

SANOFI GENZYME and REGENERON Alliance
Medical Affairs
Request for Proposal

Date: May 6, 2021	
Disease State/Therapeutic Area: Immunology	
Area of Interest: Chronic Spontaneous Urticaria (CSU)	
Geographic Scope: US	
Internal Requestor Information:	
Sharon Barnett Grants Manager Sanofi Genzyme 908.981.6036 Sharon.Barnett2@sanofi.com	Holly Murray Associate Director, Medical Education Regeneron 914.348.5185 Holly.murray@regeneron.com
Due Date: Noon ET on June 7, 2021	
Submission Portal: https://sgrants.envisionpharma.com/vt_sgrants/	
RFP Name: CSU-RFP-1-2021	

Burden of Disease/Educational Gap

Chronic spontaneous urticaria (CSU) is a chronic immune-mediated condition characterized by the sudden development of wheals (hives) and/or angioedema and debilitating symptoms (e.g., itching and/or burning sensation) recurring for 6 weeks or more resulting in substantial physical, mental, emotional, and socio-economic effects on patients' quality of life.^{1,2,3,4,5} CSU has a point prevalence of approximately 0.5–1%, although considerable regional differences have been observed. Adults are more commonly affected than children, with most patients aged 20–40 years, and twice as many women are affected than men.^{6,7,8} The diagnosis of CSU is complex. Urticaria needs to be differentiated from other medical conditions where wheals, angioedema or both can occur.^{1,3}

CSU is primarily a mast cell-driven disease. Wheals and angioedema in CSU results from the degranulation of mast cells and the release of histamine and inflammatory mediators that induce vasodilatation, increase vascular permeability, and stimulate sensory nerve endings that lead to swelling, redness and itch.^{3,9,10,11,12} Two types of autoimmunities are thought to be highly involved in the pathogenesis of CSU. Autoimmune mechanisms involve the production of IgG antibodies against IgE or against the high-affinity IgE receptor FcεRI on effector cells. Autoallergy mechanisms refers to the production of IgE antibodies against self-antigens. The binding of autoantibodies and then cross-linking of the FcεRI receptors promote the spontaneous mast cell and basophil degranulation.^{13,14,15} Elements of type 2 inflammation may play an underlying role in the pathophysiology of CSU. The major effector responses in type 2 immunity include B-cell mediated humoral responses such as IgG1 and IgE antibody class switching and the recruitment of inflammatory effector cells such as mast cells, basophils and eosinophils. Activated mast cells release inflammatory mediators, including histamine, leukotrienes, prostaglandins, and cytokines, including IL-4, IL-5, IL-13 and IL-31. A CSU lesion is characterized by edema, mast cell degranulation, and a perivascular infiltrate of CD4+ lymphocytes, monocytes, neutrophils, eosinophils and basophils and a cytokine profile shows T cell expression of IL-4, IL-5, and gamma interferon.^{3,16} IL-4 and IL-13 are two key cytokines that drive the type 2 immune response. IL-4 enhances proliferation and mediator release in mast cells. Both IL-4 and IL-13 promote B cell class switching, IgE mediated activation of mast cells and recruitment of inflammatory cells. IL-4 also enhances FcεRI expression, stimulate the production of IL-13 from mast cells, increase IgG-mediated degranulation and cytokine production, and proliferation of Th2 cells, further sustaining the type 2 immune response.^{3,15,16,17,18,19,20,21,22}

CSU is a heterogeneous disease with several different possible clinical characteristics, associated factors, and different degrees of response to the given drugs. Therefore, it could be informative and clinically important to identify the biomarkers able to classify patients according to their phenotype, possibly identifying underlying immunological mechanisms (and therefore setting the disease “endotype”), to stratify patients according to their severity and prognosis, and to identify best responders to any given therapy, particularly to biologics.²³ The diagnosis and management of CSU is complex, requiring differential exclusion from other medical conditions where wheals, angioedema or both can occur and

a stepwise approach to treatment, using often off label doses of current therapies for optimal control. Despite currently available treatment options, many CSU patients remain inadequately controlled, leaving a significant unmet need for safe and effective, targeted therapies.^{1,4,24,25} In approximately 1 of 5 CSU patients, these treatment options are not sufficient. Novel drugs are needed and are under development. When new and better medication for the prevention and symptomatic treatment of CSU are sought, the ultimate goal is to develop strategies and drugs that can cure CSU, rather than stop the signs and symptoms. The exploration of novel therapeutic targets for their role and relevance in CSU can help to achieve this, by providing a better understanding of its etiopathogenesis.¹⁰

Currently, there are US and international guidelines that provide recommendations on the diagnostic and management of CSU. One international observational study that assessed a cohort of 673 adult patients with CSU identified incorrect treatment patterns in the real-world practice, and the high cost of unnecessary investigations and treatments is due to poor compliance with guidelines and best practices.^{1,4,26} Available guidelines are not well utilized based on real-world studies; sedating antihistamines and oral steroids are overutilized. The gap between the guidelines for diagnosis and treatment and what is happening in the real world needs to be closed to reduce the cost and morbidity associated with this disorder.²⁷

Call for Grants

The Sanofi Genzyme and Regeneron Pharmaceuticals Alliance is seeking to close independently identified gaps and provide education for US Health Care Providers involved in the diagnosis and treatment of CSU (eg, Dermatologists, Allergists, Specialty Nurse Practitioners, Specialty Physician Assistants) and Managed Care/Pharmacy Directors, and other clinicians who diagnose, treat, and/or manage patients with CSU. Proposals can target one or multiple audiences and should focus on key evidence-based data to support recognized healthcare gaps and independently identified and referenced educational needs. Grants should address issues specific to CSU and be inclusive of appropriate available data for current/emerging treatments options.

Learning objectives for the proposed initiative should provide measurable objectives for improving clinicians' knowledge, competence, and/or performance with the ultimate goal of improving patient care.

The Sanofi Genzyme and Regeneron Pharmaceuticals Alliance will consider grants including, but not limited to, the following:

- 2022 Symposia (face-to-face live or virtual real-time) with enduring (eg, AAAAI, AAD, Managed Care Congresses [AMCP Annual, Asembia Specialty Pharmacy])
 - Securing slots are the responsibility of the grant recipient(s)
 - Applicants should articulate considerations for addressing anticipated limitations and/or challenges due to pandemic conditions
- Self-directed online programs (eg, Virtual, Mobile, Social Media, Podcast, Point-of-Care, Print). May include scientific/clinical simulation, case-based learning formats, microlearning. Comprehensive, interactive, and innovative online educational formats designed for engagement using various proven distribution channels are eligible.
- Proposals should clearly demonstrate the initiative's applicability to the target audience. Single supported and multi-supported proposals will be considered with a maximum request not to exceed **\$300,000**.

Please note that proposals are expected to include an analysis of educational gap(s) and how the proposed intervention(s) would address the identified gap(s), with consideration for learner preferences and potential clinical impact. 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 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, as 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. The Sanofi Genzyme/Regeneron Alliance 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:** The Sanofi Genzyme/Regeneron Alliance 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.^{a,b,c}
- 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 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.^d Objective and quantitative methods are preferred for each outcomes level.
- **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 the Sanofi Genzyme/Regeneron Alliance informed of progress. If applicable, include description of how the results of this educational intervention will be presented, published or disseminated.

References

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