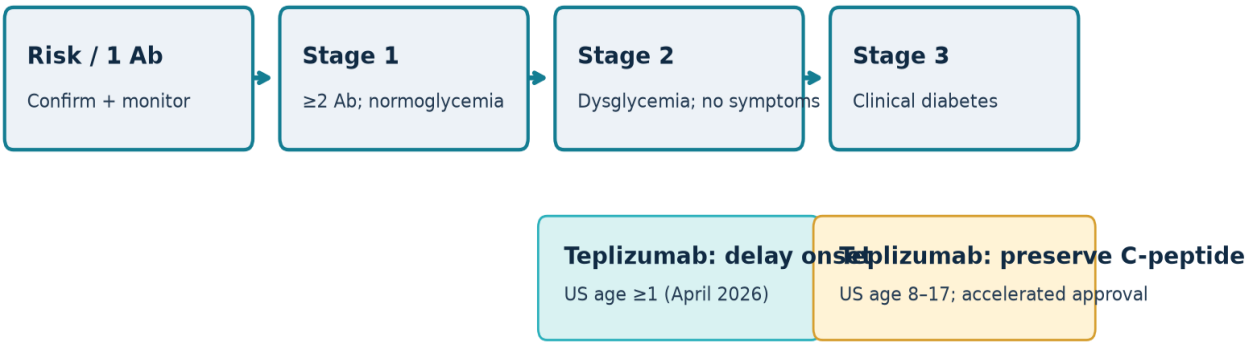
TYPE 1 DIABETES IN 2026

Breakthroughs in Cure Research, Cell Therapy, Immunomodulation, and Advanced Management

Disease modification is stage-specific



Insulin, CGM/AID, education, acute-safety planning, and complication prevention continue at stage 3.

A clinical evidence review current to 21 July 2026

For endocrinologists, specialist teams, and translational researchers

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Evidence review current to 21 July 2026 Audience: endocrinologists, diabetologists, transplantation clinicians, diabetes-technology teams, and translational researchers

Clinical boundary. This is a professional evidence synthesis, not individualized medical advice. Experimental cell products, off-label adjunct pharmacotherapy, and immunomodulators require trial or specialist governance. Insulin must never be stopped on the basis of a research result or detectable C-peptide alone.

Executive summary

Type 1 diabetes (T1D) entered 2026 with two distinct forms of progress. First, replacement biology has crossed a credibility threshold: manufactured stem-cell-derived islets can restore glucose-responsive insulin secretion and, in selected recipients receiving chronic immunosuppression, produce insulin independence. Second, disease modification is now a clinical reality, although not a cure: teplizumab can delay progression in presymptomatic disease and, after a June 2026 US accelerated approval, can be used to delay loss of endogenous insulin production in recently diagnosed children and adolescents. At the same time, automated insulin delivery (AID) has become the practical standard against which any “breakthrough” must be judged.

The strongest cell-replacement evidence is the phase 1–2 FORWARD study of zimislecel, an allogeneic, pluripotent-stem-cell-derived islet product infused into the portal vein. In 14 adults with longstanding T1D, impaired hypoglycemia awareness, and recurrent severe hypoglycemia, all 12 who received the full dose had engraftment and no severe hypoglycemic events after day 90; 10 of 12 were insulin-independent at day 365. The study was small, single-arm, selected for extreme clinical need, and required chronic immunosuppression. It demonstrates biologic efficacy—not yet broad safety, durability, comparative effectiveness, or a population-scale cure [1].

The immune barrier remains decisive. FDA-approved donor-islet therapy, donislecel (Lantidra), can confer years of insulin independence in some adults with recurrent severe hypoglycemia, but donor scarcity, portal-infusion risk, variable potency, and immunosuppressive toxicity restrict its role. Among 30 registrational recipients, 21 achieved at least one year of insulin independence, while five achieved none; most experienced at least one serious adverse reaction related to infusion or immunosuppression [2]. A single-person 2025 report of gene-edited, hypoimmune donor islets surviving and secreting insulin without immunosuppression is scientifically important but is not evidence of insulin independence, scalability, or long-term immune escape [3]. An autologous chemically reprogrammed islet transplant produced one-year insulin independence in one woman, but interpretation is complicated by concomitant immunosuppression for a prior liver transplant and by the bespoke manufacturing model [4].

Immunomodulation is advancing from “whether” to “when, for whom, and at what burden.” Teplizumab’s stage 2 indication was expanded in April 2026 to adults and children aged one year and older; in June 2026, the FDA granted accelerated approval for recently diagnosed stage 3 T1D in patients aged 8–17. In the 328-participant PROTECT trial, two 12-day courses improved stimulated C-peptide at week 78 (least-squares mean difference 0.13 pmol/mL; 95% CI 0.09–0.17), but insulin dose, HbA1c, time in range, and clinically important hypoglycemia did not differ significantly. The 2026 label adds a boxed warning for serious and life-threatening viral reactivation and requires infection, hematologic, hepatic, and vaccination planning [5–7]. Thus, preserved C-peptide is demonstrated; immediate glycemic benefit is not.

For most people living with T1D in 2026, the highest-yield “breakthrough” is reliable access to CGM, AID, structured education, rapid-acting insulin, ketone and rescue planning, and psychosocial support. A 2025 meta-analysis of 16 fully automated systems trials (669 participants) found a mean 9.99-percentage-point improvement in time in range versus pooled control therapies (95% CI 3.75–16.22), but fully automated systems did not outperform contemporary hybrid AID overall [8]. The 2026 ADA Standards recommend CGM from diagnosis and remove C-peptide, autoantibody, and insulin-duration prerequisites before pump or AID initiation [9]. Technology narrows physiologic risk; it does not remove the need for infusion-set failure protocols, exercise and meal strategies, sick-day rules, or equitable coverage.

The clinically defensible conclusion is therefore precise: manufactured islet replacement is now convincingly functional; immune-evasive replacement is promising but preliminary; immune therapy can alter trajectory but has stage-specific benefit and nontrivial toxicity; and advanced management already improves outcomes at scale. A universal cure—durable normoglycemia without exogenous insulin, chronic immunosuppression, device dependence,

or unacceptable risk—has not been demonstrated.

Key findings

• Functional cell replacement is demonstrated; a general cure is not. Full-dose zimislecel produced one-year insulin independence in 10 of 12 highly selected adults, but all required chronic immunosuppression and comparative data are absent [1]. Evidence: moderate for short-term efficacy; limited for durability and net benefit.

• Donor islets validate the therapeutic principle. Lantidra is FDA approved only for adults with recurrent severe hypoglycemia despite intensive management. Its benefit can be durable, but procedure and immunosuppression risks are substantial [2]. Evidence: moderate, restricted population.

• Avoiding immunosuppression is the field's central bottleneck. One hypoimmune-islet recipient showed graft survival and C-peptide without immunosuppression; this is proof of concept, not a clinical cure [3]. Encapsulation remains attractive, but the VX-264 program stopped after efficacy was insufficient to support further development [10]. Evidence: limited and mixed.

• Teplizumab changes disease course, not daily insulin dependence. It delays stage 2 progression and preserves C-peptide after diagnosis; clinical secondary outcomes in PROTECT were null [5–7]. Evidence: strong for surrogate preservation; moderate for delay of stage 3; unproven for long-term complication reduction.

• Other immune interventions preserve C-peptide, inconsistently translate to glycemia, and remain unapproved for T1D. Network evidence favors several agents—including low-dose antithymocyte globulin (ATG), golimumab, baricitinib, and teplizumab—but cross-trial ranking is uncertain and adverse effects differ [11–14]. Evidence: mixed.

• AID is the present-tense population intervention. It generally increases time in range and reduces burden without increasing hypoglycemia, although performance, usability, and access vary [8,9,15]. Evidence: strong.

• Adjunct drugs can help selected adults but do not replace insulin. Semaglutide improved time in range and reduced insulin and weight in a small crossover trial with AID, while euglycemic ketosis occurred; GLP-1 receptor agonists are not approved specifically for T1D. SGLT2 inhibitors carry a clinically important ketoacidosis risk and are not FDA-approved for T1D [16,17]. Evidence: moderate for short-term metabolic effects; safety-limited.

1. What counts as a cure?

The word "cure" hides several endpoints. **Biochemical engraftment** means detectable glucose-responsive C-peptide. **Insulin independence** means no exogenous insulin while meeting a prespecified glycemic target. A **functional cure** usually implies durable insulin independence and protection from severe hypoglycemia. A **disease cure** would also extinguish the autoimmune process. A population-ready cure must add manufacturability, retrievability or safety control, freedom from chronic immunosuppression, durable graft function, affordability, and acceptable cancer, infection, alloimmune, and procedural risk.

These distinctions matter because insulin independence is not synonymous with immune tolerance. A graft protected by tacrolimus-based immunosuppression may function while exposing a recipient to infection, renal injury, malignancy, metabolic toxicity, and drug interactions. Conversely, partial graft function that prevents severe hypoglycemia may be clinically valuable even when insulin continues. Trials should therefore report stimulated C-peptide, HbA1c, CGM time in range and below range, severe hypoglycemia, exogenous insulin dose, patient-reported burden, graft durability, immunosuppression toxicity, and rescue or explant procedures—not a single celebratory endpoint.

2. Cell replacement: the strongest breakthrough

Zimislecel establishes manufactured-islet efficacy

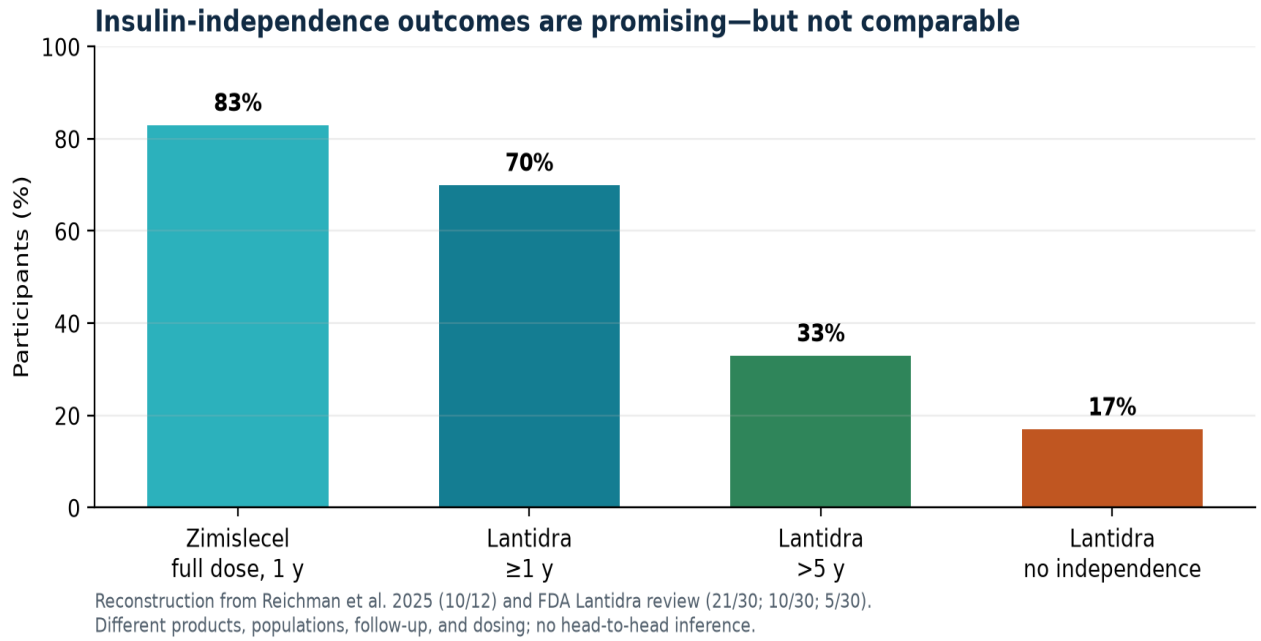


Figure 1. Original reconstruction from cited trial and FDA data; cohorts are not directly comparable.

Zimislecel (formerly VX-880) consists of fully differentiated allogeneic islet cells made from pluripotent stem cells. Cells are infused through the portal vein and require chronic immunosuppression against alloimmunity; suppression may also blunt recurrent autoimmunity. The phase 1–2 FORWARD cohort enrolled 14 adults aged 18–65 with at least five years of T1D, impaired awareness, and severe hypoglycemic events despite optimized care. This is a high-risk, low-frequency phenotype, not representative of the broader AID-treated population [1].

All 14 recipients developed detectable C-peptide. Among 12 full-dose recipients evaluable at one year, all met the composite primary endpoint of freedom from severe hypoglycemic events after day 90 with HbA1c below 7%, and 10 were insulin-independent at day 365. That absolute insulin-independence proportion—83% among the full-dose one-year evaluable group—is compelling. It is not a randomized comparison, however, and the denominator is small. The most relevant comparator for future trials is not poorly controlled injection therapy but optimized contemporary AID plus education and hypoglycemia-avoidance care.

Safety cannot be separated from the regimen. Serious adverse events occurred, including events attributed to immunosuppression and the portal-infusion procedure; no deaths, malignancies, or severe treatment-related hypoglycemia were reported in the published short follow-up [1]. Open questions include attrition of graft function, renal and infectious toxicity over years, repeat dosing, alloantibody development, manufacturing consistency, health-system capacity, pregnancy implications, and whether benefit exceeds modern technology for anyone without recurrent severe hypoglycemia. A pivotal phase 3 expansion is registered within NCT04786262; as of the review date, zimislecel remains investigational and no FDA marketing approval has been identified [18].

Donor islets: an approved, narrow real-world precedent

Donislecel-jujn (Lantidra) is deceased-donor pancreatic islets infused into the hepatic portal vein. FDA approval in 2023 covers adults who cannot approach target HbA1c because of current repeated severe hypoglycemia despite intensive management and education, with concomitant immunosuppression. Two prospective, single-arm studies included 30 participants and allowed up to three infusions. Twenty-one were insulin-independent for at least one year: 11 for one to five years and 10 for more than five years. Five never achieved insulin independence [2].

This is a documented clinical example of durable functional benefit, but not a scalable cure. The label emphasizes portal-pressure and thrombosis monitoring, bleeding and procedural complications, immunosuppressant toxicities, and transmission risk inherent to human cellular products. Repeat intraportal infusion is not recommended after prior portal thrombosis except limited branch thrombosis. Candidate selection belongs in an experienced multidisciplinary transplant program after verified failure of intensive diabetes technology and education.

Autologous reprogrammed cells: elegant, but one confounded case

In a phase 1 report from China (ChiCTR2300072200), a 25-year-old woman received 19,843 islet equivalents/kg of autologous chemically induced pluripotent stem-cell-derived islets beneath the anterior rectus sheath. She became insulin-independent 75 days after transplantation and maintained target glycemia for one year [4]. The extrahepatic site offered imaging and potential surgical access.

The result is a documented person-level example, not a generalizable efficacy estimate. She was already receiving immunosuppression after liver transplantation, so the study cannot establish that autologous cells evade recurrent autoimmunity without immune therapy. Patient-specific manufacturing is resource-intensive; genomic stability, residual pluripotent cells, teratoma risk, batch release, time to treatment, and cost require larger and longer studies. Autologous identity removes classic allorejection but does not erase the autoimmune memory that caused T1D.

Immune-evasive islets: the decisive experiment has begun

UP421 combined deceased-donor islets with gene edits that reduced HLA class I and II recognition and increased CD47, an innate “do not eat me” signal. In a first-in-human report, a small intramuscular forearm graft in one adult survived and secreted insulin without systemic immunosuppression, while unedited comparator cells elicited immune responses [3]. This validates immune evasion in a human environment. It did not produce insulin independence: the transplanted dose was intentionally subtherapeutic.

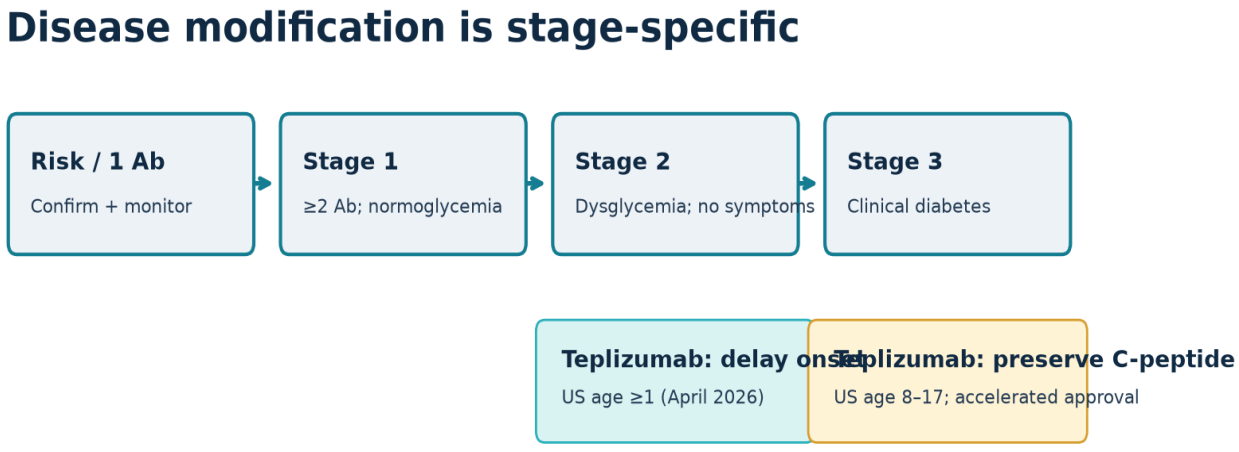
For an off-the-shelf successor, investigators must show consistent editing, adequate vascularization and oxygenation, glucose-responsive secretion at therapeutic dose, protection from adaptive and innate rejection, and a credible control strategy if cells proliferate or transform. Reduced HLA display may impair immune surveillance; CD47 overexpression has theoretical oncologic and infection implications. Longitudinal biopsy, imaging, circulating donor DNA, alloantibodies, cellular immune assays, viral surveillance, and a retrievable or kill-switch design are logical monitoring domains. These risks are hypotheses and engineering concerns, not demonstrated clinical harms from a one-person study.

Encapsulation: biologically sensible, technically unforgiving

Encapsulation attempts to allow diffusion of glucose, insulin, oxygen, and nutrients while excluding immune cells and antibodies. The recurrent failure modes are foreign-body fibrosis, hypoxia, limited cell mass, uneven maturation, and devices that are either poorly vascularized or not fully immune-isolating. Vertex ended further development of VX-264 in March 2025 after full-dose implanted-cell data were safe but not sufficiently efficacious [10]. That negative result is informative: cell quality alone cannot compensate for mass-transfer and host-response limitations. Encapsulation remains unproven as a route to therapeutic insulin independence without immunosuppression.

3. Immunomodulation across the T1D continuum

Stage 1 and stage 2: find disease early enough to modify it



Insulin, CGM/AID, education, acute-safety planning, and complication prevention continue at stage 3.

Figure 2. Stage-specific US regulatory pathway as of 21 July 2026.

Stage 1 denotes persistent multiple islet autoantibodies with normoglycemia; stage 2 adds dysglycemia without symptoms; stage 3 is clinical diabetes. Screening relatives enriches risk, but most incident T1D occurs without an affected first-degree relative, making population screening, confirmatory testing, counseling, surveillance capacity, and equitable infusion access integral to disease modification.

In TN-10, 76 relatives with stage 2 T1D were randomized to one 14-day teplizumab course or placebo. Stage 3 developed in 43% versus 72% at the original analysis; median time to diagnosis was 48.4 versus 24.4 months [6]. The FDA's current record lists approval to delay stage 3 onset from age one as of 20 April 2026 [5]. Benefit is delay, not prevention: some treated participants still progress, and long-term retreatment strategies remain unsettled.

Before teplizumab, confirm stage, age, metabolic status, and absence of clinical T1D where the stage 2 indication is used. The 2026 label requires attention to complete blood count and liver enzymes, serious or chronic infection, EBV/CMV risk, hypersensitivity, cytokine-release syndrome, pregnancy, and vaccine timing. Live vaccines are avoided around treatment; inactivated and mRNA vaccine timing also follows label intervals. The boxed warning reflects serious viral reactivation reports [7]. Infusion burden, travel, missed work or school, insurance authorization, and access to specialty centers can determine real-world uptake as much as efficacy.

Recent-onset stage 3: beta-cell preservation without proven near-term glycemic gain

PROTECT enrolled 328 patients aged 8–17 within six weeks of diagnosis and randomized them 2:1 to teplizumab or placebo, delivered as two 12-day courses 26 weeks apart. At week 78, the least-squares mean difference in stimulated C-peptide was 0.13 pmol/mL (95% CI 0.09–0.17; P<0.001). A clinically meaningful peak C-peptide threshold was retained by 94.9% of treated participants and 79.2% of controls. Yet insulin dose, HbA1c, time in range, and clinically important hypoglycemia—the prespecified key secondary endpoints—were not significantly different [6].

The June 2026 indication is accelerated approval based on C-peptide as a surrogate reasonably likely to predict clinical benefit; a postapproval study must verify benefit [5]. Clinicians should communicate both halves: residual C-peptide is biologically and prognostically desirable, but families should not be promised easier glucose control, lower insulin dose, or fewer complications on current evidence. Insulin and technology remain standard care.

Other agents: signals, not a single winning pathway

T1D involves autoreactive T cells, antigen presentation, B-cell help, inflammatory cytokines, beta-cell stress, and impaired regulation. Accordingly, anti-CD3, ATG, anti-TNF, CTLA4-Ig, anti-CD20, JAK inhibition, low-dose IL-2, antigen-specific therapy, and combinations have been tested. A 2025 network meta-analysis of 60 randomized trials and 4,597 participants found several interventions associated with higher 12-month C-peptide than comparators, but benefits in HbA1c and insulin dose were inconsistent and comparisons were mostly indirect [11]. This is hypothesis-generating ranking, not a license to prescribe the "top" drug.

Low-dose ATG has reproducibly preserved C-peptide in recent-onset disease, but infusion reactions, cytokine release, serum sickness, cytopenias, and infection risk constrain use; it is not FDA-approved for T1D. Golimumab preserved beta-cell function in youth during treatment, with infection and immunosuppression considerations [12]. Baricitinib, an oral JAK1/2 inhibitor, preserved mixed-meal C-peptide over 48 weeks in 91 recently diagnosed adults, but requires continuous exposure and carries class risks including serious infection, thrombosis, malignancy, and laboratory abnormalities [13]. Verapamil produced a modest C-peptide signal in newly diagnosed children, plausibly through reduction of TXNIP-mediated beta-cell stress; it is not immune tolerance and remains off-label [14].

The likely future is rational combination: remove or reprogram pathogenic lymphocytes, reinforce regulation or antigen tolerance, and support beta-cell survival. Combinations increase mechanistic coverage but also infection, malignancy, reproductive, vaccine-response, and monitoring burdens. Adaptive trials with harmonized C-peptide and CGM endpoints, biomarker-defined responders, and multi-year follow-up are preferable to small disconnected studies.

4. Advanced management in 2026

Automated insulin delivery is the active comparator

AID links CGM data to an insulin pump algorithm that adjusts basal delivery and/or correction doses; most commercial systems remain hybrid because users announce meals. Across 16 trials of fully automated systems (669 participants), time in 70–180 mg/dL increased by 9.99 percentage points versus pooled controls (95% CI 3.75–16.22). The gain was larger versus non-AID therapy, while fully automated approaches underperformed hybrid AID in subgroup comparison, emphasizing that “hands-free” does not automatically mean better physiology [8]. Real-world review across 171,209 users broadly confirmed improved time in range and stable or reduced time below range, but observational selection and manufacturer ecosystems limit causal comparison [15].

Implementation should include individualized glucose targets, insulin action settings, carbohydrate ratios, correction factors, sleep and exercise modes, infusion-site rotation, connectivity and charging plans, and explicit backup basal insulin or injection calculations. Persistent hyperglycemia on pump therapy demands immediate evaluation of infusion failure and ketones; algorithm corrections cannot deliver insulin through an occluded or dislodged cannula. Pregnancy, very young children, dialysis, steroid exposure, gastroparesis, high-intensity sport, and shift work require tailored protocols.

The ADA’s 2026 technology direction is access-forward: CGM at diagnosis and thereafter for those who benefit, and no requirement for C-peptide, autoantibodies, or a minimum insulin-treatment duration before pump or AID initiation [9]. This matters because administrative “step therapy” can prolong preventable hypoglycemia and hyperglycemia.

Adjunct pharmacotherapy: useful phenotype targeting, narrow safety margins

In a double-blind crossover trial, 28 adults completed semaglutide and placebo phases while using AID. Semaglutide increased time in range without increasing time below range and reduced insulin dose, carbohydrate intake, and body weight; no DKA or severe hypoglycemia occurred, but two episodes of euglycemic ketosis occurred during semaglutide use [16]. Short duration, small size, crossover design, and enrollment of adults able to use AID limit generalizability. GLP-1 receptor agonists are not insulin substitutes and are not specifically FDA-approved for T1D; nausea, delayed gastric emptying, rapid insulin reduction, low carbohydrate intake, illness, and pump failure can complicate ketosis risk.

SGLT2 inhibitors lower glucose independently of insulin and may improve time in range and weight, but increase DKA risk, sometimes with only modest hyperglycemia. They are not FDA-approved for T1D. If used off-label in exceptional specialist-managed cases, blood ketone access, education, sick-day cessation, perioperative holds, avoidance of ketogenic diets, cautious insulin adjustment, and immediate action for nausea or malaise are essential [17]. Pramlintide is approved as an insulin adjunct in the United States but adds injections and hypoglycemia complexity. None of these agents is a cure.

Prevention of complications remains part of “advanced” care

Technology should not eclipse blood pressure and lipid management, kidney screening, retinal examination, neuropathy and foot assessment, celiac and thyroid surveillance where indicated, vaccination, contraception and preconception planning, smoking cessation, sleep, mental health, eating-disorder screening, and affordable insulin access. Severe hypoglycemia requires glucagon availability and trained close contacts. Recurrent DKA or missed insulin is often a signal of access barriers, depression, diabetes distress, disordered eating, housing or food insecurity—not simply “nonadherence.”

5. Four documented examples—and what each actually proves

1. FORWARD full-dose cohort (multicenter). Ten of 12 full-dose zimislecel recipients evaluable at one year were insulin-independent. This proves manufactured stem-cell-derived islets can replace physiologic insulin secretion under immunosuppression in selected adults; it does not prove long-term safety or broad eligibility [1].

2. Lantidra registrational program (United States). Ten of 30 donor-islet recipients remained insulin-independent for more than five years, while five never achieved independence. This demonstrates both durability and heterogeneity, with a substantial procedure/immunosuppression burden [2].

3. Autologous CiPSC-islets (China). One woman achieved insulin independence from day 75 through one year after an abdominal-wall graft. This proves feasibility in one immunosuppressed recipient; it does not isolate immune protection or establish reproducibility [4].

4. UP421 hypoimmune donor islets (Sweden). A subtherapeutic forearm graft survived and produced insulin without systemic immunosuppression in one person. This supports human immune-evasion biology; it did not eliminate insulin therapy [3].

These examples are deliberately bounded. They are not interchangeable, and none supports direct-to-consumer stem-cell treatment. Unregulated clinics marketing “stem cell cures” without a regulator-authorized protocol, product characterization, adverse-event reporting, and long-term follow-up should be considered unsafe and scientifically unsupported.

Practical synthesis

For current clinical practice

• Optimize proven management first. Offer CGM and AID early, pair them with structured education, and maintain injection and ketone backup plans. Review severe hypoglycemia and DKA as system failures as well as biomedical events.

• Screen strategically. Offer autoantibody screening through evidence-based programs, especially to relatives, with a defined pathway for confirmation, staging, metabolic monitoring, counseling, and teplizumab referral. Screening without follow-up capacity can create anxiety without benefit.

• Use teplizumab with endpoint honesty. For stage 2 disease, discuss delayed—not prevented—stage 3. For recently diagnosed patients aged 8–17, explain accelerated approval, C-peptide preservation, null key glycemic secondary endpoints, infusion burden, viral-reactivation boxed warning, laboratory monitoring, and the required confirmatory evidence [5–7].

• Reserve approved islet transplantation for its label population. Adults with repeated severe hypoglycemia despite optimized education and technology may merit referral to an experienced islet-transplant center. For well-controlled T1D, immunosuppressive risk is not justified by current evidence [2].

• Treat experimental cell therapy as research. Trial enrollment should address source and manufacture, dose, delivery site, immune regimen, rescue/explant plan, reproductive precautions, long-term tumor surveillance, costs, and what happens if graft function declines.

A decision hierarchy for specialist teams

Clinical state	Evidence-backed 2026 action	What not to infer
At-risk, single autoantibody	Repeat/confirm in a qualified pathway; risk-stratify	Not inevitable T1D
Stage 1	Metabolic surveillance, education, trial discussion	No approved drug proven to prevent T1D
Stage 2, age ≥1 in US	Consider teplizumab after confirmation and safety review	Delay is not permanent prevention
Recent stage 3, age 8–17 in US	Consider teplizumab under 2026 label; continue full insulin care	C-peptide benefit does not mean insulin independence
Established T1D	CGM/AID, education, complication prevention, psychosocial care	Adjunct drugs do not replace insulin
Recurrent severe hypoglycemia despite optimized care	Transplant-center assessment; Lantidra may be an option for eligible adults	Cell therapy is not safer than technology for most people
Interest in stem-cell “cure”	Authorized clinical trial or regulated transplant program only	Testimonials are not evidence

Evidence and caveats

The evidence hierarchy is uneven. AID rests on multiple randomized trials and large real-world cohorts. Teplizumab has randomized stage-specific trials and regulatory review, but the new stage 3 indication relies on a surrogate under accelerated approval. Lantidra has long follow-up but only 30 nonrandomized recipients. Zimislecel has striking efficacy with a very small selected cohort and limited duration. Autologous and hypoimmune approaches are one-person reports. Comparisons across cell products are invalid because dose, site, immune regimen, eligibility, endpoints, and follow-up differ.

Important uncertainties include whether stem-cell grafts remain functional beyond five to ten years; whether chronic immunosuppression produces net benefit compared with modern AID; whether hypoimmune cells can evade rejection without compromising tumor and infection surveillance; whether recurrent autoimmunity emerges after autologous grafting; how grafts can be stopped or removed; which immune biomarkers predict benefit; and whether preserved C-peptide translates into fewer severe events and microvascular complications.

Equity is not an appendix. Autoantibody screening, two-week or repeated infusion courses, transplant evaluation, cell manufacturing, CGM, pumps, supplies, broadband connectivity, and specialist follow-up are all unevenly distributed. Trials have often underrepresented racial and ethnic minority groups, rural populations, people with low income, those with high HbA1c, and people with psychiatric or social complexity—the groups who may carry the greatest acute risk. Enrollment criteria that maximize signal can narrow generalizability. A cure that requires scarce centers and lifelong immunosuppression is not yet a public-health cure.

Finally, the field is moving rapidly. Regulatory indications and pipeline programs should be checked against current FDA/EMA records and trial registries at the point of care. Company statements can clarify operational status but cannot substitute for peer-reviewed outcomes. As of 21 July 2026, the evidence supports guarded optimism: beta-cell replacement works; selective immune modification works; integrating the two safely, durably, and equitably remains the unsolved problem.

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