

Gene Therapies for Rare Diseases

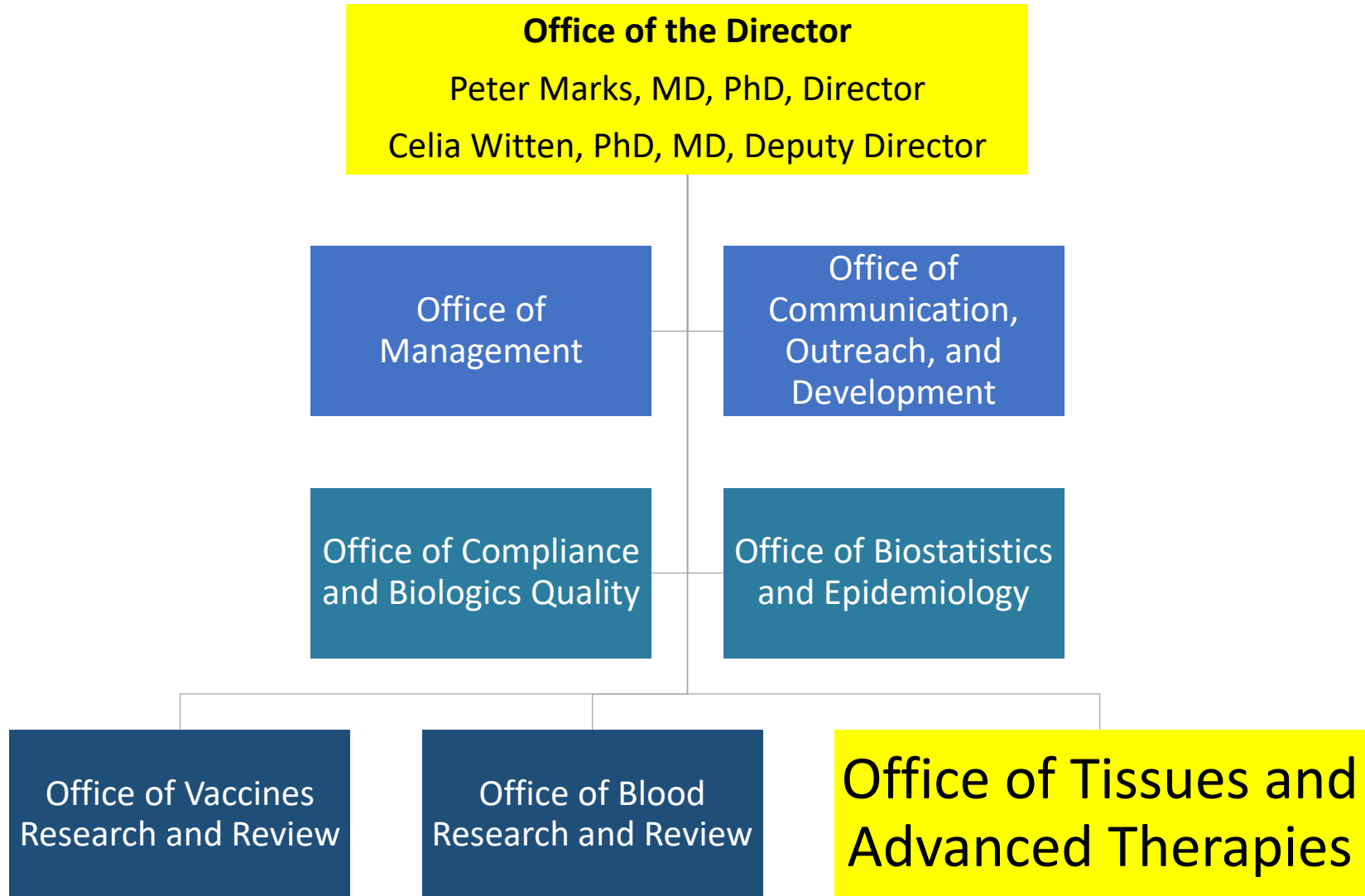
September 13, 2018

Rare Disease Scientific Workshop
Everylife Foundation for Rare Diseases
Washington, DC

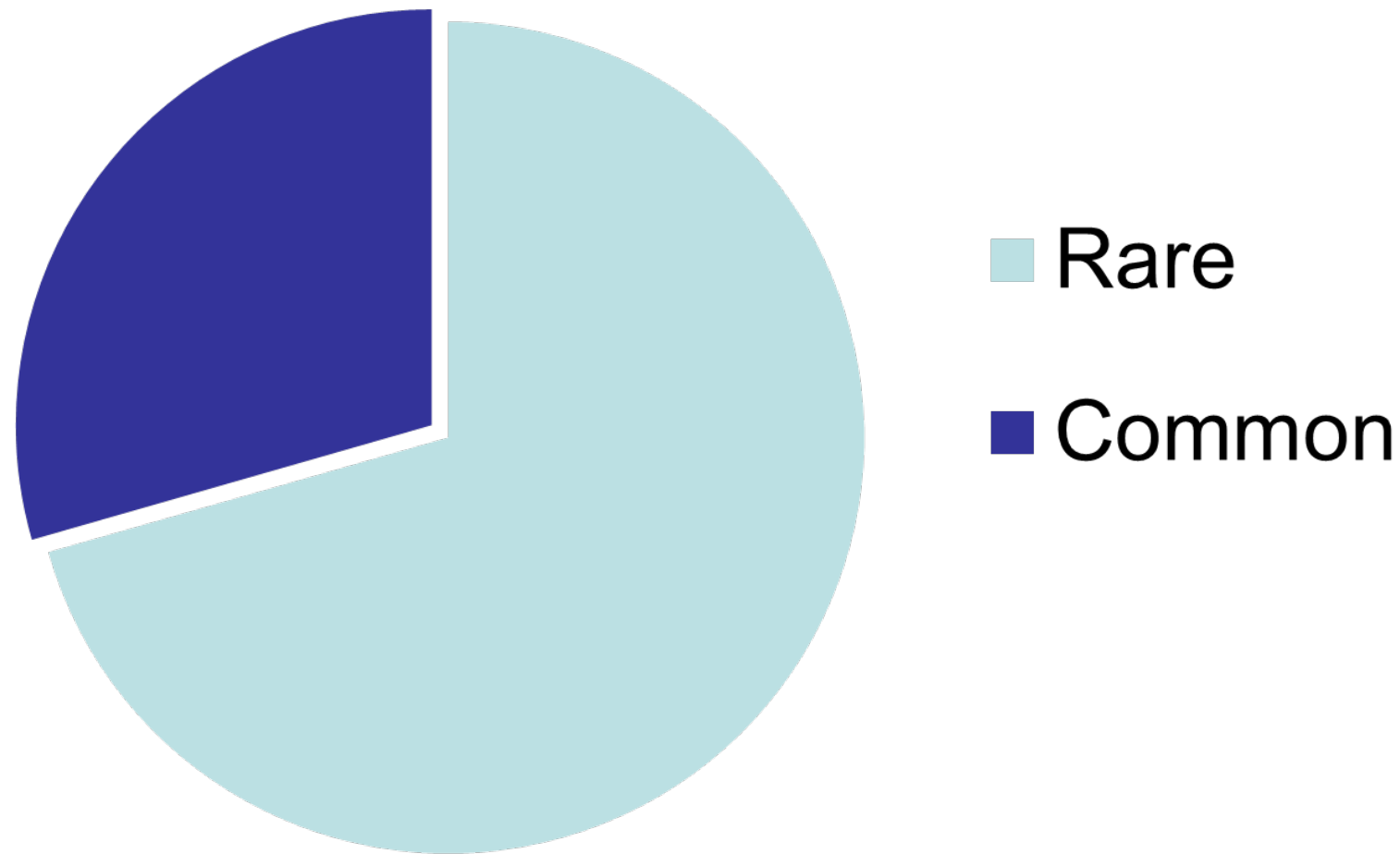
Wilson W. Bryan

Office of Tissues and Advanced Therapies (OTAT)
Center for Biologics Evaluation and Research (CBER)
United States Food and Drug Administration (US FDA)

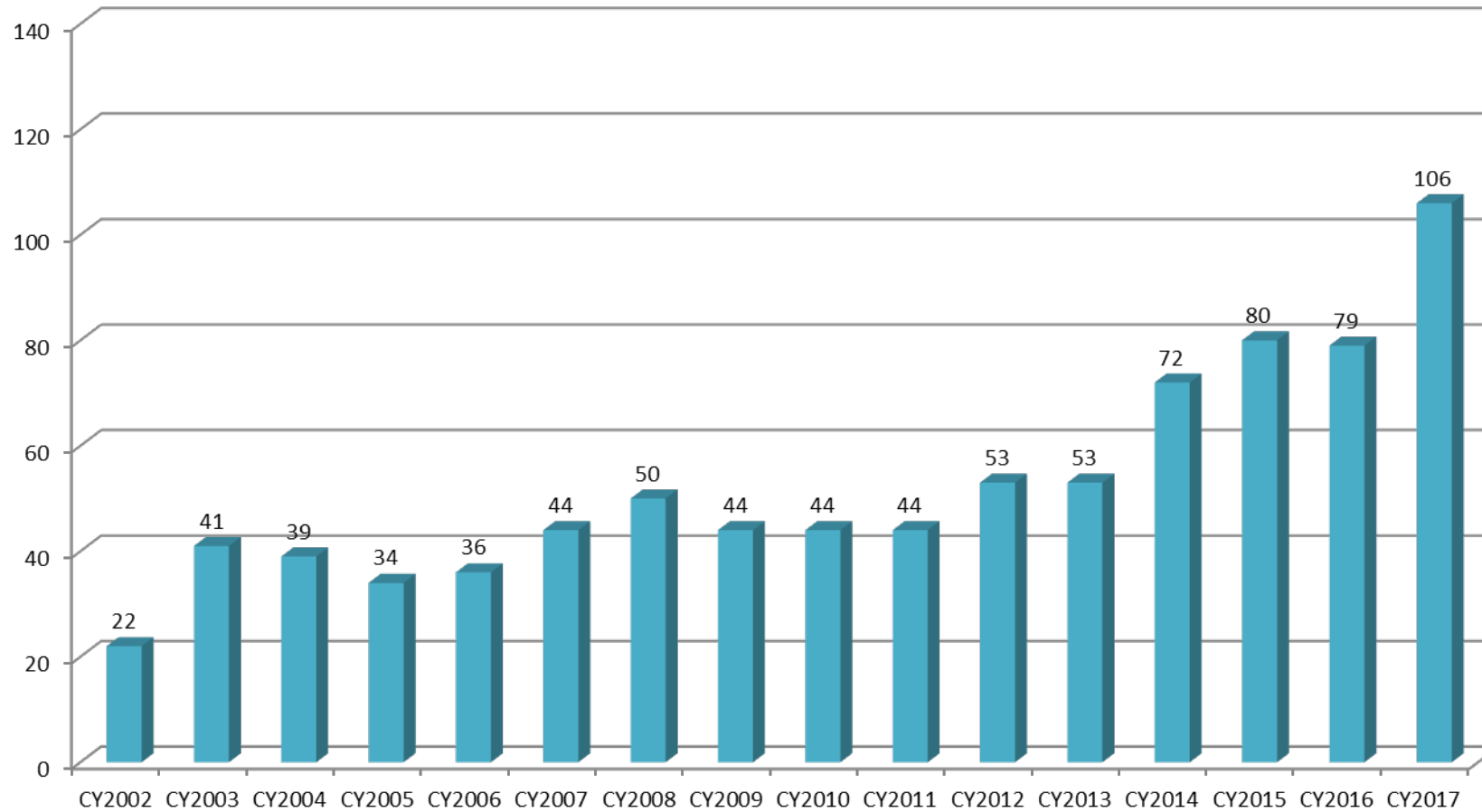
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Cell and Gene Therapy Investigational New Drug Applications



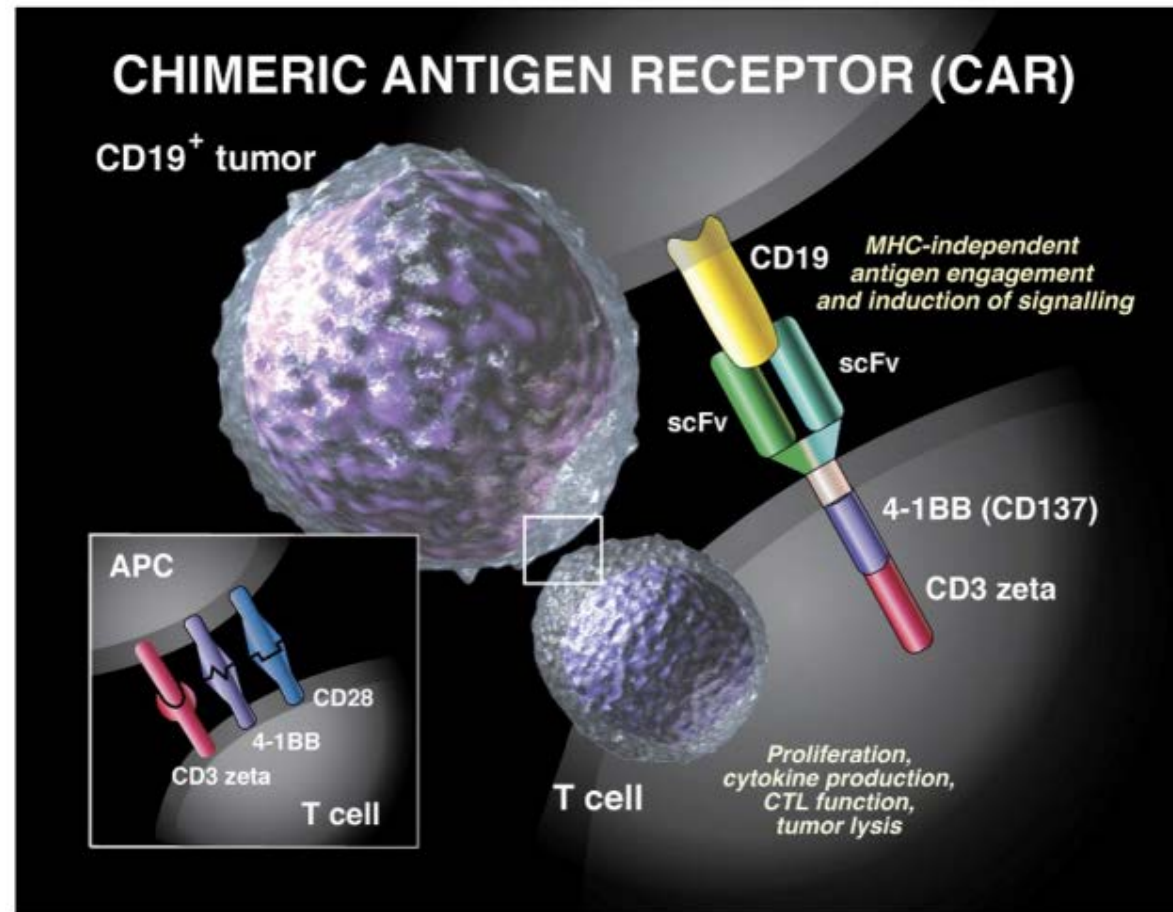
Investigational New Drug Applications (INDs) for Gene Therapy Products, 2002-2017



Gene Therapy: Scientific Advances

- Human Genome Project
 - Completed in October 2003
 - 99% of human genes sequenced to 99% accuracy
- Development of new vectors
 - Adeno-associated virus (AAV)
 - Lentivirus
- Genome editing

CAR T Cells: A Novel Way to Treat Cancer



Shannon L. Maude et al. Blood 2015

CTL, cytotoxic T lymphocyte; MHC, major histocompatibility complex

Gene Therapy

United States Marketing Approvals in 2017

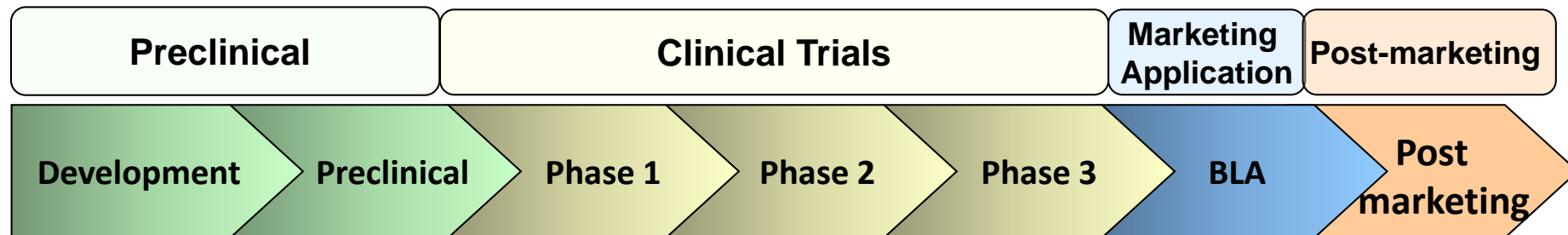
- **Kymriah** (tisagenlecleucel; Novartis)
 - CAR T cells (target – CD19)
 - Refractory childhood lymphoblastic B cell leukemia
- **Yescarta** (axicabtagene ciloleucel; Gilead (Kite))
 - CAR T cells (target – CD19)
 - Adult patients with relapsed or refractory large B cell lymphoma
- **Luxturna** (voretigene neparvovec-rzyl; Spark Therapeutics)
 - Gene therapy (adeno-associated virus vector)
 - Biallelic RPE65 mutation-associated retinal dystrophy

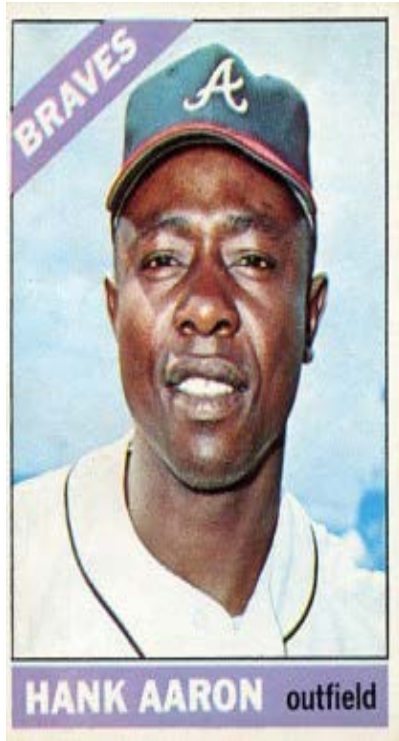


Baseball

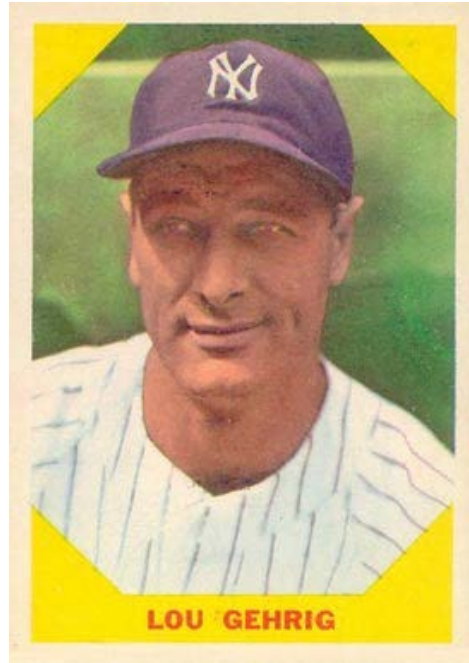


Drug Development

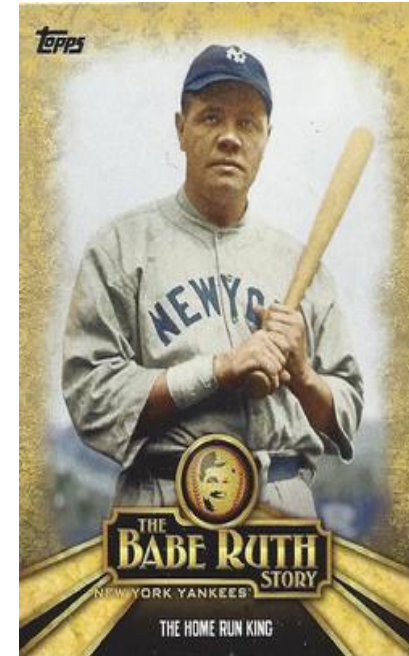




Hank Aaron



Lou Gehrig



Babe Ruth

Gene Therapies for Rare Diseases

FDA Draft Guidance (July 2018):

Human Gene Therapy for Rare Disease

... consider designing ... first-in-human study to be an adequate and well-controlled investigation that has the potential ... to provide evidence of effectiveness to support a marketing application.

Efficient Development of Gene Therapies

1) Teamwork

Requires collaboration of scientists, academic investigators, sponsors (e.g., pharmaceutical industry), funding organizations, patients, patient advocacy groups, and regulatory agencies

Efficient Development of Gene Therapies

2) Preparation

- Design and conduct Natural History studies that will support subsequent drug development
- When preclinical studies are beginning, draft the design of the clinical study(ies)
- Resolve manufacturing issues, as much as possible, before first-in-human clinical trial

Efficient Development of Gene Therapies

3) Try to hit a home run!

Design first-in-human clinical trial to provide evidence of effectiveness (e.g., include randomized controls)

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

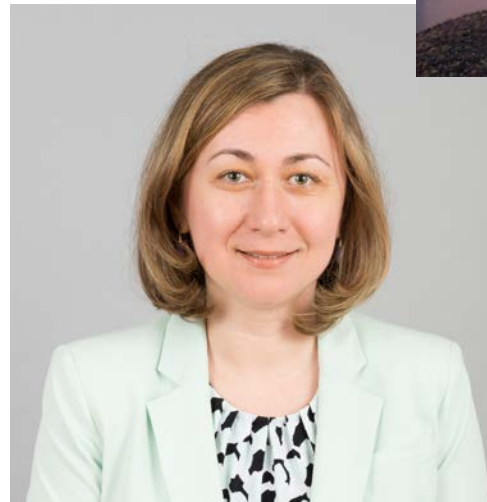
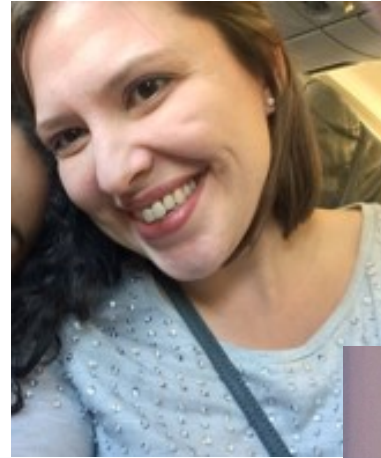
- **Manufacturers Assistance and Technical Training Branch:** industry.biologics@fda.hhs.gov

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



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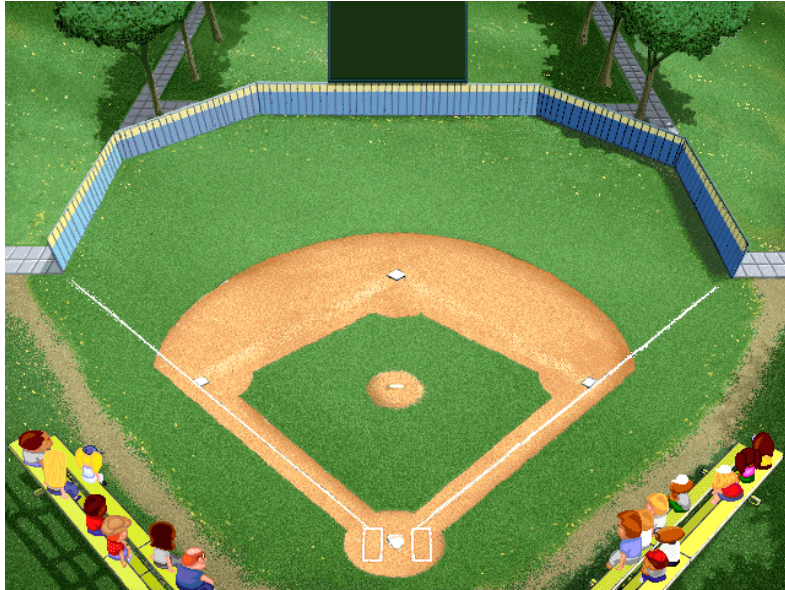
Gene Therapy: Efficient Drug Development

Drug development is like baseball:

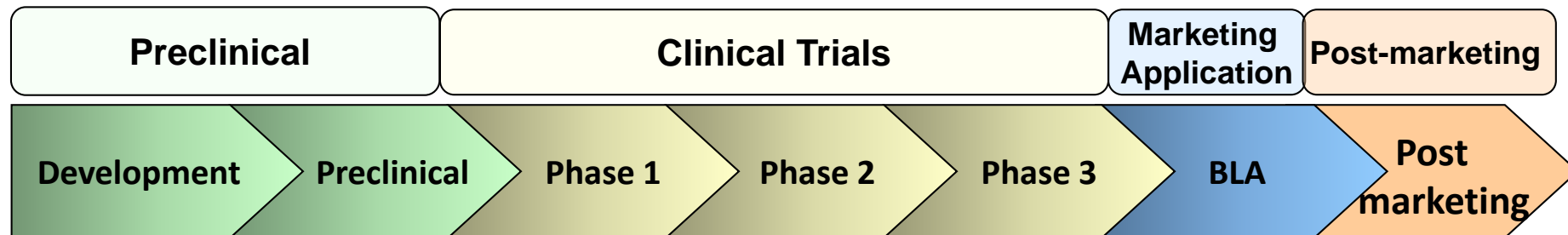
- 1) Preparation
- 2) Teamwork
- 3) The heroes try for the home run!



Baseball



Drug Development



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