Building Research Capacity in West Virginia

NINDS Overview

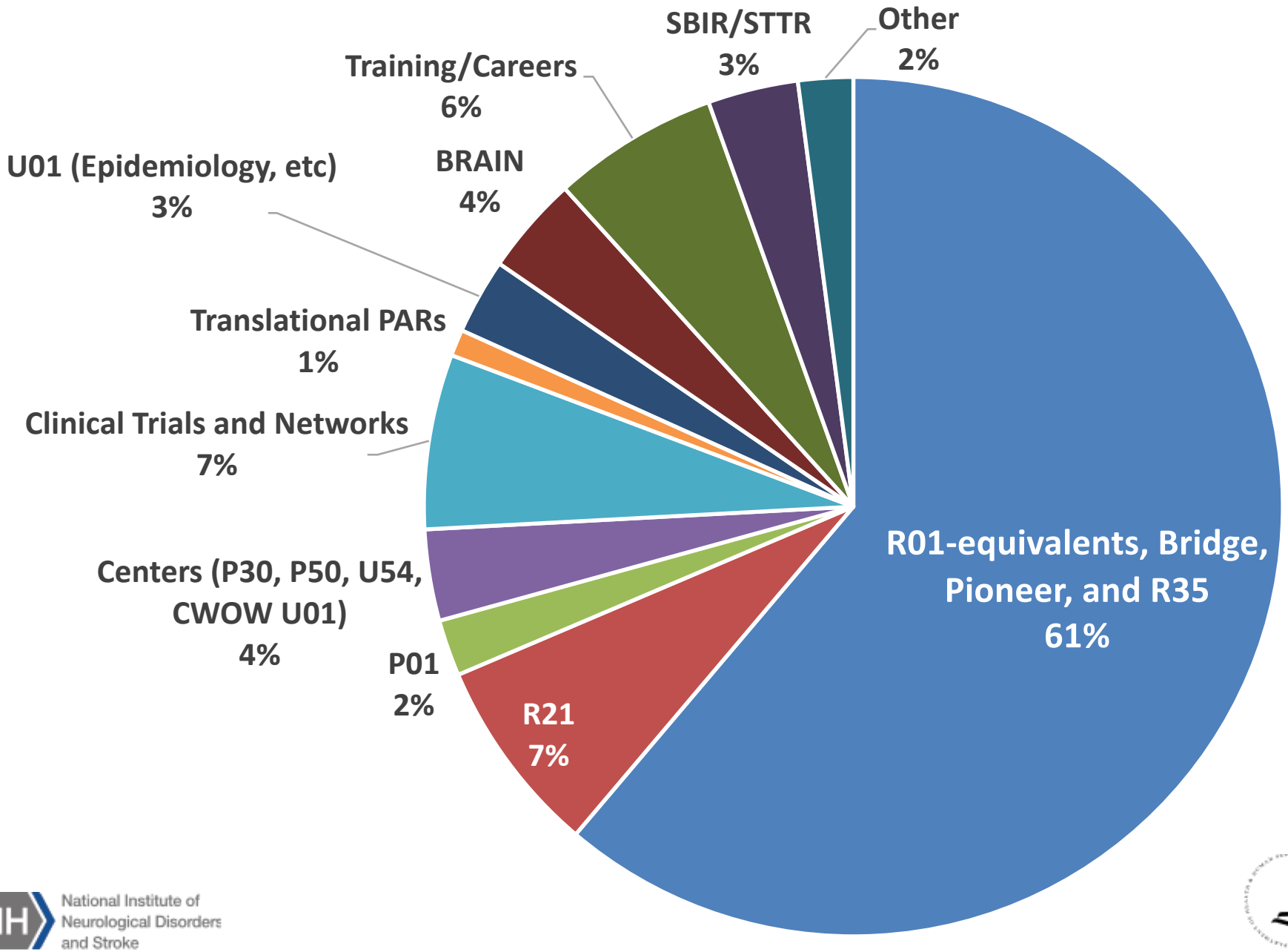
and Clinical Trial Funding Opportunities

September 19, 2018

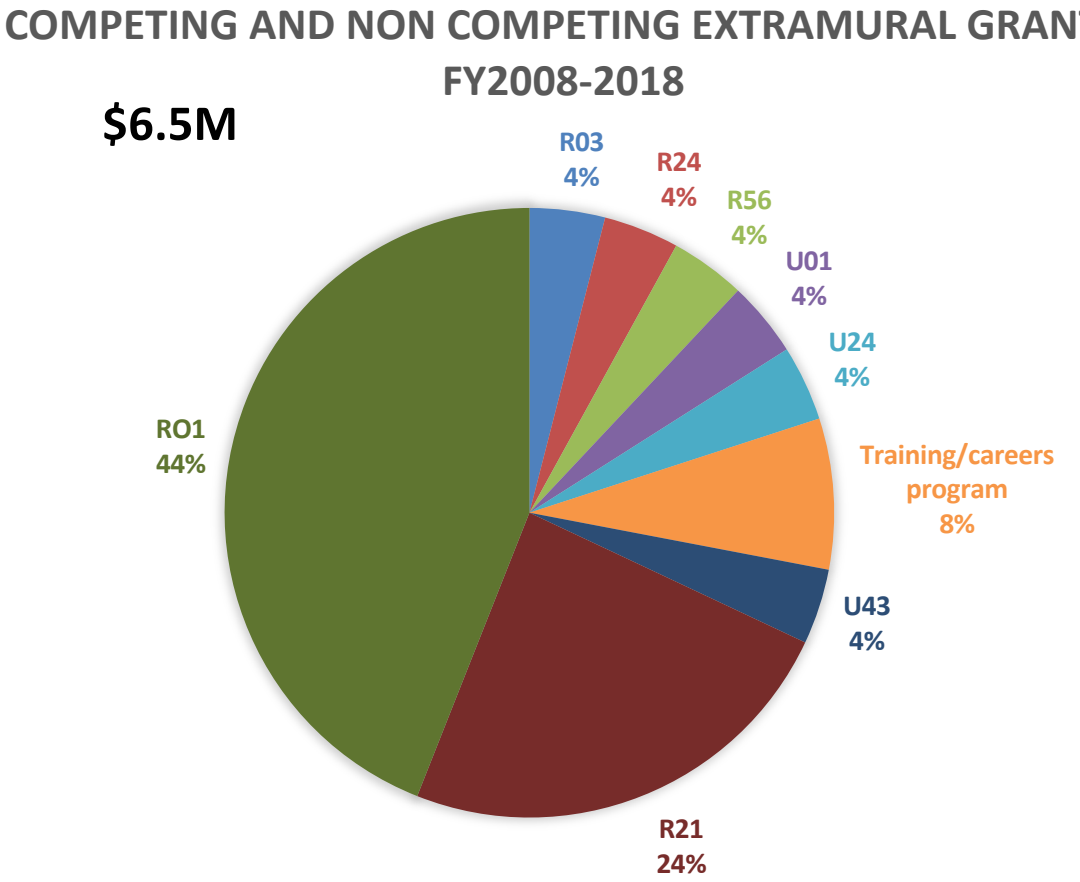
Clinton Wright, MD, MS

NINDS

Competing and Noncompeting Extramural Grants FY 2016



Active NINDS Research Funding in West Virginia

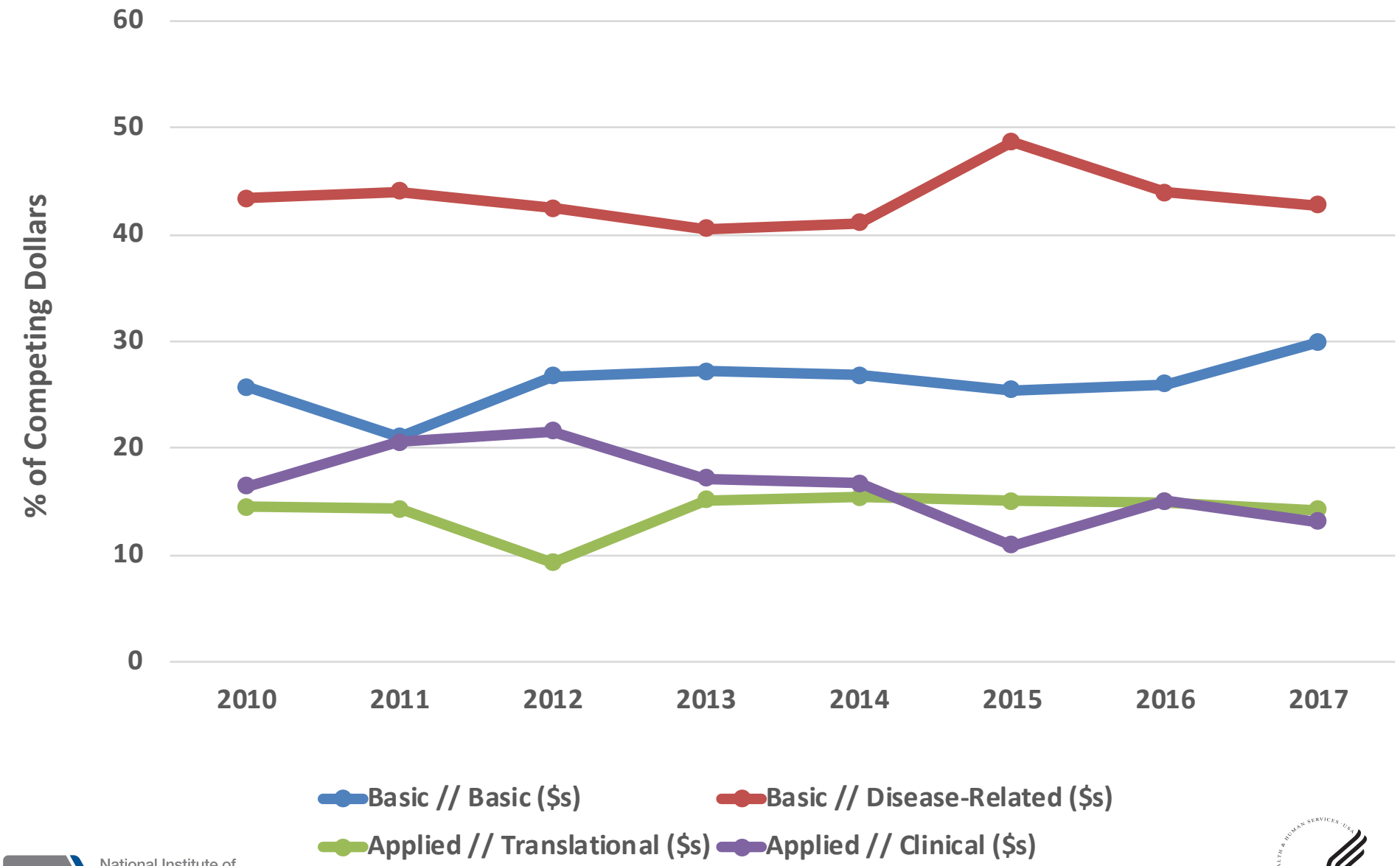


- NINDS Funding since 2008: $6.5 M

NINDS supports a range of basic and applied research projects, including active grants:

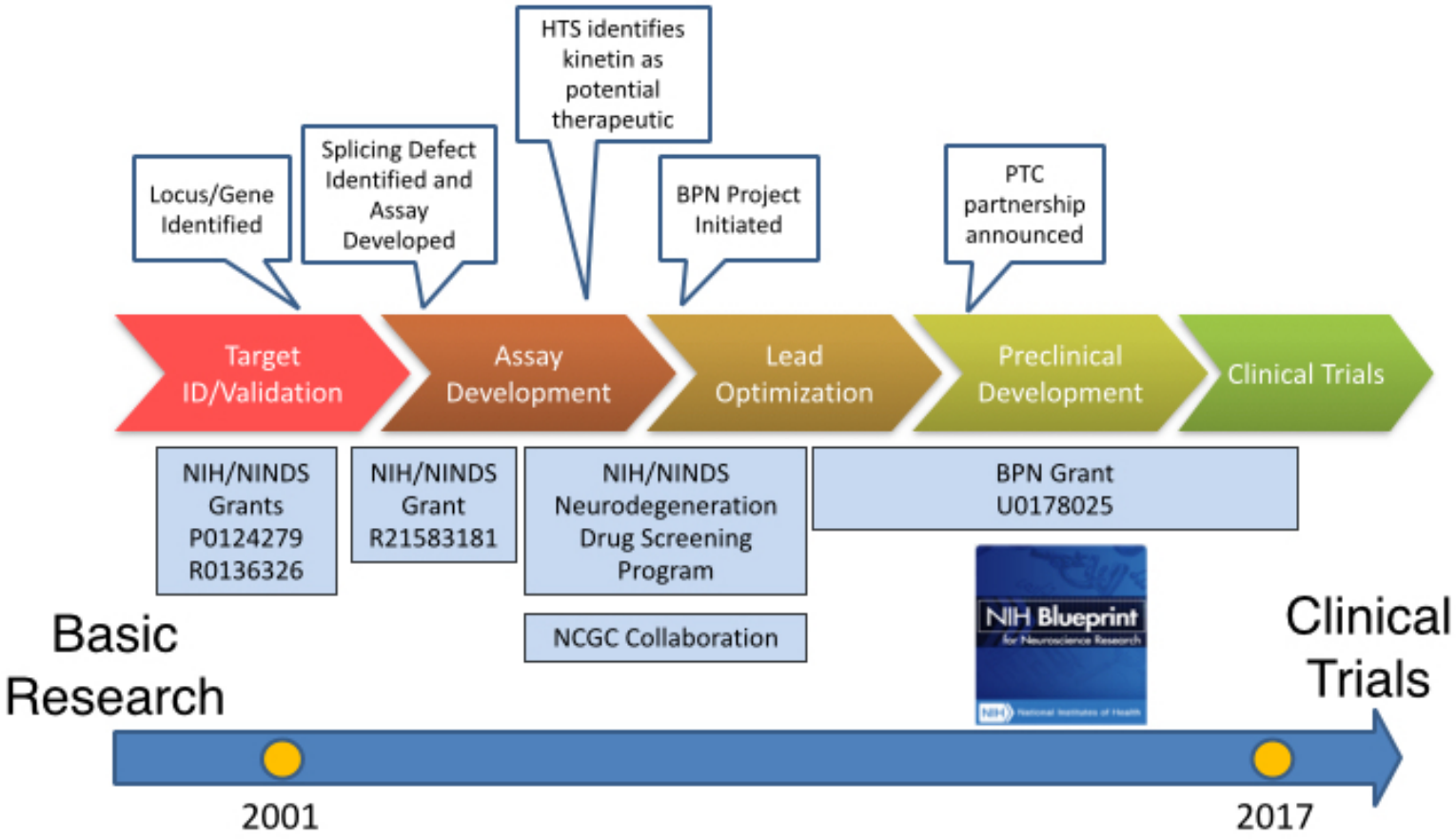
- Therapeutic use of Bryostatin-1 to extend TPA time window following MCAO
- Perk dependent mechanism of Neuroinflammation
- Adverse consequences of light at night for cerebral ischemia
- Role of C-JUN N-terminal kinase signaling in cortical interneuron migration

Subcategory Research Trends: *Dollars*



NIH Funding and Timelines Advancing Basic research to Clinical Trials

Case Study: Prof. Susan Slaugenhaupt (Massachusetts General Hospital)



Expertise – Staff and Consultants

Staff

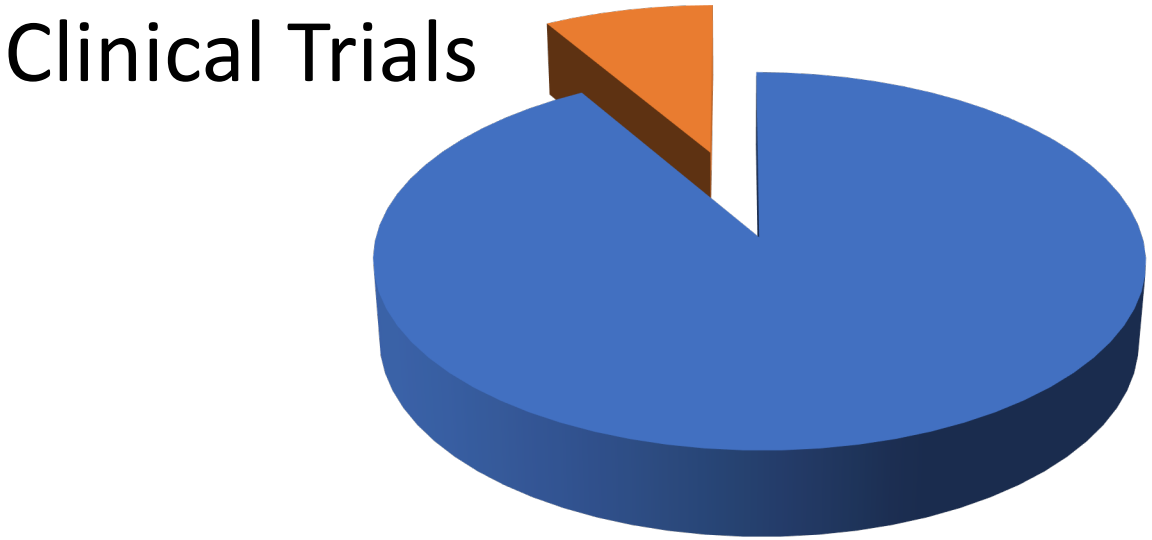
- ✓ Medicinal Chemistry
- ✓ Gene therapy/editing
- ✓ Assay Development
- ✓ High Throughput Screening
- ✓ Pharmacology
- ✓ Toxicology
- ✓ In vivo pharmacology
- ✓ Product development
- ✓ Scale up and Formulation
- ✓ Project management
- ✓ Business Development
- ✓ Device manufacture
- ✓ Electrochemistry

Consultants

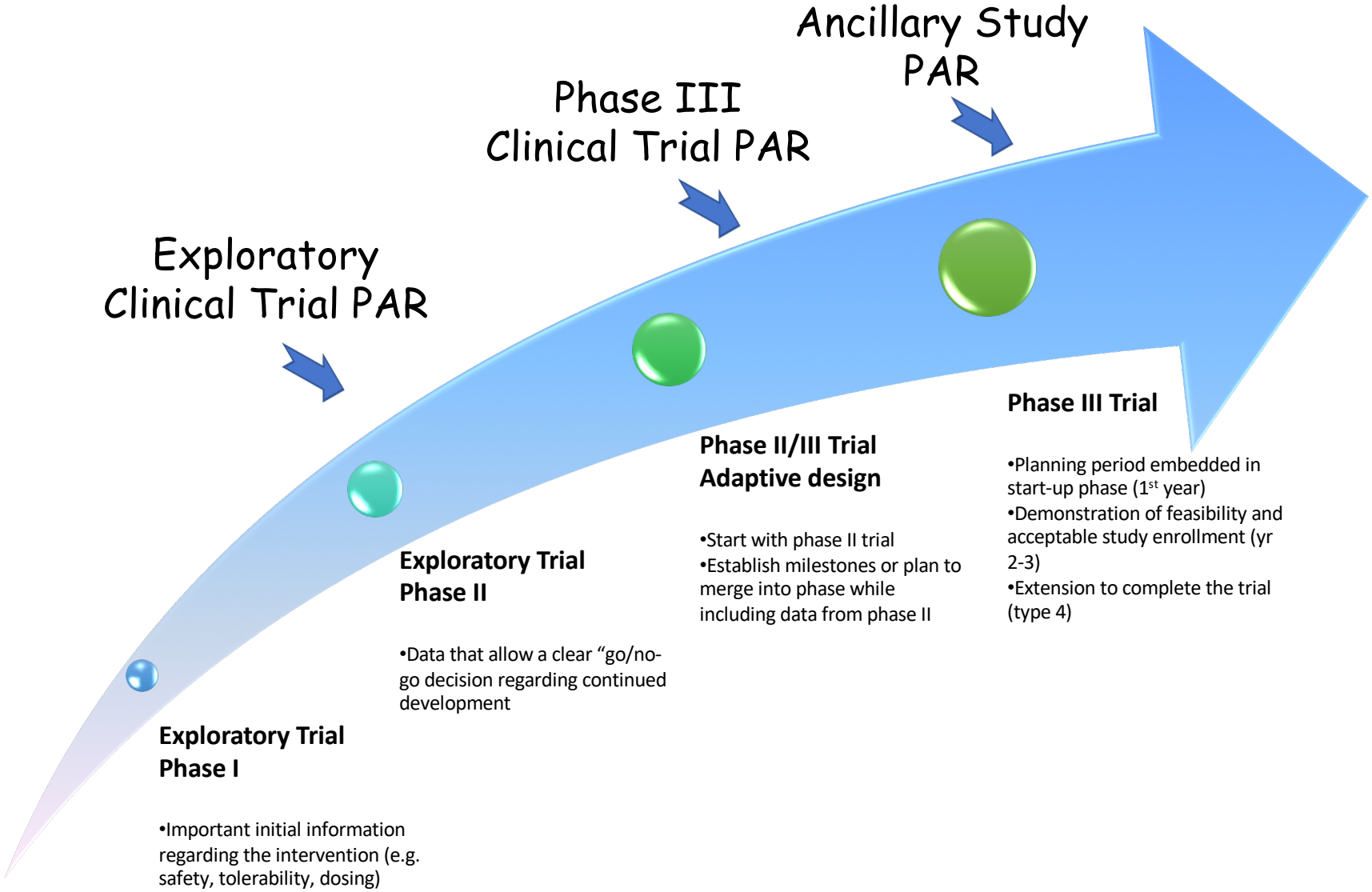
- ✓ Assay development
- ✓ Pharmacology
- ✓ Medicinal chemistry
- ✓ DMPK
- ✓ Toxicology
- ✓ Development
- ✓ Regulatory
- ✓ Exploratory clinical trials
- ✓ Venture capital investment
- ✓ Due diligence
- ✓ Merger and acquisitions
- ✓ Medical device expertise
- ✓ Engineering

Clinical Research at NINDS

- NINDS Grants Portfolio ~ 1.3 billion, including ~ 10% for clinical trials



Clinical Trial Implementation Process



NINDS Clinical Trial Networks

- NeuroNEXT: https://www.neuronext.org
  - Relevant FOAs:

  https://grants.nih.gov/grants/guide/pa-files/PAR-18-528.html
  https://grants.nih.gov/grants/guide/pa-files/PAR-18-628.html

- StrokeNET: https://www.nihstrokenet.org
  - Relevant FOAs:

  https://grants.nih.gov/grants/guide/pa-files/PAR-18-561.html
  https://grants.nih.gov/grants/guide/pa-files/PAR-18-563.html

- SIREN: https://siren.network
  - Relevant FOA:

  https://grants.nih.gov/grants/guide/pa-files/PAR-18-304.html

Network Goals

- **Establish efficient clinical trials infrastructure**
- **Central IRB**
- **Master clinical trial agreements**
- **Optimal use of NINDS CDEs (reproducibility, data sharing)**
- **Coordinate public/private sector efforts**
- **Conduct clinical trials/biomarker studies with expertise in one entity**
- **Lowered barrier to entry for investigators: several PIs had not had NIH funding before their NN trial!**

NEURONEXT

NeuroNEXT – CCC (MGH), DCC (Iowa), 25 clinical sites

- **Increase efficiency of clinical trials before embarking on large, confirmatory studies**
  - Central IRB / Master Clinical Trial Agreements / Design assistance from experienced clinical trialists
- **Network infrastructure to support Phase II and biomarker studies in neuroscience**
- **Ongoing biomarker efforts:**
  - NN101 (PI: Kolb) – Identified prognostic and surrogate biomarkers of disease progression to facilitate therapeutic infant SMA clinical trials
  - NN102 (PI: Fox) – Evaluated activity of ibudilast (MN-166) using imaging biomarker endpoint (MRI brain atrophy)
  - NN106 (PI: Griguer) – Evaluation of Cytochrome C Oxidase activity as marker of overall survival with newly diagnosed glioblastoma
  - NN107 (PI: Berry-Kravis) – Fragile X intervention study involving auditory ERP and eye tracking

NIH StrokeNet Overview:

- NINDS created StrokeNet in 2013 to support clinical trials in stroke **prevention, treatment,** and **recovery**
- CCC (Cinncinnatti), DCC (MUSC), 25 hubs with over 300 total sites
- The network responded to Stroke Progress Review Group and NINDS Stroke Planning efforts in 2012
  - Working groups in Prevention (CREST-2, ARCADIA), Acute Treatment (DEFUSE 3, MISTIE), and Recovery (Telerehab)
- Designed to support early exploratory phase 2 to confirmatory phase 3 clinical trials
- Use of a centralized IRB and master trial contracts and to provide centralized support for data management, integration, and data sharing

Strategies to Innovate EmeRgENcy Care Clinical Trials Network (SIREN)

PARTNERS

NINDS

NHLBI

NCATS

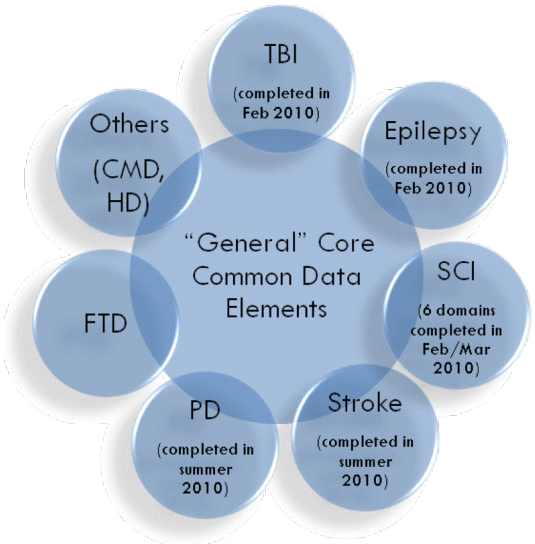
OECR

- Mission to transform emergency research.
- Exploring clinical trial design innovations with adaptive design, registry based methodology, and more
- Innovating with improvement in early patient engagement, collaborative research planning, and site- and practice-standardization to maximize generalizability
- Structure: DCC, CCC, 11 hubs
- Funded studies:
  - HOBIT Hyperbaric oxygen in severe TBI (start date ~Spring 2018)
  - BOOST-3 Intracranial oxygen monitoring for TBI (start date TBA)

Common Data Elements (CDEs)

NINDS Common Data Elements
Harmonizing information. Streamlining research.

- 23 diseases
- 1 General
- ~ 80 studies



GOALS

- Reduce barriers in clinical research
- Avoid redundancy
- Facilitate research in rare diseases
- Accelerate meta-analysis of data across studies

Features

- Data collection terms
- Harmonization and simplification of data standards
- Easily accessible tools for investigators
- Encourage focused and simplified data collection
- Improve data quality and data sharing
- Working groups (experts and community stakeholders)

Common Data Elements

- Website: www.commondataelements.ninds.nih.gov
  - Data dictionaries
  - Template data collection forms
  - Manuals of Procedures (MOPs)

- General CDEs include:
  - Demographic Information (age, race, ethnicity, education level etc.)
  - Modified Rankin Scale and Trail Making Test*
  - Adverse events data
  - Concomitant medications data
  - Medical history data