JOHNS HOPKINS
UNIVERSITY & MEDICINE

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LAB eN²
EVOTEC AND NOVO NORDISK
BRINGING ACADEMIC SCIENCE TO PATIENTS

Request for Pre-proposals

for

Novo Nordisk and Evotec LAB eN^2 – Johns Hopkins University Collaboration

1. Background

Johns Hopkins University has entered into a research collaboration with Novo Nordisk and Evotec called LAB eN^2 to accelerate the translation of academic discoveries into IND-ready candidates with the potential to improve patient care in cardio-metabolic diseases and rare blood disorders. The goal of the collaboration is to fund research at Johns Hopkins University facilitating the identification of new targets, disease biology insights and novel research tools for the treatment of cardio-metabolic diseases. Ideas for a proposed project should be submitted in a Project Concept Form to be considered for a full proposal application.

2. Awards

Successful proposals will receive funding of up to $1-4 million per project. All project related direct and indirect costs should be included in the budget.

All funded projects will have a Project Team established to review the progress. These proposals are for early-stage research projects and not applicable for clinical trials. Support will include funding and close collaboration with Novo Nordisk and Evotec experts during the design and execution of the project.

3. Research Areas of Interest

Diabetes

- **Insulin sensitization (muscle, liver, adipose and interorgan cross talk)**
- **Improving glucose homeostasis without risk of hypoglycaemia and weight gain**
- **Novel mechanism for glucose control with added benefit on weight and/or comorbidities**
- **Improvement of beta-cell health/function**
- **Next generation of incretin and amylin-based therapies**
- **Novel targets/pathways based on human centric approach (genetics, multiomics, clinical data)**
- **Strategies addressing immune-tolerance for type 1 diabetes**
- **Transformational insulin therapy e.g. glucose responsive insulin therapy**

Obesity

- **Energy intake**
  - **Homeostatic control of feeding circuits in the CNS, peripheral GI control of appetite/hunger including vagal afferent, nutrient/chemical sensing mechanism**
  - **Hedonic feeding and reward circuits to modulate feeding**
- **Energy expenditure**
  - **Mitochondrial biology including mitochondrial biogenesis and controlled uncoupling mechanism**
  - **Substrate futile cycling, hepatic lipid oxidation and fuel utilization**

        - Non-canonical thermogenesis pathways, such as selective sympathetic nervous system activation
    - Healthy weight management
        - Lean mass preservation: understanding of proteostasis (muscle proteolysis and autophagy), muscle hypertrophy, muscle fiber type switch
        - Anti-inflammation and oxidative stress
    - Body weight control
        - Counter-regulatory mechanism on weight regain, putative body weight setpoint control mechanism
        - Vascular dynamics in metabolic active tissues including fat and brain
        - Regulation of hormonal sensitivity (i.e. Leptin, ghrelin) in metabolic relevant tissues including adipose tissue, brain, skeletal muscle and liver

Chronic Diseases

- Cardiovascular disease (CVD)
    - Address unmet needs in ASCVD (tackle the residual risk left after standard of care by targeting inflammation, dyslipidemia, endothelial & smooth muscle biology), and heart failure (HFpEF, HFrEF, cardiomyopathies, and fibrosis)
    - Out-of-scope: anti-platelets/anti-coagulants & Stroke
- Chronic kidney disease (CKD)
    - Prioritized indications are cardio-renal-metabolic kidney diseases including diabetes- and obesity-related CKD, CKD with hypertension, CKD with heart failure
    - Mechanisms of interest include preserving vasculature and glomerular integrity, targeting metabolism and reducing inflammation as well as complement inhibition
- Metabolic dysfunction-associated steatohepatitis (MASH)
    - Fibrosis resolution/inhibition of fibrogenesis, suppression of chronic inflamaation, liver regenerative approaches. Non-invasive diagnostic biomarkers

Rare Diseases

- Rare renal
    - Primary Hyperoxaluria (PH)
- Hemobloginopathies
    - Beta-thalassemia
    - Sickle cell disease (SCD)
- Hemolytic anaemia
    - Rare anemias
    - Paroxysmal nocturnal hemoglobinuria (PNH)
    - Thrombotic thrombocytopenic purpura (TTP)
- Iron disorders
    - Hereditary haemochromatosis (Hh)
- Hemophilia
    - Hemophilia A(HA)
    - Hemophilia B (HB)

Technology Platforms

- Novel technology platforms for oligonucleotide or RNA-based therapies
- Formulation and drug delivery technologies; focus on oral delivery
- Intracellular tissue targeting (extra-hepatic) technologies
- Drug modalities, and new applications of known modalities, that can enable protein up- and down-regulation and gain-of-function – both of transient and permanent nature
- Approaches overcoming limitations of established drug modalities such as mitigating frequent dosing intervals, off-target effects and undesired immune stimulation

Modality Agnostic

- Small molecules
- Peptides
- Monoclonal and bispecific antibodies
- RNA & RNA targeted therapeutics
- Antibody Drug Conjugates
- Protein degraders and covalent drugs

- **Cell therapies**
- **Oligonucleotide therapeutics**

4. Examples of projects to be in scope

- **Target validation**
- **Screening and hit identification**
- **Medicinal chemistry**
- **Antibody development**
- **RNA and cell therapy**
- **Structural biology**
- **In vitro validation**
- **In vivo validation**

5. Eligibility

All JHU faculty (Assistant, Associate and Full Professors) are eligible to submit a pre-proposal.

6. Pre-proposal submission guidelines

Please use attached Project Concept Form Word document to submit your proposal ideas–include only non-confidential information and data in this form. The form is intended to be a short pre-proposal describing the proposed project at a high level.

7. Submission

Your pre-proposal should be submitted electronically to the JHU Alliance Manager, (Tom Ng, Ph.D., Director, Corporate Partnerships, Johns Hopkins Technology Ventures at tom.ng@jhu.edu). There is a rolling submission deadline. Prior to completing and submitting the Project Concept Form, the principal investigator should meet with Tom Ng to discuss the proposed project. Once the form has been submitted, Tom Ng will initiate discussions with the Novo Nordisk and Evotec leads to see if the proposed project concept is a good fit. If the pre-proposal is recommended for the next step, the principal investigator, in consultation with the JHU Alliance Manger (Tom Ng), Novo Nordisk and Evotec leads, will prepare and submit a full proposal application to the Funding Board for review and funding consideration.

8. Selection Process

Funding Board composed of Novo Nordisk and Evotec leaders will review the pre-proposal form. This process usually takes about 2 months. If the pre-proposal is selected then a full proposal in the form of a Discovery Award Application will be developed for review by the Funding Board. This review process usually takes about 3 months. Selected projects will be funded with a Discovery Award to reach key preclinical value-inflection points.

9. Intellectual property

Novo Nordisk has the option to in-license the project-related intellectual property (IP). If Novo Nordisk chooses not to in-license the project IP, Novo Nordisk, Evotec and the University may alternatively pursue the creation of a start-up company to further develop the technology.