Cover Page

Release Date: June 16, 2025

ClinicalTrials.gov ID: NCT07033585

Unique Protocol ID: ANDA219975 + ANDA220011

Brief Title: Generic Drugs (Dapagliflozin and Saxagliptin) Treat Type 2 Diabetes Patients with Controlled Cancers (GD-T2D)

Official Title: Generic Drugs (Dapagliflozin and Saxagliptin) Treat Type 2 Diabetes Patients with Controlled Cancers

Secondary IDs: NPI-1831468511 [Registry ID: HHS, Health Care Provider Individual]
NPI-1023387701 [Registry ID: HHS, Health Care Provider Organization]
FWA00015357 [Registry ID: HHS, Human Protections Administrator]
IORG0007849 [Registry ID: HHS, IORG]
IRB00009424 [Registry ID: HHS, IRB]
ANDA219975 [Registry ID: FDA, ANDA]
ANDA220011 [Registry ID: FDA, ANDA]

Contents

21 CFR 312.23(a)(1)(v)
A commitment to conduct the investigation in accordance with all other applicable regulatory requirements.

Statement

I write the **commitment** with respect to each clinical study involving human subjects that it either will be conducted in compliance with the institutional review board regulations in part 56 or will not be subject to the regulations under §56.104 or §56.105; and that it either will be conducted in compliance with the informed consent regulations in part 50 or will not be subject to the regulations under §50.23 and §50.24.

Study Protocol [21 CFR 312.23(a)(6)(iii)] for ANDA Type 2 Diabetes Clinical Trial

ANDA SNP - NCT07033585 Clinical Trial

Han Xu, **Sponsor-Investigator** will initiate and conduct the Study Protocol [21 CFR 312.23(a)(6)(iii)].

- **ClinicalTrials.gov ID: NCT07033585**
- **Sponsor:** Han Xu, M.D., Ph.D., FAPCR, **Sponsor-Investigator**, IRB Chair
- **Responsible Party:** Sponsor-Investigator
- **Sponsor-Investigator:** Han Xu, M.D., Ph.D., FAPCR
- **Study Principal Investigator [Principal Investigator (PI)]:** Han Xu, M.D., Ph.D., FAPCR

My protocol will follow the requirements of 21 CFR 312.23(a)(6)(iii).

The protocol is to contain the following, with the specific elements and detail of the protocol reflecting the above distinctions depending on the Phase 2 of the ANDA type 2 diabetes clinical study:

(a) A statement of the objectives and purpose of the study.

Generic Drugs Treat Type 2 Diabetes Patients with Controlled Cancers (GD-T2D).

(b) The name and address and a statement of the qualifications (curriculum vitae or **other statement of qualifications**) of sponsor-investigator or each investigator, and the name of each Principal Investigator or sub-investigator (e.g., research fellow, resident) working under the supervision of the sponsor-investigator; the name and address of the research facilities to be used; and the name and address of each reviewing Institutional Review Board.

M**y investigation will follow the requirements of 21 CFR 312.23(a)(6)(iii)(b).**

The name of sponsor-investigator: Han Xu, M.D., Ph.D., Sponsor-Investigator, IRB Chair, Medical Director
The address of sponsor-investigator: 5545 Burnside Drive, Online Site, Rockville, Maryland, 20853

The name of the IRB: IRB00009424 -- Medicine Invention Design Incorporation (MIDI) IRB #1
The Address of the IRB: 5545 Burnside Drive, Online Site, Rockville, Maryland, 20853

The name of the research facility: IORG0007849 -- Medicine Invention Design Incorporation (MIDI)
The address of the research facility: 5545 Burnside Drive, Online Site, Rockville, Maryland, 20853

The statement of the qualifications of Sponsor-Investigator:

- 2020 - Active Member, **Fellow of the APCR (FAPCR)**, Academy of Physicians in Clinical Research (APCR) - APCR Membership Eligibility - Physician Investigator
  - Certificate of Fellow of Academy of Physicians in Clinical Research (FAPCR)
  - Academy of Physicians in Clinical Research (APCR)
    - **PI (Principal Investigator) in clinical trials**
    - **Medical Director of Clinical Research Site**
- 2025-06 - FDA Pre-Assignment IND 177776 for Type 2 Diabetes Oral Mix Prescription
  - **Sponsor:** HAN XU
- 2025-06 - **ClinicalTrials.gov ID:** NCT07033585
  - **Sponsor:** Han Xu, M.D., Ph.D., FAPCR, **Sponsor-Investigator**, IRB Chair
  - **Responsible Party:** Sponsor-Investigator
  - **Sponsor-Investigator:** Han Xu, M.D., Ph.D., FAPCR
  - **Study Principal Investigator [Principal Investigator (PI)]:** Han Xu, M.D., Ph.D., FAPCR

(c) The criteria for patient selection and for exclusion of patients and an estimate of the number of patients to be studied.

- Criteria:
  - Select 600 type 2 diabetes patients with controlled cancers.
  - Dosage Duration at least 90 days

- ✧ The usual approach group - Recruit 300 no-placebo double blind random group separated type 2 diabetes patients currently using Oral Mix Prescription - 1 as follows:
- ✓ NDC 0310-6210-30 (FARXIGA - dapagliflozin tablet, film coated) (NDA202293) (Mix-1)
- ✓ NDC 0310-6105-30 (ONGLYZA - saxagliptin tablet, film coated) (NDA022350) (Mix-1)
- ✓ NDC 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) (ANDA077880) (Mix-1)
- ✧ The study approach group - Recruit 300 no-placebo double blind random group separated type 2 diabetes patients currently using Oral Mix Prescription - 2 as follows:
- ✓ China Import - dapagliflozin tablet (ANDA 219975) -- 10 mg orally once daily
- ✓ China Import - saxagliptin tablet (ANDA 220011) -- 5 mg orally once daily
- ✓ NDC 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day
- ✧ If any participating patients have serious side effects, they will stop the research.
- ✧ If any participating patients have no therapeutic effects, they will stop the research.

➢ Inclusion Criteria:

1. Clinical diagnosis of type 2 diabetes
2. Controlled cancers
3. Suitable for enough blood-drawing
4. Random and double blind
5. Measurable disease
6. Adequate organ functions
7. Adequate performance status
8. Age 24 years old and over
9. Sign an informed consent form
10. Receive blood-drawing

➢ Exclusion Criteria:

1. Uncontrolled cancer
2. Pregnancy
3. Breast-feeding
4. The patients with other serious intercurrent illnesses or infectious diseases
5. Have more than one different kind of cancer at the same time
6. Serious Allergy to Drugs
7. Serious Bleed Tendency
8. Serious Risks or Serious Adverse Events of the drug product
9. The prohibition of drug products
10. Have no therapeutic effects

(d) A description of the design of the study, including the kind of control group to be used, if any, and a description of methods to be used to minimize bias on the part of subjects, investigators, and analysts.

The usual approach group will try to do the following:

- ➢ Detect Hemoglobin A1c (HbA1c)
- ➢ Detect fasting blood glucose (FBG)
- ➢ Detect 2-hour postprandial blood glucose (2 hPBG)
- ➢ Detect fasting insulin (FINS)
- ➢ Detect 2-hour postprandial insulin (2 hPINS)

The study approach group will try to do the following:

- ➢ Detect Hemoglobin A1c (HbA1c)
- ➢ Detect fasting blood glucose (FBG)
- ➢ Detect 2-hour postprandial blood glucose (2 hPBG)
- ➢ Detect fasting insulin (FINS)
- ➢ Detect 2-hour postprandial insulin (2 hPINS)

The detailed methods:

Usual Approach Group: 300 double blind random group separated type 2 diabetes patients with controlled cancer
Oral Mix Prescription - 1:
NDC 0310-6210-30 (FARXIGA - dapagliflozin tablet, film coated) -- 10 mg orally once daily
NDC 0310-6105-30 (ONGLYZA - saxagliptin tablet, film coated) -- 5 mg orally once daily
NDC 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day

Study Approach Group: 300 double blind random group separated type 2 diabetes patients with controlled cancer
Oral Mix Prescription - 2:
China Import - dapagliflozin tablet (**ANDA 219975**) -- 10 mg orally once daily
China Import - saxagliptin tablet (**ANDA 220011**) -- 5 mg orally once daily
NDC 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day

- Detect Hemoglobin A1c (HbA1c)
- Detect fasting blood glucose (FBG)
- Detect 2-hour postprandial blood glucose (2 hPBG)
- Detect fasting insulin (FINS)
- Detect 2-hour postprandial insulin (2 hPINS)

(e) The method for determining the dose(s) to be administered, the planned maximum dosage, and the duration of individual patient exposure to the drug.

The method for determining the dose(s) to be administered:

- Usual Approach Group: 300 type 2 diabetes patients with Controlled Cancers
- ✧ Oral Mix Prescription - 1:
- ✓ **NDC** 0310-6210-30 (FARXIGA - dapagliflozin tablet, film coated) -- 10 mg orally once daily
- ✓ **NDC** 0310-6105-30 (ONGLYZA - saxagliptin tablet, film coated) -- 5 mg orally once daily
- ✓ **NDC** 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day

- Study Approach Group: 300 type 2 diabetes patients with Controlled Cancers
- ✧ Oral Mix Prescription - 2:
- ✓ China Import - dapagliflozin tablet (**ANDA 219975**) -- 10 mg orally once daily
- ✓ China Import - saxagliptin tablet (**ANDA 220011**) -- 5 mg orally once daily
- ✓ **NDC** 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day

The planned maximum dosage(s):

- The usual approach randomization of double-blinding active treatment concurrent control group:
- ✧ Oral Mix Prescription - 1:
- ✓ **NDC** 0310-6210-30 (FARXIGA - dapagliflozin tablet, film coated) -- 10 mg orally once daily
- ✓ **NDC** 0310-6105-30 (ONGLYZA - saxagliptin tablet, film coated) -- 5 mg orally once daily
- ✓ **NDC** 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day

- The study approach randomization of double-blinding active treatment concurrent control group:
- ✧ Oral Mix Prescription - 2:
- ✓ China Import - dapagliflozin tablet (**ANDA 219975**) -- 10 mg orally once daily
- ✓ China Import - saxagliptin tablet (**ANDA 220011**) -- 5 mg orally once daily
- ✓ **NDC** 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day

The duration of individual patient exposure to the drug(s):

- The usual approach randomization of double-blinding active treatment concurrent control group:
- ✧ Oral Mix Prescription - 1:
- The study approach randomization of double-blinding active treatment concurrent control group:
- ✧ Oral Mix Prescription - 2:
- **The duration of individual patient exposure to the drugs:** 90 days

(f) A description of the observations and measurements to be made to fulfill the objectives of the study.

- Detect Hemoglobin A1c (HbA1c)
- Detect fasting blood glucose (FBG)
- Detect 2-hour postprandial blood glucose (2 hPBG)
- Detect fasting insulin (FINS)
- Detect 2-hour postprandial insulin (2 hPINS)

(g) A description of clinical procedures, laboratory tests, or other measures to be taken to monitor the effects of the drug in human subjects and to minimize risk.

The clinical procedures:

- Recruit 600 type 2 diabetes patients with controlled cancers.
- The usual approach randomization of double-blinding active treatment concurrent control group:
  - ✧ 300 type 2 diabetes patients
  - ✧ Oral Mix Prescription - 1:
    - ✓ **NDC** 0310-6210-30 (FARXIGA - dapagliflozin tablet, film coated) -- 10 mg orally once daily
    - ✓ **NDC** 0310-6105-30 (ONGLYZA - saxagliptin tablet, film coated) -- 5 mg orally once daily
    - ✓ **NDC** 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day
- The study approach randomization of double-blinding active treatment concurrent control group:
  - ✧ 300 type 2 diabetes patients
  - ✧ Oral Mix Prescription - 2:
    - ✓ China Import - dapagliflozin tablet (**ANDA 219975**) -- 10 mg orally once daily
    - ✓ China Import - saxagliptin tablet (**ANDA 220011**) -- 5 mg orally once daily
    - ✓ **NDC** 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day

The laboratory tests:

- Detect Hemoglobin A1c (HbA1c)
- Detect fasting blood glucose (FBG)
- Detect 2-hour postprandial blood glucose (2 hPBG)
- Detect fasting insulin (FINS)
- Detect 2-hour postprandial insulin (2 hPINS)

The measures to be taken to monitor the effects of the drug in human subjects:

- Detect Hemoglobin A1c (HbA1c)
- Detect fasting blood glucose (FBG)
- Detect 2-hour postprandial blood glucose (2 hPBG)
- Detect fasting insulin (FINS)
- Detect 2-hour postprandial insulin (2 hPINS)
- Every type 2 diabetes patient will receive blood test one time per week.

The measures to be taken to minimize the risks of the drug in human subjects:

- Every type 2 diabetes patient will receive blood test one time per week.
- **LABEL:** FARXIGA - dapagliflozin tablet, film coated (https://dailymed.nlm.nih.gov)
- **LABEL:** ONGLYZA - saxagliptin tablet, film coated (https://dailymed.nlm.nih.gov)
- **LABEL:** METFORMIN HYDROCHLORIDE - metformin tablet (https://dailymed.nlm.nih.gov)
- **Nan Fang Yi Ke Da Xue Xue Bao:** 2019 Nov 30; 39(11): 1305-1311.

21 CFR§56.102 (i)
Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

The IRB00009424 must let all subjects sign a written consent form and will let the research NCT07033585 present no more than minimal risk of harm to subjects as well as will let the research NCT07033585 involve no procedures for outside the written consent document context.

21 CFR§56.111 (a) (1)
Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design, and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

- Usual Approach Group: 300 type 2 diabetes patients with Controlled Cancers
  - Oral Mix Prescription - 1:
  - ✓ **NDC** 0310-6210-30 (FARXIGA - dapagliflozin tablet, film coated) -- 10 mg orally once daily
  - ✓ **NDC** 0310-6105-30 (ONGLYZA - saxagliptin tablet, film coated) -- 5 mg orally once daily
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- Study Approach Group: 300 type 2 diabetes patients with Controlled Cancers
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  - ✓ China Import - dapagliflozin tablet (**ANDA 219975**) -- 10 mg orally once daily
  - ✓ China Import - saxagliptin tablet (**ANDA 220011**) -- 5 mg orally once daily
  - ✓ **NDC** 65162-175-10 (METFORMIN HYDROCHLORIDE - metformin tablet) -- 500 mg twice a day
- If any participating patients have serious side effects, they will stop the research.
- If any participating patients have no therapeutic effects, they will stop the research.

21 CFR 56.102(g)
Institutional Review Board (IRB) means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects.

21 CFR 56.102(m)
IRB approval means the determination of the IRB that the clinical investigation has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.

21 CFR 56.107(e)
No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

I (Han Xu, M.D., Ph.D. i.e., Sponsor i.e., Sponsor-Investigator) as IRB Chair of our IRB (IRB00009424) will only organize the IRB meeting but give up my voting power in the determination of IRB, when I conduct my clinical investigation (NCT07033585).

- 2020 - Active Member, Fellow of the APCR (FAPCR), Academy of Physicians in Clinical Research (APCR) - APCR Membership Eligibility - Physician Investigator
  - Certificate of Fellow of Academy of Physicians in Clinical Research (FAPCR)
  - Academy of Physicians in Clinical Research (APCR)
    - **PI (Principal Investigator) in clinical trials**
    - **Medical Director of Clinical Research Site**
- 2025-06 - FDA Pre-Assignment IND 177776 for Type 2 Diabetes Oral Mix Prescription
  - **Sponsor:** HAN XU
- 2025-06 - **ClinicalTrials.gov ID:** NCT07033585
  - **Sponsor:** Han Xu, M.D., Ph.D., FAPCR, **Sponsor-Investigator**, IRB Chair
  - **Responsible Party:** Sponsor-Investigator
  - **Sponsor-Investigator:** Han Xu, M.D., Ph.D., FAPCR
  - **Study Principal Investigator [Principal Investigator (PI)]:** Han Xu, M.D., Ph.D., FAPCR

21 CFR 56.102(k)
Sponsor-investigator means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, … The term does not include any person other than an individual, e.g., it does not include a corporation or agency. The obligations of a sponsor-investigator under this part include both those of a sponsor and those of an investigator.

21 CFR §50.3 (f)
Sponsor-investigator means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, … The term does not include any person other than an individual, e.g., corporation or agency.

I (**Han Xu, Sponsor-Investigator**) can both initiate and conduct, alone or with others, my clinical investigation. So, I am a qualified investigator for my ANDA diabetes drugs' clinical trial.

21 CFR 312.23(a)(1)(v)
A commitment to conduct the investigation in accordance with all other applicable regulatory requirements.

Statement

I write the **statement** with respect to each clinical study involving human subjects that it either will be conducted in compliance with the institutional review board regulations in part 56 or will not be subject to the regulations under §56.104 or §56.105; and that it either will be conducted in compliance with the informed consent regulations in part 50 or will not be subject to the regulations under §50.23 and §50.24.

Han Xu, M.D., Ph.D., FAPCR, Sponsor-Investigator, Medical Director, Medical Monitor, Safety Officer

- NPI 1831468511 - Individual
  - Clinical Ethicist - (Code - 174V00000X)
  - Specialist Research Study - (Code - 1744R1102X)
  - Pharmacist, Pharmacist Clinician (PhC) / Clinical Pharmacy Specialist (Code - 1835P0018X)
- **Certificate of Fellow of Academy of Physicians in Clinical Research (FAPCR)**
  Academy of Physicians in Clinical Research (APCR)
  - Principal Investigator (PI) in clinical trials
  - Medical Director of Clinical Research Site
- **Medicine Invention Design Incorporation (MIDI) (IORG0007849)**
  - IORG Director (IORG0007849)
- **Medicine Invention Design Incorporation (MIDI) IRB #1 (IRB00009424)**
  - IRB Chair (IRB00009424)
- **Federal-wide Assurance (FWA) for the Protection of Human Subjects (FWA00015357)**
  - Human Subjects Administrator (FWA00015357)
- **FDA Wholesale Drug Distributor (Maryland License Number: D11379922)**
  - Medical Director (D11379922)
- NPI 1023387701 - Organization
  - Multi-Specialty Group (Code - 193200000X)
  - Research Clinic/Center - (Code - 261QR1100X)
  - Clinical Medical Laboratory - (Code - 291U00000X)
  - **Health Maintenance Organization - (Code - 302R00000X)**
  - Managed Care Organization Pharmacy (Code - 3336M0003X)
  - Mail Order Pharmacy - (Code - 3336M0002X)
  - FDA Wholesale Drug Distributor (Maryland License Number: D11379922)
  - Distribute human drug products under own private label (FDA NDC Labeler Code - 69891)
  - FDA Establishment Identifier (FEI Number - 300363713)
- My IND has been granted. My pre-assigned number is IND 177776.
  - Sponsor: HAN XU
  - Sponsor: Medicine Invention Design Incorporation
- **ClinicalTrials.gov ID: NCT07033585** under **42 CFR Part 11**
  - Responsible Party: **Sponsor-Investigator:** Han Xu, M.D., Ph.D., FAPCR
  - Study Principal Investigator [**Principal Investigator (PI)**]: Han Xu, M.D., Ph.D., FAPCR
  - Study Director (**Medical Director**): Han Xu, M.D., Ph.D., FAPCR
  - Study Chair (**IRB Chair**): Han Xu, M.D., Ph.D., FAPCR

Company Name: Medicine Invention Design, Inc.
Contact Name: Han Xu, M.D., Ph.D., FAPCR, Sponsor-Investigator, Medical Director, IRB Chair
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