

The Global Commission to End the Diagnostic Odyssey for Children with a Rare Disease

October 2018

GLOBAL
COMMISSION



to End the Diagnostic Odyssey
for Children with a Rare Disease

CONFIDENTIAL

The time has come to significantly shorten the multi-year journey patients, and those who care for them, endure to receive a rare disease diagnosis.

What are the barriers to diagnosis?

In our research, we found that...



New interventions are needed to help physicians identify patients with a rare disease.

Primary care physicians are on the frontline of care and need to be knowledgeable about fundamental issues in medical genetics. However, interventions – beyond continuing medical education – are needed to help physicians identify patients with a rare disease.



There is opportunity to apply new technology to the rare disease field.

There have been many advancements in clinical technology, however these innovations have not been fully realized and applied to finding patients with a rare diseases.



We do not have to wait for more geneticists and other specialists.

The lack of geneticists and other specialists is a challenge for patients in accessing specialized care, but this challenge can be mitigated without waiting for a larger workforce.



Streamlining processes in a complicated healthcare system can improve time to diagnosis.

The ability for a patient to successfully navigate the diagnosis process is compounded by complexities in the healthcare system such as difficult referral processes and insurance coverage limitations.



Commission Overview

WHO The Commission is led by:

- Flemming Ornskov, MD, MPH – CEO, Shire
- Simon Kos, MD - Chief Medical Officer & Senior Director, Microsoft Worldwide Health
- Yann Le Cam – CEO, EURORDIS

These leaders have come together to tackle the barriers to diagnosis that leave patients living in uncertainty for an average of 5 years. They have invited 13 diverse experts to leverage their unique skills and capabilities to **solve issues** affecting the rare disease community and **develop actionable recommendations** to overcome them.



Microsoft



WHAT Produce a roadmap for the rare disease field that **focuses on solutions to core barriers** preventing timely diagnosis for ALL rare diseases – with an emphasis on those **affecting children**.

HOW Publish a **groundbreaking report** with recommendations and a **roadmap** to reduce diagnosis time. After the publication, Shire will track progress against the roadmap, providing annual reports on the changes affecting patient lives.

WHEN The Global Commission was announced on February 20, 2018 and the final report/roadmap is expected to be published on February 20, 2019.



Barriers to Diagnosis for each Track

1 Barriers for Patient and Family Empowerment:

- Difficulty navigating a complex, fragmented healthcare system
- Not alerting physicians to seemingly unrelated symptoms – lack of knowledge about symptom clusters (i.e., knowing to tell a cardiologist about a liver problem)
- Parents' lack of medical credibility (i.e., “crying wolf” scenario)
- Lack of patient-centered information

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2 Barriers for First-line Providers:

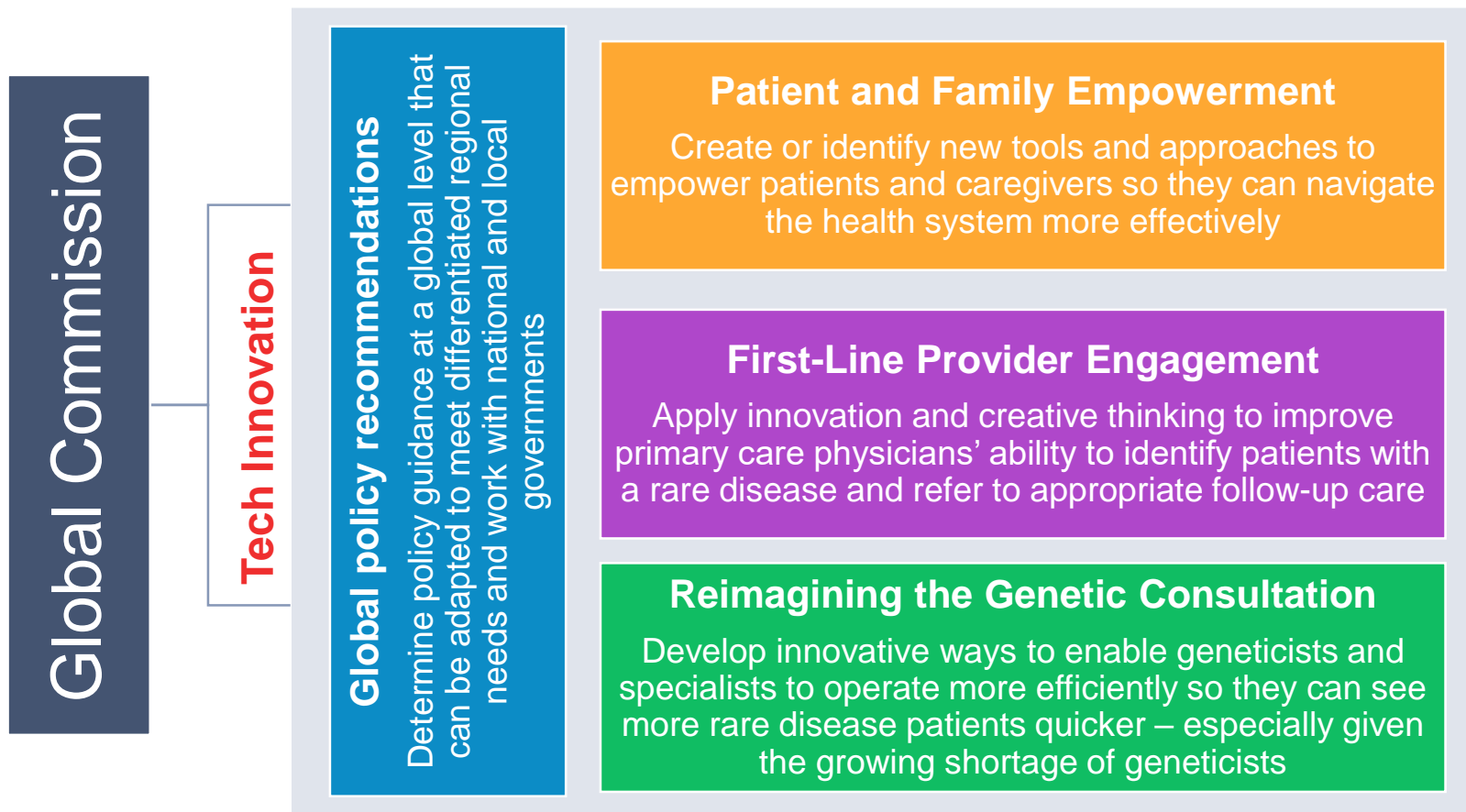
- Minimal/non-existent training or exposure to rare disease
- Lack of standard criteria to help diagnose many rare diseases
- Poor communication between PCPs and specialists
- Lack of awareness around which specialty to refer
- Access to diagnostic tools

3 Barriers for the Genetic Consultation:

- Shortage of geneticists
- High workload = inability to see more patients
- Fewer specialists in rural areas
- Inefficient practices that limit productivity (e.g., diagnosed patients making follow up visits, tests not ordered in advance of patient visit)

Commission Tracks

The Commission will focus on developing solutions in four areas that will lead to accelerating the time to diagnosis – and will organize its work accordingly



Track 1 Solutions

Patient and Family Empowerment

1 Empowering patients to ask their doctor to *think differently*

Vision: All families are empowered and have the tools they need to ask the right questions to expedite diagnosis

A social media campaign would focus on common signs, or “**triggers**,” that may indicate the need to explore whether a patient has a rare disease. If a parent relates to these triggers, the campaign then prompts parents to more carefully track symptoms, consultations, and recommendations of physicians in a digital “journal” provided by the campaign. Parents can then bring this journal, as well as key questions for consideration, when meeting with physicians to have more informed discussions.

2 Portable Blockchain Health Records

Vision: All patients and their caregivers are able to easily share detailed medical records with multiple physicians and specialists quickly and efficiently.

Using blockchain technology, this system would aggregate all patient data from physicians and parents, including electronic health records, notes from multiple physicians, and test results. Parents manage the information in a patient-owned system, maintaining control of their child’s data and allowing them to easily transport the information through their personal “passport”. By bringing this passport to each new physician, parents can ensure that the entire care team has all relevant patient information to make the best decision for the child.

Track 2 Solutions

Equipping First-line Providers with Tools for Diagnosis and Referral

1 Use Artificial Intelligence to Identify Rare Diseases

Vision: Support first-line physicians to identify patients with a suspected rare disease

The technology “learns” from medical literature based on identified symptoms for each rare disease. Then, usually globally aggregated data, the technology scans diagnosed patient health records to continue matching symptoms to diagnoses, becoming more accurate over time. Physicians can then use the technology by inputting a range of data on undiagnosed patients to narrow down possible diagnoses. Eventually, this technology will be applied preemptively, scanning health records to flag patients who may have an undiagnosed rare disease.

2 Facilitate and Expand access to Diagnostic Testing

Vision: Provide greater access to diagnostic testing for patients who would benefit most

This platform allows first-line providers to provide patient information to a panel of experts via an online input system. These experts will then work together with the physician to make informed decisions about whether genetic testing is warranted and, if so, which test to order. Ideally, the first-line provider who requested the consult will be able to order the test immediately, reducing unnecessary testing and better pinpointing the right test. The results are faster and more accurate diagnosis and savings to the health care system

Track 3 Solutions

Reimagining the Genetic Consultation

1 Establish early-access centers in genetics clinics

Vision: Facilitate access to genetic consultations more quickly and efficiently

As part of a referral for a genetic consultation, first-line providers will input patient data into a standardized, digital system and order any needed tests. Before the appointment, a genetics team reviews the information to understand the child's current health needs and determines whether a genetic consultation is needed and, if so, which additional tests should be conducted beforehand. This collaboration allows for a more effective and efficient visit with a geneticist, saving valuable time for both the patient and the geneticist. Ultimately, this technology could be used to prioritize the most urgent needs of patients.

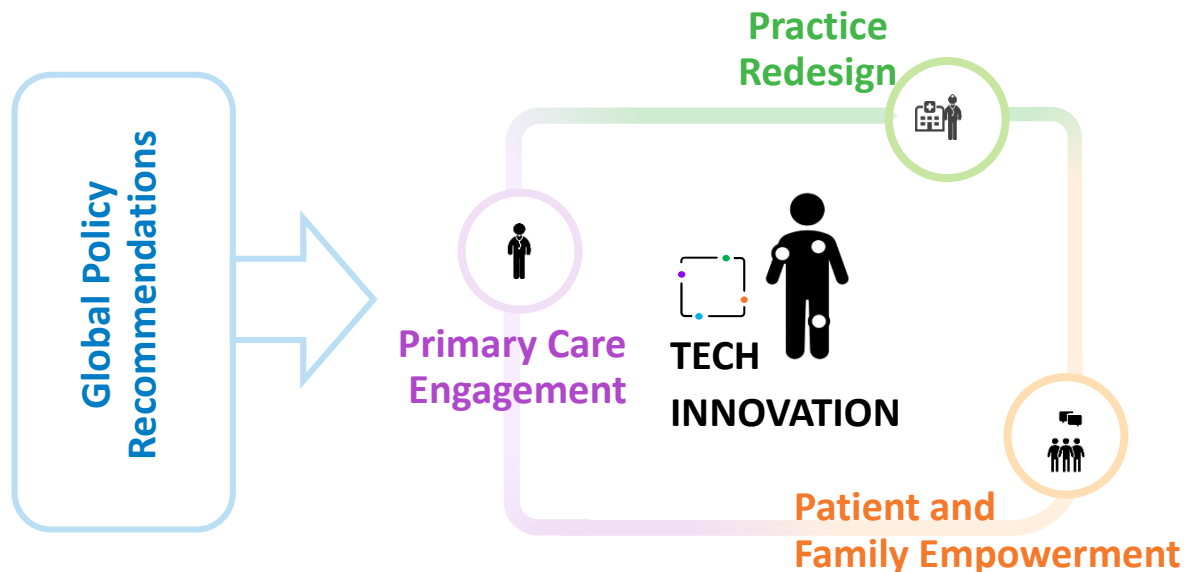
2 Information capture and tele-consultations for rural/remote patients

Vision: Ensure that patients in remote areas have access to the quality and type of diagnosis and care that they need

Families complete an online form in advance of an initial genetics consultation with the help of the referring physician. The form is sent to the specialist before the appointment to ensure an informed, productive first visit and avoiding the need for multiple in-person appointments. Then, a virtual consultation takes place as a first appointment, to avoid unnecessary travel and time. Only when an in-person visit is deemed essential will the family travel for a physical visit

Global Policy Recommendations

Originally, the Global Commission had been considering the Solutions as part of four Tracks. Upon further consideration, the Global Policy Recommendations outlined by the Commission will support and enable each solution the group has put forward (e.g., Tracks 1-3). It is crucial that the proper support, advocacy, and legislation is in place to create an enabling environment for each platform to succeed.



Policy Recommendations

These policy recommendations support the solution tracks and do not represent an exhaustive list of policies that would support diagnosis of rare diseases in general

Centers of Excellence

National healthcare systems should issue guidance on collaboration between primary care centers and centers of excellence to ensure consistent, effective and efficient diagnostic and referral protocols. The guidance should address coordinating care, laboratory resources, and knowledge sharing across country borders.

Genetic screening

As countries develop policies around genetic screening, these should incorporate next generation sequencing given its declining cost and potential to more quickly pinpoint a diagnosis, thus generating savings in unnecessary provider visits and diagnostic tests.

Data sharing

To fully leverage the global benefit of cloud-based data storage – of particular value to countries with limited patient data (common in the case of rare disease) – health policies should encourage data sharing across borders to increase the likelihood of a match to determine a diagnosis.

Privacy

In encouraging patients to provide medical and other information about their symptoms to help expedite diagnosis, it's critical that countries implement adequate privacy safeguards.

Policy recommendations

Centers of Excellence (Part 1 of 2)

CoEs: National healthcare systems should issue guidance on collaboration between PCCs and CoEs to ensure consistent, effective and efficient diagnostic and referral protocols. The guidance should address coordinating care, laboratory resources, and knowledge sharing across country borders.

TRACK 1

Government support for platforms for shared action across stakeholders

Governments should provide a platform for uniting patients, patient advocacy groups, healthcare professionals and policymakers to increase awareness and understanding of the issues patients face in rare disease diagnosis.

Enable cross-country sharing of electronic medical records to improve diagnosis efficiency

Governments should find optimal ways for cross-country sharing of electronic medical records to increase diagnosis efficiency, while preserving patient privacy and enabling physicians to adopt these systems.

Recognise benefits of cross-country rare disease research networks on best practice sharing

National healthcare systems and medical societies should recognise the benefits that cross-country rare disease research networks have on diagnosis and encourage national organisations to exchange knowledge and best practices.

TRACK 2

Standardization of diagnostic and referral protocols between PCCs and CoEs

National healthcare systems should issue guidance on the collaboration between primary care centers (PCCs) and centers of excellence (CoEs) to ensure standardization of diagnostic and referral protocols within a common user interface.

Policy recommendations

Centers of Excellence (Part 2 of 2)

CoEs: National healthcare systems should issue guidance on collaboration between PCCs and CoEs to ensure consistent, effective and efficient diagnostic and referral protocols. The guidance should address coordinating care, laboratory resources, and knowledge sharing across country borders.

TRACK 3

Establishing regional CoEs and networks to speed up diagnosis

International, regional and national public authorities should engage in activities that encourage and support the establishment of regional centers of excellence and networks that directly facilitate timely diagnosis and act as regional hubs for best practices in the diagnosis of rare diseases

Healthcare systems to improve coordination and standardization of clinical practice

National healthcare systems should aim to increase operational efficiencies in routine practice through better coordination and national standardization between healthcare professionals, geneticists and specialists.

Governments to issue plans to establish CoEs in support of diagnosis

Governments should issue clear plans to develop Centres of Expertise (CoE) for rare diseases to support diagnosis and treatment across the full national or regional population.

Ensure interoperability across established CoE to optimize data sharing

National healthcare systems should not only ensure the availability of novel technologies, but also seek to address system interoperability across the healthcare system, particularly between CoE for rare diseases.

Support investment in data network and connectivity to ensure uniform adoption of technologies

Governments should support investment in immature data networks and connectivity to support adoption of novel healthcare technologies.

Policy recommendations

Genetic Screening

Genetic screening: As countries develop policies around genetic screening, these should incorporate next generation sequencing given its declining cost and potential to more quickly pinpoint a diagnosis, thus generating savings in unnecessary provider visits and diagnostic tests.

TRACK 2

Development and implementation of a genomic sequencing strategy

Genomic sequencing strategy setting out how to screen more patients using sufficiently broad, targeted gene panels should be developed and implemented to support diagnosis of rare diseases with known interventions.

Access pathways that ensure access to diagnostic tools

Dedicated access pathways that account for the value of diagnostics should be developed and adequate funding for diagnostic tools should be available so that patients have timely and broader access to these technologies.

Infrastructure that supports the development and implementation of NGS

Forward-looking vision on infrastructure investments, specifically supporting the development of next-generation sequencing infrastructure (i.e. molecular genetics labs), should be developed and implemented.

Primary care technical training to incentivize adoption of novel approaches

The development of new training programmes with technical specifications should be incentivised to increase familiarity with novel diagnostic approaches, 'big data' and AI.

Policy recommendations

Data Sharing

Data sharing: To fully leverage the global benefit of cloud-based data storage – of particular value to countries with limited patient data (common in the case of rare disease) – health policies should encourage data sharing across borders to increase the likelihood of a match to determine a diagnosis.

TRACK 1

Government support for platforms for shared action across stakeholders

Governments should provide a platform for uniting patients, patient advocacy groups, healthcare professionals and policymakers to increase awareness and understanding of the issues patients face in rare disease diagnosis.

Establish privacy guidelines for health data to encourage data sharing

Policymakers should establish privacy guidelines for health data to ensure dissemination of information to patients, while allowing use for 'big data' analysis to improve diagnosis.

Enable cross-country sharing of electronic medical records to improve diagnosis efficiency

Governments should find optimal ways for cross-country sharing of electronic medical records to increase efficiency in diagnosis, while preserving patient privacy and enabling physicians to adopt these systems.

TRACK 3

Ensure interoperability across established CoE to optimize data sharing

National healthcare systems should not only ensure the availability of novel technologies, but also seek to address system interoperability across the healthcare system, particularly between CoE for rare diseases.

Support investment in data network and connectivity to ensure uniform adoption of technologies

Governments should support investment in immature data networks and connectivity to support adoption of novel healthcare technologies.

Policy recommendations

Privacy

Privacy: In encouraging patients to provide medical and other information about their symptoms to help expedite diagnosis, it's critical that countries implement adequate privacy safeguards.

TRACK 1

Establish privacy guidelines for health data to encourage data sharing

Policymakers should establish privacy guidelines for health data to ensure dissemination of information to patients, while allowing use for 'big data' analysis to improve diagnosis.

Enable cross-country sharing of electronic medical records whilst preserving privacy for EHR

Governments should find optimal ways for cross-country sharing of electronic medical records to increase efficiency in diagnosis, while preserving patient privacy and enabling physicians to adopt these systems.

Policy Recommendations

Areas for Discussion: What policy recommendations could support the concepts listed below?



**Empowerment of
Physicians**



**Community of Rare
Diseases**

Pilot Projects



Rare Disease Diagnosis: Pilot Overview

- Shire and Microsoft have been at work developing Pilot Projects that are aligned to the Commission members suggestions to accelerate time to diagnosis. **Currently, there are several pilot projects in various states of development.**
- The Working Group has suggested that we **prioritize 3-4 pilots** in order to focus our efforts, deploy resources, and deliver initial findings by November for inclusion in the roadmap being published in February.
- The following pilots are **Priority Pilots** in development:
 - Technology-based:
 - Multifactorial machine learning to recognize symptom patterns
 - Enable Collaboration Tools for “Intelligent Triage” and Clinical Geneticist Virtual Panel Consultation
 - Explore a Blockchain-based patient registry and RD Passport
 - Challenge Pitch for Rare Disease

Pilot Projects Overview Criteria

In order to prioritize the Commission's Pilot Projects, the following criteria were developed. Pilots that meet these criteria will be pursued and included in the final Commission Report:

- By November 1, 2018:
 - Pilot focuses specifically on diagnosis of rare disease
 - Pilot has a clear vision and goal
 - Partners and Commission Members have been identified and engaged to support the pilot
 - Site(s) and scope of the effort have been determined
 - Pilot can be publicly discussed (i.e., permission from all partners)
 - Start date has been decided and agreed to by all partners
 - Options for scalability have been considered
 - Intended outcomes and success factors have been identified

Multifactorial machine learning to recognize symptom patterns

Summary	Leveraging the power of machine learning, this collection of digital technologies will integrate with EMR systems to support primary care physicians and pediatricians by recognizing symptom patterns that they may not immediately associate with a rare disease, expediting patient diagnosis. It will be piloted in three areas: (1) medical records data, (2) patient-reported data, and (3) integration with genomics
Detail	<ul style="list-style-type: none"> Phase 1 will support existing efforts at Hospital La Paz de Madrid in Madrid, Spain <i>(Proposed)</i> Phase 2 will expand to Taipei Veteran's Hospital in Taipei, Taiwan and King Faisal Hospital in Riyadh, Saudi Arabia
Expected Outcomes	<ul style="list-style-type: none"> Test the efficacy of the AI algorithms for symptom extraction and disease mapping. This includes exploring potential collaboration with the International Society for Pediatric Innovation (ISPI) to test an AI tool with patients from the NICU enrolled in Trial at US pediatric health centers Establish workflow guidelines for clinician engagement and build infrastructure to support additional users
Next Steps	<ul style="list-style-type: none"> 20 patients already enrolled for first clinical study planned to finish on Oct 1st. Functional prototype at https://health29-dev.azurewebsites.net (select Demo at login screen) AI being used for symptoms extraction and gene prioritization

Potential Partner(s)	Project Manager	Commission Member Engagement
Microsoft	Julian Isla Gomez (Microsoft)	Marshall Summar <i>Proposed: Dau-Ming Niu, Moeen Al-Sayed</i>

TRACK 3: Reimagining the Genetic Consultation

Enable Collaboration Tools for “Intelligent Triage” and Clinical Geneticist Virtual Panel Consultation

Summary	This pilot will leverage virtual communication tools to increase access to genetic counselling and to reduce the time/cost burden to the patient for in-person consultations. Building on a virtual consultation app being used at Children’s National Hospital in Washington, DC, this technology will utilize collaboration tools and health templates to design reliable, innovative solutions to deliver genetic counseling remotely to patients and PCPs.
Detail	The Commission will partner with the Accenture’s Digital Health team and Univ. of New Mexico’s Project ECHO to create hubs of expertise on rare diseases to first improve education for primary care physicians, eventually aiming to shorten the wait for diagnosis by a geneticist.
Expected Outcomes	<ul style="list-style-type: none">• An integrated platform with a suite of communications tools to enable effective and efficient virtual consultation by geneticists• Establish workflow rules for geneticist engagement and enable infrastructure for multi-institution and multi-market participation
Next Steps	<ul style="list-style-type: none">• Conduct an in-person workshop in October at Children's National Medical Center with Dr. Marshall Summar, Shire, and Accenture. Purpose of this meeting is to understand current state and gain alignment on future state deliverables around collaboration.• Post workshop, gain alignment with team members on key areas of focus and opportunities to pilot

Potential Partner(s)	Project Manager	Commission Member Engagement
University of New Mexico ECHO Platform	Carlos Pelayo	<i>Proposed: Roberto Giugliani, Marshall Summar</i>



Explore a Blockchain-based patient registry and RD Passport

Summary	Utilizing Blockchain technology, this tool will manage patient data and maintain a patient registry for global rare disease patients. Because blockchain technology will be used, patient privacy will be protected, patient consent for data use and storage can be monitored, and patient health records can be easily transported. The data will be owned by the patient, giving them the power and information they need to seek additional opinions and lead their own pursuit of a diagnosis.
Detail	A digital ledger will map the patient journey from the first consultation to diagnosis, recording medical data, symptoms, diagnosis and all medical interactions. The ledger will be used to build a digital registry for patients with a rare disease and can be administered/monitored by patient groups. The ledger will facilitate interactions among patients with the same disease and will connect them to the right specialists and organizations. A digital wallet containing medical records (an “RD passport”) will be controlled by the patients, who will authorize and monitor the data access.
Expected Outcomes	<ul style="list-style-type: none"> • Proposal and written framework for a global registry of rare disease patients • A digital ledger that registers patients’ diagnostic journeys and patient data/ consent • A business case for potential models to support and empower patients to control their data
Next Steps	<ul style="list-style-type: none"> • Met with Blackberry about data security on September 26 • Kick-off meeting with project team via WebEx • Work on defining Scope of Work

Potential Partner(s)	Project Manager	Commission Member Engagement
Blackberry, Microsoft	Rune Wetlesen	TBD

Challenge Pitch for Rare Disease

Summary	<p>Leveraging Shire's Diamond Partnership with Pulse@MassChallenge, this pilot is crowd-sourcing innovative ideas from the startup community to overcome barriers to diagnosis.</p> <p>Pulse@MassChallenge is recruiting digital health companies on a global scale to pitch viable ideas and accelerate a best-in-class technology solutions to solve challenges associated with early diagnosis of rare disease.</p>
Detail	<ul style="list-style-type: none">Challenge topic: Facilitating early diagnosis of rare disease (the Commission can further refine)Shire opened up the challenge to digital health startups on September 13 at Microsoft's NERD Center. Scheduled to view live pitches in December 2018. If viable options are found, pilots will commence in 2019. Dr. Anne O'Donnell-Luria was present at September 13 event.
Expected Outcomes	<ul style="list-style-type: none">5-10 innovative solutions to challenges in rare disease diagnosis, delivered by cutting-edge startups in the health spaceThe opportunity for the Commission to be involved with the winning pilot
Next Steps	<ul style="list-style-type: none">View live pitches December 4th and 5th. Include Anne O'Donnell, MD, Clifford Goldsmith, MD, Uzma Atif and/or Ekaterina Musaeva, MD.

Potential Partner(s)	Project Manager	Commission Member Engagement
MassChallenge	Dawn Irish	TBD pending project