Cover Page

Release Date: August 26, 2023

ClinicalTrials.gov ID: NCT03348670

Unique Protocol ID: IND 168800 to be IND EXEMPT

Brief Title: Pharmacogenomics IND EXEMPT SNP Clinical Study - Abiraterone and Single Nucleotide Polymorphisms (Drugs-SNPs)

Official Title: Explore the Relationship Between Single Nucleotide Polymorphisms and Abiraterone Response and Toxicity in Patients with Prostate Cancer.

Secondary IDs: FWA00015357 [Registry ID: HHS, Human Protections Administrator]
IRB00009424 [Registry ID: HHS, IRB]
IORG0007849 [Registry ID: HHS, IORG]
NPI - 1831468511 [Registry ID: HHS, Health Care Provider Individual]
NPI - 1023387701 [Registry ID: HHS, Health Care Provider Organization]
IND 168800 [Registry ID: FDA IND EXEMPT]

Contents

21 CFR 312.2(b)(1)(iv)

The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50

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.

Study Protocol [21 CFR 312.23(a)(6)(iii)] for IND EXEMPT SNP Clinical Trial

IND EXEMPT SNP - NCT03348670 Clinical Trial is an **IC & IRB** Clinical Study.

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

- **ClinicalTrials.gov ID: NCT03348670**
- **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§312.2(b)(1)
The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements of this part……

According to 21 CFR 312.2(b)(1), my clinical investigation of the drug product (**Abiraterone Tablet**) that is lawfully marketed in the United States is exempt from the requirements of this part, which this part means 21 CFR Part 312. **Therefore, my protocol will be exempt from 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 SNP study:

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

Explore the relationship between single nucleotide polymorphisms and abiraterone response and toxicity in patients with prostate cancer.

- Correlate CYP17 Gene Single Nucleotide Polymorphisms (SNPs) to Therapeutic Effects of Using abiraterone to Treat Prostate Cancer (PC), based on precisely sequencing drug target gene via Peripheral Blood DNA.
- Correlate SULT2A1 Gene Single Nucleotide Polymorphisms (SNPs) to Side Effects of Using abiraterone to Treat Prostate Cancer (PC), based on precisely sequencing drug target gene via Peripheral Blood DNA.

(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.

According to 21 CFR 312.2(b)(1), my clinical investigation of the drug product (**Abiraterone Tablet**) that is lawfully marketed in the United States is exempt from the requirements of this part, which this part means 21 CFR Part 312. **Therefore, my investigation must be exempt from 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**

- 2023-08 - FDA Pre-Assignment IND 168800 for Abiraterone Tablet
  - **Sponsor:** HAN XU
- 2023-08 - **ClinicalTrials.gov ID:** NCT03348670
  - **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 Prostate Cancer (PC) Patients without prostate resection.
- Duration at least 90 days
- The usual approach group - Recruit 300 no-placebo double blind random group separated PC patients currently used High Dose Combined Chemotherapy on Abiraterone Tablet plus Prednisone Tablet plus Relugolix Tablet after clinical diagnosis of prostate cancer, like as the usual approach group.
- The study approach group - Recruit 300 no-placebo double blind random group separated PC patients currently used Low Dose Combined Chemotherapy on Abiraterone Tablet plus Prednisone Tablet plus Relugolix Tablet after clinical diagnosis of PC, like as the study approach group.
- If any participating patients have serious side effects, they will be stopped the research.
- If any participating patients have no therapeutic effects, they will be stopped the research.

- Inclusion Criteria:
- Clinical diagnosis of prostate cancer without prostate resection
- Random and double blind
- Measurable disease
- Adequate organ functions
- Adequate performance status
- Age 22 years old and over
- Sign an informed consent form.
- Receive blood-drawing.

- Exclusion Criteria:
- Treatment with other anti-cancer therapies and the therapies cannot be stopped currently.
- The patients with other serious inter-current illness or infectious diseases
- Have more than one different kind of cancer at the same time
- Serious Allergy Tendency
- Serious Bleed Tendency
- Serious Risks or Serious Adverse Events of the drug product
- The prohibition of the drug product
- The participating patients have serious side effects.
- The participating patients 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, 300 double blind random group separated prostate cancer patients currently used High Dose Combined Chemotherapy on Abiraterone Tablet plus Prednisone Tablet plus Relugolix Tablet, based on precisely sequencing drug targets' genes, it will try to do following:

- Correlate CYP17 Gene SNP to Therapeutic Effects of Using Abiraterone to Treat Prostate Cancer (PC), via Testing Peripheral Blood DNA.
- Correlate SULT2A1 Gene SNP to Side Effects of Using Abiraterone to Prostate Cancer (PC), via Testing Peripheral Blood DNA.

The study approach group, 300 double blind random group separated prostate cancer patients currently used Low Dose Combined Chemotherapy on Abiraterone Tablet plus Prednisone Tablet plus Relugolix Tablet, based on precisely sequencing drug targets' genes, it will try to do following:

- Correlate CYP17 Gene SNP to Therapeutic Effects of Using Abiraterone to Treat Prostate Cancer (PC), via Testing Peripheral Blood DNA.
- Correlate SULT2A1 Gene SNP to Side Effects of Using Abiraterone to Prostate Cancer (PC), via Testing Peripheral Blood DNA.

The detailed methods:

1) Detect each drug target whole gene precision sequence of everyone patient for all 600-recruited double-blind prostate cancer patients.

- Oxford Nanopore Technologies Ltd - Nanopore DNA Sequencing uses electrophoresis to transport an unknown sample through an orifice of 10^{-9} meters in diameter. A nanopore system always contains an electrolytic solutions- when a constant electric field is applied, an electric current can be observed in the system. The magnitude of the electric current density across a nanopore surface depends on the nanopore's dimensions and the composition of DNA or RNA that is occupying the nanopore. Sequencing is made possible because, when close enough to nanopores, samples cause characteristic changes in electric current density across nanopore surfaces. The total charge flowing through a nanopore channel is equal to the surface integral of electric current density flux across the nanopore unit normal surfaces between times t_1 and t_2.
- DNA Sequencing
- Prepare
- ✓ Streamlined library prep in as little as 10 minutes.
- ✓ PCR-free library prep using 400 ng DNA.
- ✓ PCR option for very low input amounts
- ✓ Multiplexing options for more cost-effective analysis
- Sequence
- ✓ Real-time sequencing on MinION, GridION or PromethION
- Analyses
- ✓ Real-time analysis with on device or local infrastructure base-calling
- ✓ Detect DNA modifications using open-source tools.

2) Mutually compare everyone patient drug target whole gene precision sequence for total 600-recruited double-blind NSCLC patients.
3) Calculate each drug target gene SNP in all 600-recruited double-blind prostate cancer patients.
4) Correlate everyone patient drug target gene SNP to everyone patient drug efficacy.
5) Correlate everyone patient drug target gene SNP to everyone patient drug safety.
6) Mutually compare the usual approach group SNPs (300 double blind random group separated PC patients) with the study approach group SNPs (300 double blind random group separated PC patients).
7) Confirm the relationship between drug target gene SNPs and drug efficacy.

(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:

- **LABEL:** ZYTIGA - Abiraterone Tablet (**DAILYMED:** https://dailymed.nlm.nih.gov)
- **LABEL:** DELTASONE - Prednisone Tablet (**DAILYMED:** https://dailymed.nlm.nih.gov)
- **LABEL:** ORGOVYX - relugolix tablet, film coated (**DAILYMED:** https://dailymed.nlm.nih.gov)

The planned maximum dosage(s):

- ✧ The usual approach randomization double-blinding active treatment concurrent control group:

- ✓ ZYTIGA - abiraterone acetate tablet, film coated -- 2 x 500 mg tablets orally once daily (12 weeks)
- ✓ DELTASONE - prednisone tablet -- 5 mg orally twice daily (12 weeks)
- ✓ ORGOVYX - relugolix tablet, film coated -- 360 mg orally first day -- 120 mg orally once daily (12 weeks)

- ✧ The study approach randomization double-blinding active treatment concurrent control group:
- ✓ ZYTIGA - abiraterone acetate tablet -- 4 x 250 mg tablets orally once daily (12 weeks)
- ✓ DELTASONE - Prednisone tablet -- 5 mg orally once daily (12 weeks)
- ✓ ORGOVYX - relugolix tablet, film coated -- 360 mg orally first day -- 120 mg orally once daily) (12 weeks)

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

- ✧ **The usual approach randomization double-blinding active treatment concurrent control group:**
- ✓ ZYTIGA - abiraterone acetate tablet, film coated -- 2 x 500 mg tablets orally once daily (12 weeks)
- ✓ DELTASONE - prednisone tablet -- 5 mg orally twice daily (12 weeks)
- ✓ ORGOVYX - relugolix tablet, film coated -- 360 mg orally first day -- 120 mg orally once daily (12 weeks)
- ✧ **The study approach randomization double-blinding active treatment concurrent control group:**
- ✓ ZYTIGA - abiraterone acetate tablet -- 4 x 250 mg tablets orally once daily (12 weeks)
- ✓ DELTASONE - Prednisone tablet -- 5 mg orally once daily (12 weeks)
- ✓ ORGOVYX - relugolix tablet, film coated -- 360 mg orally first day -- 120 mg orally once daily (12 weeks)
- ➢ **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.

- ➢ Sequence precisely each target gene DNA whole chain in peripheral blood like as following: CYP17, SULT2A1, GnRH-R, CYP3A (CYP3A4, CYP3A5, CYP3A7, CYP3A43), CYP2C8.
- ➢ Correlate CYP17 Gene SNP to Therapeutic Effects of Using Abiraterone to Treat Prostate Cancer, based on precisely sequencing drug target gene via Peripheral Blood DNA.
- ➢ Correlate SULT2A1 Gene SNP to Side Effects of Using Abiraterone to Treat Prostate Cancer, based on precisely sequencing drug target gene via Peripheral Blood DNA.
- ➢ Oxford Nanopore Technologies Ltd - Nanopore DNA Sequencing uses electrophoresis to transport an unknown sample through an orifice of 10^{-9} meters in diameter. A nanopore system always contains an electrolytic solutions- when a constant electric field is applied, an electric current can be observed in the system. The magnitude of the electric current density across a nanopore surface depends on the nanopore's dimensions and the composition of DNA or RNA that is occupying the nanopore. Sequencing is made possible because, when close enough to nanopores, samples cause characteristic changes in electric current density across nanopore surfaces. The total charge flowing through a nanopore channel is equal to the surface integral of electric current density flux across the nanopore unit normal surfaces between times t_1 and t_2.
- ➢ DNA Sequencing
- ➢ Prepare
- ✓ Streamlined library prep in as little as 10 minutes.
- ✓ PCR-free library prep using 400 ng DNA.
- ✓ PCR option for very low input amounts
- ✓ Multiplexing options for more cost-effective analysis
- ➢ Sequence
- ✓ Real-time sequencing on MinION, GridION or PromethION
- ➢ Analyses
- ✓ Real-time analysis with on device or local infrastructure base-calling.
- ✓ Detect DNA modifications using open source tools.

(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 patients of Prostate Cancer (PC) without prostate resection.

- ✧ The 600 prostate cancer patients are randomly separated into 2 groups via computer.
- ✧ The usual approach group is 300 prostate cancer patients.
- ✧ The study approach group is 300 prostate cancer patients.
- ✧ Every prostate cancer patient will receive peripheral blood-drawing.
- ✧ Keep storing all peripheral blood.
- ✧ Every PC patient will receive testing each Target Gene SNP in Peripheral Blood DNA like as following: CYP17, SULT2A1, GnRH-R, CYP3A (CYP3A4, CYP3A5, CYP3A7, CYP3A43), CYP2C8.
- ✧ The usual approach group (300 prostate cancer patients) for everyone:
- ✓ ZYTIGA - abiraterone acetate tablet, film coated -- 2 x 500 mg tablets orally once daily (12 weeks)
- ✓ DELTASONE - prednisone tablet -- 5 mg orally twice daily (12 weeks)
- ✓ ORGOVYX - relugolix tablet, film coated -- 360 mg orally first day -- 120 mg orally once daily (12 weeks)
- ✓ Sequence precisely each target gene DNA whole chain in Peripheral Blood like as following: CYP17, GnRH-R.
- ✓ Correlate CYP17 Gene SNP to Therapeutic Effects of Using Abiraterone to Treat Prostate Cancer (PC), via Testing Peripheral Blood DNA.
- ✓ Sequence precisely each target gene DNA whole chain in peripheral blood like as following: SULT2A1, CYP3A (CYP3A4, CYP3A5, CYP3A7, CYP3A43), CYP2C8.
- ✓ Correlate SULT2A1 Gene SNP to Side Effects of Using Abiraterone to Treat Prostate Cancer (PC), via Testing Peripheral Blood DNA.
- ✧ The study approach group (300 prostate cancer patients) for everyone:
- ✓ ZYTIGA - abiraterone acetate tablet -- 4 x 250 mg tablets orally once daily (12 weeks)
- ✓ DELTASONE - Prednisone tablet -- 5 mg orally once daily (12 weeks)
- ✓ ORGOVYX- relugolix tablet, film coated -- 360 mg orally first day -- 120 mg orally once daily) (12 weeks)
- ✓ Sequence precisely each target gene DNA whole chain in Peripheral Blood like as following: CYP17, GnRH-R.
- ✓ Correlate CYP17 Gene SNP to Therapeutic Effects of Using Abiraterone to Treat Prostate Cancer (PC), via Testing Peripheral Blood DNA.
- ✓ Sequence precisely each target gene DNA whole chain in peripheral blood like as following: SULT2A1, CYP3A (CYP3A4, CYP3A5, CYP3A7, CYP3A43), CYP2C8.
- ✓ Correlate SULT2A1 Gene Single Nucleotide Polymorphisms (SNPs) to Side Effects of Using Abiraterone to Treat Prostate Cancer (PC), via Testing Peripheral Blood DNA.
- ✧ Every prostate cancer patient will receive an image test one time per month.
- ✧ Every prostate cancer patient will receive blood test one time per week.
- ✧ Every prostate cancer patient will receive urine test one time per week.
- ✧ Every prostate cancer will receive ECG test one time per week.
- ✧ The clinical study endpoint is prostate cancer metastasis or growth.
- ✧ The drug efficacy standard is to avoid prostate cancer metastasis or growth in 90 days.
- ✧ Mutually compare the usual approach group SNPs (300 double-blind random group separated PC patients) with the study approach group SNPs (300 double-blind random group separated PC patients).
- ✧ Confirm the relationship between drug target gene SNPs and drug efficacy.
- ✧ If the peripheral blood samples of the usual approach group have the same CYP17 Gene SNP as the peripheral blood samples of the study approach group, the relationship between the Abiraterone drug target gene SNP and the Abiraterone drug efficacy can be confirmed, i.e., this CYP17 Gene SNP is the Abiraterone drug target gene SNP relating to the Abiraterone drug efficacy.
- ✧ Confirm the relationship between drug target gene SNPs and drug risk.
- ✧ If the peripheral blood samples of the usual approach group have the same SULT2A1 Gene SNP as the peripheral blood samples of the study approach group, the relationship between the Abiraterone drug target gene SNP and the Abiraterone drug risk can be confirmed, i.e., this SULT2A1 Gene SNP is the Abiraterone drug target gene SNP relating to the Abiraterone drug risk.

The laboratory tests:

- ✧ Recruit 600 patients of Prostate Cancer (PC) without prostate resection.
- ✧ Every prostate cancer patient will receive peripheral blood-drawing.

- ✧ Keep storing all peripheral blood.
- ✧ Detect every drug target's whole gene precision sequence of every patient for all 600 PC patients.
- ➢ Oxford Nanopore Technologies Ltd - Nanopore DNA Sequencing uses electrophoresis to transport an unknown sample through an orifice of 10^{-9} meters in diameter. A nanopore system always contains an electrolytic solutions- when a constant electric field is applied, an electric current can be observed in the system. The magnitude of the electric current density across a nanopore surface depends on the nanopore's dimensions and the composition of DNA or RNA that is occupying the nanopore. Sequencing is made possible because, when close enough to nanopores, samples cause characteristic changes in electric current density across nanopore surfaces. The total charge flowing through a nanopore channel is equal to the surface integral of electric current density flux across the nanopore unit normal surfaces between times t_1 and t_2.
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- ➢ Sequence
- ✓ Real-time sequencing on MinION, GridION or PromethION
- ➢ Analyses
- ✓ Real-time analysis with on device or local infrastructure base-calling.
- ✓ Detect DNA modifications using open-source tools.
- ✧ Every prostate cancer patient will receive sequencing of each target gene DNA whole chain in peripheral blood like as following: CYP17, GnRH-R.
- ✧ Every prostate cancer patient will receive sequencing of each target gene DNA whole chain in peripheral blood like as following: SULT2A1, CYP3A (CYP3A4, CYP3A5, CYP3A7, CYP3A43), CYP2C8.
- ✧ Mutually compare every drug target whole gene precision sequence of every patient for total 600 PC patients.
- ✧ Obtain every-one Target Gene SNP for every PC patient in Peripheral Blood DNA like as following: CYP17, GnRH-R.
- ✧ Obtain every-one Target Gene SNP for every PC patient in Peripheral Blood DNA like as following: SULT2A1, CYP3A (CYP3A4, CYP3A5, CYP3A7, CYP3A43), CYP2C8.
- ✧ Every prostate cancer patient will receive an image test one time per month.
- ✧ Every prostate cancer patient will receive blood test one time per week.
- ✧ Every prostate cancer patient will receive urine test one time per week.
- ✧ Every prostate cancer patient will receive an ECG test one time per week.

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

- ✧ The clinical study endpoint is prostate cancer metastasis or growth.
- ✧ The drug efficacy standard is to avoid prostate cancer metastasis or growth in 90 days.
- ✧ Every prostate cancer patient will receive an image test one time per month.

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

- ✧ Every prostate cancer patient will receive an image test one time per month.
- ✧ Every prostate cancer patient will receive blood test one time per week.
- ✧ Every prostate cancer patient will receive urine test one time per week.
- ✧ Every prostate cancer patient will receive ECG test one time per week.

The study patients of prostate cancer follow up the <u>standard of care treatment with drug therapy</u> in the ZYTIGA - Abiraterone Tablet DAILYMED Label

If any participating patients have serious side effects, they will be stopped the research.
If any participating patients have no therapeutic effects, they will be stopped the research.
21 CFR 312.2(b)(5) exempts from the IND requirements my clinical investigation that involves use of a placebo.

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 NCT03348670 present no more than minimal risk of harm to subjects as well as will let the research NCT03348670 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.

The study patients of NSCLC follow up the standard of care treatment with drug therapy in the ZYTIGA - Abiraterone Tablet DAILYMED Label
If any participating patients have serious side effects, they will be stopped the research.
If any participating patients have no therapeutic effects, they will be stopped the research.
21 CFR 312.2(b)(5) exempts from the IND requirements my clinical investigation that involves use of a placebo.

My clinical investigation (**NCT03348670**) intends to explore the relationship between **single nucleotide polymorphisms (SNP)** and abiraterone response and toxicity in patients with prostate cancer. My investigation information is from exploratory studies and is research data from general gene expression analyses in white blood cells of humans and from **single-nucleotide polymorphism (SNP)** analysis of trial participants. So, my pharmacogenomic data submission to **an IND is NOT required**, (i.e., my information does **not** meet the criteria of 21 CFR § 312.23).

My clinical study (**NCT03348670**) meets all of the requirements for exemption from the IND regulations and, therefore, **an IND is not required** to conduct my clinical investigation; i.e., my clinical investigation of oncology drug product (**Abiraterone Tablet**) that is lawfully marketed in the United States is exempt from the requirements of **this part** (i.e. 21 CFR Part 312): i.e., my clinical investigation is exempt from the requirements of 21 CFR §312.305 (c)(1) and 21 CFR §312.305 (c)(3). Although I am **not** a licensed physician, I still can be a qualified investigator for my IND EXEMPT SNP oncology drug clinical investigation.

IND 168800 should be IND EXEMPT. In my APCR documents, Han Xu, M.D., Ph.D., FAPCR had been defined as **PI (Principal Investigator)** in clinical trials. According to **42 CFR Part 11**, in my document **ClinicalTrials.gov ID:** NCT03348670, I (**Han Xu, M.D., Ph.D., FAPCR**) am defined as **Responsible Party (Sponsor-Investigator)**, Study Principal Investigator [Principal Investigator (PI)], Study Director (Medical Director), and Study Chair (IRB Chair) in my clinical trial. So, I must be the **sponsor-investigator (S-I)** of my clinical trial. And I (**Han Xu, M.D., Ph.D.** i.e., **Sponsor** i.e., **Sponsor-Investigator**) can both initiate and conduct, alone or with others, my clinical investigation. At the same time, I am a qualified investigator for my **IND EXEMPT SNP** oncology drug clinical trial.

My clinical investigation (**NCT03348670**) is not intended to be reported to FDA as a well-controlled study in support of a new indication for use, **nor** intended to be used to support any other significant **change** in the **labeling** for my oncology drug (**Abiraterone Tablet**). My investigation does **not** involve a change in route of administration, dosage level, or patient population, or other factors that significantly increase the risks (or decreases the acceptability of risks) associated with use of the drug product.

My IND 168800 should be IND EXEMPT. My investigation (**NCT03348670**) is conducted in compliance with the requirements of 21 CFR 312.7, i.e., the oncology drug (**Abiraterone Tablet**) may not be represented as safe or effective for the purposes for which it is under investigation, nor may it be commercially distributed or sold. So, my clinical investigation (**NCT03348670**) of oncology drug product (**Abiraterone Tablet**) that is lawfully marketed in the United States is exempt from the requirements of **this part** (i.e., 21 CFR Part 312): i.e., my clinical investigation is exempt from the requirements of **21 CFR §312.23 (a)(1)(iii)**.

Our IRB's review of the investigator's qualifications and the sponsor's qualifications, including any institutional requirements for sponsor-investigator studies, will surely abide by **21 CFR 312.2(b)(1)**.

21 CFR 312.2(b)(1)
The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements of this part ……

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.

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 (NCT03348670).

- 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**
- 2023-07 - FDA Pre-Assignment IND 168800 for Abiraterone Tablet
  - **Sponsor:** HAN XU
- 2023-08 - **ClinicalTrials.gov ID:** NCT03348670
  - **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

21CFR§50.3 (f)
Sponsor-investigator means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., corporation or agency.

IND 168800 should be IND EXEMPT. In my APCR documents, Han Xu, M.D., Ph.D., FAPCR had been defined as **PI (Principal Investigator)** in clinical trials. In my document **ClinicalTrials.gov ID:** NCT03348670, I (Han Xu, M.D., Ph.D., FAPCR) am defined as Responsible Party (Sponsor-Investigator). So, I (**Han Xu, M.D., Ph.D.)** must be the **sponsor-investigator (S-I)** of my clinical trial. And I (**Han Xu, Sponsor** i.e., **Sponsor-Investigator**) can both initiate and conduct, alone or with others, my clinical investigation. At the same time, I am a qualified investigator for my IND EXEMPT SNP oncology drug clinical trial.

21 CFR 312.2(b)(1)(iv)
The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50

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.