Community Congress: Annual Meeting

November 16th, 2016
Emil Kakkis, M.D. PhD
President, EveryLife Foundation for Rare Diseases
Community Congress
Uniting Industry & Patient Organization Partners to Solve the Drug-Development Puzzle

Philip Reilly, M.D., J.D.
Venture Partner, Third Rock Ventures
What does the Election mean for rare diseases?
Dr. Richard Pan
California State Senator
NETWORKING BREAK

Thank you Sponsors & Members
Foundation Mission, Milestones & Goals

Julia Jenkins
Executive Director

No Disease Is Too Rare to Deserve Treatment
Mission and Core Principles

Accelerating biotech innovation through science-driven public policy

What We Believe:
- No disease is too rare not to deserve treatment
- Rare disease therapies should be safe and effective
- We could do more with the science we already have

What We Do:
- Advocate for evidence-based public policy and regulatory reform

How We Get it Done:
- Grassroots action
- Scientific and policy expertise
Our Team

- **Julia Jenkins**, Executive Director
- **Max G. Bronstein**, Senior Director, Advocacy & Science Policy
- **Stephanie Fischer**, Senior Director, Patient Engagement & Communications
- **Carol Kennedy**, Chief Development Officer
- Sue Colton, Director of Development
- Grant Kerber, Deputy Director of Communications & Patient Programs
- **Vignesh Ganapathy**, Manager of Advocacy & Government Relations
- Lisa Schill, RDLA Special Events Program Coordinator
- Lindsey Cundiff, Office and Special Events Manager
Our Board of Directors

- **President & Founder Emil D. Kakkis**, MD, PhD, President/CEO, Ultragenyx
- **Secretary Julia Jenkins**, Executive Director, EveryLife Foundation
- **Treasurer Matt Wilsey**, President, Grace Science Foundation
- **Mark Dant**, Executive Director, National MPS Society
- **Ritu Baral**, Managing Director/Senior Biotechnology Analyst, Cowen & Company
- **Vicky Seyfert-Margolis**, PhD, Founder and CEO MyOwnMed
- **Mike Astrue**, Former Commissioner, Social Security Administration
- **Frank Sasinowski**, Director, Hyman, Phelps & McNamara, P.C.

*3 former FDA - 5 with family affected by rare disease*
We Succeed by Giving Rare Disease Patients a Voice

- We do not speak on behalf of patients
- Our programs seek to
  - Educate patients about the challenges of drug development and the legislative and regulatory process
  - Train advocates on how to tell their stories to affect policy change
  - Create opportunities to allow patients to be heard by policy makers and to build relationships with elected officials
  - Provide financial resources to ensure patients can travel to policy events
- Patients will be the key to fighting for any innovation policies in the next Congress - We must double down to support of our patient communities
Community Support & Outreach

North American Metabolic Academy encourages & trains the next generation of rare disease physicians and scientists

RareGiving gives $100,000+ to the community in grants and scholarships to ensure FDA & Congress hears from patients

Rare Artist promotes awareness of rare diseases & highlights the talents of our community

Rare Affair promotes investment in rare disease treatments during the JP Morgan Health Care Conference in San Francisco, CA
Brings 300 patients to Washington DC to learn about how legislation impacts access to treatments & to meet with Congress

Allows advocates who cannot come to DC to meet with their Members during August Recess, Regional Conferences train advocates

Ensures the Rare Disease Community has a permanent voice on Capitol Hill through regular briefings to educate Congress

TONIGHT!!! Honors Advocates who give patients a voice in state & federal government

www.RareAdvocates.org
Public Policy Objectives

The Foundation seeks practical policy solutions that will:

- Close the innovation gap for the 95% of rare diseases that have no FDA-approved treatment
- Ensure patients receive earliest access to diagnostic and treatment opportunities
- Improve the regulatory process and advance regulatory science for rare disease therapies
- Enhance the patient voice in policymaking, drug development and regulatory decision-making
Brings together FDA, NIH, industry and patients to address urgent regulatory challenges through case examples and expert led discussion.

Bipartisan legislation granting 6 months of market exclusivity for repurposing a drug for a rare disease.

Seeks to improve newborn screening policies at the State and Federal levels.

Fosters COLLABORATION between industry and patient organizations to seek policy solutions!!
Improving access to the Accelerated Approval Pathway

- Need pathway to qualify biomarkers
- Need clear guidance on qualification criteria, case by case basis does not improve predictability of the process
- Unlocking Lifesaving Treatments for Rare diseases Act (ULTRA)/Faster Access to Specialized Therapies (FAST ACT) language incorporated into PDUFA V bill (FDASIA, S. 3187)

- Passed: Sec. 901. FDASIA Enhancement of accelerated patient access to new medical treatments.
  - Considerations. – In developing the guidance . . . . the Secretary shall consider . . . . for drugs designated for a rare disease or condition under section 526 of the Federal, Food, Drug, and Cosmetic Act; and
  - (2) how to incorporate novel approaches to the review of surrogate endpoints based on pathophysiologic and pharmacologic evidence in such guidance, especially in instances where the low prevalence of a disease renders the existence or collection of other types of data unlikely or impractical.”
Improving FDA regulatory process

- Improve Specialization of FDA Review
  - Allow dual appointments with academia and/or NIH-NCATS (like CBER)
  - Allow for travel to scientific conferences
  - Lifting salary caps
  - Create new ODE unit with more specialized divisions
  - Could enable enhanced recruitment, which is currently a major challenge
Increasing the Flexibility for FDA Toxicology Requirements

- Longer FDA toxicology requirements were preventing early-stage clinical trials from starting in the U.S., delaying access to lifesaving treatments for U.S. patients.

- 2014 Foundation Scientific Workshop “Rationalizing Safety Testing to Enable Clinical Studies and Approval in the US for Rare Disease Treatments” sought to address the issue.

- In the spring of 2015, the FDA outlined their new toxicology requirements in their draft guidance for industry, titled “Investigational Enzyme Replacement Therapy Products: Nonclinical Assessment.”
  - The guidance potentially allows for only three months of chronic toxicology animal studies if there are no adverse findings, which is a significant improvement in policy.
California Newborn Screening Legislation – SB 1095

- California has the largest number of babies born in the US
- New legislation was needed every time a new disease was added to the RUSP
- Introduced by Dr. Richard Pan in February 2016
- Requires that California screen for a disease within two years of it being added to the RUSP
- Supported by more than 120 patient organizations
- Passed unanimously through the Assembly & Senate
- Requires screening of MPS I & Pompe disease by Sept. 2018
- Governor Jerry Brown signed on Friday, September 16th 2016 (7 months after introduction)
2016 Publications

- **Op-Ed: Closing the Rare Disease Innovation Gap** Morning Consult – October 7th, 2016, by Emil Kakkis, MD PhD and Max Bronstein (Support of the FDA’s approval of the novel therapy for Duchenne based on BioMarkers)

- **Patients as Key Partners in Rare Disease Drug Development** – Nature Reviews Drug Discovery – July 22nd, 2016, by Emil Kakkis, MD PhD and Max Bronstein (Outcome of 2015 Scientific Workshop)

- **Accessing the Accelerated Approval Pathway for Rare Disease Therapeutics:** *The need for an improved qualification process for biomarkers as primary endpoints in pivotal clinical studies of treatments for the rarest of diseases* – Nature Biotechnology – April 7th, 2016, by Emil Kakkis, MD PhD and Max Bronstein
New Partnerships

- Partnered with NORD & Global Genes on a United Day of Action
- New partnership with Global Genes host regional patient advocacy conferences
- Providing financial sponsorship & promotion of the State House Events for Rare Disease Day
- Partnering with March of Dimes to advance state newborn screening legislation

TIME IS RUNNING OUT
WE NEED #CURESNOW
Closing the Innovation Gap - 21st Century Cures Initiative

• **Foundation Priorities:**
  – Orphan Product Extensions Now, Accelerating Cures & Treatments (OPEN ACT)
  – Improve biomarker qualification
  – Improve FDA’s ability to recruit & retain staff & keep up on the latest science
  – Billions in NIH & hundreds of millions in FDA Funding

• **Foundation supported efforts:**
  – Expanding Hope Act (Priority Review Vouchers)
  – Neurological Disease Surveillance
  – Compassionate Use Reform & Enhancement Act
  – Patient Focused Drug Development
THE 21ST CENTURY CURES ACT CAN CHANGE THESE STATISTICS. CURES WAS PASSED OVERWHELMINGLY BY THE HOUSE 344-77 IN 2015.

16 MONTHS LATER IT STILL HAS NOT REACHED THE PRESIDENT’S DESK!

PATIENTS CAN’T WAIT A DELAY IN LEGISLATION IS A DELAY IN LIFE-SAVING TREATMENTS #CURESNOW
Community Congress Overview

Max Bronstein
Senior Director, Advocacy & Science Policy

No Disease Is Too Rare to Deserve Treatment
We Can Achieve More When We Work Together
A Divided Environment
The Dynamic

- Rare disease advocates can help bridge this divide
- Patient organizations and industry are key stakeholders in developing new treatments for rare diseases
- Each brings a unique but critical perspective
- When patient organizations and industry align, we can achieve more and make an IMPACT
- Successful policy is shaped by bringing many stakeholders to the table
Program designed to foster collaboration between patient organizations and industry

- Strategic advisory committees
- On call to respond to urgent policy issues
- Provide a forum for discussion with a goal of taking action
Our Structure

Newborn Screening
Co-Chairs:
Jay Greissing, BioMarin
Elisa Seeger, Aidan Jack Seeger Foundation

Public Policy
Co-Chairs:
Ted Buckley, Shire
Christina Might, NGLY1.org

EveryLife Foundation – Staff Support

Regulatory Science
Co-Chairs:
Lynne McGrath, RegenxBio
Steve Smith, National MPS Society

No Disease Is Too Rare to Deserve Treatment
Self-Selected Issues in 2016

- Public Policy – Early Access
- Newborn Screening – Legislation in California
- Regulatory Science – Navigating the Accelerated Approval Pathway
Joining

- You can sign-up today
- **FREE** for patient organizations to join
- Fee structure for industry – funding enables us to keep the program free for patient organizations and helps support events and programming
- [www.everylifefoundation.org](http://www.everylifefoundation.org)

---

**EveryLife Foundation Community Congress**

![EveryLife Foundation Logo]

Click here to register for the November 16, 2016 in-person meeting

**What is the Community Congress?**

The Community Congress is a membership-based program of the EveryLife Foundation dedicated to bringing patient organizations, industry leaders, and other rare disease stakeholder organizations together. The Congress acts as a strategic advisory council, providing key advice and insight on existing Foundation programs. Members of the Congress have the opportunity to help shape and drive Foundation policy initiatives and will have access to exclusive members-only content through webinars and annual, in-person meetings in Washington, D.C.

**Current working groups include:**

**Public Policy** – Focusing on the topic of expanded/early access and guiding the development of the Foundation’s annual Scientific Workshop.

**Regulatory** – Focusing on improving the drug approval process at FDA through the qualification of biomarkers and enhanced specialization.

**Newborn Screening** – Focusing on expanding newborn screening for rare diseases through state-level legislation.

Each working group is co-chaired by a patient organization participant and industry participant. Working groups engage on an ongoing basis and meet annually in November in Washington D.C. Ultimately, Community Congress serves as a platform for engagement with rare disease stakeholders and provides critical guidance to the Foundation and leadership to the rare disease community.
Today

- Next up: Working Group Updates
- Networking Lunch
- 12:30pm-2:30pm Working Group Breakout Meetings
  - Newborn Screening
  - Public Policy
  - Regulatory Science
Updates from the Public Policy Working Group: Expanded Access

Cristina Casanova Might
Founder & Executive Director
NGLY1.org
Expanded Access Public Policy Working Group

Co-Chairs: Ted Buckley (Shire) & Cristina Might

Abeona Therapeutics
ALD Life
ALS Emergency Treatment Fund
American Behcet’s Disease Association
Amgen
Bluebird Bio
BRBN Alliance
Dercums Foundation
EDSers United Foundation
GIST Cancer Awareness Foundation
Global Genes
Immunophotonics
Insmed
Let’s Breathe Sarcoidosis Support
National Fragile X Foundation
National MPS Society
Parent Project Muscular Dystrophy
Pulmonary Fibrosis Advocates
Rare & Undiagnosed Network
Sarcoma Foundation of America
Stiff Person Syndrome Action Network, Inc.
United Leukodystrophy Foundation
Vaculitis Patient-Powered Research Network
Why I Care About Expanded / Early Access...
Eliminating the challenges of N-glycanase deficiency through research, awareness & support.
N-glycanase Deficiency

- Congenital Disorder of De-glycosylation
- Estimated 500-1500 worldwide
- Discovered in 2012
- Neurodegenerative Disorder
  - Global Developmental Delay
  - Movement Disorder
  - Seizures
  - Neuropathy
  - Lack of Tears

No Disease Is Too Rare to Deserve Treatment
A Personal Perspective

No Disease Is Too Rare to Deserve Treatment
Mort Migh and Cristina Casanova met in the spring of 2002, as twentieth-year-old undergraduates at the Georgia Institute of Technology. Cristina was an industrial-design major with an interest in philosophy; Matt was a shy computer geek obsessed with "Star Trek." At first, Cristina took no notice of him, but the two soon became friends, and their full worry. Matt and Cristina described Bertrand to friends as being "jiggy"; his body appeared always to be in motion, as if he were wearing a coat of jelly. He also seemed to be in near-constant distress, and Matt's efforts to comfort him just enraged him," Matt says. "I felt like a failure as a father." When the Mighs raised their concerns with Bertrand's city, and the first available appointment fell on the same day as a mandatory family retreat. That afternoon, when Matt was able to check his phone, he saw that Cristina had left several messages. "I didn't notice them," he told me in an e-mail. "I didn't have to. The number of them told me this was really bad."

Bertrand had brain damage—er, at least, that was the diagnosis until an MRI revealed that his brain was perfectly normal. After a new round of lab work was done, Bertrand's doctors concluded that he likely had a rare, inherited movement disorder called ataxia-telangiectasia. A subsequent genetic screen ruled out that diagnosis. When Bertrand was fifteen months old, the Mighs were told that urine screening suggested that

Until recently, Bertrand Migh was the only known patient with a certain genetic disorder. His parents began searching for others.
Soul Searching

Three of my 70+ kids.

No Disease Is Too Rare to Deserve Treatment
Our Barriers to Access

Why we could...
- Drug
- Pharma Support
- Willing Clinicians

Why we didn’t...
- Natural History
- Quality > Quantity
- Insurance Concerns
Natural History Study

ACMG 2015

No Disease Is Too Rare to Deserve Treatment
The Next 5 Minutes

- Background
- Scientific Workshop
- Breakout Session
Expanded Access 2016

- Definition
- Individual v. Groups
- Importance to Rare Disease
- Hot Topic
  - Right to Try
  - Precision Medicine
  - FDA Expanded Access Navigator & New Form 3926
Scientific Workshop

- Origins & History
- Navigating Expanded Access
- Frameworks & Models
- Industry Case Studies
- Public Policy Landscape
Breakout Session

- Provide Additional Input &/or Questions
- Work on Expanded Access Publication
- Select Public Policy Topic for 2017
Thank You!

info@ngly1.org

NGLY1.org | NGLY1 Foundation

No Disease Is Too Rare to Deserve Treatment
Regulatory Science Working Group

EveryLife Foundation for Rare Diseases
Rare Disease Community Congress
Update: November 16, 2016

Steve Smith, SteveSmithPlans LLC
SteveSmithPlans.com

No Disease Is Too Rare to Deserve Treatment
Steve Smith

- SteveSmithPlans.com
- MPS Parent since 1990
- Pharma Companies
- Software, Data Collection, Analysis
- CureTheProcess 160 Advocacy Groups
- 21st Century Cures
- Volunteer National MPS Society
  - Committee Federal Legislation
Objectives

Regulatory Science Working Group

Examine issues that impede rare disease drug development and approvals

- Build awareness
- Facilitate discussion
- Encourage collaboration
- Suggest approaches
More Trials & Approvals Possible

Trial Design
- Endpoint Selection & Validation
- Biomarkers as Surrogate Endpoint
- Long-Term Studies

More Rapid Trials
- Accelerated Approvals
- Adequate and Well-controlled Studies

New Approval Paths
- Small Patient Populations
- Heterogeneity
Activities & Resources

Activities

- **Conference Call 2015**: Biotech, Patients: FDA Guidance
- **Webinar: October 2016**: FDA, Biotech, Patients
- **Annual Meetings** (Nov 16, 2016)

Resources

- **White Papers**
- **FDA Guidance & Response**
- **Webinar Replay & Slides**

Response to FDA Guidance: 

*Guidance is too general; need specifics*

- Small patient populations
- Heterogeneity of disease and response
- Endpoint Selection
- Biomarkers as surrogate endpoints
- Long term studies
White Papers on Regulatory Science

http://everylifefoundation.org/foundation-papers/

- Recommendations for the Development of Rare Disease Drugs using the Accelerated Approval Pathway and for Qualifying Biomarkers as Primary Endpoints in Pivotal Clinical Studies – Orphanet Journal of Rare Diseases – February 10, 2015 by Emil D KakakisEmail author, Mary O’Donovan†, Gerald Cox†, Mark Hayes†, Federico Goodsaid†, PK Tandon†, Pat Furlong†, Susan Boynton†, Mladen Bozic†, May Orfali† and Mark Thornton†

- Accessing the Accelerated Approval Pathway for Rare Disease Therapeutics – Nature Biotechnology – April 7th, 2016, by Emil Kakakis, MD Ph, Sara Kowalcyk, and Max Bronstein


- FDA’s Flexibility in Subpart H Approvals: Analysis Shows Wide Variances Between the Quantum and Quality of Evidence for Approval – August 2016, Hyman, Phelps & McNamara, Frank Sasinowski and Alexander Varond
FDA’s Flexibility
Not a Product of Working Group But Helpful

August 04, 2016

FDA’s Flexibility in Subpart H Approvals: Analysis Shows Wide Variances Between the Quantum and Quality of Evidence for Approval

by Hyman, Phelps & McNamara, P.C’s Frank Sasinowski and Alexander Varond

...researched the bases for FDA’s determinations when an unvalidated surrogate or intermediate clinical endpoint is “reasonably likely to predict clinical benefit.

... takeaway from the paper is that a robust showing on the key factors in FDA’s May 2014 Guidance is not required, or, as the authors write: “you don’t need to knock it out of the park” on all 3 factors.

... For their efforts, the authors “hope to promote a better understanding of the circumstances under which Subpart H may be employed

... mobilize expanded FDA use of Subpart H.”
Webinar October 2016 - Speakers

- Max Bronstein – Chair
- Steve Smith – Patients & Data Perspective
- Dr. John Goldsmith – FDA Perspective
- Lynn McGrath, VP Regulatory Affairs, Cases
- Shamim Ruff – Sarepta SVP Regulatory Affairs, Etepliensen Case Study
- Isabelle Lousada – CEO Amyloidosis Research Consortium
Webinar

Approval Pathways

• **Both** pathways must meet the statutory standards:
  • Substantial evidence based on adequate and well-controlled clinical study(ies)
• Accelerated approval expedites new drug availability for *serious unmet need* by relying on a more readily measured *surrogate* or *intermediate clinical endpoint*
Webinar: Case Studies – Lynn McGrath

- Lynn McGrath – Cases on Rare and Metabolic, Ultra-Rare Metabolic, Rare Cancer: accelerated approvals vs full approvals and whether they got Fast Track, Priority Review, Accelerated Approval, and Breakthrough Therapy Designation.
Conclusion

- Multiple FDA guidance available for industry to gain insights into drug development and approval process
- FDA considers the unique characteristics of patients, unmet need, rarity of disease and the challenges in conducting trials
- FDA provides multiple opportunities for industry sponsors for rare diseases with an unmet need discuss and facilitate development
- FDA does not compromise study quality in any approval
Eteplirsen Case: Dystrophin as surrogate endpoint and whether it was reasonably likely to predict clinical benefit, the issues, and decision based on totality of evidence. And reactions thereto.
Types of Biomarker Studies Done by ARC

- Retrospective studies using clinical specimens, known clinical outcomes and research or analytically validated assays
- Prospective validation studies
- Exploratory (correlative) studies using clinical biospecimens and research assays
- Prospective natural history and biomarker studies
- Standardization of data collection across Collaborative Network
- Biobank
Working Group Next Steps?

- Nov 16, afternoon. All welcome.
- Watch EveryLife Foundation Website

Steve Smith 630 779 9560
SteveSmith@stevesmithplans.com
SteveSmithPlans.com
Community Congress
Newborn Screening WG Update

Mark Dant
President and CEO, National MPS Society
Board Member, EveryLife Foundation for Rare Diseases

No Disease Is Too Rare to Deserve Treatment
No Disease Is Too Rare to Deserve Treatment
No Disease Is Too Rare to Deserve Treatment
No Disease Is Too Rare to Deserve Treatment
• Each state has its own newborn screening panel—some states screen for nearly 60 diseases while other screen for as few as 29
• To screen for a new disease, each state has to introduce new legislation, so there’s a patchwork of laws
• Patients and parent advocates have to testify in front of each legislature, while children get sicker
• Many children are missed and slip through the cracks because of where they were born
• A federal committee of experts recommends a screening panel, but states take up to 8 years before screening for a disease after it’s recommended
Sib 1
7 yrs old
Treatment from 3 yrs old

Sib 2
3.6 yrs old
Treatment From Birth

• We can do better!
• Universal screening will ensure that no baby is left behind
• If all states screen for what is recommended by experts, we can save lives and money
SB 1095

- Introduced by Senator Richard Pan, a pediatrician
- Allows state to screen for a disease within two years after the disease is recommended by the committee of experts
- Eliminates legislative delay in screening
- Allows for earliest treatment possible, saving many patients' lives
- Patients can now work on adding diseases to the RUSP instead of going to every state legislature
SB 1095

- Over 120 patient organizations showed support.
- Governor Jerry Brown signed SB 1095 on Friday, September 16th!
- California will *have* to screen for MPS I & Pompe by August 26, 2018
Community Congress Working Group

- Provided advice and expertise for patients and public health perspectives
- Instrumental in getting other organizations to support this legislation
What’s Next...?

Give advocates the resources they need to improve newborn screening in their states

- State Newborn Screening RUSP Alignment Toolkit
- California was the first state. We would like to introduce similar efforts in states with the highest birthrates, to screen for “at a minimum” what’s on the RUSP
What’s Next...?

Improve the federal newborn screening infrastructure

• “How to Add your Disease to the RUSP” Webinar.
• Newborn Screening Saves Lives Act reauthorization in 2018
Thank you Sponsors & Members

mbronstein@everylifefoundation.org