Background-Type 1 Diabetes Consortium (T1DC)

• Issue/Need statement: Currently no therapies are approved for the delay or prevention of type 1 diabetes (T1D)

• Solution: Qualification with FDA and EMA of islet autoantibodies (AAs) as enrichment biomarkers for use in T1D prevention clinical trials to enable proper patient selection in clinical investigations of earlier interventions in T1D, allowing:
  • Sponsors of drug development programs to have confidence incorporating biomarkers into their trial designs
  • Regulatory authorities to have confidence relying on biomarkers during their review process
  • Aid the development of therapies and the design of clinical trials to delay and ultimately prevent clinical diagnosis

• Goal of T1DC:
  • Develop a model from patient-level data that will quantitatively describe the relationship of the islet AAs and other relevant patient features to the probability of a T1D diagnosis during the course of T1D prevention clinical trials
  • Qualify the islet AAs as enrichment biomarkers to identify subpopulations at highest risk of a T1D diagnosis in T1D prevention trials
## Background-T1DC membership

T1DC is a public-private-partnership currently composed of the following Industry and Foundation Members, Academics, and Observers/Advisors:

- Janssen
- JDRF
- Helmsley Trust
- Novo Nordisk
- Provention Bio
- Benaroya Research Institute
- Helmholtz Zentrum München
- Lund University, Sweden
- University of Bristol
- University of Colorado Denver
- University of Florida
- University of Helsinki
- University of Leuven
- University of Munich
- University of Oulu
- University of Tampere
- University of Turku
- FDA
- NIH
- INNODIA
Autoantibodies are the Foundation for Staging\(^1\) of Presymptomatic T1D

\[^1\text{Diabetes Care 2015 Oct; 38(10): 1964-1974}\]

But we are running trials today using autoantibodies...

- Provide valuable information to reduce uncertainty in regulatory decisions
  - Approving an investigatory trial that will expose even a few hundred people to risk is a very different proposition for regulators than approving a drug that will possibly be used in tens of thousands for years to come
  - It is vital that, when we can, we provide regulators with the body of evidence that removes uncertainty for them, particularly when considering medicines for children

- Enable the FDA/EMA as partners
  - The regulators want to enable progress and desire to be in the best possible position to help all of us achieve that for patients
  - Providing the regulators with data in the form that they need enables a deeper understanding of the disease and greater confidence that new medicines will have appropriate risk: benefit
  - A qualified biomarker can serve as the foundation upon which future biomarkers may stand
Challenges/Considerations for Qualification

- Three biggest challenges are data, data, and data
  - Who has it?
  - What does it take to get it?
  - How fit for purpose is it (appropriate, complete, validated?)

- Precision in the Context of Use Statement
  - Understand what the data can support and don’t overreach
  - Keep the long goal in mind
  - Make it as easy as possible for the regulators to agree to qualification

- Keep focused on implementation

- Qualification is the main goal, but there are other benefits
  - Deeper understanding of disease “subtypes”
  - Tools that can aid in clinical development/trial planning
Value to Stakeholders

Endorsed model supporting the islet AAs as enrichment biomarkers for T1D = Drug Development Tool (DDT) that can be used with confidence

- **Patients:**
  - Catalyze risk screening, reduce DKA hospitalizations and means of reimbursement
  - Development of therapies that may delay or ultimately prevent beta cell loss

- **Industry:**
  - Identification of a patient-pool of known trajectory for inclusion in prevention studies
  - Quantitative benefit risk analysis for outcomes assessment and trial duration
  - Knowledge that the regulatory agencies are familiar with and utilizing the same tool

- **Academics:**
  - Translation of the scientific research into drug development
  - Enables the translation of cutting-edge research by providing a regulatory benchmark
  - Integrated database can provide a means for further investigations

- **Regulatory Agencies:**
  - Vetted and approved disease progression tool in T1D for evaluation of sponsor trial data
“The patients are waiting...”
- Paul Janssen

Thank You