Realizing the Collaborative Advantage in Pediatric Research

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Boston Children’s Hospital
President, Dana-Farber/Boston Children’s Cancer and Blood Disorders Center
Leland Fikes Professor of Pediatrics
Harvard Medical School
Disclosures

• License shRNA^{mir} architecture for hemoglobinopathies bluebird bio
• Consultant: Novartis (pediatric aplastic anemia)
• SAB and Co-Founder: Orchard Therapeutics
• Co-founder: Alerion Biosciences
Outline

• Overview of BCH Research
• Patient-centered science at BCH
• Our vision and how we interact with biopharma
• An example of academic/biopharma interactions in rare disease
• Our future in genomics and post-genomics era of pediatric diseases
Family and patient-centered science-driven vision for BCH

- Can you help me understand what problem my child has, why did it happen? Are you studying the reason this happened?
- Are there new treatments?
- Is there evidence that new treatments are effective?
- Are you doing new clinical trials?
- Is there a treatment that is correct for my child?
- Are you developing treatments that reduce side effects?
- Can you predict the long-term, natural history of disease that my child will experience?
Boston Children’s: Partner of Choice for Industry

A Leader in Clinical Care:
• Ranked #1 US News & World Report, 2017-2018 - 4 consecutive years
• >600,000 inpatient/outpatient visits
• >40 Clinical Departments
• >225 Specialized Clinical Programs
• 800 Faculty Members and 2000 Fellows

A Leader in Biomedical Research:
• Largest pediatric research program in the world based on extramural research funding
• Broad research areas that span diseases affecting all ages
• >$330 Million in research funding
• 2 Nobel Prize Winners
• 11 members, HHMI
• 7 members, National Academy of Sciences
• 11 members, National Academy of Medicine (formerly Institute of Medicine)
Total NIH Funding to Children’s Hospitals 2009-2016

Millions

Boston Children's Hospital
The Children's Hospital of Philadelphia
Cincinnati Children's Hospital Medical Center
St. Jude Children's Research Hospital

2009
2010
2011
2012
2013
2014
2015
2016
Scope of Research

Children’s has comprehensive research and clinical programs, including:

• Departments
  • Anesthesiology, Cardiac Surgery, Cardiology, Dentistry, General Surgery, Gynecology, Laboratory Medicine, Medicine (Pediatrics), Neurology, Neurosurgery, Nursing, Ophthalmology, Orthopedics, Otolaryngology, Pathology, Plastic Surgery, Psychiatry, Radiology, Urology

• Divisions (Medicine)
  • Adolescent Medicine, Developmental Medicine, Emergency Medicine, Endocrinology, Gastroenterology, General Pediatrics, Genetics and Genomics, Hematology/Oncology, Immunology/Allergy/Dermatology/Rheumatology, Infectious Diseases, Laboratory of Molecular Medicine, Medicine Critical Care, Neonatology, Nephrology, Pulmonology

• Interdepartmental Research Programs
  • Computational Health Informatics Program (CHIP), Program in Cellular and Molecular Medicine (PCMM), Neurobiology, Stem Cell, Vascular Biology
Research Areas of Expertise

- Gene and Cell Therapy
- Rare Diseases in all disease categories
- Vascular Biology and Cancer
- Genomics and Informatics
- Neurobiology and neuromuscular degeneration
- Stem Cells
- Cardiology
- Autism and Epilepsy
- Ophthalmology
- Immunology

Natural selection on a small scale: Immune cells called B cells battle each other to produce the best antibody. Here, green represents the B cells that are producing the "winning" antibody, which stamp out competing B cells (other colors). *Cell* 170 (5) 2017

3D organoids and RNA sequencing reveal the crosstalk driving lung cell formation. *Cell* 170 (6), 2017
Family and patient-centered science-driven vision for BCH

How we implement

Genes and environment
   →
Deep phenotyping
   →
Identifying and validating disease pathways
   →
Precision in diagnosis
   →
Targeted intervention and cures
   →
Improved long-term outcomes

Disease phenotype of GAMOS patients. Left: Kidney cells show signs of nephrotic syndrome. Right: Anomalies in brain development

Nature Genetics (2017) DOI: doi:10.1038/ng.3933
BCH Research Cycle: From Bench to Patient (and back again)

DISCOVERY
- Early Phase Discovery
- Discovery
- Target Validation
- Optimize Leads
- Process Chemistry
- Preclinical
- Phase I
- Phase II
- Phase III
- FDA
- Phase IV

TRANSLATIONAL RESEARCH
- Optimization

EARLY CRITICAL HUMAN TRIALS
- Phase I
- Phase II
- Phase III
- FDA
- Phase IV

WIDESPREAD APPLICATION
- Process Chemistry
- Preclinical
- Early Critical Human Trials
- FDA
- Phase IV
BCH Research

To support the translation of promising innovations into products for patient care

Each year, BCH invests ~$40 million into research infrastructure
BCH Research

To support the translation of promising innovations into products for patient care

BCH has specific programs in translational and clinical research

Focus on first in human studies

Translational Research Program and Translational Investigator Program
Mooney Family Initiative for Translational and Clinical Studies in Rare Diseases
Institutional Centers for Clinical and Translational Research
Nation-leading regulatory infrastructure in pediatric trials
Since 2009, BCH has committed $7M to 64 projects, resulting in:

- 7 startup companies garnering $42M in VC investment
- 9 license agreements
- $13M in additional funding at BCH
BCH Research

To support the translation of promising *innovations into products* for patient care

Technology and Innovation Development (TIDO)
Dedicated liaison to biopharma
BCH Research

To support the translation of promising *innovations into products* for patient care

Proven ability to carry out Phase III trials
Rare disease research platform and repository: Manton Center for Rare Diseases

- 1200+ families enrolled to date: Over 3800 individuals
- Enrolled for next generation sequencing, functional analysis, diagnosis and gene discovery
- Referrals from 23 departments/divisions
- N of 1 cases as well as large cohort studies

Capability to recruit broadly consented patients

Courtesy of Alan Beggs
Our vision: Disease expertise, unique patient cohorts and outstanding discovery science

- Genomic Info
- Samples
- Medical Data
- Boinformatics
- Research
- Population Sciences
- New Therapies
- Point-of-Care Innovations
- Academia
- Licenses, start-ups
- Biopharma, industry partners

Our vision:
Disease expertise, unique patient cohorts and outstanding discovery science
How do we interact with Biopharma?
### Selected Products Invented at Boston Children’s

**On the Market**

<table>
<thead>
<tr>
<th>Name</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>VonVendi</td>
<td><img src="shire.png" alt="Shire" /></td>
</tr>
<tr>
<td>Pomalyst and Revlimid</td>
<td><img src="celgene.png" alt="Celgene" /></td>
</tr>
<tr>
<td>Thalidomide</td>
<td></td>
</tr>
<tr>
<td>Namenda - Memantine</td>
<td><img src="forest.png" alt="Forest Laboratories" /></td>
</tr>
<tr>
<td>Neumega – IL-11</td>
<td><img src="pfizer.png" alt="Pfizer" /></td>
</tr>
<tr>
<td>Dystrophin Diagnostic</td>
<td></td>
</tr>
<tr>
<td>INF2 (FSGS) DNA Sequencing Test</td>
<td><img src="athena.png" alt="Athena Diagnostics" /></td>
</tr>
<tr>
<td>T3 Patient monitoring software</td>
<td><img src="etiology.png" alt="Etiometry" /></td>
</tr>
<tr>
<td>Surgical Sam Simulator</td>
<td><img src="chamberlain.png" alt="The Chamberlain Group" /></td>
</tr>
<tr>
<td>ACT.md Platform</td>
<td><img src="act.md.png" alt="ACT.md" /></td>
</tr>
<tr>
<td>Patient Communication Board</td>
<td><img src="vidatak.png" alt="VIDATAK" /></td>
</tr>
<tr>
<td>Quickchange Mutagenesis Kit</td>
<td><img src="agilent.png" alt="Agilent Technologies" /></td>
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</table>

**On the Market**

<table>
<thead>
<tr>
<th>Name</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprolix™ - Fc-Factor IX</td>
<td><img src="biogen.png" alt="Biogen Idec" /></td>
</tr>
<tr>
<td>Eloclate - Fc -Factor VIII</td>
<td><img src="biogen.png" alt="Biogen Idec" /></td>
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</tbody>
</table>

**In Clinical Trials**

<table>
<thead>
<tr>
<th>Name</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>MyChoice HDR test</td>
<td><img src="myriad.png" alt="Myriad" /></td>
</tr>
<tr>
<td>Omegaven - Omega 3-based parenteral nutrition</td>
<td><img src="fresenius.png" alt="Fresenius Kabi" /></td>
</tr>
<tr>
<td>Premiplex</td>
<td><img src="shire.png" alt="Shire" /></td>
</tr>
<tr>
<td>APZ2</td>
<td><img src="ticeba.png" alt="TICEBA" /></td>
</tr>
<tr>
<td>Neosaxitoxin</td>
<td><img src="grunenthal.png" alt="Grunenthal" /></td>
</tr>
<tr>
<td>Neuro-Spinal Scaffold</td>
<td><img src="invivo.png" alt="iN Vivo" /></td>
</tr>
<tr>
<td>TBX-01</td>
<td><img src="therabio.png" alt="TherabioLogics" /></td>
</tr>
<tr>
<td>mRNA 1440</td>
<td><img src="moderna.png" alt="Modern" /></td>
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</tbody>
</table>
## Selected Boston Children’s Startup Companies

<table>
<thead>
<tr>
<th>Therapeutics/Platform</th>
<th>Diagnostic/Devices</th>
<th>Digital Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphic Therapeutics</td>
<td>Claritas Genomics</td>
<td>Circulation</td>
</tr>
<tr>
<td>Orchard Therapeutics</td>
<td>Fate Therapeutics</td>
<td>REBIScan</td>
</tr>
<tr>
<td>INVIVO Therapeutics</td>
<td>DeclImmune Therapeutics</td>
<td>ACT.md</td>
</tr>
<tr>
<td>Scholar Rock</td>
<td>Affinivax</td>
<td>epidemico</td>
</tr>
<tr>
<td>Piper</td>
<td>Emulate</td>
<td>etiolmetry</td>
</tr>
<tr>
<td>Magenta Therapeutics</td>
<td>Quartet Medicine</td>
<td>neuro'motion</td>
</tr>
<tr>
<td>Alerion</td>
<td>Selecta Biosciences</td>
<td></td>
</tr>
</tbody>
</table>
Overview of Licenses / Revenue 2015*

US biomedical research institutes ranked by licenses executed, together with revenue, startups and US National Institutes of Health (NIH) awards and funding in 2015.

<table>
<thead>
<tr>
<th>Research institute</th>
<th>Licenses and/or options executed</th>
<th>Gross licensing revenue received</th>
<th>Startups</th>
<th>NIH awards(^a)</th>
<th>NIH funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mayo Foundation for Medical Education and Research</td>
<td>96</td>
<td>$36,773,336</td>
<td>7</td>
<td>395</td>
<td>$207,634,203</td>
</tr>
<tr>
<td>Massachusetts General Hospital</td>
<td>75</td>
<td>$74,628,784</td>
<td>N/A</td>
<td>769</td>
<td>$350,848,744</td>
</tr>
<tr>
<td>Brigham &amp; Women’s Hospital</td>
<td>56</td>
<td>$9,787,501</td>
<td>N/A</td>
<td>539</td>
<td>$333,214,883</td>
</tr>
<tr>
<td>Memorial Sloan Kettering Cancer Center</td>
<td>49</td>
<td>$201,643,367</td>
<td>3</td>
<td>254</td>
<td>$117,253,758</td>
</tr>
<tr>
<td><strong>Boston Children’s Hospital</strong></td>
<td>48</td>
<td>$7,677,274</td>
<td>5</td>
<td>319</td>
<td>$137,431,827</td>
</tr>
<tr>
<td>Wistar Institute</td>
<td>28</td>
<td>$19,285,000</td>
<td>1</td>
<td>44</td>
<td>$24,222,301</td>
</tr>
<tr>
<td>Cleveland Clinic</td>
<td>25</td>
<td>$27,244,088</td>
<td>6</td>
<td>210</td>
<td>$95,453,745</td>
</tr>
<tr>
<td>Cedars-Sinai Medical Center</td>
<td>12</td>
<td>$11,027,000</td>
<td>2</td>
<td>95</td>
<td>$41,464,366</td>
</tr>
<tr>
<td>Fred Hutchinson Cancer Research Center</td>
<td>11</td>
<td>$18,056,932</td>
<td>3</td>
<td>265</td>
<td>$232,612,758</td>
</tr>
</tbody>
</table>

\(^a\)NIH data shown for fiscal year 2015. Source: Association of University Technology Managers, university technology transfer offices, NIH.
Nature Biotechnology Top Academic Spinouts

2014
- emulate
- Scholar Rock
- Intellia
- Quartet Medicine

2016
- magenta

FierceBiotech’s Fierce 15

2013
- moderna

2015
- Intellia

2016
- Orchard therapeutics
Champion discovery

Deploy genomics in everyday medicine

Translate wealth of research into more effective, precisely targeted therapies

Invest in excellence

Build collaboration
Gene Therapy Medicinal Products

1) Isolation of the target cells (autologous or allogeneic)
2) Gene transfer
3) Re-Infusion of the genetically modified cells

Genetically modified human cells

Vectors, nucleic acids, replicating micro-organism (not including live vaccines)

Direct application:
- Viral vector
- Non-viral vector
- Naked DNA
- Replicating rec. micro-organism (adenovirus, Salmonella)
Strategy for *ex vivo* gene correction of monogenic diseases using HSC

**Advantages of gene therapy:**

- No donor search
- No chance of Graft-vs-Host Disease
- Cross-correction with supra-physiological expression of transgene

Dr. Sung-Yun Pai
Severe Combined Immunodeficiency (SCID): ‘Bubble Boy Disease’

Good candidate for treatment with GT

Fatal if not treated
Gene mutation known

Corrected by HSCT
Retroviral insertion near oncogenes associated with leukemia in X-SCID

Out of 20 patients, 5 (4 in Paris, 1 in London) have developed T acute leukemia

Insertion site

<table>
<thead>
<tr>
<th>Insertion</th>
<th>Gene(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P4</td>
<td>LMO2</td>
</tr>
<tr>
<td>P5</td>
<td>LMO2</td>
</tr>
<tr>
<td>P7</td>
<td>CCND2</td>
</tr>
<tr>
<td>P10</td>
<td>LMO2, BMI1</td>
</tr>
<tr>
<td>P8</td>
<td>LMO2</td>
</tr>
</tbody>
</table>

Clinical outcome

1 patient died (P4)
4 patients treated successfully
now have normal T cell number and diversity

Gene transfer for SCID-X1 using a self-inactivating (SIN) gammaretroviral vector

A multi-institutional phase I/II trial evaluating the treatment of SCID-X1 patients with retrovirus-mediated gene transfer

Sites:
Great Ormond Street Hospital, UK
Hôpital Necker Enfants Malades, France
Children’s Hospital Boston, US
Cincinnati Children’s Hospital Medical Center, US
Mattel Children’s Hospital, Los Angeles, US

BCH: US lead clinical site, FDA IND holder (DAW) and NIH grant lead site

Funding: NIAID U01
## Patient characteristics

<table>
<thead>
<tr>
<th>Pt #</th>
<th>Age at GT (mo)</th>
<th>Infection history</th>
<th>Months f/u</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.3</td>
<td>BCG, pneumonitis</td>
<td>61</td>
<td>Alive and well</td>
</tr>
<tr>
<td>2*</td>
<td>5.8</td>
<td>Viral ulcers</td>
<td>61</td>
<td>Alive and well</td>
</tr>
<tr>
<td>3</td>
<td>5.5</td>
<td>Bronchiolitis, BCG, CMV,EBV,RSV</td>
<td>51</td>
<td>Alive and well</td>
</tr>
<tr>
<td>4</td>
<td>6.8</td>
<td>BCG, Pneumocystis</td>
<td>45</td>
<td>Alive and well</td>
</tr>
<tr>
<td>5</td>
<td>9.0</td>
<td>Adenovirus, hepatitis</td>
<td>died</td>
<td>died</td>
</tr>
<tr>
<td>6*</td>
<td>10.5</td>
<td>BCG</td>
<td>45</td>
<td>Alive and well</td>
</tr>
<tr>
<td>7*</td>
<td>3.9</td>
<td>None</td>
<td>Off 6m</td>
<td>s/p cord blood</td>
</tr>
<tr>
<td>8*</td>
<td>8.2</td>
<td>Pneumocystis</td>
<td>43, 25</td>
<td>Alive, 2\textsuperscript{nd} GT</td>
</tr>
<tr>
<td>9</td>
<td>8.0</td>
<td>Pneumocystis, rotavirus</td>
<td>28</td>
<td>Alive and well</td>
</tr>
<tr>
<td>10</td>
<td>14.0</td>
<td>BCG, resp/GI sx</td>
<td>26</td>
<td>Alive and well</td>
</tr>
<tr>
<td>11*</td>
<td>8</td>
<td>Polymicrobial bacteremia</td>
<td>24, 14</td>
<td>Alive, 2\textsuperscript{nd} GT, s/p URD</td>
</tr>
<tr>
<td>12*</td>
<td>3</td>
<td>Adenoviremia</td>
<td>23</td>
<td>Alive and well</td>
</tr>
<tr>
<td>13*</td>
<td>3.9</td>
<td>None</td>
<td>8</td>
<td>Alive and well</td>
</tr>
</tbody>
</table>

No leukemias to date
(Median follow-up for 11 patients now 47 months)

Hacein-Bey-Abina, Pai et al, NEJM 2014, unpublished
A Modified γ-Retrovirus Vector for X-Linked Severe Combined Immunodeficiency


(DAW corresponding author)
Orchard Therapeutics

Founding Institutions:
Boston Children’s, University College London/
Great Ormond Street Hospital, UCLA, U of Manchester
Phase I/II trial of lentiviral gene transfer for SCID-X1 with low dose targeted busulfan conditioning

United States
Boston Children’s Hospital (lead site)
Sung-Yun Pai

UCLA Mattel Children’s Hospital
Donald Kohn

Europe
Great Ormond Street Hospital (London)
Adrian Thrasher
H. Bobby Gaspar

IND Sponsor:
David Williams, Boston Children’s Hospital
IND # 17679

Primary objective
To measure event-free survival and T cell immune reconstitution at 1 year

Secondary objective
To measure overall survival, safety, humoral immune reconstitution and multi-lineage gene marking

Funding: NIAID U01-AI125051 (Pai)
Vector produced by Yposkesi (France), Funded by Orchard Therapeutics
Target enrollment n=20, Boston (5), LA (5), Europe (10)
2 years of follow-up on this study
Long-term follow-up to 15 years post on separate protocol
## Under development Gene (and Cell) Therapy Trials

<table>
<thead>
<tr>
<th>Indication</th>
<th>PI(s)</th>
<th>Sponsor</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene therapy for SCID-X1 with low dose busulfan and a SIN-lentiviral vector</td>
<td>S. Pai</td>
<td>D. Williams Orchard Therapeutics (vector)</td>
<td>Regulatory stages: pending IND submission planned for Sept., plan for study opening in Fall</td>
</tr>
<tr>
<td>A Phase I trial of <em>intra-ventricular hematopoietic stem cell transplantation</em> for neurometabolic diseases</td>
<td>A. Biffi, C. Duncan, L. Goumnerova, S. Nikiforow</td>
<td>A. Biffi</td>
<td>Regulatory Stages: Pre IND meeting held in February, preclinical work proceeding to support IND application</td>
</tr>
<tr>
<td>HSC gene therapy for Type IIIA Mucopolysaccharidosis</td>
<td>A. Biffi</td>
<td>Orchard Therapeutics</td>
<td>Pre-clinical development phase: received Orphan Drug Designation, regulatory and gap analysis on going, clinical protocol complete</td>
</tr>
<tr>
<td>Gene Therapy for Hemophilia A</td>
<td>S. Croteau, A. Biffi</td>
<td>Spark Therapeutics</td>
<td>Site visit complete, IRB/IBC submission in progress</td>
</tr>
<tr>
<td>A Phase 1/2, Open-Label Safety and Dose-Finding Study of Adeno-Associated Virus (AAV) Serotype 8 (AAV8)-Mediated Gene Transfer of Human Ornithine Transcarbamylase (OTC) in Adults with Late-Onset OTC Deficiency</td>
<td>W.H. Tan</td>
<td>Dimension Therapeutics (Regenixbio)</td>
<td>Active: SRC review stage, plan for early summer enrollment</td>
</tr>
<tr>
<td>SMA type I &amp; II (IV and IT)</td>
<td>B. Darras</td>
<td>AveXis</td>
<td>Regulatory Stages: Protocols redesigned, GT SRC review stage, plan for early fall enrollment</td>
</tr>
<tr>
<td>CNL7 (Batten Disease) – AAV</td>
<td>A. Biffi</td>
<td>PI Initiated</td>
<td>Pre clinical development-18 mon to open</td>
</tr>
</tbody>
</table>
Family and patient-centered science-driven vision for BCH

How we implement

Genes and environment

Deep phenotyping

Identifying and validating disease pathways

Precision in diagnosis

Targeted intervention and cures

Improved long-term outcomes
Family and patient-centered science-driven vision for BCH

Courtesy of Ken Mandl
What is GRIN?

A collaborative effort to:

• Capture the extraordinary genomic and phenotypic variability across the largest, most diverse and complex pediatric populations.

• Provide scaffolding for deep collaboration around data and sample collection, sequencing, analysis and discovery.

• Be the founding institutions in an extensible, scalable network (strong interest expressed already by outside hospitals and health systems).
GRIN’s Intended Impact

Gene discovery:
• Rare diseases
• Rare/extreme phenotypes
• Pharmacogenetics

Cohort expansion:
• By genotype ➔ find patients with same genotype to enroll in clinical trials or perform more phenotyping
• By phenotype ➔ find patients with same phenotype to discover new genomic causes

Identify genetic attributes and contributors to health:
• Study genetic determinants of healthy children
• Provide control cohorts for genomic studies
Key outcomes:
GRIN will set the standards by which future large scale collaborative pediatric genomics research will be performed.
Target Populations

- Participants in funded research studies in which genomic information is collected (e.g. NIH funded)
- Community/Healthy Controls
- Patients having clinical exome testing
- Participants with specific disease or drug reactions

GRIN Cohort
Key outcomes: GRIN will set the standards by which future large scale collaborative pediatric genomics research will be performed.
Broad Consent

Agreement to share

- Molecular/genomic data
- Phenotype data (fully de-identified, aggregate, limited data sets)
- De-identified sample metadata
- Biospecimens
- Potentially full medical record data

Preserve ability to return medically actionable results

Ability to re-contact patients for future research
**Key outcomes:**
GRIN will set the standards by which future large scale collaborative pediatric genomics research will be performed.
Stored Samples

- DNA = minimum sample for inclusion
- Aligned sample metadata across sites
- Leverage power of institutional biobanks
- Potential to share samples upon request
**Key outcomes:**
GRIN will set the standards by which future large scale collaborative pediatric genomics research will be performed.
Genomic Data

Data sources
- Whole exome
- Whole genome
- Gene panels
- SNP array

Standardized data processing pipeline
- Hosted in the cloud
- Harmonized across institutions
- Standardized genomic sequencing metadata

Potential cloud analysis
- Variant Analysis
- Genomic Warehouse
- Tools: myBIC, Harvest, i2b2/tranSMART, Jupyter Notebook, gNOME
Standardize & Harmonize

Key outcomes:
GRIN will set the standards by which future large scale collaborative pediatric genomics research will be performed.
Phenotypic Data

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shallow Phenotype</td>
<td>• PCORNet Data Model&lt;br&gt;• OMOP</td>
</tr>
<tr>
<td>Medium Phenotype</td>
<td>• Standardized data collected for institutional biobank participants&lt;br&gt;• “GRIN standard”</td>
</tr>
<tr>
<td>Deep Phenotype</td>
<td>• Data collected for specific funded research projects</td>
</tr>
</tbody>
</table>
Key outcomes: GRIN will set the standards by which future large scale collaborative pediatric genomics research will be performed.

Domains:
- Data Sharing
- Phenotypic Data
- Genomic Data
- Target Populations
- Broad Consent
- Stored Samples

Standardize & Harmonize
Data Sharing

Data sharing supported by:

Legal
MTA and Investigator Collaboration Agreements

Regulatory
Aligned Protocol/Consent
Institutional Biobanks

Bioinformatics
Amazon Cloud Sharing
Aligned Metadata
How to address challenges of innovative therapies in rare disease in children?

- Lack of drugs studied, approved for pediatric indications
- Costs vs future margins on drugs
- Accrual time-lines for rare diseases; finding the subjects for trials
- Lack of accurate, annotated natural history data for many diseases
- Regulatory burden
- Regulatory disharmony across multiple countries and multiple agencies
- Differences in health care insurance across states and countries:
  - Payment for care given during clinical trials
  - Research harm financial obligations related small biotech/’academic reagents’ (IRB, NIH)
Key outcomes:
GRIN will set the standards by which future large scale collaborative pediatric genomics research will be performed.
Global Center for Pediatric Transformative Therapies at BCH

The BCH Global Curative Medicines Initiative

**Discovery & Translational Sciences**

**Disease Models**

**Regulatory**

**Cellular processing, IPS**

**GMP/GLP Research Pharmacy**

**Experimental Therapeutics Unit**

**Advanced Experimental Therapeutics**

**Biologics**

GMP/GLP

Cell manufacturing Research Pharmacy

**Validation and Disease Models**

**New Drugs**

**Biopharma**

Start-ups Licenses

**Genomics and Rare Diseases**

- genotype/omics/phenotype
- biological samples
- population sciences
- point of care innovations

**Novel therapeutics**

- Repurposing FDA approved drugs for pediatric conditions
- Devices
- Cellular therapies
- Molecular therapies
gene therapies
small molecules
antibodies

"Domestic and international collaborations"