



Type 1 Diabetes: Vision for the Next 5 Years

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T1DX-QI Learning Session | November 15, 2023

JDRF: Purpose

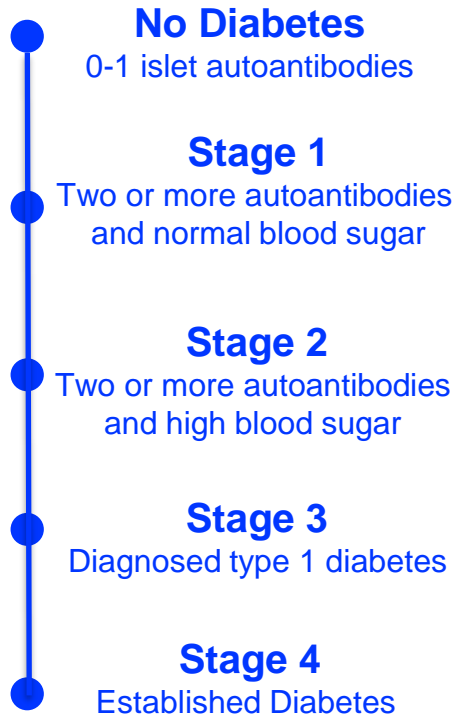
Our Vision:

A world without T1D

Our Mission:

Improving lives today and tomorrow by accelerating life-changing breakthroughs to cure, prevent and treat T1D and its complications.

Stages of Type 1 Diabetes



Risk of a
Type 1 Diabetes Diagnosis:

~70%

10 YEARS

~84%

15 YEARS

**Two or more persistent autoantibodies are a
“near certain predictor of clinical diabetes.”**

Lifetime risk approaches 100%

JDRF Research Priorities



**Global Universal
Screening**



**Disease Modifying
Therapies**



Cell Therapies



Improving Lives



**Training of
Researchers and Clinicians**

Screening

Reality and Vision of Screening for Risk of T1D

TODAY

- Low awareness about T1D stages and the benefits of knowing your risk
- Limited eligibility for and access to screening
- Insurance coverage for T1D screening is inconsistent at best
- Disease-modifying therapies are progressing slower due to these barriers

FUTURE

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

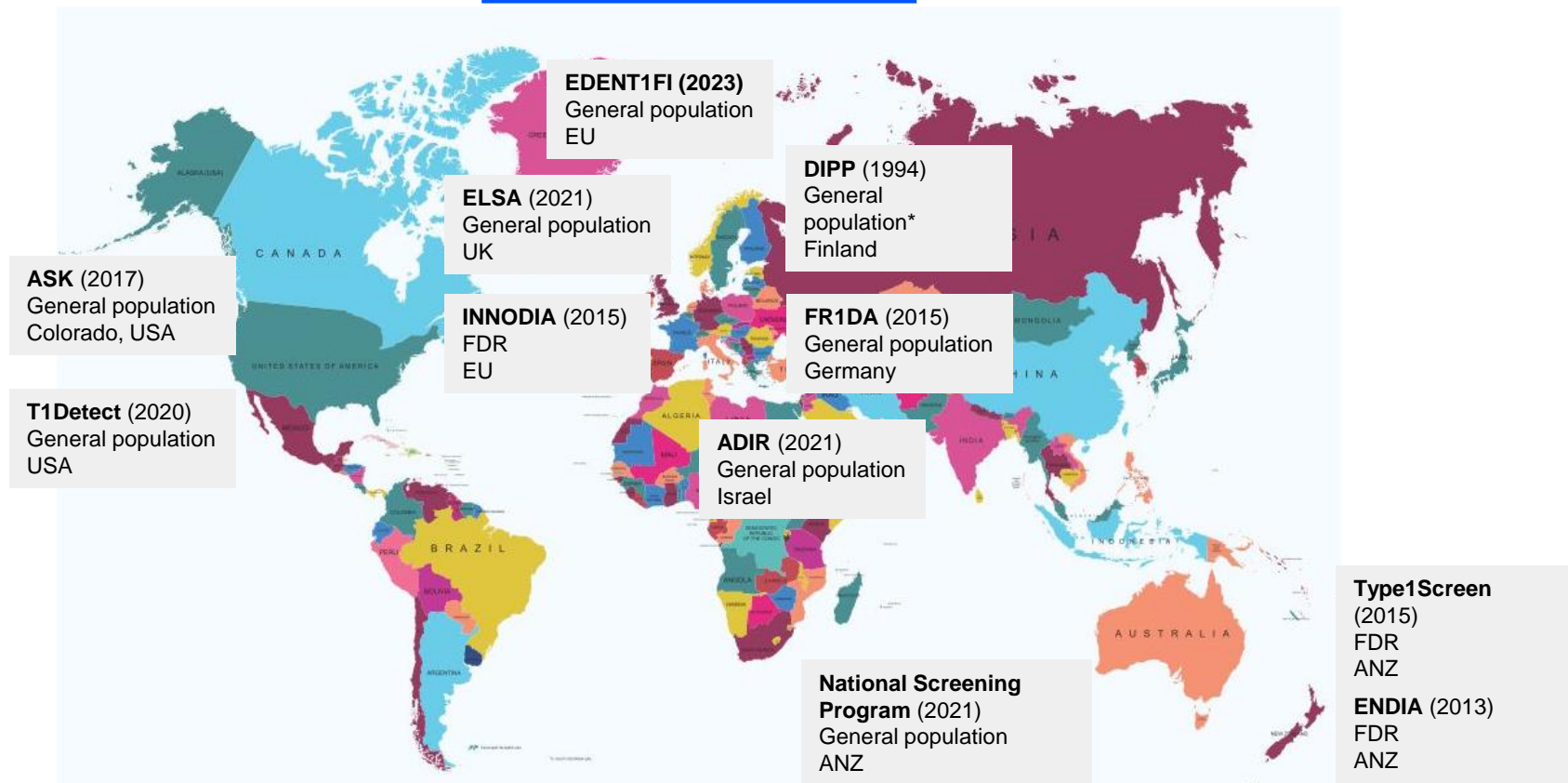
Why Screening and Monitoring for T1D risk?



General Population Screening

- Expand screening pathways to
 - reduce health consequences of DKA at diagnosis
 - increase trial recruitment
 - access to FDA approved therapies

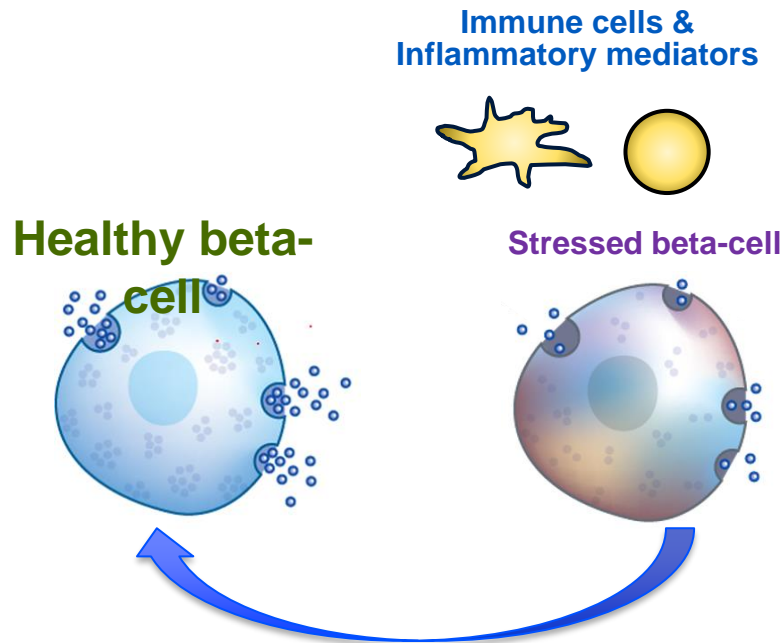
JDRF Supported Screening Programs



Disease Modifying Therapies

Reversing the Course of T1D

- Disease-Modifying Therapies (DMTs) are therapies that change the course of a disease aimed at people **at every stage of T1D**
- The goal: prevent, halt, or reverse the loss of beta cells by:
 - Rebalancing the immune system and Preserving/regrowing the beta cells
- Several DMTs are in JDRF-supported clinical trials around the world—and one, Tzield™, was just FDA approved!



The Reality and Vision of Disease Modifying Therapies

TODAY

- One FDA-approved Teplizumab-mzwv (Tziel) and several promising disease-modifying therapies in clinical trials 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
- Barriers to pivotal trials remain staggeringly high!

FUTURE

- Commercially available disease modifying therapies that slow, halt and/or reverse the progression of T1D
- Choice, access and adoption of therapies for all

First major FDA-approved therapy since insulin

Teplizumab-mzwv is the first approved disease-modifying therapy for T1D

Clinical Treatment Begins

A landmark study shows teplizumab delays the onset of T1D by 2 years in at-risk individuals

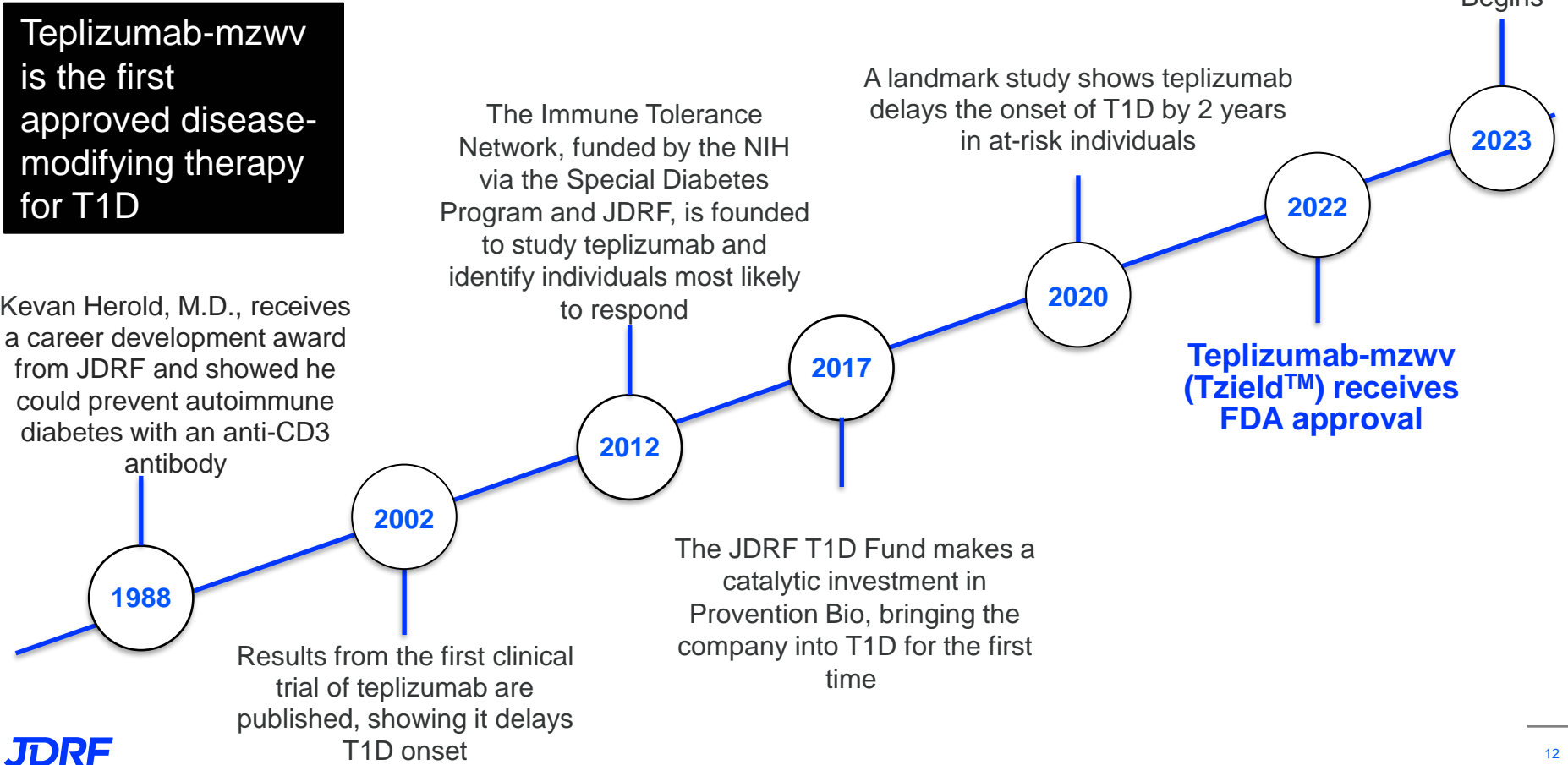
The Immune Tolerance Network, funded by the NIH via the Special Diabetes Program and JDRF, is founded to study teplizumab and identify individuals most likely to respond

Teplizumab-mzwv (Tzield™) receives FDA approval

The JDRF T1D Fund makes a catalytic investment in Provention Bio, bringing the company into T1D for the first time

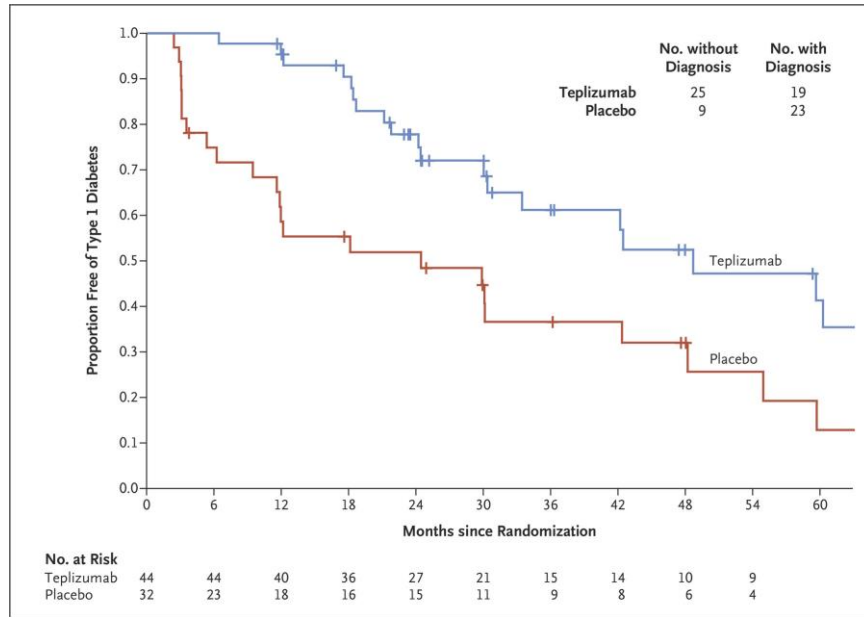
Results from the first clinical trial of teplizumab are published, showing it delays T1D onset

Kevan Herold, M.D., receives a career development award from JDRF and showed he could prevent autoimmune diabetes with an anti-CD3 antibody

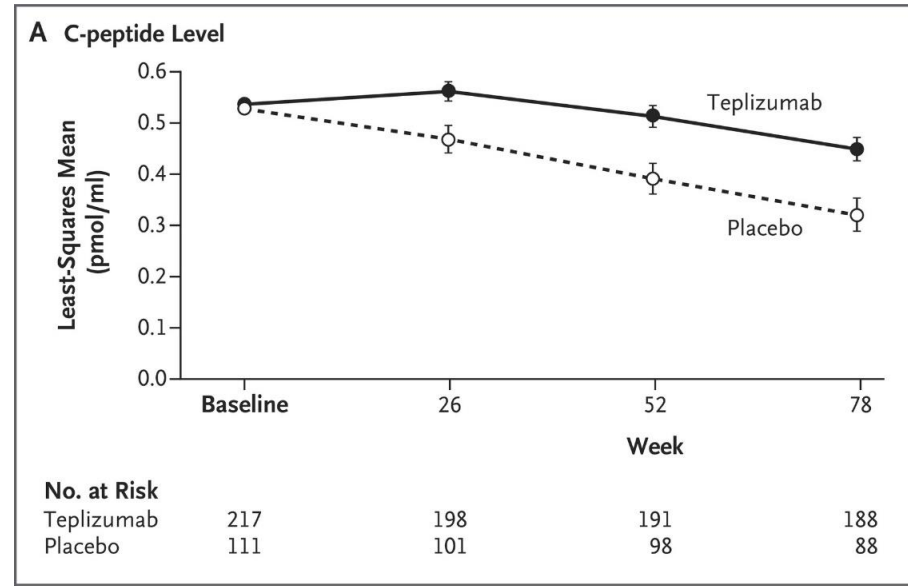


Teplizumab in Stage 2 and Stage 3 Individuals

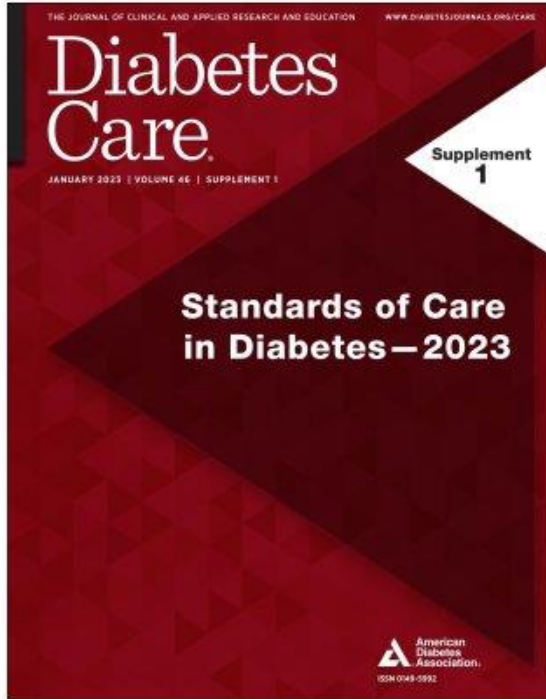
TN10 Study (Stage 2)



PROTECT Study (Stage 3)



Mid-Year Update to Clinical Guidelines



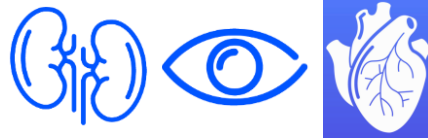
- The American Diabetes Association’s Standards of Care in Diabetes has been updated to include **Teplizumab-mzww (Tzield™)** to delay T1D in at-risk, or Stage 2, individuals
- The diagnostic criteria for T1D screening has also been updated, to be more in line with the label

Improving Lives

How we are improving lives



Drugs for glucose and
metabolic control



Drugs for complications



Devices for
glucose control



Therapies for
psychosocial burden

Unmet needs remain for people with T1D

Unmet clinical needs

- Blood glucose control is still a challenge
- Broader metabolic control is unaddressed by current therapies
- Complications remain a reality for many with T1D

Unmet mental health and quality of life needs

- People with T1D are disproportionately affected by mental health issues, which affect T1D outcomes
- Burden of disease (e.g. inconvenience of therapies, careful monitoring of diet and insulin administration, etc.) imposes a toll on all people with T1D

We have come a long way and have further to go. The IL program is developing therapies to improve health and reduce the burden of living with T1D!

The present and future of drugs and devices for T1D

TODAY

- Insulins: basal and rapid-acting
- Glucagon (rescue only); Symlin (US - limited adoption)
- SGLT inhibitors (mainly Japan)
- “Hybrid closed loop” AP systems, pumps, factory calibrated CGMs, other

FUTURE

- Next-generation insulins, widely used adjunctive therapies
- *Fully* closed loop AP systems, user-friendly devices, CGM-CKMs
- Reduced disease management burden

Breakthroughs in the last year of T1D tech

Dexcom G7 cleared by FDA and launched in US



Abbott Freestyle Libre 3 cleared by FDA



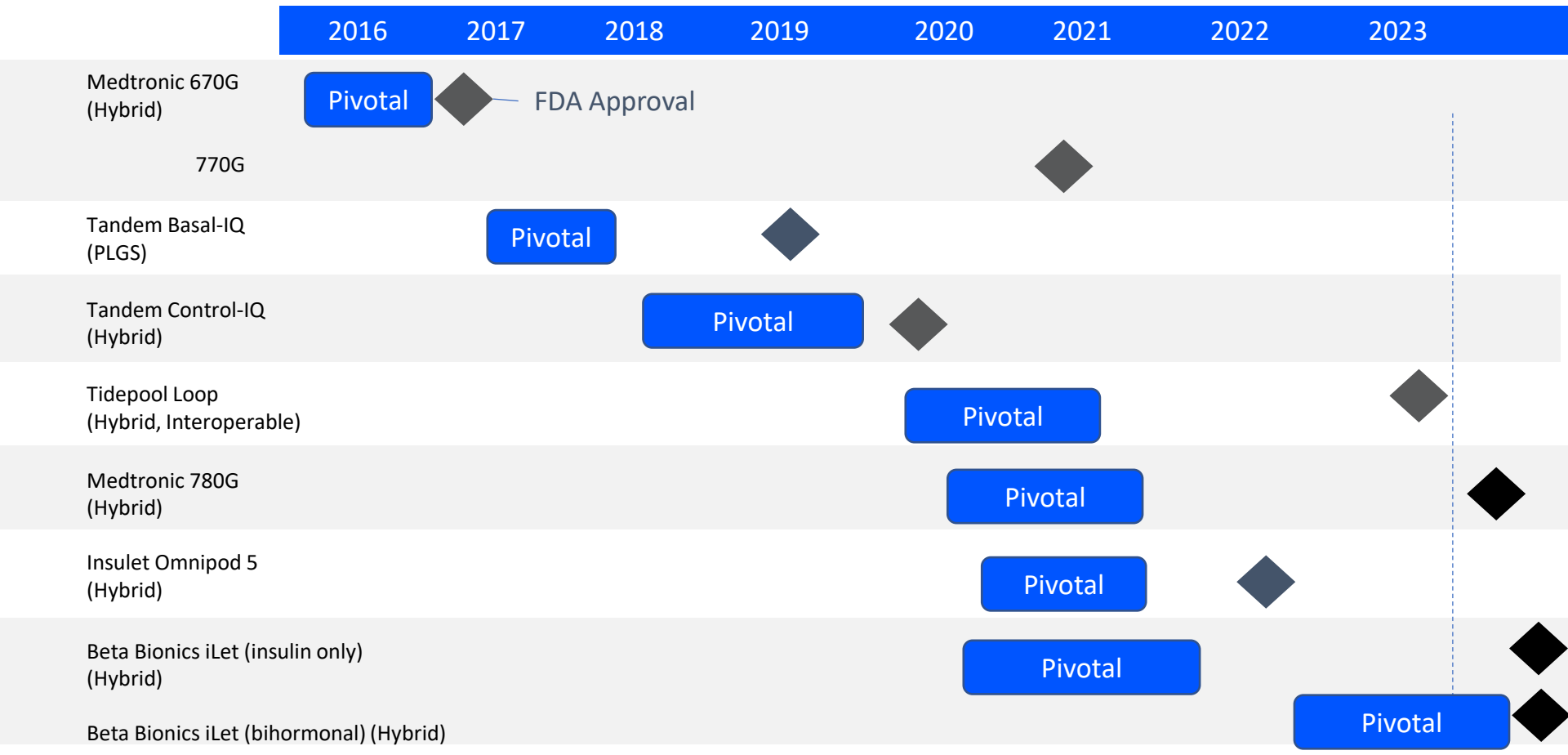
Tandem Control-IQ remote insulin bolus delivery FDA cleared



Medtronic Extended Wear Infusion Set launched



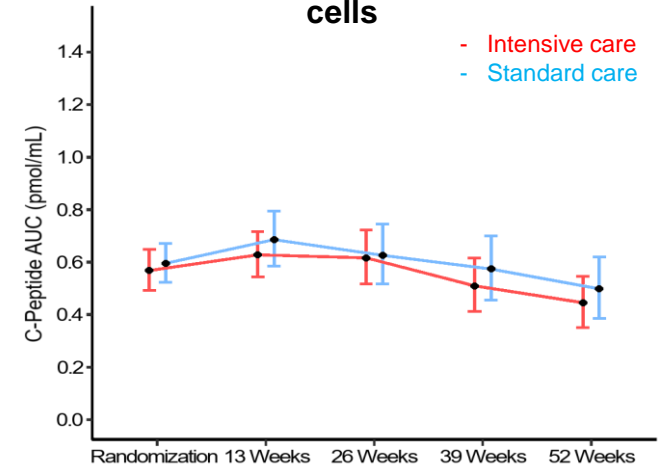
AP Systems in Development: Current Status



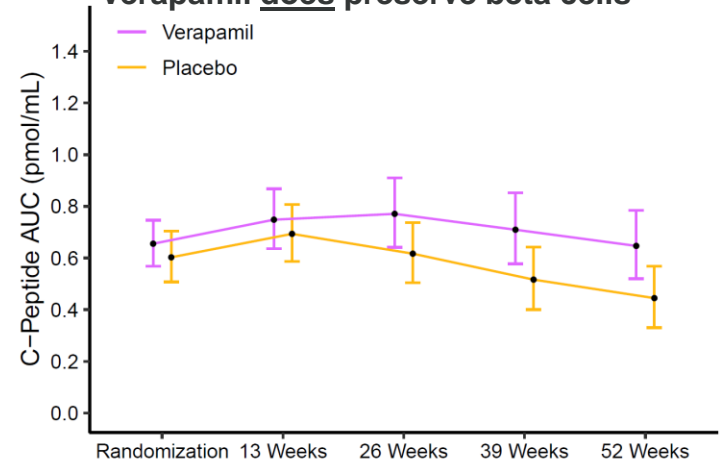
CLVer trial: AP systems and verapamil immediately after diagnosis

- Can AP systems and/or verapamil preserve beta cells (i.e. extend the honeymoon period) in the new onset population?
- **Results:**
 - **AP systems did not preserve beta cells but did provide exceptionally good glucose control in the new onset period**
 - **Verapamil preserved beta cells (~30%)— meaning they make more insulin for longer!**
- JDRF will continue to pursue research into verapamil, including using it with other drugs

Tight glucose control does not preserve beta cells



Verapamil does preserve beta cells



Urgent need for next-generation insulins

NEXT-GEN INSULINS

	Endogenous	Standard of care (s.c. insulin)	URI	LTI	GRI
Fast kinetics	✓		✓		
Physiologic distribution	✓			✓	
Glucose responsivity	✓				✓

URI: ultra-rapid insulin: lowers blood glucose quickly

LTI: liver targeted insulin: functions at the liver

GRI: glucose responsive insulin: only active when blood glucose is high

Fully closing the loop

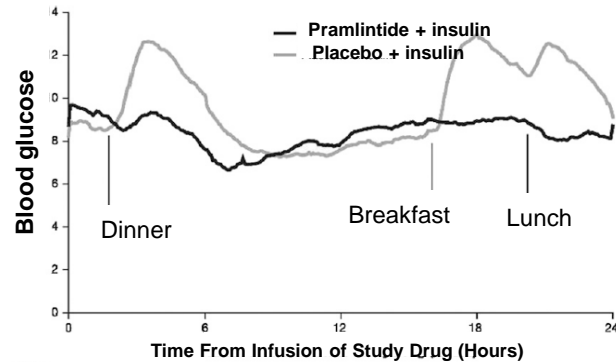
It is a JDRF priority to move from hybrid closed loop to fully closed loop systems. But how?

Ultra-rapid insulin



- Using fast-acting snail insulin as a model for new therapeutic insulins

Insulin-pramlintide co-formulation



- Co-formulation of insulin and pramlintide
- Clinical trials testing administration of insulin and pramlintide from separate pumps

Algorithms



- Trial testing a new algorithm in adolescents and young adults with high HbA1c
- Trial testing Android APS without boluses

Continuous Ketone Monitoring (CKM)

- DKA remains a dangerous complication of T1D
- Risk of DKA is further elevated in people with T1D undergoing intense exercise or taking SGLT inhibitors, which is a huge barrier to SGLTi adoption
- DKA is caused by elevated ketones
- Target product: CGM-CKM to warn of impending DKA (which can be averted by insulin and carbohydrates) with no additional on-body or mental health burden
- We have funded 5 projects!

**Funded projects-
diverse scientific
approaches to CGM-
CKM**

Koji Sode, UNC

Joseph Wang, UCSD

**Mahla Poudineh,
University of Waterloo**

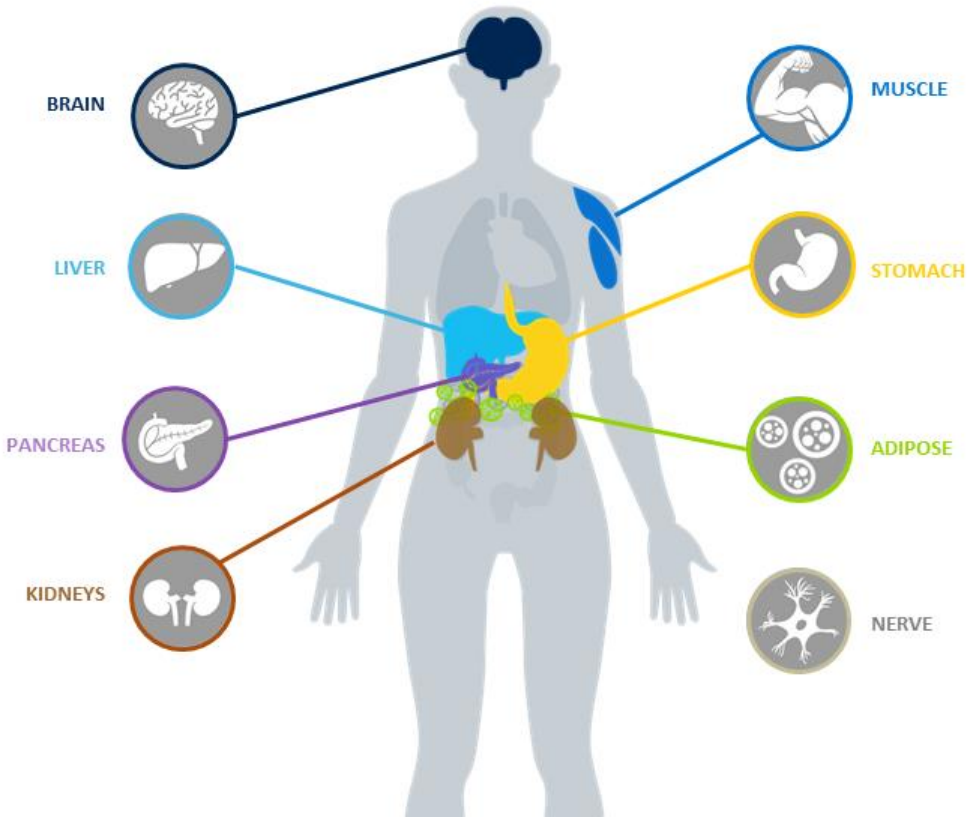
QuLab Medical

**Integrated Medical
Systems**

Co-
funded
with the
Helmsley
Charitable
Trust

ABBOTT PARK, Ill., June 3, 2022 [/PRNewswire/](#) -- Abbott (NYSE: ABT) today announced it's developing a new biowearable that will continuously monitor glucose and ketone levels in one sensor. The system has secured breakthrough device designation from the U.S. Food and Drug Administration, which is designed to expedite the review of innovative technologies that can improve the lives of people with life-threatening or irreversibly debilitating diseases or conditions.

Adjunctive therapies for T1D: Glucose control AND metabolic control



T1D metabolic imbalances

- Glucose control
- Glucagon dysregulation
- Insulin resistance
- Obesity (2/3 of adults with T1D in US registry)
- Ketones
- Lipids...

... all of these contribute to complications!

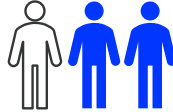
Adjunctive therapies can improve glucose control AND other metabolic imbalances, leading to better outcomes

JDRF adjunctive therapy strategy

Among people with T1D in the US:



~70% do not consistently achieve target blood-glucose control levels



2/3 of adults have obesity or overweight



~1 in 3 will develop kidney disease



~2 in 3 will develop heart disease

- Goals: To develop adjunctive therapies to be approved for T1D and included in clinical guidelines
- De-risk private sector investment
- Spread the message: **The future of T1D care is multiple drugs taken safely and conveniently for glucometabolic control and long-term health**

Foster NC, et al. *Diabetes Technol Ther.* 2019;21(2):66-72.

Wallace AS, et al. *JCEM.* 2022;107(5):1247-1256.

Diabetes - a major risk factor for kidney disease. *National Kidney Foundation.*

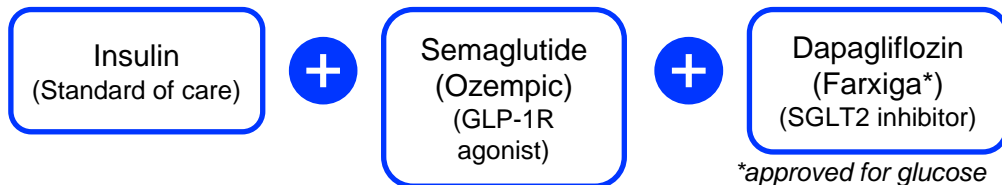
Schofield J. *Diabetes Ther.* 2019;10(3):773-789.

Multi-drug approach to metabolic control and prevention of complications

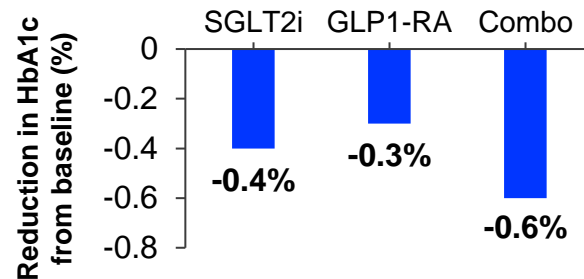
- State of the art drug combinations improve outcomes in T2D
- The future of T1D care is multiple drugs taken safely and conveniently to improve short- and long-term health
- “Glucose +” approach: obesity, insulin resistance, lipids, blood pressure, heart and kidney health, etc.

JDRF Role:

- These drugs and drug combinations need to be tested in T1D to guide clinical care and “de-risk” private sector investment
- JDRF-supported multi-drug trial: Effects of Insulin + Ozempic + Farxiga on metabolic control



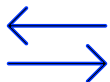
**approved for glucose control in T1D in Europe and Japan*



Retrospective analysis of the EHRs of 296 people with T1D over 12 months found the combination of SGLT2i + GLP-1RA therapy to be most effective in reducing HbA1c

- Other JDRF support for drug combinations under evaluation
- SGLT + GRA
 - SGLT + pioglitazone

Adjunctive therapies – What should the future look like for T1D care?



Develop novel and repositioned treatments

Many drugs for T2D and other indications are beneficial for T1D too!
Trials in T1D are essential!



Reduce the burden

Oral drugs, once weekly injectables are more convenient



Shift the paradigm

Not just glucose control!
We need greater focus on glucometabolic health and preventing long-term complications



Maximize lasting benefits

Multiple therapies are needed to achieve optimal metabolic control

Complications and Psychosocial Health

The reality and vision of Improving Lives

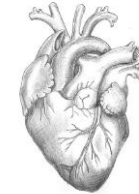
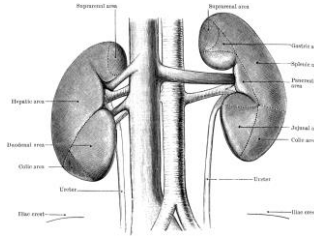
TODAY

- Lucentis/Eylea/Vabysmo/Beovu (eye disease)
- **No** targeted therapy for kidney or heart disease
- Need for more, validated psychosocial interventions

FUTURE

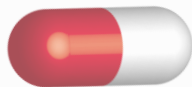
- Therapies that prevent, delay, or reverse diabetic retinopathy, renal decline, and cardiovascular disease
- Diabetes-focused behavioral health interventions that improve the mental health of people with T1D

Long-term Complications: Eye, Kidney, Heart



- Diabetic retinopathy (DR): a long-term complication of T1D that can cause vision loss
- Global estimate for proliferative DR in people with >20 years T1D is 40%. But rates in different populations vary widely!
- Approved therapies represent a major advance but have limitations (health risks, effectiveness, access)
- Diabetic nephropathy (DN): a long-term complication of T1D that affects kidney function
- Estimated that more than half of people with T1D will be affected by DN
- No approved, targeted therapies for T1D
- CVD : a long-term complication of T1D that affects the cardiovascular system (heart, brain, other)
- Major cause of mortality in T1D
- No approved, targeted therapies for T1D

T1D-exclusive trials with drugs in development (or approved) for T2D heart and kidney disease

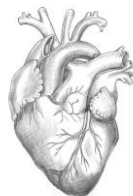


Sotagliflozin (Inpefa)

SGLT inhibitor

Approved for HF in T2D

T1D HF: Dr. Ify Mordi

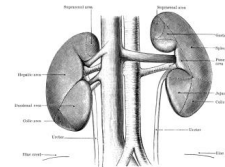


Semaglutide (Ozempic)

GLP-1

Approved for CVD in T2D

T1D trial: Dr. Viral Shah



Semaglutide (Ozempic)

GLP-1

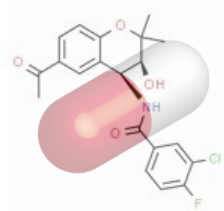
Under investigation for DN in T2D

T1D trial: Dr. Ian de Boer

Oral medications for DR

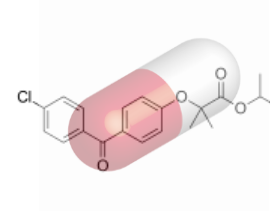
Current therapies are life-changing, but we also need new ones— especially non-invasive options

Xiflam



- Anti-inflammatory drug
- Repurposed drug-- safe and convenient
- Clinical trial is about to kick off!
- Potential benefits for kidney as well
- Collaboration with DRCR Network, NIH, InflammX Therapeutics

Fenofibrate



- Generic lipid-lowering medication
- Repurposed drug— safe, convenient and cheap
- Definitive clinical trial is ongoing
- Collaboration with DRCR Network, NIH, Roche, and Helmsley Charitable Trust

Potential benefits: protection of vision *and* quality of life

Driving Better Outcomes in T1D

Today

Current therapies are a major advance but have limitations

There are no approved, targeted therapies for T1D

There are no approved, targeted therapies for T1D



Future

New therapies are developed to both treat vision loss due to diabetic retinopathy and, eventually, restore vision

People with T1D are included in clinical trials, leading to approval of new therapies to treat diabetic nephropathy and cardiovascular disease

JDRF Psychosocial Strategy



Standardize measures of psychological outcomes



Increase the number of psychosocial interventions



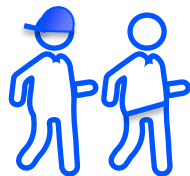
Increase the number of trained psychology professionals



Increase access to psychosocial interventions



Children



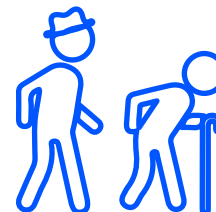
Adolescents



Young adults



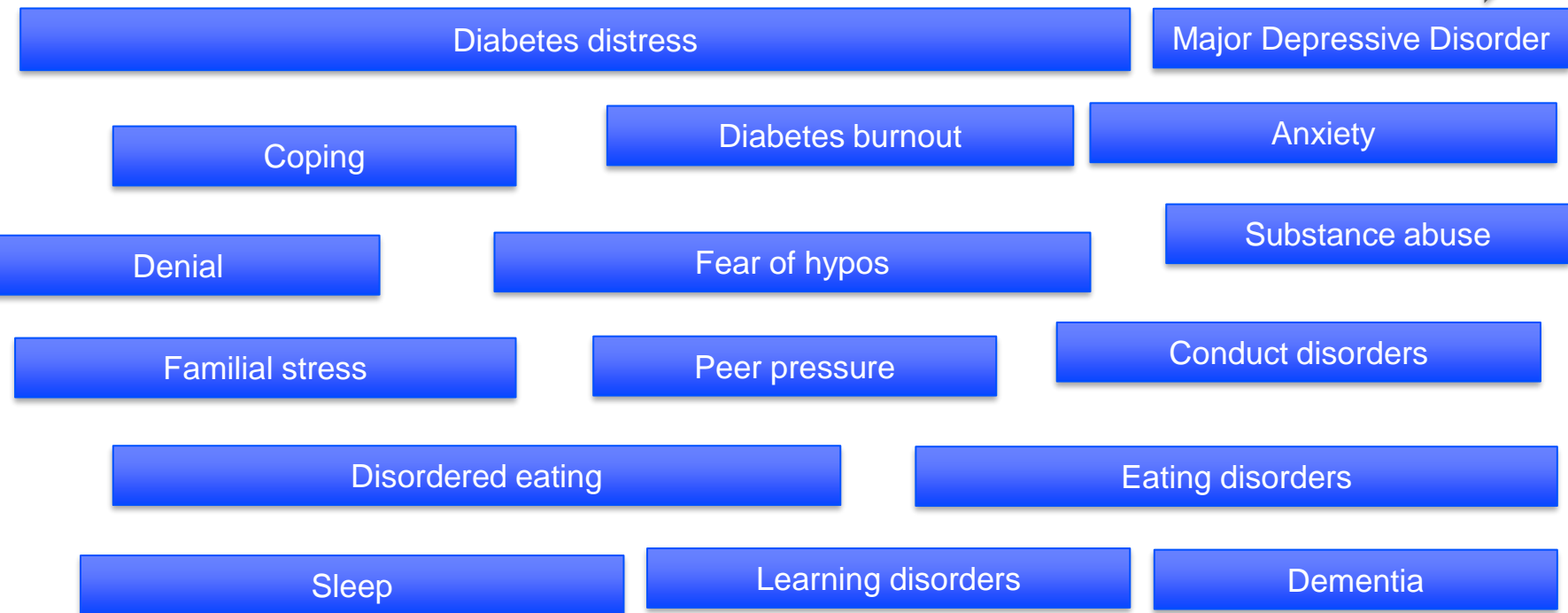
Adults



Older adults

Subclinical symptoms

Diagnosed psychiatric conditions



Subclinical symptoms

Diagnosed psychiatric conditions

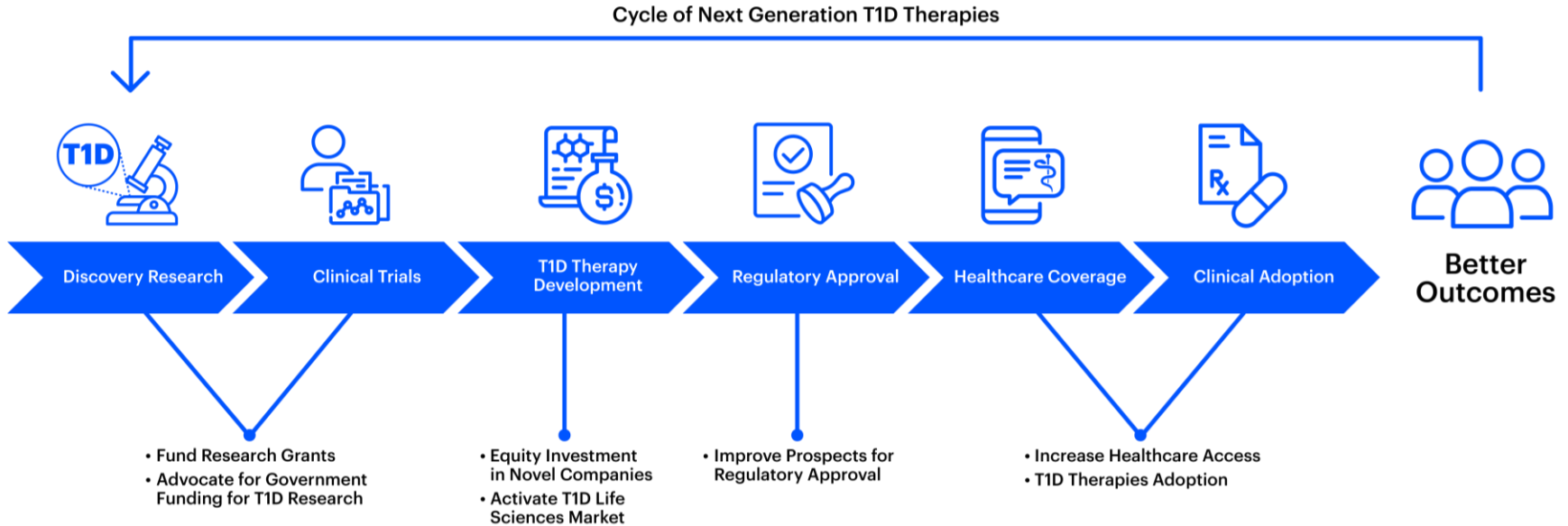


Psychosocial Clinical Trials

ReDUCE	Reducing Diabetes Distress in Young Adults Using Cognitive Behavioral Therapy	Diabetes Distress
THRIVE app	Positive psychology	Diabetes Distress
Tripple T	Family support during first year after diagnosis	Diabetes Distress
The UP study	CBT based approach that takes a holistic view on depression and anxiety	Anxiety & Depression
BodyProject	eating disorder prevention program for young people with T1D	Disordered Eating
iACT	a novel mHealth intervention for eating disorders in T1D	Disordered Eating

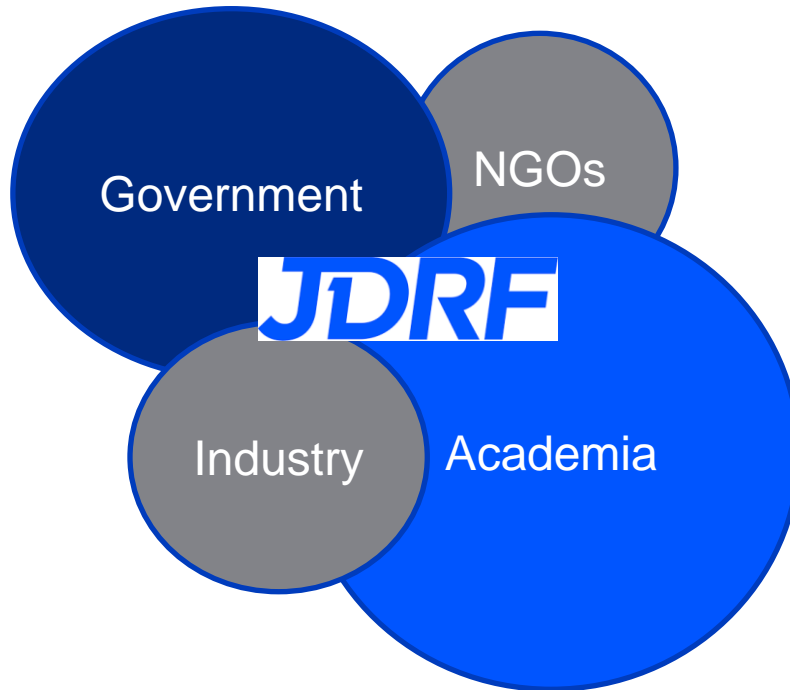
Advance Therapies: Our Strategic Approach

Drive more new therapies through the research and development (R&D) pipeline, from discovery research and clinical trials to therapy development, regulatory approval, and healthcare access. We call this our “pipeline strategy.”



Accelerating Research through Strategic Collaborations

JDRF collaborates on T1D research and advocacy efforts with a variety of partners



THANK YOU

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