U.S. FOOD & DRUG ADMINISTRATION

Multiple Versions of Gene Therapy Products

Cellicon Valley '21: Future of Cell and Gene Therapies

May 6, 2021

Wilson W. Bryan, MD
Office of Tissues and Advanced Therapies (OTAT)
Center for Biologics Evaluation and Research (CBER)
United States Food and Drug Administration (FDA)

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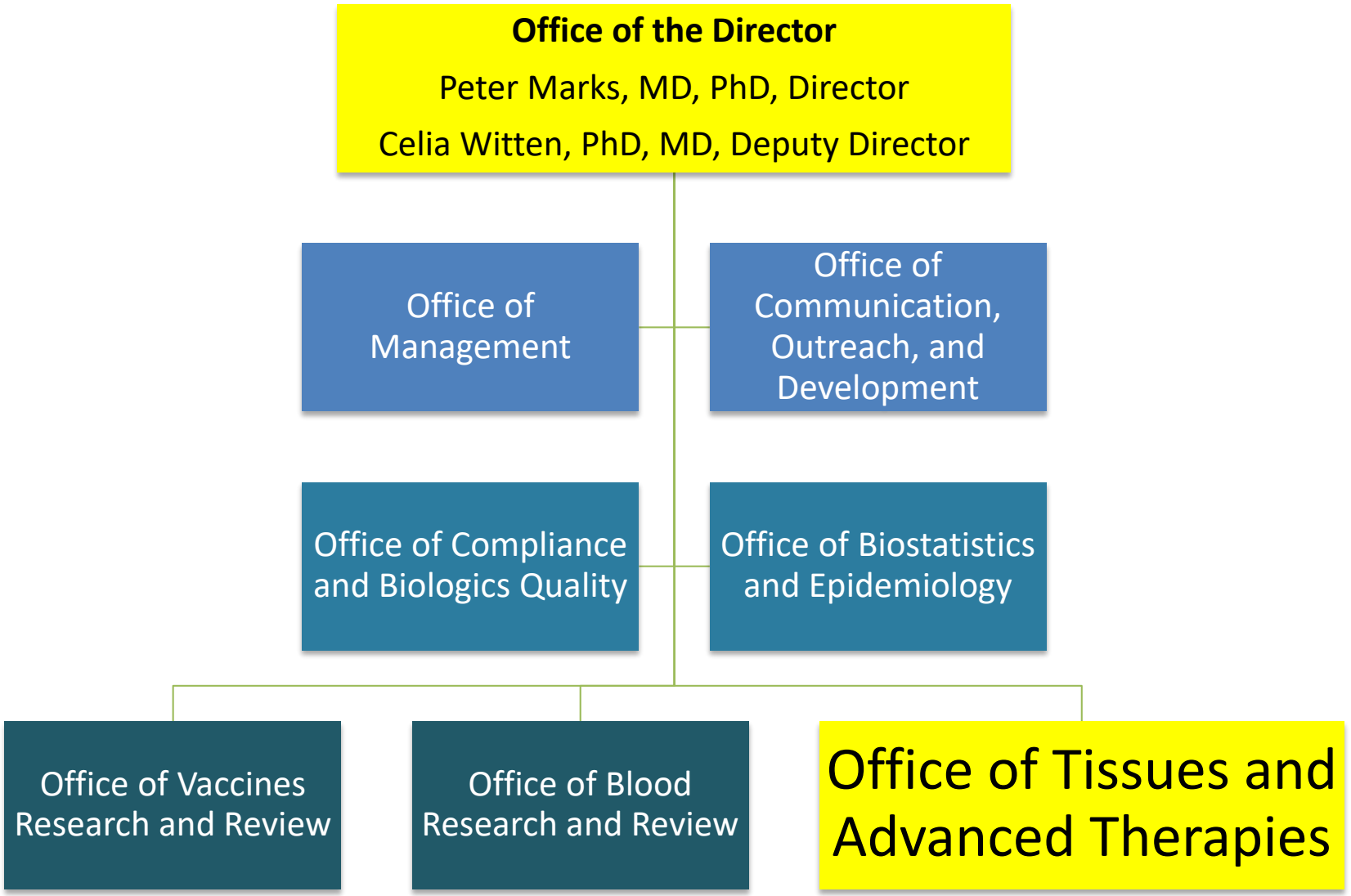
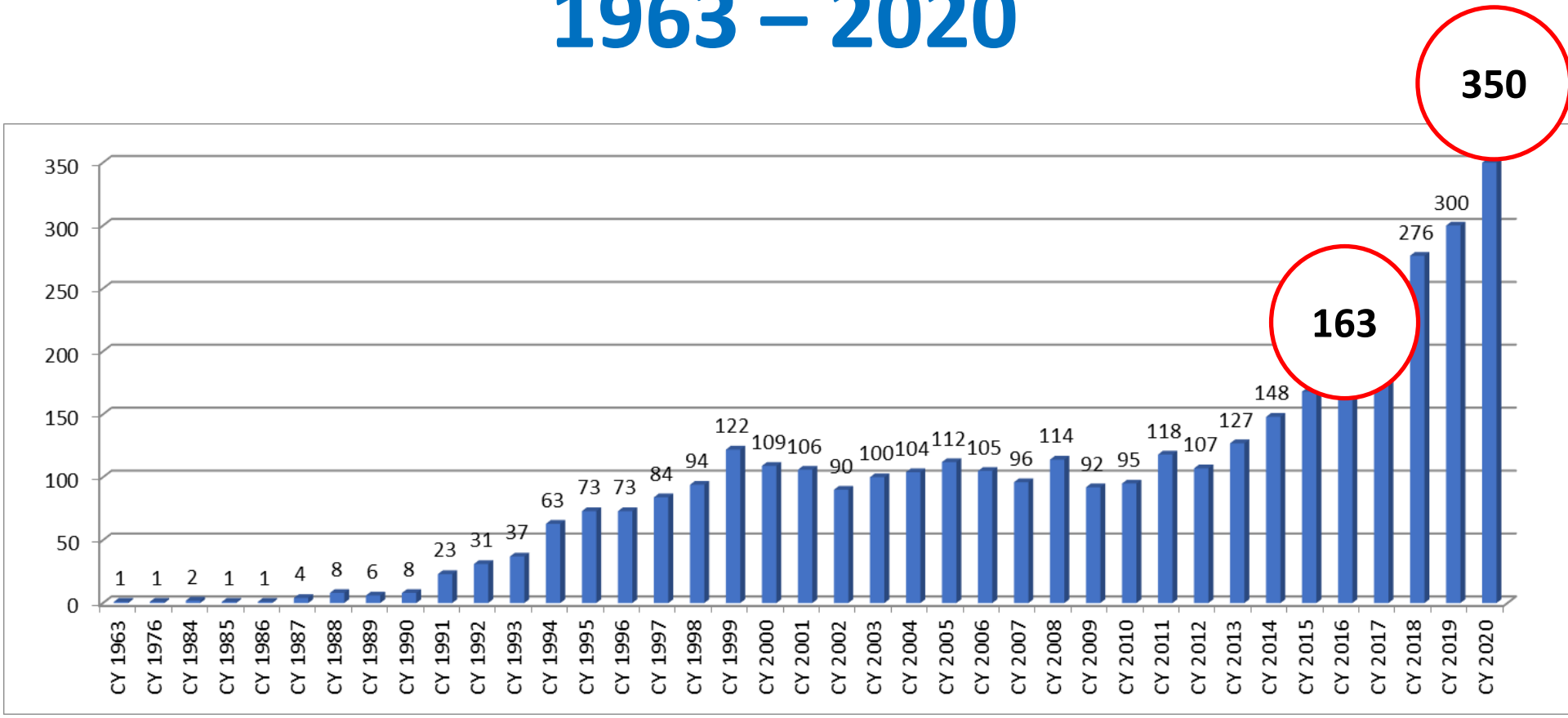


OTAT Research Investigational New Drug Applications (INDs) 1963 – 2020



Clinical Development

- Phase 1 objectives
  - Safety, tolerability, maximum tolerated dose (MTD), and activity / efficacy (if feasible)
  - Guide dosing and monitoring of subsequent Phase 2 studies

- Phase 2 objectives
  - Determine dose, route, regimen, population, endpoints, and estimated magnitude of effect
  - Guide design of subsequent confirmatory (Phase 3) studies

- Phase 3 objectives
  - Evidence of effectiveness and safety to support a marketing application (e.g., Biologics License Application (BLA))

Challenges

The development of gene therapy products often requires multiple iterations

- Redesign product to improve safety or efficacy
- Parallel first-in-human studies compare different versions of the product
  - A “winner” may emerge to move forward into later-phase trials.
- Each version of the product generally requires new nonclinical and manufacturing (CMC) information.
- Manufacturing methods for each version may evolve over the course of the trial.

Challenges

These INDs become very complex to review and keep track of.

When a new version of a product is added sequentially to an existing IND, FDA has no statutory 30-day review period.

Current Regulatory Flexibility

- Regulations do not limit the number of products or protocols per IND.

- FDA sometimes allows multiple products in one IND if the products work together and are being codeveloped, even if the products are very different.

- Stakeholders have requested guidance on how to structure these INDs and facilitate “umbrella” studies.

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Studying Multiple Versions of a Cellular or Gene Therapy Product in a Clinical Trial

Draft Guidance for Industry

Date: Coming in 2021

Draft Guidance: Studying Multiple Versions of a Cellular or Gene Therapy Product in a Clinical Trial: Projected Scope

- Cell and gene therapy products
- Early-phase products
- Related versions of a product
- All products have the same sponsor
- All versions of the product target the same disease
- Products submitted to FDA either simultaneously or sequentially

Acknowledgements

- Rachael Anatol, PhD
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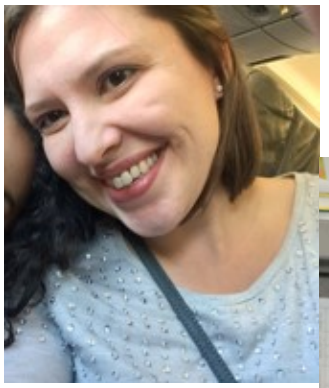

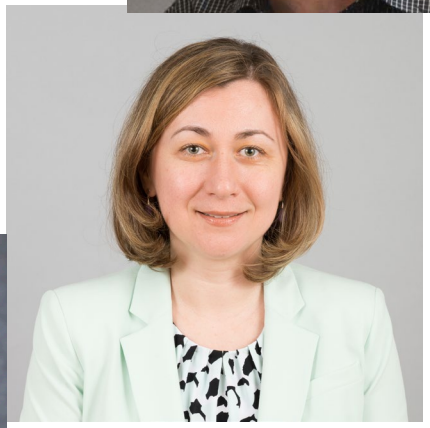

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FDA Headquarters

- **OTAT Learn Webinar Series:**

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

- **CBER website:** www.fda.gov/BiologicsBloodVaccines/default.htm
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