Innovative Medicines Initiative

DIRECT
Diabetes Treatment Gets Personal

IMI and personalised medicine –
20 March 2013 – Dublin, Ireland

Bernd Jablonka, Ewan Pearson, Hartmut Rütten,
Bernd Stowasser

Challenges of Diabetes Treatment

- **Novel therapeutic approaches**
  - **Novel targets for the treatment of diabetes**
    - Identification of novel genes or cellular pathways that are involved in pancreatic beat-cell regeneration / degeneration, proliferation / apoptosis and demise
  - **Reliable probes for in vivo imaging of beta-cells**
    - Assessment of beta-cell function, mass and disease progression, treatment response

- **Individual therapy of diabetes patients (personalized medicines approach)**
  - **Prediction of disease progression and treatment response**
    - Identification of biomarkers that are predictive for progression of glycaemic deterioration in pre-diabetes patients or patients with early onset of diabetes
    - Identification of biomarkers that are predictive of treatment response to current standard therapies

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DIABETES RESEARCH ON PATIENT STRATIFICATION

- **Prediction of cardio-vascular risk of diabetes patients**
  - Identification of biomarkers that are predictive for the development of diabetic macro- and micro-vascular complications

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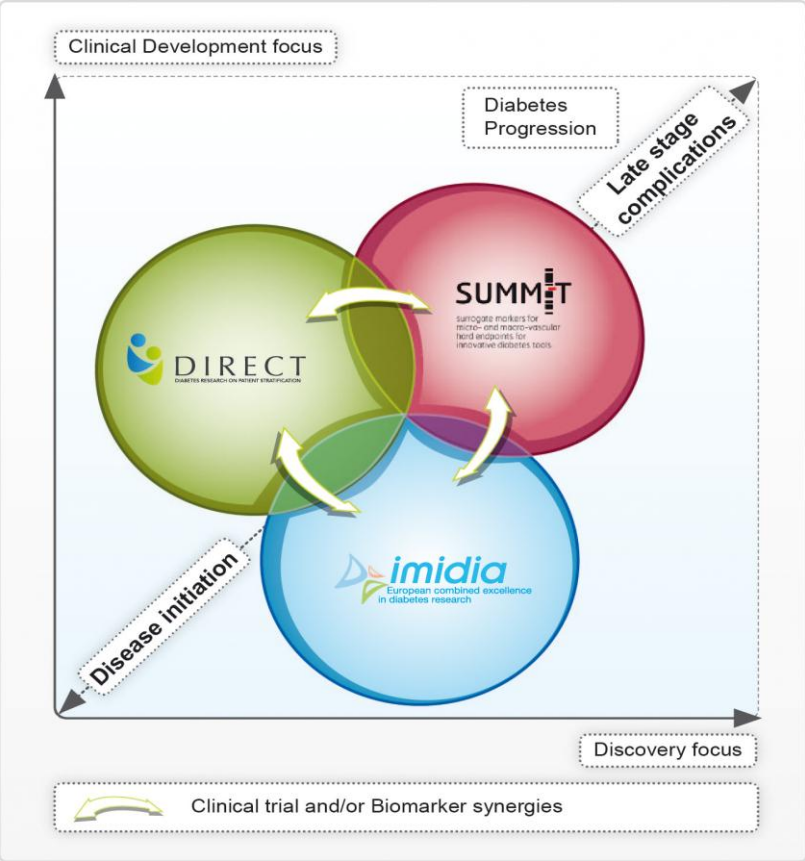
The IMI* Diabetes Platform



IMIDIA – DIRECT – SUMMIT:

3 DIABETES PROJECTS

bringing together experts from academia, industry and biotech to generate novel approaches for diabetes research and treatment in a unique European Public-Private-Partnership (PPP)

* Innovative Medicines Initiative – Joint Undertaking: a Public-Private-Partnership between the European Commission (EC) and the efpia European Federation of Pharmaceutical Industries and Associations (EFPIA)

Novel Treatment Strategies in Diabetes

Current treatment of diabetes

- No estimation of diabetes onset is possible in high-risk pre-diabetes patients
- No prediction of disease progression is applicable in patients with early onset of diabetes
- First line therapy for Type 2 Diabetes (T2D) patients is metformin or sulfonylureas for all
- Substitution therapy with insulins
- Second line therapy with GLP-1 receptor agonists

Need for novel prediction and treatment strategies to

- classify high-risk pre-diabetes patients, who will develop diabetes as early as possible
- improve control of diabetes development and disease progression
- identify individual therapy options immediately after onset of diabetes
- avoid non-response to diabetes therapy or treatment intolerance

PPP for Personalized Medicines in Type 2 Diabetes (T2D)

Scientific contributions of DIRECT participants to the consortium

- Availability of large cohorts of T2D patients from academic partners
- Use of improved risk prediction models for high-risk pre-diabetes patients and patients with early onset of diabetes
- Access to “omics” labs of leading European academic experts for the analysis of patient samples
- Development of joint database and installation of analysis server accessible to all participants
- Provision of Pharma expertise in the preparation and conduct of clinical validation studies

Unique opportunities of the consortium

- to elucidate mechanisms of glycaemic deterioration and treatment response to current standard therapies in T2D patients
- to identify novel biomarkers predictive for disease progression and treatment response
- to validate biomarker candidates in clinical study(ies)
- to develop selective treatment options of T2D in a personalized medicines approach
- to establish diabetes network among scientists and between Academia and Pharma across Europe

Rationale for the implementation of DIRECT as PPP

- Each single participant cannot undertake this holistic approach alone
- Close collaboration between expert institutes for diabetes research and clinical development is required to achieve the ambitious goals of the consortium

Concept and Goals

For further information see: www.direct-diabetes.org

The DIRECT consortium is working towards developing a personalized medicines approach for the treatment of type 2 diabetes with existing or novel therapies

- **The scientific program of the consortium aims at delivering:**

  <u>Part 1 of the project (years 1-4)</u>

  - **Complete phenotyping of**
    - **extreme phenotypes of patients with rapid and slow glycaemic deterioration**
    - **extreme glycaemic response to therapeutic intervention**
      - **in already well-characterized subjects from large cohorts available throughout Europe**
  - **Identification of**
    - **biomarker for subtypes with rapid diabetes development and progression**
    - **biomarkers for altered response to diabetes treatments**
      - **based on transcriptional and functional genomics, proteomics, lipidomics and metabolomics analyses of patient plasma samples**
    - **surrogate response biomarkers that reflect the underlying disease progression**

Concept and Goals

For further information see: www.direct-diabetes.org

Part 2 of the project (years 5-7)

– **Validation of biomarker candidates as surrogate response markers in**

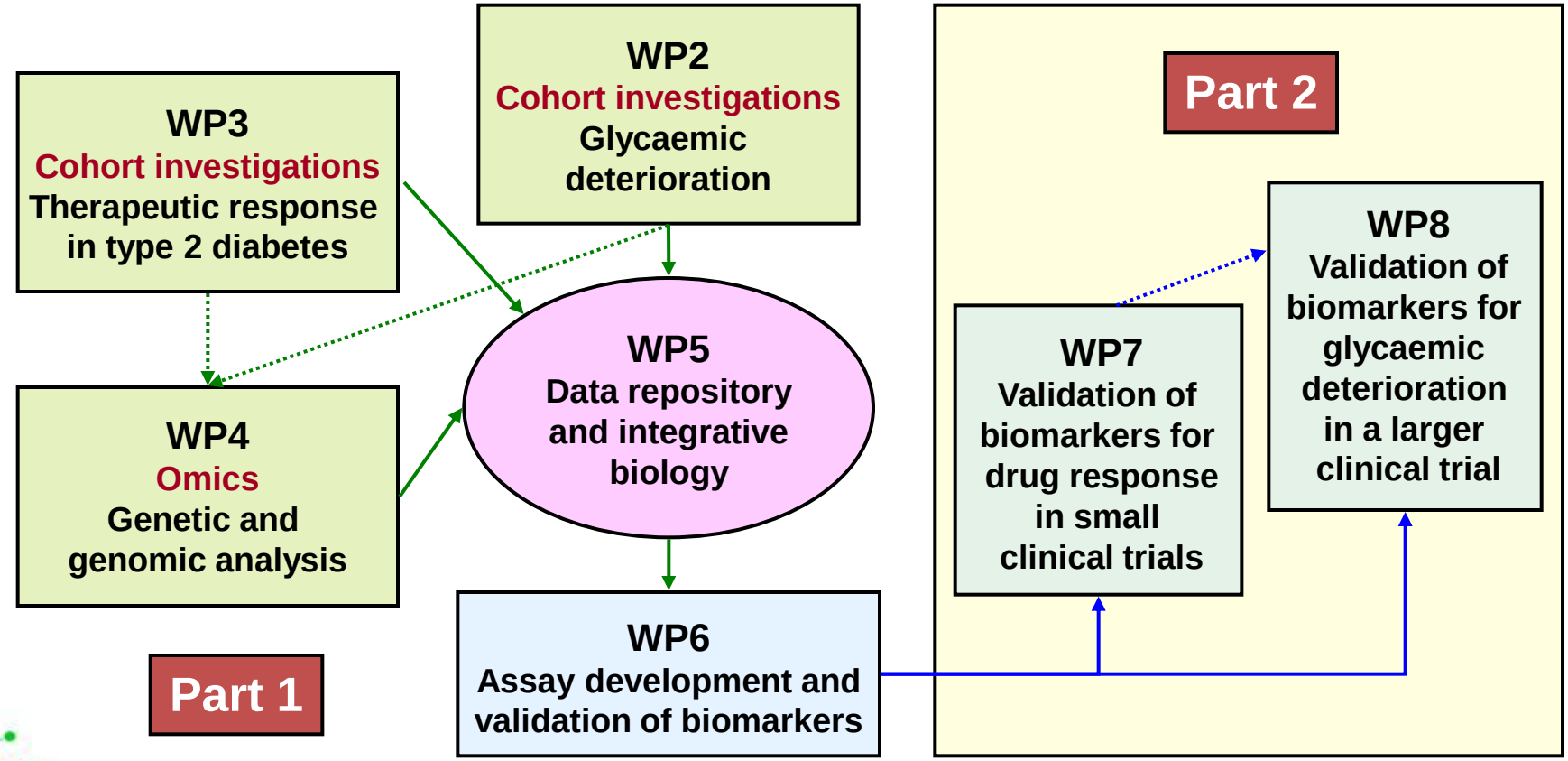
- **a large intervention trial for the delay progression of diabetes or pre-diabetes**

Or

- **smaller trials for therapeutic response**

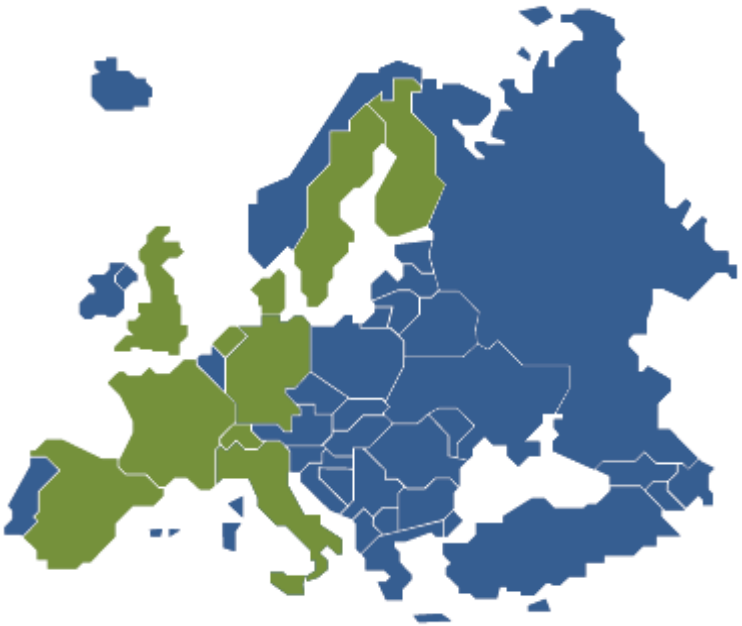
Organisation of Project Activities

The DIRECT consortium is organized as a highly integrative and synergistic structure dividing the project into seven interacting work packages as described below



Participants and Participating EU Countries

Sanofi-Aventis Deutschland GmbH (Coordinator)
Eli Lilly (Co-coordinator)
University of Dundee (Academic Lead)



The IMI diabetes project DIRECT was launched on February 01, 2012

University of Bath
Consiglio Nazionale delle Ricerche
Technical University of Denmark
Eberhard Karls Universitaet Tuebingen
Helmholtz Zentrum München – Deutsches Forschungszentrum für Gesundheit u. Umwelt GmbH
Consorci Institut D'Investigacions Biomediques August Pi i Sunyer
Imperial College London
Kungliga Tekniska Högskolan
University of Lille- CNRS
Leiden University Medical Center
University of Copenhagen
University of Eastern Finland
Lunds Universitet
University of Newcastle upon Tyne
University of Exeter
Université de Genève
University of Oxford
Universitaet Ulm
VU University Medical Center
Novo Nordisk A/S
Servier
Lille University Hospital

Deliverable Timelines

Part 1

- **Start of patient recruitment:** **PY1 (2012)**
- **Availability of baseline data:** **PY3 (2014)**
- **Selection of "extremes" for follow-up:** **PY3 (2014)**
- **Availability of follow-up data:** **PY4 (2015)**
- **Selection of biomarker candidates predictive for glycaemic deterioration and treatment response:** **PY5 (2016)**

Part 2

- **Start of clinical validation study(ies):** **PY5 (2016)**
- **Completion of biomarker assay development and up-scaling:** **PY6 (2017)**
- **Availability of clinical validation data:** **PY7 (2018)**

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Budget and Funding

No. of participants: 25

- 21 Academia and 4 EFPIA participants

- **Dedicated resources from EFPIA partners: 16.5 mio. €**
- **Dedicated resources from public and SME* partners: 26.6 mio. €**
- **Total project budget: 43.1 mio. €**
- **IMI funding to public and SME partners: 21.5 mio. €**

Project duration: 7 years

*** Small to Medium Enterprises**

efpia

Benefit of personalized medicines for the T2D patient

- Early classification of high-risk, pre-diabetes patients for development of T2D
- Improved prognosis of glycaemic deterioration after onset of T2D
- Individual therapy after T2D diagnosis
- Better control of blood glucose levels
- Less side effects
- Less cost for society

→Can only be achieved through large collaboration among public and private partners across borders and institutions

On behalf of the DIRECT Consortium

Thank you for your attention !