Strategic Governing Group
Diabetes / Metabolic Disorders

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

Bernd Stowasser, PhD, MS,
Associate Vice President, Head of European Public Private Partnerships Office
Sanofi R&D – Strategy, Science Policy & External Innovation
on behalf of the SGG Diabetes / Metabolic Disorders
AbbVie, Astra-Zeneca, Boehringer Ingelheim, GSK,
Janssen, Lilly, MSD, Novartis, Novo Nordisk, Pfizer, Sanofi,
Servier

efpia imi2

Background

Strategic Governing Group
Diabetes / Metabolic Disorders

- **Problem**
  - 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 altering the course of the disease
  - Gaps exist to improve feasibility of drug development to restore cellular health and
    - Prevent progression of prediabetes to T2D or to
    - Delay or prevent disease progression in individuals with T2D

Need

Strategic Governing Group
Diabetes / Metabolic Disorders

- Robust approaches are needed to select the individuals most in need of and most likely to benefit from new potential disease-modifying therapies for clinical trials.

- Validated biomarkers and diagnostic assays are needed to identify individuals with rapidly declining health of cells that function in maintaining blood glucose levels, including insulin-producing pancreatic beta cells and glucose-metabolizing liver, muscle, and fat cells.

- Innovative clinical trial designs are needed to improve the feasibility of drug development for disease-modifying therapies in prediabetes and diabetes.

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

Overall Objectives

Strategic Governing Group
Diabetes / Metabolic Disorders

Prioritize and /or validate biomarkers (and assays):

To enable prospective selection of subjects with rapid progression from prediabetes to type 2 diabetes and type 2 diabetes subjects with accelerating type 2 diabetes disease progression prioritize and/or validate panels of human biomarkers or assays of

- **pancreatic beta cell stress, function, mass, and death** (validation and discovery components)
- **impaired hepatic, skeletal muscle, and/or adipose cellular functions contributing to progression of insulin resistance** (validation and discovery components)

Develop innovative potential regulatory approaches

In collaboration with regulatory experts, including adaptive clinical trial designs, enabling feasible and robust benefit/risk assessments in clinical trials 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

Overall key deliverables

Strategic Governing Group
Diabetes / Metabolic Disorders

Validation and/or discovery of human phenotypes and biomarker panels predictive of rapid declines in

- Pancreatic beta cell health and function
- Insulin action-targeted hepatic, skeletal muscle, and/or adipose cellular functions

to enable prospective identification of a) "rapid progressors" from prediabetes to type 2 diabetes and *b)* accelerating type 2 diabetes disease progression for patient identification for clinical trial recruitment or therapeutic intervention

Prioritization and selection of robust phenotypes and biomarker panels that enable feasible prospective patient segmentation/selection, clinical trial design and regulatory paths to assess new therapeutic options for

- Prevention of progression from prediabetes to type 2 diabetes and
- Prevention of acceleration of type 2 diabetes disease progression

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

Benefit/risk models for public health and economic impact of therapeutic intervention to prevent or delay progression from prediabetes to type 2 diabetes

Applicant Consortium

Strategic Governing Group
Diabetes / Metabolic Disorders

- Network of academic basic, translational, clinical research scientists with expertise in
  - biomarker discovery across the range of specified technologies,
  - human pancreatic beta cell, hepatic, muscle, and adipose biology
  - conducting intensive clinical phenotyping of prediabetes and type 2 diabetes patients

- Investigators with expertise in and ability to leverage existing retrospective cohorts and collaborations with ongoing studies of individuals with prediabetes and with type 2 diabetes
  - including clinical phenotype data, biomarker data, longitudinal outcomes data and available biobank biofluids and/or tissues

Suggested project structure

Strategic Governing Group
Diabetes / Metabolic Disorders

WP1: Administration, management, and communications

WP2: Data integration, analysis, and informatics

WP3: Pancreatic beta cell biomarker prioritization and selection

WP4: Insulin action target (*liver, muscle, adipose*) cell biomarker prioritization and selection

WP5: Assays and technologies development

WP6: Regulatory consensus for disease modification

WP7: Modeling economic and public health impact of disease modification

Further details and timelines

Strategic Governing Group
Diabetes / Metabolic Disorders

- Indicative project duration: 4 years

- Anticipated Timelines:
  - Currently in consultation process with IMI stakeholders
  - 7th October 2014: Publication of indicative topic text on IMI Website
  - 12th Dec 2014: Launch of call
  - 24th March 2015: Deadline for submission of Expression of Interest