Sample manuscript of the informed consent form

Phase I Clinical Trial of Evaluating [^{68}Ga] Ga-NOTA-SNA002 for the Safety Tolerance, Radiation Absorbed Dose and Dosimetry in Patients with Solid Tumor

SN-SNA002-2023-001

Informed Consent Form

Name initials of subject: _____

Subject selection No.: _____

Version: V4.0, June 24, 2024

Hospital name: _____ **Address**: _____

Principal investigator: _____ **Tel.**: _____

Informed Consent Form

Dear subjects,

We would like to invite you to participate in a phase I clinical trial to evaluate the safety, tolerance, radiation absorbed dose, and distribution of SNA002, and the correlation between PET imaging and histological expression in patients with solid tumor. Before you decide whether to participate in this study, please read the following contents carefully. These contents can facilitate your understanding about this study and why conducting it, procedure and cycle of the study, as well as the benefits, risks, and inconveniences arising from your participation.

Below is a brief introduction to the clinical trial:

1 Background and objectives of the clinical trial

According to the latest data released by the International Agency for Research on Cancer of WHO, the number of newly diagnosed cancer patients in China is about 4.285 million in 2018, and the number of cancer-related deaths reaches up to 2.865 million. In the last decade, the annual incidence and mortality of cancers in China have been rising at a rate of 3.9% and 2.5%, respectively.

PET scan represents a major breakthrough in cancer diagnosis. PET imaging that uses radionuclides to label the specific receptor molecules on cancer cell surface offers a precise diagnosis of cancers and hence lays the basis for precise treatment. According to the current clinical practice, a preliminary diagnosis is first made based on your medical history, symptoms, signs, and radiographic evaluation. Next, you may receive a biopsy of the tumor lesions. If you have received a surgery, the resected cancer tissues will be sampled for pathological examination. The conventional methods used for pathological examination include immunohistochemistry, DNA testing, and fluorescence in situ hybridization. Therefore, the pathological typing of your tumor lesions and the expressions of specific receptors on the cancer cell surface will be understood. So far, conventional pathological examination of cancer tissues is still considered the gold standard for clinical diagnosis of tumors.

At present, there are many anti-PD-1 /PD-L1 monoclonal antibody products on the market. Among them, the approved indications of Opdivo (Nivolumab, Bristol-Myers Squibb, anti-PD-1 monoclonal antibody) are recurrent or metastatic squamous cell carcinoma of the head and neck which progresses during or after the cisplatin-containing regimen and positive for PD-L1 expression (tumor proportion score (TPS) ≥ 1% or tumor proportion score(CPS) ≥ 10). the approved indications of Keytruda (Pembrolizumab, Merck Sharp & Dohme Ltd., anti-PD-1 monoclonal antibody) are locally advanced or metastatic non-small cell lung cancer with PD-L1 TPS ≥ 1％ and negative for EGFR and (or) ALK as the first-line monotherapy. Apparently, there

is usually the need to determine the PD-L1 expression status of the tumor lesions before the use of such products. During the CheckMate-078 and KEYNOTE-042 clinical trials, the results showed that the patients with PD-L1 TPS ≥ 1% benefited more significantly.

The most commonly used method to detect PD-L1 expression in tumor tissues is immunohistochemistry kit. At present, two PD-L1 immunohistochemistry kits are commercially available in China: PD-L1 IHC 22C3 pharmDx (where tumor cells are the cells evaluated and the threshold is set to 1% and 50% in clinical trials), and PD-L1 IHC 28-8 pharmDx (where tumor cells are the cells evaluated, and the threshold is set to 1%, 5%, and 50% in clinical trials). The former can be used for companion diagnostics for Keytruda (developed simultaneously with Keytruda), and the latter for supplementary diagnosis for Opdivo (developed after Opdivo has come to the market). Both PD-L1 IHC 22C3 pharmDx and PD-L1 IHC 28-8 pharmDx are intended to screen the patients that can benefit the most from the monoclonal antibodies. However, IHC has some obvious defects when used to detect the PD-L1 expression: 1) It is an invasive detection method that requires the acquisition of sufficient samples, which is often difficult in patients with distant metastasis. 2) IHC assessment is time consuming and requires the collaboration of multiple laboratories. 3) This method is unable to show the dynamic changes in PD-L1 expression. 4) This method is limited by the sensitivity and specificity of the anti-PD-1/anti-PD-L1 antibodies used.

Suzhou SmartNuclide Biopharmaceutical Co., Ltd. (hereafter referred to as "SmartNuclide") has developed the SNA002 (^{68}Ga-NOTA-Nb109), a molecular imaging agent that is a coupling of the anti-PD-L1 antibody with ^{68}Ga. By PET imaging using SNA002, the radioactivity uptake of the tumor lesion can be calculated semi-quantitatively. PET imaging using SNA002 can directly visualize the PD-L1 expression in all tumor lesions throughout the body. Besides, by delineating the region of interest on the PET images, the maximum and mean SUV values (SUV_{max} and SUV_{mean}) of the lesions concerned can be directly calculated. A comprehensive quantification of the PD-L1 expression in tumor lesions lays an important basis for treatment decision-making. The anti-PD-L1 antibody contained in SNA002 is a single domain antibody, also known as nanobody. Having a molecular weight of about 15 kDA, it has an excellent tumor permeability. The radionuclide ^{68}Ga has been approved for marketing in some western countries. The dose of 37 to 200 MBq chosen for the clinical trial falls within the safety range. Briefly, SNA002 can determine the PD-L1 expression of the tumor lesions in a non-invasive, timely, accurate, convenient, comprehensive, and dynamic manner.

The clinical trial is intended to evaluate the safety, tolerance, radiation absorbed dose, distribution of SNA002, and the correlation between PET imaging and histological expression in patients with solid tumor. The objective is to develop an auxiliary method or a replacement for IHC to detect

PD-L1 expression, so as to better guide the treatment decision-making for patients with solid tumor. This clinical trial is wholly funded by SmartNuclide.

2 Design of the Clinical Trial

This is an open-label dose-escalation clinical trial. This trial includes four dose groups, namely, the 0.1 mg, 0.3 mg, 0.5 mg, and 0.9 mg dose groups. Based on the imaging results under the prior dose level, the clinical trial may be actually terminated after finishing the tests under three doses. The total sample size is estimated as 12-28 subjects. For each dose group, the sample size is 3–7 subjects.

All subjects participating in the clinical trial (including you) are required to receive one dose of SNA002. The subjects are assigned to different dose groups based on the enrollment sequence. Then they are given the corresponding doses of SNA002.

Throughout the clinical trial, you are expected to be present and involved at the following time points whatever the dose group to which you are assigned: the screening period (D-14 to D-2), the baseline period (D-1), the study period (D1 to D5), the safety follow-up period (D6 to D28). If new AEs occur to you during the safety follow-up period, the AEs will be followed up until recovery to normal or to the pre-trial level or stabilization, which is at most 28 days. Therefore, the duration of study participation will be approximately 42 days, including a screening period up to 14 days and a follow-up period up to 28 days.

During the clinical trial, the general principles of dose escalation are as follows:

Range of dose escalation: 0.1 mg, 0.3 mg, 0.5 mg and 0.9 mg, a total of 4 dose groups (these doses are specified based on the protein components). For all dose groups, the radiation dose of the radionuclide ^{68}Ga at the time of release should be range from 111 MBq to 200 MBq, with a maximum of 200 MBq, allowing a range of 37 to 200 MBq at the time of administration.

1. The 0.1 mg dose group has 3–7 subjects, in which the imaging situation is observed to determine the actual number of enrolled subjects in this group and whether they are enrolled into the escalated dose group.
2. The 0.3 mg dose group has 3–7 subjects, in which the imaging situation under the prior dose level is observed to determine the actual number of enrolled subjects in this group and whether they are enrolled into the escalated dose group.
3. The 0.5 mg dose group has 3–7 subjects, in which the imaging situation under the prior dose level is observed to determine the actual number of enrolled subjects in this group and whether they are enrolled into the escalated dose group.
4. The 0.9 mg dose group has 3–7 subjects, in which the imaging situation under the prior dose level is observed to determine the actual number of enrolled subjects in this group.

In this clinical trial, the in vivo metabolism, distribution and elimination of the protein components of SNA002 (PD-L1 nanobody) are observed, and a sparsely spaced BPK blood sampling design was carried out. Blood samples are collected at eight time points, namely, at 30 min before the administration and at 2 min, 5 min, 10 min, 30min, 50 min, 100 min and 150 min after the administration.

How can a subject be enrolled in the clinical trial? To be enrolled in the clinical trial, you need to satisfy all of the inclusion criteria below:

Inclusion criteria:

General conditions

- 18–75 years old (inclusive).
- Has the capacity to participate in this clinical study voluntarily and has signed the informed consent form (ICF).
- ECOG performance status score 0–2 (See Appendix 1 for details).
- Baseline heart rate 60–100 beats/min (inclusive).
- Blood pressure value is < grade 1 hypertension (including patients with a history of hypertension whose systolic blood pressure is < 140 mmHg and diastolic blood pressure is < 90 mmHg after exercise or drug treatment).

Disease conditions

- Patients diagnosed with solid tumors (including but not limited to NSCLC, breast cancer, oesophagea cancer, squamous cell carcinoma of the head and neck, ovarian cancer, and malignant melanoma,).
- Obtain pathological results within one year.
- Patients with the imaging results showing at least 1 tumor lesion that can be sampled by aspiration biopsy (enhanced CT, enhanced MRI or ^{18}F-FDG PET/CT results are acceptable).

Laboratory tests

- Blood routine: WBC 3.0-10.0 × 10^9/L, TNC 1.5-7.0 × 10^9/L, PLT 75-300 × 10^9/L, and HGB ⩾ 90 g/L.
- Liver function: Total bilirubin (TBIL) ≤ 2.5 times the upper limit of normal (ULN), alanine aminotransferse (ALT) and aspartate aminotransferase (AST) ≤ 3 times the ULN.
- Renal function: Serum creatinine (Scr) and blood urea nitrogen (BUN) ≤ 1.5 times the ULN.
- Coagulation time and prothrombin time ⩽ 1.5 times the upper limit of normal values.

However, if you satisfy any of the exclusion criteria below, you will be excluded from the clinical trial for the sake of protecting your benefits and interests:

Exclusion criteria:

General conditions

- Unable to proceed with the follow-up visits or receive relevant tests or receive treatments specified by the clinical trial protocol.
- Extremely poor nutritional status, BMI<18.5, unable to tolerate the test subjects.
- Known or suspected active autoimmune disorders (diagnosed as vitiligo, diabetes, residual hypothyroidism due to autoimmune disorders that only require hormone replacement therapy, or psoriasis that does not require systemic treatment. patients with diseases that are not expected to relapse without external inducers can be included in the study).
- Receiving high dose hormones, such as > 20 mg hydrocortisone or 5 mg prednisone in the morning, or > 10 mg hydrocortisone or 2.5 mg prednisone in the evening.
- Major comorbidities, including but not limited to:
  Other concurrent malignancies (except for those that have already been cured or do not require additional treatment since a year ago).
- Known serious allergic to SNA002, similar drugs or excipients

Disease conditions

- Unable to provide pathological results of biopsy samples.
- With symptomatic brain metastases.

Laboratory tests

- Serum virology test: Positive for hepatitis B surface antigen, antibody to hepatitis C virus or anti-syphilis antibody or unable to confirm human immunodeficiency virus negativity.
- Total protein < 50 g/L or albumin < 30 g/L during screening.

Other

- History of other severe diseases: ① cardiovascular disease, such as acute myocardial infarction/myocardial infarction within 1 year, acute myocarditis, acute pancarditis, acute heart failure, chronic heart failure NYHA heart function class ⩾ II, CCS class II or higher stable angina pectoris, unstable angina pectoris, rheumatic heart disease, malignant arrhythmia [ventricular tachycardia/ventricular fibrillation, frequent ventricular premature beats (more than 5 beats in one minute), II/III degree atrioventricular block, rapid atrial fibrillation/atrial flutter (ventricular rate > 110 beats/min)]. ② brain disease, such as cerebral hemorrhage/cerebral infarction (excluding lacunar infarction), history of epilepsy, pituitary/hypothalamic lesions. ③ lung disease (except lung cancer patients), such as asthma, acute obstructive pulmonary infection, acute bronchitis or acute tracheobronchitis. ④ liver disease (except liver cancer patients), such as cirrhosis (child-pugh score more than 7 points) etc.

- Active severe infections (excluding clinical remission period of chronic bronchitis).
- Drug/alcohol abuse or severe mental disorder.
- Patients have received high-dose radiation therapy or annual radiation dose>50mSv within 1 year (inquire about their previous radiation therapy and radiation examination within 1 year, and record them in the screening medical record).
- Has claustrophobia, emotional instability, acute persistent spasm, or inability to keep both arms raised and to lie down for 15–30 min. Participated in other clinical trials within 3 months prior to screening (excluding participants who only participated in the screening of this clinical trial and have not used the investigational drug).
- Female subjects who are pregnant or lactating, or female subjects who have had unprotected sex within 2 weeks before screening, or with positive blood pregnancy test; male subjects (or their partners) or female subjects who have fertility plan or sperm or egg donors throughout the trial and within 6 months after the end of the study, and are unwilling to take contraceptive measures during the trial and within 6 months after the end of the study.
- Women of childbearing age do not use sufficient non hormonal contraceptive methods.
- Patients who are deemed unsuitable for the study by the investigator.

3 Schedule and steps of the clinical trial

The clinical trial is divided into four stages, nmely the screening period, baseline period, study period, and safety follow-up period. The schedule and steps of each period are shown below:

Screening Period

D-14 to D-2

You are expected to read and sign the ICF within 2 weeks before the start of the clinical trial. After signing the ICF, you should receive inquiry and examinations by the study doctor to confirm whether you are eligible for the clinical trial: First, you should provide truthful information about the medical history, personal history, allergic history, history of tumors, surgical history, usage of drugs, and pathological examination results. It is preferable that the pathological examination results contain the information about tumor staging and results of previous IHC of PD-L1. second, you should receive vital sign measurement, including body temperature, blood pressure, and heart rate. Next, your study doctor will perform a physical examination, along with 12-lead ECG, chest X-ray, and enhanced CT/enhanced MRI/PET-CT. If you have received chest X-ray or CT within one month, the radiographic results will be acceptable. third, if you are a female, you should receive serum pregnancy test. You should receive all laboratory tests, including blood routine, blood biochemistry, electrolyte, coagulation function, urine routine, serum virology, and thyroid function.

Serial number	Schedule for the Screening Period
1	Sign the ICF.
2	Provide demographic information and medical history (including past medical history, tumor history, etc.), medication history, and allergy history.
3	Observe vital signs (blood pressure, pulse, respiratory rate, and body temperature) and conduct physical examinations.
4	Fasting blood test: blood routine, blood biochemistry, coagulation function, electrolytes, thyroid function, serum virology test, blood pregnancy test (for women of childbearing age) (Note: Serum virology acceptable up to 28 days prior to screening, other tests acceptable up to 7 days prior to screening).
5	Urinary routine examination.
6	Physical condition ECOG score.
7	Cardiac function score.
8	12-lead ECG
9	Chest X-ray (If there are chest CT results, It can be ignored).
10	CT/MRT/PET-CT (imaging results of this site or other tertiary hospitals within 1 month before screening).

After the above tests are finished, your study doctor will review your data and examination results according to the inclusion and exclusion criteria of the clinical trial. You can be enrolled in the clinical trial if you meet all of the inclusion criteria and none of the exclusion criteria. All of the above tests will be conducted at the study site at which you are enrolled. If you pass all of the screening tests, the time span from the start of the screening to your enrollment shall not be longer than 14 days. If you are not enrolled in 14 days, you should receive the above examinations for the second time. Your study doctor will review your data and examination results again according to the inclusion and exclusion criteria of the clinical trial.

Baseline Period

D-1

If you pass all of the screening tests, your study doctor will review your examination results again just before the enrollment for the sake of your benefits. After that, your study doctor will arrange your admission into the ward at D-1 and record your concomitant medications:

Serial number	Schedule for D0 of the treatment period
1	The study doctor will review your eligibility again for the clinical trial based on the inclusion/exclusion criteria.
2	Go through the admission procedures.
3	Provide truthful information about concomitant medications.

Study period

D1

During this period, we need your cooperation in the following matters: At 08:30 ± 0.5 h in the morning of D1, receive SNA002 through intravenous injection. Insert intravenous catheter within

30 min before the injection of SNA002 for subsequent blood collection and infusion, and receive the first blood sampling for PK analysis of anti-SNA002 antibodies and SNA002. The blood samples are sent to the central laboratory (Junke Zhengyuan (Beijing) Pharmaceutical Research Co., Ltd) for detection. The subsequent time points for PK blood sample collection are as follows: within 30 minutes before administration, at 2 min, 5 min, 10 min, 30min, 50 min, 100 min and 150min after drug administration. In the meantime, the PK blood samples collected at the above time points are detected for the radiation dose of ^{68}Ga using a γ-counter.

Urine sample will be collected to evaluate the renal excretion of radioactivity before injection, at 90±30 minutes, 180±30 minutes and 300±30 minutes post injection. Counts in aliquots of serum or urine will be obtained using a γ-well-type detector and measured activity concentrations will be converted to percentage injected activity/L.

Three systemic PET scans are performed at 15 min, 1 h, and 2 h after drug administration. The ambient radiation dose is measured at 4 ± 0.5 h after the drug administration. Blood routine coagulation function test, electrolyte test, and vital sign measurement are conducted at 6 ± 1 h after drug administration.

Serial number	Schedule for D1 of the Study Period
1	Collect blood samples within 30 min prior to administration for the detection of anti-SNA002 antibody in the central laboratory.
2	Two indwelling needles were placed intravenously: one for blood sampling and one for injection of study drug.
3	SNA002 is slowly injected intravenously at 08:30 ± 0.5 h in the morning. The time of injection should be no less than 1 min.
4	Blood samples are collected. ^{68}Ga in the blood samples and centrifugated serum samples are measured using a γ-counter, and the blood samples are sent to the central laboratory for SNA002 detection.
5	Urine sample will be collected. ^{68}Ga in the urinal samples are measured using a γ-counter
6	Three systemic PET scans are performed at 15 min, 1 h, and 2 h after drug administration.
7	Ambient radiation dose is determined at 4 ± 0.5 h after drug administration.
8	Blood routine, coagulation, and electrolyte tests are conducted at 6 ± 1 h after drug administration on D1. The corresponding results are obtained before biopsy on D2.
9	Vital signs: The vital signs are measured at 6 ± 1 h after drug administration on D1.
10	If you are not hospitalized, a subject diary card will be issued to you today upon completion of the relevant tests. If you use any combination of medications or have any adverse events while you are not hospitalized, you will be required to record them on your diary card.

D2 to D5

During this period, we need your cooperation in the following matters: The study doctor will evaluate the position and number of lesions for puncture according to the results of the three systemic PET scans. The lesion samples are collected and submitted for preprocessing by the

pathologist authorized by your study do ctor (the preprocessing method is determined by the study site). the biopsy specimens after preprocessing are sent to the central pathology laboratory for IHC examination of PD-L1 expression.

If you have undergone a biopsy within 2 weeks prior to enrollment and have obtained a biopsy specimen, and have not undergone chemotherapy, radiation therapy, or immunotherapy until enrollment, there is no need for another biopsy (Note: If you do not need another biopsy, in order to avoid affecting subsequent treatment and reduce your waiting time, you can directly enter the safe follow-up period).

Serial number	Schedule for D2 to D5 of the Study Period
1	If biopsy is performed, it will be performed on the second day through endoscopy (such as gastroscopy, bronchoscopy, laparoscopy, etc.) or puncture biopsy. If surgical resection is performed, it can be performed on the D2 to D5. Immunotherapy, chemotherapy, or radiation therapy should not be performed on the primary tumor disease during the injection of experimental drugs until the surgery period.
2	The biopsy specimens are sent to the central pathology laboratory for IHC examination of PD-L1 expression.
3	Evaluate vital signs at 6 ± 2 h after surgery/biopsy.

Safety follow-up period

D6 to D28

During the safety follow-up period, you will receive follow-up by your study doctor at the outpatient clinic. The study doctor will handle and record all AEs occurring to you as well as your concomitant medications. You are expected to pay a visit to the study site on D6 and D28 for the second blood sample collection for the detection of anti-SNA002 antibody. The samples will be sent to the central laboratory for detection.

Serial number	Schedule for D6–D28 of the Safety Follow-up Period
1	You need to undergo fasting blood sampling, testing for blood routine, blood biochemistry, coagulation, electrolytes at D6.
2	Anti-SNA002 antibody: The blood samples are collected on D6, D28(extra visit for ADA analysis) and sent to the central laboratory for the detection of anti-SNA002 antibody.
3	If you are hospitalized during the study period, a diary card will be issued to you on the day of discharge, and you will be required to record any comorbid medications or adverse events that occur while you are not hospitalized in the hospital.
4	Finish the study at D28 (D28 will recall your diary card).

At this point, you have completed all the contents and processes of this clinical study.

If you withdraw from the study in advance, you will proceed with the following content and process:

Serial number	What should be done to withdraw from the study
1	Monitor your vital signs;

2	12-lead ECG (If you withdraw after D6 and the test has already been performed at D6, it may not be performed again);
3	You need to undergo fasting blood sampling, complete blood routine, blood biochemistry, coagulation, electrolyte testing (if you withdraw after the D6 and have undergone laboratory testing on the D6, testing may not be conducted), and anti SNA002 antibody testing;
4	Record adverse events;
5	Record all concomitant medications.

Blood sampling

1) If you have completed all screening period checks but failed the screening, please refer to the table below for the number of times and amount of blood collected:

Testing items	**Number of blood samples taken**	**Each blood collection volume**	**Maximum blood collection volume**
Laboratory tests (blood routine, blood biochemistry, coagulation function, electrolyte).	once	about 10mL	about 10mL
Thyroid function test	once	about 5mL	about 5mL
Virology test	once	about 5mL	about 5mL
Serum pregnancy test (for women of childbearing age)	once	about 5mL	about 5mL
Total · If you are a male or non reproductive age woman, completing the entire study will result in a maximum of 20mL of blood collected. · If you are a woman of childbearing age, completing the entire study will result in a maximum of 25mL of blood being collected.			

2) If you are successfully enrolled and complete all the clinical research processes, the number of blood samples and blood volume are shown in the table below:

Testing items	**Visiting points**	**Number of blood samples taken**	**Each blood collection volume**	**Maximum blood collection volume**
PK	Study period	8 times	about 2 mL	about 16mL
Laboratory tests (blood routine, blood biochemistry, coagulation function, electrolyte).	Screening period, Safety follow-up period	twice	about 10mL	about 20mL
Thyroid function test	Study period	once	about 5mL	about 5mL
Anti SNA002 anti drug antibody（ADA）	Study period、Safety follow-up period	3 times	about 3mL	about 9mL
Virology test	Study period	once	about 5mL	about 5mL
Serum pregnancy test (for women of childbearing age)	Study period	once	about 5mL	about 5mL
Total · If you are a man or a woman not of childbearing age, a maximum of 55mL of blood will be taken to complete the entire study. · If you are a woman of childbearing age, a maximum of 60mL of blood will be collected upon completion of the entire study.				

Note: ∗During the experimental period, blood samples were collected at 8 time points: 30 minutes before and 2 minutes (± 1 minute), 5 minutes (± 1 minute), 10 minutes (± 1 minute), 30 minutes (± 2 minute), 50

minutes (± 5 minute), 100 minutes (± 5 minute), and 150 minutes (± 10 minute) after the injection of the investigational drug.

During the clinical trial, the collected blood samples for blood routine, blood biochemistry test, electrolyte test, coagulation function test, serum virology test, and thyroid function test will be sent to the central clinical laboratory at the study site. The blood samples collected for BPK study of SNA002 and anti-SNA002 antibody will be first centrifuged at the study site to collect the serum. Then the serum samples will be regularly transported by an independent third-party cold-chain logistics company (Shanghai Shengsheng Logistics Co., Ltd.) to a third-party central laboratory (Junke Zhengyuan (Beijing) Pharmaceutical Research Co., Ltd) for detection.

The blood samples detected at the study site will be processed according to the relevant procedures at the study site. The blood samples needed to be detected at the central laboratory will be sent to the central laboratory that has signed an agreement with the sponsor.

Your samples will be only used for clinical tests described in the ICF and not for any other purposes. If the sponsor wants to use your blood samples for other tests, you will be invited to sign a new ICF.

4 Your responsibilities arising from participation in the clinical trial

You are supposed to bear the following responsibilities during the clinical trial: Provide truthful information about your medical history and test results during the trial and finish all trial procedures as per the protocol and the ICF. You cannot use immunomodulatory inhibitors or agonists during study period (D1 to D5), including inhibitors of PD-1, PD-L1, and CTLA-4 (e.g., BMS-936559, MPDL3280A, MK-3475, and MEDI4736). Neither will you be allowed to use large doses of hormones. For example, > 20 mg hydrocortisone or 5 mg prednisone in the morning, and > 10 mg hydrocortisone or 2.5 mg prednisone in the evening. The use of immunostimulatory Chinese herbal medicines (e.g., mistletoe extract) or those known to interfere with important organ functions (e.g., hypericin) are prohibited.

If you experience any discomfort or encounter any conflict with your routine treatment during the clinical trial, you should contact your study doctor in the first time. You should make sure that you have not participated in any other clinical trial within three months before the screening. Neither are you allowed to participate in any other clinical trial while you are involved in this clinical trial. You are not allowed to participate in this clinical trial if you are pregnant or lactating or have a plan for pregnancy. You should cooperate with all of the laboratory tests during the clinical trial. If you drop out in the middle of the clinical trial, you should cooperate with your study doctor during the last follow-up for the sake of your safety.

5 Benefits from participation in the clinical trial

The objective of the clinical trial is to evaluate the safety, tolerance, radiation absorbed dose, distribution of SNA002, and the correlation between PET imaging and histological expression in patients with solid tumor. Therefore, you will at least know of the PD-L1 expression in the tumor lesions by participating in the clinical trial and whether there are distant metastases of the primary lesions through PET imaging.

During the clinical trial, the study doctor will evaluate whether you are suitable for and benefit from the PD-1/PD-L1-targeting anti-tumor therapy based on the PET imaging results and the PD-L1 expression of the tumor lesion determined after imaging. The tests and examinations you receive during the clinical trial can provide basis or evidence for precise clinical decision-making. Besides, this clinical trial will provide us with some data/evidence. Your participation contributes to our development of SNA002 for the evaluation of PD-L1 expression in the primary and/or metastatic lesions in patients with solid tumor and to the determination of indications for the use of SNA002. We would like to express our sincere gratitude for your participation.

6 Potential risks that you may encounter during the clinical trial

6.1 Risk of the use of SNA002

Protein components of SNA002: According to the "Technical Guidelines for the Clinical Evaluation of In Vivo Diagnostic Radiopharmaceuticals", the radiopharmaceuticals are generally non-therapeutic, and the administered dose of the product is far lower than its pharmacologically active dose. The dose of the protein components of SNA002 has a magnitude of microgram and it has no pharmacological activity under this dose. Therefore, it has high safety. However, there is an extremely low probability of allergic reaction. In that case, please contact your study doctor for antianaphylactic treatment.

Radionuclide ^{68}Ga: The adminstration dose of ^{68}Ga used in the study is ange of 37 to 200 MBq, which is associated with a small risk of exposure to radiation and falls within the acceptable range. However, if the washing solution used for the preparation of ^{68}Ga is not completely filtered, the injection of the ^{68}Ga-labeled imaging agent may cause local irritation to the veins. If you have the above conditions, please contact your study doctor first to receive wet dressing at the site of skin irritation. Then quality control of the imaging agent should be reconducted.

NOTA (2-[4,7-bis(carboxymethyl)-1,4,7-triazonan-1-yl] acetic acid): No risk associated with the coupling agent NOTA has been found.

6.2 Risks associated with blood collection

The conventional venous blood collection procedure will be used in the clinical trial. extract a certain amount of venous blood through a venous catheter. Mild pain in venous catheters: pain or congestion may occur at the site of blood collection. infection may also occur at the site of blood

collection (which is very rare). there is also the possibility of dizziness or syncope during blood collection. Even if you have pain or congestion, they are generally mild and will relieve spontaneously some time later. If you have dizziness or syncope, please rest a while in a sitting position and timely contact your study doctor. If you have an infection, please contact your study doctor in the first time and receive anti-infective therapy.

6.3 Risks associated with radiology

During the screening period, you will receive chest X-ray once, CT scan once, enhanced CT or enhanced MRI or PET-CT once. Throughout the clinical trial, you will receive three systemic PET scans. If you are very concerned with radiation exposure, or you have already received too many X-rays or radiological scans, you can discuss this problem with your study doctor.

6.4 Risks associated with pregnancy, contraception, and reproductive organs

The influence of the investigational drug SNA002 on fetuses or suckling infants remains unclear. The females enrolled in this clinical trial should have gone through menopause, have received sterilization surgery (tubal ligation or hysterectomy) or consent to the adoption of one contraceptive measure approved by the doctor (birth control pills, intrauterine device (IUD) or diaphragm or condom containing spermicides). If you are a female of childbearing age, you should receive blood pregnancy test before the enrollment. The enrolled males should consent to the use of one medically acceptable contraceptive measure or have already received vasoligation. If you are a female of childbearing age and are pregnant during the clinical trial, you should inform your study doctor immediately.

6.5 Risks associated with pathological biopsy

You may need to undergo a biopsy during the study by your study doctor or an authorized doctor. You may experience pain during the biopsy, which can relieve spontaneously. If the pain is unbearable, please inform your study doctor. you may also experience hemoptysis, while the symptoms may be mild. You should rest in bed and avoid vigorous activities. If you cough up too much blood, please inform your study doctor to receive timely treatment. You may also have infections at the puncture site, but the probability is extremely low. In case of infections, please timely inform your study doctor and receive anti-infective therapy. Under the most serious circumstances, you may also have pneumothorax, though the probability is very low. In that case, you will need help from your study doctor in receiving proper treatment or handling.

To ensure you safety, the study doctor will keep a close watch of any changes in your health condition. You will be truthfully informed of any changes and the recently confirmed AEs during the study period. During your hospitalization, the ward is equipped with first aid medicine and equipment. During the study period, you will receive medical monitoring from experienced staff,

who keep a close watch of any AEs. In case of any AEs, you will receive timely and appropriate treatments.

7 Compensations you may receive by participating in the clinical trial

You will receive compensations for the costs of transportation to the study site, blood collection and hospitalization related to the clinical trial. SmartNuclide will cover these costs by offering subsidies for transportation, nutrition, lost labor hours, and accompanying. The payment amount and the calculation method of subsidies are listed below (all are after-tax amounts):

After each visit, you will receive a transportation subsidy of **RMB200.00** to cover the cost incurred in traveling to the study site and back. The time points of visits to the study site covered by the transportation subsides are as follows: screening period (D-14 to D-2), baseline period (D-1), study period (D1 to D5), and safety follow-up period (D6 to D28). The total amount of the transportation subsidy is **RMB1000.00**. If you withdraw early from the clinical trial, you will receive transportation subsidies according to the visits you have already paid.

After finishing all of the scheduled visits, you will receive a nutrition subsidy of **RMB 1350.00**. If you withdraw early from the clinical trial, you will receive transportation subsidies according to the actual numbers of blood collection you have already received.

Except for the above, you will receive no other subsidies by participating in the clinical trial.

8 your participation

1. Obtain [^{68}Ga] Ga-NOTA-SNA002 injection free of charge

The study drug for this study ([^{68}Ga] Ga-NOTA-SNA002) is provided free of charge by SmartNuclide.

2. Free examination (specified in the study protocol)

Intelligent Nuclear Biology will also bear the examination costs specified in the study protocol that you perform during your participation in this study (after signing the informed consent form). Tests include: hematology, blood biochemistry, coagulation, electrolytes, virology, thyroid function, blood pregnancy test (women of childbearing age), urinalysis, electrocardiogram, and chest X-ray, CT or MRI or ^{18}F-FDG PET-CT, [^{68}Ga] Ga-NOTA-SNA002 PET-CT. Routine treatment and examinations required for other concomitant diseases will not be free of charge.

3. free access to a biopsy and possible determination of PD-L1 expression

9 Costs that may be incurred by you participating in the clinical trial

Participating in this clinical study is not the only way to test PD-L1 expression. At present, the most used method to detect PD-L1 expression is immunohistochemical detection of tumor tissue samples. Usually, tumor tissue samples are obtained by CT-guided needle biopsy, endoscopic biopsy and surgical sampling.

10 Important information update during the clinical trial

We will timely inform you if there are any major findings or risks from recent trials that may influence your decision to continue to participate in the clinical trial. You can discuss such information and your health status with your trusted doctors, friends, and family members to help you decide whether to continue or not. In that case, we will update the original ICF and add the updated information to the original one. You may be required to sign the new ICF.

11 Your participation in the clinical trial is a voluntary act

Your participation in the clinical trial is completely a voluntary act. You can choose not to participate in this clinical trial or withdraw at any time without reason after the trial begins. Your decision will not impair your access to other treatments at the study site or other due benefits arising from the damages.

12 Protection of your personal information during the clinical trial

If you decide to participate in the clinical trial on a voluntary basis, the study doctor will collect your personal information. Personal information includes medical records and trial records. Specifically, it includes the procedures and results of examinations you have received during and before the clinical trial, your response to the investigational drug, and other medical information related to your participation in the clinical trial. The information related to this clinical trial will be disclosed to the sponsor, contract research organization (CRO) entrusted by the sponsor, CRA, auditor, relevant institutions, ethics committee, and supervisory bodies. However, your name, address and other identifiable private information will be concealed and kept confidential.

SmartNuclide is the sponsor of this clinical trial and has the right to use the information coming from this trial. All or part of the results of this clinical trial will be displayed at conferences or published in journals. However, your ID will not be disclosed.

The information related to this clinical trial will be provided to FDA as well. For the purpose of registration or administration, the following institutions may review and/or copy your medical records and the signed ICF:

- Sponsor.
- FDA.
- Other national or local supervisory bodies.
- Other participating study institutions

In case of medical emergencies, your information related to this trial may be provided to your attending doctor and first-aid staff.

Since the information related to this clinical trial will be supplied to each party involved, it cannot be kept absolutely confidential.

Once you have signed the ICF, it means that you have given your authorization to the contents in the current section. This authorization has no expiry date and it will be valid in the long-term. This is because the information collected from this clinical trial will be used for analytical purposes for many years thereafter. It is still uncertain when such analyzes will be finished. If you decide to withdraw from this trial, you have the right to withdraw your permission for the usage and disclosure of your medical information after the withdrawal. However, if you do decide to withdraw your permission for the usage and disclosure of your medical information, the information already included in your clinical records can be still used and disclosed as described above.

13 Termination of your participation in the clinical trial

Your participation in the clinical trial may be terminated due to the following reasons:

1. You do not follow the instructions of the study doctor.
2. Some serious conditions that may need to be treated have happened.
3. The study doctor considers that it will be most beneficial for your health and welfare by terminating your participation in the trial.
4. Intelligent nuclear biology has terminated this clinical study;
5. Or other reasons.

14 Compensation for any damages that may be incurred by your participation in the clinical trial

SmartNuclide has purchased insurance from Ping a Property Insurance Co., Ltd. in China for this study, and will bear the cost of treatment and corresponding economic compensation for subjects who suffer from damage or death related to the study. In addition, the applicant also bears the cost of damage related to this trial that cannot be covered by the subject's insurance.

15 Approval and registration of the clinical trial

This clinical trial has been approved by FDA (approval number: 155846) on April 4th 2022 and registered at the website. You can log onto this website to look for relevant information of this trial.

16 Contact information of your study doctor and the ethics committee in the clinical trial

If you have any questions or doubts concerning your participation in the clinical trial, or if you have any damage or discomfort associated with this trial at any time, or if you have any concerns or complaints about this trial, please contact your study doctor:

Study doctor: _____, Tel.: _____.

If you have any questions about your rights as a subject in this trial or if you have any questions,

concerns or complaints about this trial, you can also contactthe ethics committee of the XXXXXX hospital. Contact number: _____, E-mail:_____.

The ethics committee is responsible for conducting an independent review of this clinical trial.

Unless you have the chances to raise questions and all your questions have been satisfactorily answered, you have the right to choose not to sign the ICF.

The ICF is in duplicate. One copy is preserved by the investigator, and the other by the subjects.

If you consent to participate in this clinical trial, you will receive a copy of this ICF that has been signed and dated for your keeping.

——————————— (The page below is intentionally left blank) ———————————

Signature page of the ICF

I have read and understood this ICF. I am fully informed about this clinical trial in different aspects, including the investigational drug, trial steps, possible risks, discomforts, and AEs. If I have any other questions about this trial or suffer trial-related damage during this trial, I will contact with the above personnel. I participate in this clinical trial on a completely voluntary basis after being fully informed.

I have the right to decide not to participate in this trial or to withdraw at any time after informing the investigators about my decision without incurring discrimination or punishment. My medical care or benefits will not be affected by my decision. The study doctor can terminate my participation in this trial if I need other treatments or if I do not abide by the trial protocol, or if there are trial-related injuries or due to any other reasons.

I have been informed that I will get the copy of this ICF.

Subject name: ID card No.:

Address/E-mail:

Contact number:

Date: Hour Min Month Day, Year

Signature of the legal representative (if necessary): ID card No.:

Address/E-mail:

Contact number: Relationship with the subject:

Date: Hour Min Month Day Year

Signature of the witness (if necessary):

Contact number:

Date: Hour Min Month Day, Year

Signature of the informed doctor: Contact number:

Address/E-mail:

Date: Hour Min Month Day, Year