Assessing Risk and Progression of Prediabetes and Type 2 Diabetes to Enable Disease Modification

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Need for public-private collaboration- I

- **The incidence of type 2 diabetes (T2D) is increasing at epidemic proportions**
  - Declining cellular health in T2D likely begins before glucose levels rise or diagnosis of disease
  - Current T2D therapies focus more on blood glucose control than on improving cellular health or modifying disease
  - Additional therapeutic approaches are needed to attenuate progression of the disease

- **Gaps exist to enable feasible and successful drug development of new therapies to restore cellular health and**
  - prevent progression of prediabetes to T2D or to
  - delay or prevent disease progression in individuals with T2D

Need for public-private collaboration- II

- More intensive phenotyping and molecular biomarker identification and validation is needed to select the individuals
  - at risk of rapid progression from prediabetes to T2D
  - at risk of rapid progression in T2D

- Identification and validation of robust markers is needed to characterize
  - function of insulin-producing beta- cells
  - cellular function of insulin action target cells such as hepatic, skeletal muscle and /or adipose tissue
  - patient segmentation for assessing new therapeutic options

- Collaboration and dialogue with regulatory and economic experts is needed to advance development of disease-modifying therapies to prevent or delay progression of T2D

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Pre-competitive nature

The scale of the problem is too large for individual researchers or companies to address alone. To address these challenges a pre-competitive research effort is needed including:

- Pharmaceutical company scientist experts in drug discovery
- Academic investigators with diabetes research experience
- Hospitals, clinical research centers, and practicing physicians with access to patients
- Patient donations of biofluids and tissue samples
- Biotechnology and diagnostics company expertise in assay development
- Regulatory authorities
- Health care payers and economists

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Objectives of the full project- I

Overall Aim: Discover and validate the molecular taxonomy of type 2 diabetes to enable

- Feasible patient segmentation
- Innovative clinical trial design
- Regulatory paths for diabetes prevention and / or modification of disease progression

- **Prioritize and validate a panel of human biomarkers (and assays) to identify patients at risk for**
  - rapid progression from prediabetes to Type 2 diabetes
  - rapid progression in Type 2 diabetes

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Objectives of the full project- II

- **Develop innovative potential regulatory approaches in collaboration with regulatory experts for**
  - therapeutic intervention in prediabetes to prevent or delay onset of type 2 diabetes
  - therapeutic interventions in type 2 diabetes for disease modification to reduce the rate of disease progression

- **Model short- and long-term economic and public health benefit/risk assessments for**
  - therapeutic intervention in prediabetes to prevent or delay onset of type 2 diabetes
  - therapeutic interventions in type 2 diabetes for disease modification to reduce the rate of disease progression

Expected impact on the R&D process

A successful project is expected to advance diabetes research and drug development by

- increasing knowledge of cellular and molecular phenotypes in the progression of prediabetes to diabetes and of disease progression within T2D
- discovering and validating biomarkers that enable patient segmentation of prediabetes and diabetes patients to expedite clinical trials of disease-modifying therapies in diabetes
- addressing gaps that restrict the development of new therapies for diabetes disease modification to improve public health

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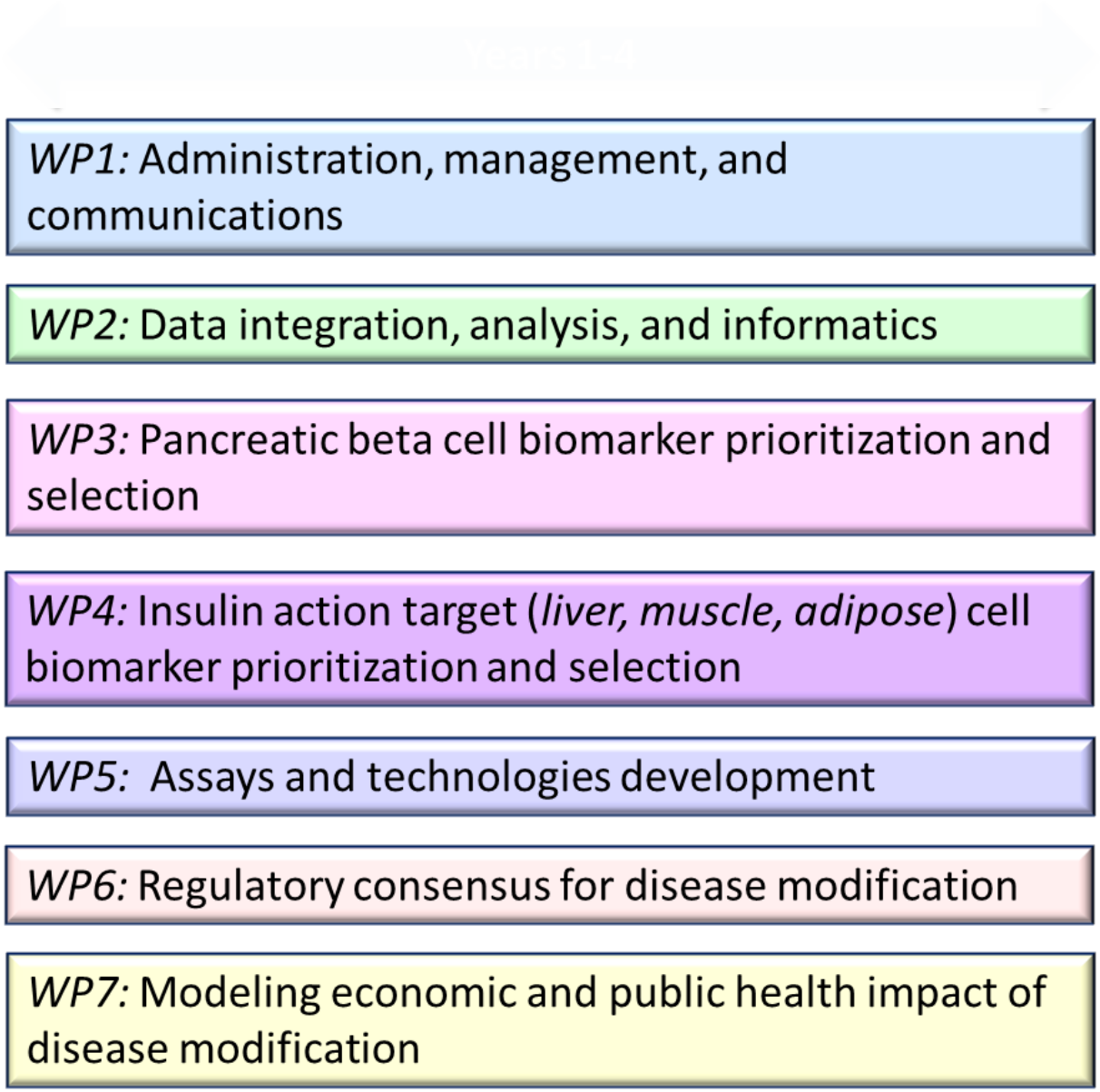
Suggested architecture of the project



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Expected contributions of the applicants

- Network of academic basic, translational, clinical research scientists with
  - *expertise in biomarker discovery and clinical assay implementation across the range of specified technologies*
  - *expertise in intensive clinical phenotyping of prediabetes and type 2 diabetes patients in retrospective and prospective longitudinal cohorts and biobanks*
  - *confirmed access to cohorts for biomarker discovery and validation*
- Experts with regulatory knowledge and experience
- Economic and public health modeling experts
- Professional project management organization

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Expected (in kind) contributions of EFPIA members

Participating pharmaceutical companies in the project:

Lilly (Project leader), Servier (Project Co-leader),

Janssen, Novo Nordisk, Sanofi

EFPIA companies will contribute expertise in

- diabetes drug discovery and development
- regulatory, economic, and logistical challenges for developing drugs for disease prevention or modification
- biomarker discovery and validation
- data analysis
- assay development and scaling
- prospective clinical trial design

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What's in it for you?

Participation in this project will enable

- academic researchers to access resources to advance diabetes research and drug development
- SMEs to contribute technical expertise to support diabetes research, project management, and diagnostics development
- regulators to influence development of new approaches for disease modification
- economic experts and payers to influence development of approaches to improve public health

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Key deliverables of the full project- I

- **Validation and/or discovery of human phenotypes and biomarker panels to enable prospective identification of "rapid progressors" from**
  - prediabetes to type 2 diabetes and
  - type 2 diabetes disease progression
- **Validation and/or discovery of human phenotypes and biomarker panels predictive of rapid declines in**
  - beta cell function
  - insulin action-targeted cellular function of hepatic, skeletal muscle, and/or adipose tissue

Key deliverables of the full project- II

- Development of new regulatory approaches or standards enabling innovative and feasible clinical trial designs for disease modification in patients with prediabetes or type 2 diabetes

- Models for public health benefit and economic impact of therapeutic intervention to prevent or delay progression from prediabetes to type 2 diabetes

Questions?

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