Phase 3 Clinical Trial Protocol – “Glucofix” vs Placebo in Diabetes (Phase III Study)

Protocol Synopsis

- **Study Design:** Phase 3 randomized, double-blind, placebo-controlled trial conducted across ~50 sites in India. Eligible participants will be assigned in a 2:1 ratio to Glucofix or placebo, in parallel groups. Both patients and investigators will be blinded to treatment (identical placebo provided). Treatment duration is 24 weeks, with a subsequent 4-week off-treatment follow-up (total study length per patient: 28 weeks).
- **Study Population:** Approximately 450 adult patients with type 2 diabetes mellitus (T2DM) will be enrolled. Key population criteria include inadequately controlled T2DM (HbA1c ~7.0–10.0%) on diet/exercise therapy or stable metformin monotherapy cdek.pharmacy.purdue.edu. Patients are recruited from outpatient clinics; the sample size (~450) is chosen to provide adequate power to detect a clinically meaningful HbA1c difference between Glucofix and placebo.
- **Investigational Product: Glucofix** (an investigational anti-hyperglycemic medication) administered at a fixed dose (e.g. 50 mg oral tablet once daily) for 24 weeks. **Comparator:** Matching placebo tablet once daily for 24 weeks. Both Glucofix and placebo will be dispensed in identical packaging. Patients will continue background therapies (e.g. metformin) if applicable, unchanged during the trial.
- **Objectives:** The primary objective is to evaluate the efficacy of Glucofix in improving glycemic control compared to placebo over 24 weeks of treatment. Secondary objectives include assessing effects on other metabolic parameters and safety/tolerability of Glucofix in the target population.
- **Primary Endpoint:** Change in glycated hemoglobin **(HbA1c)** from baseline to Week 24 of treatment accessdata.fda.gov. This endpoint assesses improvement

in chronic glycemic control (a standard primary efficacy measure in diabetes trials).

- **Secondary Endpoints:** Key secondary endpoints will include the proportion of patients achieving target HbA1c <7.0% at Week 24, change in fasting plasma glucose (FPG) from baseline to Week 24, change in body weight, change in lipid profile (e.g. LDL cholesterol), and measures of beta-cell function or insulin resistance if applicable. Safety endpoints (incidence of adverse events, hypoglycemia episodes, laboratory changes) will also be evaluated.
- **Sample Size and Randomization:** ~450 patients will be randomized (300 to Glucofix, 150 to placebo). Randomization is stratified (for example, by baseline HbA1c category or site) to ensure balance between treatment arms. The 2:1 allocation favors more patients on Glucofix to gather extensive safety data without compromising power. A centralized randomization system will assign treatment codes; study drug and placebo are identical in appearance to maintain blinding.
- **Duration:** Each patient will participate for about 28 weeks total: a screening period (up to 2–4 weeks), a 24-week double-blind treatment period, and a 4-week post-treatment follow-up period. Efficacy assessments occur through Week 24, and safety is monitored through Week 28 (follow-up).
- **Visit Schedule:** Patients will attend regular clinic visits at Screening, Baseline (Week 0), and at Weeks 4, 8, 12, 16, 20, 24 during treatment, plus a follow-up visit at Week 28. Interim phone contacts may be used as needed for patient support or safety checks. On-treatment visits are approximately every 4 weeks (monthly), with an allowable window (e.g. ±7 days) to accommodate scheduling.
- **Safety Monitoring:** Patient safety is closely monitored throughout. An independent Data Monitoring Committee (DMC) will periodically review unblinded safety data. **Rescue Medication:** If a patient's diabetes worsens significantly (e.g., confirmed FPG above a pre-specified threshold or HbA1c >10% on two visits), rescue therapy (such as insulin) may be initiated at the investigator's discretion for ethical reasons. Patients who require rescue will discontinue study drug (considered treatment failures for efficacy) but will continue in the trial for safety follow-up. All adverse events will be recorded and evaluated. Routine

laboratory tests (chemistry, liver enzymes, renal function, etc.) are scheduled more frequently early in the study and at key time points thereafter for proactive safety monitoring.

- **Endpoint Analysis:** The primary efficacy analysis will compare the mean change in HbA1c from baseline to Week 24 between the Glucofix and placebo groups (e.g., using an ANCOVA or mixed model, with baseline HbA1c as covariate). A clinically significant HbA1c reduction is expected with Glucofix vs placebo, based on the trial hypothesis and prior data. For example, GLP-1 agonists and SGLT2 inhibitors in similar 24-week trials have shown HbA1c improvements on the order of 0.5–1.5% versus placebo pubmed.ncbi.nlm.nih.gov. The trial is powered (e.g. 90% power at two-sided alpha 0.05) to detect an HbA1c difference of ~0.5% or greater between groups. Secondary endpoints will be analyzed descriptively and with appropriate statistical tests (with adjustment for multiplicity if confirmatory). Safety data will be summarized by treatment group, and any emerging safety signals (lab abnormalities, events) will be closely examined.

In summary, this Phase 3 study will evaluate whether Glucofix can significantly improve glycemic control in type 2 diabetic patients over 24 weeks compared to placebo, while monitoring safety in a large Indian multicenter patient population. The study's rigorous design (randomized, placebo-controlled, double-blind) and comprehensive assessments aim to ensure robust efficacy and safety data to support potential regulatory approval of Glucofix.

Schedule of Assessments

The 28-week study schedule includes a Screening visit, a Baseline (Week 0) visit, six on-treatment monthly visits (Weeks 4, 8, 12, 16, 20, 24), and an end-of-study follow-up visit at Week 28. Table 1 below summarizes the schedule of assessments for each visit. Early in the trial, visits are more frequent and include more extensive evaluations – the first couple of months are often the busiest period in a clinical trialmds-foundation.org – to closely monitor safety and efficacy as therapy is initiated. As the study progresses, later visits involve relatively fewer assessments, focusing on essential safety labs and efficacy endpoints, with continued monitoring of adverse events and adherence.

Table 1: Schedule of Assessments (Screening to Week 28)

Assessment	Screening	Baseline (Week 0)	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24 (End of Treatment)	Week 28 (Follow-up)
Demographics (age, sex, etc.)	X								
Medical history & medication history	X								
Physical examination (complete)	X	X						X	X
Vital signs (BP, HR, weight)	X	X	X	X	X	X	X	X	X
12-lead ECG	X							X	
HbA1c (glycated hemoglobin)	X				X			X	
Fasting plasma glucose (FPG)	X	X	X	X	X	X	X	X	
Lipid profile (Total-C, LDL, HDL, TG)		X						X	
Liver function tests (ALT, AST, ALP, bilirubin)	X		X		X			X	X
Renal function tests (serum creatinine, eGFR, BUN)	X		X		X			X	X
Complete blood count (CBC)	X		X		X			X	X
Study drug accountability (pill count)			X	X	X	X	X	X	
Adverse events (AE) review			X	X	X	X	X	X	X
Concomitant medications review	X	X	X	X	X	X	X	X	X

Note: All on-treatment visits (Week 4 through Week 24) have a visit window of approximately ±7 days (to allow scheduling flexibility). The follow-up visit at Week 28 has a window of ±7 days as well. Assessments marked “X” are performed at that visit. Blank cells indicate the assessment is not scheduled for that visit.

- **Screening (Week -4 to 0):** After informed consent, comprehensive data collection is done to determine eligibility. Demographics and full medical history are recorded. A complete physical exam is performed. Vital signs (blood pressure, heart rate, weight) are measured. A 12-lead electrocardiogram (ECG) is done to screen for cardiac conditions. Blood samples are taken for laboratory tests: HbA1c (for glycemic status), fasting plasma glucose, liver function tests (ALT, AST, alkaline phosphatase, bilirubin), renal function (serum creatinine, estimated GFR, BUN), CBC, and other safety labs. (A lipid profile may be optionally measured at screening or at baseline.) Women of childbearing potential undergo a pregnancy test. Concomitant medications are reviewed (recording any current treatments). These screening assessments ensure the patient meets inclusion criteria and has no exclusionary conditions. **Visit window:** Screening may occur up to 2–4 weeks before baseline; all inclusion labs (e.g. HbA1c) must be within protocol-defined ranges.

- **Baseline (Week 0):** Occurs after eligibility is confirmed. Vital signs are measured and a brief physical check (to note any changes since screening) is done. Fasting plasma glucose is measured on the day of randomization as a baseline reference. A blood sample is collected for any outstanding baseline labs (e.g., lipid profile, or repeat safety labs if screening results were borderline or out of window). Eligible patients are then randomized to a treatment arm (Glucofix or placebo) and receive the first dose of study medication. Study drug dispensing occurs (patients are given a supply of Glucofix or placebo to take until the next visit). Concomitant medications are reviewed/updated. Investigators counsel patients on study procedures (e.g. how to take the medication, lifestyle advice, how to perform self-monitoring of blood glucose at home, and to report any symptoms). **Adverse events** are monitored from this point forward (any issue arising after the first dose is considered an adverse event).

- **Treatment Visits (Weeks 4, 8, 12, 16, 20, 24):** During the 24-week double-blind treatment phase, patients return for regular visits approximately every 4 weeks. **At each visit:** vital signs (including weight) are measured and interim medical history is taken. A targeted physical exam is performed if needed (if patient

reports new symptoms). Study drug **accountability** is done – patients bring their pill bottles, and any unused tablets are counted to assess compliance. A new batch of study medication is dispensed (with dosing adherence reinforced). **Concomitant medications** are reviewed (any changes or new therapies recorded). **Adverse events** are actively queried and all new or ongoing AEs are documented at each visit. **Laboratory tests:** Fasting blood samples are collected at select visits:

- **Week 4:** Early safety check – liver function and renal function tests (ALT, AST, etc., and creatinine) are measured at this early time point to detect any acute drug-related abnormalities. CBC may also be checked at Week 4 as part of the safety panel. (HbA1c is not repeated at Week 4, as significant changes are not expected yet.)
- **Week 8:** No routine labs scheduled (unless needed for safety follow-up of prior abnormal results). Clinical assessment continues (vitals, AE, compliance).
- **Week 12: Mid-point efficacy/safety labs** – HbA1c is measured at the halfway point to observe the glycemic trend (not for formal endpoint, but for interim monitoring). Liver and renal function tests and CBC are repeated at Week 12 to monitor any emerging trends (e.g. cumulative effects on liver enzymes or hematology). FPG is measured to track short-term glycemic changes. Lipid profile is optional at this mid-point (not required, but could be measured if an interim lipid assessment is of interest).
- **Week 16 and 20:** No scheduled blood tests (except FPG and any necessary safety labs if prior issues). These visits focus on clinical monitoring (vitals, AE review, compliance) and ensuring continued study drug adherence. By design, the frequency of lab monitoring is reduced in the later half of the treatment period, as early visits establish safety mds-foundation.org.
- **Week 24: End-of-treatment assessments** – this is the final on-treatment visit. A comprehensive evaluation is done. Vital signs and a **complete**

physical exam are performed to assess overall health at end of treatment. Efficacy and safety labs are collected: HbA1c (primary endpoint) is measured at Week 24 to determine treatment effect accessdata.fda.gov, and fasting plasma glucose is measured. A repeat **lipid profile** is done to compare to baseline (to see if Glucofix improved cholesterol/triglycerides). Liver function tests, renal function tests, and CBC are measured again at Week 24 to identify any changes after 24 weeks of therapy. Study drug accountability is performed (patients return all remaining study medication — this is the final pill count). Concomitant medications are reviewed one more time. All **adverse events** since the last visit are reviewed and documented; particular attention is given to any events that might warrant follow-up even after stopping the drug. Patients are instructed to stop taking study medication after this visit (if any doses remain) and are scheduled for the follow-up.

- **Follow-Up (Week 28):** Approximately 4 weeks after treatment cessation, patients return for a safety follow-up. The purpose is to check for any **late-occurring or persistent adverse effects** after stopping Glucofix. Vital signs are taken and a brief physical exam is conducted, focusing on any unresolved issues from treatment. Key safety labs are repeated: for example, liver enzymes and creatinine are tested to ensure any treatment-related lab changes have resolved after 4 weeks off drug. (HbA1c is not typically measured at follow-up, since the primary efficacy evaluation was at Week 24 and HbA1c would not markedly change in 4 weeks; however, if a patient had an exceptionally high HbA1c at Week 24, a follow-up value may be checked for medical management.) Concomitant medications are reviewed to note if any new therapies were started in the interim. All **adverse events** are reviewed – investigators check if any prior AEs are ongoing or if new events occurred since stopping medication. Any continuing drug-related adverse events may prompt further follow-up until resolution. After the follow-up visit assessments, the patient's participation in the study is complete.

(All data from visits are recorded in case report forms. Investigators will ensure protocol adherence at each step. Compliance, concomitant therapy changes, and adverse

events are carefully tracked to maintain data integrity.) The schedule above balances thorough early monitoring (to quickly identify safety signals) with practicality in later visits as the safety profile becomes clearer. This systematic schedule helps ensure patient safety while collecting all necessary efficacy data through the primary endpoint at Week 24 and beyond.

Inclusion Criteria

Eligible participants **must meet all** of the following inclusion criteria:

1. **Age 18 to 75 years:** Adults in this age range, of any gender, who are capable of giving consent. (Patients >75 or <18 are excluded to minimize age-related confounders and because the safety/efficacy in those groups is not established.)
2. **Confirmed Type 2 Diabetes Mellitus (T2DM):** Diagnosis of type 2 diabetes for at least 6 months prior to screening (per ADA/WHO criteria or medical records). This ensures a stable, established diagnosis (not transient hyperglycemia).
3. **Glycated Hemoglobin (HbA1c) 7.0% to 10.0% at screening:** Patients must have an HbA1c in this moderately uncontrolled range at the screening visit to qualify cdek.pharmacy.purdue.edu. This range indicates suboptimal glycemic control suitable for improvement, but not so high as to mandate immediate insulin therapy. (HbA1c is measured in a central lab; one re-test is allowed during screening if an initial value is slightly out of range.)
4. **Current Treatment Regimen:** Patients should be either managing diabetes with diet and exercise alone **or** on a stable dose of metformin monotherapy for ≥3 months prior to screening cdek.pharmacy.purdue.edu. “Stable” means no changes in dose; this criterion ensures that baseline glycemic control is stable and that the effect of Glucofix vs placebo can be isolated. No other glucose-lowering medications are permitted during this period (e.g., no recent use of sulfonylureas, DPP-4 inhibitors, GLP-1 agonists, SGLT2 inhibitors, insulin, etc., before trial entry).
5. **Body Mass Index (BMI) 18.0 to 40.0 kg/m²:** BMI in this range is required. This excludes underweight individuals and those with morbid obesity for whom extreme BMI might affect drug pharmacokinetics or safety. Patients should have

a BMI within 18–40 at screening (with no unexplained weight loss >5% in the last 3 months).

6. **Able to provide informed consent:** The patient is mentally and physically capable of understanding the trial requirements and has voluntarily signed the Institutional Review Board (IRB)-approved informed consent form. Participants must be willing to comply with all study procedures and visits.
7. **Women of childbearing potential:** Must have a negative pregnancy test at screening and baseline, **must not be pregnant or breastfeeding**, and must agree to use **effective contraception** during the study and for a defined period after (e.g., oral contraceptive, IUD, implant, abstinence, or partner sterilization). Women who are post-menopausal (≥1 year without menses) or surgically sterile are exempt from contraception requirements, but if <1 year since menopause, they should be treated as of childbearing potential.
8. **Male participants:** Men with partners of childbearing potential must agree to use a medically acceptable form of contraception (e.g., condom plus spermicide) during the study and for a period after, to avoid impregnating their partner. Male participants must also agree to refrain from sperm donation during the trial.
9. **Willingness and ability to comply with study procedures:** Patients must be willing to adhere to the study visit schedule, medication instructions, and other protocol requirements. This includes willingness to perform self-monitoring of blood glucose (SMBG) at home as instructed (e.g., fasting glucose readings or if symptoms of hypoglycemia occur), maintain a medication diary, and follow dietary/exercise advice given for the study duration. The participant should have a reliable means of contact and be likely to complete the full study.
10. **General health status acceptable for the study:** Patients should be in generally stable health aside from diabetes. Chronic medical conditions (e.g., hypertension, dyslipidemia) are permitted if **stable and well-controlled** (with or without medication). Screening evaluations (physical exam and labs) should show **no significant abnormalities** that would pose undue risk or interfere with interpretation of results. Key organ function parameters (renal, hepatic, hematologic) must be within acceptable ranges: e.g., serum creatinine within normal limits for age (or eGFR above a minimum threshold, such as >60

mL/min/1.73m²), ALT/AST not exceeding 2.5× the upper limit of normal (ULN), etc. Participants should have no active infection or acute illness at enrollment.

Rationale: These inclusion criteria select for adult type 2 diabetic patients who have suboptimal glycemic control and can potentially benefit from a glucose-lowering therapy. By requiring a specific HbA1c range and stable pre-trial treatment, the study ensures that the population has measurable room for improvement and that any HbA1c change is attributable to the investigational drug rather than recent medication changes. Ensuring patients are generally healthy (apart from diabetes) and can comply with the protocol helps maintain patient safety and data quality.

Exclusion Criteria

Patients **will be excluded** from the trial if **any** of the following criteria apply:

1. **Type 1 diabetes or other non-T2DM etiology:** Patients with Type 1 diabetes mellitus (autoimmune β-cell destruction) are excluded, as are those with any other forms of diabetes besides type 2 (e.g., latent autoimmune diabetes of adults, monogenic diabetes/MODY, or secondary diabetes due to pancreatic disorders). **History of diabetic ketoacidosis (DKA)** or hyperosmolar hyperglycemic state/coma (HHS) at any time is also exclusionary cdek.pharmacy.purdue.edu, as such history suggests unstable or Type 1 diabetes physiology unsuited for a placebo-controlled trial.

2. **Use of prohibited diabetic medications:** Use of any glucose-lowering medications other than metformin in the 3 months prior to screening is not allowed. This includes insulin of any kind, sulfonylureas, thiazolidinediones (TZDs), DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, meglitinides, or any investigational anti-diabetic agent. Patients who require more than one oral agent to control diabetes, or who have been on insulin recently, are excluded because their inclusion would confound efficacy results and could pose safety issues on placebo. (Short-term prior insulin use for an acute issue may be reviewed case-by-case, but generally patients needing insulin are not eligible.)

3. **Recent acute cardiovascular events:** Any history of a **myocardial infarction** (heart attack), **unstable angina**, **stroke**, or transient ischemic attack (TIA) in the **6 months** prior to screening excludes the patient. These conditions pose high risk for near-term recurrence and would make the trial interventions and assessments unsafe or difficult. Patients with **New York Heart Association (NYHA) Class III or IV heart failure** or **severe uncontrolled arrhythmias** are also excluded. In summary, significant cardiovascular disease – such as recent acute coronary syndrome or advanced heart failure – is exclusionary due to safety concerns and potential impact on outcomes.

4. **Uncontrolled hypertension:** Resting blood pressure >160/100 mmHg at screening (despite treatment) is exclusionary. Patients with hypertension should be on a stable regimen and have blood pressure below this threshold. This

criterion ensures cardiovascular risk is mitigated and avoids confounding effects of severe hypertension on outcome measures.

5. **Significant renal impairment: Chronic kidney disease** with **estimated GFR <30 mL/min/1.73m²** (Stage 4 or worse) or patients on **dialysis** are excluded. Severe renal dysfunction could affect drug metabolism/excretion (if Glucofix is renally cleared) and heightens the risk of drug accumulation or adverse effects (and such patients may need different glycemic targets and therapies). A screening serum creatinine corresponding to eGFR <30 is exclusionary. (Note: If eGFR is 30–45, patients may also be excluded or limited, depending on Glucofix's safety in moderate CKD – here we choose <30 as a strict cutoff; investigators will use caution for eGFR 30–45 as well.)

6. **Hepatic impairment:** Active liver disease or significant hepatic impairment is exclusionary. Specifically, patients with **ALT or AST >3× ULN** at screening are excluded (even if asymptomatic), as this may indicate liver injury. Patients with liver cirrhosis (Child-Pugh B or C), active hepatitis (e.g. hepatitis B or C with significant elevation in liver enzymes), or other serious hepatic disorder are not eligible. The trial drug's effects on the liver need to be evaluated in a population without confounding pre-existing liver disease, and to ensure patient safety.

7. **Active malignancy:** Patients with any active cancer are excluded (with the exception of adequately treated non-melanoma skin cancer or in situ cervical cancer). Additionally, any history of malignancy within the past 5 years (prior to screening) is exclusionary, unless the cancer was definitively treated and is considered cured. This criterion prevents enrolling patients with serious comorbid conditions that could both affect short-term health and interfere with trial participation (and certain diabetes drugs have contraindications in patients with a history of specific tumors).

8. **History of pancreatitis:** A past history of acute or chronic **pancreatitis** (inflammation of the pancreas) excludes the patient cdek.pharmacy.purdue.edu. This is because some diabetes medications (e.g., GLP-1 analogs) carry a risk of pancreatitis, and a predisposition could be exacerbated by the study drug. Although Glucofix's mechanism is not fully known, the study errs on caution by excluding those with pancreatitis history.

9. **Diabetic retinopathy requiring acute treatment:** Patients with **proliferative diabetic retinopathy** or significant **diabetic macular edema** that currently requires therapeutic intervention (such as laser therapy or intraocular injections) are excluded cdek.pharmacy.purdue.edu. Ongoing active retinal treatment could confound outcomes (e.g., vision changes, stress) and indicates unstable diabetes complications. (Patients with background or non-proliferative retinopathy not needing urgent treatment can be included, but should continue routine ophthalmologic care.)

10. **Pregnancy or lactation:** Pregnant women or women who are breastfeeding are **excluded**. Any female participant who tests positive on a pregnancy test at screening or baseline is not eligible. Women who become pregnant during the study will discontinue study drug immediately. This criterion is to protect unborn children from any potential drug exposure and because pregnancy itself alters glucose metabolism significantly.

11. **Substance abuse: Alcohol or drug abuse** that could interfere with study compliance or patient safety leads to exclusion. Specifically, a history of alcohol abuse, or drinking more than a threshold amount (e.g., >14 drinks per week) in the past 6 months, is exclusionary. Similarly, any illicit drug use or dependency (excluding caffeine/nicotine) within the past year is exclusionary. These conditions raise concerns about medication adherence, accurate reporting of AEs, and potential drug interactions.

12. **Allergy to study medication:** Known **hypersensitivity to "Glucofix" or its excipients** (inactive ingredients) excludes the patient. If the investigational product contains a drug in the same class as Glucofix, patients with a history of allergy to that class are also excluded. For example, if Glucofix were a sulfonylurea, patients with sulfonylurea allergy would be excluded. This is to prevent any allergic adverse reactions during the trial.

13. **Recent participation in another clinical trial:** Participation in any investigational drug trial within 3 months (or 90 days) prior to screening is exclusionary. This "washout" period avoids carry-over effects from a previous study drug and prevents overlapping study commitments. Additionally, patients cannot enroll if they plan to participate in another clinical trial concurrently.

14. **Concurrent therapy affecting glucose:** Chronic use of systemic corticosteroids or other medications known to significantly affect glucose metabolism is not allowed. For example, patients on high-dose prednisone or other glucocorticoids (for chronic conditions like rheumatoid arthritis or severe asthma) are excluded, as these drugs induce hyperglycemia and would confound efficacy assessment. (Intermittent short courses of steroids may be evaluated case-by-case, but generally such patients are not ideal for a glycemic control trial.) Other medications that may interfere with glucose levels or study drug pharmacokinetics (e.g., certain anti-psychotics causing metabolic effects, or strong CYP450 inhibitors if Glucofix is metabolized by those pathways) may also be criteria for exclusion if applicable.

15. **Any condition that, in the investigator's judgment, makes the patient unsuitable for the study:** This is a catch-all criterion. Examples include: significant psychiatric illness or cognitive impairment that would impair the ability to follow instructions or give informed consent; history of non-compliance with medical regimens; any acute life-threatening illness; or expected survival <1 year due to any medical condition. The investigator should not enroll patients who are unlikely to safely complete the trial or adhere to protocol requirements.

Rationale: The above exclusion criteria are designed to ensure patient safety and to obtain a clean assessment of Glucofix's efficacy. Patients with other types of diabetes or severe diabetic complications (like recent DKA or proliferative retinopathy) are excluded to maintain a homogeneous T2DM population and because such patients may require urgent therapies incompatible with a placebo period cdek.pharmacy.purdue.edu. Excluding recent cardiovascular events and advanced organ disease (renal, hepatic, cardiac) protects those patients from potential risk and avoids confounding the interpretation of results by other health issues. Pregnancy and substance abuse exclusions are standard for safety and compliance reasons. By removing these high-risk or confounding conditions, the trial can more safely and clearly determine Glucofix's true therapeutic effect versus placebo.

References:

1. FDA Center for Drug Evaluation and Research – Statistical Review for a diabetes drug (NovoLog). *"The primary efficacy endpoint is change from baseline in HbA1c after 26 weeks of randomized treatment."* accessdata.fda.gov
2. Clinical Trial Eligibility Example (Tirzepatide SURMOUNT-2 study): Demonstrates typical criteria – *Type 2 diabetes patients with HbA1c 7–10% on stable therapy for ≥3 months were included; Type 1 diabetes or history of ketoacidosis were excluded* cdek.pharmacy.purdue.edu cdek.pharmacy.purdue.edu. Also, history of pancreatitis and active retinopathy were exclusion criteria in that trial cdek.pharmacy.purdue.edu cdek.pharmacy.purdue.edu, similar to this protocol.
3. MDS Foundation – Clinical Trials Guide: *Early trial visits are often busiest with frequent assessments, while later visits are less intensive as safety is established* mds-foundation.org.
4. Efficacy of GLP-1 therapy (Dulaglutide) vs placebo: Example outcome from a 24-week trial – *Dulaglutide was superior to placebo in HbA1c reduction by ~1.3% at 24 weeks* pubmed.ncbi.nlm.nih.gov, illustrating the magnitude of change a potent therapy can achieve, which informs the effect size this Glucofix trial may target.