# Leveraging Data to Advance Sanfilippo Syndrome Therapeutic Development

A publication summarizing the February 21, 2023, meeting of academia, biopharmaceutical companies, and patient advocacy organizations in a first-of-its-kind discussion to address the sharing of existing data sets to further the development of therapies for Sanfilippo syndrome

CURE SANFILIPPO FOUNDATION

# Leveraging Data to Advance Sanfilippo Syndrome Therapeutic Development

Meeting Summary

## INTRODUCTION

Sanfilippo syndrome is an ultra-rare, neurometabolic disease which leads to severe neurodegeneration and multisystemic impacts for those affected. Individual heterogeneity, the protracted timespan of disease evolution across body systems, limitations of currently-available clinical outcome measures in symptomatically-impaired patients, near inability to identify pre-symptomatic patients due to lack of newborn screening, and the small, geographically-dispersed patient population are some of the barriers faced in the development of urgently-needed treatments. To date, there are no approved therapies for any of the four subtypes of Sanfilippo syndrome (Types A, B, C, or D).

Finding ways to increase the power of our learnings through utilization of existing datasets has been proposed as a useful strategy in the rare disease space and specifically the Sanfilippo community over the past several years. **Patients and their families who participate in research studies are overwhelmingly supportive of data sharing** and expect that the sacrifices they make to participate in clinical studies will contribute to a greater common good. However, by and large, **existing Sanfilippo datasets remain in silos, limiting our ability to effectively and efficiently build upon those learnings**. With increasing interest in broader collaborations, we recognized that this is an opportune time to address this gap and to convene stakeholders around this topic.

**Cure Sanfilippo Foundation hosted 30 leaders representing academia, biopharmaceutical companies, and patient advocacy organizations in a first-of-its-kind discussion to address the challenges, needs, and goals of sharing of existing data sets to further the development of therapies for Sanfilippo syndrome**, also known as mucopolysaccharidosis type III or MPS III. The meeting was held Feb. 23, 2023, from 10:00 a.m. - 1:00 p.m., in Orlando, Florida, as a prelude to the 2023 WORLD*Symposium*, a scientific meeting attracting nearly 3,000 participants from across the globe to share research updates on lysosomal diseases. The setting for this highly-focused session provided participants the opportunity to continue discussions and follow-up throughout the week.

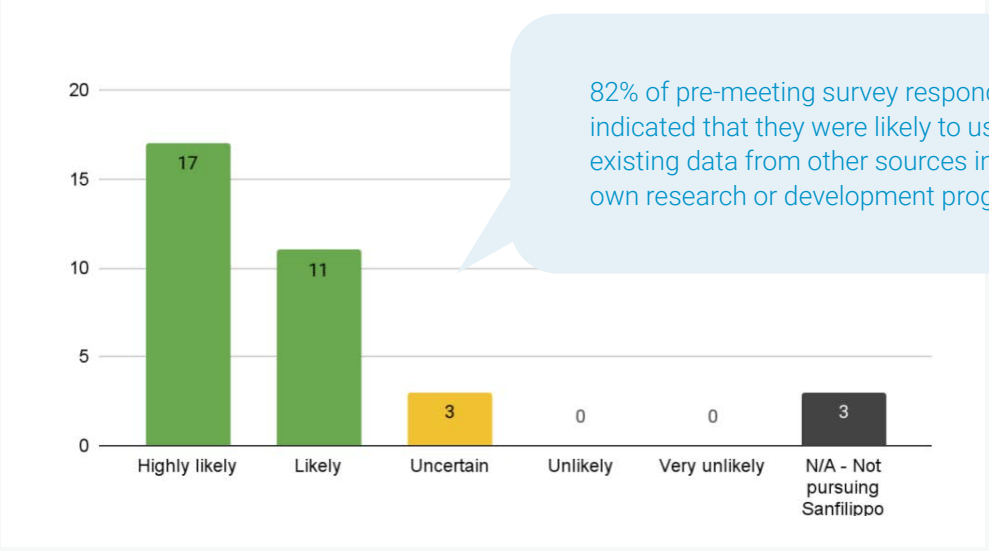

 

# MEETING SUMMARY

> "Data sharing refers to the practice of making data available to other research stakeholders, including other investigators, research subjects, and the broader public."
>
> – National Library of Medicine

In preparation for the meeting, a planning team comprised of Cure Sanfilippo Foundation staff and volunteers and the Kith Collective explored a range of topics related to the complex terrain of data sharing, narrowing in on the possibilities for expanding access to data that has been collected in Sanfilippo observational and interventional research studies. The **team explored existing data-sharing policies, identified various data-sharing models, and engaged in discussions with hosts of data-sharing platforms**. The team also began to **inventory observational and interventional research studies in Sanfilippo**. Finally, a **survey of individuals connected to Sanfilippo data sets** (including invited meeting participants) was circulated to better understand perspectives on and prior experiences with sharing data. Responses from 34 individuals were received and compiled to inform the meeting agenda.

Pre-meeting Survey Question: How likely would you be to utilize others' data for research or to inform your own or your organization's/company's research if it were available to you? (n=34)

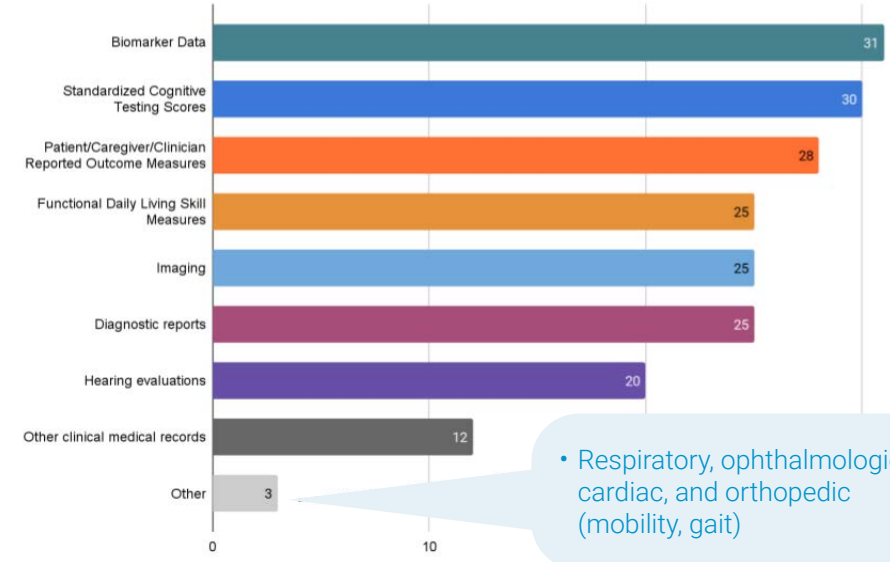



82% of pre-meeting survey respondents indicated that they were likely to use existing data from other sources in their own research or development programs.

**Graph 1: Survey respondents reported likelihood of utilizing external data**

Pre-meeting Survey Question: What type of data would be most valuable to have available through shared datasets? (check all that apply) (n=33)




**Graph 2: Survey respondents indicated valued types of data for cross dataset analysis**

The advantages of data sharing are gaining broad recognition. Funders of medical research such as the National Institutes of Health (NIH) and patient advocacy organizations are introducing policies that require funded researchers to share data. In January 2023, NIH issued the Data Management and Sharing (DMS) policy to promote sharing of scientific data (NIH, 2023). In January 2021, the Health Research Alliance (HRA), a cooperative of non-profit biomedical research funders, surveyed member organizations about data-sharing requirements of grantees. Of the 29 organizations that responded to the survey, 18 reported having a data-sharing policy practice in place, including some of the nation's largest private research funders (HRA, 2021).

There are special efforts within the rare disease community to foster data sharing, given the substantial burden on those immediately affected as well as to the healthcare system. Efforts by the U.S. Food and Drug Administration (FDA), National Organization for Rare Disorders

(NORD), Global Genes, and others are creating platforms and methods to leverage existing knowledge and data across rare diseases that have potential for immense positive impact (*Orphanet Journal of Rare Disease*, 2022). Despite all these initiatives, there are numerous practical, legal, and economic challenges that willing data holders must overcome to make data sharable and useful to the field (Science, 2023).

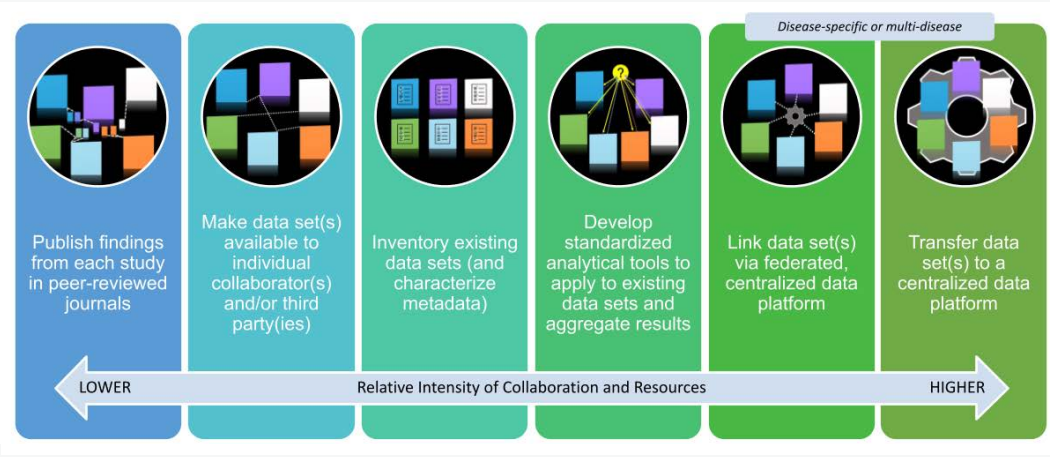



**Figure 1: Range of data sharing modalities to gain insights from different data sources**

At the meeting, **participants were invited to identify potential research questions** that existing Sanfilippo datasets might be able to address, **as well as "must-haves" for an approach to data sharing** that will attract participation from data holders and users alike. Dr. Cara O'Neill, Cure Sanfilippo Foundation, and Kim McCleary, Kith Collective, provided context on the relevance of data sharing for the Sanfilippo community and shared learnings from the survey and other preparatory work.

**Cure Sanfilippo Foundation also brought perspectives external to the Sanfilippo community into the discussion** to illustrate a range of approaches being taken to foster data sharing, as depicted in the figure above (Figure 1). Christine Waggoner, Cure GM1 Foundation, and Kathleen Kirby, Viridian Strategies, shared Cure GM1 Foundation's experiences spearheading a data-sharing initiative. To promote sharing of data from natural history and clinical studies, a working group convened by Cure GM1 Foundation is developing a charter to guide data-sharing efforts, based on a publication by the International Rare Disease Research Consortium

(IRDiRC, 2015). They will also perform an assessment of the study conduct and data from each data contributor, with help from a dedicated project manager and a biostatistician. Meeting participants were also introduced to a case study from the Amyloidosis Research Consortium (ARC). As an interim strategy to pool data from disparate data sources to validate a surrogate endpoint, ARC collaboratively developed a way to conduct a federated analysis of a limited set of data elements. Patient-level data from four separate clinical trials were analyzed locally by the individual trial sponsors, eliminating the need for cross-institution data transfers. Results from the local analyses were pooled centrally to produce final evidence (ARC, 2022). Meeting attendees then engaged in robust discussion about how these examples and others might be translated into use for the Sanfilippo community.

# KEY OBSERVATIONS

The entire meeting was filled with fast-moving and dynamic discussion among attendees and yielded several **key observations:**

- **Data sharing is a high priority for Sanfilippo stakeholders** in academia, biopharmaceutical companies, and patient advocacy, as demonstrated by the discussion and through the survey results. Some holders of Sanfilippo datasets have identified ways to share their data and others have committed to do so.

  89% of pre-meeting survey respondents indicated that a framework for data sharing was important for the field.

- There is also a **high level of interest in making use of Sanfilippo data shared by other investigators**. While the survey results indicated interest in a great variety of data types, at the meeting there was general consensus that starting with a select core of data elements might be a pragmatic way to establish good practices, ensure data quality, and conserve resources.

- To advance therapeutic development in Sanfilippo, **there is an urgent need to align study endpoints and outcome measures** in a manner that will be accepted by regulatory agencies, and this might represent the highest shared purpose for a data-sharing initiative. Use of a primary disease biomarker should not be delayed by these efforts, but rather data sharing may offer a longer term view and ability to further explore and validate various biomarkers across the spectrum of disease.

- There have been about a dozen studies of the natural history of Sanfilippo from 2006 to present, with some studies limited to specific subtypes. **Integrating natural history data could further strengthen the robust existing evidence from individual studies and expand collective use as an external control arm.** Where genetic information is available, efforts to investigate genotype/phenotype correlations across datasets could also provide a better understanding of disease progression.

- **Other potential uses for shared data** include generating and testing novel research hypotheses, informing future clinical trial designs, and refining clinical care guidelines, especially following introduction of new interventions.

- **The field would benefit from a more-detailed inventory and analysis of existing Sanfilippo datasets**, both to catalog the types of data that have been collected and whether there is sufficient synergy to establish a core dataset for comparison across sources. It was suggested that making case report form templates available could be one strategy to speed this effort.

- Based on the information gathered from meeting participants and others, **existing data-sharing platforms are actively evolving and it is not yet clear if there is a single, optimal solution for priority use cases in Sanfilippo.** All would require some level of effort and additional resources, either by the data holder or a centralized resource, to curate and standardize existing data. Collaborators in this initiative could conduct a more formal assessment of the existing platforms, define terms for use by data holders, and agree upon policies for access by data users.

- While the discussion was focused on existing data, **there was strong interest in coordination among researchers and clinicians to standardize prospective collection of data**. Specific areas of focus to increase harmonization include measures of cognition and behavior and laboratory tests that are not standard in clinical practice (heparan sulfate and other biomarker analyses, especially for precious limited cerebrospinal fluid samples).

- In parallel with future collaborations to increase data-sharing efforts and to strengthen the impact of existing datasets, **stakeholders voiced the importance of continuing to engage with decision-makers** in order to provide them with timely information on emerging science and family-centered priorities for the development of treatments, improved diagnosis and care upon which they can rely. FDA, NIH, and the Department of Health and Human Services and the Health Resources & Services Administration's Advisory Committee on Heritable Disorders in Newborns and Children [which are responsible for the Recommended Uniform Screening Panel (RUSP)] are chief among the entities that the Sanfilippo community should continue to engage in this process.

During the meeting and in the days following it, meeting participants expressed interest in exploring these possibilities and forming a group to pursue one or more approaches.

# NEXT STEPS

- Cure Sanfilippo Foundation will leverage the ideas and enthusiasm generated by the meeting to **forge a collaborative effort aimed at promoting and facilitating data sharing**.

- Collaborators will continue efforts to **inventory and characterize the components of existing datasets in order to generate focused and achievable research analyses for high-priority questions**.

- Inform and share among stakeholders the best practices to **incorporate broader data-sharing language into informed consent documents**.

- This effort to accelerate research and advance therapeutic development will be **driven by science and inspired by the urgent unmet need of affected children and their families**.

# MEETING PARTICIPANTS

Thank you to the participants of the meeting for their valuable insights and discussion.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