GENZYME, A SANOFI COMPANY
Medical Affairs
Request For Proposal

Date: April 21, 2015

Therapeutic Area: Genetic Disease

Area of Interest: Neurology and Neuromuscular (AANEM CME program)

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TAG ID: SP-D9K99
Due Date: May 26, 2015

HEALTH CARE GAP:

Limb-girdle muscle weakness (LGMW) presents a diagnostic challenge for physicians due to the genetic and phenotypic heterogeneity [1]. In addition to over 30 types of limb-girdle muscular dystrophy (LGMD), other hereditary muscular dystrophies (Emery-Dreifuss muscular dystrophy, Becker muscular dystrophy), hereditary myopathies (hereditary Inclusion Body Myopathy) and metabolic myopathies (late onset Pompe disease) can also present with progressive proximal muscle weakness. Diagnosis typically relies on clinical features, distribution of weakness, associated symptoms and inheritance patterns. However, along with the phenotypic overlap, there can be various presentations within a diagnosis and timing within the progression of the disease making it a challenge when a patient first presents [1]. Muscle biopsy and electromyography have been utilized to aid in the diagnosis. However, there can be non-specific findings or non-diagnostic findings depending on the site of biopsy or EMG. Concise genetic confirmation of the diagnosis is important for defining the long-term prognosis, directing care and management more effectively, helping to determine risks to offspring, and avoiding repetitive diagnostic tests [1]. The AAN and AANEM have developed a guideline summary to the diagnosis and treatment of limb-girdle muscular dystrophies [1].

Late onset Pompe disease (LOPD) is a progressive disorder of proximal muscle weakness with or without respiratory, gastrointestinal and cardiac involvement [2-5]. Studies have shown that as many as 3-5% of patients with LGMW may have LOPD [6-7]. Diagnosis is complicated by non-specific clues on muscle biopsy [8] and EMG [9-10]. Due to the rarity and phenotypic overlap with other disorders of LGMW, the diagnosis of Pompe is often delayed by years from onset of symptoms [11].

Genzyme, a Sanofi Company, is seeking proposals to close the following independently identified educational gaps for healthcare professionals treating patients with LGMW.

1. Due to the genetic heterogeneity of limb-girdle muscle weakness (LGMW), there is a diagnostic challenge to the approach with a broad diagnostic differential including late onset Pompe disease (LOPD). LOPD may be the etiology in 3-5% of this population (studies from Europe [6-7]), however a gap exists in the recognition of LOPD in the phenotypic presentation of LGMW.

2. While both muscle biopsy and EMG can aid in the evaluation of LGMW; which muscle groups are
tested and technician and evaluator variability can affect the results. [8-10]. Ensuring optimal performance and interpretation of these tests is key to the successful diagnosis of LGMW.

3. Newer genetic testing, including Next generation panel testing and whole exome testing has an increased utility in clinical practice. However, its utility in the diagnostic evaluation of limb-girdle muscle weakness has not been fully evaluated [1]. Clinicians need to better understand the limitation of this testing and understand when, and to whom, they should refer patients with LGMW to ensure optimal diagnosis.

4. The delay from symptom onset to diagnosis within LGMW, especially LOPD [11] is significant. Decreasing the time between onset and diagnosis will aid in patient relevant outcomes including long-term prognosis, directing care and management more effectively, recurrence risks to offspring, and avoidance of repetitive diagnostic tests [1].

The AANEM has announced the possibility of Forums for accredited educational activities during their 2015 Annual meeting in Honolulu, HI (October 28-31, 2015), and Genzyme, a Sanofi Company is considering proposals for this forum.

Please note that proposals are expected to include an analysis of the barriers and root causes for this gap and appropriately designed educational interventions. In addition, proposals may include physician education and/or patient education.

PROPOSAL FOR PHYSICIAN EDUCATION 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 (i.e., ACCME accreditation element 2). The needs assessment must be independently developed and validated by the accredited provider.

• **Target Audience and Audience Generation**: Proposal should describe why AANEM attendees are an appropriate target audience for education that would help close the identified healthcare gaps. In addition, please describe methods for reaching the target audience(s) including description of and 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. 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, as appropriate. Explain how content will be updated if necessary throughout the program period, and how accuracy will be ensured.

• **Educational Methods**: The ACCME calls for educational methods that are 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 issues as they relate to the gaps in the knowledge, competence, or performance of the targeted audience. Education methods and design should be based on current literature in continuing education best practice and consistent with ACCME accreditation elements 3,4,5,6. 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. 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 12, 13, 14, 15). Describe methods that will be used to determine the extent to which the activity has served to close the identified healthcare gap. (For ACCME accredited programs refer to accreditation elements 10, 11, 12), 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 of level 4-6.15

- **Budget:** Include a detailed budget with rationale including breakdown of costs, clear explanation of the units, and calculations of:
  - Content cost per activity
  - Out-of-pocket cost per activity
  - Management cost per activity

- **Accreditation:** Programs must be accredited by an appropriate accrediting body and fully compliant with the accrediting body’s criteria and applicable government guidelines and regulations. If you are a non-accredited provider, the accredited provider must be involved from the concept origin, fully knowledgeable of the grant submission and documentation should be provided on the website grant application section entitled, “Other Information.”

- **Resolution of Conflict:** The proposal should briefly describe methods for ensuring fair and balanced content, identification and resolution of conflict of interest, with particular emphasis on ACCME criteria 7, 8, 9 for ACCME accredited programs.

- **Communication and Publication Plan:** Provide a description of how the provider will keep the supporter informed of progress. If applicable, include description of how the results of this educational intervention will be presented, published or disseminated.

**REFERENCES:***

12. Davis, D, Barnes, BE, Fox, R. (2003). The continuing professional development of physicians – From Research to practice; Chicago, IL: AMA