INSMED CALL FOR MEDICAL EDUCATION GRANT APPLICATIONS (CGA)
NON-CYSTIC FIBROSIS BRONCHIECTASIS

Insmed is committed to improving the lives of patients with serious and/or rare lung diseases through funding independent education programs that advance the clinical knowledge, competence, and performance of healthcare providers. This may ultimately lead to improved health outcomes in patients with these diseases and a better overall health status in the patient community.

Insmed issues Calls for Medical Education Grant Applications (CGA) as an additional method to notify organizations that grant funding is available for specific programs and focus areas where Insmed has identified an unmet need addressable through education. Insmed CGAs are publicly posted on the Alliance for Continuing Education in the Health Professions (ACEHP) website for Request(s) for Proposals (RFP), Call for Grants Notification (CGN) and CGA opportunities:

- https://www.acehp.org/Resources/RFP-CGN-and-CGA-Opportunities

Please refer to https://insmed.com/culture/responsibility/grants-funding/ for medical education grant submission requirements. For additional questions about this CGA funding availability or general questions about grant processes please contact Insmed Medical Education at grants@insmed.com.

Insmed will have funding available to support independent medical education that reaches national audiences through Medical/Academic Society conferences and enduring programs. Insmed is interested in receiving grant requests that align with the specifications outlined below.

Therapeutic Area	Non-Cystic Fibrosis Bronchiectasis (NCFBE)
Educational format & scope	Independent medical education that can address the unmet needs of clinicians and researchers who have a role in the diagnosis and treatment of patients with NCFBE who work in pulmonology, respiratory and primary care to include live, enduring, or multiple components (where in-person programs may not be possible). We want to ensure that programs are targeting education on early patient diagnosis, guidelines-focused treatment, disease state awareness, risk factors, burden of disease, comorbidities and evaluations that reflect on clinicians' confidence within the therapeutic area. Preference will be given to applications that utilize engaging and unique methods that have been shown to result in practice improvements, and/or with data on the effectiveness of other programs of the same type. Accreditation Council for Continuing Medical Education (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.
Meetings of interest	In addition to the educational programs above, proposals for independent satellite symposia at meetings including, but not limited to the following will be considered: • ERS 2023 • CHEST 2023 • RSNA 2023 • ATS 2024 Hybrid participation for live programs (live simulcasts, enduring webcasts, etc.) to engage the greatest number of learners is preferred, if possible.

<table>
<tr><td>Submission deadline</td><td>
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<tr><th>Focus</th><th>Insmed Submission deadline</th><th>Important deadline</th></tr>
<tr><td>NCFBE</td><td>November 22, 2022*</td><td>Ensure submission at least 60 days before funding commitment is needed</td></tr>
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If your organization plans on submitting requests for more than one activity (live and/or enduring), please structure the proposal(s) to ensure:
• Deadlines can be met
• Cost efficiencies are clear –budget summaries should be included for each activity
• Rationale/justification is clear, including relevance to potentially different audiences

*Insmed accepts grant applications on a rolling basis. This deadline is strongly suggested for programs that begin in Q1 2023.
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<tr><td>Accreditation</td><td>Grant requests must adhere to any Medical/Academic/Scientific Society requirements regarding accreditation, if applicable.</td></tr>
<tr><td>Budgets</td><td>When submitting budgets please clearly differentiate out of pocket costs (i.e., direct cost) from management fees, management cost per activity, content cost per activity, and note optional costs. Please include costs associated with the continuous promotion and recruitment of leaners throughout the posting of the enduring program. Organizations may use their own template or request a form from Insmed.</td></tr>
<tr><td>Intended audience</td><td>Education should address the needs of clinicians and who have a role in the diagnosis and treatment of patients with NCFBE, including, but not limited to pulmonologists, radiologists, and primary care or family medicine practitioners (MDs, NPs, PAs, etc.). Intended audience regions should include <u>only</u> USA and/or Europe.</td></tr>
<tr><td>Areas of educational focus</td><td>1. Enhance awareness of NCFBE and assessment of disease burden, unmet needs, associated patient risk factors, and comorbidities.
2. Enhance the clinician’s assessment of the natural history, clinical course, and impact of pulmonary exacerbations on progression of the disease.
3. Educate on appropriate diagnosis, disease management recommendations, and emerging therapies.
4. Improve clinician’s understanding of the role of neutrophilic inflammation and Neutrophil Serine Proteases (NSPs) in NCFBE.</td></tr>
<tr><td>Outcomes measures</td><td>Moore’s Level 4 (competence) outcomes will be the minimum expected. (Moore et al. Achieving desired results and improved outcomes: integrating planning and assessment throughout learning activities. JCEHP. 2009; 29 (1):1-15).</td></tr>
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<u>Needs Assessment and Healthcare Gap</u>

Note*: It is expected that any education provider submitting a grant application conduct their own independent needs assessment when identifying gaps in patient care and learning objectives that aim to reduce those gaps.*

<u>Background/Disease Burden</u>

Non-cystic fibrosis bronchiectasis (NCFBE) is a pulmonary disorder that is irreversible and characterized pathologically by permanent bronchial dilatation and severe bronchial inflammation. Clinically, it presents with chronic productive

cough and recurrent pulmonary exacerbations. NCFBE is the result of a pathological process involving vicious cycles of impaired mucus clearance, neutrophilic inflammation, recurrent infections, and bronchial wall damage that occurs due to its association with various primary causes, including many patient-specific factors such as infectious, genetic, inflammatory, environmental, and allergic conditions. (Chalmers J et al.,2015; Aksamit T et al., 2017). To further describe the complexity and interconnectivity between these pathophysiological processes, Flume et al. (2018) proposed a "vicious vortex" model suggesting that the process can be initiated at any step with each step contributing to all others, rather than follow a specific sequence. This model reinforces a multimodality approach to treatment that addresses all aspects of bronchiectasis. (Flume P et al., 2018).

The prevalence of NCFBE in adults over the age of 18 years old is 139 cases per 100,000 persons in the US. There is an estimated 340,000 to 522,000 adults having NCFBE and receiving treatment in the United States. The prevalence of bronchiectasis is much more common than previously reported with an annual growth rate since 2001 of 8% per year, due to at least in part to recent advances in, and increased use of, radiologic techniques. (Weycker D et al., 2017). In the United Kingdom bronchiectasis is common and is increasing in incidence and prevalence, particularly in older age groups. Bronchiectasis is also associated with a markedly increased mortality. (Quint J et al., 2016).

Clinical manifestations of NCFBE are cough, daily sputum production, dyspnea, rhinosinusitis, hemoptysis, and recurrent pleurisy. Common physical findings include crackles and wheezing. (King P et al., 2006).

Inflammation in bronchiectasis is dominated by neutrophils (Chalmers JD et al., 2017; Finch S et al., 2019). Activation of neutrophils in the airway leads to release of Neutrophil Serine Proteases (NSPs), including Neutrophil Elastase (NE), which is believed to be central to the pathophysiology of bronchiectasis (Chalmers JD and Chotirmall SH, 2018). Elevated NE, Proteinase 3 (PR3), and Cathepsin G (CatG) overwhelm natural inhibitors, such as alpha-1 antitrypsin and secretory leukoproteinase inhibitor (Dubois AV et al., 2012), (Sibila O et al., 2019), which leads to damaged airway walls (Chalmers JD, Chotirmall SH, 2018), mucus hypersecretion (Voynow JA et al., 1999), exacerbated inflammation (Finch S et al., 2019), and disabled neutrophil and macrophage functions, increasing the risk of infection.

Current Therapies

There is currently no FDA-approved treatment for NCFBE. (Smith T, 2018). NCFBE treatment options include physiotherapy for patients with excessive secretions, with techniques directed at improved clearance of broncho-pulmonary secretions, ACT (Airway Clearance Techniques), combined with a pulmonary rehabilitation program to improve exercise tolerance. (Lee A et al., 2014).

Macrolides are a treatment option due to their anti-bacterial and anti-inflammatory properties. According to the British Thoracic Society Guideline for bronchiectasis of 2019, long-term antibiotics should be considered in patients with three or more exacerbations yearly and are suffering from chronic symptoms. (Altenburg J et al., 2013; Serisier D et al., 2013; Hill A et al., 2019).

Unmet Medical Need

The importance of proper and timely diagnosis and guidelines-based treatments are paramount to controlling NCFBE exacerbations in patients who present symptoms. Bronchiectasis is underrecognized as a serious and treatable disease and its diagnosis is often delayed or misdiagnosed as asthma or COPD. The severity and frequency of bronchiectasis exacerbations significantly impact the quality of life, daily symptoms, the decline in lung function, risk of mortality and are associated with increased health care costs. (Maselli DJ et al., 2017).

There is limited understanding by the medical community of the key role of neutrophils and NSPs in NCFBE and other respiratory conditions. There are currently no products approved for NCFBE and no current guideline-recommended pharmacotherapies that target neutrophilic inflammation. Emerging data on the horizon is important to be aware of

as future tools to inform treatment decisions in patients with NCFBE. Utilizing independent medical education can be a useful tool in educating healthcare providers to diagnose and treat NCFBE patients and requires regular and consistent educational opportunities over time to build an educational foundation to enhance diagnosis and treatment options for their patients. (Solomon G et al., 2017).

Selection Criteria

Grant requests are reviewed and prioritized for funding based on the following:

- Educational need and plan to deliver the educational activity to the intended audience
- Learning objectives that are achievable and align with the educational need and areas of focus
- Experience in designing educational programs and assessing the effectiveness of the activity
- Extension of the reach and accessibility of educational content by including plan to present, publish or use QR codes, if applicable
- Inclusion of patient(s) in development of application and/or activity or as faculty, speaker or panelist preferred
- History of timely provision of final budget reconciliation and outcomes reports in the desired format, if applicable
- Complete budget as requested above
- Accreditation and compliance with ACCME Standards for Commercial Support
- Compliance with Insmed policies and procedures

References:

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Chalmers JD, Chotirmall SH. Bronchiectasis: new therapies and new perspectives. *Lancet Respir Med.* 2018;6(9): 715-26).

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