NeuroNEXT

The NEXT Generation of Neurologic Treatments

NIH-Network for Excellence in Neuroscience Clinical Trials

Clinical Trial Networks: The Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT)

August 21, 2018

National Institute of Neurological Disorders and Stroke

The University of Iowa

MGH Massachusetts General Hospital

What Is NeuorNEXT?

- NIH - Network for Excellence in Neuroscience Clinical Trials
- Website: https://www.neuronext.org
- Network funded by NINDS in 2011
- 1 Clinical Coordinating Center (CCC); 1 Data Coordinating Center (DCC); 25 Clinical Study Sites (CSS)
- Network renewed in 2018
- 1 CCC, 1 DCC and 25 CSS (17 original sites and 8 new sites)

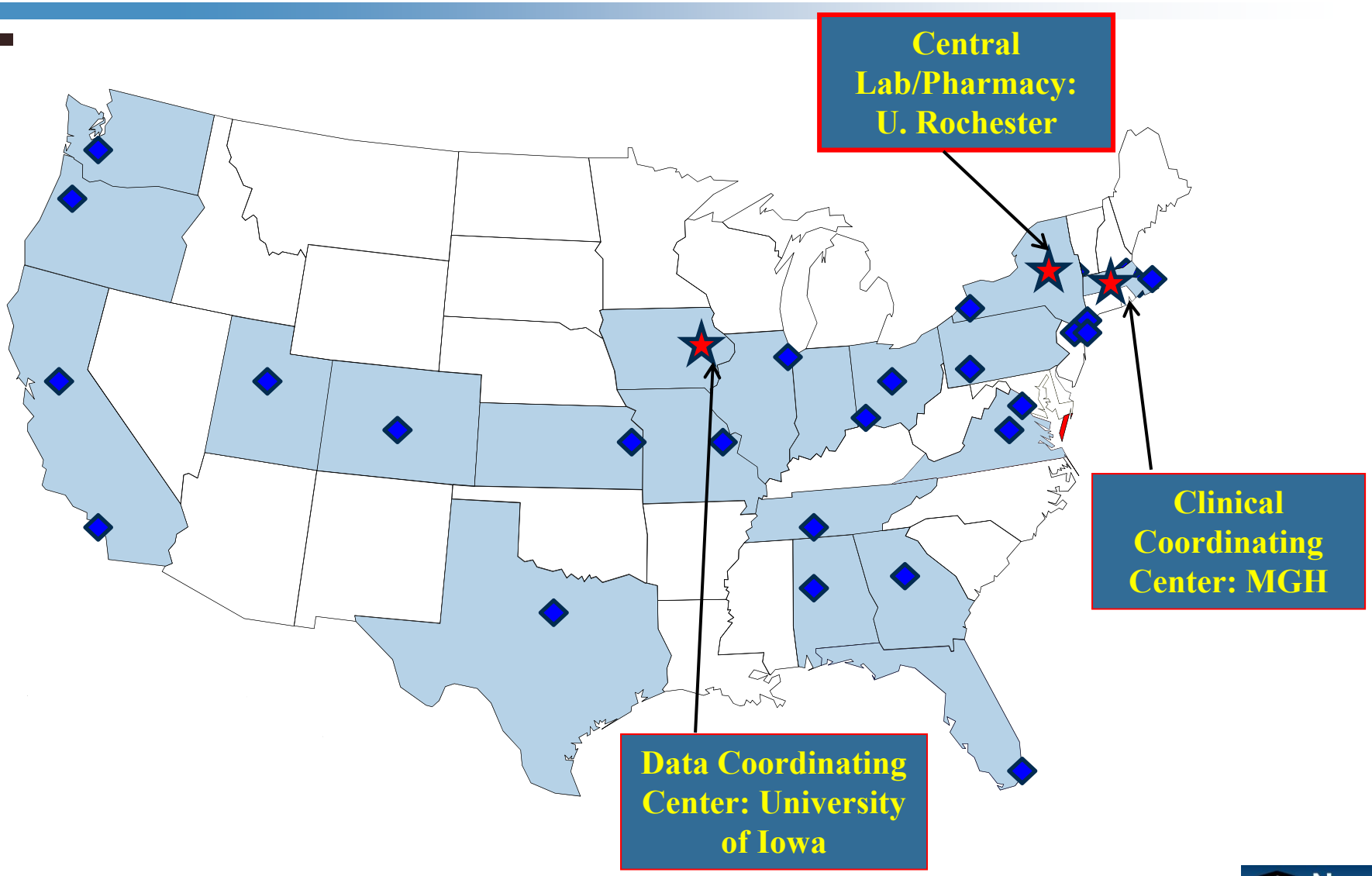
Network Vision

Conduct studies in neurological diseases through partnership with academia, private foundations and industry

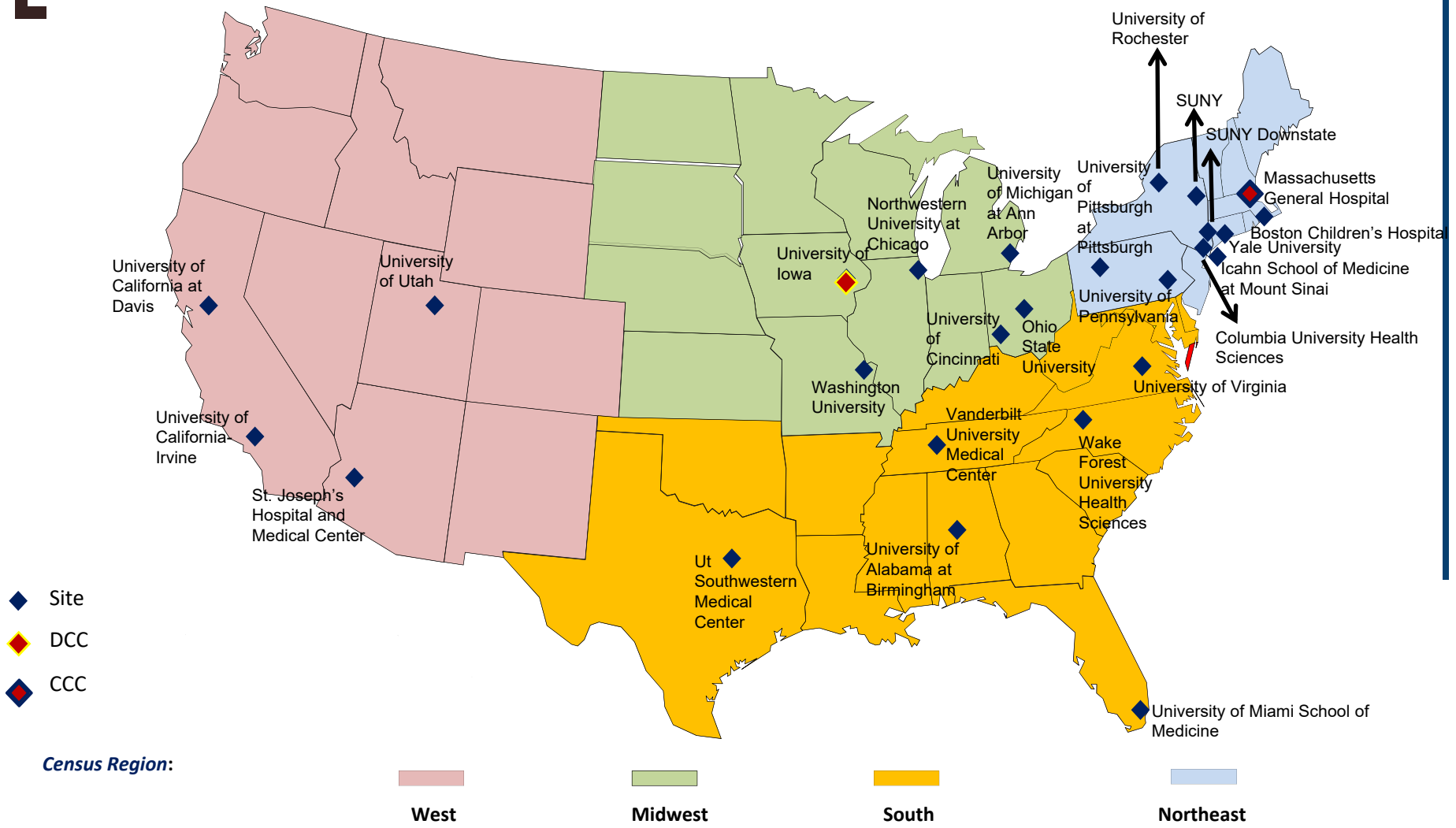
Expand the NINDS capability to:

- *Test promising new therapies*
- *Increase efficiency* of clinical trials before embarking on larger studies
- *Respond quickly* as new opportunities arise to test promising therapies for people with neurological disorders

Network: Funded in 2011



Network: Funded 2018



Network Infrastructure

- NIH/NINDS
  - Janice Cordell, PhD
    Robin Conwit, MD
    Codrin Lungu, MD

- Clinical Coordinating Center
  - Massachusetts General Hospital
    (Merit Cudkowicz, MD, MSc)

- Data Coordinating Center
  - University of Iowa
    (Christopher S. Coffey, PhD)

National Institute of Neurological Disorders and Stroke

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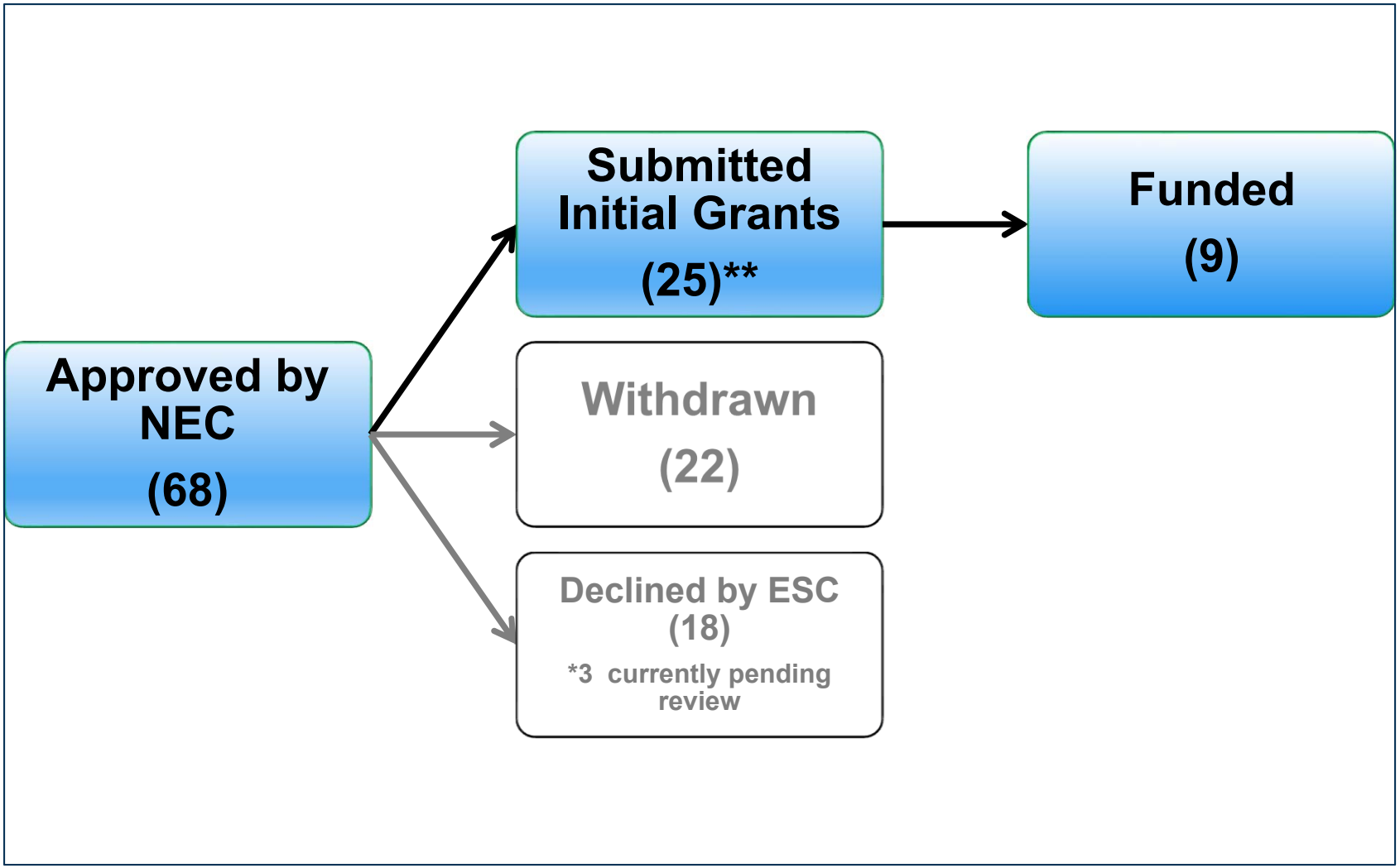
NeuroNEXT

Nine Funded Studies



** 12 by investigators submitting their 1st NIH grant

Network Studies to Date

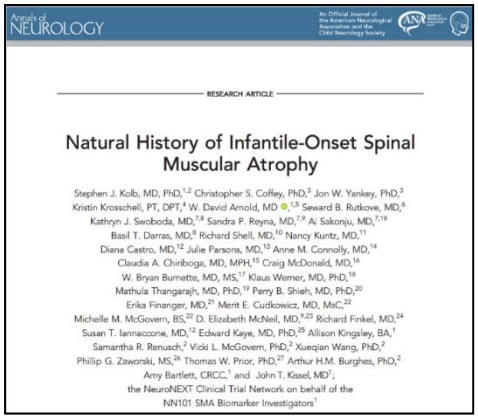
- ☑ **Spinal Muscular Atrophy** Biomarker Study
- ☑ Ibudilast in Progressive **Multiple Sclerosis**
- ☑ Rituximab in **Myasthenia Gravis**
- ☑ 3K3A-APC in **Acute Stroke**
- ☑ SRX246 for Irritability in **Huntington's Disease**
- ☑ Cytochrome C as Biomarker for **Glioblastoma Multiforme**
- ☑ AFQ056 for Language Learning in **Fragile X Syndrome**
- ☑ Topiramate for **Cryptogenic Peripheral Neuropathy**
- ☑ ManNAc for **GNE Myopathy**

Network Accomplishments

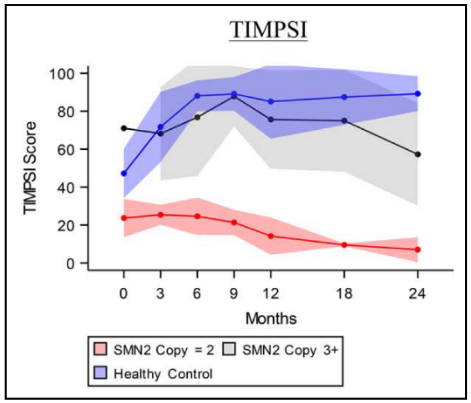
- ☑ **Test promising (new) agents in Phase 2 clinical trials**
  - NN102, NN104, NN105, NN107, NN108, NN109
- ☑ **Establish efficient clinical trials infrastructure**
  - Central IRB (first for NINDS)
  - Master clinical trial agreements
  - Optimal use of NINDS CDEs
- ☑ **Coordinate public/private sector efforts**
- ☑ **Conduct clinical trials/biomarker studies with**
  - Academics – NN101, NN102, NN103, NN104, NN106, NN107, NN108
  - Small business – NN105
  - Industry partnerships – NN102, NN104, NN109
- ☑ **All studies meeting enrollment goals and sites providing high quality data!**

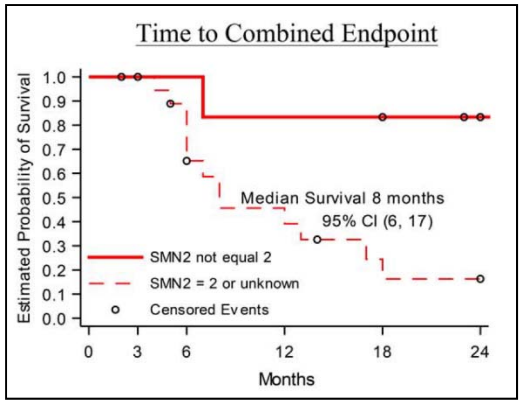
NN101 – Spinal Muscular Atrophy

☑ Dec 2017: Primary Manuscript Published



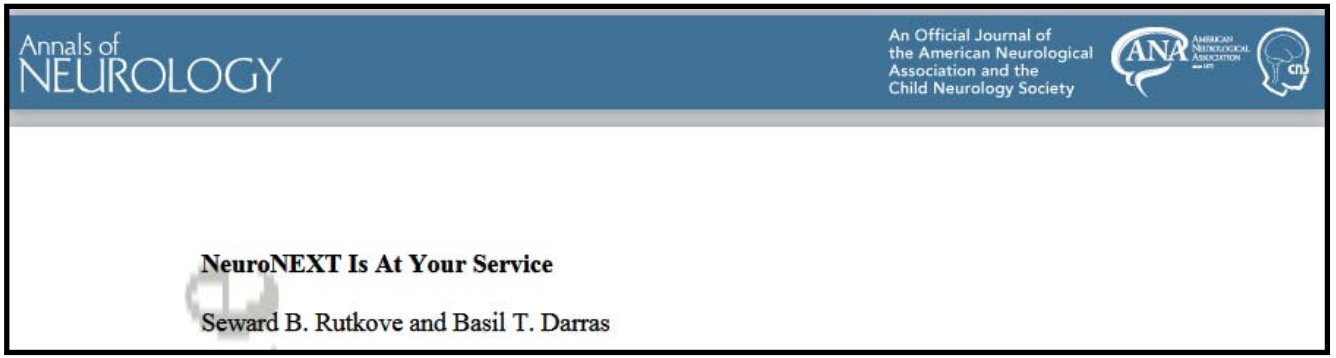
- Motor function scores decreased rapidly in SMA infants, versus rapid increase in healthy infants
- Post hoc analysis of survival to combined endpoint in SMA infants with 2 copies of SMN2 indicated a median age of 8 months at death or need of ventilation (95% CI: 6, 17)





NN101 – Spinal Muscular Atrophy

☑ Jan 2018: Accompanying Editorial



- *"Perhaps the most remarkable aspect of this study is that it is already serving as the gold-standard for the natural history of untreated infantile SMA."*
- *"NeuroNEXT is clearly trying to change the landscape of clinical trials in neurology, helping to empower the academic investigator to pursue research efforts that would otherwise be impossible.*
- *So what's next for NeuroNEXT? That is up to you.*

Why Apply to Use NeuroNEXT

- Allows access to NeuroNEXT infrastructure
- Novel initiatives to increase efficiency of conducting clinical trials in the network:
  - Utilization of a Central IRB (CIRB) of record
  - Pre-existing Master Clinical Trial Agreements (MCTA) between the CCC and all clinical study sites
  - Availability of experienced trial design staff to assist with protocol and grant development
  - Experienced sites with full time funded coordinator and record of high enrollment and quality study conduct

Submitting Proposals to NeuroNEXT

- Contact Codrin Lungu, MD at NINDS
  - lunguci@ninds.nih.gov / 301-496-9135
- Complete Concept Form, submit to NINDS
- NINDS initial review to determine if proposal meets goals and missions of NeuroNEXT
  - If yes, proposal sent to:
    - NeuroNEXT Executive Committee (NEC) for feasibility review
    - NINDS Extramural Science Committee (ESC) for scientific merit & budget review
  - If no, NINDS informs Protocol PI and discusses other funding options

Summary Statements

Primary reasons for studies not funded are primarily concerns with:

- Scientific Rationale/Significance
- Dosing/PK/PD
- Trial Design
- Outcome Measures