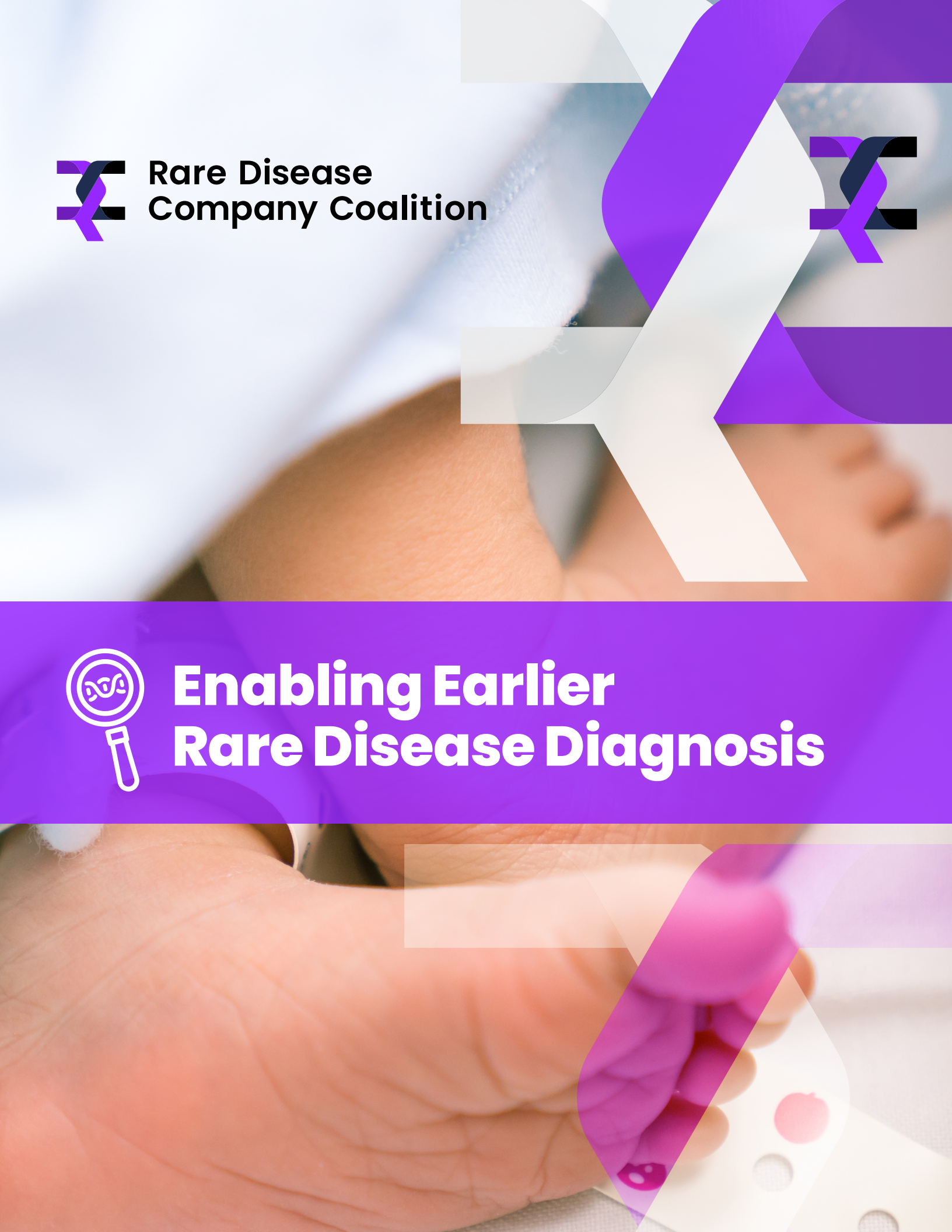
Rare Disease
Company Coalition

Enabling Earlier Rare Disease Diagnosis



Contents

Enabling Earlier Diagnosis:

Supporting more equitable and timely access to life-saving testing and diagnostics for rare diseases.

Rare disease diagnosis is uniquely complex. With over 10,000 known rare diseases, it can be challenging to pinpoint a diagnosis, especially when patient populations are as small as just a few dozen. Furthermore, the very nature of the rare disease means that physicians may not have the specialized knowledge needed to achieve an accurate diagnosis.

As a result, rare disease patients and families face the "diagnostic odyssey." Typically, it takes over 5[1] years to receive a correct rare disease diagnosis, and over a third of rare disease patients receive at least one misdiagnosis along the way.[2] Even when a successful diagnosis occurs, only 5 percent of known rare diseases have an FDA-approved treatment available. This process costs rare disease patients and caregivers precious time and resources. According to an EveryLife Foundation for Rare Diseases (EveryLife) study, the economic impact of rare diseases reached nearly $1 trillion in the U.S. in 2019 - a number that could be reduced with earlier diagnosis.[3]

To address these challenges, RDCC recommends the following:

1. Modernize Newborn Screening in the United States
2. Advance the Availability and Accessibility of New Testing Technologies
3. Provide Equitable Access to Specialists by Advancing Telemedicine Consults Across State Lines and Improving Training
4. Advance Education of and Access to Disease-Agnostic Biomarker Testing
5. Transform Rare Disease Research with Federated Data Models

1 Modernize Newborn Screening in the United States

Newborn Screening (NBS) is the process by which, in the first 24 to 48 hours of a baby's life, a small blood sample is taken to detect serious, often fatal, genetic conditions that can be treated if diagnosed early. According to a 2020 National Organization for Rare Disorders (NORD) survey, 44 percent of respondents that received NBS were diagnosed within 0-6 months, compared to 27 percent of all survey participants.[4] This is a critical and proven public health program that has yet to be adopted nationally because the current system is not equipped to keep pace with the current wave of medical innovation and new therapies.

"Since the sequencing of the human genome, we have the power to identify one of the many genes that can be defective in a child. When we see a child with these diseases, we have to be able to do the sequencing to help figure out what they have. Instead of spending 5 to 7 years or longer in a diagnostic odyssey, we need to support genetic tests for patients with symptoms so that they can get diagnosed promptly and participate in trials or receive better treatment for their conditions. It's unconscionable that we leave patients with rare diseases undiagnosed because we're not supporting genetic testing for those diseases."

~ Emil Kakkis, Chief Executive Officer and President, Ultragenyx

Policy Solutions:

- **Increase NBS Funding:** RDCC encourages Congress to establish a new stream of federal funding to incentivize national harmonization among states, accelerate review of a greater number of conditions each year, and enable states to support and improve their patient/family and pediatrician/provider follow-up programs. In addition, Congress should advance legislation authorizing funding to states that expand the number of preventative services for rare disease patients under the recommended uniform screening panels (RUSP).
- **Reauthorize the *Newborn Screening Saves Lives Act*:** *The Newborn Screening Saves Lives Act* provides funding for state programs that screen newborns for a panel of disorders, as recommended by experts, and educate parents and providers about the disorders. The Act was first passed in 2008 and expired in 2019, leaving a critical gap in lifesaving programs. The RDCC urges Congress to reauthorize these federal NBS programs to save lives, improve healthcare outcomes, and reduce long-term healthcare costs by allowing for early detection and intervention.
- **Increase Recommended Uniform Screening Panel (RUSP) Resources:** The RUSP is a list of disorders that the Secretary of the Department of Health and Human Services (HHS) recommends for states to screen as part of their state programs. However, most states do not screen for all 37 core RUSP conditions. In addition, many states view the RUSP prescriptively, which prevents states from considering new conditions even as new treatments for rare diseases are increasingly available. The RDCC recommends increasing state funding so that state labs can treat the RUSP as dynamic, and have the resources necessary to add new conditions more swiftly after, or even before, RUSP approval. RDCC supports piloting the concept of a "provisional" RUSP approval that is automatically granted when a treatment is approved

that incorporates review and analysis following initial recommendations.

- **Make the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) Nimbler:** The ACHDNC provides recommendations for the inclusion of additional conditions on the RUSP and pediatric development guidelines. RDCC supports any efforts by the ACHDNC to improve and broaden data inclusion in the evidence review matrix for new conditions and to allow for fast and unambiguous votes on potential conditions. In 2022, the ACHDNC determined it has the capacity to conduct two reviews per year, which falls behind the overall pace of innovation.[5] ACHDNC has recently taken costs associated with a disease into their nomination consideration, which is historically outside their purview. Additionally, when considering the availability of therapies and associated benefits of treatment, ACHDNC has been engaging in a re-evaluation of the effectiveness of FDA-approved therapies, which undermines the authority and expertise of the FDA. Accordingly, RDCC recommends that the ACHDNC advances a consistent, predictable process that does not integrate cost but rather patient outcomes that could allow for new diseases to be nominated and considered quickly. In addition, RDCC recommends increasing the frequency of meetings annually to ensure regular incorporation of new data in ACHDNC 's recommendations.
- **Authorize an Intergovernmental NBS Working Group:** While the ACHDNC makes recommendations of conditions to be added to the federal RUSP, implementation of screening programs varies widely by state. The RDCC encourages the authorization of a State and Federal NBS Working Group to collect data and make decisions regarding the funding and implementation of NBS. Further, RDCC encourages a state and federal collaboration under the auspices of the HHS Secretary and in coordination with federal health agencies and state entities to collect data and make recommendations.
- **Support Public-Private Partnerships:** The private sector has moved quickly to address issues related to screening by creating new screening technologies and increased data collection and analysis capacity. RDCC encourages the application of grant funding to incentivize new public-private partnerships to provide scientific leadership, oversight, and funding for NBS implementation, ongoing data collection, and outcomes reporting. Such partnerships may also increase the adoption of new technologies, such as next-generation sequencing (including, but not limited to whole genome sequencing, gene panel testing, single gene testing, etc.), and their integration with NBS programs.

2 Advance the Availability and Accessibility of New Testing Technologies

Innovation in revolutionary treatments has dramatically improved Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES), which help identify genetic variations or provide incidental findings. By identifying genetic causes, patients can begin treatments and interventions earlier and potentially alter the course of a condition.

"Lowering the barriers to connecting patients and primary care physicians with rare disease experts and genetic counselors is greatly needed to shorten the diagnostic journey and improve the lives of patients suffering from a rare disease. Initiatives aimed at educating family physicians and pediatricians and helping to improve patient access to experts through telemedicine could directly address the critical need for an early, accurate diagnosis and appropriate care in a cost-effective and scalable manner."

~ Thomas Brown, Ph.D., Executive Medical Director, Alnylam Pharmaceuticals

Policy Solutions:

- **Maximize Patient Access to Current and New Testing Technologies:** Congress should ensure that patients have equitable access to new diagnostics methods such as WGS, WES, phosphate regulating endopeptidase homolog X-linked (PHEX) genetic testing and other gene panels. Furthermore, patients should have access to whatever diagnostic tests their clinicians deem necessary to accurately diagnose and, when possible, treat them. RDCC supports the newly-proposed Transitional Coverage for Emerging Technologies (TCET) procedural notice, and additional efforts to streamline the coverage of new technologies by reducing the time between the FDA approval of new diagnostic testing tools and coverage by public payers. RDCC urges regulators to facilitate the inclusion of new technologies applicable to rare disease patients in these new coverage/approval paradigms. Finally, RDCC supports exploring validated artificial intelligence-based approaches to help diagnose at speed and at scale to help patients gain access to early treatment and care.
- **Preserve Regulatory Paradigms to Allow New Testing Innovation:** Currently, many newborn screenings utilize laboratory-developed tests (LDTs). These tests, regulated under the Clinical Laboratory Improvement Amendments (CLIA), have included several technologies designed to meet unmet medical needs and to address and track rare disease diagnoses and progression. RDCC supports continued patient access to high-quality, accurate tests that promote innovation and keep pace with discovery in rare disease diagnosis and treatment. Any regulatory or legislative activity in this area should avoid disruption of patient access to genetic testing.
- **Collect Data to Promote NGS Coverage at the State Level:** While many state Medicaid programs cover various next generation sequencing (NGS), the conditions screened and offerings of state

laboratories differ from state to state. This can lead to gaps in coverage that restrict patient access to care. To further improve the availability of new NGS technology, RDCC calls upon the Centers for Medicare and Medicaid Services (CMS) to regularly perform surveys to update data on state coverage of NGS technologies and urges Congress to require the National Academies of Science, Engineering, and Medicine (NASEM) to further study this issue.

- **Protect Patient Privacy:** The *Genetic Information Nondiscrimination Act* (GINA) protects individuals from discrimination related to their genetic information in certain employment settings and in health care coverage. However, GINA does not cover discrimination related to life, long-term care, and disability insurances. Patients and families may choose to decline genetic testing due to this privacy protection gap. RDCC urges Congress to explore a "GINA 2.0" that would expand protections for patients to other scenarios beyond employment and basic healthcare coverage.
- **Promote Screening in Alternative Settings:** Many screening tests are prescribed and administered in pediatric or primary care settings. However, access to these traditional pathways of care may be limited, especially for those who are transient, have inconsistent coverage under Medicaid, or are otherwise low-income and under or uninsured. In fact, many patients' primary access to the healthcare system is through the emergency department and associated intensive care units (ICU). To ensure that the most vulnerable patients are able to receive timely and accurate diagnoses, the RDCC urges coverage of WGS in ICU settings.

3 Provide Equitable Access to Specialists by Advancing Telemedicine Consults Across State Lines and Improving Training

Telemedicine can shorten the diagnostic odyssey by enabling access to medical expertise without geographic constraints. This is especially critical for rare disease patients, as few health care providers have deep experience and expertise in specific rare diseases. Telehealth specialty consults can help bridge access gaps and address disparate health equity, providing underserved communities with much-needed care, especially in rural areas not sufficiently connected to sub-specialty provider access. In a 2019 NORD survey, nearly 40 percent of respondents reported traveling more than 60 miles for medical care.[6]

"A rare disease patient's journey to diagnosis and care shouldn't hinge on their location. Living with a rare disease is tough on its own, and the added burden of traveling long distances to reach specialized experts only compounds the challenge. Equitable access to top-notch telemedicine is vital for the rare disease community, and I urge Congress to back policies that ensure early diagnosis and treatment, no matter where patients reside"

~ Anish Bhatnagar, Chief Executive Officer, Soleno Therapeutics

Policy Solutions:

- **Build an Educated Workforce in Rare Disease Diagnosis:** While telehealth has seen a drastic increase in uptake, associated training for healthcare workers has not kept pace. The complexities of rare disease diagnosis make this issue even more acute. RDCC urges the Health Resources and Services Administration (HRSA) to expand its resources through graduate medical education and train healthcare workers to carry out telemedicine work. In particular, family physicians, nurse practitioners, physician assistants and pediatricians should receive training to recognize use cases for genetic tests and prescribe them to patients. Investment should be made to bolster graduate medical education specific to rare disease detection and the use of genetic tests.
- **Increase and Empower the Genetic Counselor Workforce:** Although the number of genetic counselors has doubled over the past decade, there are still fewer than 6,000 across the nation.[7] Therefore, the wait between genetic testing and associated follow-up with a genetic counselor is typically several months, potentially negatively impacting health outcomes. RDCC supports increased investment in the genetic counseling field, including improving care team structure and coordination, integrating genetic counselors early into patient care, ensuring adequate and predictable reimbursement for genetic counseling services by public and private payers, and ensuring sufficient telehealth training for genetic counselors to facilitate patient care. Relatedly, RDCC supports the Access to Genetic Counselor Services Act and related legislation that would expand Medicare coverage of genetic counseling similar to physician services.

4 Advance Education of and Access to Disease-Agnostic Biomarker Testing

Biomarker testing can be used to diagnose myriad diseases as well as determine whether a course of treatment is correct for a specific patient, allowing for more targeted care and precision medicine. With decreased time from diagnosis and treatment and increased positive outcomes, biomarker testing is a critical resource with significant untapped potential for the rare disease community.

"Genetic medicines for rare genetic diseases have their greatest potential when administered early, before full-blown disease progression, at which point the damage is often irreversible. Breaking the vicious cycle will require equitably deploying modernized and uniform genetic screening of newborns across the population, and making such screening data accessible to select rare disease experts through seamless data federation. "

~ Dr. Vishwas (Vish) Seshadri, Chief Executive Officer, Abeona Therapeutics

Policy Solutions:

- **Increase Information on Biomarker Use in Rare Disease:** Biomarker testing has shown significant promise for promoting the use of targeted therapies, but in many cases, payers limit coverage to oncological medicine. RDCC supports efforts to further define how biomarker testing is utilized in rare diseases and encourages state legislatures to explore expanding access to comprehensive biomarker testing across all disease groups. Finally, RDCC also urges CMS to cover biomarker testing.
- **Support Publication of Biomarker Use Cases and Incorporation in Graduate Medical Education (GME):** Due to the significant number of tests currently on the market, there are several easily administered technologies, such as urine tests, that can detect the potential for rare diseases, including severe and life-threatening diseases. However, patients and their physicians may be unaware of these technologies. RDCC supports the collection of a national compendium of use cases for existing tests in the early detection of rare diseases that would serve as a living resource for patients and physicians. In addition, these use cases may serve as a component of GME offerings nationally.
- **Support and Expand the Interstate Medical Licensure Compact (IMLC):** The COVID-19 pandemic led to an expansion of the use of telehealth across state lines. The RDCC supports the Interstate Medical Licensure Compact (IMLC), which is designed to streamline the licensing process and enable physicians to practice in multiple states. The IMLC will increase patient access to rare disease experts and the RDCC encourages the 13 non-participating states to join.

5 Transform Rare Disease Research with Federated Data Models

A lack of physician data sharing and data interoperability is a continued barrier within rare disease. Further, the rare disease registry landscape consists of small, disjointed data sets stored across different national registries and localized consortia. These data silos, coupled with strict data privacy regulations, limit the collaboration that is needed by researchers to enhance analysis.

"Advances in diagnostic technology promise to accelerate early diagnosis and treatment, and change entire life trajectories for many rare disease patients. Collaboration across the healthcare ecosystem – from technology companies to provider systems, public health labs, regulators, payers, and policymakers – will ensure access to new screening opportunities such that all patients have a chance to benefit from early diagnosis and treatment."

~ Diane Berry, Ph.D., Executive Vice President, Chief Global Policy & Advocacy Officer, Sarepta Therapeutics

Policy Solutions:

- **Create a Federated Data Model:** RDCC support creating a federated data model for clinicians nationwide, both genetic and genomic, for tracking and collaboration around rare disease diagnosis. Developing advanced registries of patients with more granular ICD-10 codes and automated ways to describe phenotypes along genotypes will help advance further research
- **Facilitate Public/Private Collaboration:** Broad coordination and collaboration should be extended between government and non-governmental organizations, local governments, scientific researchers, biobanks, and industry to build capacity, encourage investments, improve infrastructure, and build more prominent and representative data ecosystems.
- **Invest in the National Institutes of Health National Center for Advancing Translational Sciences (NCATS) Division of Rare Diseases Research Innovation:** RDCC advocates for more significant investment in the NIH NCATS Division of Rare Diseases Research Innovation efforts to expand ICD codes to rare diseases.

Endnotes

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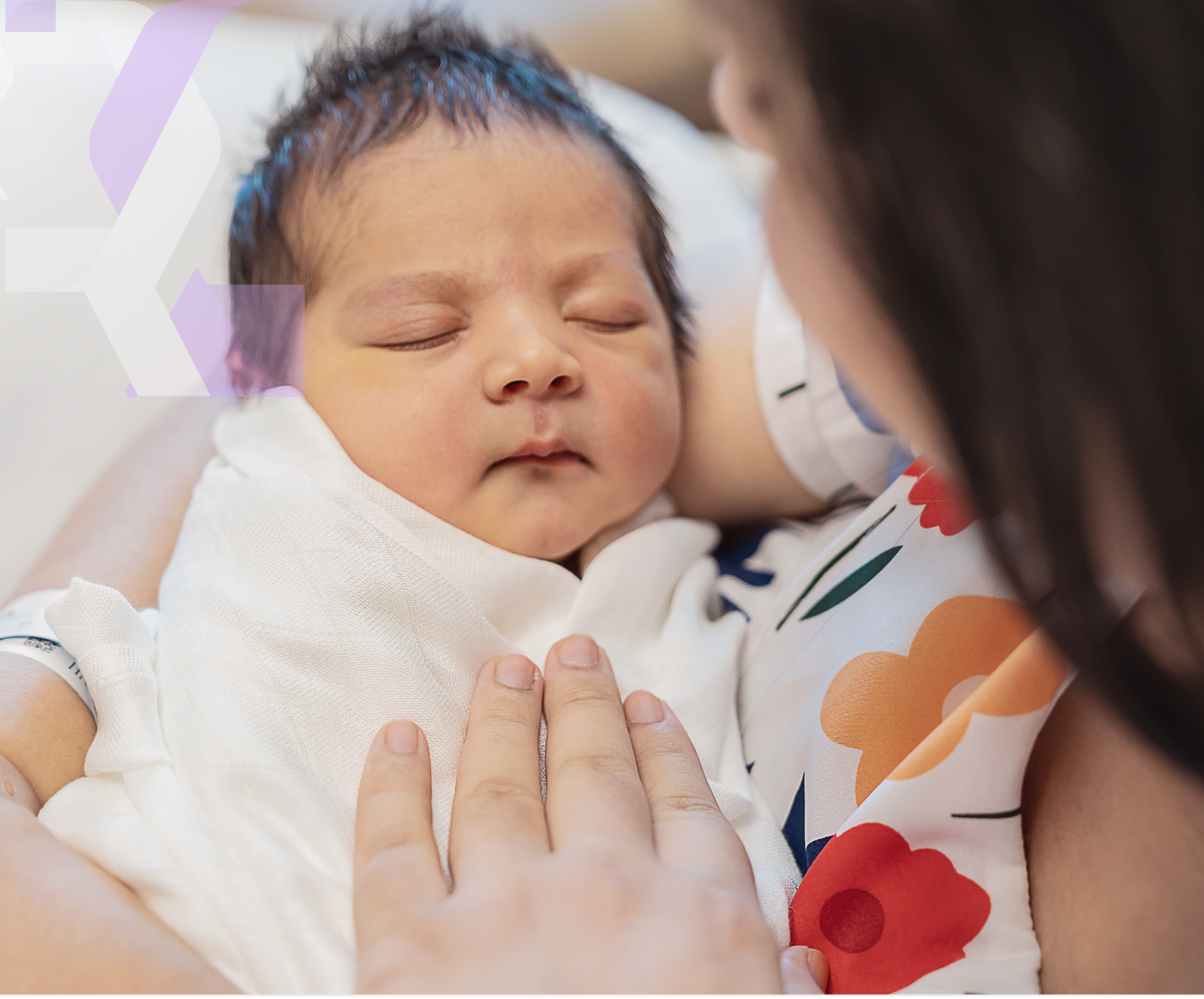

Rare Disease Company Coalition

We are dedicated to being a reliable and trusted resource for our leaders in Congress and the Administration, and a productive partner to rare disease-minded industry, academic and patient groups, by educating on the issues and opportunities that affect rare disease companies and advancing our shared mission to improve the lives of people living with rare diseases.

For more information, please visit www.rarecoalition.com or contact info@rarecoalition.com.
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