TARGETS TO THERAPIES (T2T) PROGRAM: T2T VALIDATION CORE

PRE-PROPOSAL TEMPLATE

Please upload the pre-proposal template below (as a PDF) to your online application in the Grant Portal. Use a minimum 11-pt font, with a **2-page max length**. You may use bullet points and delete instructional text, but **keep headings in the left column**. Images, graphs, and references are optional to include and do not count toward the page limit.

Principal Investigator:
Institution/Company:
Project Title:

T2T TARGET(S):

☐ Autophagy Pathway ☐ GPNMB ☐ VPS35 ☐ CTSB ☐ GALC

VALIDATION GAP: Select target validation gap(s) this project aims to address.

- ❑ **Biology:** Define how target biology is altered in PD including cell type–specific and mutation-specific effects
- ❑ **Pathway/Mechanism:** Elucidate which components of the pathways are deficient or compensatory in PD, and establish mechanistic directionality of target modulation
- ❑ **Translational:** Establish links to idiopathic and genetically defined PD through biomarker development, patient stratification, and analysis of existing cohorts to validate target engagement and pathway-relevant readouts
- ❑ **Tools:** Develop and disseminate robust preclinical models, activity assays, reporters, tagged lines, and chemical/biologic probes to enable rigorous assessment of target function and pathway modulation across in vitro and in vivo systems

VALIDATION GAP(S)	Clearly define the target validation gap(s) this project aims to address.
EXPERIMENTAL PLAN	Provide a detailed validation plan, including a brief description of: • the models to be used (e.g., *in vitro*, *in vivo*, or *ex vivo* models, including patient-derived samples, add RRID# where known) • the key assays and techniques (e.g., biochemical, imaging, molecular, and functional assays) that will be employed to evaluate critical target endpoints such as target expression, function, and engagement. • the approach for data analysis, specifying statistical models (e.g., ANOVA, regression, Bayesian inference)

	• the use of controls and replicates to ensure data robustness and reproducibility.
OUTCOME	• Define the key milestone or inflection point this project aims to achieve and its impact on filling the validation gap(s). • Describe any resources that will be leveraged or generated along with their availability status.
PROGRAM SUPPORT	Identify areas where MJFF can provide support (e.g., expertise, model advice, generation of tools & reagents, or PD patient samples).
RISKS	Highlight the primary risks associated with the project and potential mitigation strategies.
TIMELINE	Provide an estimated timeline for project completion, including key milestones.
INTELLECTUAL PROPERTY	Describe any intellectual property considerations or restrictions (e.g., freedom-to-operate) that may impact data or resource sharing with the broader PD community.
BUDGET	Present a high-level budget estimate, including anticipated costs.