Lundbeck Medical Education: Request for Independent Medical Education Grant Proposals	
Therapeutic Area	Treatment Resistant Schizophrenia
	The objective of this RFP is to support activities that improve healthcare provider (HCP) education on topics related to treatment resistant schizophrenia.
Intended Audience	Enduring Online Programs/Materials • Primary audiences: Psychiatrists, Schizophrenia Specialists; Forensic Psychiatrists • Secondary audience: NPs, PAs
Date Issued:	September 17, 2018
Submission Timeframe:	September 17, 2018 – October 31, 2018
Program Format:	Live symposia consisting of a curriculum containing multiple interventions employing a variety of formats at a major national or regional psychiatry conference in Q1/Q2 2019. The purpose of this RFP is to close gaps in the diagnosing and treating of TRS using evidence based medicine. Interventions should support improvements in the following areas of knowledge and skills but not be limited to: 1. Treatment-Resistant Schizophrenia (TRS) poses a significant clinical challenge for mental health providers; this may lead to lack of recognition, under-diagnosis and inappropriate management of these individuals 2. TRS is a highly debilitating and wide-ranging disorder; with a significant personal, economic, familiar and societal impact 3. There appears to be a lack of awareness of the consequences in the delay in diagnosis and the need for earlier intervention in TRS 4. Treatment guidelines and evidence-based techniques may not be sufficiently known nor widely used 5. Current evidence suggests that there appears to be distinct neurobiological differences between TRS and treatment-responsive schizophrenia Providers should detail ability to attract the greatest number of potential learners and demonstrate good financial stewardship. Programs should ideally employ experiential or inquiry-based learning strategies. These may include case based discussions, HCP office simulations or other engaging and interactive educational formats to best facilitate understanding, retention, and application of content.
Maximum Lundbeck Contribution	$600,000.00
Deadline for Application:	All proposals to this RFP must be received on or before 8 PM Eastern/5 PM Pacific Time on October 31, 2018

	Proposals received after the deadline will not be considered. ****November 5, 2018 Update:** Notification regarding the status of all submitted RFP responses **is to be determined.****
Applicant Eligibility	Eligible program sponsors are third-party providers of medical or scientific educational programs and include, but are not limited to, accredited CME/CE providers, not-for-profit charities, associations, patient advocacy groups, foundations and societies, institutions, hospitals and managed care organizations. Ineligible program sponsors include, but are not limited to, non-accredited CME/CE providers, individual healthcare providers, group practices, physician practice management companies, provider medical groups, or commercial publishers, any of which is not accredited as a CME provider.
Disease Summary/Burden	Schizophrenia is a chronic mental disease associated with disturbances of thoughts, comprehension, volition, and perception. Schizophrenia is characterized by periods of partial remission interrupted by episodes of illness exacerbations. [1] It usually hits during late adolescence and is commonly manifested by three types of symptoms: positive; such as hallucinations, delusions, paranoia, and disorganized thoughts, negative; such as lack of motivation, social withdrawal, and alogia, and cognitive symptoms; where performance on tasks requiring attention and memory is poor. [2,3] Schizophrenia is associated with high economic and social burden with double the mortality rates and 12-15 years lower life expectancy when compared with healthy individuals. [4,5,6,7] Although it is a treatable condition, almost 50% of the patients do not receive proper treatment probably due to poor personal care or poverty. [4,8] 20-30% of schizophrenia patients fail to respond to treatment and almost one-third of patients do relapse despite adherence to proper maintenance therapy. [8,9] Treatment-resistant schizophrenia (TRS) was first defined by Kane et al. as failure to respond to three periods of antipsychotic agents, from at least two different classes, administered properly at fixed doses over a period of six weeks. [8] However, later studies have further defined TRS as the persistence of extensive positive symptoms despite one or more trials for therapy with appropriate doses of neuroleptic agents for adequate time periods. [10,11,12] Schizophrenia-related research and clinical data are limited by the inconsistent definitions of treatment resistance or response. In fact, TRS is a major clinical problem which is often misdiagnosed and worldwide guidelines recommend specific treatments in affected cases. [13,14,15] As a result of these imprecise definitions and the wide variety of criteria used in clinical research, clinical studies, on which some guidelines are based, may use subjects with very different characteristics from those of patients who were actually included in the clinical trial on which the guidelines were primarily based on. These perception-based errors result in limited comparisons and difficulty in reaching replicable results. [16,17] From Howes and his colleagues' point of view, the main key elements which define TRS are; a confirmed diagnosis of schizophrenia,

	adequate pharmacological therapy, and the persistence of significant symptoms despite adequate therapy. [18] The efficacy of antipsychotic agents has been proven by many studies to be related to dopamine D2 receptor blockade. [19] All antipsychotic drugs used to treat schizophrenia work by blocking dopamine D2 receptors and their relative potency is affected directly by their affinity to these receptors. [20,21] Recent studies have proved a strong association between short-term response to treatment and striatal D2 occupancy where a clinical response was found to be achieved after at least 50% D2 receptor occupancy. [22,23] Although D2 receptor occupancy is a requirement for a proper response to antipsychotic treatment, it doesn't guarantee it. Wolkin et al. conducted a study to compare the striatal dopamine D2 receptor occupancy in both groups of treatment sensitive and treatment-resistant schizophrenia patients. There was no significant difference between both groups in terms of D2 receptor occupancy indicating that D2 receptor occupancy was not the reason for treatment resistance in TRS. [24] Some studies also showed that higher striatal dopamine synaptic levels resulted in improved response to antipsychotic treatment. [25] Some data suggest that individuals who respond to antipsychotic treatment may have higher [18F]-DOPA uptake, as measured by positron emission tomography (PET), when compared to those who do not respond to treatment. [25,26] Others also suggest that treatment-resistant individuals may have exceptionally hyperactive dopaminergic systems that can not be blocked efficiently by current antipsychotic agents. Demjaha et al. studied the dopamine synthesis capacity in TRS patients in comparison to normal schizophrenic patients. The dopamine synthesis capacity was found to be significantly lower in the treatment resistant group. The findings suggest that dopamine blockade, provided by antipsychotic, may be effective in patients exhibiting an elevation in dopamine synthesis capacity rather than those with normal dopamine synthesis, as in the case of the treatment-resistant group. [27]However, it is still unclear whether individuals with TRS have a different underlying neurobiology from the beginning or their dopamine synthesis capacity is affected by antipsychotics even though they do not respond to them. The aim of the treatment of schizophrenia is to reduce eliminate most of the symptoms, decrease the frequency and severity of psychotic exacerbations and improve the overall quality of life. Treatment of schizophrenia is based on a combination of pharmacological therapy, or antipsychotic drugs, and some psychosocial interventions. There are no differences in efficacy between all different antipsychotic drugs with the exception of clozapine. Evidence shows that clozapine is the only drug likely to be effective after two prior failures or in case of TRS. [28-30] Studies also suggest that clozapine may be superior to other antipsychotics in the treatment of non-resistant schizophrenia. [31-35]The patient compliance with oral medication in cases of schizophrenia has been a great concern, this led the practitioners to prescribe depot medication and avoid some potentially effective oral medication such as clozapine. [36]However, recent studies showed that re-hospitalization rates were higher in patients receiving depot medications than in those receiving clozapine. [37]This proves that medications that guarantee compliance may still have worse patient outcomes. Patient surveys also proved the practitioners' concern about patient refusal to

	receive treatment, due to tolerability issues or blood tests, to be unreasonable.[38-40]
Educational Needs	1. Increase awareness of the prevalence, high unmet need and the significant and wide-range burden of TRS 2. Present the clinical challenges and barriers in defining and diagnosing TRS 3. Examine the current guidelines and discuss the evidence-based recommendations for the management of TRS 4. Discuss the existing evidence supporting the distinct neurobiological hypotheses underlying TRS
Outcomes measures	The educational evaluation plan must be designed to objectively measure improvements in HCP knowledge and competence (Moore's Expanded Outcomes Level 4). Ideally, the evaluation plan will include quantitative and qualitative evidence that the intervention(s) has had an impact on health care professional behavior.
Funding Guide	• Multi or sole support. The budget should demonstrate fiscal responsibility and cost effectiveness. • Each budgetary item must be clearly delineated and be in line with fair market value(FMV) • Input from Lundbeck regarding selection of speaker(s) or the content of the program is not permissible • Lundbeck personnel cannot be utilized as speakers or consultants
Submission Guidelines	Please utilize the Lundbeck medical education grant portal at www.Lundbeckincgrants.com Please include RFP code **RFP-TRS-1901** in the activity title. Only eligible registered Lundbeck grant portal users who do not currently have any overdue outcomes data or financial reconciliations may submit a request in response to this RFP. Information on how to register can be found at www.Lundbeckincgrants.com. The education should offer credits for Psychiatrists, NPs, PAs. The education must be accredited by the appropriate accrediting bodies, be fully compliant with ACCME criteria and the Standards for Commercial Support and must be in accordance with the U.S. Food and Drug Administration's Guidance on Industry-Supported Scientific and Educational Activities. If accepted, must attest to the terms, conditions, and purposes of an educational grant as described in the Lundbeck letter of agreement.

Contact Information	Please email mededgrants@lundbeck.com or call 844-634-7867

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