SANOFI GENZYME
Rare Disease
US Medical Affairs
Request for Proposals

Date: May 13, 2019		
Disease State: Lysosomal Storage Diseases: Pompe Disease and MPS 1		
Therapeutic Area: Rare Genetic Disease		
Area of Interest: Lysosomal Storage Diseases		
Geographic Scope: US		
Internal Requestor Information:		
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Due Date: No later than 5PM ET on Friday, July 19, 2019		
Submission Portal: https://sgrants.envisionpharma.com/vt_sgrants/		
RFP Title: NBS Peds RFP 19		

Background:

Although individually rare, the lysosomal storage disorders (LSDs) as a group have a frequency of about 1/8000 live births, making this disease group a major challenge for the health care system.[1,2] Diagnosis is complicated, as these disorders have a broad spectrum of clinical phenotypes; and central nervous system involvement.[3] Despite this heterogeneity in each single disorder, including significant variation regarding the age of onset, severity of symptoms, manifestations within and between LSDs, these diseases share the common feature of significant multi-organ system morbidity and reduced life expectancy.

Clinicians find the differential diagnosis/symptom recognition of LSDs a challenge, as little is taught regarding these diseases during clinical training. Additionally, there is a wide spectrum of presentations and symptoms, many of which overlap with other more common diseases. Thus, misdiagnosis is common, and there is a very long gap between onset of symptoms and diagnosis, often between 10-15 years.[6-9] Greater physician awareness of manifestations of LSDs has important clinical implications.[8,9] There is a shortage of clinicians well-trained in the diagnosis, treatment, and management of LSDs.[9]

Early diagnosis and disease management are vital for optimal outcomes in Pompe disease[11-15], MPS I[16-18]. Clear diagnostic and management guidelines have also been established for these disorders [10-11, 17, 19-22]. In regions where NBS for Pompe disease has been implemented, for example, improved outcomes have been demonstrated [10, 22]. Rarity and clinical heterogeneity contribute to significant delays in diagnosis of individuals with LSDs[26]. While there may be complexities regarding the identification of asymptomatic and pre-symptomatic patients[23], NBS

for these conditions permits closer clinical monitoring and the timely delivery of expert care[24-26].

Newborn screening is critical to early detection, diagnosis and treatment of LSDs in infants. Improving pediatricians' knowledge and understanding of LSDs, disease manifestations and causes, will undoubtedly impact patient outcomes. Unfortunately, there is a shortage of clinicians well-trained in the diagnosis, treatment and management of LSDs.[9] Pompe and MPS I were added to the Recommended Uniform Screening Panel (RUSP) in 2015 and 2016, respectively[10, 29]. Several states have adopted newborn screening for these and other lysosomal storage disorders. Thus there is a need for Physicians to learn about the clinical presentation and diagnosis of these disorders, as Primary Care Physicians (including Nurse Practitioners, Physician Assistants, etc.) are the first line of care providers seeing these patients.

Healthcare Gaps:

- Greater physician awareness of manifestations of LSDs has important clinical implications (Pediatrics Vol. 123 No. 4 April 1, 2009 pp. 1191 -1207. Rare Disease Impact Report. Shire 2013.)
- There is a shortage of clinicians well-trained in the diagnosis, treatment and management of LSDs. (http://thepersonalgenome.com/2007/12/shortage-of-geneticists-in-the-united-states/. Rare Disease Impact Report Shire 2013)

Sanofi Genzyme will consider will consider programs including, but not limited to, the following:

- Regional and/or Local distribution channels with or without enduring activity
- Accredited or Non-accredited IME activities
- Single supported and multi-supported activities

Preference will be given to proposals that recommend appropriately designed interventions that are likely to enhance a learner's knowledge of the unmet needs and employ proven strategies to overcome knowledge and performance gaps and barriers. Proposals should be submitted with a maximum request not to exceed $75,000.

Proposal should include the following information:

- **Needs Assessment/Gaps/Barriers**: Include a comprehensive needs assessment that is well referenced and demonstrates an understanding of the specific gaps and barriers of the target audiences (in alignment with ACCME criteria). **The needs assessment must be independently developed and validated by the accredited provider, if applicable.**
- **Target Audience and Audience Generation:** Proposal should indicate the target audience(s) and provide a rationale for how and why this target audience is appropriate for closing the identified healthcare gap. In addition, please describe methods for reaching the target audience including description of any rationale for recruitment and placement strategies to maximize participation according to need. Any unique recruitment efforts specific to the target audience should be highlighted.

- **Learning Objectives and Content Accuracy:** Provide clearly defined and measurable learning objectives framed as expected practice improvements in relation to the identified gaps and barriers.
- Include an overview of program content and explanation of criteria that will guide content selection, considering level of evidence and other variables. Sanofi Genzyme is committed to the highest standards in ensuring patient safety; the applicant should describe methods to ensure complete, accurate, evidence-based review of key safety data for any therapeutic entities discussed in the activity. Explain how content will be updated if necessary throughout the program period, and how accuracy will be ensured.
- **Educational Methods:** Sanofi Genzyme supports the ACCME guidance for educational methods to be clearly designed to address the knowledge, competence and/or performance gaps that may underlie an identified healthcare gap. Your proposal should demonstrate an understanding of instructional design as it relates to the gaps in the knowledge, competence, or performance of the targeted audience. Educational methods and design should be based on current literature in CME best practice and consistent with ACCME accreditation criteria, as applicable. For example, systematic reviews have suggested that the most effective continuing education is clearly linked to clinical practice, uses methods including interaction, reflection, strategies that ensure reinforcement through use of multiple educational interventions, and more. [1,2,3,] Preference will be given to applications that utilize methods that have been shown to result in practice improvements, and/or with data on the effectiveness of other programs of the same type. ACCME criteria recognize that barriers may be related to systems, lack of resources, or tools etc. and these may be included if relevant in your discussion of the gap and the educational methods you propose. In addition, the educational preferences of the target audience(s) may be considered to maximize attendance/participation and lead to practice improvements.
- **Faculty Recruitment and Development:** Provide Information on the expected qualifications of contributors and description of methods to ensure recruitment of course directors and faculty who meet the qualifications. Explain any methods that will be used to ensure that faculty are fully trained in the program expectations and any skills that may be needed to ensure effective delivery of intended education.
- **Program Evaluation and Outcomes:** Provide a description of the approach to evaluate the reach and quality of program delivery; methods for monitoring individual activities and for ensuring ongoing quality improvements. For ACCME accredited programs, refer to accreditation elements and criteria, as applicable. Describe methods that will be used to determine the extent to which the activity will close the identified healthcare gap, and the qualifications of those involved in the design and analysis of the outcomes. Preference will be given to programs with Objectives and Outcomes Plans with objective measures of changes in knowledge, and/or additional measures of improvements in competence, performance, patient health, population health, and/or system improvements, as aligned with the design of the intervention.4

- **Budget:** Include a detailed budget with rationale and breakdown of costs, per unit, and description of each budget line item. In addition, please include any registrations fees paid by the learner, and how the fees will be applied.
- **Accreditation**: If proposal involves an accredited program, the accreditation must be provided by an appropriate accrediting body and fully compliant with the accrediting body's criteria and applicable government guidelines and regulations.
- **Fair Balance:** The proposal should briefly describe methods for ensuring fair and balanced content, identification and resolution of conflict of interest, in alignment with applicable ACCME criteria.
- **Communication and Publication Plan**: Provide a description of how the provider will keep Sanofi Genzyme informed of progress. If applicable, include description of how the results of this educational intervention will be presented, published or disseminated.

1. Cervero RM, Gaines JK. The Impact of CME on Physician Performance and Patient Health Outcomes: An
1. Updated Synthesis of Systematic Reviews. J. Contin. Educ. Health Prof., 2015:35: 131–138.
2. doi:10.1002/chp.21290
3. McMahon GT. Advancing Continuing Medical Education. JAMA. 2015; 314(6):561-562.
4. doi:10.1001/jama.2015.7094.
2. Mostofian F, Ruban C, et al. Changing Physician Behavior: What Works? AJMC. 2015; 21(1):75-84
3. Moore DE, Green JS, and Gallis HA . Achieving Desired Results and Improved Outcomes: Integrating Planning and Assessment Throughout Learning Activities. JCEHP. 2009;29(1):1-15.
5. Lysosomal Storage Disorders. www.ncbi.nlm.nih.gov/books/NBK6177/.
6. JIMD Rep. 2013;9:117-20.
7. Am J Med Genet A. 2013 Oct;161(10):2431-43.
8. J Inherit Metab Dis. 2010 Dec;33 Suppl 3:S429-33.
9. Rare Disease Image Report Shire 2013.
10. http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/nominatecondition/reviews/mps1finalreport.pdf
11. Chien et al., 2009. Pompe disease in infants: improving the prognosis by newborn screening and early treatment. *Pediatrics* 124: e1116–e1125.
12. Chien et al., 2013. Pompe disease: early diagnosis and early treatment make a difference. *Pediatrics and Neonatology* 54: 219-227
13. Chien et al., 2015. Long term prognosis of patients with infantile-onset Pompe disease diagnosed by newborn screening and treated since birth. *J Pediatr* 166: 985-91.
14. Kishnani et al., 2006. Pompe disease diagnosis and management guideline. *Genet Med* 8: 267-288.
15. Cupler et al., 2012. Consensus treatment recommendations for late onset Pompe disease. *Muscle Nerve* 45: 319–333.

16. Beck et al., 2014. The natural history of MPS I: global perspectives from the MPS I Registry. *Genet Med*16(10): 759-65.
17. Muenzer et al., 2009. Mucopolysaccharidosis I: Management and Treatment Guidelines. *Pediatrics* 123 (1): 19-29.
18. D'Aco et al., 2012. Diagnosis and Treatment Trends in mucopolysaccharidosis type 1: findings from the MPS I Registry. *Eur J Peds* 171: 911-919.
19. Goldstein et al., 2009. Screening for Pompe disease using a rapid dried blood spot method: experience of a clinical diagnostic laboratory. *Muscle Nerve* 40: 32-36.
20. 2009. Diagnostic criteria for late-onset (childhood and adult) Pompe disease. *Muscle Nerve* 40: 149-160.
21. Kishnani et al., 2014. Methods of diagnosis of patients with Pompe disease: Data from the Pompe Registry. *Mol Genet Metab* 113: 84-91.
22. Yang et al., 2016. Very early treatment for infantile-onset Pompe disease contributes to better outcomes. *J Pediatr* 169: 174-80.
23. Wang et al., 2011. Lysosomal storage diseases: diagnostic confirmation and management of presymptomatic individuals. *Genet Med* 13: 457-484.
24. Chien et al., 2011. Later onset Pompe disease: early detection and early treatment initiation enabled by newborn screening. *J Pediatr* 158: 1023-1027.
25. Chien et al., 2012. Early pathologic changes and responses to treatment in patients with later-onset Pome disease. *Ped Neurol* 46: 168-171.
26. Kishnani et al., 2013. Timing of diagnosis of patients with Pompe disease: Data from the Pompe Registry. *Am J Med Genet Part A* 161A: 2431–2443.
27. Kishnani and Hwu, 2017. *Pediatrics* 2017 Jul; 140 (Suppl 1):S1-S50
28. Clarke et al., 2017. Mucopolysaccharidosis type I Newborn Screening: Best Practices for Diagnosis and Management. *J Pediatrics* 182: 363-370.
29. http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/recommendations/correspondence/secretaryfinalresponse.pdf