Coordination of Screening and Early Detection Efforts

Esther Latres, Ph.D. | SVP Research

8th Annual Diabetes Screening Symposium, Denver

November 10, 2025

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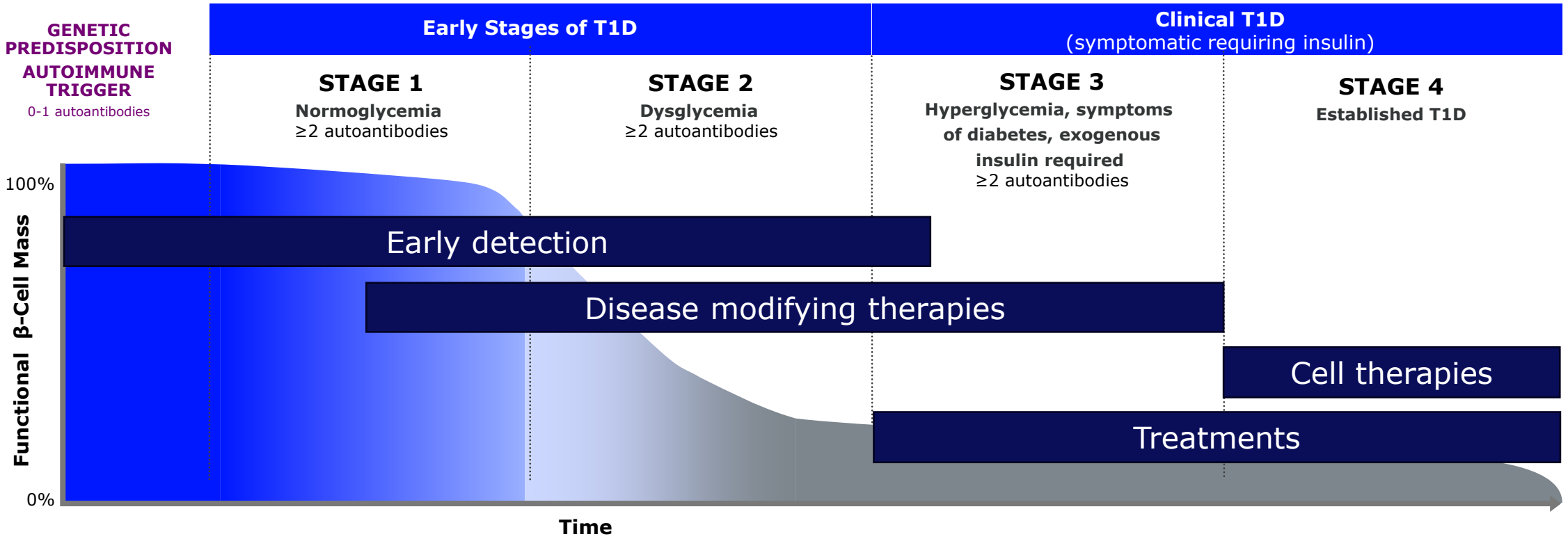
Create a Strategy to Meet our Vision “A world without T1D”



Insel et al. Diabetes Care 2015;38(10):1964–1974

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Our vision for early detection

A future where T1D is:

- Identified years before individuals need insulin
- Accompanied by effective preventive therapies
- Integrated into healthcare systems globally

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Breakthrough *T1D Early Detection* History

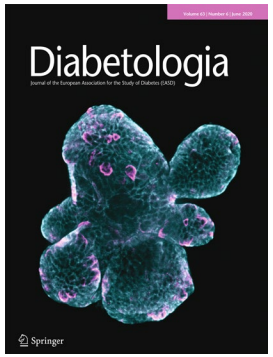
Past: Providing evidence for screening in research

- Feasibility of screening
- Ability to predict disease progression – Staging of T1D
- Benefits of screening, including DKA prevention, time to plan and prepare, potential to participate in research aimed at identifying therapies to delay and prevent T1D

Priorities in Early Detection and Monitoring to:

1. Delay insulin dependence through approved disease-modifying

- Accelerate clinical trial recruitment and drug development
  - Clinical study design
  - Immune/glycemic/molecular biomarkers of progression



2. Access: Clinical guidelines for expansion into clinics- Diabetes Care and Diabetologia in 2024

What's next- **SCREENING CONSENSUS GUIDANCE**

3. Move towards adoption by healthcare systems

- The strongest evidence for a T1D recommendation is in children with family history
- There is robust evidence supporting early detection of T1D in the general pediatric population, and we continue to build evidence to support broader implementation

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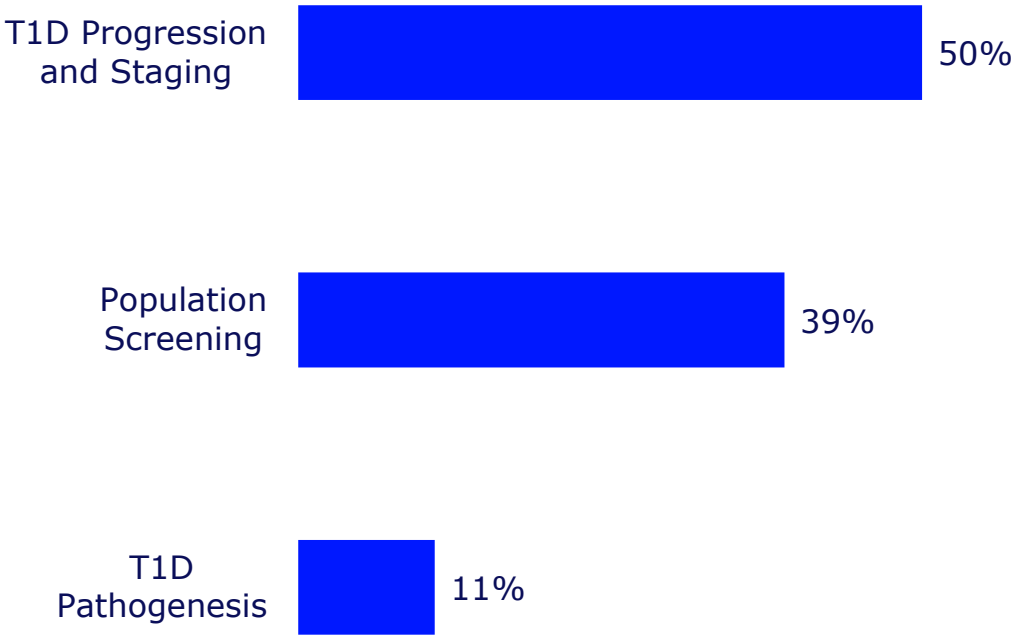
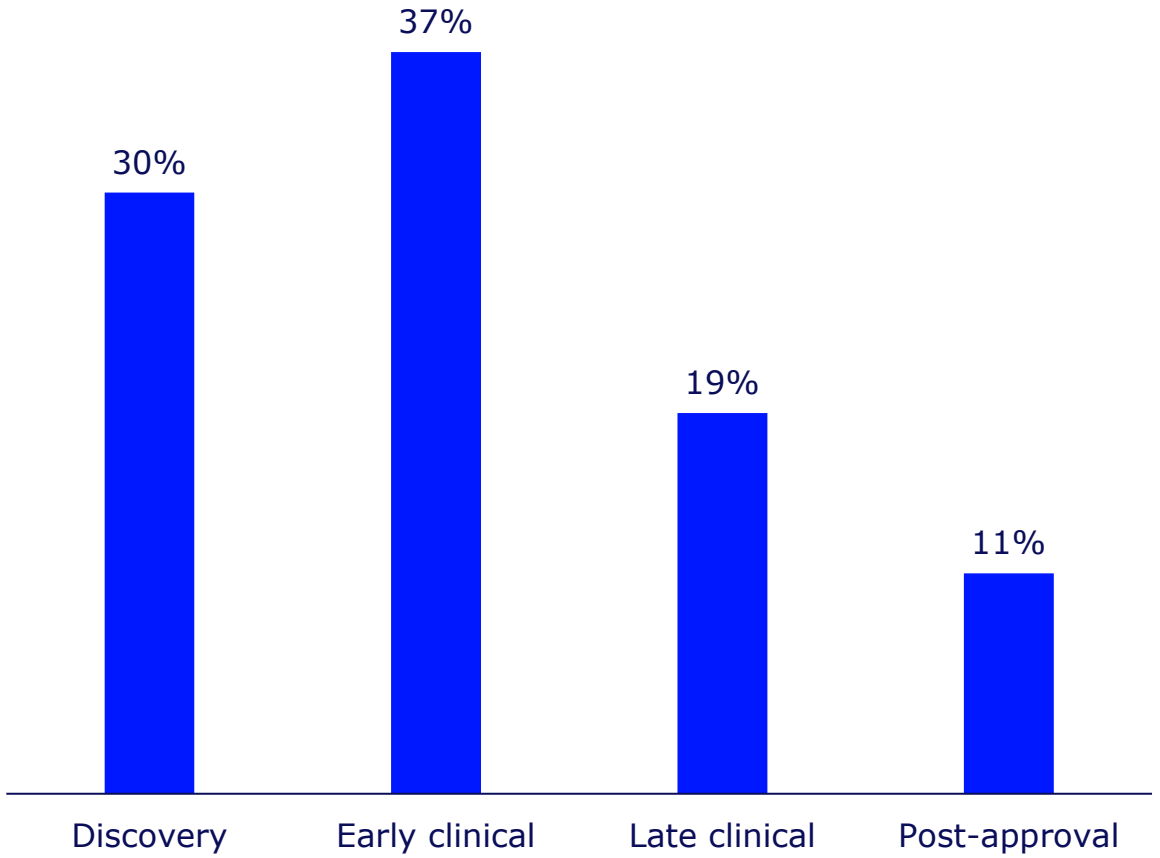
Breakthrough T1D Early Detection Portfolio Overview

$60M funded across 84 grants

Early Detection Funding Areas



Early Detection Development Pipeline



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Research Priority:
Provide evidentiary research for clinical implementation of screening and monitoring

- Improve glycemic assessment of disease progression in individuals at early stages, as they transition from presymptomatic disease to clinical diagnosis:
  - RFA ”Glycemic and Beta Cell Monitoring in Individuals at Risk of Type 1 Diabetes” (FY24)
  - Broader harmonization/standardization program is needed for current and emerging CGM devices to be implemented in early stages of T1D.
- Validate a comprehensive Genetic Risk Score to expand global screening (Newborn Screening)
- Improve Adult T1D Detection

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Current Screening Programs Landscape

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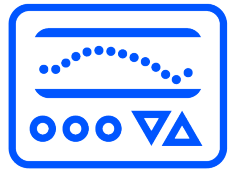
FY25 Breakthrough T1D Early Detection RFAs Addressing Monitoring, Adult-onset, and Genetics

Beyond Pediatrics: Advancing Early Detection in Adult-Onset Type 1 Diabetes

- Improve the diagnosis of adult onset T1D, with a focus on early detection and understanding of disease progression

Advancing Genetic Risk Assessment for Type 1 Diabetes: Improving Prediction and Clinical Translation

- Develop population specific and trasn-ancestry T1d genetic risk scores that advance toward clinical validation and regulatory approval



Development of Continuous C-Peptide Monitoring Technologies

- Develop and advance continuous C-peptide monitoring (CCPM) technologies to enable real-time, user-friendly assessment of beta cell function.

Focus: Technology, detection in interstitial fluid (ISF)

Goal: enhance research capabilities, deepening understanding of progression, and support development and evaluation of disease-modifying and cell therapies.

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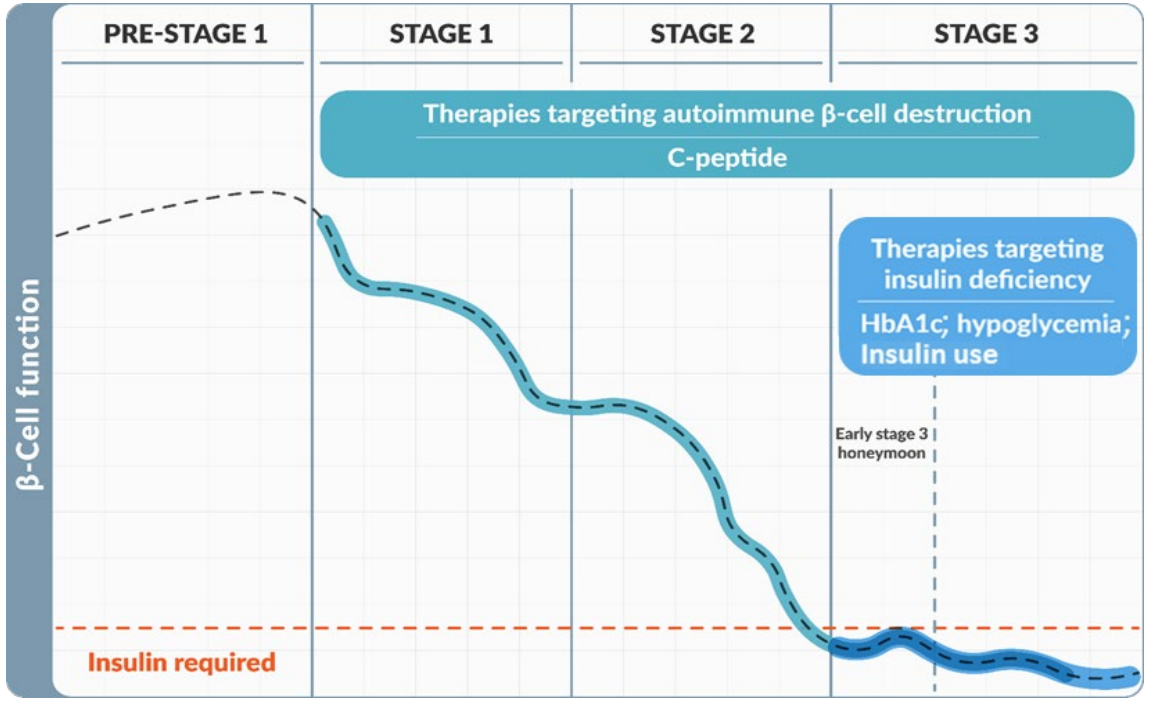
Research Priority:
Accelerating clinical trials of disease modifying therapies



Therapies that address the **insulin deficiency** of T1D aim to improve **glycemic control**

- **Assessment:** HbA1c, hypoglycemia, insulin use, time-in-range, others

Disease modifying therapies (DMTs) target the underlying **autoimmune disease** and aim to **preserve beta cell function**

- **Assessment:** beta-cell function (typically via **C-peptide**)

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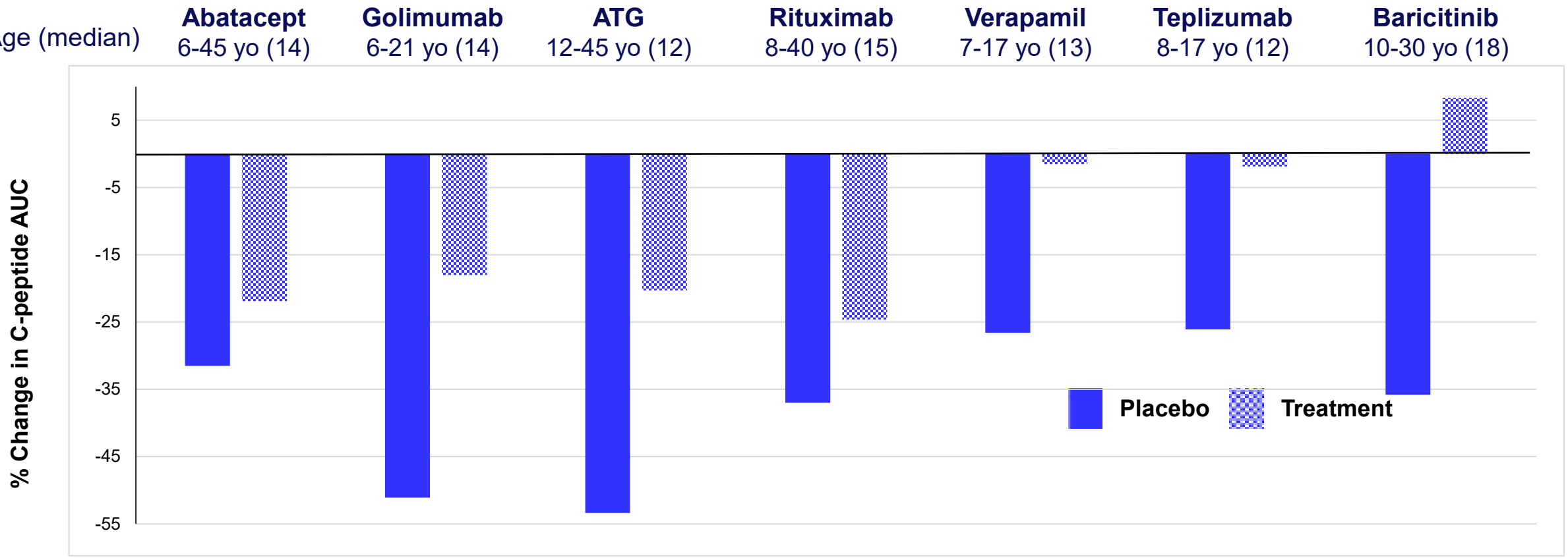
Multiple therapies show efficacy (preservation of β-cell function) in pediatric and adult **Stage 3 T1D**

Changes in C-peptide, baseline vs endpoint (12 months)



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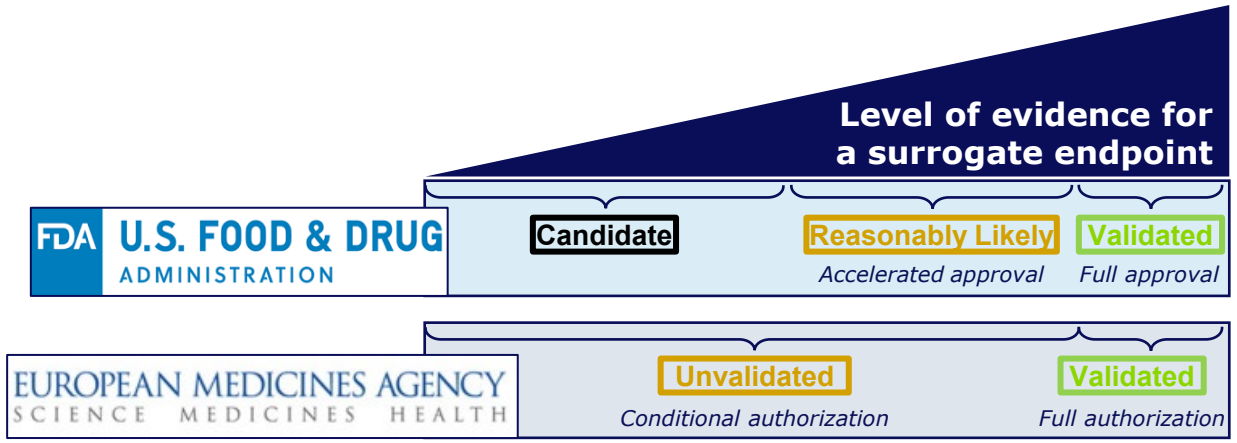
Accelerating Stage 3 T1D clinical trials of disease modifying therapies:

Regulators consider C-peptide a surrogate endpoint

- Predicts, but does not directly measure, a therapy's benefits
- Allows clinical trials to be shorter, smaller, less complex, and/or less burdensome for trial participants

Regulatory status of C-peptide:

- FDA: **reasonably likely surrogate endpoint** that can support *accelerated approval*
- EMA: **unvalidated surrogate endpoint** that *could* support *conditional marketing* (*unlikely in T1D)



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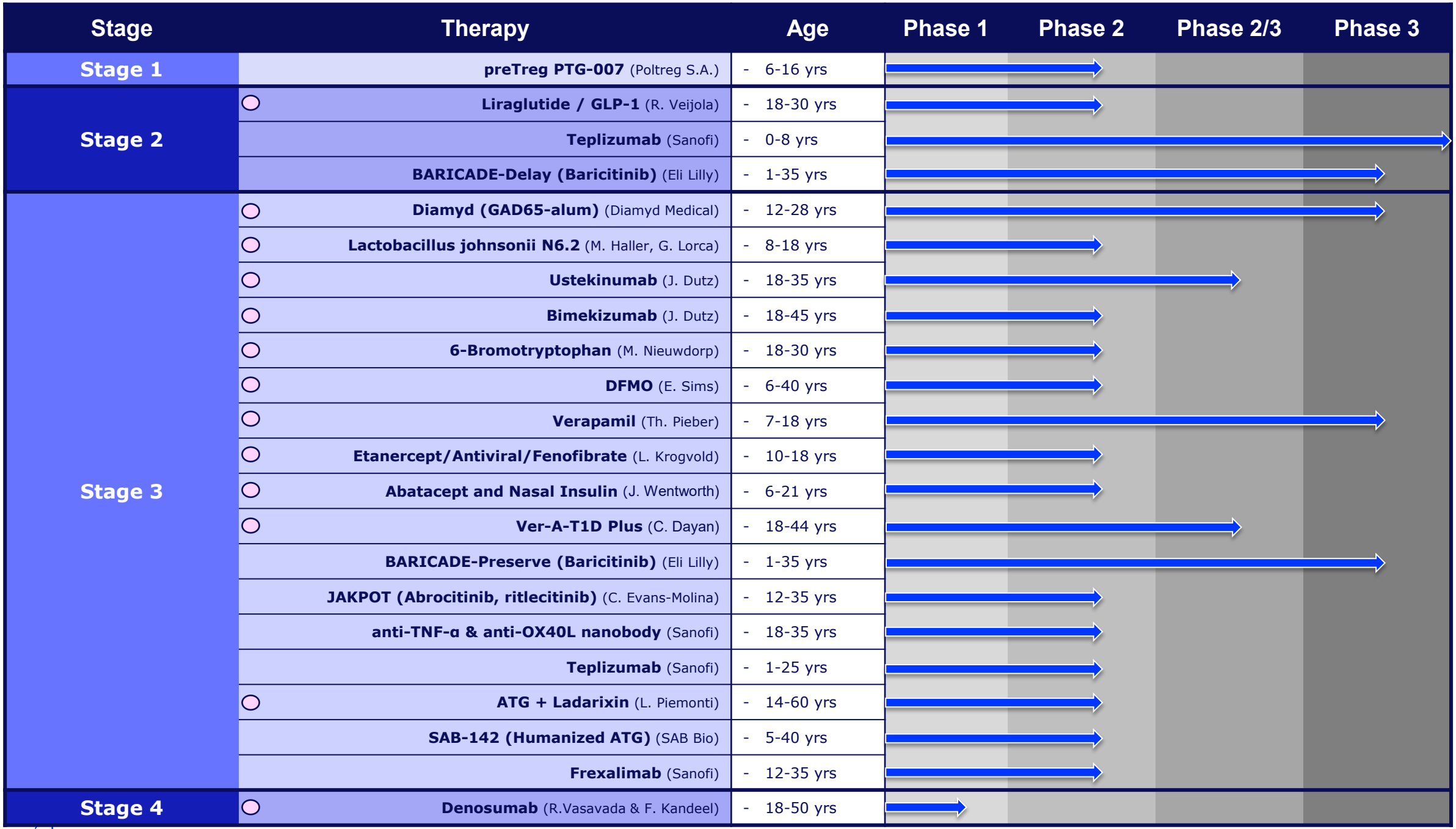
Stage
Therapy
Age
Phase 1
Phase 2
Phase 2/3
Phase 3
Stage 1
preTreg PTG-007 (Poltreg S.A.) - 6-16 yrs
Stage 2
Liraglutide / GLP-1 (R. Veijola) - 18-30 yrs
Teplizumab (Sanofi) - 0-8 yrs
BARICADE-Delay (Baricitinib) (Eli Lilly) - 1-35 yrs
Stage 3
Diamyd (GAD65-alum) (Diamyd Medical) - 12-28 yrs
Lactobacillus johnsonii N6.2 (M. Haller, G. Lorca) - 8-18 yrs
Ustekinumab (J. Dutz) - 18-35 yrs
Bimekizumab (J. Dutz) - 18-45 yrs
6-Bromotryptophan (M. Nieuwdorp) - 18-30 yrs
DFMO (E. Sims) - 6-40 yrs
Verapamil (Th. Pieber) - 7-18 yrs
Etanercept/Antiviral/Fenofibrate (L. Krogvold) - 10-18 yrs
Abatacept and Nasal Insulin (J. Wentworth) - 6-21 yrs
Ver-A-T1D Plus (C. Dayan) - 18-44 yrs
BARICADE-Preserve (Baricitinib) (Eli Lilly) - 1-35 yrs
JAKPOT (Abrocitinib, ritlecitinib) (C. Evans-Molina) - 12-35 yrs
anti-TNF-α & anti-OX40L nanobody (Sanofi) - 18-35 yrs
Teplizumab (Sanofi) - 1-25 yrs
ATG + Ladarixin (L. Piemonti) - 14-60 yrs
SAB-142 (Humanized ATG) (SAB Bio) - 5-40 yrs
Frexalimab (Sanofi) - 12-35 yrs
Stage 4
Denosumab (R.Vasavada & F. Kandeel) - 18-50 yrs
Breakthrough T1D - Funded

Looking Ahead: Disease Modifying Therapies

Accelerators and Initiatives to Drive Clinical Progress

DMTs for Stage 1/2

Product Development: Generation 1/2/3

- Stage-Specific Considerations for DMTs
- Adaptive Combination Trial Platform
- Clinical Translation of Targeted Delivery of Regen DMTs
- Guidance for Early-Stage Clinical Trials
- International T1D Clinical and Mechanistic Minimal Protocol
- Regulatory Advancement of Tolerizing DMTs
- Translation of DMTs to Beta Cell Replacement
- DMT Clinical Trial Guidelines
- T1D Cures Accelerator Biomarkers of Progression/Response
- Markers of Beta Cell Health Consortium
- B Cell-Directed Therapies for T1D

DMTs for Stage 3/4

Product Development: Generation 1/2/3

- Publications and Guidance
- International Consortia / Initiatives
- Strategic Funding Priorities

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Disease Modifying Therapies

IDDPs: Supporting Gap-filling **Products** through Industry Collaborations

Company	Product	Status
DIAMYD MEDICAL	TOLERIZING THERAPY Intralymphatic injection of GAD-alum for tolerization in individuals who are HLA-DR3-DQ2 positive	Phase 3 ongoing. Interim analysis in April 2026 for Accelerated Approval in Stage 3. Fast Track Designation for Stages 1 and 2.
Integrated nanotherapeutics	TOLERIZING THERAPY LNP co-delivery of mRNA-based antigen and immunomodulation	Continuing preclinical development.
EVOQ THERAPEUTICS	TOLERIZING THERAPY Novel "Nanodisc" delivery of tolerizing antigens	Promising preclinical data. Licensing deal with Sanofi for continued development of the platform.
NEURODON	BETA CELL SURVIVAL Developing SERCA activators to improve β-cell ER function and reduce β-cell stress	Completing synthesis and characterization of pre-clinical leads in *in vivo* models.
insphero	ENABLING REGENERATION TX High-throughput islet organoid platform (hIsMT) for pre-clinical pharmacological development of regenerative and combination tx	Completing testing and validation experiments for multiple identified targets in the islet organoid platform.

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Breakthrough T1D is focused on driving early detection forward with three approaches

Research

Building evidence for the feasibility and acceptability of early detection and monitoring in the clinical setting

Health Policy

Affordable access to T1D early detection, monitoring, and disease modifying therapies

Clinical Adoption

Health care provider education, clinical guidelines, and implementation science

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Advocacy Efforts to Expand T1D in Early Detection

Application to USPSTF

- Submitted on May 19th
- Application recommended general population pediatric screening for T1D
- Letters of support for T1D screening
  - Congressional letter
  - Letter signed by 13 diabetes focused organizations and 40+ KOLs

What's Next for 2026

- Continue to engage USPSTF in application process
- Directly engage Congress and senior leaders at HHS on USPSTF and T1D early detection

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Medical Affairs Progress to Date

Consensus Clinical Guidelines

- Early Stage Monitoring
- Screening
- Continuous Ketone Monitoring
- ADA Ketone and DKA Guidance

Educate Healthcare Professionals

- 7,707+ HCPs received accredited CME to date
- European CME under contract
- HCP landing page launched

Early Detection Pilot Clinics

- 10+ contracts
- 40+ sites
- 2500+ screened to date
- IAb+ individuals identified
- 1 teplizumab infusion

Clinical Trial Education Program

- 53 active clinical trial education volunteers
- 13,000+ people opt in to Clinical Trial Communication
- Participant Advisory Council widely utilized

Recent workshops:
International Consensus on the Clinical Adoption of Cell Replacement Therapies, Now and in the Future
Pilot workshop establishing Centers of Reference for Cell Therapies

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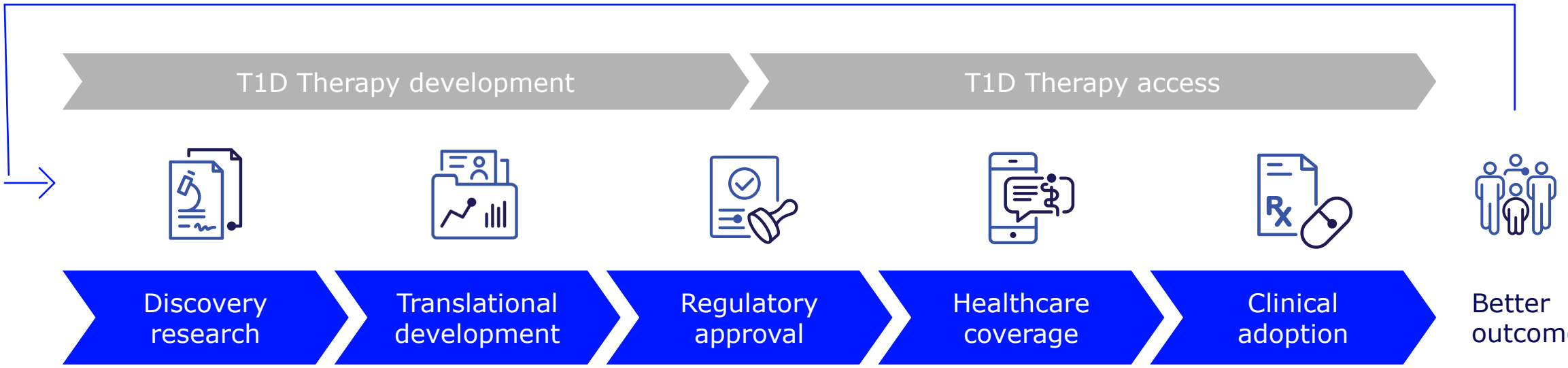
Progress at every step of the pipeline

Cycle of next generation T1D therapies



- 450+ active grants right now (including 75+ clinical trials)
- Provide research evidence for the benefits of screening
- First manufactured islet therapy in pivotal trials
- GLP-1 receptor agonists in trials for T1D

- Advocating for C-peptide as a clinical trial endpoint
- Upcoming publications to streamline regulatory pathway to approval

- Unique ICD-10 codes for stage 2 T1D
- Application submitted to USPSTF to cover screening

- Creation of Medical Affairs unit
- Development of HCP education
- Workshops for consensus guidelines

Patient Reported Outcome (PROMs)

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Thank you.

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Lilly launches DMT trials in Stage 2 and 3 T1D

- Lilly announced two clinical trials to determine the effectiveness of baricitinib in stage 2 and 3 T1D.
  - BARICADE-DELAY is investigating if it can delay progression from stage 2 T1D to stage 3 T1D
  - BARICADE-PRESERVE is investigating if it can preserve beta cell function of newly diagnosed stage 3
- Breakthrough has supported JAK inhibitors in T1D for years.
- These studies are built on the findings of the Breakthrough T1D-funded BANDIT study.
- **Help recruit!**

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Tzield receives voucher for expedited review in stage 3 T1D

What it is:

- Sanofi's Tzield has been accepted into the FDA Commissioner's National Priority Voucher (CNPV) program for people with stage 3 T1D.
- This could reduce the review time to 1—2 months.

Why it matters:

- If Tzield is approved for stage 3, newly diagnosed individuals will have the option to treat the root cause of T1D, not just the symptoms, and preserve critical beta cell health.
- If approved, it would be the first disease-modifying therapy approved for use in adults and children ages 8 and older in stage 3 T1D.

Sanjoy Dutta, Ph.D.
Chief Scientific Officer

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