



美迪西生物医药



**Integrated Preclinical Drug
Discovery Services**

SHANGHAI MEDICILON INC.



Company Profile

Shanghai Medicilon Inc. is one of the top contract research organizations (CRO) in China. Since its establishment in 2004, Medicilon has been striving to offer fully integrated pharmaceutical services for the global scientific community. Our services span across chemistry, biology, formulation and preclinical studies. Therefore, we have the capability to help our clients to develop their researches and discovery programs from the stage of initial ideas to the Investigational New Drug (IND) filing phase.

Our headquarters is located in Zhangjiang High-Tech Park in Shanghai, China, with an additional facility in Chuansha Economic Park, Shanghai, China. We occupy over 300,000 sq. ft. in lab space and have over 800 employees cross biology, chemistry and preclinical research. Over 30% of our employees have M.S. and Ph. D. degrees.

Medicilon is one of the first CRO in China to provide integrated services, including compound synthesis, biological activity screening, structural biology, pharmacodynamics, pharmacokinetics, toxicology, and IND filing. Our high quality services are well-recognized internationally.

Medicilon is fully accredited by the International Laboratory Animal Assessment and Accreditation (AAALAC) and in compliance with the US Food and Drug Administration's (US FDA) Good Laboratory Practice (GLP). The standard of laboratories is certified by the China Food and Drug Administration (CFDA) for GLP compliance. Therefore, experimental reports generated at Medicilon can be used for China and USA dual filing to facilitate the evaluation of the safety and marketing of life-changing compounds for our clients.

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Innovation Platform

- The GLP for Safety Evaluation Platform
- The Protein and Antibody Pharmacokinetic Platform
- The Animal Disease Models Platform
- The Isotopic Platform
- The Protein Crystallography Platform
- The New Drug Formulations and The Generic Drug Platform

Why Choose Medicilon?

- A CRO to Provide Full Set of Preclinical Research Which Comply with Both China and US GLP Standards
- A CRO to Provide Structural Biology and Chemical Biology Services
- A CRO to Provide "Foreign Pharmaceutical Company - CRO - Domestic Pharmaceutical Company" Three Parties Collaboration
- One of the Largest Preclinical Drug Safety Evaluation CRO in Shanghai

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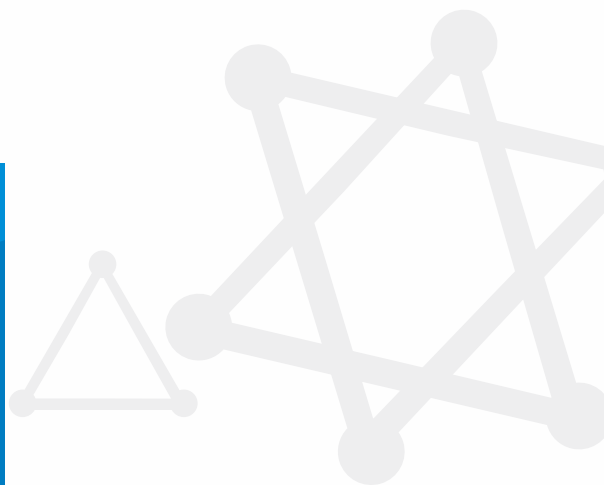


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CAPABILITIES



■ Integrated and Comprehensive Drug Research and Development Service Platform



■ Chemistry Services

Medicinal Chemistry: Drug Design, Structure-Activity Relationship Campaign, Lead Optimization and Druggability Test

Synthetic Chemistry: Intermediates, Reference Compounds, Metabolites, Impurities, and Other Small Molecule Chemicals

Process Development: Development and Optimization of Synthetic Process, Quality Analysis

■ Biology Services

Recombinant Protein Expression and Purification, Crystallization and Structure Determination, Discovery Biology, SeMET Growth Media Kits and Packages, Computational Biology and Molecular Modeling, Isotope Experiments and Biomarker Testing

■ Formulation:

Solid Formulation: Tablets, Capsules, Granules, Injectable Powder

Semi-Solid Formulation: Ointments, Creams, Gels

Liquid Formulation: Injections, Oral Liquid Preparations, Sprays, Tinctures

Innovative Dosage Forms: Slow Release Formulations, Nano Preparations, Pellets, Fat Emulsions

■ Pharmaceutical Analysis

API Analysis, Formulation Analysis, Analytical Method Development and Validation, Impurity Studies, Regular Chemical Analysis

■ Preclinical Services

Pharmacokinetics: In Vivo Assays, In Vitro Assays, BE Research, A Full Set of Studies for IND (CFDA & US FDA)

Drug Safety Evaluation: Single Dose Toxicity Test, Repeated Dose Toxicity Test, Safe Pharmacology Study, Immunogenicity Test, Toxicokinetics, Reproductive Toxicology Study, Genotoxicity Study

Pharmacology: Oncology, Digestive Diseases, Endocrine and Metabolic Diseases, Inflammation and Immune Diseases, Nervous System Disease Models

Bioanalysis: Small Molecule Drugs, Biologics (Proteins & Antibody)



PHARMACOLOGY



- The Pharmacology department at Medicilon has developed hundreds of reliable diseased animal models for efficacy test. The species we work on include non-human primate, dog, mouse, rat, rabbit, guinea pigs, and mini pigs. Our scientists have strong background knowledge and vast hands-on experience, which can largely facilitate the efficacy test of new drugs for our sponsors.



Cancer Models

1. Xenograft Models

| Cancer Type | Human Cancer Cell Lines |
|-----------------------------------|--|
| Head and Neck | FaDu, Detroit 562, CAL-27 |
| Oral Epithelial Carcinoma | KB |
| Lung Cancer | DMS114, NCI-H69, NCI-H146, NCI-H209, NCI-H446, NCI-H526, NCI-H1688, 95-D, A549, Calu-1, Calu-3, Calu-6, HCC827, NCI-H226, NCI-H292, NCI-H358, NCI-H441, NCI-H460, NCI-H520, NCI-H522, NCI-H1299, NCI-H1437, NCI-H1650, NCI-H1975, NCI-H1993, NCI-H2009, NCI-H2122, NCI-H2126, NCI-H2228, PC-10, QG-56, A427, H23, H1568, H2110 |
| Breast Cancer | SUM159, MDA-MB-231, MDA-MB-468, Bcap-37, 2LMP, ZR-75-1, ZR-75-30, HCC70, HCC1954, MDA-MB-361, MCF-7, BT474 |
| Gastric Cancer | MKN-45, NCI-N87, BGC-823, HGC-27, MKN-28, NUGC-3, SCH, SGC-7901, SNU-5, SNU-16, MGC-803 |
| Pancreatic Cancer | AsPC-1, BxPC-3, Capan-1, Capan-2, CFPAC-1, HPAF-II, MIAPaCa-2, PANC-1, PANC-10.05 |
| Renal Cancer | ACHN, OS-RC-2, 786-O, A498 |
| Hepatocellular Carcinoma | Bel-7402, Hep-3B, Huh-7, PLC/PRF/5, QGY-7703, SK-HEP-1, SMMC-7721, HepG-2, JHH7 |
| Glioblastoma | U87-MG |
| Colon and Cecum Cancer | COLO 201, COLO 205, COLO 320 DM, CW-2, DLD-1, HCT-8, HCT-15, HCT-116, HT-29, LoVo, LS1034, LS174T, LS411N, NCI-H716, RKO, SW48, SW620, WiDr, SW948, DiFi |
| Prostate Cancer | DU145, PC-3, LNCap, CL-1 |
| Urinary Bladder | HT-1197, HT-1376, RT4, SCaBER, SW780, T24 |
| Ovary Cancer | ES-2, HO-8910PM, PA-1, SK-OV-3, OVCAR-3 |
| Endometrium/ Hystero carcinoma | An3 CA, HEC-1-A, ME-180, MFE-280 |
| Cervical cancer | SiHa, HeLa |
| Skin Cancer | A431, Colo829 |
| Melanoma | A375, A2058, C32, HMCB, SK-MEL-30, MDA-MB-435s, WM-226-4 |
| Osteosarcoma | MG-63, SJSA-1 |
| Fibrosarcoma | HT-1080 |
| Muscle, Striated | SJCRH30 |
| Myeloma | KMS-11, KMS-26, RPMI-8226, MM.1S |
| Leukemia / Lymphoma | U937, THP-1, MV-4-11, HEL, TF-1a, ML-2, HL-60, K562, KARPAS-299, Daudi, RL, Mino, Raji, Ramos, ARH-77, KMS-12-BM, KG-1, JeKo-1, MAVER-1, CML-T1, MOLM-13, TMD-8, OCI-LY10, Nalm-6 |

2. Orthotropic Models

| Cancer Type | Cell Line | Luciferase Cell Line | Cancer Type | Cell Line | Luciferase Cell Line |
|------------------|---|----------------------|-----------------|-------------------------------------|----------------------|
| Breast carcinoma | MDA-MB-231, HCC1954, HCC70, MDA-MB-361, MCF7, HCC1954 | MDA-MB-231-luc | Glioblastoma | U87-MG | U87-MG-luc |
| Lung cancer | NCI-H1650 | A549-luc, LLC-luc | Ovary carcinoma | SK-OV-3 | |
| Colon carcinoma | HCT-116 | CT26.WT-luc | Prostate Cancer | Pc3 | |
| | | | Leukemia | RL, MAVER-1, Karpas299, K562, HL-60 | |

3. Syngeneic Models

| Cancer Type | Cell Line |
|------------------|------------------------------------|
| Breast carcinoma | 4T1,4T1-luc, EMT6, JC, C1271 |
| Lung cancer | LLC1, LLC1-luc, KLN205 |
| Colon carcinoma | CT26.WT, CT26.WT-luc, CMT-93, MC38 |
| Kidney carcinoma | RENCA |
| DLBCL lymphoma | A20 |
| T cell lymphoma | Ei4 |

| Cancer Type | Cell Line |
|--------------|----------------------------------|
| AML | C1498 |
| Leukemia | L1210, WEHI-3 |
| Hepatoma | H22 |
| Melanoma | B16-F10 |
| Plasmacytoma | J558, MPC-11 |
| Lymphoma | P388D1, L5178-R (LY-R), E.G7-OVA |

4. Transgenic Models

| |
|--------------------|
| hPD-1 Mouse Model |
| hCTLA4 Mouse Model |

5. Humanized Mice Models

| |
|-------------------|
| hCD34 Mouse Model |
| hPBMC Mouse Model |

Pharmacology Models

1. Neurological Disorders

| Disease | Model | Species |
|---|---------------------------------------|------------|
| Analgesia | Hot-Plate | Mouse/Rat |
| | Tail flick | Mouse/Rat |
| | Radiant heat pain | Mouse/Rat |
| | Pressing pain | Mouse/Rat |
| | Formalin test (phase I & phase II) | Mouse/Rat |
| | Complete Freund's adjuvant, CFA | Rat |
| | Acetic acid induced writhing | Mouse |
| | LPS-induced thermal hyperalgesia | Guinea pig |
| | Selective spinal nerve ligation (SNL) | Rat |
| | Sciatic nerve injury model (SNI) | Rat |
| | STZ-induced diabetic neuropathy | Rat |
| Hippocampal cell apoptosis and behavioral performance after hypoxia-ischemia brain injury | Mouse | |

| Disease | Model | Species |
|-----------------------------------|--|-----------|
| Sedative-hypnotic and antianxiety | Potentiated pentobarbital-induced sleep | Mouse |
| | Open field test | Mouse/Rat |
| | Elevated plus maze test | Rat |
| | Shuttle box test | Rat |
| Anticonvulsant Tests | Toxicity enhancement experiment with yohimbine | Mouse |
| | Pentylenetetrazol convulsions | Mouse |
| | Picrotoxin convulsions | Mouse |

| Disease | Model | Species |
|----------------------|---|-----------|
| Antidepressant Tests | Forced swimming test | Mouse/Rat |
| | Tail suspension test | Mouse |
| | 5-HTP-induced head twitches potentiation (5-HT) | Mouse |
| | Reserpine-induced ptosis | Mouse |
| | Yohimbine-induced lethality | Mouse |
| | High-dose apomorphine antagonism | Mouse |
| | Chronic unpredictable mild stimulations (CUMS) | Mouse |
| | MAO-A、MAO-B activity test | Rat |
| Anti-Parkinson Tests | Oxotremorine-induced Tremors/Salivation | Mouse |
| | Reserpine Antagonism | Mouse |
| | MPTP model | Rat |

| Disease | Model | Species |
|---------------------|--|-----------|
| Antidementia Tests | Morris water maze | Mouse/Rat |
| | In light –dark box test | Mouse |
| | Memory retrieval impairment | Mouse |
| | Memory consolidating impairment | Mouse |
| | Activity of acetylcholinesterase test | Mouse |
| | D-galactose model | Mouse |
| | APP/PS1 | Mouse |
| Antipsychotic Tests | Mk801 induced schizophrenia with positive/negative symptom | Mouse |
| | Ketamine induced schizophrenia with positive symptom | Mouse |
| | Catalepsy | Rat |

2. Digestive System and Other Disease Models

| Diseases | Models | Species |
|------------------------|--|---------|
| Renal failure | Nephrectomy (5/6) | Rat |
| Anemia | Anemia model induced | Rat |
| Gastric acid secretion | Pylori ligation | Rat |
| | Histamine induced | Rat |
| Gastric ulcer | Ethanol induced | Rat |
| | Non-steroidal anti-inflammatory drug induced | Rat |
| | Cold water stress induced | Rat |
| | Acetic acid chronic | Rat |

3. Inflammation and Immune System Disease Models

| Diseases | Models | Animals |
|------------------|---|------------|
| Arthritis | CIA induced | Mouse/Rat |
| | AIA adjuvant induced | Mouse/Rat |
| | PIA desilane induced | Mouse/Rat |
| Psoriasis | Estrogen induced vaginal epithelium mitosis | Mouse |
| | Tail scales | Mouse |
| | IL-23 induced auricle epidermal dysplasia | Mouse |
| | Imidocriptine induced | Mouse |
| | Propranolol induced ear | Guinea pig |
| Acute ammatation | Toe swollen | Mouse/Rat |

4. Cardiovascular and Metabolic Diseases

| Diseases | Models | Animals |
|--------------------------|--|--------------------|
| Obesity and Diabetes | Streptozotocin induced diabetes | Mouse/Rat |
| | Spontaneous diabetes | db/db, ob/ob Mouse |
| | Spontaneous diabetes | Rat ZDF |
| | High fat and high sugar diet induced | Mice |
| Nonalcoholic fatty liver | Hereditary atherosclerosis | APOE Mouse |
| | Nonalcoholic fatty liver | Rat |
| Thrombus model | Arteriovenous bypass thrombosis | Rat/Mouse |
| | Carrageenan induced tail vein thrombosis | Mice |
| | Deep vein thrombosis | Rat |
| | Carotid thrombosis | Rat/Mouse |

| Diseases | Models | Animals |
|----------------|--|------------|
| Hyperuricemia | Potassium oxonate induced | Rat/Mouse |
| | Hypoxanthine-induced | Mouse |
| | Adenine + ethambutol induced | Rat |
| Liver Fibrosis | Biliary ligation | Rat |
| | TAA-induced | Rat |
| | Composite factor method induced | Rat |
| | ConA induced | Mouse |
| Dyslipidemia | Porcine serum induced | Rat |
| | High fat / cholesterol / fructose diet induced | Hamster |
| | Hereditary atherosclerosis | APOE Mouse |

5. Other Disease Models

| Diseases | Models | Animals |
|--------------|----------------------------|---------|
| Skin Healing | Full-thickness skin trauma | Rat |
| | Pressure ulcers | Rat |
| | Skin Scald | Rat |



PHARMACOKINETICS

- Medicilon's pharmacokinetics (PK) and pharmacodynamics (PD) department is composed of a team of highly educated and well-trained scientists who carry out experimental designs and implementations as well as bio-analysis, formulation and data analysis to provide highly quality service and reports to our sponsors. All experimental research comply with ICH & CFDA & FDA guidance. Medicilon Preclinical Research team can design and carry out PK study according to the requirements of customers and provide the reliable and complete data. Our services have been well-recognized by our clients.





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In Vitro Study

Evaluation Capacity

Every year, Medicilon's PK/PD department completes thousands of in vitro and in vivo PK/PD studies. Our test articles range from small molecules, biologics, and natural products.

Service Items

- Protein Binding Studies
- Plasma Stability Test
- Liver Microsomal / S9 Stability
- CYP450 Inhibition Test
- CYP450 Induction Test
- Metabolites Prediction
- Metabolites Verification
- Metabolic Pathway Prediction
- Metabolic Pathways Verification
- Caco-2 Permeability
- Uptake and Efflux Transporter Studies
- Kinetic Solubility
- Metabolic Phenotype
- Hepatocyte Stability Test

In Vivo Study

Operation Capability

The test articles include small molecules, biologics, and natural products.

Animals: Mice, Rats, Dogs, Monkeys, Rabbits, Mini Pigs

Software

WinNonlin and Watson LIMS are used for pharmacokinetic data analysis and laboratory management, respectively.

Service Spectrum

- Pharmacokinetic Studies
- Excretion Study
- BBB Penetration
- Tissue Distribution Studies
- Mass Balance
- Cassette Dosing



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BIOANALYSIS



- The Bioanalysis Department of Medicilon, which consists of a number of highly experienced managing scientists, provides comprehensive bioanalytical services which include the development and drug screening of small molecule drug, biologics, vaccine and biomarker for clients. Our lab implements a comprehensive system management to keep track of the sample handling record and experimental data processing, tracking and storage. All of our bioanalysis studies are in compliance with FDA/OECD/CFDA GLP regulations.





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Biologics

Capability

- Development of Immunoassays and Method Validation
- Analysis of Proteins, Antibodies and Peptide Drugs
- Screening and Analysis of Biomarkers
- Drug Resistance Test (Immunogenicity)
- Vaccine Test

Advanced Equipment

- MSD Sector Imager 6000
- Molecule Devices M2/M4/M5 Reader
- UV 2600 Spectrometer
- Biotech ELx405 Select
- Hamilton Workstation

Small Molecule Drugs

Small Molecule Drug Analysis

- Development, transfer, and optimization of LC-MS / MS methods for the determination of drug concentration in biological samples
- Clinical Sample Bioanalysis
- Bioequivalence Experiments for Generic Drugs
- Supports Early DMPK Screening

Advanced Equipment

- SCIEX Triple Quad 6500+
- SCIEX Triple Quad 5500
- SCIEX API 4000
- Shimadzu LCMS 8050
- Shimadzu UHPLC
- Waters UPLC

Standards and Isotopic Internal Standard Synthesis Services

- Medicilon's Chemistry department and Radioactive Synthesis Laboratory offers stable isotopic internal standard synthesis services.

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DRUG SAFETY EVALUATION



Medicilon Preclinical Research (Shanghai) has a group of experienced professional scientific research team and built up the system of assessment of drug safety conforming to the national standards, with guidance of ICH & CFDA & USFDA & OECD. Medicilon Preclinical Research (Shanghai) provides cost-effective technical services in order to reduce the developing cost for customers by the strict enterprise management and efficient services. Since 2012, Medicilon Preclinical Research has successfully filed IND to CFDA, USFDA, TGA and MPA (Sweden) for more than 50 customers and was successfully passed both US FDA and CFDA auditing.



GLP Qualification and AAALAC

Medicilon Preclinical Research was certified by CFDA in 2011 and passed CFDA GLP inspection again in 2015. In addition, Medicilon Preclinical Research was certified by AAALAC in 2009 and was successfully passed the US FDA GLP inspection in 2017.



IND Applications

Since 2012, Medicilon has completed more than 60 toxicology packages for IND applications and hundreds of individual toxicity studies. These data has all been used by our sponsors in CFDA, US FDA and Australian TGA IND applications.

Drug Safety Services

- Single-Dose Toxicity Studies (Rodents and Non-Rodents)
- Repeated- Dose Toxicity Studies (Rodents and Non-Rodents)
- Safety Pharmacology Studies: Central Nervous System, Cardiovascular System, Respiratory System, hERG (Telemetry and Non-Telemetry in Dog and NHP)
- Genotoxicity Studies
- Reproductive Toxicity Studies [Fertility and Early Embryo Developmental Toxicity Studies (Reproductive Phase I), Embryo Fetal Developmental Toxicity Studies (Reproductive Phase II)]
- Immunogenicity Studies
- Toxicokinetics
- Local Toxicity Test (Hemolysis, Allergy Tests, Irritation Tests)
- Toxicity Tests of New Drug Delivery Technologies: Inhalation Toxicology
- Clinical Pathology Capabilities: Hematology, Urinalysis, Clinical Chemistry, Coagulation
- Histology Services: E&H Stain and IHC



PHARMACEUTICAL ANALYSIS



- Medicilon Pharmaceutical Analysis Department is equipped with a team of experienced professionals, advanced laboratories, and analytical equipment. Our experts have accumulated extensive experience through our collaboration with large pharmaceutical companies in the United States.

Medicilon is familiar with GMP, GLP, ICH, and CFDA regulations and guidelines. We provide rigorous, one-stop, comprehensive, and systematic studies for the quality of APIs, formulation products, and formulation processes.

We support simultaneous FDA, CFDA, and EMEA IND applications. Our services include method development and validation, impurity research, comparative labeling, stability studies, and a variety of routine chemical analysis.





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Quality of API

- Method Development and Validation
- Impurity Research
- Stability Research
- Report for IND Application

Quality of Formulation

- Pre-formulation Analysis
- Method Development and Method Validation
- Impurity Research
- Stability Study
- Report for IND Application

Method Development and Validation

- Weight Content and Purity
- Relative Substance
- Moisture Content
- Chiral Analysis
- Solvent Remains
- Trace Elements
- Content Uniformity
- Determination of Dissolution

Impurities

- Impurity Preparation, Separation and Structural Identification
- Study on Impurity Spectrum
- Development and Verification of Potential Genotoxic Impurities Analysis Methods

Routine Services

- NMR 1D2D (Including H-NMR, C-NMR, P- NMR, F-NMR, HSQC, HMBC, COSY, NOESY)
- LC-MS, GC-MS, HPLC Analysis (Including ELSD Detection)
- Separation of Chiral Compounds and Preparation of High Performance Liquid Phase
- General Physical and Chemical Testing (ROI, LOD, Cl-, SO42-, mp, HM, Optical Rotation, Moisture Determination, Heavy Metal Residues, etc.)



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