2015 Cure SMA Research Update

Jill Jarecki, PhD

June 20, 2015

Make today a breakthrough.

2015 Research Update Session

- **Presentation on Cure SMA Research Activities**
  - Jill Jarecki PhD, Cure SMA Research Director - 15 min

- **Talks and Question & Answer Panels**
  - Complexity of Clinical Trials for SMA, John T. Kissel MD – 15 min
  - Complexity of Clinical Trials Panel Discussion - 45 min
  - SMA Drugs in Development Q&A Panel - 45 min

$57 Million in Total Research Funding
-$1.85M in New FY2015 Funding

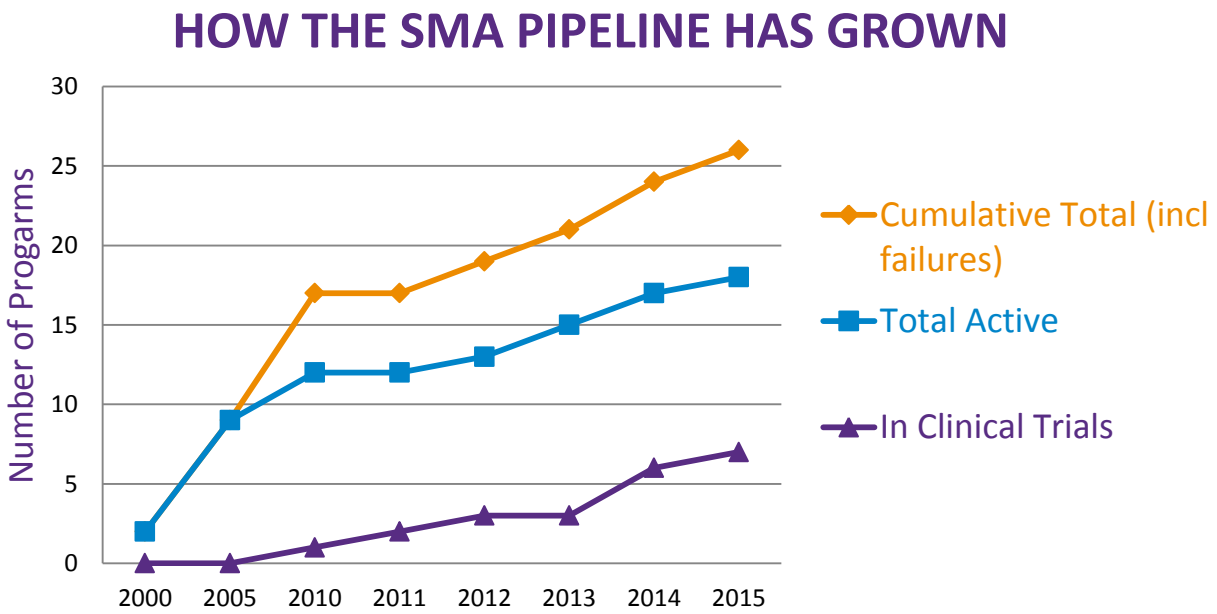
- **Basic research** to understand disease biology
- **Drug discovery** to make practical new therapies
- **Clinical research** tools to effectively test new therapies
- **Care research** to improve patient care and quality of life
- **Researcher meeting** to share and promote progress

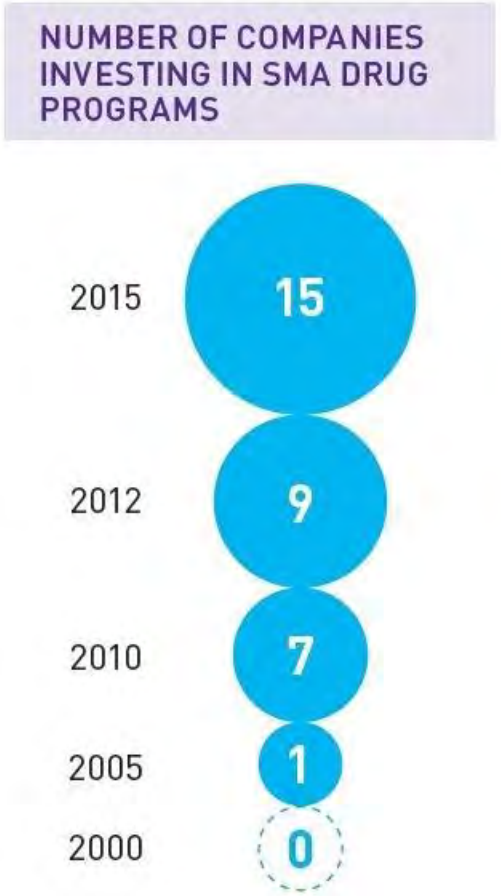
The Cure SMA funding model is based on independent and expert review by our SAB, TAC, and MAC.

Cure SMA Funds 24 Projects during FY2015 With $1.85M in New Funding

- **12 Basic Research Projects**
- **4 Drug Discovery Projects**
  - $845,000 to Brian Kaspar PhD at Nationwide ($445,000 new in 2015)
  - $925,000 to Peter Schultz PhD at CALIBR ($315,00 new in 2015)
  - $105,000 to Chien-Ping Ko PhD at USC (new in 2015)
  - $150,00 to Adrian Krainer PhD at Cold Spring Harbor Laboratory
- **3 Clinical Research Projects**
- **5 Clinical Care Projects**
- **SMA Researcher Meeting**

Cure SMA Funding - Leverage





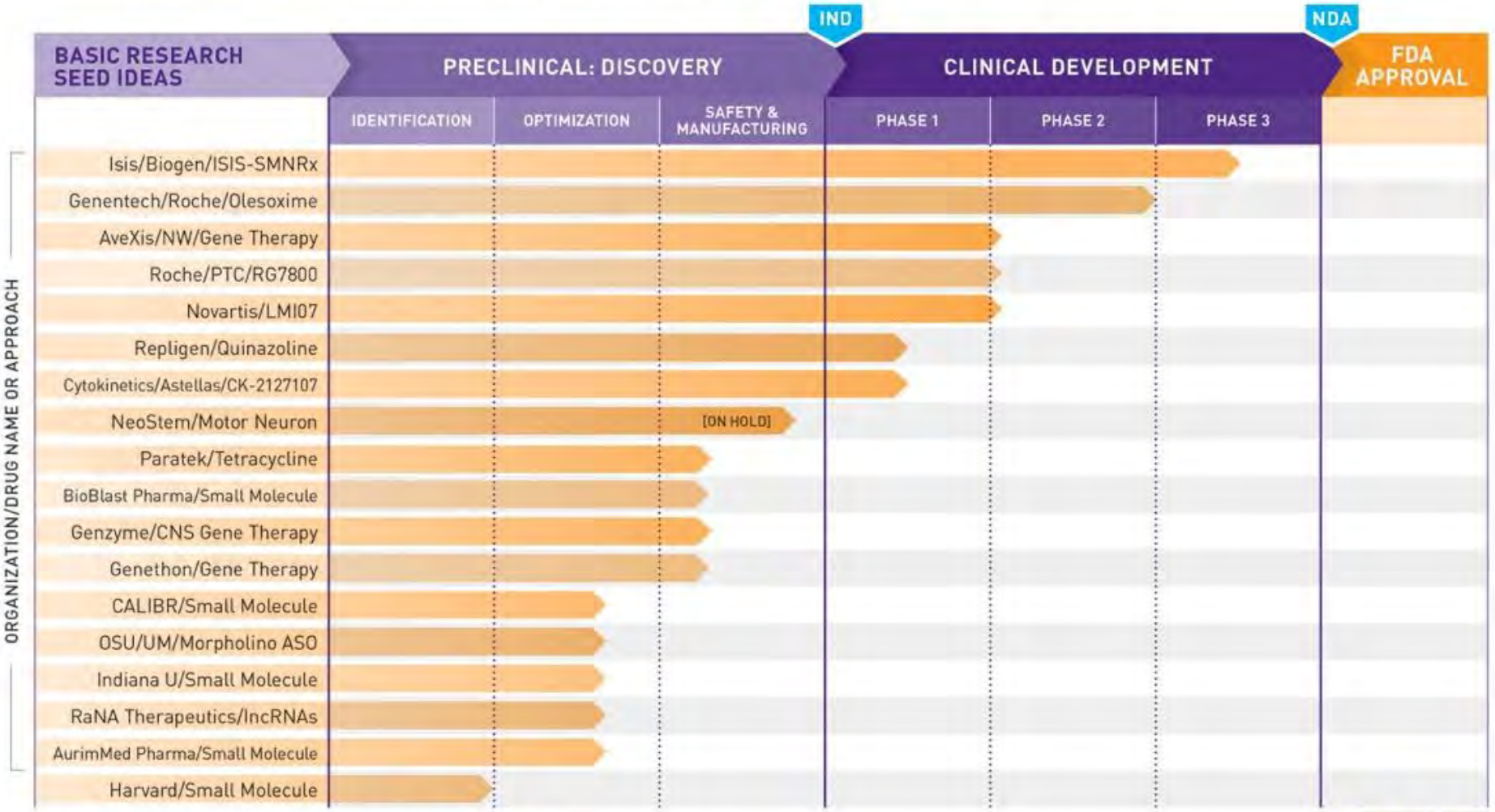
-Antisense (2003-07, $550K): U Mass licensed to ISIS

-Gene Therapy (2010-15, $850K): $4 million NINDS grant

FROM 2005 THROUGH 2013
CDER HAS AVERAGED
25
NOVEL NEW DRUG
APPROVALS PER YEAR

SMA DRUG PIPELINE: JUNE 2015

This year, we are funding research with more breadth, depth, and diversity than ever before. This chart shows the drugs and therapies that are currently in the pipeline for SMA, including a few that are just steps away from potential FDA approval.



IND = Investigational New Drug **NDA** = New Drug Application

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Facilitating Clinical Trials and Drug Development

- **Trial Outcomes / Endpoints**
  - Develop FDA sanctioned trial measures for SMA
    - Cure SMA Funding for trial endpoints to Dr. Lowes and Dr. Heatwole
- **Providing Patient Perspective to FDA**
  - Growing emphasis at FDA on patient focused drug development
    - Focus groups on meaningful benefit and impact on daily living
    - Surveys on clinical trial participation and expectations
    - Patient meetings with FDA
    - Further collection of data on patient point of view (risk / benefit)

Focus Groups: Experiences of Individuals and Families Affected by SMA and Their Views on Living with SMA

- **Participants:**
  - 96 people in 16 focus groups and 37 phone interviews
- **Identified 10 Psychosocial Impacts:**
  - 1) Confronting premature death, 2) difficult treatment choices, 3) fearing the loss of functional ability, 4) lost expectations, 5) fatigue & stress, 6) stigma, 7) limits on social activities, 8) independence, 9) uncertainty, 10) finances
- **Meaningful Change:**
  - Beneficial change is relative to current functional status
  - Avoiding further decline is very important
  - Small changes have big impact on quality of life & independence
- **Current Outcomes:**
  - Other disease features to measured: respiratory, swallowing, fatigue / endurance, activities of daily living

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Survey: Hopes and Expectations of Parents of Clinical Trial Participants

- 53 parents of children with SMA who participated in a clinical trial
- Altruistic & individual anticipated benefits critical to participation
  - Trial finds a drug that will work
  - Scientists learn important information about SMA
  - Trial results in a better future for other children with SMA
  - Trial would result in a better quality of life for my child
  - Trial would cause my child to get stronger
  - Trial would cause my child to live longer
- Anticipated harms were not critical factors in participation
- **Anticipated benefits were much more influential on decisions than anticipated harms**
  - Formal risk / benefit analysis of likely utility in SMA

Survey: Reasons Why Parents Have Not Involved Their Children in Clinical Trials

- 222 parents children who have not participated in a clinical trial
- 73% want" or "very much want" to have child in a clinical trial
- 67% child's doctor "never" or "not very often" talks trials
- 3 of top 5 reasons for not being in trial were on lack of info
  - Don't have enough information about the potential risks of clinical trials
  - Don't have enough information about day-to-day requirements of trials
  - My child could receive the placebo (which is inactive medication)
  - Don't have enough information about the potential benefits of trials
  - My child may not get any better in a clinical trial
- **Education needed about clinical trials from advocacy groups, physicians, clinical trial sites, & sponsors**

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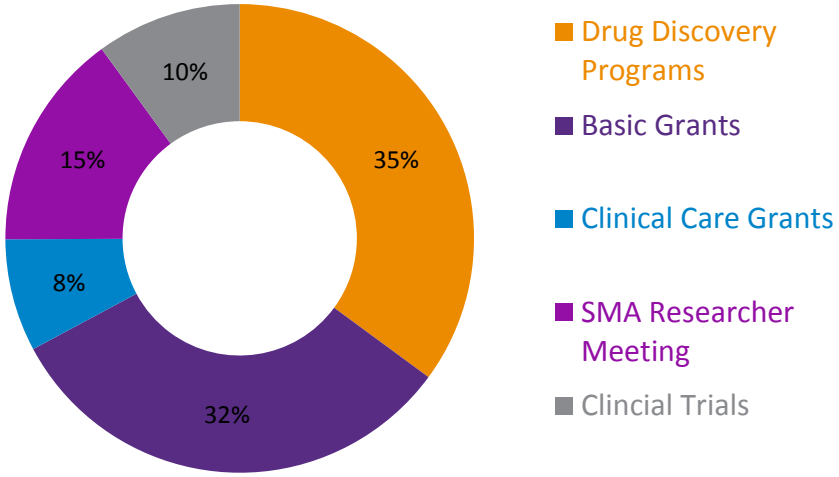
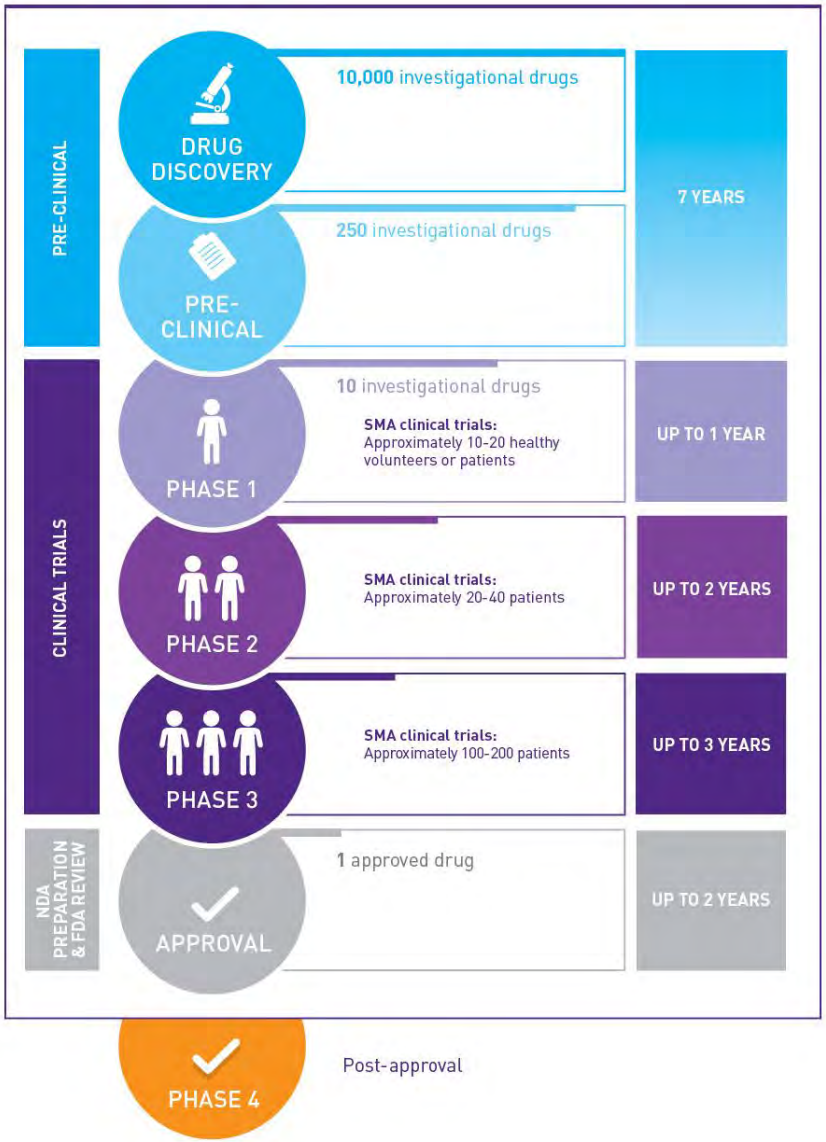
Another $1.995M in New Research Funding in 2016





Why more research funding is needed?

- **Approval rates:** only 10% receive FDA approval
- **Volume:** if one fails another is ready
- **Breadth:** attack with different biology approaches
- **Treatments for all:** drugs (or combinations) for
- every type and every stage of SMA

Moderated Panel Discussion: Complexity of SMA Clinical Trials

- **John T. Kissel MD,** Chair, Department of Neurology, The Ohio State University – **Moderator**
- **Richard Finkel MD**, Division Chief, Division of Neurology, Nemours Children's Hospital
- **Katherine Klinger PhD,** Sr. Vice President, Genetics and Genomics and Presidential Fellow, Genzyme Corporation
- **Thomas H. Murray PhD**, Senior Research Scholar, President Emeritus, The Hastings Center
- **John Whyte MD, MPH,** Director of Professional Affairs & Stakeholder Engagement, Center for Drug Evaluation & Research, FDA

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Expanded Access Programs

Expanded access, also called "compassionate use," is a way some drug companies can make investigational drugs available to patients with a serious disease like SMA who cannot participate in a clinical trial.

- FDA allows drug companies to provide expanded access for investigational drugs in particular circumstances
  - Serious disease or life threatening condition
  - No other treatment option available
  - Possible benefit justifies possible risks
  - Evidence the investigational drug will not expose patients to unreasonable risk
  - Access to investigational drug will not hurt overall development program
- The drug company must be willing and able to make drug available
  - Small companies may not have the resources available

http://www.fda.gov/ForPatients/Other/ExpandedAccess/

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