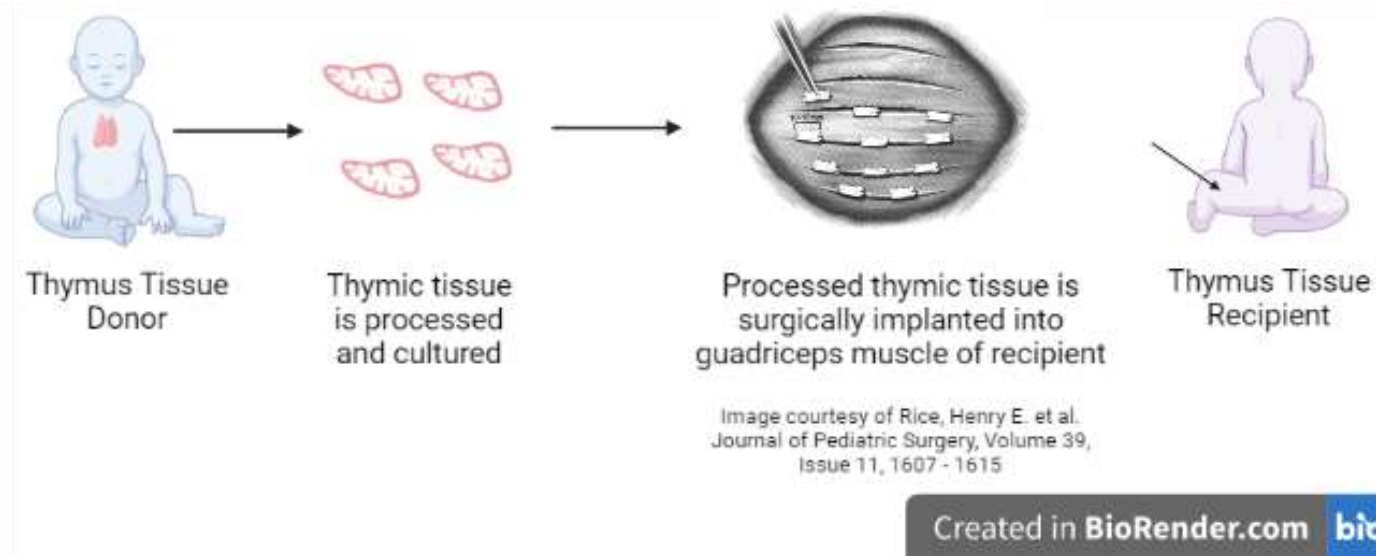
- RYPLAZIM (plasminogen, human-tvmh)
- Treatment of plasminogen deficiency type 1 (hypoplasminogenemia)
 - Disorder can impair normal tissue and organ function, may lead to blindness

Effect of RYPLAZIM on Ligneous Lesions



Allogeneic Processed Thymus Tissue

- RETHYMIC (allogeneic processed thymus tissue-agdc)
- Immune reconstitution in pediatric patients with congenital athymia
 - Rare immune disorder, typically leads to death within first two years of life

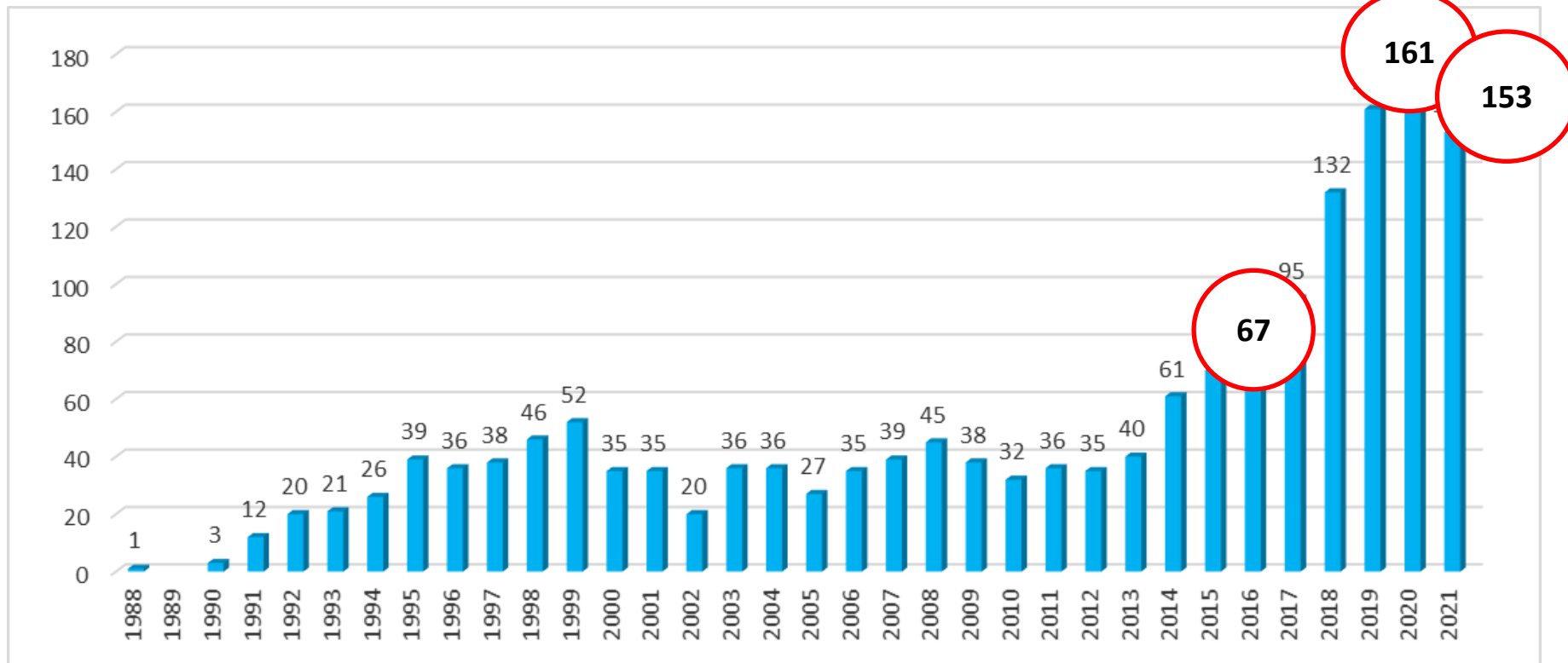




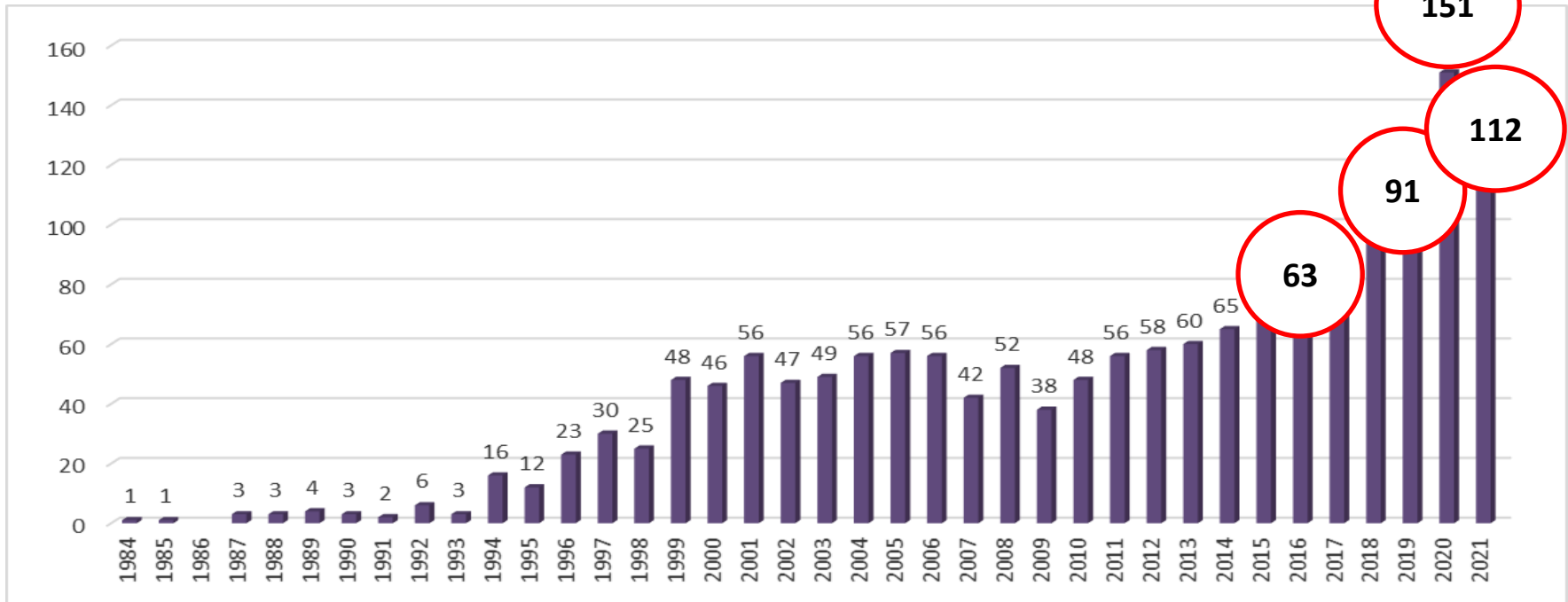
OTAT Products

Facilitating Development

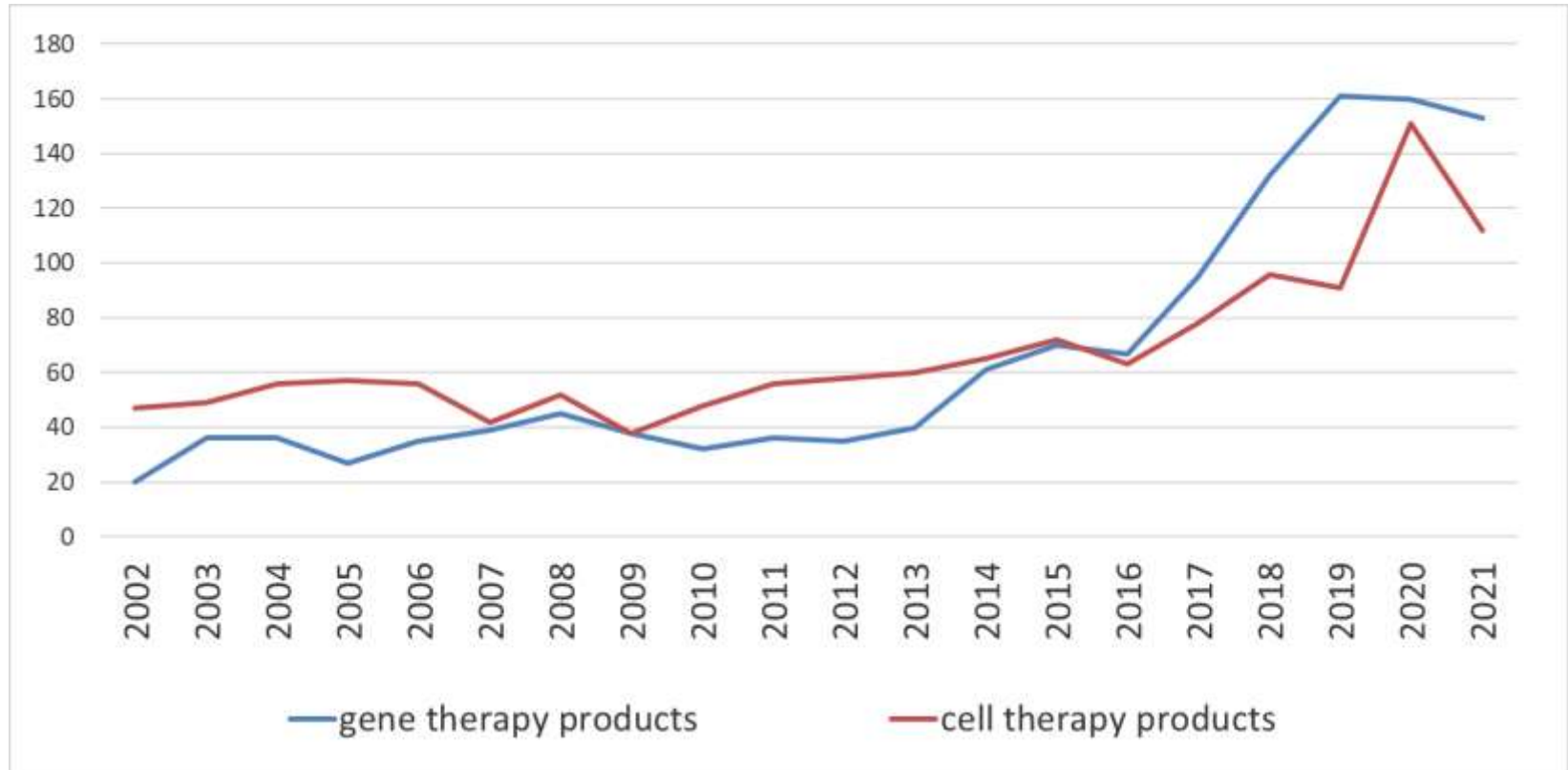
Research INDs: Gene Therapy



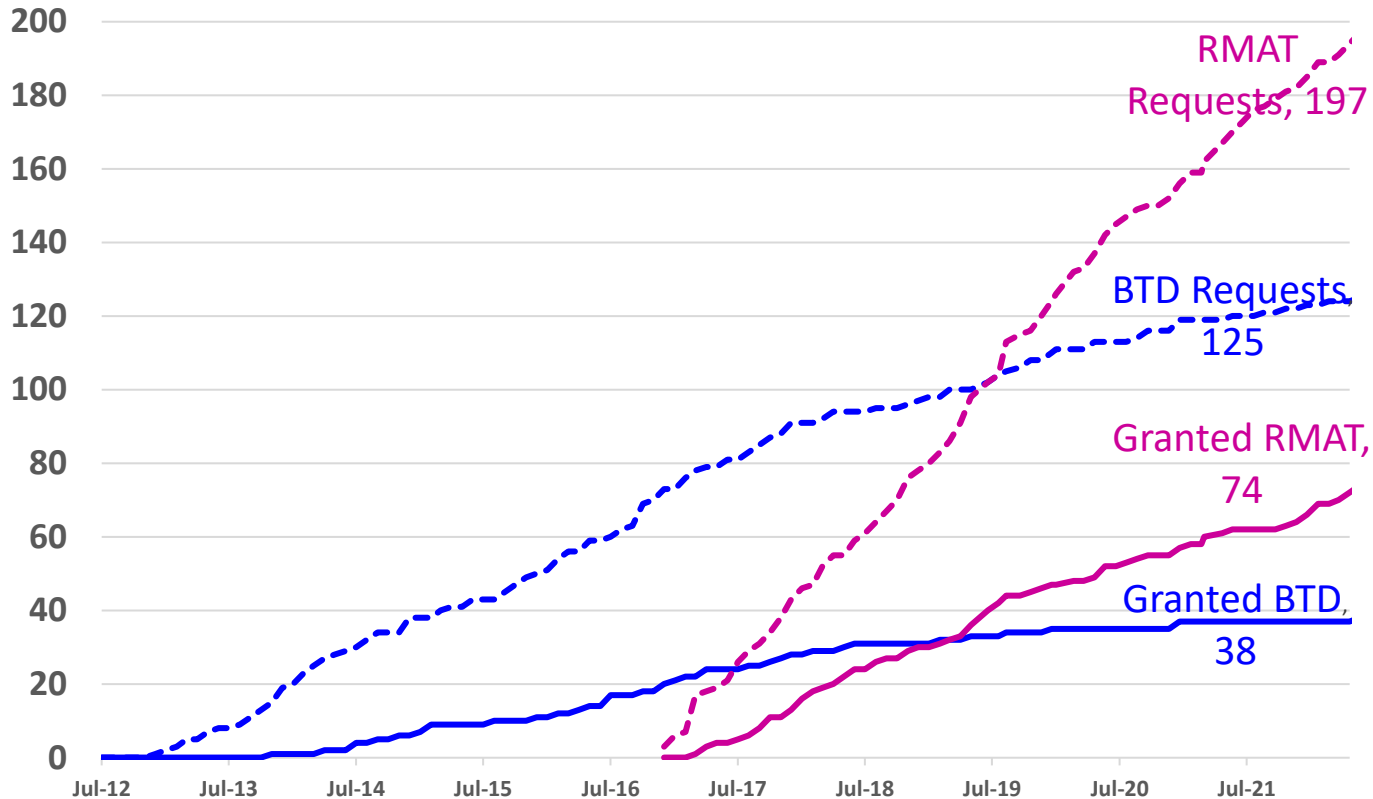
Research INDs: Cell Therapy



Cell and Gene Therapies: Research INDs 2002 – 2021



Cumulative Overview of BTD and RMAT Designation Requests (excludes withdrawn and pending requests)



Summary



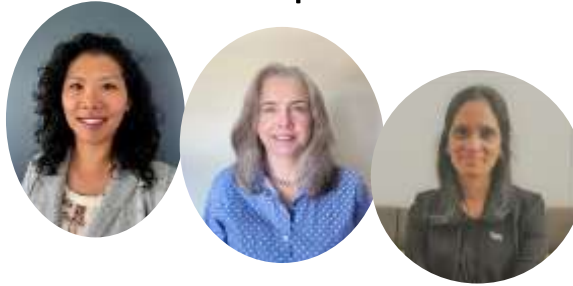
- Scientific advances have spurred recent growth in research and development of advanced therapies.
- OTAT is dedicated to facilitating the development of novel products to treat serious and life-threatening diseases.

Acknowledgements



- Division of Cellular and Gene Therapies

- Alyssa Kitchel, PhD
- Carrie Laurencot, PhD
- Archana Siddam, PhD



- Division of Clinical Evaluation and Pharmacology/Toxicology

- Patricia Beaston, MD, PhD
- Asha Das, MD
- Larissa Lapteva, MD, MHS, MBA
- Rosa Sherafat-Kazemzadeh, MD
- Melek Sunay, PhD



Acknowledgements



- Division of Plasma Protein Therapeutics

- Mikhail Ovanesov, PhD



- Division of Regulatory Project Management

- Eden Chane
- Crystal Melendez, MT, RN, BSN, DCPM



- Immediate Office of the Director

- Judith Arcidiacono, MS
- Anne Rowzee, PhD



Acknowledgements



- OCBQ/Division of Manufacturing and Product Quality

- Emnet Yitbarek, PhD



- Office of Biostatistics and Pharmacovigilance

- Meghna Alimchandani, MD
- Joyce Obidi, PhD



- Office of the CBER Center Director

- Manuel Osorio, PhD



Acknowledgements



- CBER Planning Committee

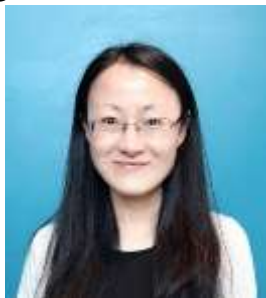
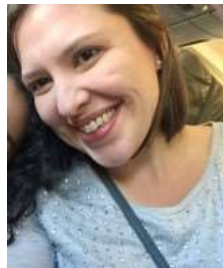
- Scott Brubaker
- Juliane Carvalho, MS
- Safa Karandish
- Larissa Lapteva, MD, MHS, MBA
- Graeme Price, PhD
- Stacey Rivette
- Irina Tiper, PhD
- Loni Warren Henderson



Acknowledgements



- Guidance and Analysis
 - Rachael Anatol, PhD
 - Larissa Lapteva, MD, MHS, MBA
 - 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



FDA Headquarters

- **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

- **Manufacturers Assistance and Technical Training Branch:** industry.biologics@fda.hhs.gov

- **Follow us on Twitter:** <https://www.twitter.com/fdacber>







Wilson W. Bryan, M.D.

wilson.bryan@fda.hhs.gov