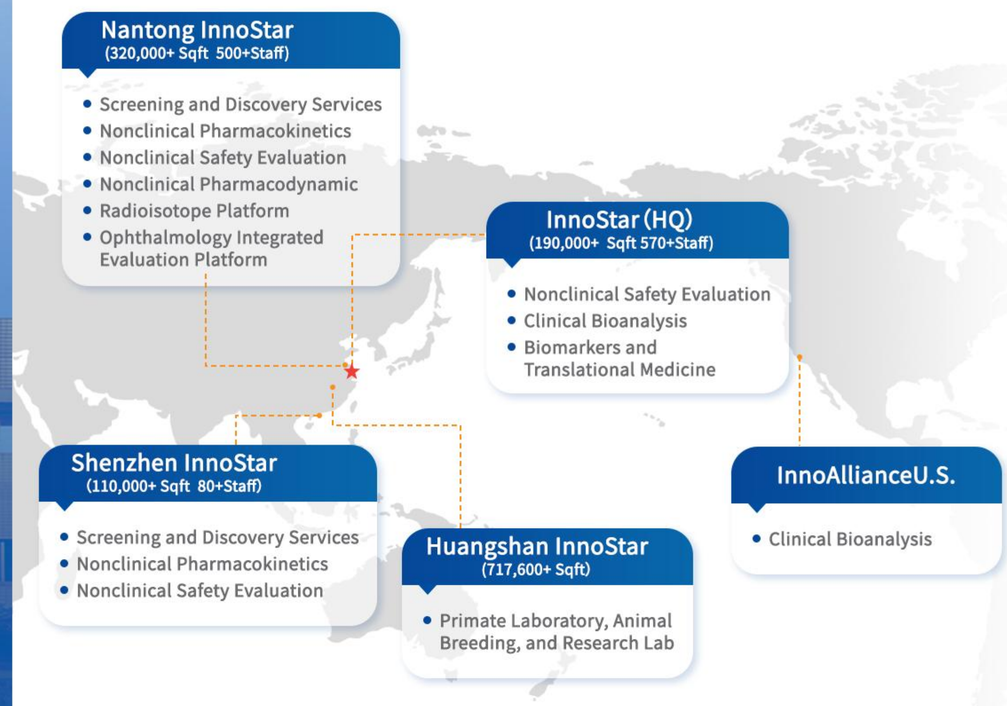
InnoStar

non-clinical pharmacokinetics platform

Focus on R&D services
Empowering the healthcare industry

Shanghai InnoStar Bio-tech Co., Ltd. (InnoStar) was established in 2010. As a leading contract research organization, we strive for excellence through our services with high quality, win customers by recognized reputation, add values by technical innovation, and maintain efficiency by streamlined management. Our business scope covers screening and discovery services, nonclinical pharmacodynamics, nonclinical pharmacokinetics, nonclinical safety evaluation, clinical sample bioanalysis, biomarkers and translational research. InnoStar was listed on the STAR Market of Shanghai Stock Exchange on September 3, 2024 (Stock code: 688710).



NMPA GLP AUT | U.S.FDA GLP INSP | OECD GLP AUT | AAALAC AUT | 美国CAP AUT

SCOPE OF BUSINESS

InnoStar Provides One-stop Service From Nonclinical to Clinical Translation

PCC
- Screening and Discovery Services

IND
- Nonclinical Pharmacodynamics
- Nonclinical Pharmacokinetics
- Nonclinical Safety Evaluation

NDA
- Clinical Biological Sample Testing
- Biomarkers and Translational Research

Services of differentiated solutions designed by experts covering the life cycle of drug development

PROJECT EXPERIENCE

920+
Already served
New drug development clients

100+
Annual average IND package completed amount

30+
Annual NDA/BLA package completed amount

200+
We have served on both international and domestic "first-of-its-kind" innovative drug research and development projects.

140
Overseas IND Application Successful

3
FDA NDA/BLAs

注: 数据统计区间:2015-2024.12.31

Scan the QR code for more business inquiries

TOC

www.innostar.cn

Main instruments and equipment

LC-MS/MS

- AB SCIEX API4000
- AB SCIEX API5500
- AB SCIEX API6500
- AB SCIEX API6500+ X6
- AB SCIEX API7500
- Shimadzu 8060
- Waters Xevo GS-XS QTOF
- Sciex TripleTOF HRMS

Protein and cytokines

MSD

Luminex

ELISPOT

PCR terrace

figure PCR

Realtime PCR

Nucleic acid extraction by automatic method

Streaming platform

CytoFLEX

FACSLyric

Aurora Spectral flow

Radioisotope platform

freezing microtome

Cathode ray screen exposure instrument

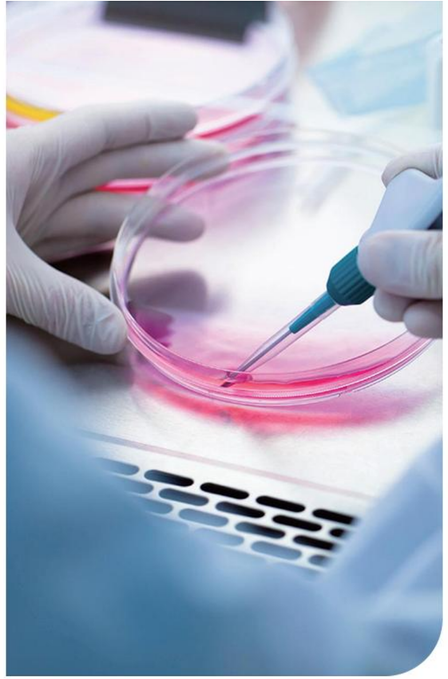
Micro-PET/MR

Grouping platform

10x, single cell

Hua Da MGISEQ-2000

Bioinformatics



non-clinical pharmacokinetics platform

Introduction to the Platform

- InnoStar non-clinical pharmacokinetics platform provides comprehensive DMPK services. The platform has a full life cycle quality management system in line with global standards, and follows the guidelines of ICH, NMPA and FDA to provide a full range of IND, NDA/BLA trial project research services required by regulations.
- The research team specializing in non-clinical pharmacokinetics at InnoStar has facilitated the approval of multiple drugs for clinical INDs. The types of drugs under review include small molecule chemical drugs, peptides, antibody-based drugs (monoclonal antibodies, bispecific/tandem-specific antibodies, nanobodies, etc.), fusion proteins, ADCs, cell and gene therapy products (immune cell therapy products, stem cell therapy products, oncolytic viruses, AAV vector-based gene therapy products, etc.), nucleic acid drugs, and radiopharmaceuticals. The platform is equipped with advanced analytical instruments, and an experienced analytical team can provide comprehensive and professional one-stop solutions from non-clinical to clinical stages.

service content

In vitro pharmacokinetic study

- Absorption studies
- Distribution studies
- Metabolic studies
- Drug interaction (DDI) studies

In vivo pharmacokinetic studies

- Sample type
- The site where the blood sample was taken
- InnoStarserves

Radioactive ADME study

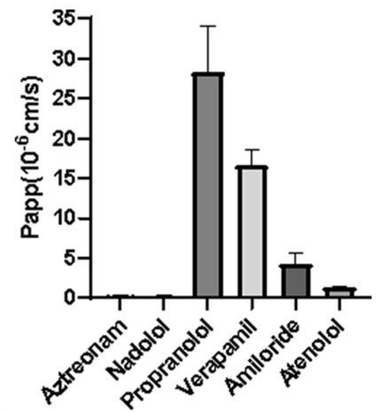
- Non-clinical evaluation of radiopharmaceuticals
- 125 The marker I is a macromolecular drug Organizational distribution
- Micro-PET Molecular imaging studies
- ^{3}H / ^{14}C non-clinical Pharmacokinetic studies

In vitro pharmacokinetic study

Absorption studies

- **Permeability studies**

  -Permeability study in Caco-2 cells



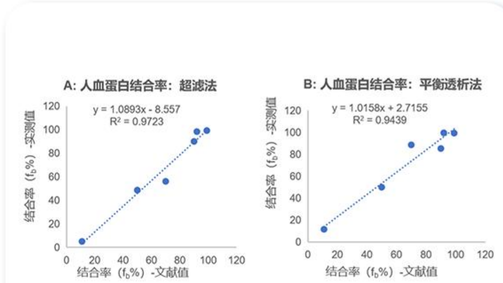
Distribution studies

- **plasma protein binding rate**

  -The free concentration of drugs in plasma was calculated by using the balance dialysis method/supercritical membrane method to compare the species differences

- **Whole blood plasma distribution ratio**

  -Provide basis for selecting analytical matrix



血浆蛋白结合率验证数据

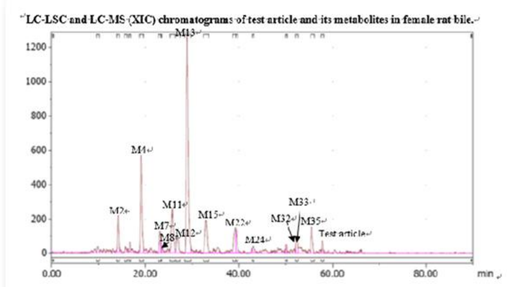
Metabolic studies

- **In vitro metabolite identification**

  -Study on identification of metabolites in hepatocytes/liver microsomes/liver S9/renal S9

- **Metabolite identification in vivo**

  -Study on identification of metabolites in plasma, urine, feces and bile after administration
  -Study on identification of metabolites labeled with isotopes



放射性同位素代谢产物鉴定研究

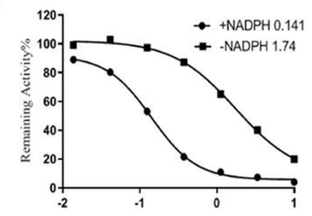
Drug interaction (DDI) studies

- **Metabolic phenotype identification experiment:**

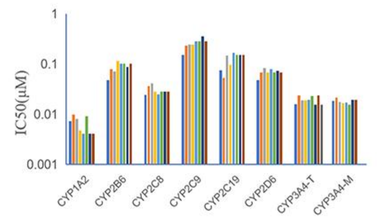
  -It includes the experiment of inhibition of microsomal system and the experiment of contribution rate of recombinant enzyme

- **CYP inhibition test:**

  -CYP1A2、2B6、2C8、2C9、2C19、2D6、3A4



Schematic diagram of time-dependent inhibition experiment



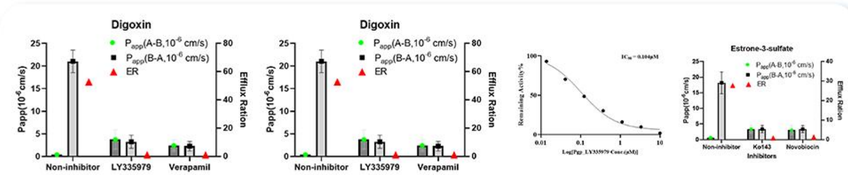
Schematic diagram of repeated validation tests for enzyme inhibition at different times

- **CYP induction assay*:**

  -mRNA levels were evaluated in CTP1A2, 2B6 and 3A4

- **Transporters*:**

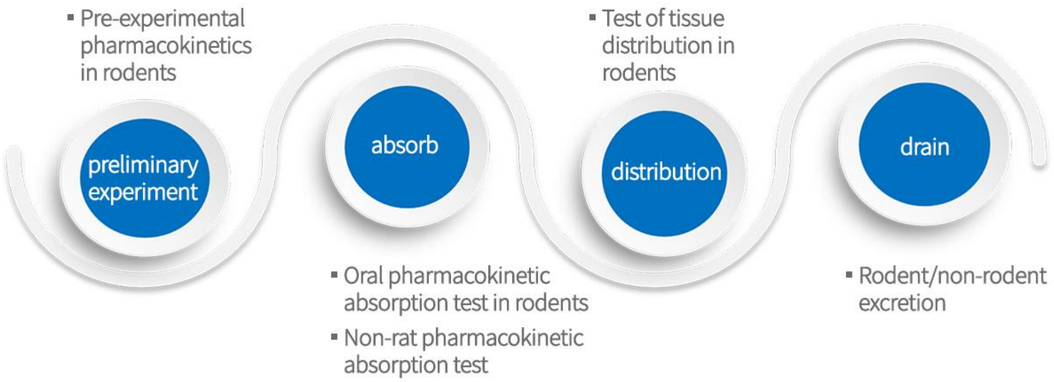
  -Substrate inhibition test of ABC transporters (P-gp and BCRP);
  -SLC transporter substrate assays (OATP1B1, OATP1B3, OAT1, OAT3, OCT2, MATE1, MATE2K)
  -SLC transporter inhibition test (OATP1B1, OATP1B3, OAT1, OAT3, OCT2, MATE1, MATE2K)



BCRP substrate　BCRP restrain　BCRP substrate　BCRP restrain

In vivo pharmacokinetic study

In vivo drug metabolism studies and in vitro pharmacokinetic studies play crucial roles in the discovery and development of new drugs. In vivo drug metabolism primarily investigates how the concentration of the drug and its metabolites in plasma or serum changes over time after administration through a specific route. Drugs can be administered directly into the body via blood vessels (intravenous injection or infusion).
The main routes of administration are extravascular administration, including oral administration, subcutaneous administration and intraperitoneal injection. Once drugs enter the body through the extravascular administration route, they will interact with the body in a variety of ways, including absorption, in vivo distribution, metabolism and excretion (ADME).



Sample type

- Blood samples
- Cerebrospinal fluid (CSF)
- bile
- urine
- excrement and urine
- organization
- joint fluid

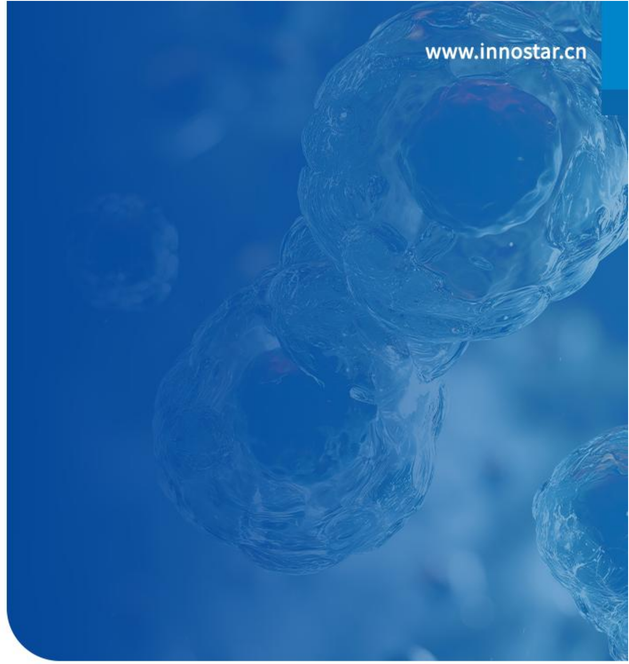
The site where the blood sample was taken

- jugular vein
- Four limb veins
- Heart blood draw
- Submental vein
- Venipuncture of the auricular vein
- Posterior limb hidden vein
- Orbital venous plexus
- femoral vein

InnoStarserves

- In vivo ADME studies were conducted in rats, mice, guinea pigs, rabbits, dogs, monkeys and small pigs
- Administration methods include but are not limited to oral administration, subcutaneous administration, intraperitoneal injection, intravenous injection, intramuscular injection, intradermal injection, inhalation administration, skin application and ocular administration

Radioactive ADME study



Non-clinical evaluation of radiopharmaceuticals

- Radioactive drug ADME study

125 The marker I is a macromolecular drug Organizational distribution

- 125 The distribution of ^{125}I labeled protein peptide drugs in rodent/non-rodent tissues was studied

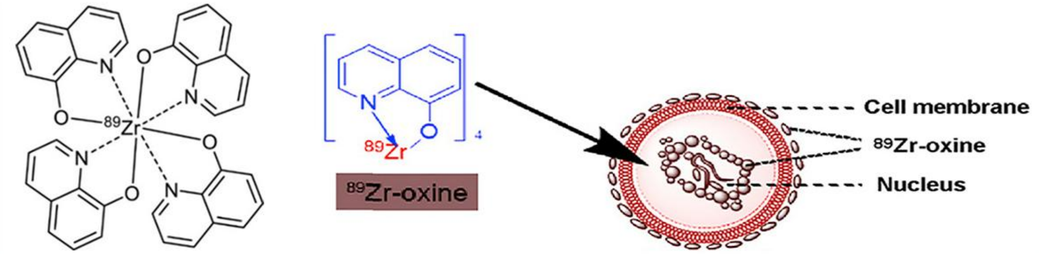
Micro-PET Molecular imaging studies

- Study on the distribution, migration and homing of Zr labeled cells in vivo animals
- Study on the distribution of 89Zr / 124 I labeled antibodies in vivo tissues of animals
- Study on the distribution and efficacy of positron radionuclide diagnostic drugs in tissues

^{3}H / ^{14}C non-clinical Pharmacokinetic studies

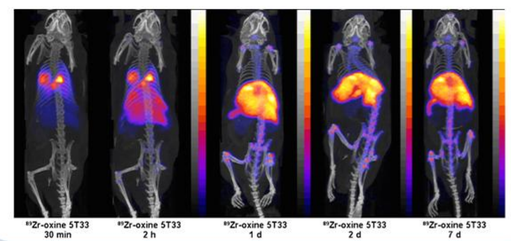
- Absorption in animals
- Organizational distribution (QWBA)
- Bile excretion (BDC rats)
- Material balance study
- Metabolite spectrum analysis and identification

Study on the distribution of radioisotope labeled cell therapy products



- **Principle of 89Zr-Oxine labeling**

-Oxine is highly lipophilic as a carrier of 89 Zr
-It enters the cell by passive diffusion
-After 89Zr-Oxine enters the cell, the carrier flows out and 89Zr stays in the cell and binds to the cytoplasm



Radioactive ADME study

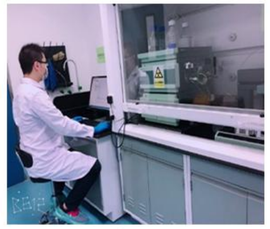
125 The study of tissue distribution of macromolecular drugs was marked with ^{125}I

- **service content:**

-125 The distribution of protein peptide drugs labeled with ^{125}I in rodent/non-rodent tissues was studied

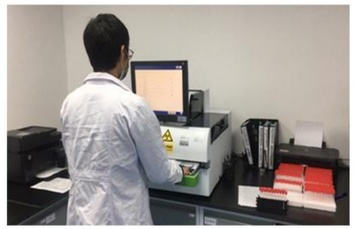
- **Type of drug used:**

-Protein, ADC, polypeptide, polysaccharide, etc

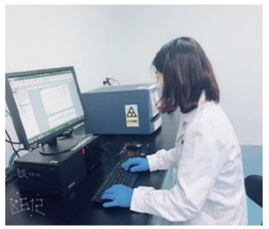


Protein purifier

Ridio-HPLC/TLC



γ counter



Microplate reader

PET/MR study of in vivo tissue distribution

PET/MR in vivo imaging studies Types of drugs used: antibodies, stem cells, positron-emitting drugs

- **service content:**

-Large and small animal PET live imaging
(Comprehensive animal studies are conducted in collaboration with the First Affiliated Hospital of Soochow University, using clinical PET scans)

-Marked with ^{89}Zr, ^{68}Ga and ^{124}I

-Study on in vivo tissue distribution of macromolecular drugs labeled with ^{89}Zr and ^{124}I

-In vivo distribution imaging study of stem cell isotope (^{89}Zr) labeling

-Study on tissue distribution of ^{18}F and ^{68}Ga radiopharmaceuticals

Micro-PET/MR

^{3}H/^{14}C ADME and one-stop service for clinical material balance

Preclinical ^{3}H/^{14}C labeled compound ADME study

- **service content:**

-Study on the distribution of ^{3}H/^{14}C compounds in rodent tissues

-Study on bile excretion and material balance in rat BDC model

-Study on material balance of normal rats

-Biotransformation (metabolite spectrum) and metabolic pathways of drugs in animals

-Olinda Estimation of internal exposure dose in human body

Study of human material balance ^{14}C

- **service content:**

-Radioactive drug preparation configuration, stability, radiochemical purity testing

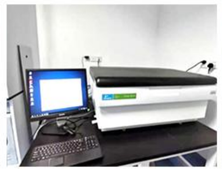
-Prodrug and major metabolite (LC-MS/MS)

-Total radioactivity of human plasma (liquid flash detection)

-^{14}C Marking compounds for human material balance

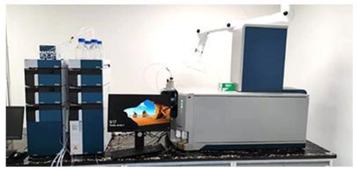
-Biotransformation (metabolite spectrum) and metabolic pathways of drugs in the body

Biological oxidation burner



liquid scintillation counter

solid-state scintillation counter



AB 7600 High resolution mass spectrometry

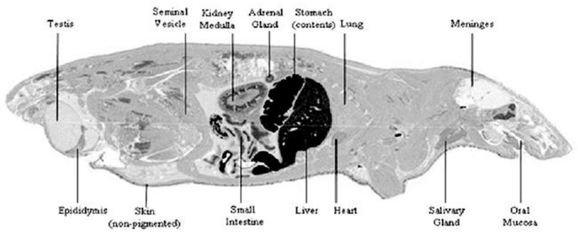
Study on tissue distribution of ^{3}H/^{14}C labeled compounds QWBA

- **service content:**

-Study on tissue distribution of ^{3}H/^{14}C compounds in rodents (QWBA)

-Study of drug crossing the placental barrier (QWBA)

-Estimation of human internal radiation dose



freezing microtome

Cathode ray screen exposure meter

Project experience

Experience in ADC projects

- **Antibody type:**

  -MSLN, HER2, CLDN18.2, CD38, CD20, C-met, trop-2, BCMA, mesothelin, EGFR-HER3 bisantibody

- **Small molecule type:**

  -MMAE, MMAF, DM1, SN38, DUO-5, a topoisomerase inhibitor, a DNA break agent.....

  -MSLN+MMAE、HER2+MMAE、T-DM1(HER2+DM1)

  -CLDN18.2+MMAE、CD38+X、HER2-DM-1、HER2-MMAF、CD20-MMAE, C-met -MMAE

Experience in cell-based projects

- **CAR-T**
  (only showing the experience of the first project in China/globally):

  -The worlds first non-viral PD-1 targeted integration CAR T cell therapy product

  -The first CAR-T cell therapy product prepared in non-virus carrier in China

- **Stem cell**
  (only domestic/globally first case project experience is displayed):

  -The first clinically approved hiPSC-derived cardiomyocytes in China

  -The first gene-edited autologous CD34+ hematopoietic stem cell for the treatment of thalassemia in China

  -The first approved clinical human amniotic epithelial stem cell product in China

  -Chinas first iPSC derived pre-brain neural precursor cell product

- **else:**

  -Exosomes, stem cell gene editing, UCAR-T, CAR-NK, production cells, trophoblasts, DC-effect T cells

Experience in antibody projects

- **Antibody target:**

  -PD-1, PD-L1, CTLA-4, LAG3, OX40, 4-1bb, PCSK-9, HER2, EGFR, TNF-a, VEGF, CD20, CD147, P40, TIM-3, RANKL, IL6R, IgE, TIGIT, GITR, IL-4R, Sclerostin, IL-17, CD47, IL-5, TGF-b, IL23…

- **Dual antibodies:**

  -PD-1-CTLA4、PD-1-CD40, PD-L1-41BB、CD3-X…

Gene therapy products

- **AAV class:**

  -AAV2, AAV8, AAV9, AAV5; Indications: ophthalmic diseases, central nervous system diseases, hematological diseases, etc

- **Gene editing:**

  -CRISPR-CAS9

Experience in oncolytic projects

- **The worlds first approved clinical oncolytic bacterial product:**
- **The worlds first oncolytic virus product approved in China, the United States and Australia at the same time:**
- **Oncorvirus products completed by Yinos that have entered clinical trials:**

  -Herpes tumor virus T3011; recombinant human PD-1 antibody for injection herpes simplex virus; VG161

Project experience overview covers all categories

mRNA class

- **Preventive products**
- **Therapeutic products**

Small nucleic acid drugs

- **siRNA**

  -The first siRNA drug for treating hyperlipidemia approved in Australia (the first case in China)

- **适配体**

Innovate small molecules

- **PROTAC:**

  -IRAK4 target

- **Molecular glue:**

  - GSTP1 target

- **AI design of small molecules:**

  -c-Met/HGFR, VEGFR2 and FLT3 inhibitors, CCR8 receptor, CSF-1R inhibitors.....

radiopharmaceuticals

- **Therapeutic products:**
- **Diagnostic products:**

  -The first targeted Tau protein radiological diagnostic drug approved for clinical use in China (the first case in China)

polypeptide

- **Non-oncologic indications**

Gliadin (only first project experience shown)

- **The first mutant IL-2 fusion protein targeting PD-1 in China**
- **The first domestic long-acting recombinant coagulation factor 8 product**

Preventive vaccines

- **attenuated vaccine**
- **inactivated vaccine**
- **Conjugate/multivalent**

traditional Chinese medicine

- **Chinese herbal compound**
- **Active ingredient extract**

INNOSTAR

益诺思 INNOSTAR

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