U.S. FOOD & DRUG ADMINISTRATION

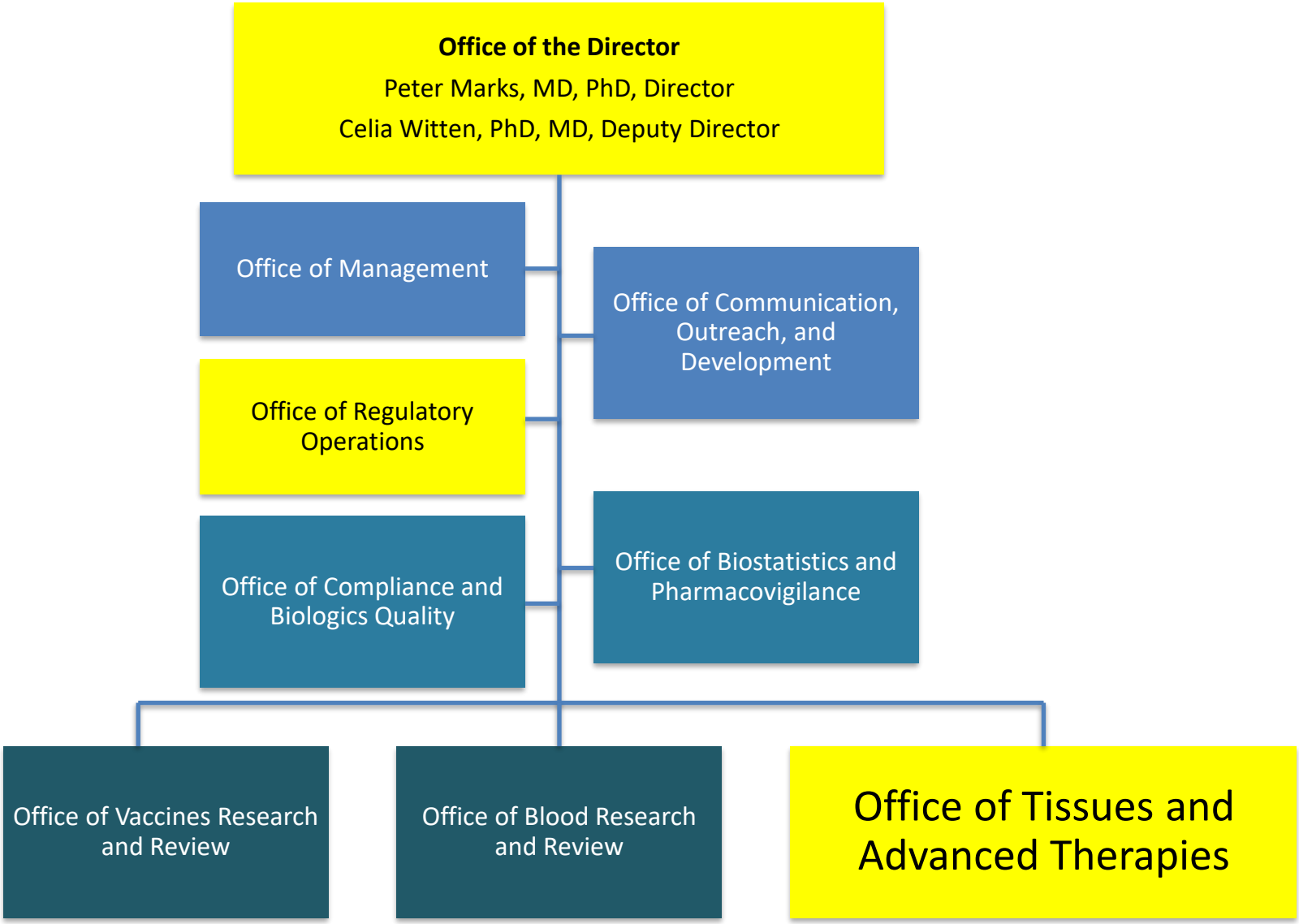
FDA / CBER
Office of Tissues and Advanced Therapies (OTAT)
Update

American Society of Gene & Cell Therapy (ASGCT)
Liaison Meeting

November 14, 2022

Wilson W. Bryan, MD

Center for Biologics Evaluation and Research (CBER)



Diversity of OTAT-Regulated Products

- **Gene therapies (GT)**
  - Ex vivo genetically modified cells
  - Non-viral vectors (e.g., plasmids)
  - Replication-deficient viral vectors (e.g., adenovirus, adeno-associated virus, lentivirus)
  - Replication-competent viral vectors (e.g., measles, adenovirus, vaccinia)
  - Microbial vectors (e.g., Listeria, Salmonella)
- **Stem cells/stem cell-derived**
  - Adult (e.g., hematopoietic, neural, cardiac, adipose, mesenchymal)
  - Perinatal (e.g., placental, umbilical cord blood)
  - Fetal (e.g., neural)
  - Embryonic
  - Induced pluripotent stem cells (iPSCs)
- **Products for xenotransplantation**

- **Functionally mature/differentiated cells** (e.g., retinal pigment epithelial cells, pancreatic islets, chondrocytes, keratinocytes)
- **Therapeutic vaccines and cellular immunotherapies** including antigen-specific active immunotherapies
- **Blood- and Plasma-derived products**
  - Coagulation factors
  - Fibrin sealants
  - Fibrinogen
  - Thrombin
  - Plasminogen
  - Immune globulins
  - Anti-toxins
  - Venom antisera for snakes, scorpions, and spiders
- **Combination products**
  - Engineered tissues/organs
- **Devices**
- **Tissues**

Approved Cellular Therapy Products

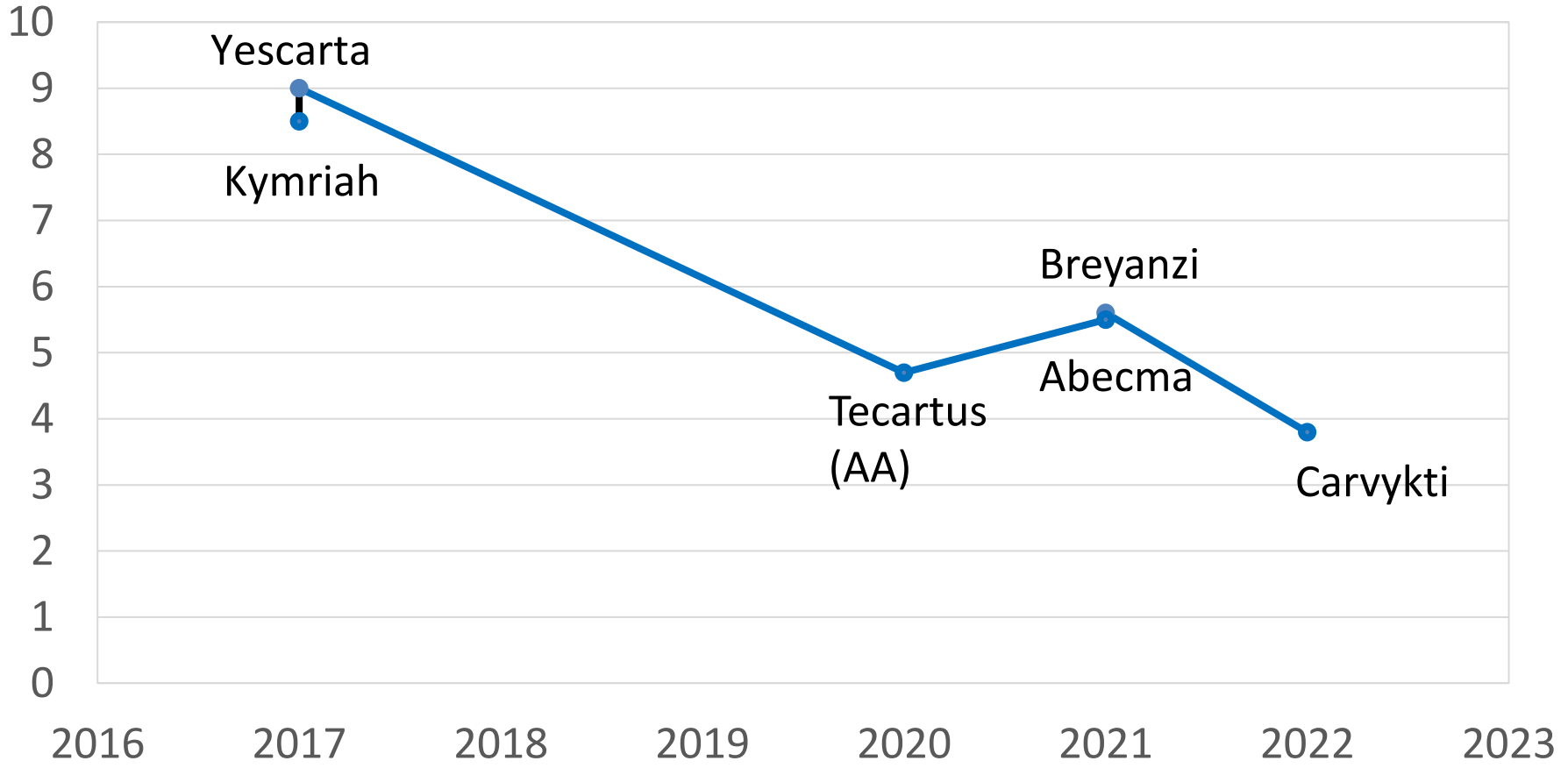
- PROVENGE (sipuleucel-T)
- Hematopoietic Progenitor Cells, Cord Blood
- LAVIV (azficel-T)
- GINTUIT (allogeneic Cultured Keratinocytes and Fibroblasts in bovine collagen)
- MACI (autologous Cultured Chondrocytes on porcine collagen membrane)
- STRATAGRAFT (allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen-dsat)
- RETHYMIC (allogeneic processed thymus tissue–agdc)

Approved Gene Therapies

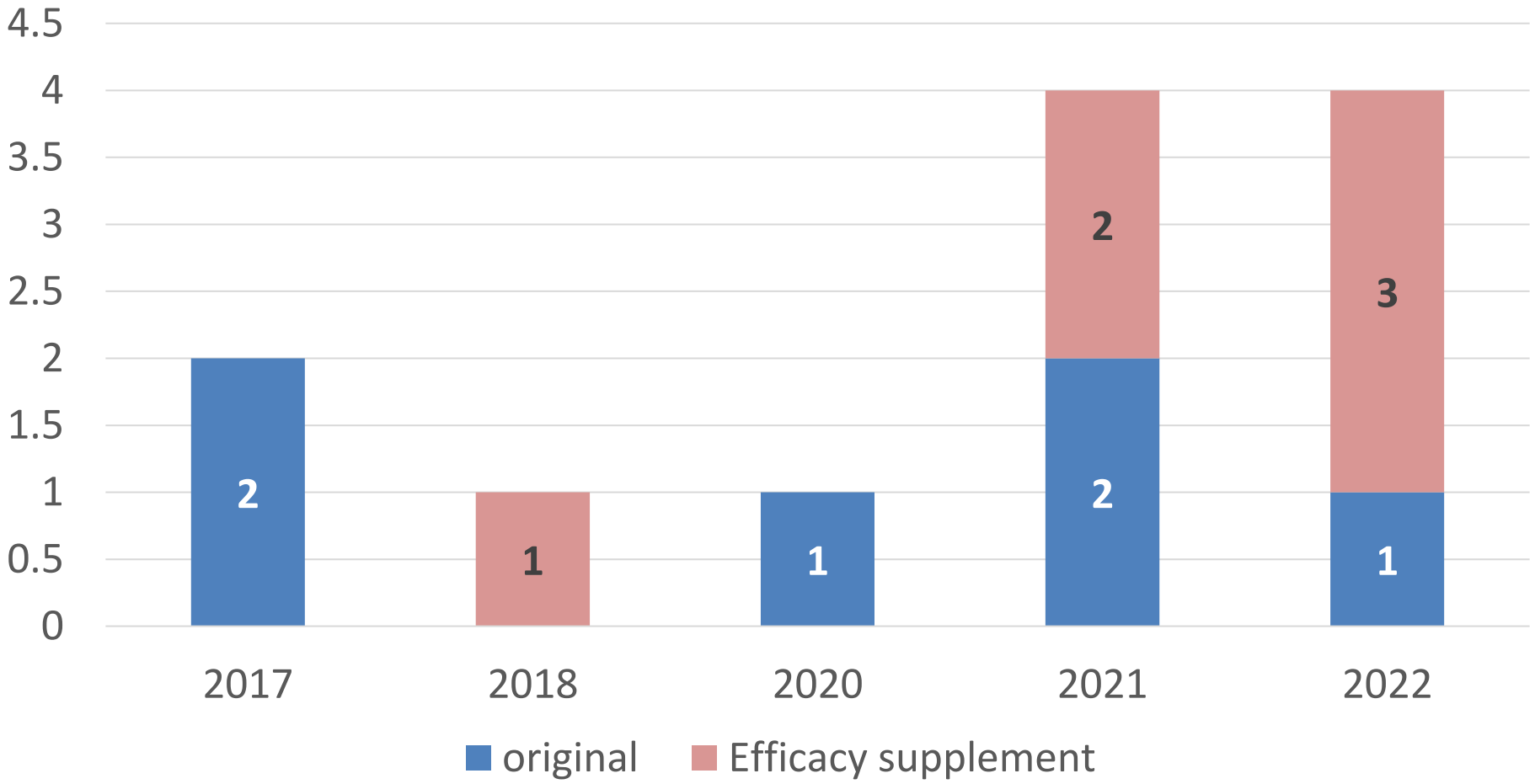
- KYMRIAH (tisagenlecleucel)
- YESCARTA (axicabtagene ciloleucel)
- TECARTUS (brexucabtagene autoleucel)
- BREYANZI (lisocabtagene maraleucel)
- ABECMA (idecabtagene vicleucel)
- CARVYKTI (ciltacabtagene autoleucel)

- LUXTURNA (voretigene neparvovec-rzyl)
- ZOLGENSMA (onasemnogene abeparvovec-xioi)
- **ZYNTEGLO** (betibeglogene autotemcel)
- **SKYSONA** (elivaldogene autotemcel)

CAR T product approval – Years from IND submission to original BLA approval



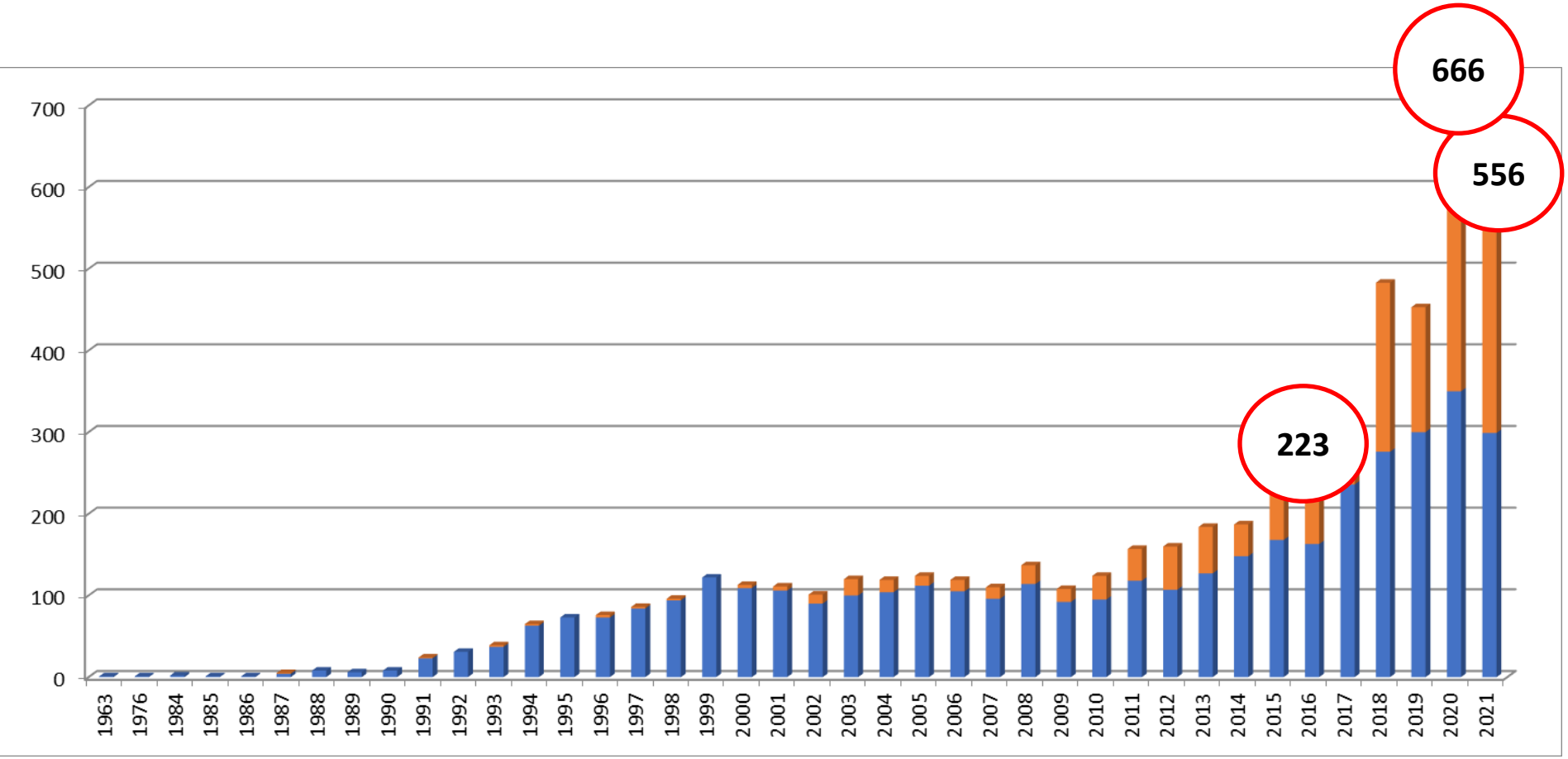
CAR T product original BLA and efficacy supplement approvals



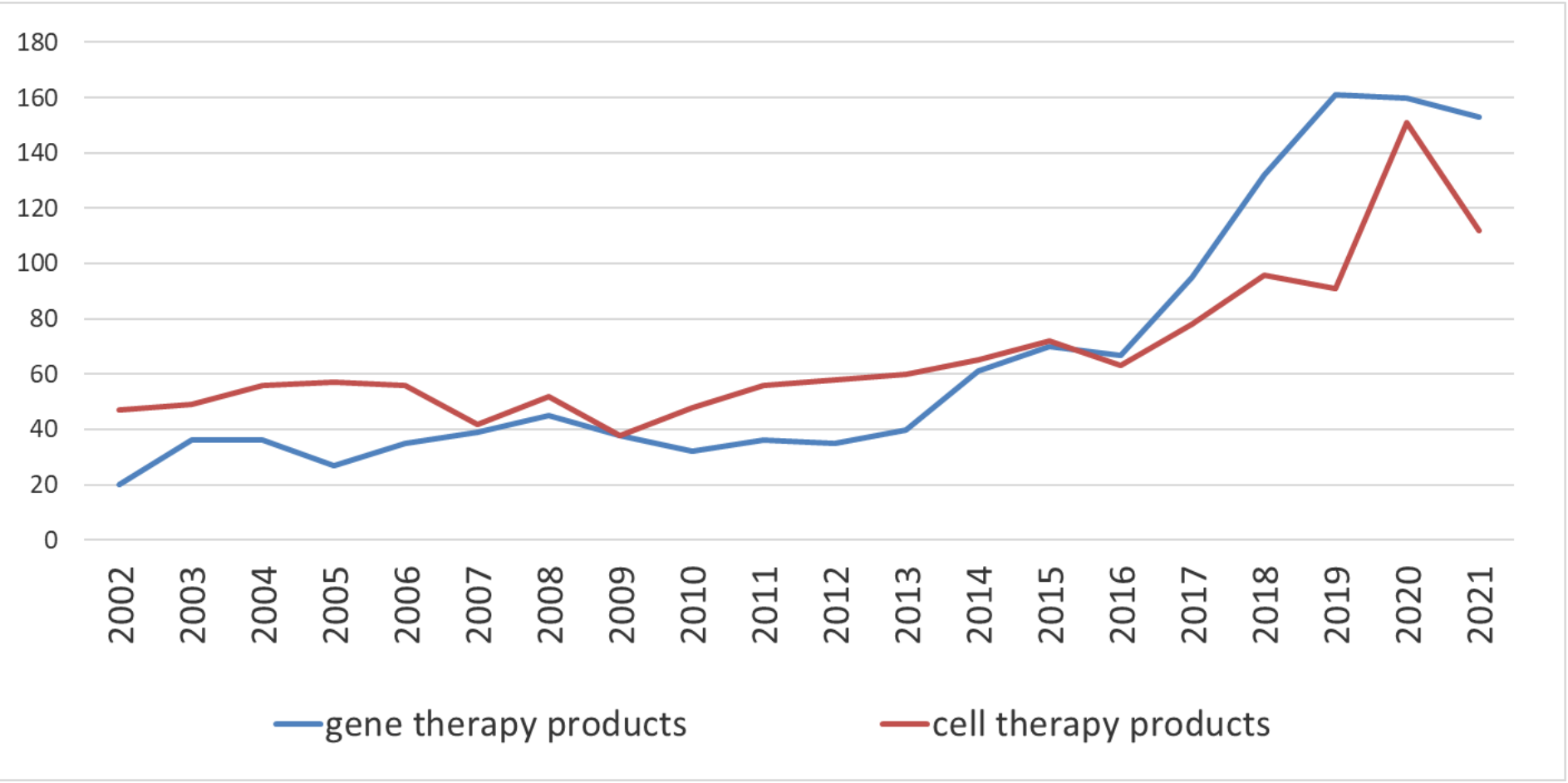
All OTAT INDS

(i.e., Research and Expanded Access (EA))

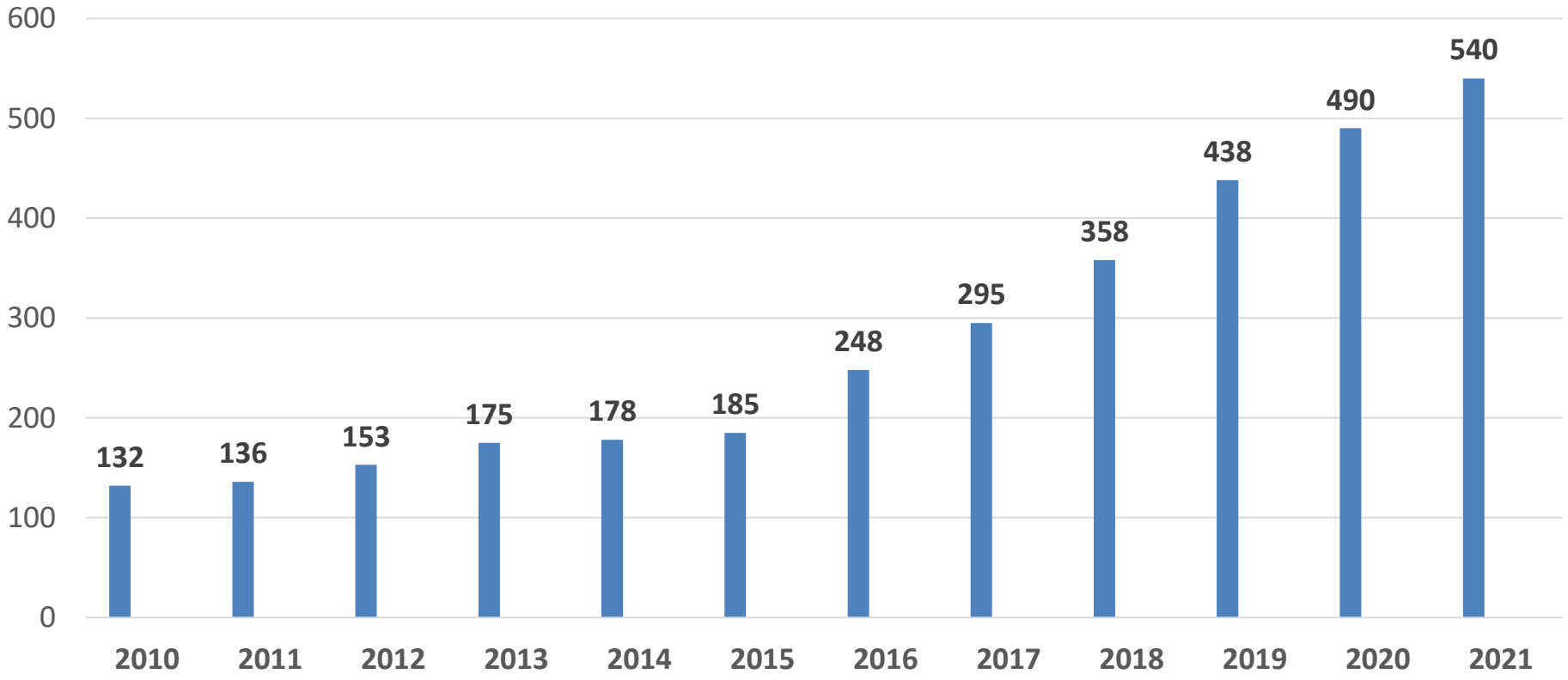
1963 – 2021



Cell and Gene Therapies: Research INDs 2002 – 2021

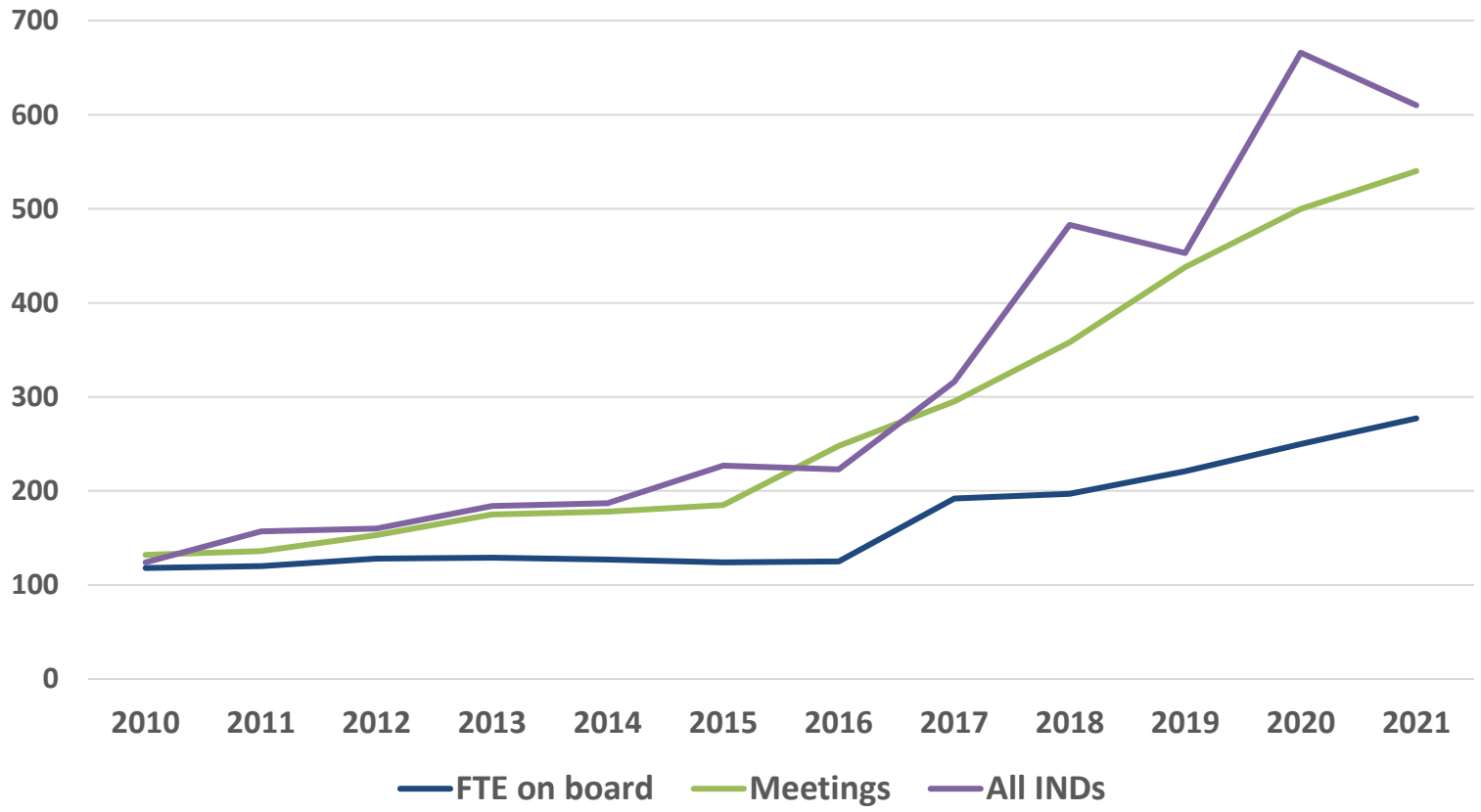


All Meetings (Type A, B, C, and Other)

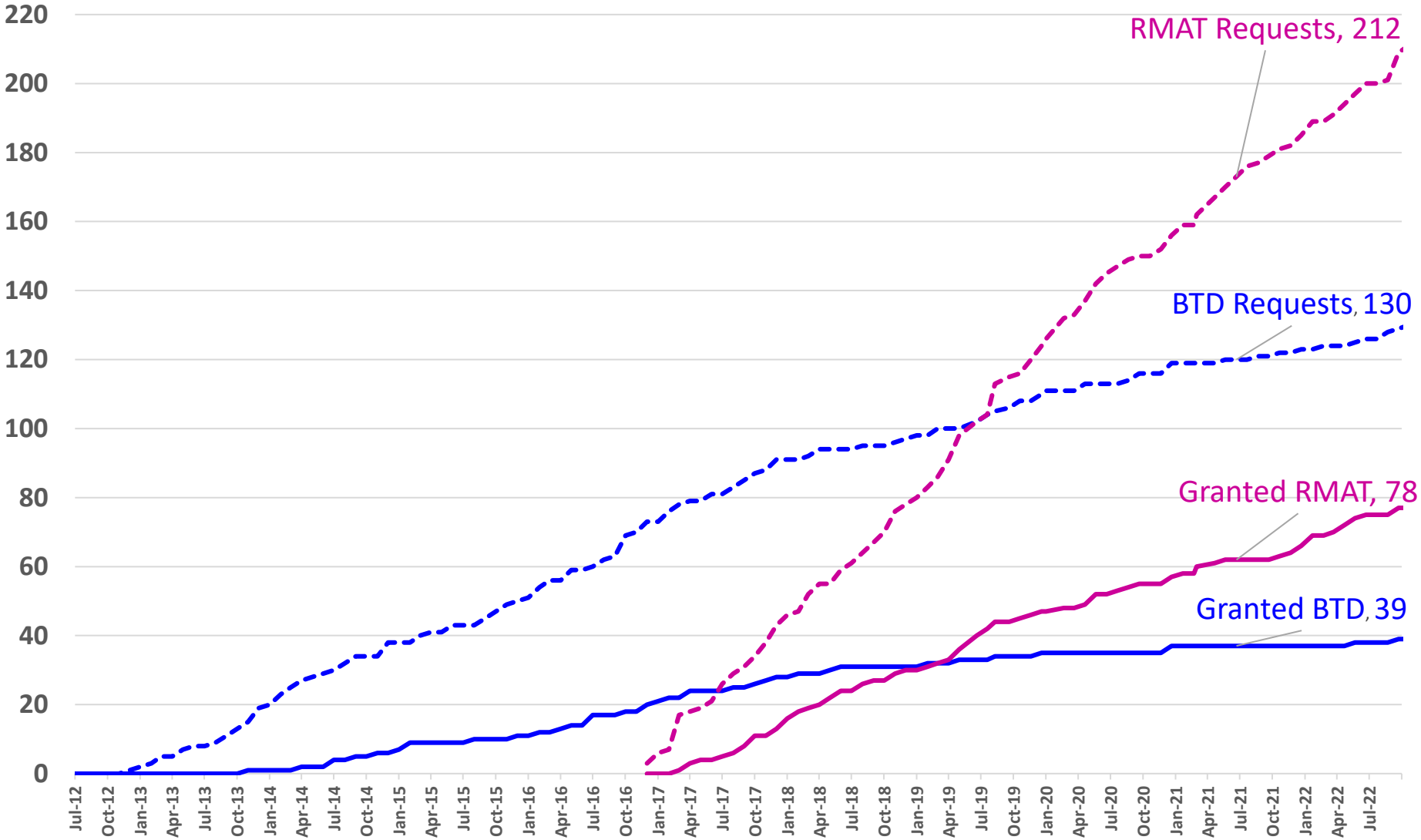


OTAT workload outpaces FTE increases

FTE, Total Meetings, and INDs (across OTAT)



Breakthrough (BTD) and RMAT Designation Requests



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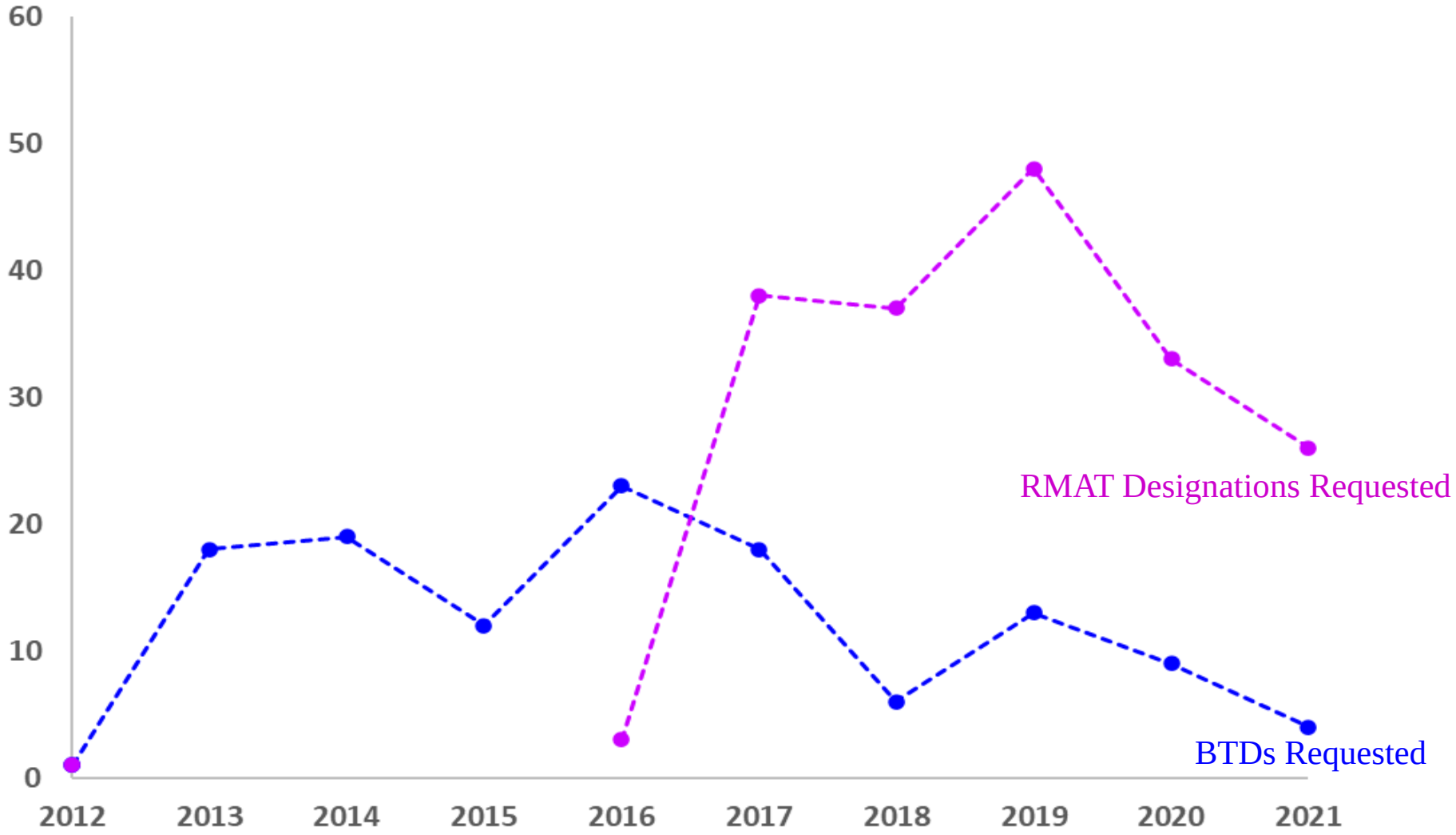
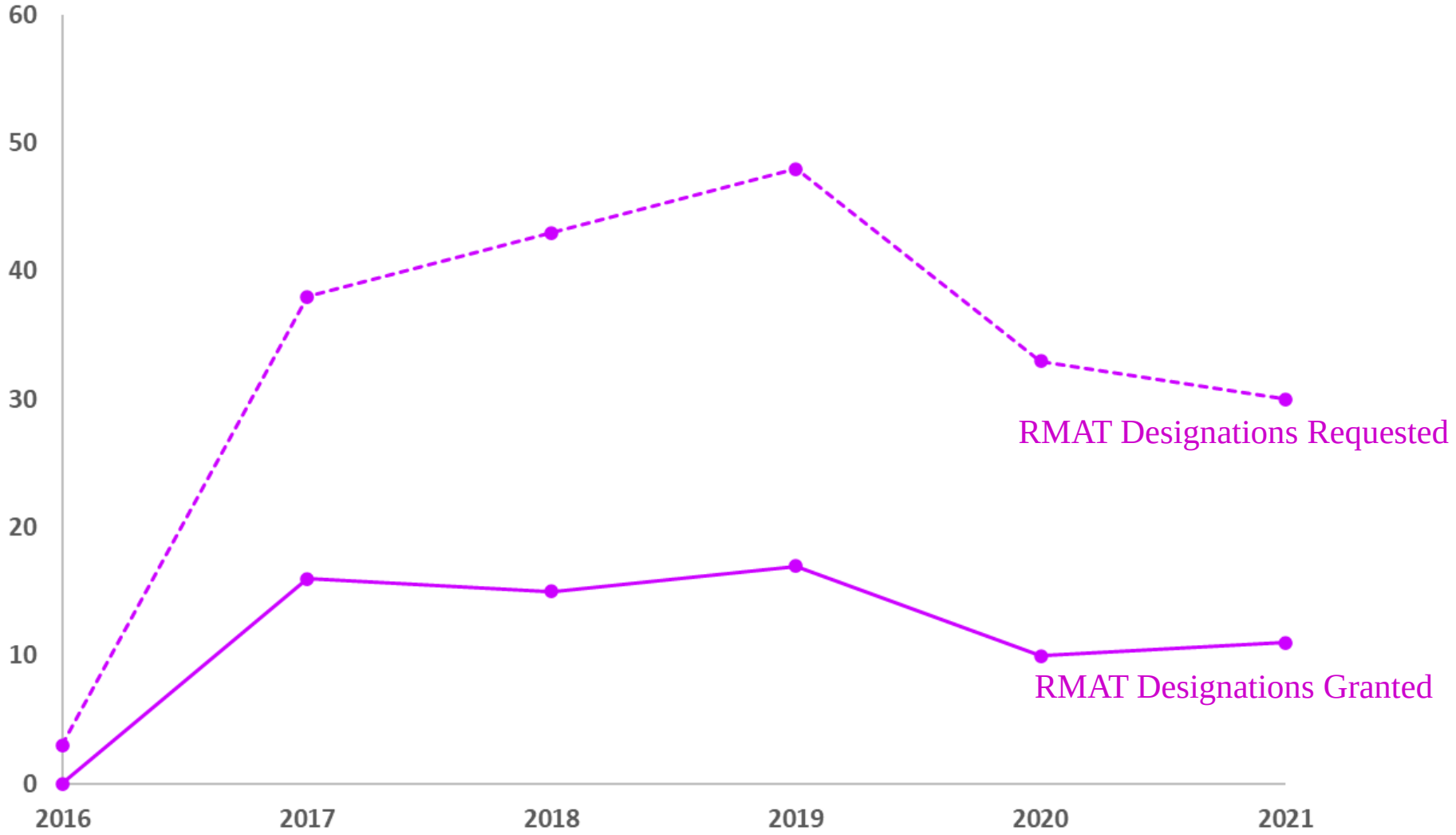
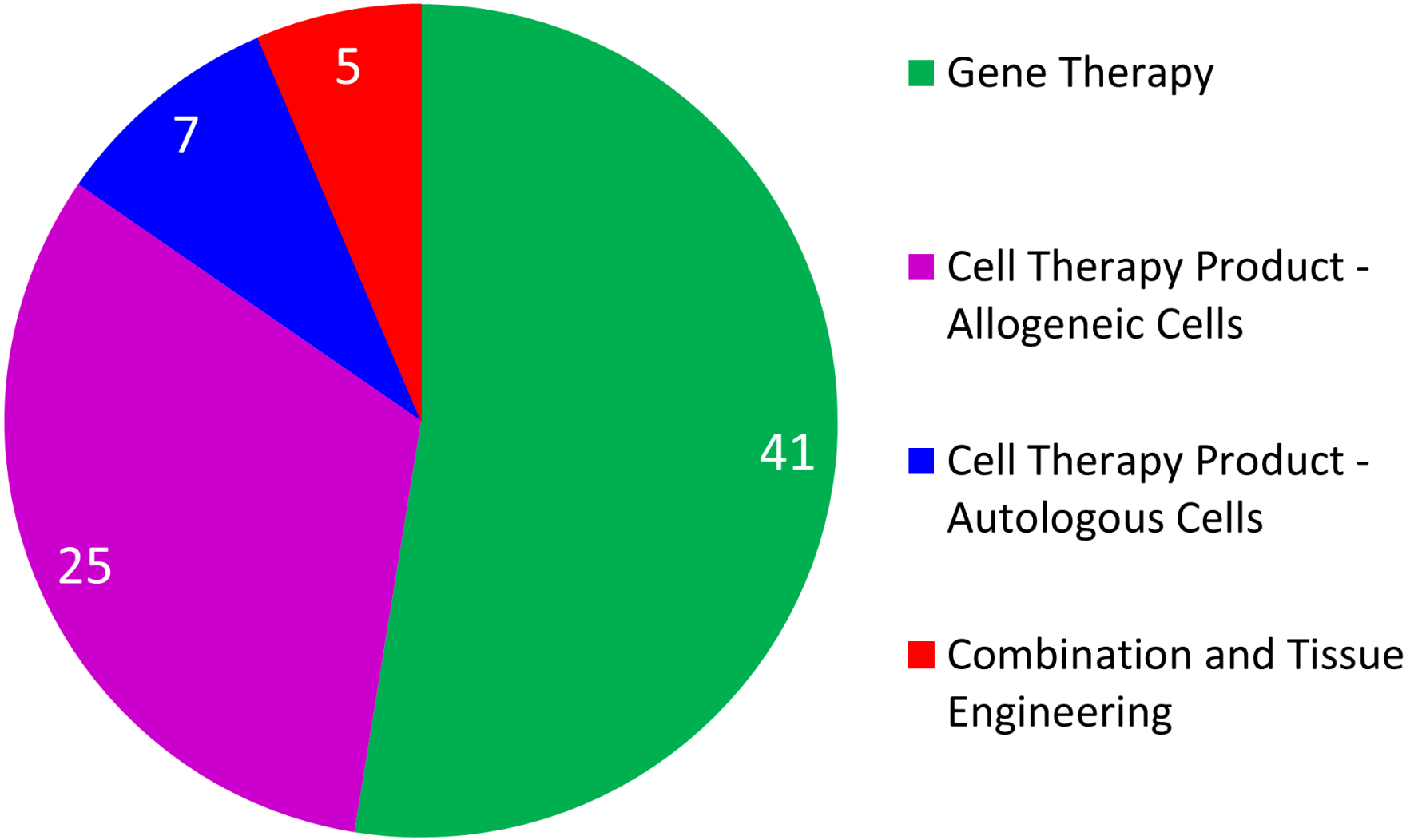


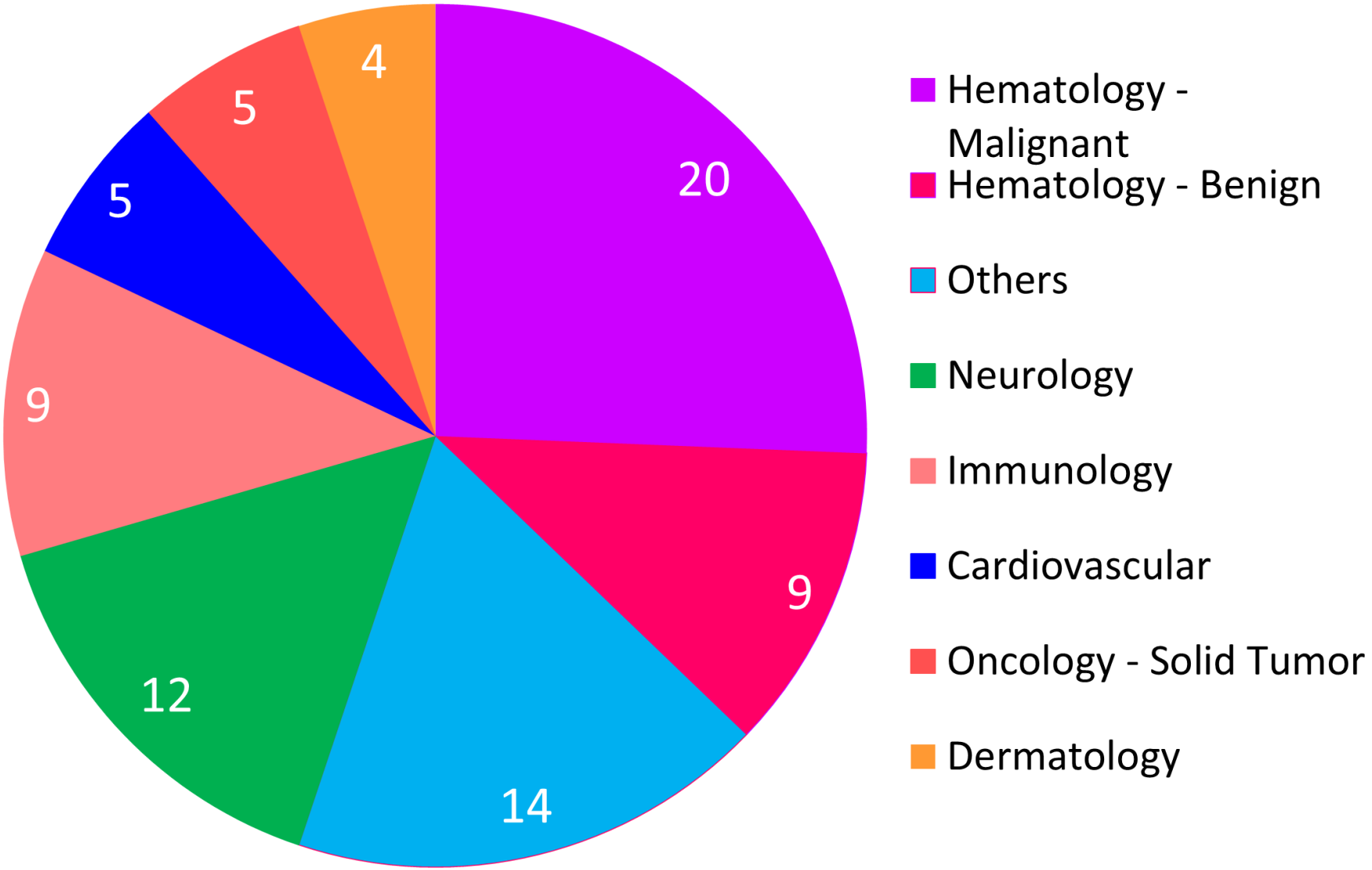
RMAT Designation Requests



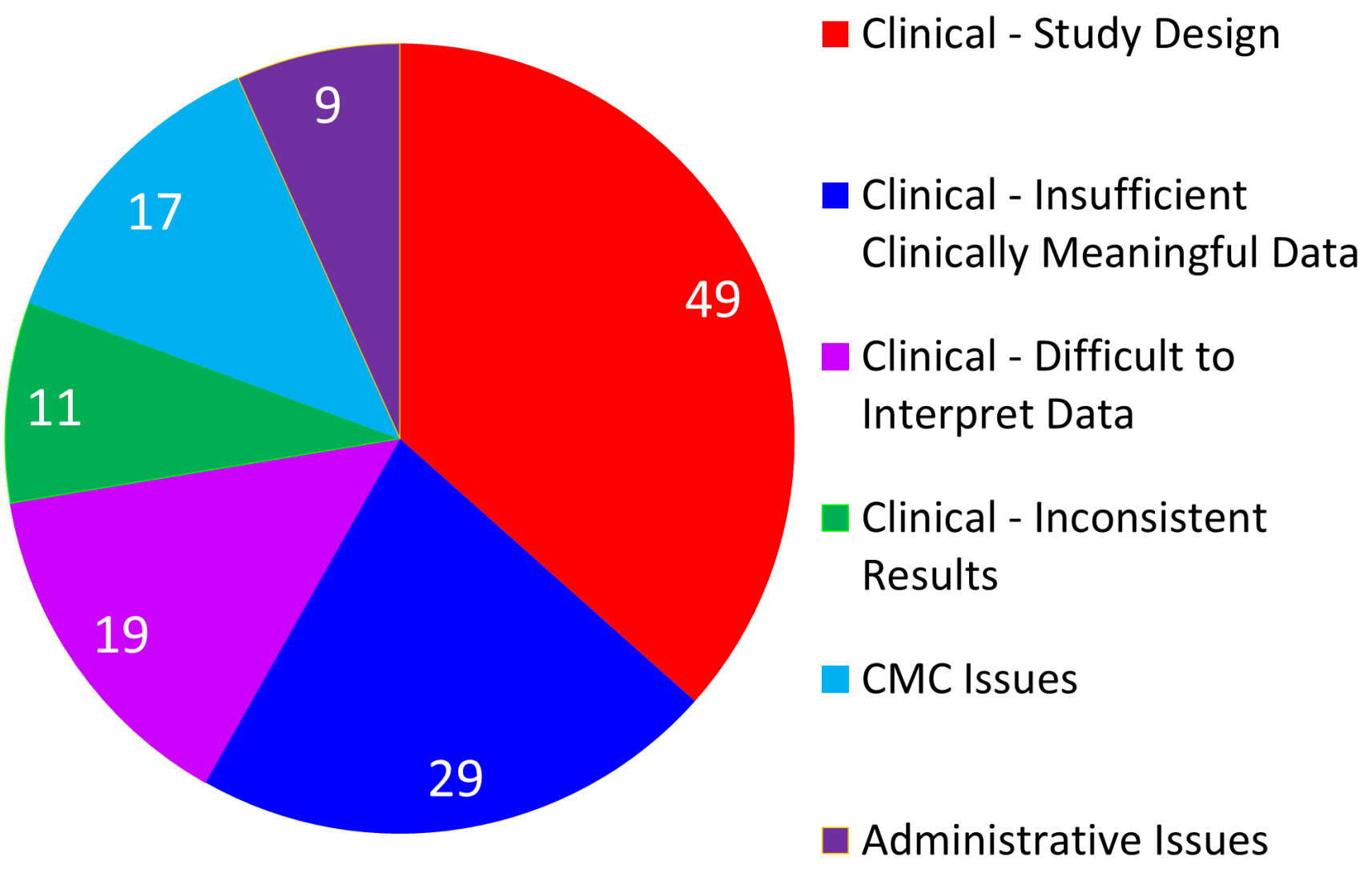
Granted RMAT Designation Requests - Distribution by Product Type



Granted RMAT Designation Requests Specialties



Reasons for Denied RMAT Designations



Reasons for Denied RMAT Designations

- Administrative Reasons
  - Inactive IND
  - No preliminary clinical evidence submitted
- CMC Reasons
  - Different product, lack of product comparability data
  - Not a regenerative advanced medicine therapy
- Insufficient Preliminary Clinical Evidence
  - Study design issues
  - Difficult to interpret data
  - Inconsistent results among endpoints or subject subgroups
  - Insufficient clinically meaningful data

Resubmissions

- 40 re-submissions
  - 33 INDs
  - 33% success rate

- Content
  - New Look
  - New Analysis
  - New Data

Marketing Approvals

- Stratagraft (allogeneic cultured keratinocytes and dermal fibroblasts in murine collagen-dsat)
- Breyanzi (lisocabtagene maraleucel)
- Rethymic (allogeneic processed thymus tissue-agdc)

Increasing CBER Capacity

1) Reorganization

   Office of Therapeutic Products (OTP);

   super-office with six sub-offices

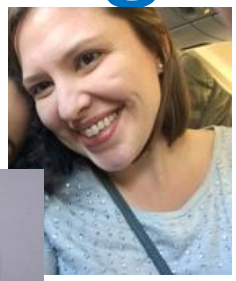
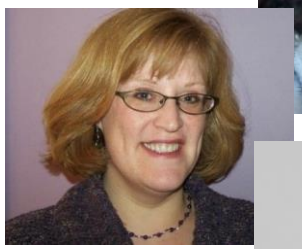
2) Increased resources (PDUFA VII)

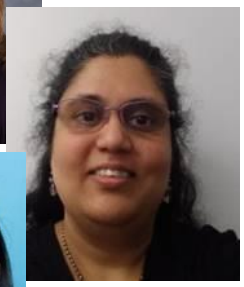
   228 FTEs for CBER

3) Enhance Communications

Acknowledgements

- Rachael Anatol, PhD
- Kim Benton, PhD
- Larissa Lapteva, MD
- Anne Rowzee, PhD
- Ramani Sista, PhD
- Xiaofei Wang, PhD
- Chris Joneckis, PhD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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
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