RARE ANSWERS™ FAQs

1. WHAT IS THE CHALLENGE IN DIAGNOSING PATIENTS WITH RARE DISEASES TODAY?

There are more than 7,000 rare diseases in the world and for people with rare diseases, it can often take years to reach the correct diagnosis. While we have more data today than ever before, much of it is untapped, disorganized, and unusable by patients and physicians. The newest science is always developing, and many patients do not have access to rare disease specialists. Even when a correct diagnosis is made, physicians may not have access to the best available medical information that can guide a patient's treatment path.

2. WHAT IS RARE ANSWERS?

RARE ANSWERS is a system of innovative and sustainable tools designed to help shorten the diagnostic journey and time to initiating treatment of children with a rare disease. Developed in collaboration with leading children's hospitals and technology and data-science companies, RARE ANSWERS tools are designed to deliver actionable data to physicians by analyzing phenotypic and genomic data and incorporating precision software, medical information, and clinical insights.

3. HOW DOES RARE ANSWERS WORK?

RARE ANSWERS is designed to be a tool to facilitate better care coordination across care team members by rapidly providing accurate information to all, as well as workflows and decision support tools to the lead clinicians. The diagnostic process begins with RARE ANSWERS extracting a patient's Human Phenotype Ontology (HPO) and Variant Call Format (VCF)*. The first capability, Provisional Diagnosis, combines HPO, VCF, and the RARE ANSWERS Rare Disease Map, to generate an initial list of potential diagnoses which are returned to the physician via web portal. The second capability, NextMove, guides healthcare providers to perform necessary tests and procedures until a physician confirms a diagnosis. The last and third capability, Gene to Treatment (GTRx), takes the confirmed diagnosis and provides medical expert curated and validated treatment options via a webpage.

4. WHAT INFORMATION IS AVAILABLE ON THE IMPACT OF PROGRAMS LIKE RARE ANSWERS?

RARE ANSWERS is a transformative approach to the diagnosis and treatment of individuals with Rare Genetic Disorders that has unique value to all stakeholders. A pilot study led by Rady Children's Institute for Genomic Medicine in California ("Project Baby Bear[1]") over 23 months to assess the extent to which rapid precision medicine for critically ill Medi-Cal babies improves clinical outcomes, improves the experience of care for families and clinicians, and reduces net healthcare expenditures. Until recently, rapid whole genome sequencing (rWGS) was a diagnostic tool used as a last resort, however, the study found that this approach could become a new standard of care for testing sick babies early in their hospitalization. Some of the key benefits from that study included:

- Completed rWGS on 178 babies and families
- Provided diagnoses for 76 babies (43%)
- Led to a change in the care of 55 babies (31%) that resulted in fewer hospital days, fewer procedures or new therapies
- Twenty-six babies (15%) were diagnosed with genetic diseases for which effective treatments are available
- Diagnosed 35 rare conditions that occur in less than one in one million births
- Achieved a three-day turnaround time for provisional results
- Reduced healthcare costs and downstream spending, primarily by empowering doctors to eliminate unnecessary procedures and discharge babies sooner

1. PROJECT BABY BEAR FINAL REPORT FROM RADY CHILDREN'S INSTITUTE FOR GENOMIC MEDICINE TO CA STATE SENATE, JUNE 2020.

*A genotype is the genetic constitution of an individual organism. A phenotype is the set of observable characteristics of an individual resulting from the interaction of its genotype with the environment.

5. WHO ARE ALEXION'S CHILDREN'S HOSPITAL PARTNERS?

Alexion has partnered with clinical experts at leading pediatric hospitals, including Rady Children's Institute for Genomic Medicine and Boston's Children's Hospital.

6. WHAT IS ALEXION'S ROLE IN RARE ANSWERS?

Alexion has acted as steward of this program for five years, investing as part of our commitment to the needs of all people with rare diseases. Along the way, we have leveraged the latest technologies for best-in-class performance and worked with a world-class ecosystem of collaborators. Pilots of the RARE ANSWERS approach have achieved world records in reducing the time to diagnosis and treatment for children in NICUs.

7. WHERE CAN I FIND RARE ANSWERS RESOURCES AND PUBLICATIONS?

For more information on RARE ANSWERS tools, download the fact sheet and FAQs, read the press releases announcing Alexion's collaboration with Rady Children's Institute for Genomic Medicine and The Manton Center at Boston Children's Hospital, or visit the Research and Development page of Alexion.com.

Alexion has also contributed to *Diagnosis of genetic diseases in seriously ill children by rapid whole-genome sequencing and automated phenotyping and interpretation* https://stm.sciencemag.org/content/11/489/eaat6177.abstract.

Other publications that support RARE ANSWERS include:

- *An RCT of Rapid Genomic Sequencing among Seriously Ill Infants Results in High Clinical Utility, Changes in Management, and Low Perceived Harm*
  The American Journal of Human Genetics 2020
  https://dx.doi.org/10.1016/j.ajhg.2020.10.003
- *Prospective, phenotype-driven selection of critically ill neonates for rapid exome sequencing is associated with high diagnostic yield*
  Genetics in Medicine 2020
  https://dx.doi.org/10.1038/s41436-019-0708-6
- *A longitudinal footprint of genetic epilepsies using automated electronic medical record interpretation*
  Genetics in Medicine 2020
  https://www.nature.com/articles/s41436-020-0923-1
- *Project baby bear pilot study implemented across the State of California to assess clinical impact of rapid precision medicine program*
  https://radygenomics.org/wp-content/uploads/2020/07/PBB-Final-Report_07.14.20.pdf
- *Detecting rare diseases in electronic health records using machine learning and knowledge engineering: Case study of acute hepatic porphyria*
  PLOS ONE 2020
  https://dx.doi.org/10.1371/journal.pone.0235574
- *Children's rare disease cohorts: an integrative research and clinical genomics initiative*
  npj Genomic medicine 2020
  https://www.nature.com/articles/s41525-020-0137-0