ISPI MEMBER HIGHLIGHT:
RARE DISEASE INNOVATION

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Global Commission: Overview and Path Forward

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Cross section of global leaders to find solutions

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Global Commission Guiding Principles

- Ensure that the Global Commission’s mission continues to benefit the entire rare disease community
- Ensure technology remains at the forefront of our efforts and pilot projects
- Leverage the strengths and skill set of each Global Commission member
- Prioritize quick wins to demonstrate progress
- Capture data, measure, and report on progress
- Adapt to changing external landscape (technology advancements, diagnostic advancements, etc.)
- Engage new partners and expertise as needed to ensure success
- Consider global needs in long-term planning, while focusing in the short-term on proof of concept in regions with appropriate infrastructure
Global Commission Recommendations

Objective: Develop tools that empower families and caregivers to become more proactive in getting a diagnosis as quickly as possible.

Objective: Equip frontline providers with the knowledge and tools to quickly and effectively identify patients who may have a rare disease and take appropriate action.

Objective: Develop innovative ways to enable medical geneticists to see priority patients more quickly — especially given the growing shortage of geneticists.

GLOBAL POLICY RECOMMENDATIONS
Policy guidance at a global level that can be adapted to meet differentiated regional needs and work with national and local governments.
Technology Pilot Programs

**Multifactorial Machine Learning to Recognize Symptom Patterns**

**Summary**
Digital tool that uses artificial intelligence to support frontline providers by recognizing symptoms and expediting patient diagnosis.

**Location**
Centro de Investigación Biomédica en red de Enfermedades Raras (CIBERER), Madrid, Spain
Hospital La Paz de Madrid in Madrid, Spain
NIMGenetics, Madrid, Spain
Idibell, Barcelona, Spain

**Technology utilized**
Multifactorial machine learning algorithms

**Diagnosis barrier targeted**
Difficulty in linking disparate symptoms to make a rare disease diagnosis

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

**Summary**
Digital collaboration tools to deliver genetic counseling remotely to patients.

**Location**
Children’s National Hospital in Washington, DC, USA

**Technology utilized**
Asynchronous physician consultation app, telemedicine technology

**Diagnosis barrier targeted**
Time and cost incurred by the patient through in-person consultations

**Explore a Blockchain-based Patient Registry and Rare Disease Passport**

**Summary**
Blockchain-based tool to manage patient data and maintain a patient registry for global rare disease patients.

**Location**
Takeda, Zug, Switzerland

**Technology utilized**
Blockchain technology to handle identity and consent management

**Diagnosis barrier targeted**
A secure way for patient ownership of their health records
Key Global Policy Focus Areas

**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 diseases) – 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.
Thought Leadership in 2019
Global Commission members have been building awareness since the February 2019 report launch

- Meeting with Dr. Tedros, Director General of the WHO
- Microsoft Executive Summit
- World Orphan Drug Congress USA
- Meeting with UK NHS stakeholders
In 2018 the Global Commission:

- Convened all members three times to develop recommendations
- Launched three technology pilot projects to test selected recommendations
- Launched the Year-One digital report-out via the updated Global Commission website February 20, 2019 ahead of Rare Disease Day

Our 2019-2020 objectives for a year of action:

- Refine and operationalize select recommendations from the Year-One Report that Global Commission members are well-qualified to address and provide leadership
- Support the implementation and scale-up of three technology pilot projects
### What we are pushing forward:

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<td>Multifactorial Machine Learning to Recognize Symptom Patterns</td>
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<td>Enable Collaboration Tools for “Intelligent Triage” and Clinical Geneticist Virtual Panel Consultation</td>
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### What we plan to achieve by May 2020:

- Continue the dissemination of the Year-One Report to inspire global action in reducing time to diagnosis. Begin work to prepare and issue a new report by April 2022
- Build the prototypes for the three technology pilots and, over the subsequent two years, beta test the pilots with scaling and implementation in markets internationally to show measurable progress
- Refine membership and explore opportunities to enlist additional partners and leverage resources to push forward implementation of recommendations
- Help achieve recognition of rare disease as a priority within the World Health Organization (WHO) global agenda
- Continue to partner with Rare Diseases International (EURORDIS, NORD, CORD) to develop a major Policy change initiative to accelerate time to diagnosis and support its dissemination by 2022
Pilot #1 Summary: Multifactorial Machine Learning to Recognize Symptom Patterns

Genetic testing is a “black box” for physicians and phenotyping is challenging. Variant filtering is conducted manually, guided by a few symptoms. Communications between physicians can be an issue and new symptom involvement is almost impossible. Ultimately the process is expensive because of all the human work needed. There is an opportunity to use AI for medical decision-making tools.

Foundation 29 has been developing a new tool (platform in beta testing at www.dx29.ai). Initial performance of the tool is high and good initial collaboration has been established with academia. Analysis using just symptoms can be useful for 10-20% of patients. Foundation 29 is evolving D29 to a platform where different algorithms can be used and is working on different strategies to have high quality data. D29 must be a platform where different CMLP algorithms could be tested.

EXPECTED OUTCOMES

• A cloud-based tool will be developed to be used for physicians during diagnosis process (free of charge for basic use)
• D29 will evolve into a platform where new diagnostic pipelines can be tested
• This tool will explore new ways of diagnosis using big data and ML for patients with complex diagnosis
• Data donor concept will be implemented (patient will have a health data locker with managed access and consent use)
Appendix
Pilot #2 Summary: Enable Collaboration Tools for “Intelligent Triage” and Clinical Geneticist Virtual Panel Consultation

• Early diagnosis of rare disease for children represents a significant challenge. HCPs/PCPs have difficulty with diagnoses due to the degree of difficulty and lack of pre-screening tools. This is a significant time/cost burden for patients and parents.

• Once a child is diagnosed with a rare disease, communication and collaboration between HCPs, Specialists, Children, and Parents is challenging. There are multiple stakeholders and various pieces of patient information that need to be shared to effectively treat the patient.

• Conduct a pilot with Children's National Hospital (CNMC-DC) in Washington, DC, that leverages virtual communication tools to increase access to genetic counselling and to reduce the time/cost burden to the patient for in-person consultations.

• Utilizing Microsoft Teams and leveraging what is already being used at CNMC-DC, this technology will utilize collaboration tools and health templates to design reliable, innovative solutions to deliver genetic counseling remotely to patients and PCPs.

EXPECTED OUTCOMES

**Wave 1 (Pre-Screening) 12 Months:** Enable PCP/HCP access to Microsoft app that allows them to intelligently triage for possible rare disease. Establish Rare Disease Patient Hub leveraging Microsoft Teams ecosystem

**Wave 2 (Post Screening Engagement) 12-24 Months:** Enable bi-directional integration of existing systems into one interface, the Patient Hub, leveraging MSFT stack. Enable efficient and timely communications between health care providers & patient

**Wave 3 (Quantitative Imaging) 12-24 Months:** Determine how proprietary software will be incorporated into ecosystem
Pilot #3 Summary: Explore a Blockchain-based Patient Registry and Rare Disease Passport

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.

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 (“Rare Disease Passport”) will be controlled by the patients, who will authorize and monitor the data access.

EXPECTED OUTCOMES

- Proposal framework and prototype implementation 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
DISCLOSURE

- The content of this presentation does not relate to any product of a commercial entity

- I have no conflict of interest and no financial relationship with commercial interest(s) to disclose
• ~25-30 million people with rare disease in US
• ~7,000 different conditions
CURRENT NEWBORN SCREENING PARADIGM

- 31 conditions recommended to be screened for
  - Only 28 states screen for all 31

- Conditions added to the NBS one-by-one based on validation studies, availability of treatment and incidence of condition

- What about the remaining ~6,900 rare diseases?
Radical solution

Process from birth to adulthood

Engage Pediatricians

Early diagnosis of all RGD

Change in medical care
RAPID WHOLE-GENOME SEQUENCING
MACHINE LEARNING
PILOT STUDY AT A GLANCE

All infants admitted to high-acuity NICU for a specific time period

Phenotype is automatically extracted using NLP

No diagnosis

FOLLOW-UP
Algorithm for re-analysis of genomic and NLP-driven phenotypic data at every pediatrician visit

As new phenotypes develop, machine learning algorithms re-analyze genomic and phenotypic data

List of possible conditions is built

Consultation with central coordinating center and referral by pediatrician to subspecialist
COMPONENTS OF THE PILOT STUDY

- Clinical, NICU - diagnostic and clinical utility
- Clinical, follow-up - diagnostic and clinical utility
- Bioinformatics/machine learning/NLP
- Molecular genetics and genomics
- Bioethics
- Healthcare economics/insurance
- Education
STEPS IN THE NEW PROGRAM

- Central and inclusive governance
- Pilot in two sites (NICUs)
- Expand to other level IV NICUs in other US states and internationally
- Expand to all level IV NICUs across the US – across other nations
- Expand to PICUs across the US – across other nations
- Expand to all newborns……
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