ZHITTYA GENESIS MEDICINE

Type 1 Diabetes

Medical Research Study Program Concept

A Vascular-First Hypothesis for Recombinant Human FGF-1 in Type 1 Diabetes

August 10, 2026

Objective

Type-1 diabetes affects around 2.1 million Americans. It is an ugly disease which causes a lifelong burden to all sufferers. As of August 10, 2026 there is no medical treatment to reverse the biological condition of type-1 diabetes. Zhittya Genesis Medicine has been advancing the medical treatment applications of a natural human molecule referred to as FGF-1 for 28 years. Zhittya has utilized the FGF-1 molecule to treat coronary artery disease, Parkinson's Disease, dementia, chronic wounds and recently Type-2 diabetes. Type-1 diabetes is a disease of the pancreas, where deficient insulin production occurs due to the destruction of beta cells by an autoimmune attack. Where Zhittya believes type-2 diabetes is a neurological disease, in which the glucose sensing neurons in the brain do not function properly, it is well agreed that type-1 diabetes results from the body's immune system attacking and destroying insulin-producing beta cells leading to a deficiency of biologically active insulin.

Zhittya as of August 10, 2026 has dosed 110 people who were type-2 diabetics and has learned a great deal from the resulting information. In February 2026, Zhittya became aware of a medical research study which inferred that FGF-1 injected into the belly enhanced liver and pancreas function. Zhittya modified its type-2 Medical Research Protocol to allow test subjects a choice to add an additional injection of FGF-1 into their belly to see if it enhanced their liver and pancreas function. Zhittya's first glance at the data is supportive of that idea. Medical research literature supports the idea that FGF-1 should enhance the regeneration of new beta cells in the pancreas. Examples of FGF-1 regenerating and rejuvenating cells are well documented in other cell groups, such as dopamine producing neurons. The enhanced insulin readings that Zhittya is seeing from its small test sample, Zhittya believes, can only come from the regeneration of beta cells in the pancreas.

Zhittya is studying whether it should undertake an additional Medical Research Study to attempt to reverse type-1 diabetes. In the almost 400 patients taking FGF-1 there has not been one adverse event reported. Zhittya believes potential type-1 Medical Research patients are at very low risk. If Zhittya's theory proves to be accurate millions of people could have their lives improved by being free of type-1 diabetes.

1. Purpose and Scope

This paper sets out the scientific reasoning behind a possible Zhittya research program in Type 1 diabetes. It explains why the company believes FGF-1 is a credible candidate in a disease where every previous approach has run into the same wall, and it describes a second source of potential benefit in this population arising from the blood vessel damage that drives most of the long-term harm in diabetes.

FGF-1 is an investigational product. The reasoning described here has not yet been tested in Type 1 diabetes in any species. This paper describes a research direction under active evaluation, not an approved therapy or a claim of efficacy.

2. The Hypothesis in Five Steps

1. The pancreatic islet, the small cluster of cells that produces insulin, is not simply an endocrine structure that happens to contain blood vessels. It is better described as a vascular structure with insulin-producing cells built into it. Beta cells do not construct their own supporting scaffold. They recruit blood vessel lining cells, called endothelial cells, and then depend on the scaffolding those vessels lay down in order to make insulin at all.
2. Published research shows that blood flow and blood vessel abnormalities inside and around the islet appear before immune cells arrive, not after. This has now been demonstrated in more than one laboratory model of autoimmune diabetes.
3. Immune cells cannot reach the beta cell unless the blood vessel wall lets them through. During the period before diabetes appears, islet blood vessels take on the molecular signature of a lymph node, which is to say they start actively recruiting immune cells. Blocking that recruitment early prevents the disease in animal models.
4. If the first three steps are correct, then blood vessel dysfunction comes before the immune attack rather than after it. Repairing the microvasculature would therefore address a cause rather than a symptom. This is the meaningful difference between Zhittya's approach and every beta-cell replacement program that has failed because the new cells were destroyed in turn.
5. FGF-1 is a candidate against this model because it acts on both halves of the problem at once. It is a blood vessel repair molecule, and the beta cell itself carries the FGF receptor and produces FGF-1. When that receptor is disabled in animals, they develop diabetes.

In addition, **the blood vessel damage that Type 1 diabetes causes over a lifetime is itself a large and measurable target that the FGF-1 platform is already built to address. That is covered in Section 6.**

3. The Wall That Previous Approaches Have Hit

The standard objection to any attempt to restore beta cells in Type 1 diabetes is well known and, on the current evidence, correct: replace or regenerate the beta cells and the immune system destroys them again. Islet transplantation works, but requires lifelong immune suppression. Stem cell derived beta cell products face the same barrier. Drugs that delay the onset of the disease do so by suppressing the immune system, with the side effects that implies.

Every one of these approaches accepts the same starting assumption: that the immune attack is the first event and the beta cell is simply its victim. Under that assumption the only available lever is immune suppression, and the ceiling on any treatment is set by how much immune suppression a patient can tolerate and for how long.

Zhittya's hypothesis questions the starting assumption. If the first injury is to the blood vessels, then the immune attack is a downstream consequence, and there is a lever available that is not immune suppression.

One further point supports the feasibility of any rescue approach. Many people who have had Type 1 diabetes for years still retain a small surviving population of insulin-producing cells. The target is not always zero. In many patients there may be something left to protect and support.

4. The Vascular-First Hypothesis

4.1 The islet cannot function without its blood vessels

Most cells in the body build their own supporting scaffold, known as a basement membrane. Beta cells do not. Instead they release a signal that attracts endothelial cells, the cells that line blood vessels, and those vessels

then lay down the scaffold the beta cells sit against. The proteins in that scaffold, principally laminins and collagen, are what switch on the insulin gene and drive beta cell growth.

The practical consequence is straightforward. A beta cell sitting next to a damaged or dying capillary is a beta cell that has lost its instructions. It will underperform long before it dies, and it will look impaired on any functional test well before a pathologist would see any sign of immune attack.

4.2 Blood vessel damage appears before the immune attack

This is the central claim, and it has published support in more than one animal model.

In the BioBreeding rat, a strain that spontaneously develops autoimmune diabetes very much like the human disease, researchers documented reduced insulin secretion, reduced beta cell mass, and reduced blood flow inside the islet at 40 days of age, before immune cells had invaded the islet and before the animals became diabetic.

In NOD mice, *the non-obese diabetic mouse, a strain bred to spontaneously develop an autoimmune diabetes closely resembling human Type 1 diabetes and the standard laboratory model for this disease*, swelling of the blood vessels and changes in the shape of the endothelial cells around the islet have been described as an early signal that immune invasion is coming. In chemically induced models of diabetes, blood vessel changes inside the islet likewise come first.

Separately, recent work using human pancreas tissue from organ donors found that beta cells were already metabolically impaired in donors who carried the antibodies that mark early Type 1 diabetes, before any widespread immune invasion of the islet. The authors specifically named endothelial cells among the possible sources of the signal driving that impairment. This does not prove Zhittya's model, but it shows that the field is no longer confident that the immune attack comes first.

4.3 The blood vessel wall is the gate the immune system comes through

Immune cells do not simply drift into tissue. They are captured, held, and passed through the vessel wall by specific adhesion molecules on the endothelial cells, which work rather like docking points. In NOD mice, a set of these docking molecules appears on islet blood vessels in the run-up to disease and is directly responsible for immune cells attaching to the islet.

The timing of the published experiments is the striking part. When these docking molecules were blocked in NOD mice starting at three weeks of age, the proportion of animals that went on to develop diabetes fell from roughly 50 percent to 9 percent. When the same treatment was started later, it did nothing. **An intervention aimed only at the blood vessel interface, given early enough, largely prevented the disease.**

This is a proof of principle for the shape of the argument: control the blood vessel interface within the right window and the autoimmune process does not take hold. It is not, on its own, evidence that FGF-1 does this.

4.4 What the hypothesis predicts

- Repairing the microvasculature in and around the islet should reduce stress on the beta cells and reduce the recruitment signal that draws immune cells in.
- Restoring the vascular scaffold should improve the performance of surviving beta cells even without any increase in their number.
- Benefit should be greatest in newly diagnosed patients, where the most beta cells remain and the vascular damage is least advanced, and smallest in patients who have had the disease for decades.
- Measures of beta cell function should improve before measures of beta cell number.

5. Why FGF-1 Is the Candidate

Four established lines of evidence, plus one clinical observation from Zhittya's own patients.

Pillar 1: FGF-1 repairs blood vessels

This is the foundation of the entire platform and the basis of Zhittya's coronary artery disease, peripheral vascular, chronic wound, and neurological programs. FGF-1 drives the growth, migration, and maturation of the endothelial cells that form microvascular networks. Whatever else in this paper is a hypothesis, this property is not.

Pillar 2: The beta cell carries the FGF receptor, and needs it

Adult beta cells express FGF receptors 1 and 2, together with FGF-1 itself and several related molecules. When FGF receptor 1 signaling is disabled in the beta cells of mice, the animals develop diabetes as they age, with fewer beta cells, impaired glucose sensing, and a breakdown in the machinery that converts proinsulin into working insulin.

This is the strongest published pillar, and it is worth stating plainly: FGF receptor signaling is not incidental to the beta cell. Take it away and the animal becomes diabetic. The beta cell is a legitimate FGF-1 target tissue, and it already produces FGF-1 itself.

Pillar 3: FGF-1 works on inflammation and tissue repair

FGF-1 is a classical wound repair molecule that operates in inflamed and poorly perfused tissue. To the extent that blood vessel activation and local inflammation around the islet are part of the initiating injury, FGF-1 is acting on the relevant biology.

Pillar 4: FGF-1 has established antidiabetic activity

A single dose of recombinant FGF-1 produces strong glucose lowering in diabetic mice without driving blood sugar dangerously low. Continued treatment increases glucose uptake into skeletal muscle and reduces glucose output from the liver. Administered centrally, FGF-1 produces sustained remission of high blood sugar in rodent models of Type 2 diabetes lasting weeks to months. FGF-1 is therefore a molecule with well characterized metabolic activity across multiple independent laboratories.

Clinical observation: improved pancreatic function in Zhittya's Type 2 patients

Zhittya has observed improvements in pancreatic function in treated Type 2 diabetes patients. This observation is consistent with Pillar 2, which establishes the beta cell as a direct FGF-1 target tissue. Further measurement in the existing Type 2 cohort, including proinsulin to C-peptide ratio and C-peptide response to a mixed meal, is planned to characterize the effect more precisely. C-peptide is released in equal amounts to insulin when the body makes its own insulin, and is therefore the standard way to measure how much insulin a patient's own pancreas is still producing.

6. A Second Source of Benefit: Vascular Complications in Type 1 Diabetes

Type 1 diabetes is not principally a disease of blood sugar. It is a disease whose damage is delivered by the blood vessels over decades. Insulin therapy manages the glucose. It does nothing to repair the vessels. A person with well-controlled Type 1 diabetes for thirty years still carries substantially elevated cardiovascular risk, and it is the complications, not the glucose itself, where the loss of quality of life and the great majority of the healthcare cost sit.

Every one of the following is a blood vessel problem, which is to say every one of them sits inside the mechanism the FGF-1 platform was built to address:

Complication	Blood vessel basis	Relevance to existing FGF-1 programs
Cardiovascular disease	Accelerated coronary artery disease and small vessel insufficiency; the leading cause of death in Type 1 diabetes	Direct overlap with the existing coronary artery disease program
Peripheral artery disease and critical limb ischemia	Blockage of large and small vessels in the lower limb	Direct overlap with existing peripheral vascular work
Diabetic foot ulcer and poor wound healing	Impaired blood vessel growth and poor perfusion at the wound	Direct overlap with the chronic wound program
Diabetic peripheral neuropathy	Loss of blood supply to the small vessels that feed peripheral nerves	Direct overlap with the chronic pain and neuropathy work
Diabetic kidney disease	Injury to the filtering vessels of the kidney and loss of small vessels around the tubules	New indication space; same mechanism
Cardiac autonomic neuropathy	Small vessel injury to the nerves controlling heart rate and blood pressure	New indication space; same mechanism
Cerebral small vessel disease and cognitive decline	Reduced blood flow to the brain and small vessel injury	Direct overlap with the neurological program and existing brain perfusion imaging capability
Erectile dysfunction	Small vessel insufficiency	Common, under-discussed, and mechanistically adjacent

Three consequences follow from this table.

- **It creates a strong base case.** Even under conservative assumptions about beta cell rescue, a demonstrated effect on limb perfusion, ulcer healing, neuropathic pain, or brain perfusion in a Type 1 population would be a clinically meaningful and commercially valuable result in its own right.
- **It creates more than one path to a successful study.** A Type 1 study can measure vascular endpoints such as limb perfusion, wound healing, and nerve function alongside measures of the pancreas such as C-peptide and daily insulin requirement. Because the vascular effects of FGF-1 are the best established part of the platform, a study in this population is not a single-outcome bet on the newest part of the science.
- **It is why this population fits the platform.** People with Type 1 diabetes carry the exact vascular disease burden that FGF-1 was developed to treat, and they carry it earlier in life and for longer than almost any other group of patients.

7. Evidence Base and Current Status

The table below separates the published science from Zhittya's own observations and from the working hypotheses that this research program is designed to test.

Statement	Status	Source
FGF receptor 1 signaling is required for normal beta cell number, glucose sensing, and insulin processing	Published research	Mouse models in which the receptor is disabled (Hart et al., Nature, 2000)
Beta cells depend on the vascular scaffold laid down by endothelial cells in order to produce insulin	Published research	Nikolova et al., Developmental Cell, 2006, and subsequent work
Blood flow and vascular deficits appear before immune invasion in autoimmune diabetes	Published research	BioBreeding rat and NOD mouse studies
Blocking blood vessel adhesion molecules early prevents diabetes in NOD mice	Published research	NOD mouse blockade studies, 1993 to 2024
FGF-1 lowers glucose and improves insulin sensitivity in diabetic animals without causing low blood sugar	Published research	Nature, 2014 and Nature Medicine, 2016
FGF-1 repairs and remodels damaged microvasculature	Zhittya clinical experience	Observed across the coronary, peripheral vascular, wound, and neurological programs
Zhittya's Type 2 patients show improved pancreatic function	Zhittya observation	Early data from the ongoing Type 2 medical research study; sample size remains small
That improvement reflects regenerated beta cells	Zhittya's working explanation	Consistent with the published role of the FGF receptor in the beta cell; further measurement planned
Blood vessel dysfunction initiates the autoimmune response in human Type 1 diabetes	Working hypothesis	Proposed by Zhittya, supported by published animal evidence, not yet tested in humans
It is hoped that rejuvenated beta cells would survive in 60 to 70 percent of cases	Zhittya's expectation	Based on the mechanism described in this paper; no clinical data yet exists in Type 1 diabetes

Key References

1. Hart AW, Baeza N, Apelqvist A, Edlund H. Attenuation of FGF signalling in mouse beta-cells leads to diabetes. Nature. 2000;408:864-868.
2. Nikolova G, Jabs N, Konstantinova I, et al. The vascular basement membrane: a niche for insulin gene expression and beta cell proliferation. Developmental Cell. 2006;10(3):397-405.
3. Medina A, Parween S, Ullsten S, et al. Early deficits in insulin secretion, beta cell mass and islet blood perfusion precede onset of autoimmune type 1 diabetes in BioBreeding rats. Diabetologia. 2018.
4. Denis MC, Mahmood U, Benoist C, Mathis D, Weissleder R. Imaging inflammation of the pancreatic islets in type 1 diabetes. PNAS. 2004.
5. Hanninen A, Taylor C, Streeter PR, et al. Vascular addressins are induced on islet vessels during insulitis in nonobese diabetic mice and are involved in lymphoid cell binding to islet endothelium. J Clin Invest. 1993;92(5):2509-2515.
6. Yang XD, et al. Mucosal addressin is required for the development of diabetes in nonobese diabetic mice. J Immunol. 1998. PMID 9637517.

7. Michie SA, et al. Mucosal addressin cell adhesion molecule-1 mediates T cell migration into pancreas-draining lymph nodes for initiation of the autoimmune response in type 1 diabetes. 2024.
8. Suh JM, Jonker JW, Ahmadian M, et al. Endocrinization of FGF1 produces a neomorphic and potent insulin sensitizer. Nature. 2014;513:436-439.
9. Scarlett JM, Rojas JM, Matsen ME, et al. Central injection of fibroblast growth factor 1 induces sustained remission of diabetic hyperglycemia in rodents. Nature Medicine. 2016.
10. Gasser E, Moutos CP, Downes M, Evans RM. FGF1, a new weapon to control type 2 diabetes mellitus. Nature Reviews Endocrinology. 2017;13(10):599-609.
11. Beta cell dysfunction occurs independently of insulitis in type 1 diabetes pathogenesis. Cell Reports. 2025.
12. Sakhneny L, et al. Pericytes contribute to the islet basement membranes to promote beta-cell gene expression. Scientific Reports. 2021;11:2378.

About this document: FGF-1 is an investigational biologic. It has not been approved by the U.S. Food and Drug Administration or any other regulatory authority for the treatment of Type 1 diabetes or any other indication. The Type 1 diabetes program described here is a research concept under evaluation and has not begun. Statements regarding future research, potential benefits, and expected outcomes are forward-looking and subject to significant uncertainty. Nothing in this document is an offer to sell or a solicitation of an offer to buy any security.