JDRF typeone nationsummit

IMPROVING LIVES. CURING TYPE 1 DIABETES. T1D

T1D Clinical Research

MCW

LEARN. LIVE. CARE. CURE.

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Assistant Professor of Pediatrics
Medical College of Wisconsin
May 6, 2017

Children's Hospital of Wisconsin

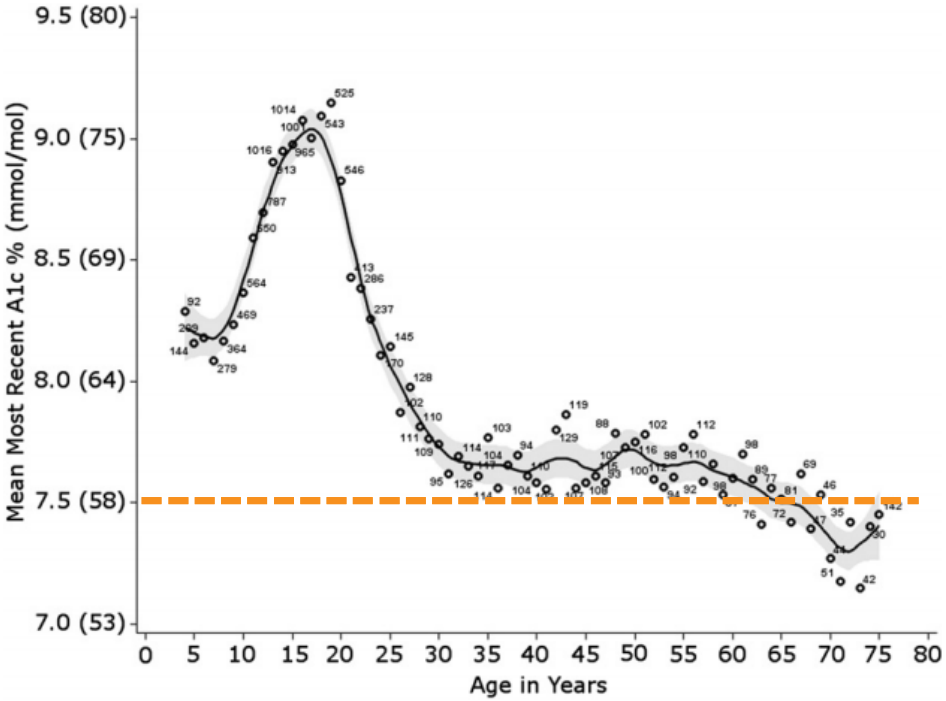
Kids deserve the best.

Why we need children and teens to participate in research

- Laboratory rats and mice are a great starting place, but they only get us so far!
- T1D is predominantly diagnosed in childhood, not adulthood
  - Typically, clinical trials occur in adults first so kids can be protected from the risks of new therapies
  - This delays getting therapies to children
  - Children have faster progression than adults, suggesting different disease processes
  - **Children are not little adults!**
    - What works in adults may not work in children and vice versa
    - Teenagers present their own unique challenges
- Research informs every single aspect of our ability to take care of your children!

There are an abundance of areas to study and improve

- The incidence of T1D is steadily increasing by 2-3% per year, especially in the youngest children
- T1D technologies and care have continued to advance but glycemic targets are rarely met
- 30-40% of people present with DKA at clinical diagnosis



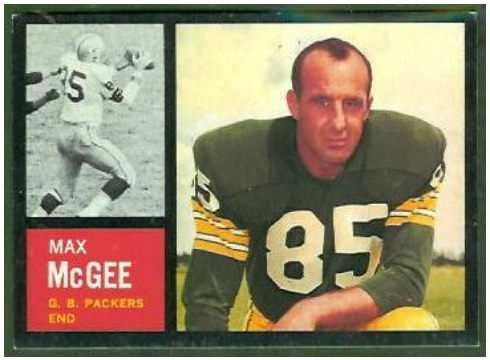
Basic tenets of clinical trials

- First, do no harm
  - All research proposals are rigorously scrutinized by Internal Review Boards (IRBs) and Drug Safety Monitoring Boards to make sure subjects are protected, all risks are being addressed, there is no coercion to participate, and that potential benefits exceed any risks
- Research participation is 100% voluntary and you can withdraw at any time
  - We will still love you and take good care of you in clinic!
- All parents sign an informed consent and children aged 7-14 sign an informed assent
- Potential side effects are very closely followed
- Any sort of lab testing needs to be done in a certified research setting
  - In SE Wisconsin, this is the Translational Research Unit at CHW

Research opportunities in Southeast Wisconsin: expanding our influence and foot print

- The CHW Diabetes Clinic is one of the highest volume clinics in the country
  - > 225 children and teens diagnosed every year
  - Very active and engaged patient population
- We have been historically under-represented
- Our goal is to continue to provide top tier clinical care and to expand our academic and research offerings
  - We're making it happen!
- Currently, 8 active research studies for T1D patients and their family members
- There are 3 more in process

Max McGee Family Study

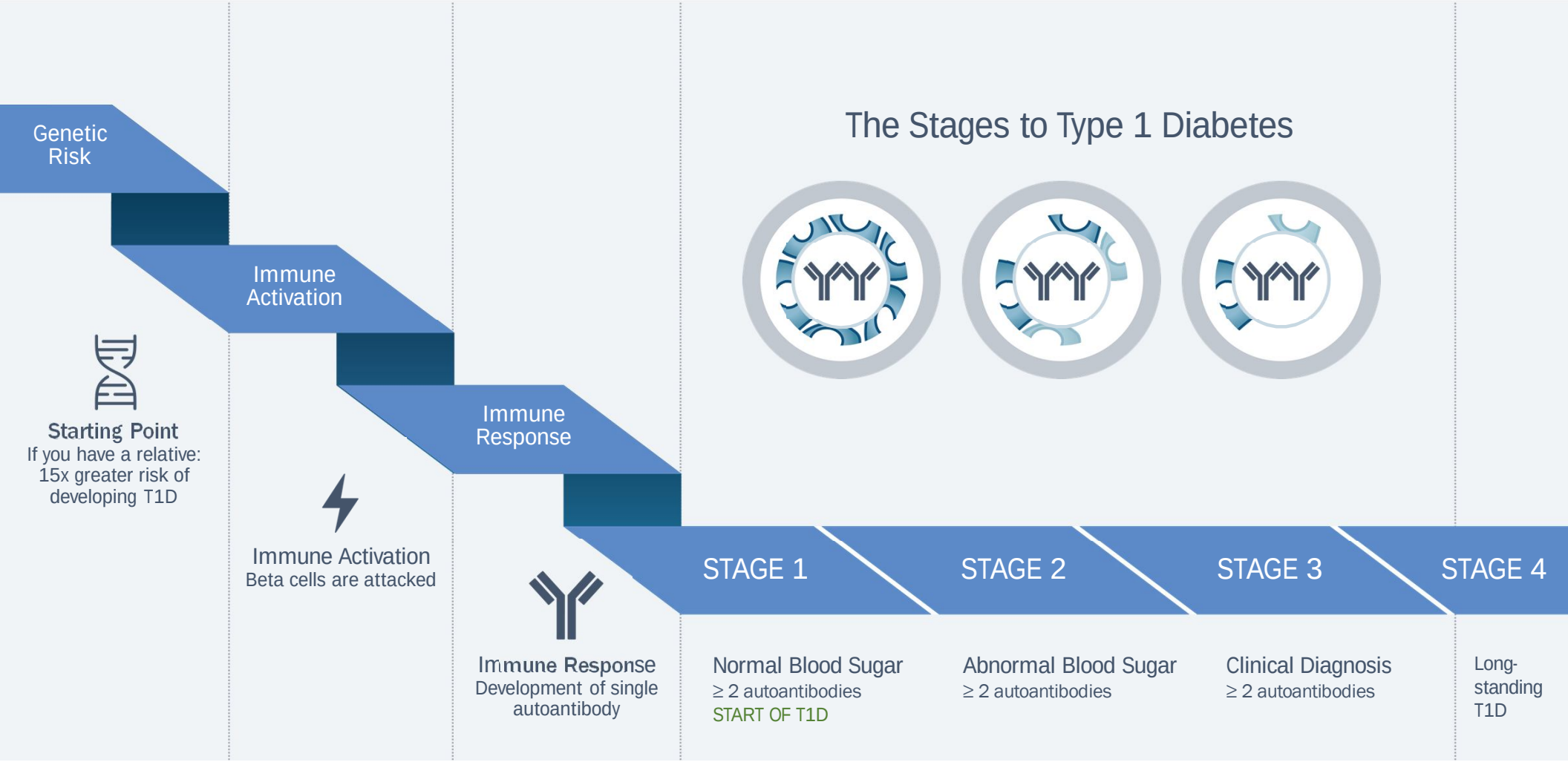


- Locally owned and operated
- Goal: to determine the immune mechanisms behind T1D to provide effective treatments, prevention measures, and a cure
- > 500 families have participated over the past 15 years
- Eligible: first degree relatives of someone with T1D (siblings, parent, children, spouse)
- Blood draw at CHW's Translational Research Unit for genetic analysis and measurement of the immune reaction and completion of a family medical history questionnaire
- Additional annual lab draws may be requested
- **Healthy controls (aged 2-39 years) are desperately needed!**
  - No family history of T1D or personal history of autoimmune disease
  - A single blood draw at CHW and a $20 gift card

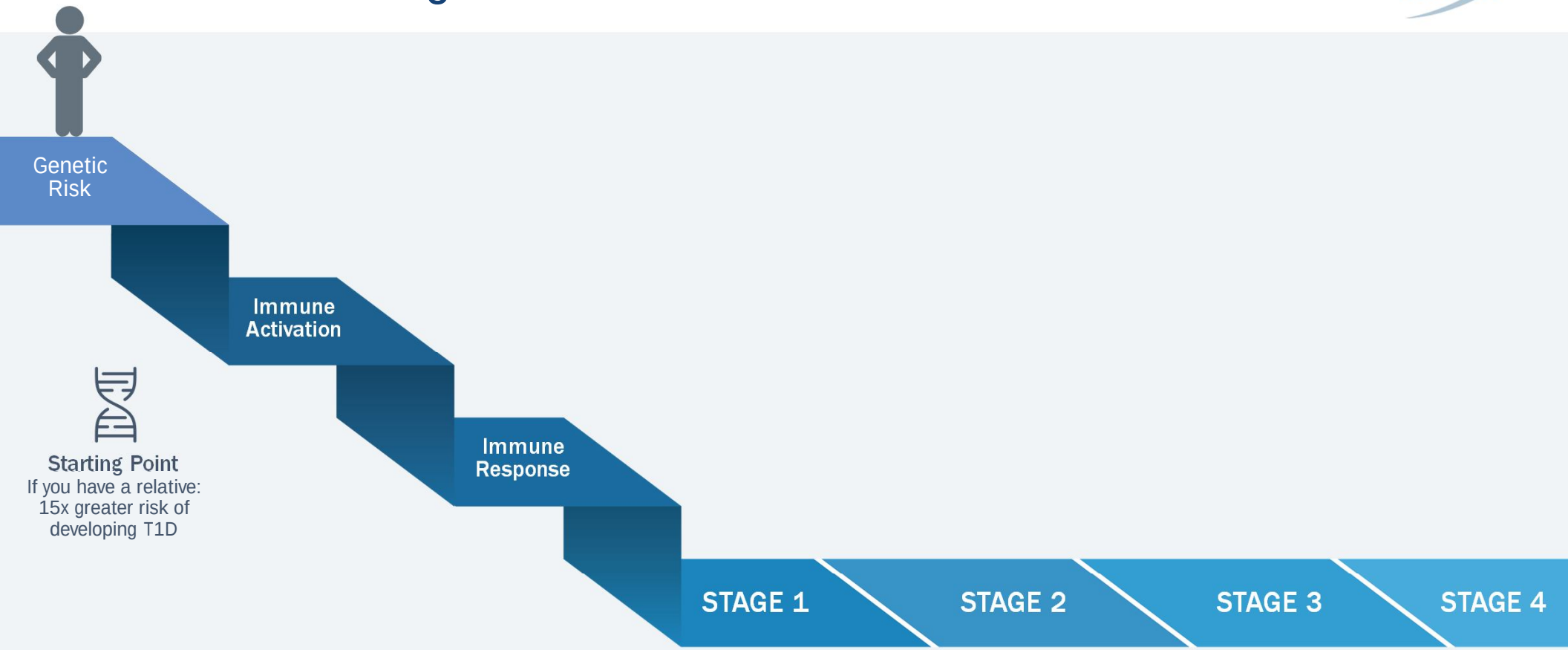
TrialNet Pathway to Prevention

- International consortium of academic institutions, research labs, healthcare teams at the forefront of T1D research
- Funded by the National Institutes of Health and the JDRF, we offer risk screening for relatives of people with T1D and innovative clinical studies to preserve insulin production
- Mission is to prevent T1D and stop disease progression by preserving insulin production before and after diagnosis

T1D Disease Progression



T1D Disease Progression



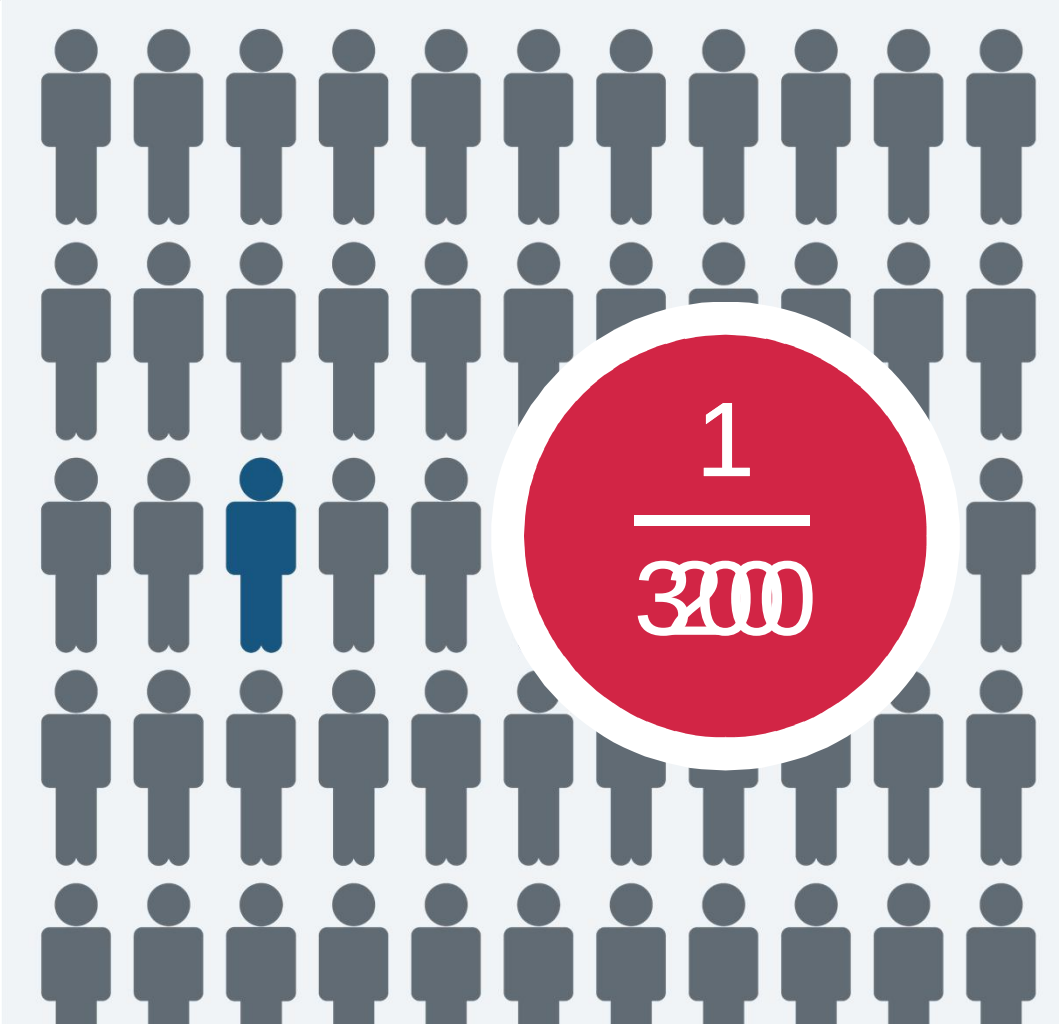
T1D Disease Progression

Type 1 Diabetes TrialNet

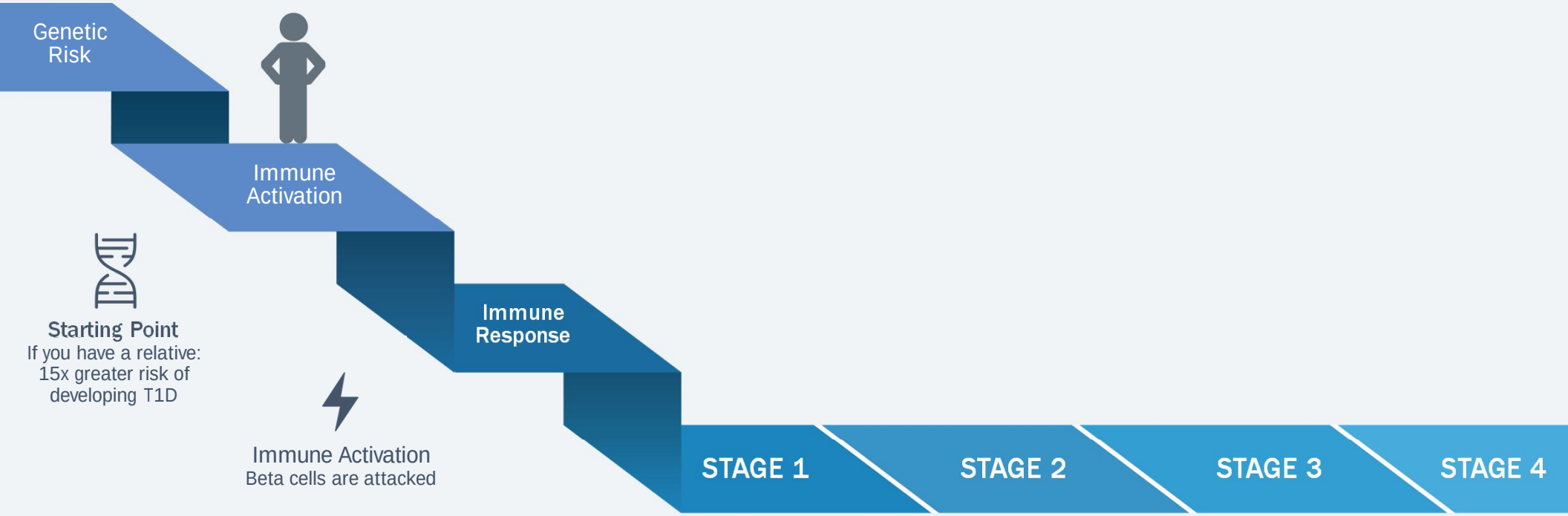
Starting Point
Genetic Risk

The path to T1D starts here

- Everyone who is diagnosed with T1D has the gene(s) associated with T1D
  - General population risk is 1 in 300
- Family members are at 15x greater risk to develop T1D
  - Relative risk is 1 in 20



T1D Disease Progression



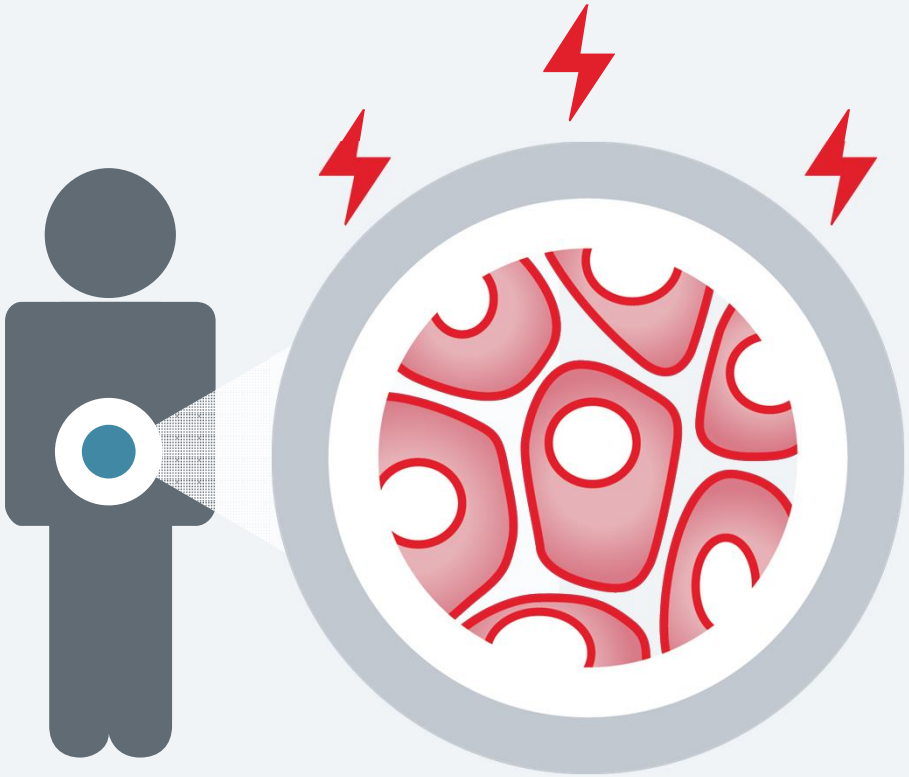
T1D Disease Progression

Immune system is activated

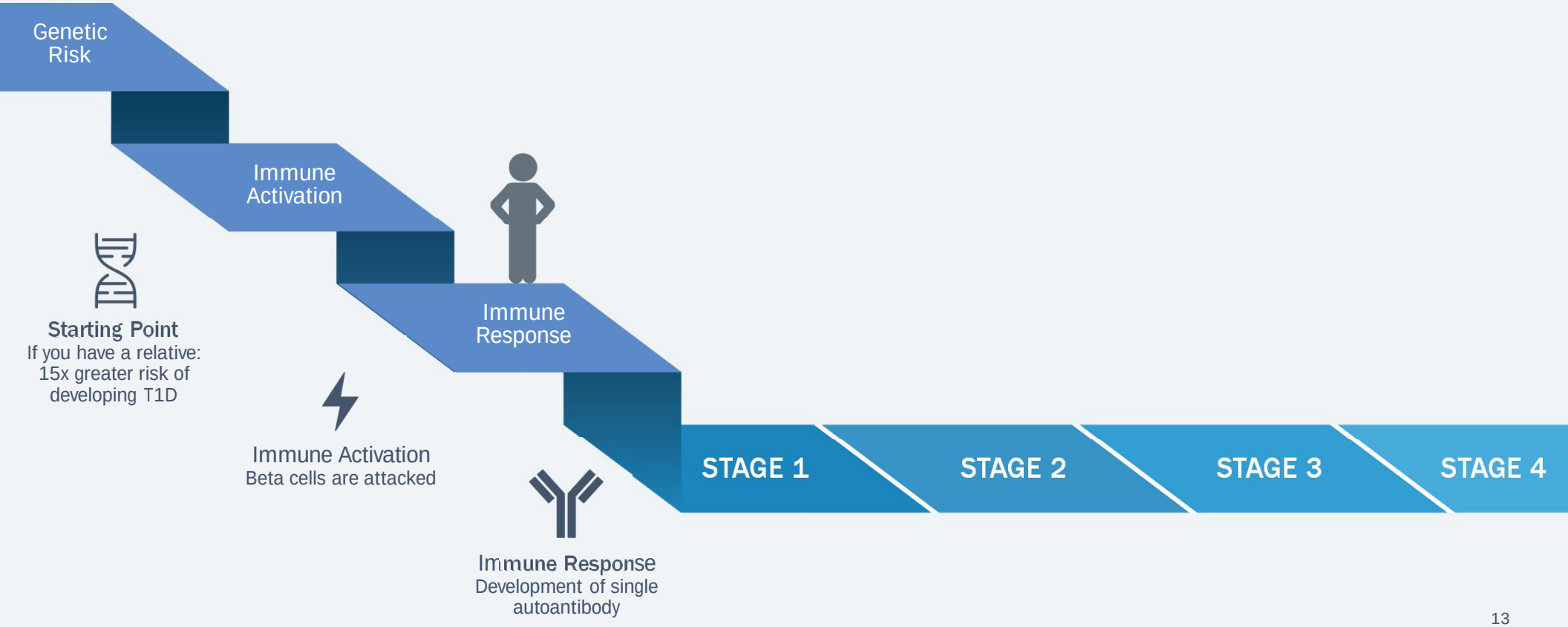
Immune Activation

Immune system attacks beta cells

- Likely a common event
- Research taking place to identify the possible “event” or combination of “events”



T1D Disease Progression



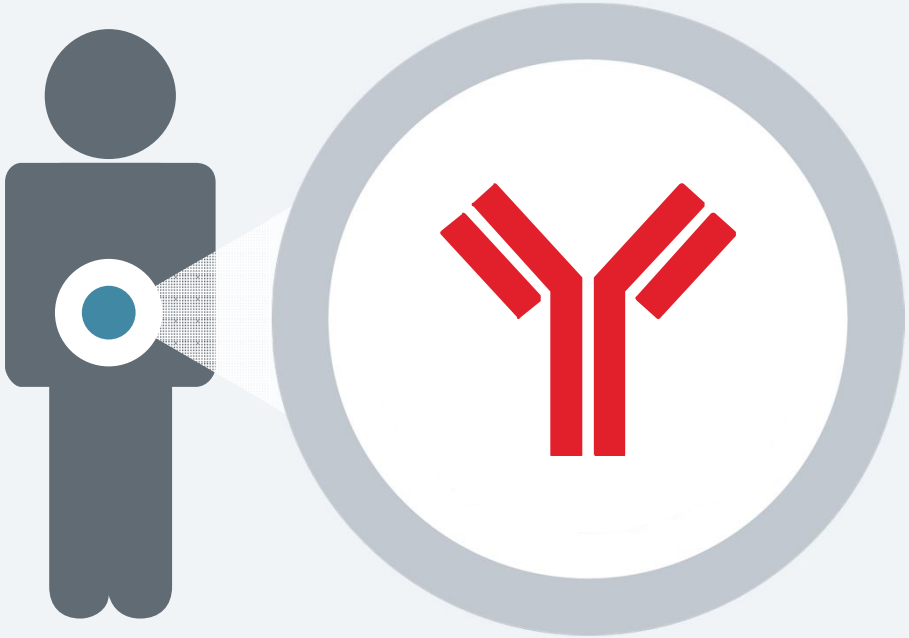
T1D Disease Progression

Type 1 Diabetes TrialNet

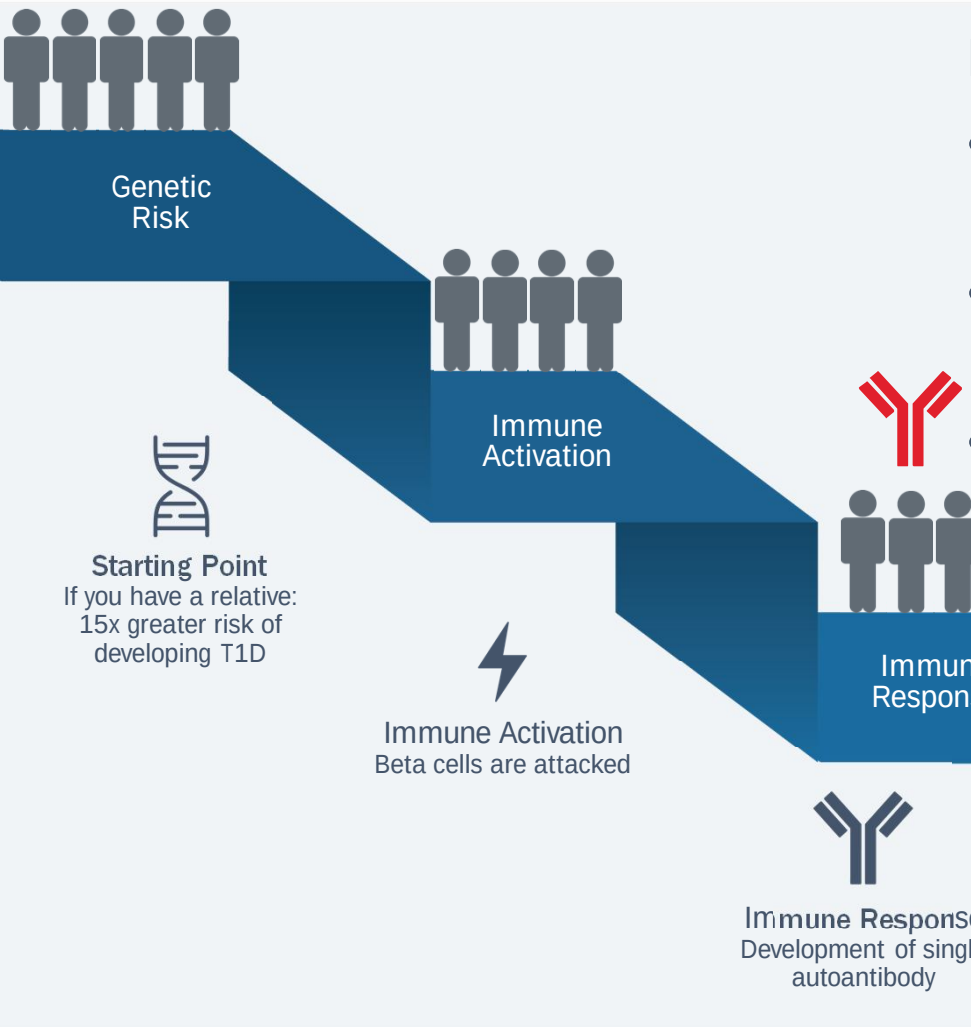
Development of single autoantibody
Immune Response

1 autoantibody

- Immune system responds to beta cells being attacked
- Results in the development of autoantibodies
- Autoantibodies are a “visible” signal that the immune system is activated



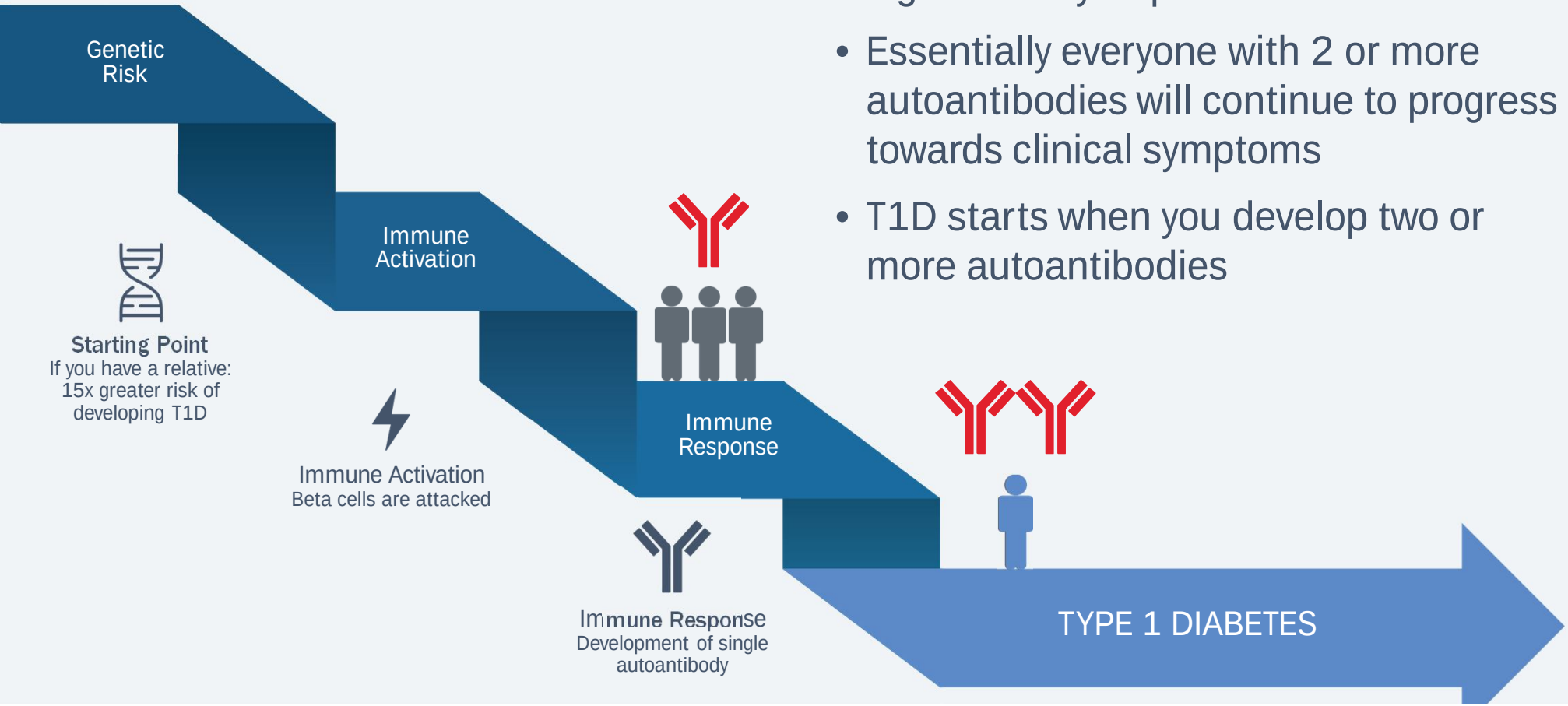
T1D Disease Progression



Progression by Population:

- Everyone who goes onto develop T1D has a genetic risk
- Immune system will be activated in some of those people
- Even fewer will go on to develop an autoantibody

T1D Disease Progression



Progression by Population:

- Essentially everyone with 2 or more autoantibodies will continue to progress towards clinical symptoms
- T1D starts when you develop two or more autoantibodies

T1D Disease Progression

Type 1 Diabetes TrialNet

Scientific Statement from JDRF, Endocrine Society, ADA

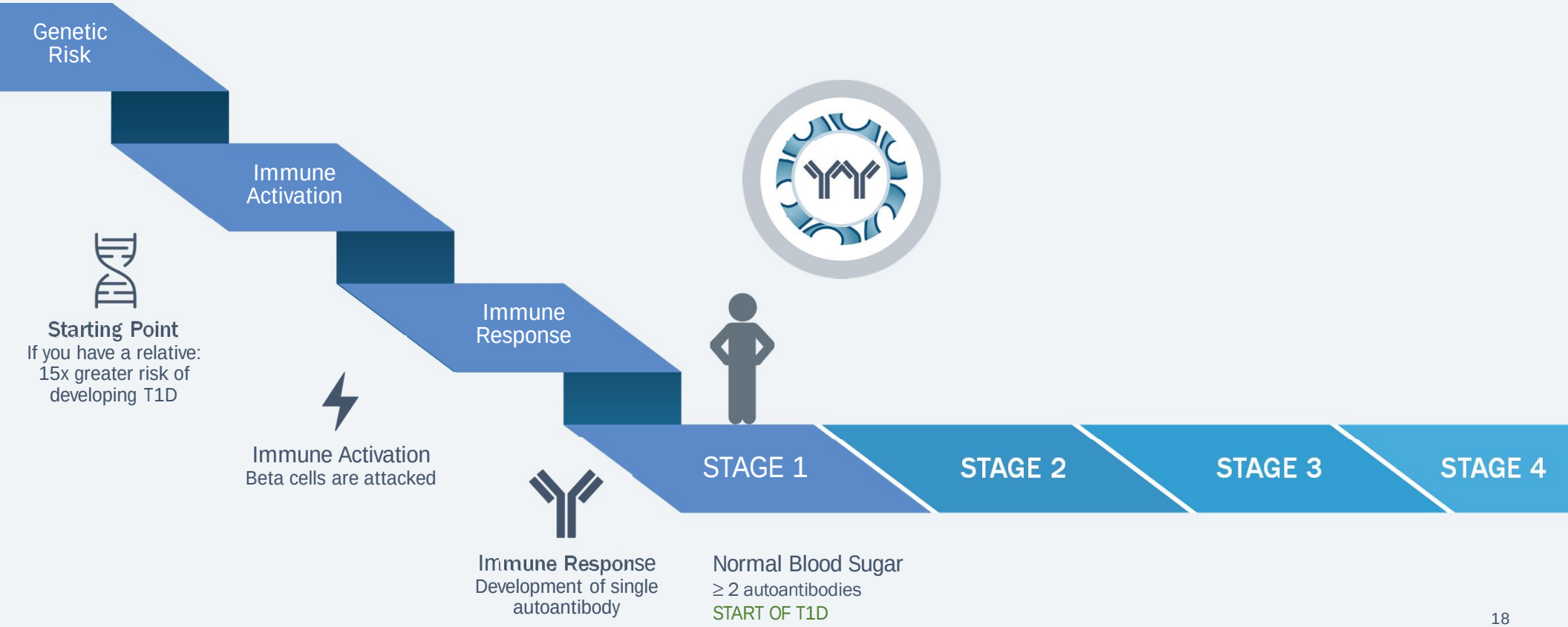
Staging Presymptomatic Type 1 Diabetes

In the January 2016 issue of Diabetes Care, the JDRF, American Diabetes Association (ADA), and Endocrine Society recommend adoption of a new type 1 diabetes staging classification.

The recommendation is largely based on an immense amount of data collected from TrialNet research spanning two decades and involving more than 150,000 relatives of people with type one diabetes.

Type one diabetes can now be most accurately understood as a disease that progresses in three distinct stages.

T1D Disease Progression



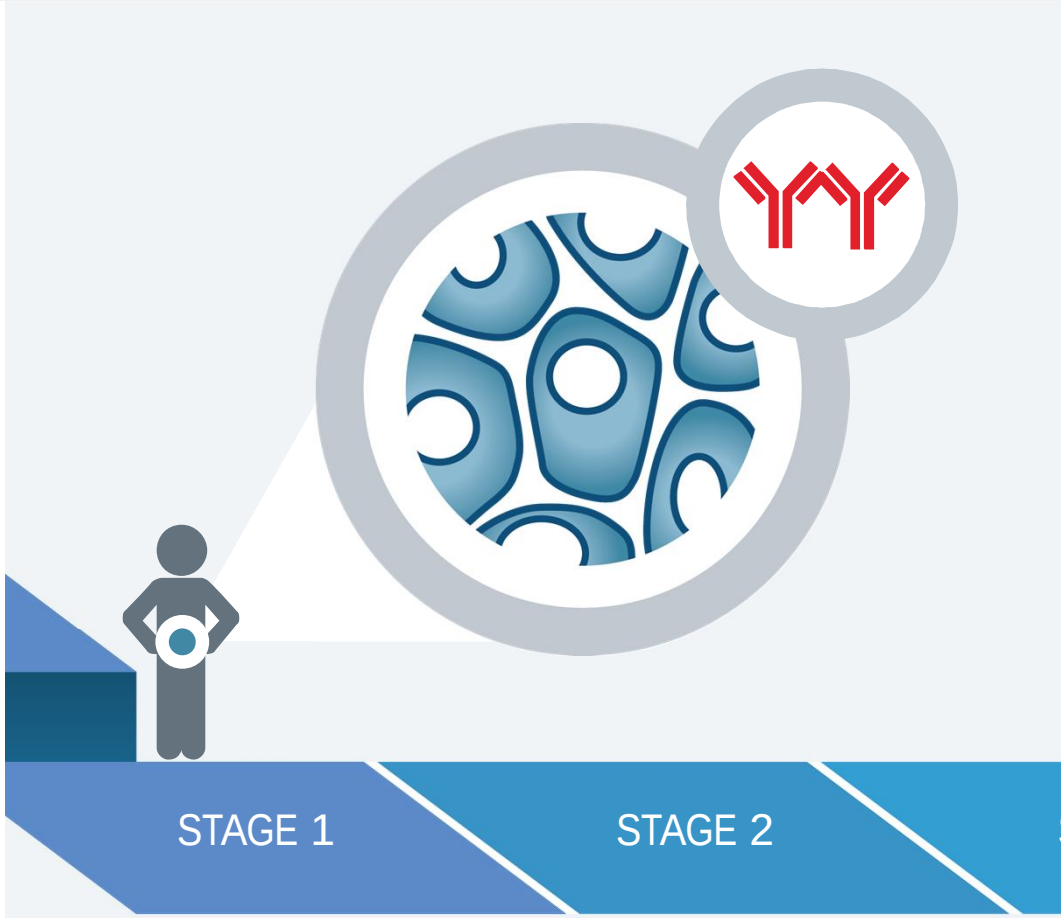
T1D Disease Progression

Type 1 Diabetes TrialNet

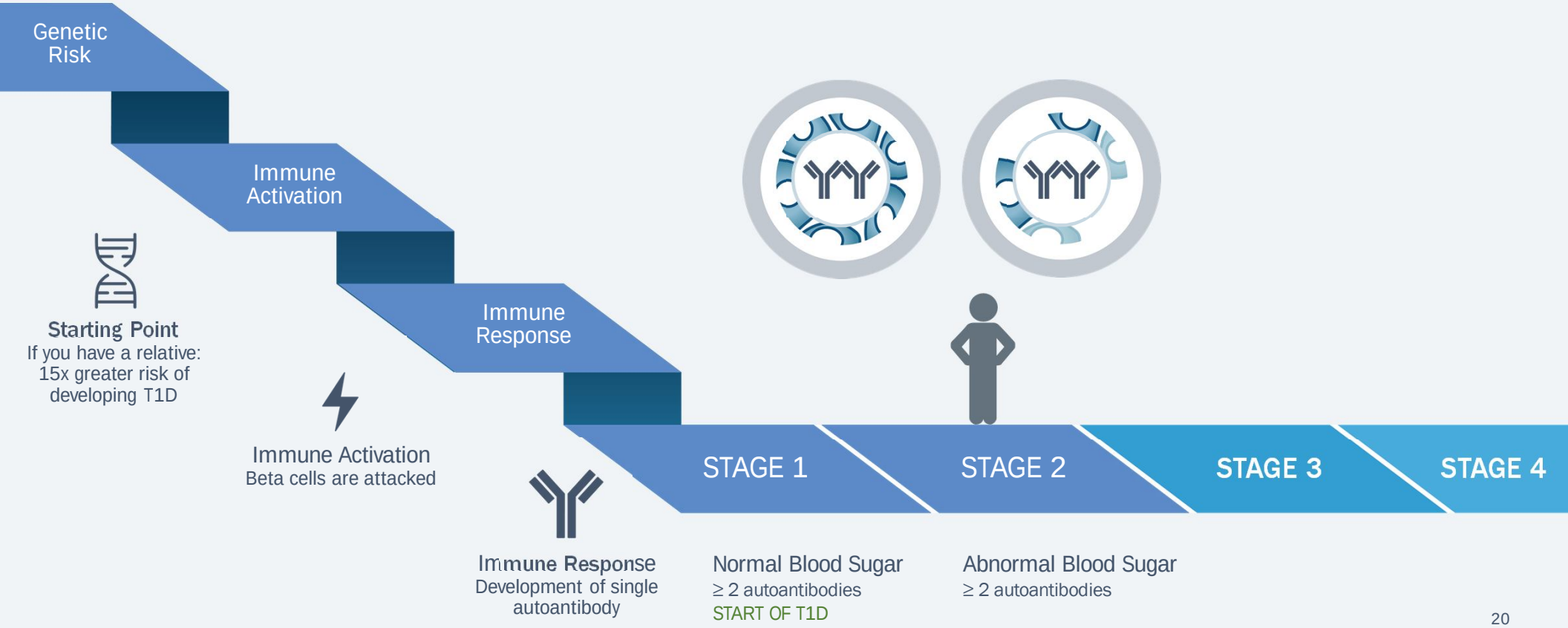
Stage 1 T1D
Normal Blood Sugar

≥ 2 autoantibodies

- START of T1D
- Two or more autoantibodies
- Normal blood sugar
- Lots of beta cells that are able to maintain blood sugar
- No symptoms



T1D Disease Progression



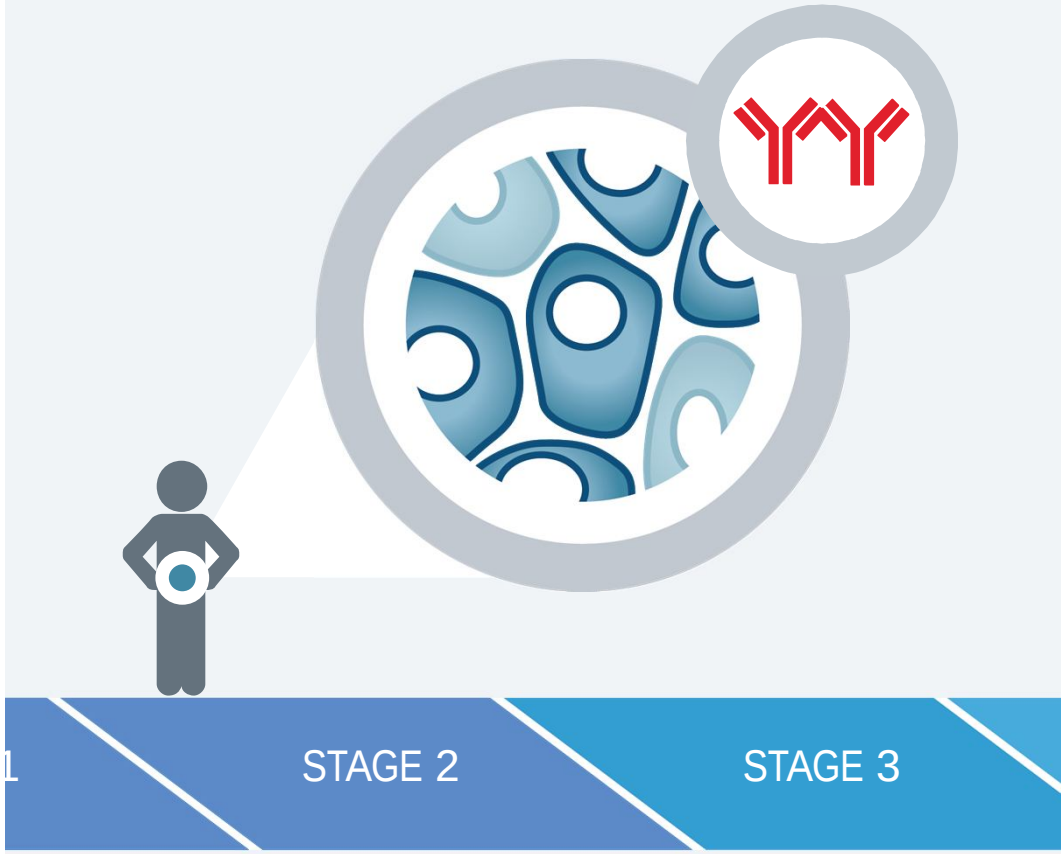
T1D Disease Progression

Stage 2 T1D

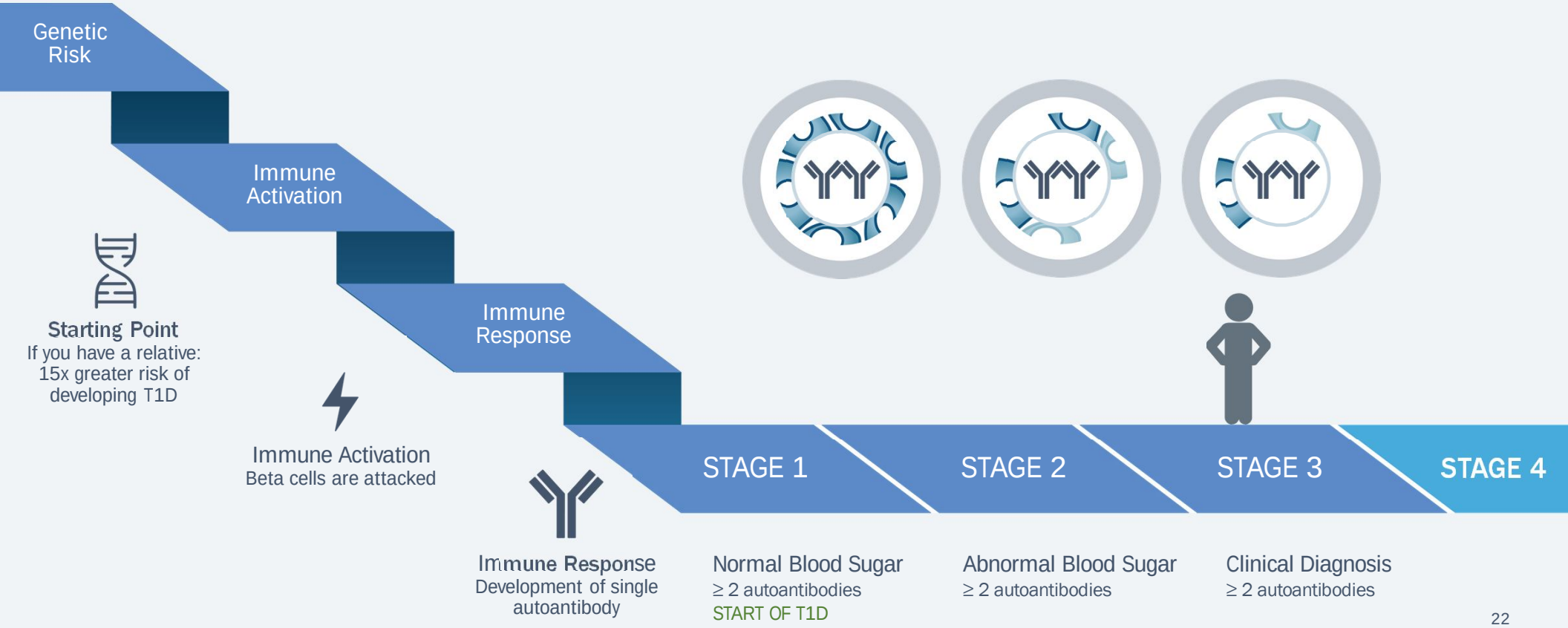
Abnormal Blood Sugar

≥ 2 autoantibodies

- Two or more autoantibodies
- Fewer beta cells, but not enough to keep blood sugar normal
- No symptoms



T1D Disease Progression



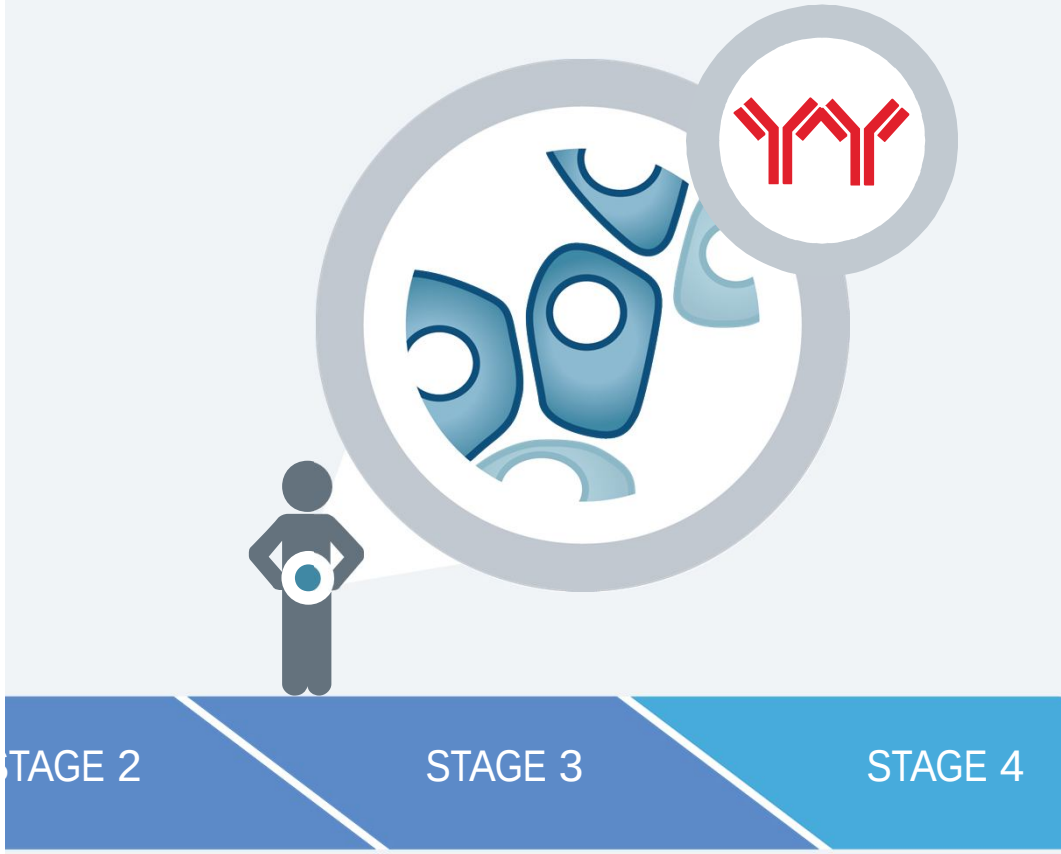
T1D Disease Progression

Type 1 Diabetes TrialNet

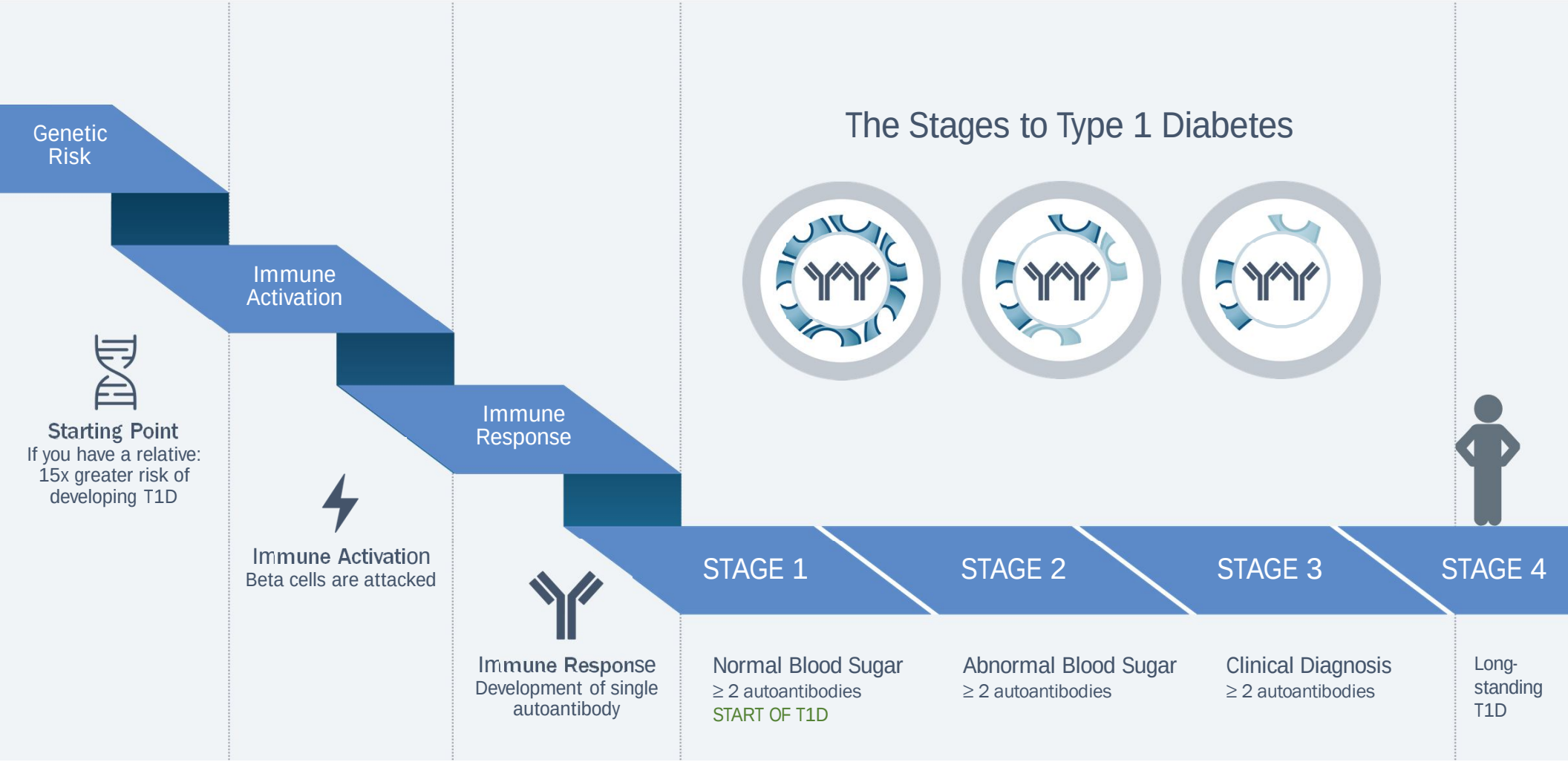
Stage 3 T1D
Clinical Diagnosis

≥ 2 autoantibodies

- Marked by clinical diagnosis (Dx)
- Formerly known as “start of T1D”
- Even fewer beta cells
- Symptoms of high blood sugar



T1D Disease Progression



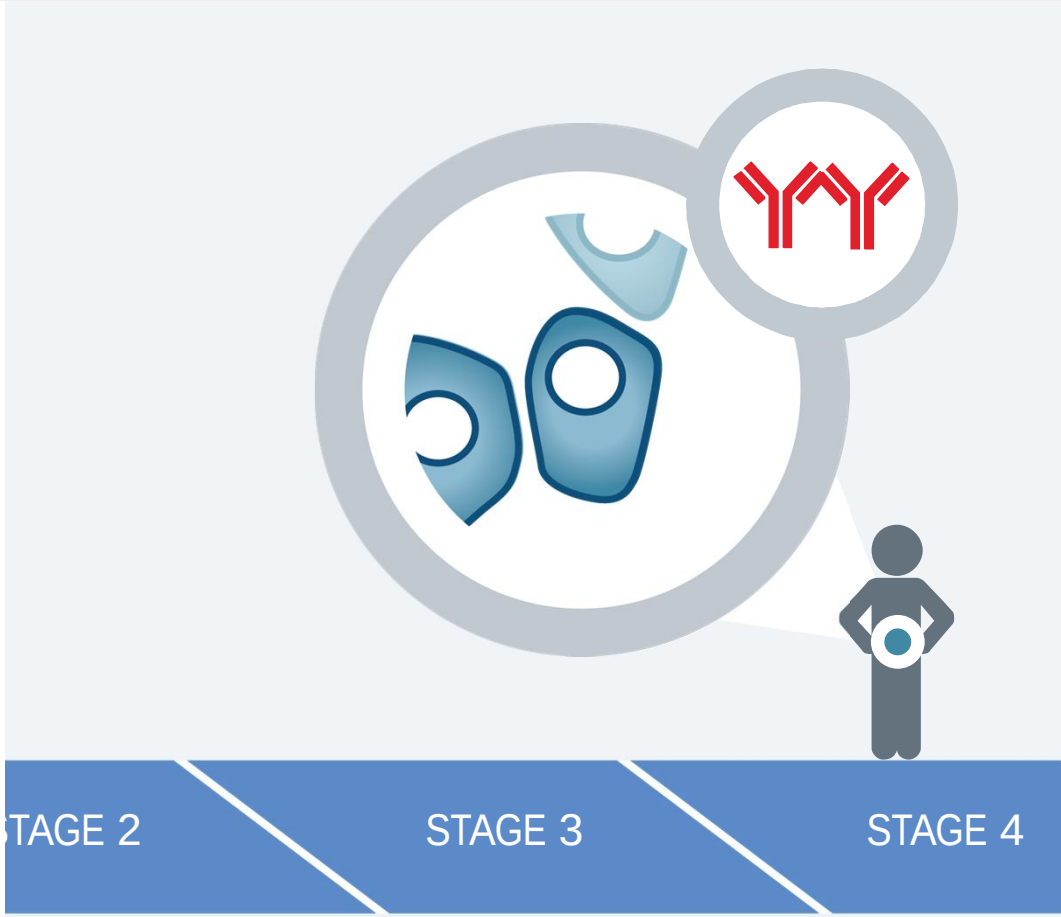
T1D Disease Progression

Type 1 Diabetes TrialNet

Stage 4 T1D
Long-Standing T1D

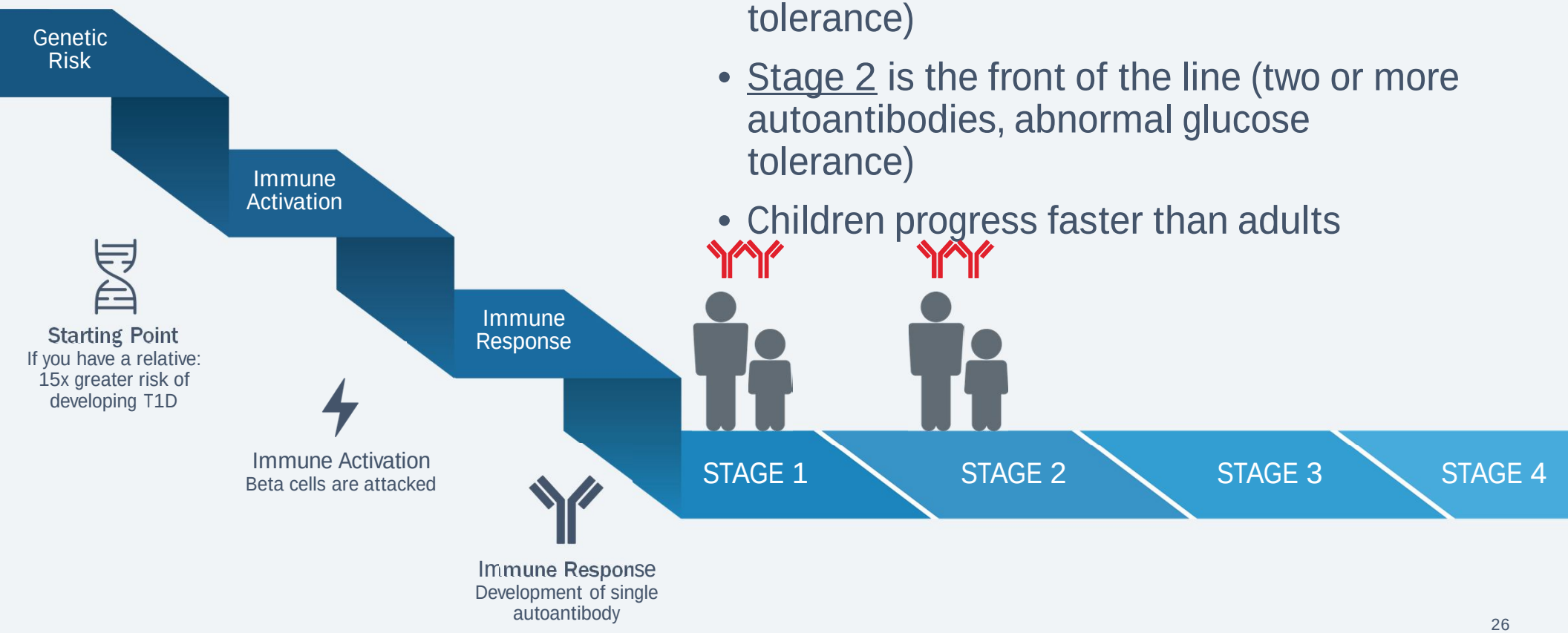
Post diagnosis

- Continued loss of beta cells over time
- Research outside of TrialNet is working to replace or replenish beta cells



T1D Disease Progression

- Stage 1 is the back of the line (two or more autoantibodies, normal glucose tolerance)
- Stage 2 is the front of the line (two or more autoantibodies, abnormal glucose tolerance)
- Children progress faster than adults



T1D Disease Progression

SUMMARY POINTS

1. Type 1 diabetes starts with two or more autoantibodies
2. There are three defined stages:
   - Stage 1: Presence of 2 or more autoantibodies with normal blood sugar
   - Stage 2: Presence of 2 or more autoantibodies with abnormal blood sugar
   - Stage 3: Clinical diagnosis (Dx) of type 1 diabetes
3. Age matters!
   1. Time from 2 or more autoantibodies to Dx is faster the younger you are
   2. Beta-cell decline is also faster the younger you are and continues through stage 4

T1D Disease Progression

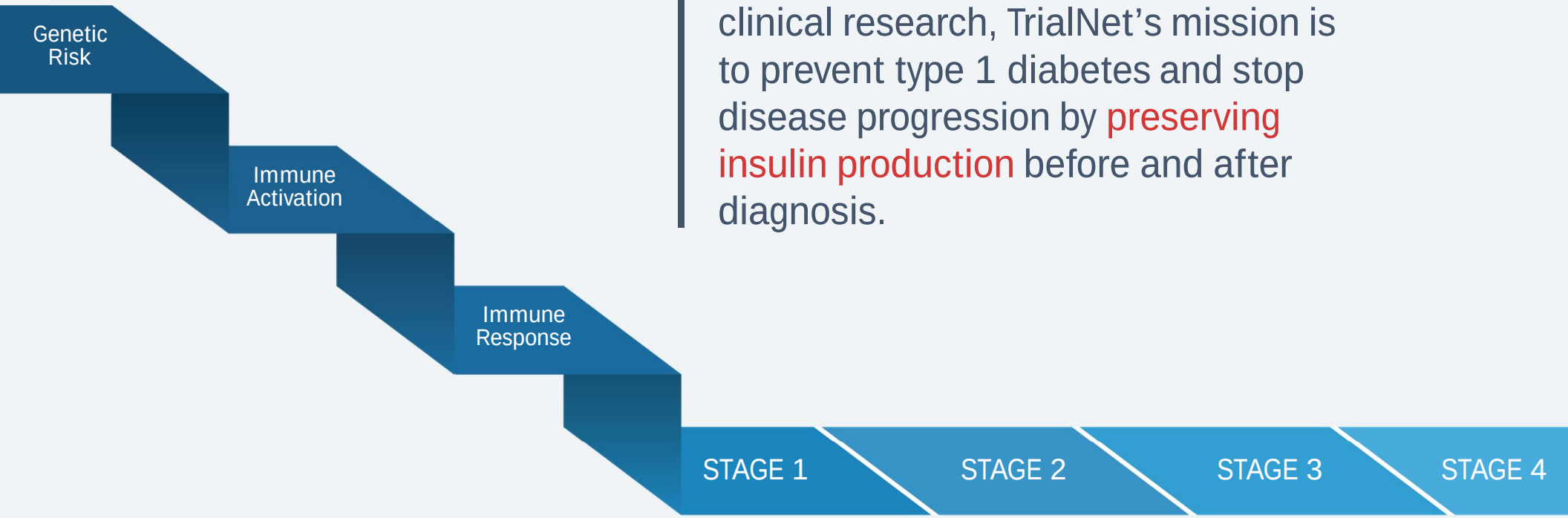
IMPORTANCE OF STAGING

1. Identification of T1D in it's earliest stages can lead to a decreased risk of diagnosis in DKA

2. Staging diabetes allows us to treat T1D early to delay progression and ultimately prevent stage 3 (symptomatic T1D)

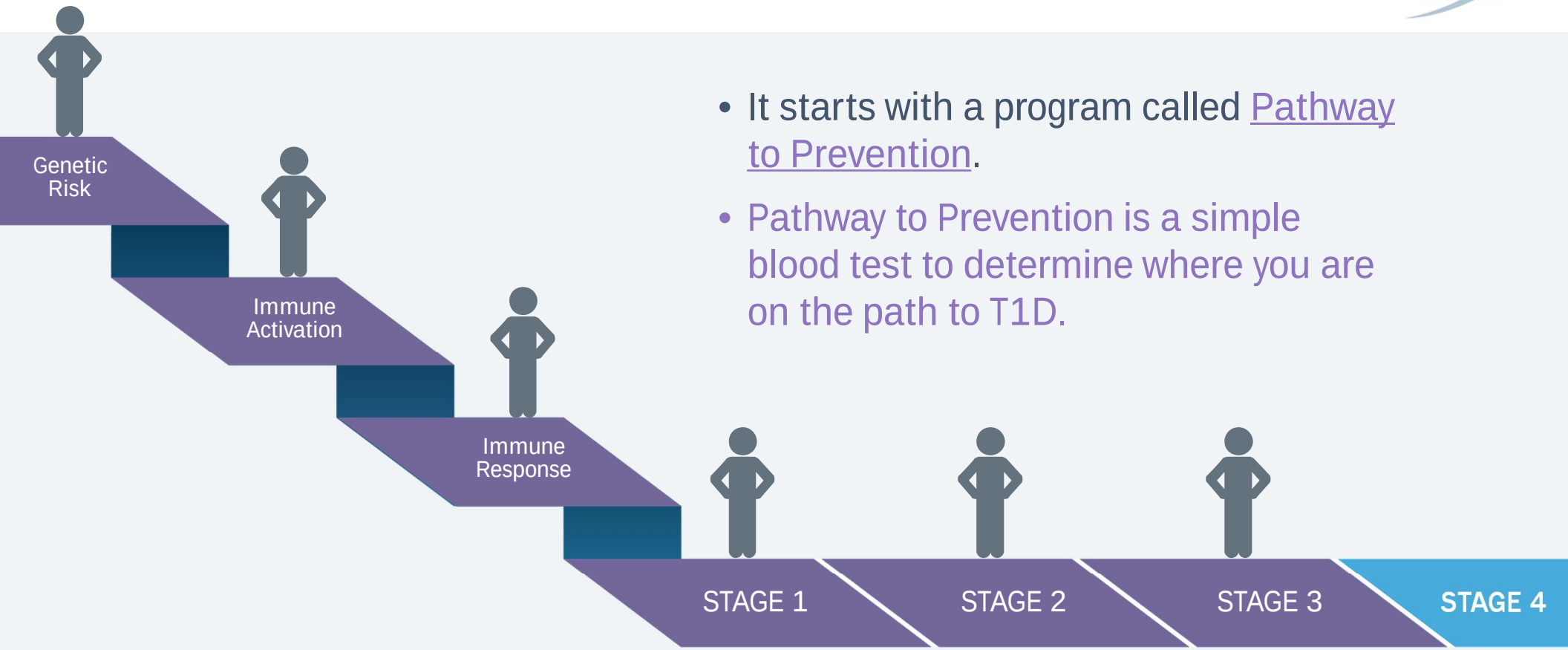
- Treating high blood pressure, allows us to treat the disease early and ultimately prevent a heart attack or stroke

TrialNet Disease Intervention



Using knowledge gained through clinical research, TrialNet's mission is to prevent type 1 diabetes and stop disease progression by preserving insulin production before and after diagnosis.

TrialNet Disease Intervention



- It starts with a program called Pathway to Prevention.
- Pathway to Prevention is a simple blood test to determine where you are on the path to T1D.

TrialNet Disease Intervention

P2P
Pathway to Prevention

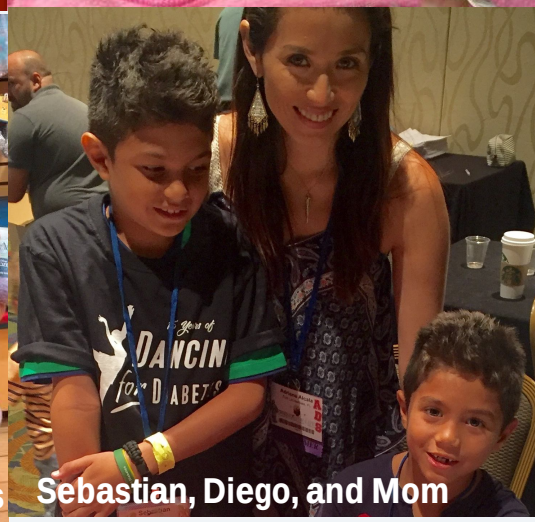
Determine where you are on the path

- No cost
- 1st and 2nd degree relatives
- Screens for autoantibodies
- Based on results
  - Look to enroll in clinical trial to preserve beta cell function
  - Or monitor for disease progression

University of Florida at Friends for Life


Keilyn
Pathway to Prevention Participant


Brooke, Emily & Ava
Pathway to Prevention Participants


Sebastian, Diego, and Mom

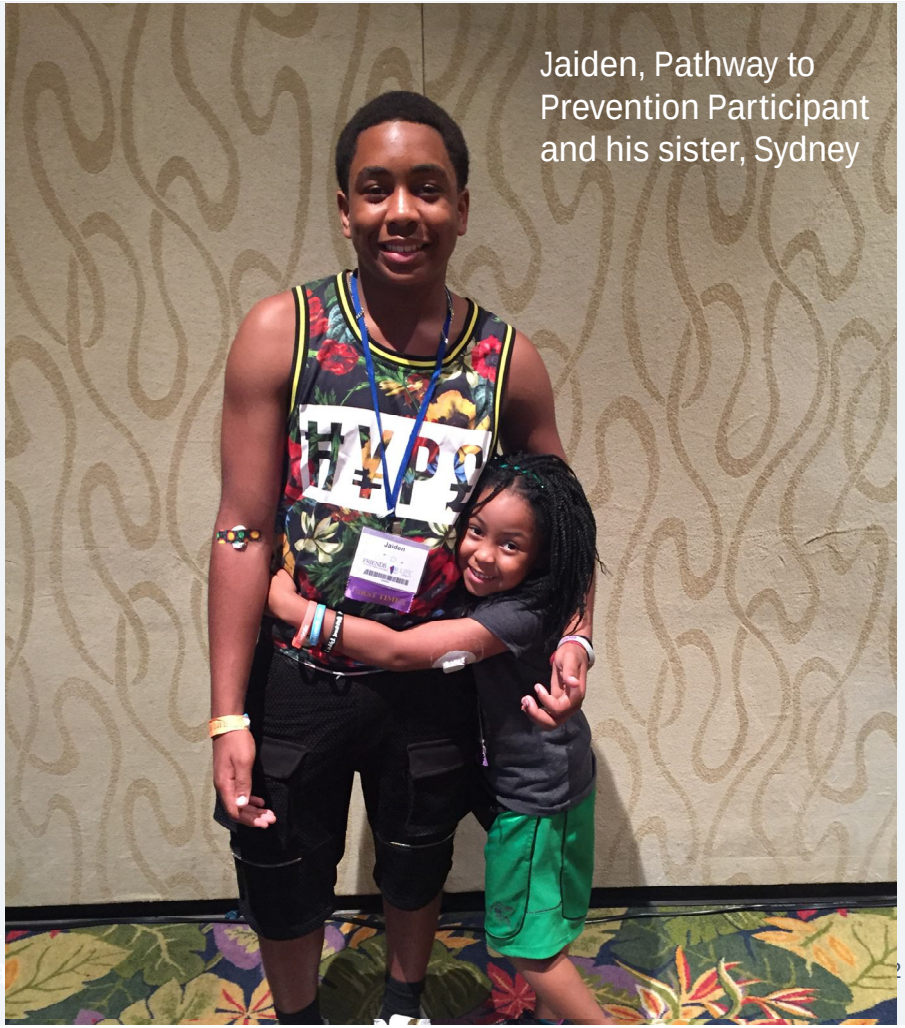
TrialNet Disease Intervention

Type 1 Diabetes TrialNet

P2P
Pathway to Prevention

Eligibility Requirements

- Anyone between age 1 and 45 with a sibling, child or parent with type 1
- Anyone between age 1 and 20 with a sibling, child, parent, cousin, uncle, aunt, niece, nephew, grandparent or half-sibling with T1D
- Those under 18 who do not have autoantibodies can be retested every year



Jaiden, Pathway to Prevention Participant and his sister, Sydney

Why enroll in Pathway to Prevention?

- TrialNet screening allows us to identify the disease at its earliest stage
  - We understand and respect this may be information you do not want to have!
  - Overwhelmingly (> 95% of the time), the test will be negative and you may have peace of mind
- TrialNet offers clinical trials for every stage of T1D
  - If you are eligible for a study current or future, it will be offered to you
  - You will be on the front line of any new intervention or study
- For people who participate in T1D prevention research, the risk of DKA at diagnosis decreases from 30% to < 4%
  - Less likely to have profound and disruptive symptoms at diagnosis or end up hospitalized
  - Tend to have a longer honeymoon period
- Even if it does not directly benefit you, it will most certainly benefit those yet to be diagnosed

Active trials

TrialNet Disease Intervention Stage 1

CURRENT & FUTURE STUDIES

1. These studies are for those identified in Stage 1 (the start of T1D)
2. Immune Effects of Oral Insulin
    - Just closed enrollment
4. Abatacept
    - Currently enrolling (CHW will be opening as a location)
    - Participate in Pathway to Prevention to identify eligibility

TrialNet Disease Intervention Stage 2

CURRENT & FUTURE STATUS

1. This study is for those identified in Stage 2 (front of the line)
2. Teplizumab
    - Currently enrolling
    - Participate in Pathway to Prevention to identify eligibility

TrialNet Disease Intervention Stage 3 (Clinical Dx)

1. This study is for those identified in Stage 3, clinical diagnosis
    - Formerly considered the start of T1D
2. ATG/GCSF
    - Currently enrolling
    - Must be enrolled in the trial within 100 days of clinical diagnosis

DFMO

- JDRF study of subjects diagnosed with T1D within the past 7 months, aged 12 to 40 years of age
- Oral medication that prevents the build-up of a toxin in the beta-cells that accelerates their demise
  - Goal is to get the beta-cells to work as well as they can for as long as they can
  - Moving towards combination approaches, recognizing that T1D is a complex disease process
- 5 study visits over 7-8 months

Primary Prevention

- Stop T1D from ever starting
- Because T1D can start as early as 6 months of age, these treatments need to be given very early and need to be very low risk
- Examples: probiotics, dietary changes
- Stay tuned! We have some interesting ideas and grants in progress!!

Contact Information

- Ask any of your clinical providers and they will get your name to the right people!
- Coordinators: Joanna Kramer and Clare Bingham-Tyson
- 414-955-4903
- T1dinfo@mcw.edu