Opening General Session
2016 Annual SMA Conference
Disneyland
The Annual SMA Conference

Support
- Family Support Workshops
- Family Networking

Research
- Scientific Updates
- Research & Clinical Trial Updates

Care
- Professional Medical Provider Education
- Cross Discipline Networking

Patient Care Workshops
The SMA Conference

- 1,500 Attendees with 300 researchers and professionals
- 23 sponsors and 23 vendors

International Research Conference
- 120 Presentations
- 100 Organizations
Key Conference Events

- **Friday Evening Poster Session.**

- **Saturday Researcher and Clinical Trials Q&A:**
  - Cure SMA Research Activities.
  - Clinical Trials and Regulatory.
  - Current Clinical Programs.

- **Saturday Disney Park and Parade**

- **Sunday Closing General Session:**
  - It’s a Wonderful Life Panel

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34 Workshops:
- Talk it outs next
- 5 Sessions
Reasons for Progress

Know:
- The cause – SMN1
- A target – SMN2

Same cause and target for all

The approach:
- 1) Volume
- 2) Breadth
- 3) Leverage
- 4) Alignment

You - The SMA Community!
- Strong and positive and unified

18 new drug programs in development, 6 in clinical trials

The Challenge:
- Low Chance of Success
- High Cost
- Rare Disease
The SMA Community

- Regulators
- Companies
- Researchers
- Payers

Rare Disease:
- Grow the community.

One Community for All Types and All Ages:
- Type I to Type IV.
- Newly Diagnosed to Adults.
- Current and Future.
2016 SMA DRUG PIPELINE
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.

<table>
<thead>
<tr>
<th>BASIC RESEARCH SEED IDEAS</th>
<th>PRECLINICAL: DISCOVERY</th>
<th>CLINICAL DEVELOPMENT</th>
<th>FDA APPROVAL</th>
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<tbody>
<tr>
<td></td>
<td>IDENTIFICATION</td>
<td>OPTIMIZATION</td>
<td>SAFETY &amp; MANUFACTURING</td>
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<td>Ionis/Biogen-Nusinersen</td>
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<td>Cure SMA-DcpS Inhibitor</td>
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<td>BioBlast Pharma-Small Molecule</td>
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<td>Genzyme-CNS Gene Therapy</td>
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<td>Calibr-Small Molecule</td>
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<td>Harvard-Small Molecule</td>
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<td>Columbia/NU-p38aDAPK Inhibitor</td>
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<td>Imago-JNK Inhibitor</td>
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IND = Investigational New Drug  NDA = New Drug Application

Last updated: June 2016
Failure is Expected and Planned for

28 Attempts

HOW THE PIPELINE HAS GROWN

TOTAL PROGRAMS*

ACTIVE PROGRAMS

PROGRAMS IN CLINICAL TRIALS


*Includes failures

2 Steps Forward 1 Back (18 Current, 10 Failures)
The Closer We Get……
Level of Frustration

Different Levels of Access
SMA Clinical Trials

• Primary goal:
  – Get approval for as many as possible as quickly as possible.

• ~40% of drugs that look good in Phase 2 eventually fail after Phase 3.

• Placebo Controls:
  – Are quicker than natural history.
  – Give stronger data for approval.

• Narrow inclusion criteria:
  – Give better data for approval.
Averages across all the data, not just the few best, to Prove.
Key Issue

• We are now up to ~30 attempts:
  – 10,000 ideas to **30 attempts** to 10 trials to **1 approved**.
  – 15 Years, $100’sM’s.

• We need to perform the final stages correctly:
  – Normally will not get a second chance.
  – Not about failing (i.e., drugs that don’t work or are not safe).
  – **We do not want to lose a good drug.**

• We have to be fair and honest to all families:
  – The whole story and all the data.
Careful Balance: When is the data good enough?

- 40% chance of approval
- Label for 20% of patients
- Sooner

- 60% chance of approval
- Label for 60% of patients
- A year later

Trying to speed up drug approvals can slow them down:
- Need to repeat a trial
  - Sometimes you only get one shot
Access to Drugs

• Priority and Dominating Goal:
  – Broad approval and coverage, as fast as possible.

• Other Methods – are good, but only if they don’t negatively impact above:
  – By participation in trials:
    • Very limited numbers, and chance of placebo.
  – By expanded access:
    • Limited by safety and efficacy criteria, and manufacturing and delivery issues.

• More people in trials can mean:
  – Longer timelines and worse data to try and get approval.

• Expanded Access can:
  – Prevent placebo controls and trial completion.
Incentives and Alignment

- Billions of dollars are on the line to align goals between industry and the community.

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<tr>
<th>Goal:</th>
<th>Families/Patients</th>
<th>Companies</th>
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<tbody>
<tr>
<td>A safe drug</td>
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<td>☑</td>
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<tr>
<td>A drug that works</td>
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<tr>
<td>For as many as possible*</td>
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<tr>
<td>As soon as possible</td>
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*vs Individual Need
Industry Activities

• Company consortium to collaborate on patient focused drug development projects:
  – Voice of the Patient Workshop with FDA
  – Further Define Clinical Meaningfulness
  – Risk / Benefit Framework for SMA
  – SMA Centers of Excellence for Clinical Trials
  – Education / Engagement: Physicians, Caregivers and Patients

• Making sure the companies:
  – Share data
  – Share ideas

Research:
- Biomarkers
- Outcome Measures
- Natural History
- Registries
Proactive Patient Voice

• Patient Voice and Data:
  – To shorten timelines and increase chances of success.

• Specific to Our Unique Disease:
  – Why:
    • Rare, Critical, Urgent.
  – What:
    • Information/Data vs Stories /Anecdotes.
    • Understanding vs Awareness.

• Clinical Trial Design and Regulatory Decisions:
  – What can you measure in SMA.
  – What should you measure in SMA.
  – Balance of what benefit for how much risk.
NDA Process

- So close! - in drug development terms!
  - 9 to 12 months.
- Includes everything about the drug:
  - Drugs are approved based on statistical data across the entire clinical trial.
- Potential for expanded access programs at this stage:
  - For some but not all.
After Approval…

• Proving it – the first step to broad access…
  – Make it.
  – Deliver it.
  – Pay for it.
  – Expand it.

• More Than 1 Therapy:
  – Slow to stop to reverse.
  – Different therapies for ages and types.
  – Multiple therapies over time.
  – Combinations to work better.
Thank you!

- You are the center!
- Raised $34 Million over last 7 years:
  - Research
  - Support
  - Care

![Fundraising Graph](chart.png)

- 2010
- 2011
- 2012
- 2013
- 2014
- 2015
- FY16
- BFY17

- $3,500,000
- $4,000,000
- $4,500,000
- $5,000,000
- $5,500,000
- $6,000,000
- $6,500,000
- $7,000,000