AN INTERNATIONAL PARTNERSHIP
TO ARREST TYPE 1 DIABETES

# INNODIA RESEARCH

## OVERVIEW INNODIA

Despite significant progress in preclinical type 1 diabetes research the important findings from in vitro models and animal studies could not yet be translated into novel and effective clinical interventions with earlier diagnosis and effective treatments to prevent development and progression of type 1 diabetes.

INNODIA is an international consortium of:

**24 ACADEMIC**
**INSTITUTIONS AND CLINICS**

**4 EFPIA**
**PARTNERS**

**2 PATIENT**
**ORGANIZATIONS**

**1 SMALL**
**& MEDIUM SIZED ENTERPRISE**

with the ambition to significantly improve our understanding of type 1 Diabetes and to pave the way to novel therapeutic options to prevent and cure this devastating disease.

# THE OVERALL OBJECTIVE OF INNODIA

The overall objective of INNODIA therefore is to advance in a decisive way how we predict, evaluate and prevent the onset and progression of type 1 diabetes (T1D), by creating novel tools, such as biomarkers, disease models and clinical trial paradigms. These tools will allow to distinguish and understand at the cellular and molecular level distinctive paths of ontogeny and progression in this heterogeneous disease, thus impacting on the future management of T1D patients and at risk individuals. For this goal, INNODIA will establish a comprehensive and interdisciplinary network of clinical and basic scientists, who are leading experts in the field of T1D research in Europe, with complementary expertise from the areas of immunology, beta□cell biology and biomarker research. The consortium will interact in a coordinated fashion with all major stakeholders in the process, in particular regulatory bodies and patients with T1D and their families.

## THE OBJECTIVES

1. Develop a European infrastructure for the recruitment, detailed clinical phenotyping and bio-sampling of a large cohort of newly diagnosed subjects with T1D and at risk family members.

2. Establish a tight collaborative network of basic and clinical researchers working in a coordinated and focused way to address key knowledge gaps in relation to b□cell autoimmunity, leading to a better understanding of the pathogenesis of T1D and a cure for this disease.

3. Advance the development and application of novel methodologies by exploiting our major strengths in bioresource and 'omics' technologies

4. Establish a unique integrated database assimilating historical data, with data from clinical and experimental sources. This will permit visualization and modelling of interactions between phenotype, genetic, immune and metabolic pathways to explore subtypes, potentially redefining ontogeny of T1D in the context of prevention and intervention strategies.

5. Conceive innovative clinical trial designs that exploit novel validated biomarkers allowing better subject stratification and functioning as surrogate endpoints, thus yielding shorter and more focused intervention studies of single or combined therapies.

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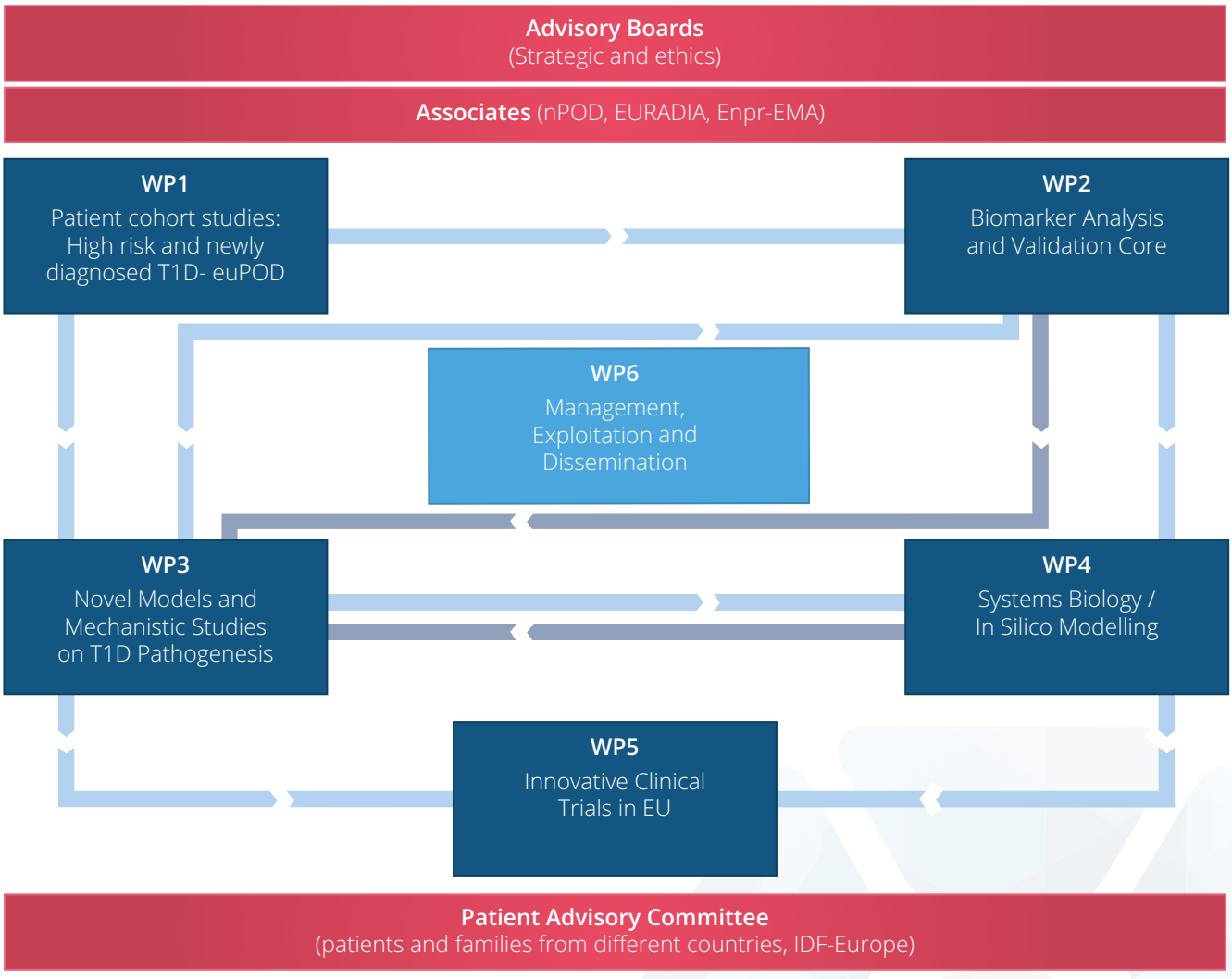
# SCIENTIFIC WORKPACKAGES

INNODIA is organized into 6 Work Packages (WP´s) focusing on distinct topics with a dedicated governance structure ensuring close interaction, communication and adherence to the objectives and deliverables of the consortium.



# WP1

WP1 creates a clinical infrastructure to enable studies of the relationship between changes in β-cell function, immune profiles, genetic and environmental factors in new onset T1D patients and subjects at risk. The workpackage will deliver standardized collections of clinically and scientifically relevant biological samples from very large populations of new onset T1D patients and at risk subjects.

## KEY OBJECTIVES OF WP1

- Capitalize on the access of clinical partners in INNODIA to large populations of new onset T1D patients and high-risk subjects through registers and national collaborations to develop a new European clinical research network
- Establish standardized procedures for patient eligibility, recruitment and sample collection, sample preparation, transport and storage
- Develop standardized protocols based on repeated measures of C-peptide (including home measurements) and comprehensive collection of appropriate biological samples for 'omics', immune, viral and microbiome studies in new onset T1D patients and high-risk subjects
- Exploit the access of clinical partners to historical cohorts to model declines in β-cell function and validate biomarkers through long-term follow up of auto Ab-positive subjects
- Establish a European tissue-biobank, based on the successful JDRF-nPOD initiative, providing access to unique pancreatic and tissues samples from T1D patients, at risk subjects, T2D patients, and control subjects.

# WP2

WP2 focuses on performing multi-dimensional analyses of T1D phenotypes and relate these singly or via integration to clinical outcomes and progression (WP4), with the intention of facilitating biomarker discovery (collaboration with WP3), surrogate marker development and patient stratification, and a better understanding of disease heterogeneity.

## KEY OBJECTIVES OF WP2

- Develop modular interrogation platforms for imaging and analysis of cellular and molecular features of T1D as they relate to the β-cell and immune cell genomes, proteomes, lipidomes and metabolomes
- Apply and integrate module datasets to T1D clinical groupings (adults/children with T1D and high-risk groups) in test and validation bio-sample sets
- Develop a systematic approach to biomarker discovery with validation of new predictive algorithms and stratifiers, new surrogates, better understanding of the molecular and cellular basis of heterogeneity and better insights into pathogenesis pathways

# WP3

WP3 will focus on the discovery of novel and better ways to model and monitor the disease process and to evaluate the effect of new therapies under well-controlled experimental conditions. For this purpose, WP3 will use as discovery and validation tools in particular primary human tissues (e.g. human islets and immune cells); human cell lines; and humanized mouse models. Novel approaches proposed in WP3 should allow progress of our understanding of the natural history of T1D, fast translation of novel therapies from the bench to the bedside, and mechanistic explanations as to why new disease-modifying therapies in T1D succeed or fail.

## KEY OBJECTIVES OF WP3

- Discover and validate in pre-clinical models biomarkers and imaging techniques to assess β-cell loss in diabetes and the outcome of novel therapies
- Elucidate the interplay between β-cells and the immune system, both innate and adaptive, in order to develop novel approaches to prevent/revert the disease
- Gain better understanding of the heterogeneous pathogenesis of human T1D through humanized models of disease, use of iPS-derived β-cells (with or without modification of selected diabetes candidate genes), human islets and immune cells, and novel human cell lines
- Test new approaches to prevent or cure human T1D in pre-clinical models

# WP4

WP4 supports the overarching aims of INNODIA relating to data management and development of integrative algorithmic approaches for prediction and discovery. WP4 algorithms will predict and evaluate the progression of T1D by combining and integrating data derived from other WPs via their multidisciplinary approaches to molecular genetics and functional genomics, cellular and molecular biology, proteomics, immunology, metabolomics, and β-cell biology together with the clinical phenotyping of subjects. WP4 will create the data management infrastructure supporting analysis of individual data types as well as integrative analyses working across readouts in a way that will be compatible with the data capture models adopted in other WPs.

## KEY OBJECTIVES OF WP4

- Establish and run the secure data-warehouse environment and server framework for management of INNODIA relevant data
- Include historical data from INNODIA partners in the data integration and include relevant publicly available T1D data and other data sets, e.g. electronic patient records and registry data sets which uncover comorbidity spectra quantitatively
- Construct tools for integrative analysis of data derived from the other work packages
- In silico modelling aiming at differential analysis of different disease pathways, e.g. slow/fast C-peptide decline and markers for heterogeneity in patients
- Identify biomarkers and biomarker signatures allowing for prediction of disease risk and progression as well as treatment responsiveness
- Cyclic iteration of the identified signatures with the other WPs for validation and implementation of innovative trial designs (WP5)

# WP5

WP5 is aiming to establish a step change in the way to evaluate novel therapeutics for newly diagnosed patients with T1D and those at risk for T1D. It will establish an EU clinical trials network, develop novel trial design models and evaluate of utility of surrogate biomarkers to accelerate clinical trial performance in T1D, moving towards prevention or cure of the disease. These strategies will be developed through an early and close engagement between the INNODIA partners (academic and industry) and stakeholders, in particular regulators and patients.

## KEY OBJECTIVES OF WP5

- Develop, qualify and accredit a collaborative clinical trial network in close relationship with regulators
- Design shorter, more efficient ways of evaluating dose, dose interval and early efficacy in new onset T1D patients and at risk subjects by developing innovative response adaptive clinical trial designs
- Produce statistical computer code that will automate interim analyses for adaptive decision making
- Develop trial designs allowing evaluation of combination therapies and the handling of stratification by biomarkers in close relationship with the regulators
- Perform at least one innovative phase II clinical trial within the accredited European paediatric and adult clinical INNODIA trial network

# WP6

WP6 provides project Management to effectively manage the INNODIA consortium and provide governance direction to the project. It supports the dissemination and exploitation of INNODIA results and is responsible for the interaction with internal and external stakeholders and implementing all management procedures required for the successful implementation and execution of the of the INNODIA workplan.

## KEY OBJECTIVES OF WP6

- Ensure efficient coordination of INNODIA
- Deliver reports on scientific, technological and financial progress as required by IMI JU and IMI legal framework
- Ensure proper execution of the contractual duties of the consortium
- Design and implement publication policies and dissemination plans
- Organize and implement the external INNODIA communication strategy, with all stakeholders i.e. patient organizations and regulators
- Ensure management of ethical issues
- Oversee and monitor project risks and propose corrective actions if needed

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# PATIENT ADVISORY COMMITEE

A clear priority of INNODIA is to keep the needs and concerns of patients with Type 1 Diabetes at the center of the project. The involvement of patients is organized by a Patient Advisory Committee.

The Patient Advisory Committee (PAC) will give voice to the experiences, opinions and desires of the patients and their relatives to help ensure that INNODIA's goals and strategy are closely aligned with the goals of people living with, and affected by Type 1 Diabetes (T1D). By bringing a powerful patient and family perspective to INNODIA, the PAC will help ensure INNODIA will deliver a patient-centric approach and specific outcomes with the potential to improve the lives of people with T1D.

Newly diagnosed type 1 diabetic patients and their relatives are encouraged to participate in this study by taking contact with one of our Clinical Centers throughout Europe. If you like to take part in this initiative, please consult our map to select a Center most nearby and complete the registration form so we can contact you.

# SPECIFIC ACTIVITIES

We (the PAC) will advise the Management Board of INNODIA, providing input in a number of areas including informed consent, clinical protocols review and relationships with regulatory authorities and patient organisations who are interested in the INNODIA project.

We will also help communicate results to a wider public throughout the duration of this 7 year project. Above all, the members of this committee will act as T1D ambassadors within INNODIA helping retain focus on what matters most: people living with this disease every day of their lives.. The PAC will work with the T1D community, taking their views into consideration for INNODIA.

Through INNODIA's scientific network, we have the chance to connect with more than 15 European countries and the possibility to connect with patients from these countries.

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# THE MEMBERS OF THE PATIENT ADVISORY COMMITTEE

**Johan Keurentjes (1967)**
I was diagnosed with T1D at the age of 11. I live in Bussum, The Netherlands and I am married and the father of two sons and a daughter. I am a director and co-owner of an e-commerce agency and I have completed 9 marathons.

**Kyle Jacques Rose**
I was diagnosed at the age of 16. I live in Aix-les-Bains, France in the foothills of the Alps. An engineer by training, I am now a specialised consultant in healthcare. My work involves the promotion of sport and healthy lifestyles leaning on my prior experience as a pro athlete. I am a big believer in new treatment/ technology and was very excited to experience a closed-loop Artificial Pancreas trial in Montpellier France!

**Anders Kristensen**
I was diagnosed with type 1 diabetes at the age of one. I live in Copenhagen, Denmark where I am studying and enjoy doing sports, both of which is often affected by my disease. I believe no one deserves to live with this disease, and find it important actively advocate for research into better treatments and ultimately a cure for type 1 diabetes. I have spoken about this at several occasions, among others at the JDRF Children's Congress in 2013, and finally I was the keynote speaker at the IMI Stakeholder Forum 2015.

**Olivier Arnaud (1955)**
I am not personally diabetic but really concerned by young children and adults in my close family and friend circle having type 1 diabetes. I share with them their stressful life and the hope for having a cure. I am proud to work for JDRF Research that I am representing in Europe and help in their vision of having a "world without T1D".

**Jaivir Pall (1994)**
I was diagnosed at the age of 4. Since a young age I have had an interest in supporting people living with diabetes like me! I now work in the national health service in Brighton, UK but support services across the UK. I believe strongly in Europeun collaboration and sharing our learning leading me to work on a project called diabetes youth advocates europe and learning from young people with diabetes from across Europe. I have swim, run, dived, flown and driven in support of diabetes research (not all at the same time!!).

**Markku Saraheimo**
I was diagnosed with T1D at the age of 7. I live in Helsinki in Finland. My wife has had her T1DM since the age of 14 and my first daughter got her diabetes at the age of 2. I´m working as a diabetologist/ researcher in Helsinki City Hospital /Helsinki University Voluntary work in Finnish Diabetes Association has been part of my life over 30 years.

**Nathalie Istas (1977)**
I was diagnosed with T1D at the age of 2. I live in Belgium, near to Brussels. I am married and a proud mother of two children. For several years, I was Benelux trainer in an American corporation, but 8 years ago, I decided to be more present at home and left business to become a teacher. I am a very dynamic, enthusiast and strong person who loves new challenges, like being part of this project. I believe new ideas can emerge out of this European collaboration. The phrase "a world without T1D" sounds like music in my ears, but in the meantime it is my goal to live my life as normal as possible with this desease.

**Dries Van Herzele (1976)**
I live in Linden, Belgium and I am married and the father of three sons and a daughter. Unfortunately, my daughter was diagnosed with T1D in 2013 on the age of 11 and as parents we follow her closely.