US Perspective on Advances for Rare Diseases

ICORD
Ede, Netherlands
9 October 2014

Sharon F. Terry, President & CEO
Elizabeth and Ian diagnosed with pseudoxanthoma elasticum (PXE) 1994

2014

Elizabeth: Teach for America
Ian: Organic Farmer
BioBank

Testing
Clinical Diagnostic Test Development via FDA & CLIA Regulatory Strategies

Patenting
Licensing & Intellectual Property Management

Gene Discovery

1995

Human Clinical Trials
2012

Drug Screening & Development Approaches

Therapeutics
--Small Molecules
--Nonsense mutants

PXE international

1999

nature genetics

Mutations in ABC6 cause pseudoxanthoma elasticum

1995

Seeing The Light
How The Terry Family's Fight Against Blindness May Change The Course Of Medical Research And IP Law

2000
Maturing Disease Advocacy

- **1950s-1960s** – **Medical Models**
  - Voluntary Health Agencies

- **1970s** – **Nascent Patient Movement** – **Missing Services**
  - Self-organized Disease Specific Organizations

- **1980s** – **Maturing Patient Movement** – **IS & IT Technology**
  - New Alliances and New Strategies Emerge, industry alliances

- **1990s** – **Powerful Momentum “Patient Power”** – **Websites & Email**
  - Institutionalized Advocacy Coalitions
  - Patient Organized Networked Research Organizations
  - Effecting Broad Change of Public Policy

- **2000s** – **Successful Models “Research Advocacy”** – **BioBanks**
  - Active Engagement in the Research Enterprise
  - Breaking Conventional Boundaries of the Medical Model
  - Demand for Quality, Services, Choice, & Personalized Delivery
  - Patient Rights Public Policy – Changing the Status-Quo

- **2010s** – **Networks in the Commons** – **Translation & Delivery**
Genetic Alliance engages individuals, families, and communities to transform health.

2003: Registry and BioBank founded
PCORnet: the National Patient-Centered Clinical Research Network

The **goal** of PCORI’s National Patient-Centered Clinical Research Network Program is to improve the nation’s capacity to conduct CER efficiently, by creating a large, highly representative national patient-centered clinical research network for conducting clinical outcomes research.

The **vision** is to support a learning US healthcare system, which would allow for large-scale research to be conducted with enhanced accuracy and efficiency.

- 1000 researchers, traditional and lay
- 29 funded entities covering all 50 states
- Focus on patient-centered outcomes research
- No “one size fits all”

CENA

- Community Engaged Network for All (CENA)
- 9 disease-specific advocacy organizations, UCSF, UCD
- From hepatitis (affects millions) to Alström syndrome (affects a several hundred)
## Clinical Data Research Network’s Disease Cohorts

<table>
<thead>
<tr>
<th>Organization</th>
<th>Common Cohort</th>
<th>Rare Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADVANCE</td>
<td>Diabetes</td>
<td>Co-infection with HIV and hepatitis C virus</td>
</tr>
<tr>
<td>CAPriCORN</td>
<td>Anemia; Asthma</td>
<td>Sickle cell disease; Recurrent C. Difficile colitis</td>
</tr>
<tr>
<td>Great Plains Collaborative</td>
<td>Breast Cancer</td>
<td>Amyotrophic Lateral Sclerosis (ALS)</td>
</tr>
<tr>
<td>Louisiana Clinical Data Research Network</td>
<td>Diabetes</td>
<td>Sickle Cell Disease, Rare Cancers</td>
</tr>
<tr>
<td>NYC-CDRN</td>
<td>Diabetes</td>
<td>Cystic fibrosis</td>
</tr>
<tr>
<td>Mid-South CDRN</td>
<td>Coronary Heart Disease (CHD)</td>
<td>Sickle Cell Disease (SCD)</td>
</tr>
<tr>
<td>PEDSNet</td>
<td>Inflammatory bowel disease</td>
<td>Hypoplastic left heart syndrome</td>
</tr>
<tr>
<td>PORTAL</td>
<td>Colorectal Cancer</td>
<td>Severe Congenital Heart Disease</td>
</tr>
<tr>
<td>pSCANNER</td>
<td>Congestive Heart Failure</td>
<td>Kawasaki Disease</td>
</tr>
<tr>
<td>P2ATH</td>
<td>Atrial Fibrillation</td>
<td>Idiopathic Pulmonary Fibrosis</td>
</tr>
<tr>
<td>SCIHLS</td>
<td>Osteoarthritis</td>
<td>Pulmonary arterial hypertension</td>
</tr>
</tbody>
</table>
**Patient Powered Research Networks span a range of conditions**

<table>
<thead>
<tr>
<th>Organization</th>
<th>PI</th>
<th>Condition</th>
<th>Proposed PPRN Population Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accelerated Cure Project for Multiple Sclerosis</td>
<td>Robert McBurney</td>
<td>Multiple Sclerosis</td>
<td>20,000</td>
</tr>
<tr>
<td>American Sleep Apnea Association</td>
<td>Susan Redline</td>
<td>Sleep Apnea</td>
<td>50,000</td>
</tr>
<tr>
<td>Cincinnati Children's Hospital Medical Center</td>
<td>Peter Margolis</td>
<td>Pediatric Crohn's Disease and Ulcerative Colitis</td>
<td>15,000</td>
</tr>
<tr>
<td>COPD Foundation</td>
<td>Richard Mularski</td>
<td>Chronic Obstructive Pulmonary Disease</td>
<td>50,000</td>
</tr>
<tr>
<td>Crohn’s and Colitis Foundation of America</td>
<td>R. Balfour Sartor</td>
<td>Inflammatory Bowel Disease (Crohn’s disease and ulcerative colitis)</td>
<td>30,000</td>
</tr>
<tr>
<td>Global Healthy Living Foundation</td>
<td>Seth Ginsberg</td>
<td>Arthritis (rheumatoid arthritis, spondyloarthritis), musculoskeletal disorders (osteoarthritis), and inflammatory conditions (psoriasis)</td>
<td>50,000</td>
</tr>
<tr>
<td>Massachusetts General Hospital</td>
<td>Andrew Nierenberg</td>
<td>Major Depressive Disorder (MDD) and Bipolar Disorder (BP)</td>
<td>50,000</td>
</tr>
<tr>
<td>Univ of California, San Francisco</td>
<td>Mark Pletcher</td>
<td>Cardiovascular health</td>
<td>100,000</td>
</tr>
<tr>
<td>University of South Florida</td>
<td>Rebecca Sutphen</td>
<td>Hereditary Breast and Ovarian Cancer (HBOC)</td>
<td>17,000</td>
</tr>
</tbody>
</table>
In both rare and common disorders

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<th>Proposed PPRN Population Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALD Connect, Inc</td>
<td>Florian Eichler</td>
<td>Adrenoleukodystrophy</td>
<td>3,000</td>
</tr>
<tr>
<td>Arbor Research Collaborative for Health</td>
<td>Bruce Robinson</td>
<td>Primary Nephrotic Syndrome (Focal Segmental Glomerulosclerosis [FSGS], Minimal Change Disease [MCD], and Membranous Nephropathy [MN] Multiple Sclerosis</td>
<td>1,250</td>
</tr>
<tr>
<td>Duke University</td>
<td>Laura Schanberg</td>
<td>Juvenile Rheumatic Disease</td>
<td>9,000</td>
</tr>
<tr>
<td>Epilepsy Foundation</td>
<td>Janice Beulow</td>
<td>Aicardi Syndrome, Lennox-Gastaut Syndrome, Phelan-McDermid Syndrome, Hypothalamic Hamartoma, Dravet Syndrome, and Tuberous Sclerosis</td>
<td>1,500</td>
</tr>
<tr>
<td>Genetic Alliance, Inc</td>
<td>Sharon Terry</td>
<td>Alström syndrome, Dyserkeratosis congenital, Gaucher disease, Hepatitis, Inflammatory breast cancer, Joubert syndrome, Klinefelter syndrome and associated conditions, Metachromatic leukodystrophy, Pseudoxanthoma elasticum (PXE)</td>
<td>50-50,000</td>
</tr>
<tr>
<td>Immune Deficiency Foundation</td>
<td>Kathleen Sullivan</td>
<td>Primary Immunodeficiency Diseases</td>
<td>1,250</td>
</tr>
<tr>
<td>Parent Project Muscular Dystrophy</td>
<td>Holly Peay</td>
<td>Duchenne and Becker muscular dystrophy</td>
<td>4,000</td>
</tr>
<tr>
<td>Phelan-McDermid Syndrome Foundation</td>
<td>Megan O’Boyle</td>
<td>Phelan-McDermid Syndrome</td>
<td>737</td>
</tr>
<tr>
<td>University of Pennsylvania</td>
<td>Peter Merkel</td>
<td>Vasculitis</td>
<td>500</td>
</tr>
</tbody>
</table>
‘Registry and BioBank in a Box’

• Add water and serve
• Deliver ‘white label product’
• Deliver technical assistance
• Cooperative – learn from each other
• Low cost and driving lower
• Community based and local trusted entities’
• Global standards and rigor
# Genetic Alliance Registry and BioBank Toolbox

<table>
<thead>
<tr>
<th>Where do I begin?</th>
<th>What is a biobank?</th>
<th>Guidelines for considering a registry/biobank</th>
<th>Advocates are leaders in biobanking</th>
</tr>
</thead>
<tbody>
<tr>
<td>How do I make this a reality?</td>
<td>Registry/repository start-up guide</td>
<td>Making your organization's biobank a reality</td>
<td>Genetic Alliance registry/repository boot camps</td>
</tr>
<tr>
<td>Is my organization ready?</td>
<td>Organizational readiness checklist</td>
<td>Biobank question &amp; answer session</td>
<td></td>
</tr>
<tr>
<td>How do I select a vendor?</td>
<td>Vendor assessment summary</td>
<td>Vendor assessment worksheet</td>
<td>Landscape analysis manuscript</td>
</tr>
<tr>
<td>Considering Genetic Alliance?</td>
<td>Genetic Alliance BioBank</td>
<td>GARB FAQs</td>
<td>Virtual tour of Genetic Alliance registry solutions</td>
</tr>
<tr>
<td>What else do I need to know?</td>
<td>Biobank governance</td>
<td>Biobank governance checklist</td>
<td>Resource list</td>
</tr>
</tbody>
</table>

*Publication* | *Training/mentoring* | *Videos* | *Webinar* | *Webpage* | *Worksheet*
CENA DAO Partners

- Alström Syndrome International
- Dyskeratosis Congenita Outreach
- Inflammatory Breast Cancer Research Foundation
- Hepatitis Foundation International
- Joubert Syndrome Foundation
- KS&A
- MLD Foundation
- National Gaucher Foundation
- PXE International
Can we connect without adding friction to people’s lives?
Needles in Haystacks
The haystack is made of needles...
...current methods of informed consent are challenged...
granular and dynamic engagement

not consent
not a transaction
not binary
not tiered
Because people have vastly different views about privacy and sharing… but all patients need a fast, simple, intuitive way to express their view (including in real time!)
High level architecture of the PEER Platform

CENA is powered by the PEER (Platform for Engaging Everyone Responsibly) Network for medical research, developed by Genetic Alliance, a 28-year old consumer health advocacy non-profit, and Private Access, Inc.

The Platform for Engaging Everyone Responsibly in Medical Research for all Disease Areas

Core components of PEER

CENA Patient Portals
- Customized for each CENA group
- Easily delivered via a secure iFrame
- “Gamified” survey questions
- Privacy preferences
- Guides to assist
- Dynamic consent
- Audit trail
- Future (request EHR, labs and Rx data)

Data Entry Facility
- Survey questionnaire, contact information, guide-based assistance, mobile interface, security and registration

PrivacyLayer®
- To create and manage permissions for sharing patient data wherever that data resides and at any level of granularity

Data Query Facility
- Search index, privacy-based ontology, simple and advanced search, alerts, access requests, security and registration

Health Data
- De-identified data patient reported

Contact Info.
- Personally identifying info

Privacy Directives
- Set by patient, dynamic & easy

Permissible Information
- From search and search alerts

Researcher Portal
- Search engine that respects patients privacy wishes
- Custom search alerts
- Bookmarks
- Do not show again
- Future (query from EHR, labs and Rx data)
How the PEER portal looks is entirely up to where it’s located.

The portal fits directly onto any web page and retains the top and bottom navigation.

Everything is patient-centric, and it supports both new users as well as individuals who may have started on a different organization’s Private Access-enabled site. Everyone benefits!
Users are assisted by highly intuitive, non-coercive “guides”

Multiple guides give an opportunity to use a variety of approaches, and selecting settings that are the most comfortable to each participant.
To enable ease **and** an extraordinary range of granularity

Each guide suggests his or her ideas as a possible starting point

For multiple categories of uses, and specified usage rights

Participants may choose to Permit, Decline, or wait for more information before deciding

Participants use privacy settings to specify who can, and cannot, access or use their de-identified and/or personal contact data, and for what purpose
Gamified questionnaire with easily customized topics

Common data elements
Standards
Ontologies – ORDO, HPO
Validated instruments

Participants see immediate feedback for how others have responded

OAuth2 authorization
Beginning in October 2014... Longitudinal data and automated reminders

The survey will become one of several sections available for participants to report information.

We’re adding ways to easily and intuitively ask about and visualize longitudinal information such as medical and family history, lab values, molecular profiles, and more.

Including the opportunity to set automated update reminders...

...and to chart longitudinal results.

With all this data being moved back into REDCap on a daily basis, and plans to eventually import it into i2b2 and TransSmart for better analytic tools.

My weight was approximately: 285 lbs

Welcome Back!

Health Survey 12% complete
Take part in our health survey; and as you respond see how your answers compare with others. Complete the whole survey, or just answer part now and finish later.

Medical History
Summarize information about symptoms, diagnosed conditions, procedures, medications and dosage levels, surgery dates, hospitalizations, and more.

Lab Results
With just a few clicks, report critical lab values and test results; and if you’d like, we’ll automatically chart these measures for you over time.

Molecular Profiling
Record information about biological markers including unique genes, proteins and other molecules derived from advanced genetic testing and molecular analyses.

Family History
Create and annotate a family tree with information about the genetic characteristics, and related ancestry information.
Each DAO creates & manages their customized PEER

Select and edit each element in the PEER portal to appear in the theme of its current website.

Curate inquiries (content, sequence, dependencies, etc) from a starting point of over 22,000 questions.

Create referral codes to use on any printed communications like letters and posters.

Also create custom badges to display on other websites.

...and view statistics for how all of these assets perform and why.

...and view a live preview of the page as it is modified.

Code is simply placed into page source and it begins working instantly.

...and data to which the group has rights can be located and downloaded in CSV format for analysis.
EspeRare: Merging patients & commercial interests

**Mission**

In partnership with patient groups, academia and medical reference centers, EspeRare uncovers the potential of existing drugs to address severe therapeutic unmet needs in neurological and immunological rare diseases.

**Strategic Goals**

- **Gives a chance to unexplored therapies in rare diseases:**
  - Identify & drive translational validation of “dormant” opportunities
  - Leverage established patient groups & biomedical networks
  - Invest foundation’s R&D revenues and grants in rare disease programs

- **De-risk early development of rare diseases programs:**
  - Combine not-for profit & public grants with commercial funds/assets
  - Bring Biopharma expertise to academia & patient groups collaborations
  - Translate patient engagement into scientific and regulatory efforts

- **Hand-over programs to commercial partners for late development:**
  - PhII/PhIII ready programs with strong network of patient groups & experts
  - Flexible partnering model, tailored to the asset & disease
“You never change things by fighting existing reality. To change something, build a new model that makes the existing model obsolete.”

Buckminster Fuller

Build the WE
Contact Information

For more information:
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CEO and President, Genetic Alliance, Inc.
(202) 966-5557, Ext. 202
sterry@geneticalliance.org

General Information: http://www.geneticalliance.org/programs/biotrust/cena

Online demo (for JSRDF shown here): http://jsrdf.org/JSLIFE-demo