Partnering Together to End the Diagnostic and Therapeutic Odyssey

Accelerating Newborn Sequencing by Whole Genome Sequencing (NBS-by-WGS) through Industry Partnerships

Winter 2022 RCIGM Conversations with Industry Partners

Rady Children's Institute
Genomic Medicine®

Rady Children's Institute for Genomic Medicine

Non-profit research organization embedded within Rady Children's Hospital-San Diego focused on improving lives through Rapid Precision Medicine

Pioneered a medical revolution to end the diagnostic odyssey for neonatal and pediatric rare disease

Trailblazers in end-to-end clinical whole genome sequencing, interpretation and analysis with a proprietary pipeline optimized for newborn screening

Successfully demonstrated **proven economic and clinical utility** capturing public, private and payor attention

Now we're moving to **end the therapeutic odyssey** with a disruptive new approach to newborn screening

Honest broker who understands the clinical landscape and has expertise in **moving things rapidly from feasibility to standard of care**

RCIGM by the numbers

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80 Hospital Partner Sites	>3,000 Genomes Sequenced	3 Avg Days to Rare Disease Diagnosis*
>$2.2M Cost Savings Generated	40% Average Diagnostic Rate	32% Change in Medical Care
#1 Largest West Coast Children's Hospital	281,469 Children Cared for in FY21	#6 NIH-Funded Ranking in FY20**

*Median # of days to delivery of provisional positive results
**University of California San Diego Department of Pediatrics

Leaders in Genomic Medicine

Rady Children's Institute Genomic Medicine®

Stephen Kingsmore
MD, DSc
President & CEO

Wendy Benson
Chief Strategy & Innovation Officer

Charlotte Hobbs
MD, PhD
VP, Research & Clinical Management

Sara Caylor
RN
Manager, Strategic Programs

Kirk Lamoreaux
Strategic Partnership Consultant

Jessica Merritt
Manager, Business Development

Looking Back on Progress

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2003
Human Genome Project

2009
Nic Volker
First Clinical Sequencing Case

2012
NSIGHT 1
at Children's Mercy

2013
GEMINI
GEnome MINIng

2014
RCIGM
Founded

2015
BabySeq

2015
SOMI
Rady + UCSD

2017
NSIGHT 2
at Rady Children's

2018
Project Baby Bear
State of California

2019
Project Baby Manatee
State of Florida

2021
Project Baby Deer
State of Michigan

2021
GTRx

The Burden of Genetic Disease is Still Unclear

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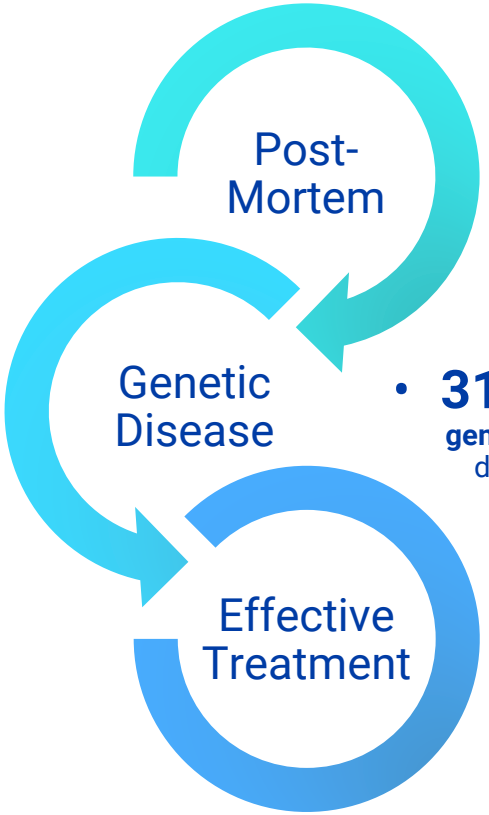
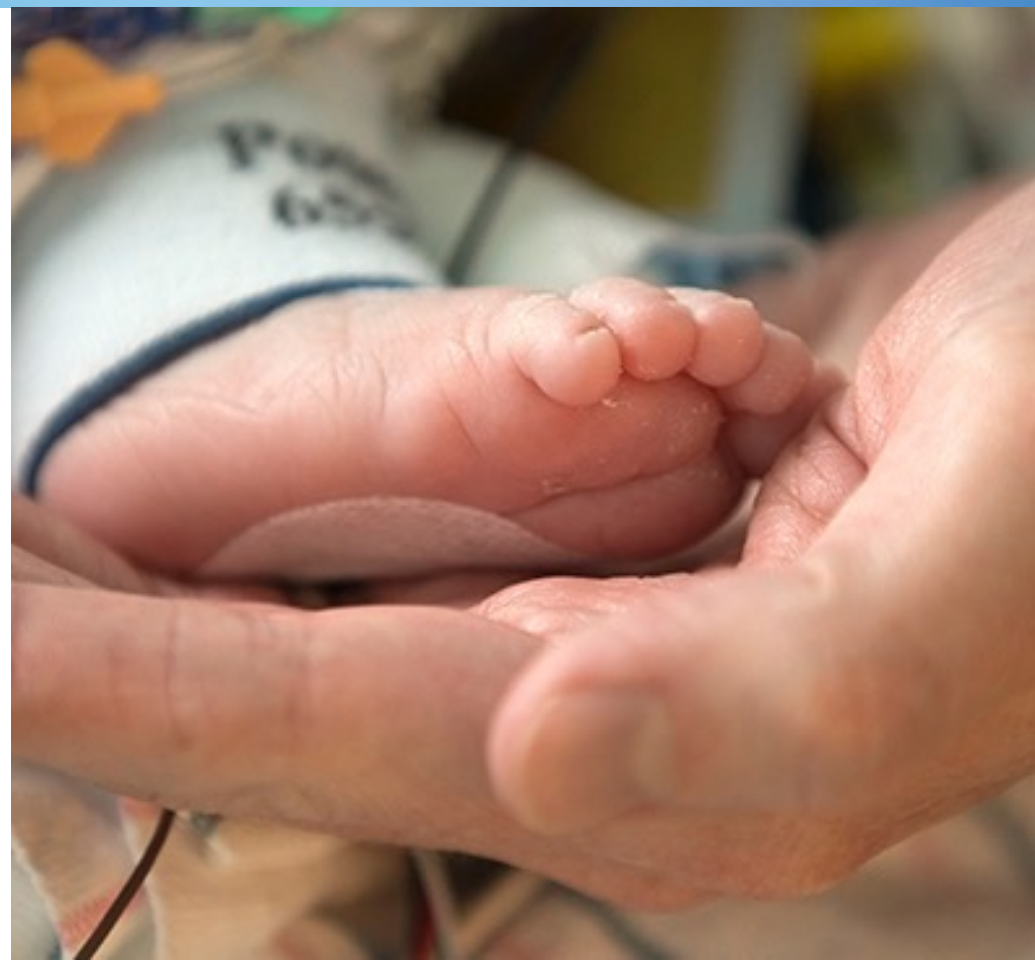
RCIGM & UCSD received an NIH grant (SOMI) to study how much infant mortality was caused by genetic disease in 2015-2020

SOMI
SAN DIEGO STUDY OF OUTCOMES IN MOTHERS AND INFANTS

NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development



- WGS performed **post-mortem** on **45 patients** who died as infants
- **31%** were found to have a **genetic disease** that was not diagnosed prior to death
- **57%** of these genetic diseases have an **effective treatment**



Infants are dying of undiagnosed genetic disease
NBS-by-WGS will help us find these patients earlier and save lives

An RCIGM-Led Consortium Will Enable the Future of Newborn Screening, Diagnosis and Treatment

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A perfect storm is accelerating access to precision medicine …

- Increasing numbers of effective and approved gene therapies
- Increasing projections of orphan drug development efforts
- Decreasing whole genome sequencing (WGS) costs and turnaround times

NBS-by-WGS

… and NBS-by-WGS will disrupt the current paradigm.

- Revolutionizing and shortening the diagnostic journey
- Intervening to change the course of a life from birth
- Force multiplying the process of slowly adding screening conditions
- Generating genomic data that empowers innovation and answers to rare diseases

Achieving Benefits by Addressing Concerns

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Benefits

- End the diagnostic odyssey for infants with treatable rare genetic diseases – saving lives and assisting families
- Screening can quickly scale as new treatments become available
- Improve our medical knowledge of genetic conditions and enable new research into treatments and cures in some instances

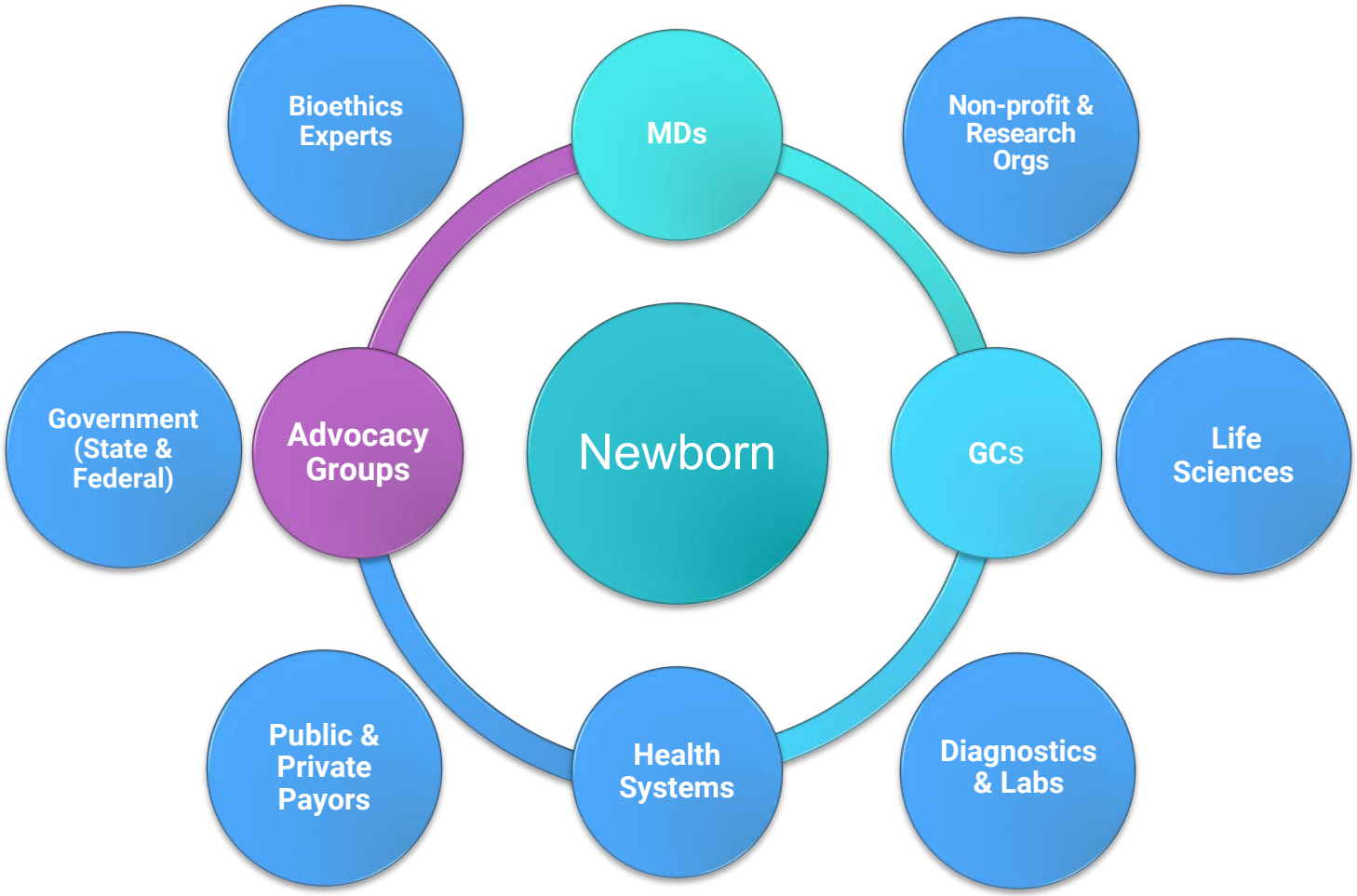
Public Concerns*

- Potential discrimination
- Fears of data breaches and loss of privacy
- (Un)certainty of WGS diagnosis
- Ensuring equitable access
- Misuse of data for social engineering
- Big data
- Is WGS the best use of money?

To earn the public trust, efforts must be transparent and include all stakeholders. Communication and education will be essential.

*As reported in Genomics England's article, "Implications of whole genome sequencing for newborn screening – A public dialogue"

Shifting the Paradigm Together



Collectively, the consortium will address important challenges related to:

- Appropriate Consent
- Data Governance
- Patient & Family Support
- Public Dialogue and Education
- Privacy & Security
- Clinical actionability
- Downstream uses of de-identified data

Closing the Gap and Accelerating Benefits

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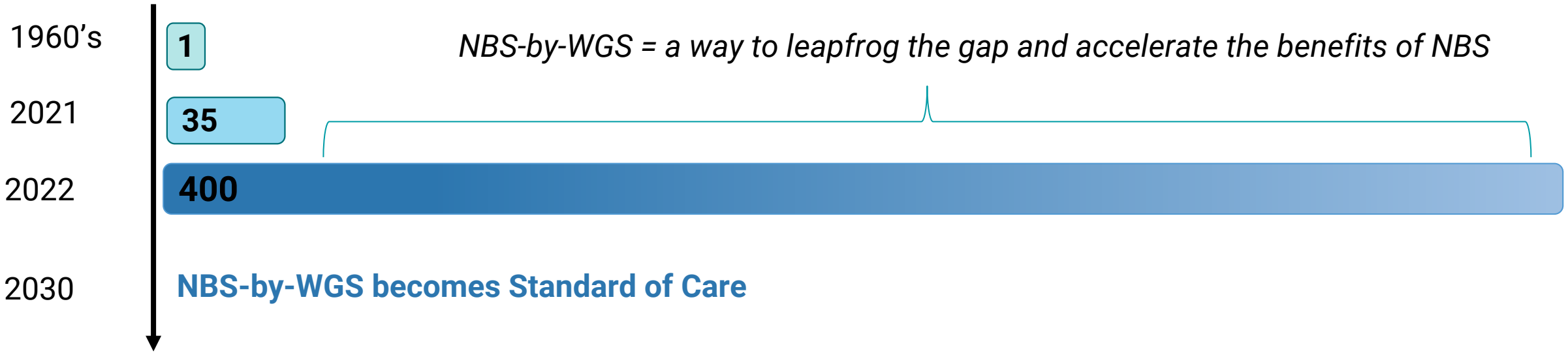
There are **~500 actionable genetic conditions** affecting newborns that could be screened by WGS for which treatments or treatment candidates in clinical trials currently exist.[1]



Without disruptive progress we will continue to see:

- Unnecessary death or irreparable damage
- Long painful diagnostic and therapeutic odysseys
- High healthcare costs
- Missed opportunities for diagnosis and treatment

rWGS Provided a Model for Moving Science to Clinical Practice

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Phase	Prototype	Alpha	Beta	…	Standard of Care
Goal	• Bioinformatics development • Faster turnaround times	• NSIGHT2 – rWGS vs rWES in neonatal intensive care unit • Project Baby Bear (PBB) – rWGS saves lives and money • 70+ partner hospitals		• Project Baby Deer – PBB spin off focused on rWGS coverage for all Michigan in-patients >18 yrs.	• Michigan Medicaid coverage of rWGS • Blue Cross Blue Shield coverage of rWGS in multiple states (CA, HI, ID, FL, NJ)
Timeline	2016	2017-2019		2020-2021	2022 and beyond
Case Volume	N/A	1,700+ patients		93 patients	TBD

rWGS is more than just a test. It is an enabler for a learning healthcare delivery system.

1 Education and Engagement

2 Testing and Confirmation

3 Translation into Precision Medicine

4 Acceleration of genetic therapy innovation

Building on the Model: A Proactive, RCIGM-led Consortium to Make Sequencing Based Screening a Reimbursed Reality

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Phase	Prototype	Alpha	Beta	…	Standard of Care
Goal	• Optimize automated sequencing and analysis pipeline • Curate a high-quality set of variants	• Demonstrate analytic performance • Quantify RWE of NBS-by-WGS • Generate economic data, create financial models • Implement and scale (e.g., sample collection, consenting, results return) • Address policy considerations (e.g., ELSI, establishment of data management rules)			• Apply infrastructure and learnings from pilot to sustainable, population-based newborn screening
Timeline	In progress	2022	2023-2024	~2026	2030
Case Volume	10,000 cases	1,000 newborns	10,000 newborns	1 million newborns cumulative	4 million US newborns

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Case Studies

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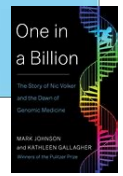
Nic

XIAP

- Developed illness at the age of 2 that caused intestinal inflammation after eating
- Over 100 surgeries by the age of 4
- Considered the sickest child at Children's Hospital of Wisconsin and his physicians feared he would die without intervention
- Clinician's suspected genetic disease
- First case of sequencing an individual's DNA clinically
- Mutation discovered in XIAP
- Bone Marrow transplant
- Nic's story was told in the Pulitzer Prize winning novel, One in a Billion



Sebastiana

KCNQ2

- Presented with seizures first day of life
- rWGS ordered on day 2 of life
- Novel mutation identified in the KCNQ2 gene – youngest child to be diagnosed
- Medication tailored treatment stabilizes Sebastiana's seizures
- Discharged home on day 18
- Read her story in Time Magazine

TIME

Fitz

DCLRE1C

- Appears healthy at birth
- Newborn test revealed he had SCID, a condition commonly referred to as "bubble boy disease"
- WGS pinpointed the exact variation of SCID
- The precise diagnosis allows Fitz to qualify for a gene therapy clinical trial
- Experimental treatment started and appears effective and successful
- Read his story in USA Today here: Baby Fitz was born without an immune system. His treatment offers hope for curing rare diseases. (yahoo.com)

USA TODAY

Sequence to Treatment Time	2009	2015	2019
	6 months	4 days	13 hours

The Time is Now.

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Newborn Sequencing by WGS (NBS-by-WGS)

Collaboration Opportunities

Together we will ***disrupt*** the current paradigm, ***shorten*** the diagnostic odyssey, and ***revolutionize*** the therapeutic journey for rare disease infants and children.

Biopharma

Become a ***Founding Partner*** of the RCIGM-led NBS-by-WGS Consortium, contributing expertise and guidance to the governance, data and advisory structure

Research, Biotech & Health Systems

Collaborate as a Consortium ***Affiliate Member,*** actively contributing expertise, thought leadership and advisory council participation

Advocacy, Governments & Payors

Become a ***Community Collaborator*** in the Consortium, contributing perspective, thought leadership and feedback

Collaborate with us
Contact Jessica Merritt, RCIGM Business Development Manager
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Help Us Make Baby Steps Toward Ending the Diagnostic Odyssey

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Please let us know if you are interested in joining as a **Founding Member** of the **RCIGM-led NBS-by-WGS Consortium** ahead of the **Alpha Phase**.

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https://radygenomics.org/