RARE / ORPHAN DISEASES

"ARE WE READY FOR THE CHANGE THAT WE NEED TO FIND EFFECTIVE TREATMENTS FOR ORPHAN DISEASE?"

CHILDREN'S TUMOR FOUNDATION
ENDING NF THROUGH RESEARCH

YES!

Rare disease is very 'popular'!

Rare disease <200,000 Americans have disease

- 7,000 different types of rare diseases and disorders
- 30 million people in the U.S. (10% of population)
- Europe has approx 30 million rare disease cases as well

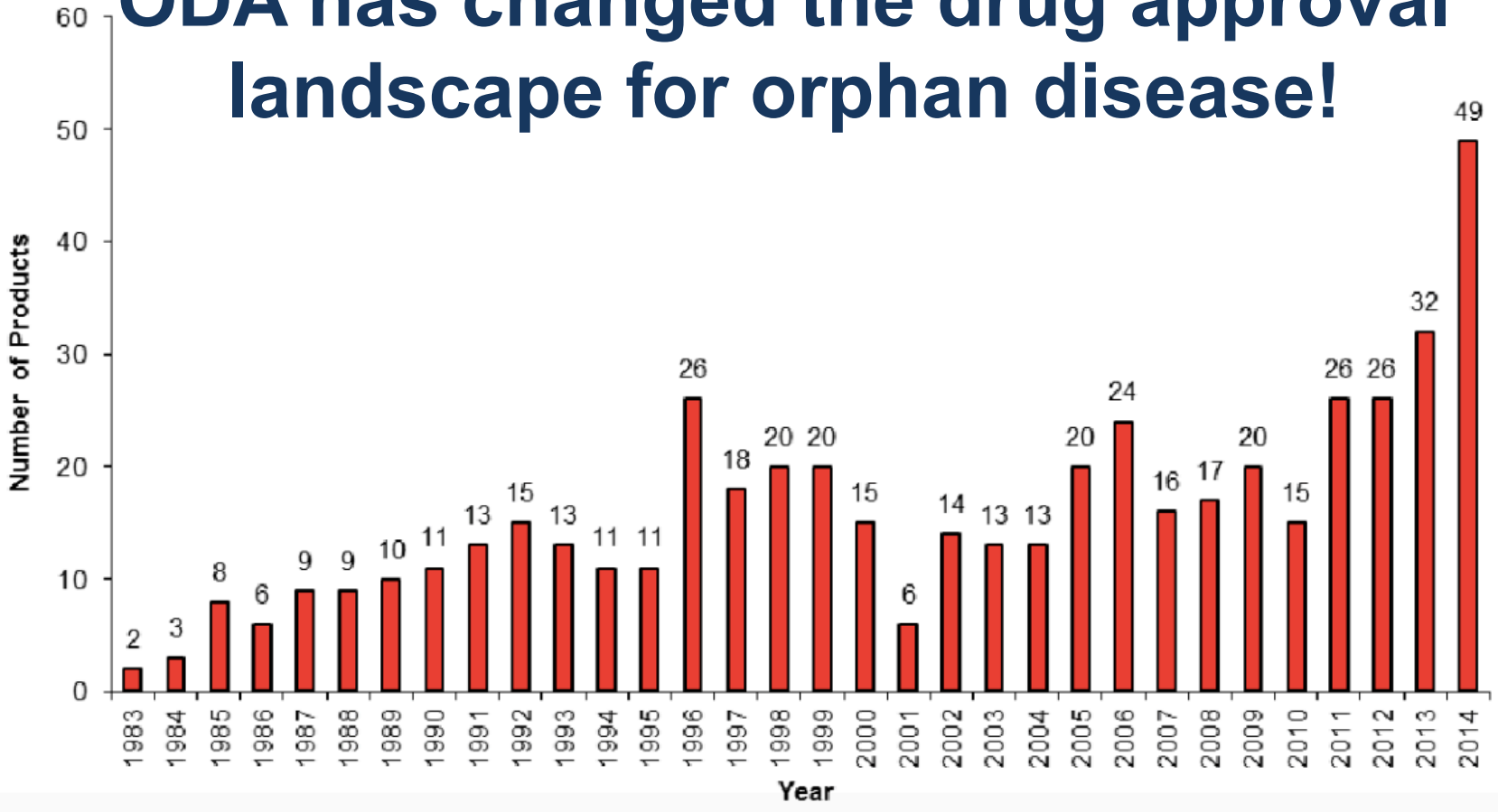
FDA Encourages…

- FDA launched the Orphan Drug Act (ODA) in 1983 to create incentives for pharma/biotech to invest in rare disease

- **Major benefits including:**

  — Funding for clinical testing
  — Tax credits
  — Assistance in clinical study designs
  — 7-year period of exclusive marketing after approval
  — Waiver of Prescription Drug User Fee Act (PDUFA) filing fees

ODA has changed the drug approval landscape for orphan disease!

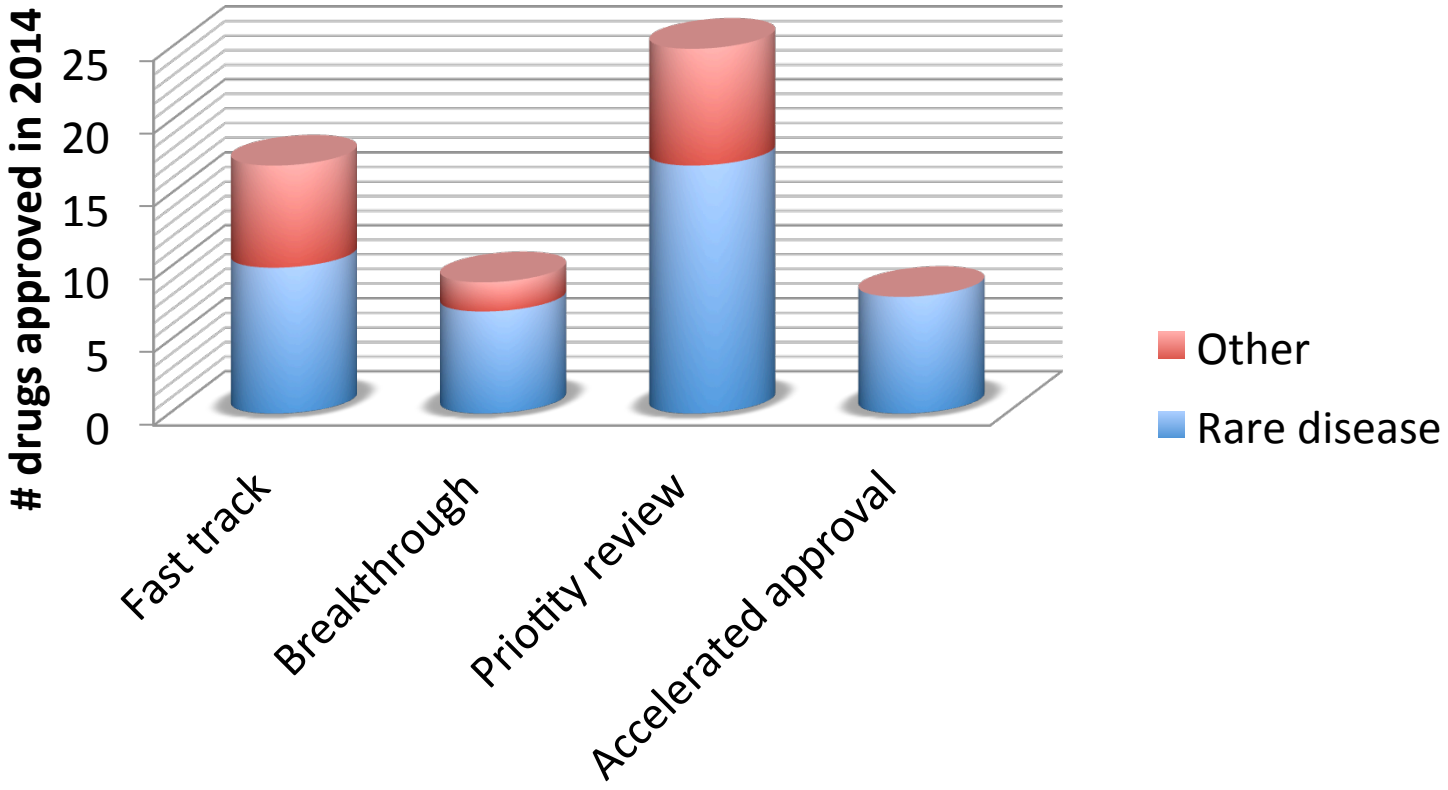


CDER for innovation…

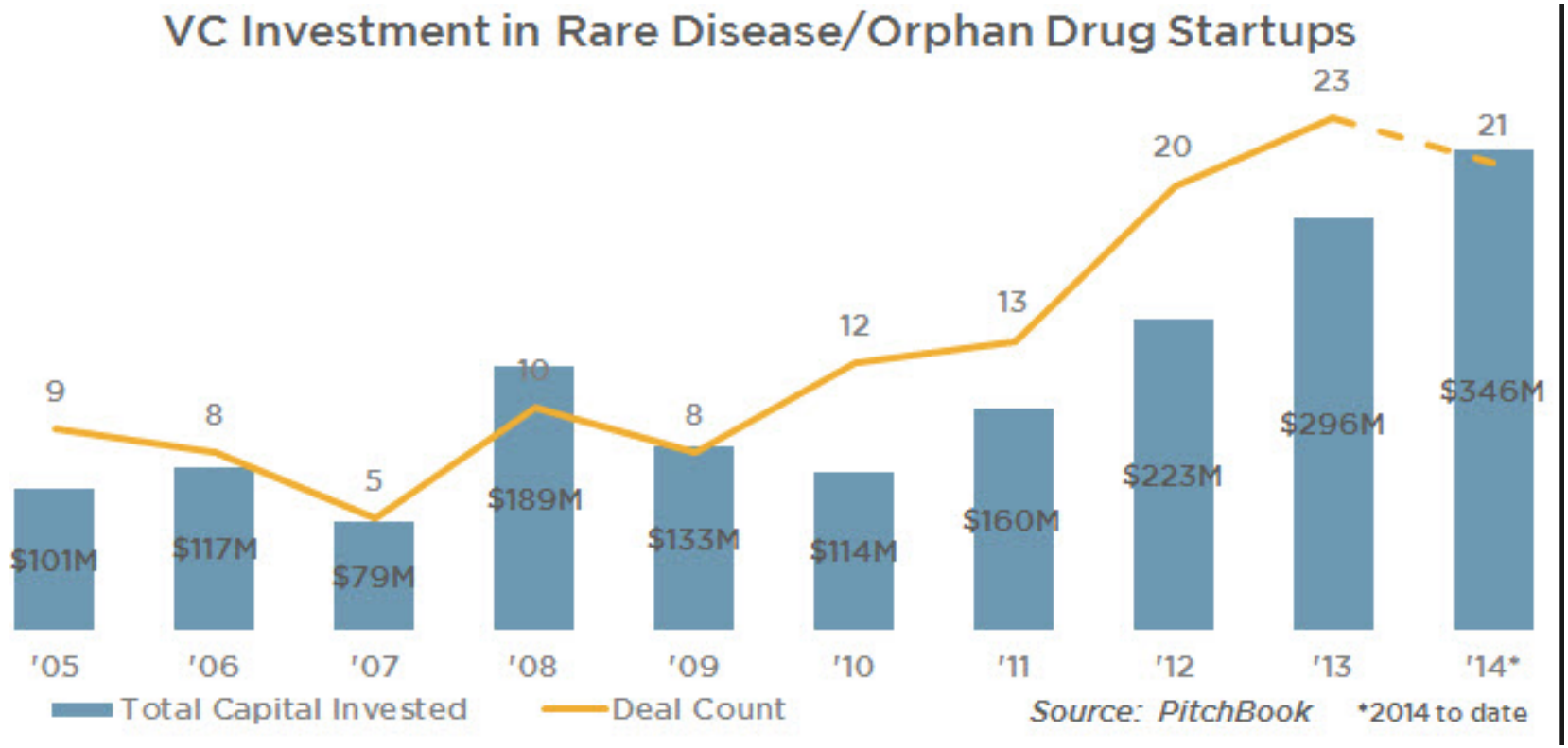
- New regulatory pathways to help speed up drug development
  - — Fast track - increased communication with FDA
  - — Breakthrough – FDA serious guidance
  - — Priority review- reduce FDA review time by half
  - — Accelerated approval- surrogate endpoint based

CDER=Center for Drug Evaluation and Research

Rare disease benefits from CDER innovation



Rare disease popular in VC space



http://blog.pitchbook.com/

BUT-

Typical roadblocks in R&D…
even more visible in rare disease sector

Roadblocks for Patients

- Patients misdiagnosed & undereducated
- Lack of knowledge around patient needs
- Limited access to clinical trial info & sites

Roadblocks for Researchers & Industry

- Tissue is very scarce
- Small often ill-defined patient population- lack of validated endpoints
- Market unknown
- Lack of tools (cells, animal models) & data
- Lack of researchers & collaboration – Slow/inefficient

FIXABLE?

Yes, but…need for change

Success stories of Children's Tumor Foundation

Children's Tumor Foundation (CTF)?

- 501(c)3 **medical foundation**

- **Focused** on rare disorder: neurofibromatosis NF
  - — Family of autosomal dominant genetic disorders-NF1, NF2, schwannomatosis
  - — Tumors grow on nerves, learning disabilities, deafness, blindness, cancer, pain etc.

- **CTF philosophy:** change to fix the roadblocks – use innovation, creative business model

CTF solutions for Patients

Roadblocks for Patients

- Patients misdiagnosed & undereducated

  NF Clinic Network / NF Forum / educational materials

- Lack of knowledge around patient needs

  Volunteer Leadership Council very involved

- Limited access to clinical trial info & sites

  NF Registry

CTF for Researchers & Industry

Roadblocks for Researchers & Industry

- Tissue is very scarce

  CTF Open Biobank

- Small often ill-defined population-lack of validated endpoints

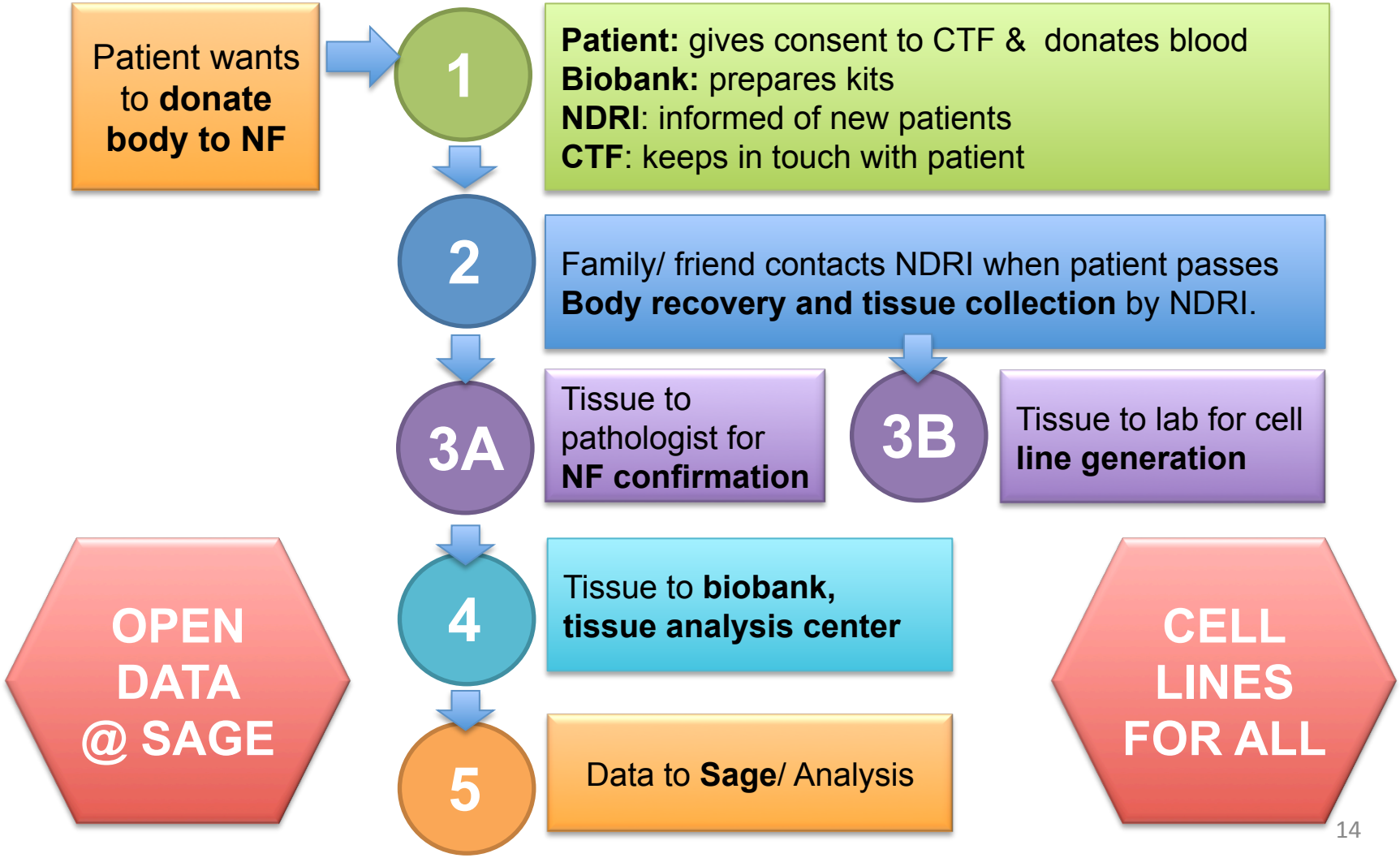
  CTF funds endpoint development

- Market unknown

  Market model developed

- Lack of tools (tissue, cells, animal models) & data
- Lack of researchers & collaboration – Slow/ inefficient

Success story 1: Lack of tissue, tools & data



Success story 2: CTF consortia science

Goal:

-Accelerate path from basic discovery to clinical benefit

-Increasing understanding by sharing failures

-Make all data public

-Break the walls between artificially divided research categories (clinical, translational, basic,..)

-Centralize data management/ analysis

NF Preclinical Consortium

— 4 academic centers -- NF1 animal models – testing drugs in parallel in multiple models

—Unpublished data gets discussed

—Clinicians involved

MEKi from target POC testing in NFPC to first clinical trial in < 3 years!

Synodos- collaborative accelerator

Characteristic	Why accelerator?
Dream team of diverse experts	No delay (mis) interpreting other scientists data sets Learn from each other
Data shared with world after 12 months	No need to wait for publications to come out Sense of urgency in team to publish data quickly
Negative data shared	No money/ time wasted refunding same failures Learn from failures
Milestone driven projects	All experiments aligned – industry quality planning

Synodos for NF2

- **12 academic centers; mix of all expertises**
- **In less than 12 months:**
  - — From unknown screening pipeline to well-defined screening system
  - — All in vitro screens finalized – undergoing in vivo testing now
  - — Efficacious combinations identified using transcriptomics & kinome analysis
  - — All data centralized at Sage Bionetworks

Thanks to our team mates:

- Sage Bionetworks team
- Synodos team
- NFPC team
- NTAP
- CTF team