JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

Type 1 Diabetes: Advances and Opportunities

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February 02, 2021

JDRF: History in the Making!

By the people, For the people:

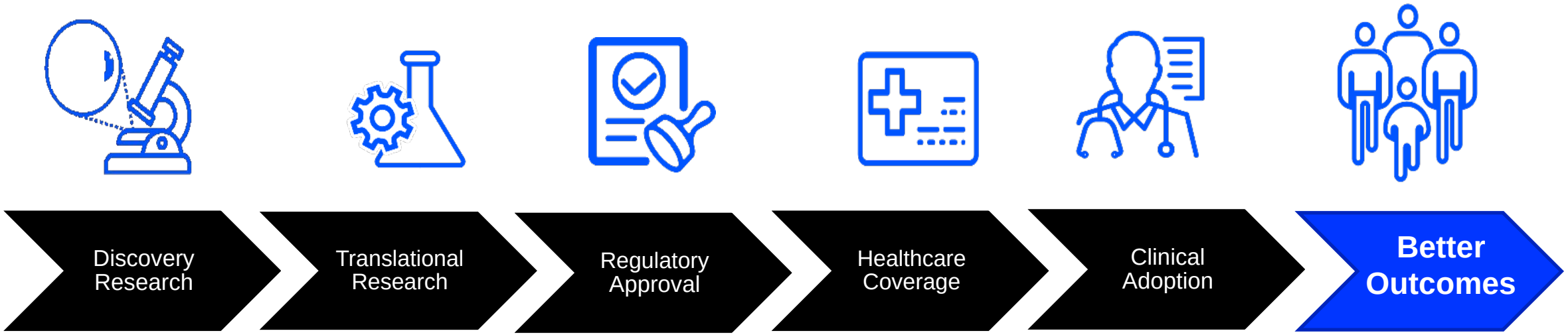
Founded 50 years ago by parents and
is today the single most powerful charitable force
and funder in the world driving T1D research

Vision & Mission:

World without T1D

Improving lives today and tomorrow by
accelerating life-changing breakthroughs
to cure, prevent and treat type 1 diabetes and its
complications

Working Across the Pipeline, Around the Globe



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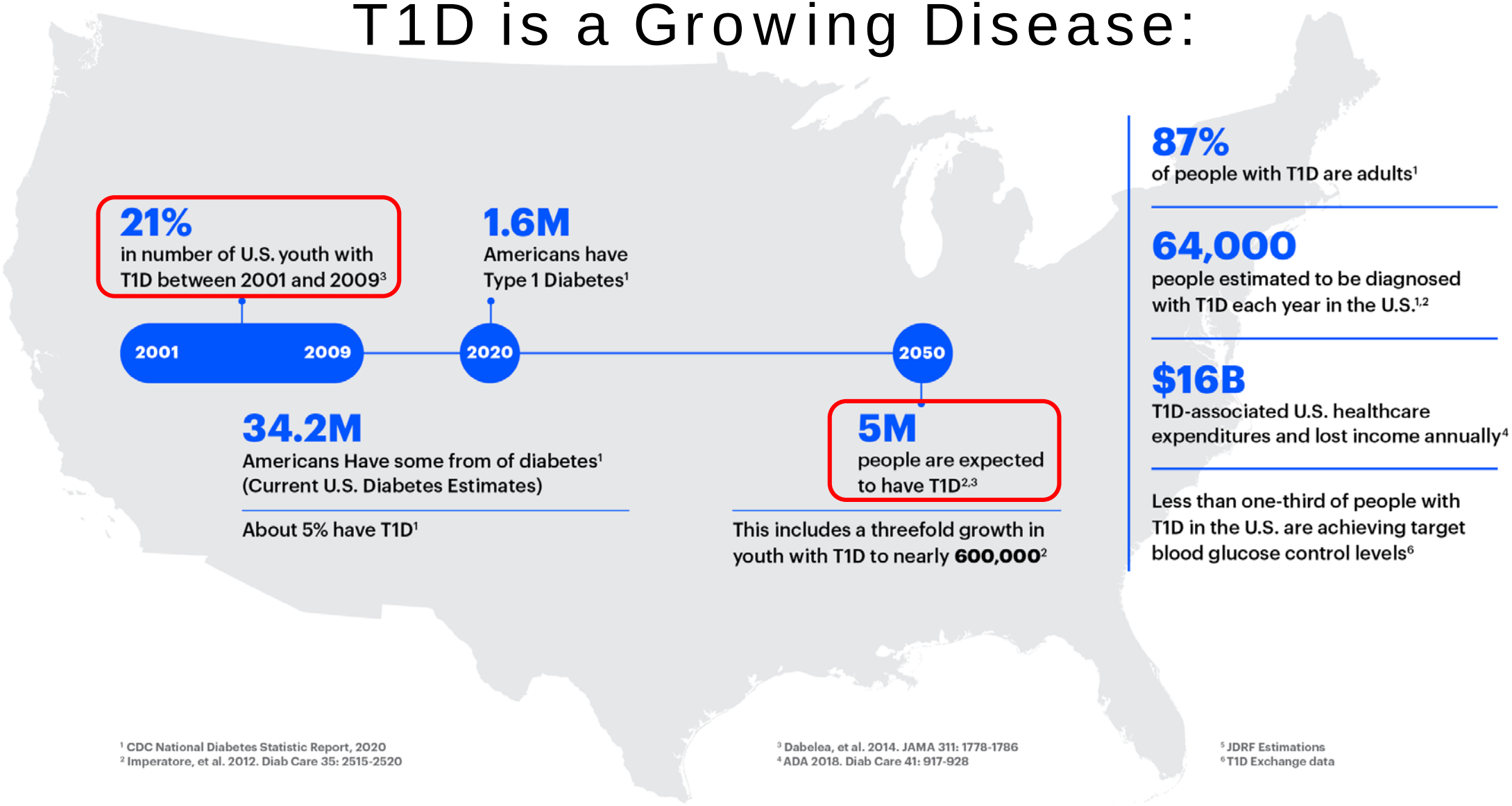
T1D is a Growing Disease:



[1] CDC National Diabetes Statistic Report, 2020
[2] Imperatore, et al. 2012. Diab Care 35: 2515-2520
[3] Dabelea, et al. 2014. JAMA 311: 1778-1786
[4] ADA 2018. Diab Care 41: 917-928
[5] JDRF Estimations
[6] T1D Exchange data

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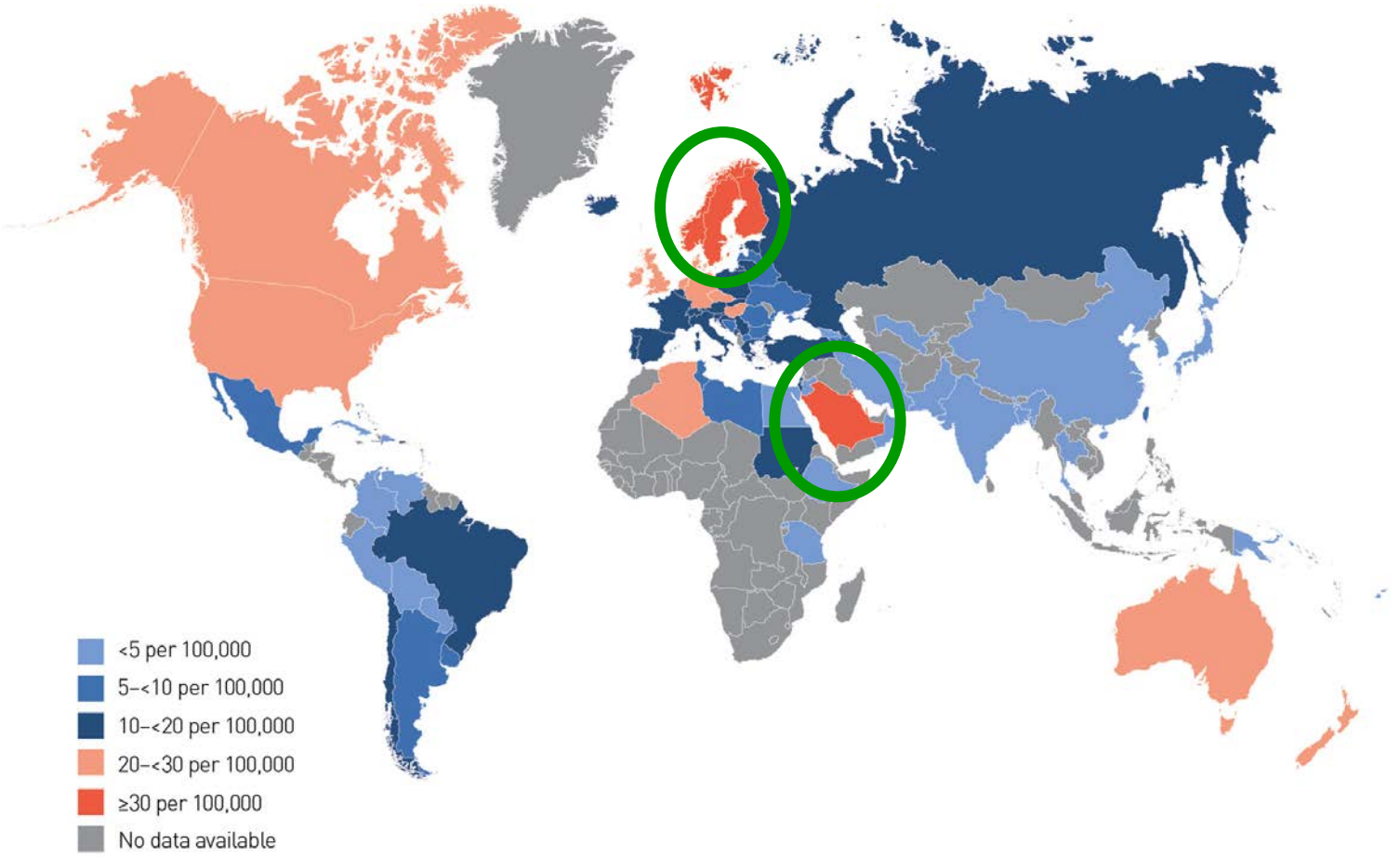
Worldwide increase in incidence of T1D in children and adolescents

T1D can affect anyone:

- **First degree relative increases risk (15x)**
- **No family history (90%)**
- **Environmental triggers**
- **Adult onset (~50%)**



Map of age-sex standardized incidence rates (per 100,000) from publications of type 1 diabetes in children aged under 15 years

[Patterson C et al, Diab Res Clin Prac 2019; 157:107842]

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JDRF Research Priorities

Global Universal Screening

Disease Modifying Therapies

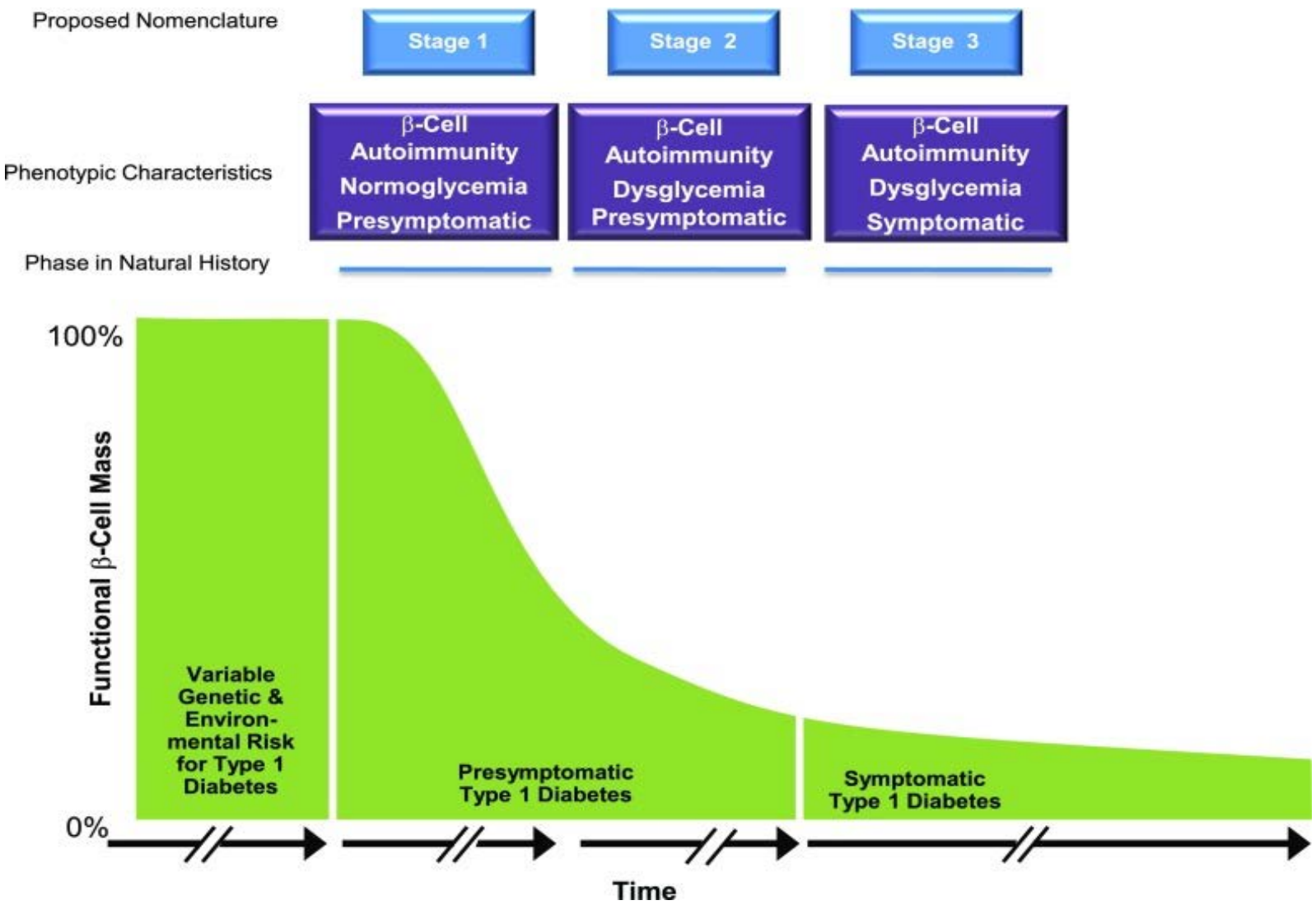
Cell Therapies

Improving Outcomes

Training of Researchers and Clinicians

Advances

T1D Stages: A Paradigm Shift



FDA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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The Reality and Vision of Screening

TODAY

- Reduces Diabetic Ketoacidosis (DKA) in new diagnoses significantly
- Low awareness about T1D stages and the benefits of knowing your risk
- Familial screening captures highest risk group but misses ~90% at risk
- Disease-modifying therapies are progressing slower due to these barriers

FUTURE

- Part of clinical preventative services, adopted by healthcare systems
- Covered by insurance, affordable and accessible to everyone
- More cures therapies in development to improve the lives of those at risk

What have we learned from T1D screening programs

1- SCREENING REDUCES DKA AT DIAGNOSIS

- From 40-60% to <5%
- Improve long-term outcomes
- **By providing screening, education, and monitoring we can almost eliminate DKA at diagnosis**

2- FAMILY SCREENING IS NOT ENOUGH

- Represents 10-15% of diagnoses, missing ~90% at risk
- DKA will remain high and decelerate drug development pipeline
- **General population screening is the solution**

3- AT-RISK POPULATION NEEDS SUPPORT

- Learning about risk status can cause significant anxiety
- Psychological burden can be reduced by education and counselling
- High risk individuals need to be followed closely by doctors to prevent DKA
- **Provision of standard counselling and PCP monitoring programs will improve lives of those at risk**

4- SCREENING SENSITIVITY CAN BE IMPROVED

- Autoantibody status can predict risk of but not when someone will become insulin dependent (T1D diagnosis)
- **Genetic and metabolic tests can more accurately predict who is at risk and also when they will need insulin**

The Reality and Vision of Disease Modifying Therapies

TODAY

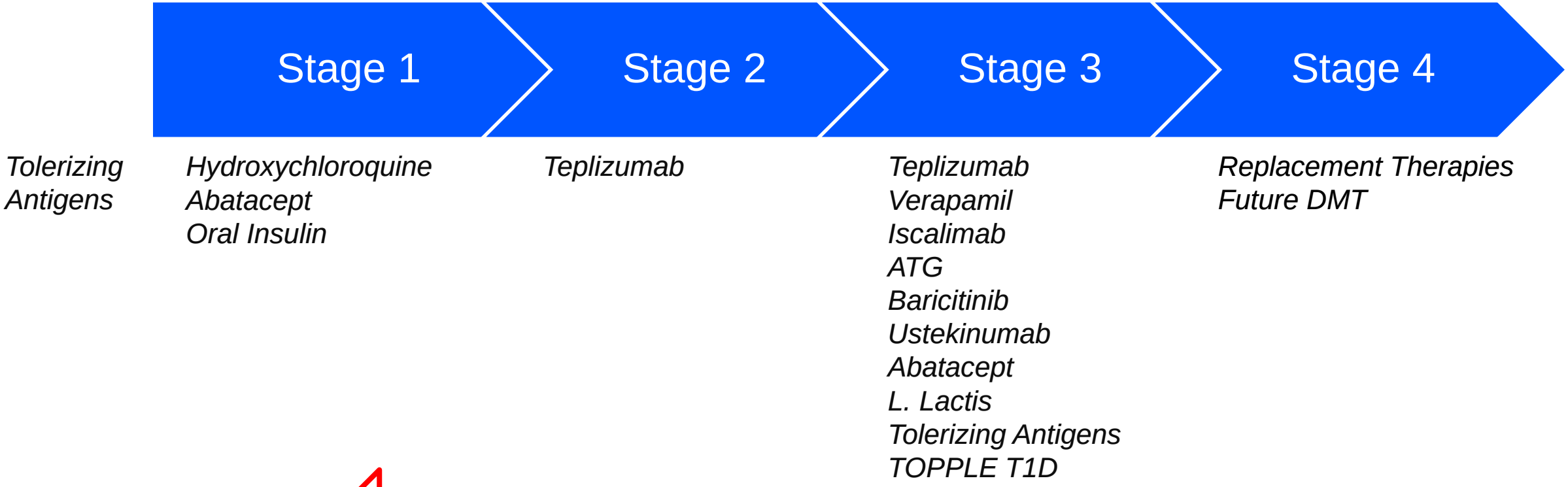
- Several promising disease-modifying therapies have shown the ability to slow or halt the progression of T1D by resetting the immune system and preserving beta cell function
- Several therapies that induce beta-cell regeneration have been discovered

FUTURE

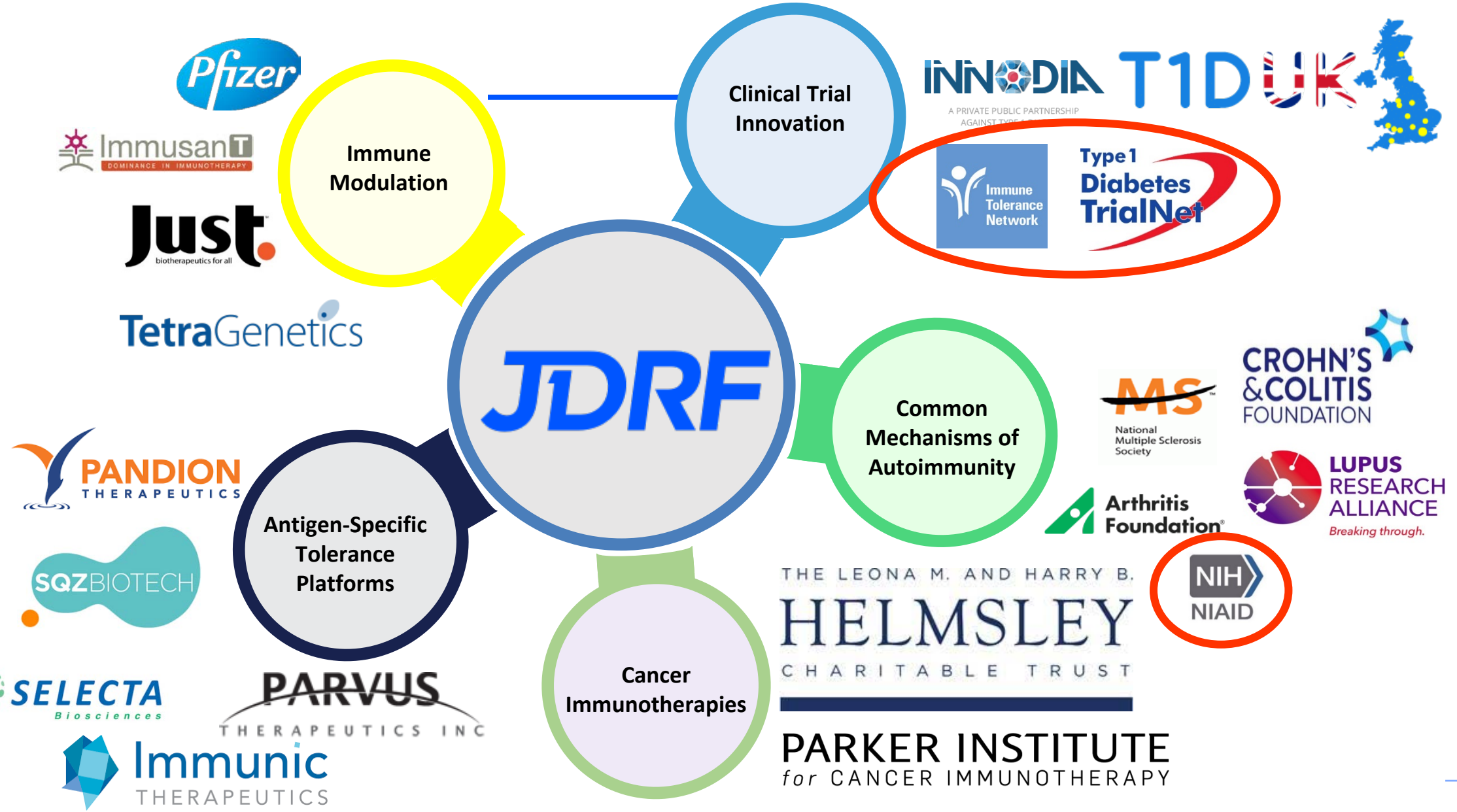
- Commercially available disease modifying therapies that slow, halt or reverse the progression of T1D

Multiple DMT in Clinical Trials Right Now
Unprecedented Exciting Time!

- Directed towards either the immune system, beta cells, or both
- Will likely require combinatorial approaches to reinstate insulin independence and immune rebalance



Global burden, global solution: Driving progress in the ecosystem



Anti-CD3 (Teplizumab) (reduces harmful immunity)

Anti-CD3 is a first in class therapy being developed for T1D that targets activated Teff and disables their activity

T1D Application: JDRF has played a *critical* role in bringing this therapy from stages of early discovery (15+ yrs) to where it is today – being developed by Provention Bio for both stage 2 and stage 3 T1D

Key Progress:

2005-2015: Efficacy shown in 6 trials in stage 3 T1D
2019-2020: Teplizumab delays stage3 disease by 3yrs
2019 - : Provention launches phase3 trial in stage3 pediatrics
2019: FDA/EMA grant coveted **Breakthough** and **PRIME** designation
2021: FDA grants **priority review** to Provention's Biologics License Application (for mid-2021) for stage2 T1D

Partners

Type 1 Diabetes TrialNet

Immune Tolerance Network

proventionbio

JDRF T1D Fund

Opportunities

What have we learned from T1D screening programs

1- ENHANCE KNOWLEDGE SHARING

- Data analytics, sample banks, searchable tools, diagnostics
- Study results (unpublished?), multi-disciplinary portals
- Best practices along the pipeline
- Globalization – efficiency, acceleration, awareness

2- CREATE PARTNERSHIP PLATFORMS

- Clinical trial protocol advancements (design, centralization, guidelines, surrogate endpoints, combinatorial approaches)
- Cross-disease fertilization – common pathways, shared genetics, mechanistic analyses, assay standardization
- Animal models and cores

3- INCENTIVIZE TRANSLATION

- Pipeline is 'leaky' at each point of inflection – there are many valleys of death!
- Strong basic research needs support for validation and creation of FIH-ready candidates
- SBIR, STTR, opportunities for academia-industry collaborations
- Regulatory pathways and guidelines

4- EXPAND PEOPLE PIPELINE

- Basic and translational researchers, clinicians, other disciplines (data scientists, biomedical engineers, pharmacologists, others)
- Diversity and Inclusion – key for disease type, care, community building and ultimately overall improved outcomes!

T1D: Take Homes

Basics:

- Autoimmune mediated loss beta cells – 5-10% of total diabetes
- Family history increases risk 15x, yet ~90% newly diagnosed do not have known family member
- Adult onset ~50% → no longer a ‘juvenile’ disease
- Insulin is the main – and essentially only – line of treatment; no disease modifying therapy available (yet!)
- Can affect anyone, anywhere, anytime

Advances:

- Understanding of pathogenesis, disease staging
- Tool for risk screening available
- Significant number of therapies in development

Opportunities:

- Collaborations to augment knowledge sharing, partnerships, translation and cross-disease research
- Training to prevent brain drain!

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THANK YOU

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