



Pharmaron's Comprehensive *in vivo* Pharmacology Solutions

Oncology and Immuno-oncology

Overview

Offering in a nutshell	3
CDX models	6
Syngenic models	7
PDX models	8
Humanized models	9
<i>in vivo</i> CRISPR screening	10
Genetically engineered tumor models	11
Drug resistant tumor models	12
Imaging	13
Biomarkers	14
Immune profiling	15
Radiation therapy	16
Quality assurance	17

Pharmaron's Oncology Capabilities in a Nutshell

Cell line-derived xenograft models (CDX)

Patient-derived xenograft models (PDX)

Syngeneic models and immune profiling

Genetically engineered tumor models

Drug resistant tumor models

in vivo CRISPR screening

Humanized tumor models

Imaging and biomarker profiling

Treatment options X-RAY ON



X-ray radiation



Small molecules



Large molecules



LNPs as vectors for therapeutics



Nucleic acids



Cell & gene therapies



Vaccines

We provide our clients with timely and accurately executed *in vivo* drug testing

Speed



24-hour philosophy for quoting, protocol generation, animal procurement, reporting of results, and study amendments.

Track Record



We perform about 1,700 *in vivo* oncology studies annually.

A Decade of Experience



Each study director has a minimum of 10 years of relevant experience.

Turnaround Times



Pharmaron provides the fastest turnaround times in the industry.



Smooth sailing with our outstanding customer service

Align the study layout with your research objectives via in-depth conversations with our scientific directors.

Choose the right model: Utilize our extensive tissue bank and tumor model profiling data.

Immediate study initiation: Within just 24 hours of the purchase order, we will:

- ↳ Provide the study protocol
- ↳ Procure the animals from accredited local or US providers
- ↳ Expedite material procurement by using in-house stock of commonly used reagents

Easy shipping: Get help from our US-based logistics team to ship your drug candidates or biological testing material.

Seamless communication: A single designated study director oversees the initiation, execution, and reporting of all study types.

1,400+ Validated Cell Line-Derived Xenograft (CDX) Models

A large collection of various CDX models in the industry

New model establishment can be performed with one of our 2,300 in-house cell lines or a custom cell line.

1,200 subcutaneous xenograft models have been established covering every relevant cancer type.

Our 190 orthotopic models comprise implantation into 15 different organs.

Metastasis can be studied through various ways of implantation:

- intracardiac
- intracranial
- intracarotid
- intravenous
- intraperitoneal

How does Pharmaron achieve outstanding reproducibility of *in vivo* studies?

- Animal studies are performed with low passage cell culture to avoid genetic drift.
- The same passage of cells is used for tumor inoculation for multiple *in vivo* studies for a single client.
- All cell lines undergo authenticity testing via STR.
- Orthotopic implantations are carried out by specialized teams, each skilled in the specific surgical techniques.

Model characterization is key for successful testing of new immunotherapeutics

- 108 syngeneic mouse models
- Covering 27 tumor types
- Subcutaneous, orthotopic, and heterotopic models

Thorough model characterization including:

- Profile of tumor infiltrating immune cells at 100 and 600 mm³
- Profile of genes associated with immune response
- Profile of PD-L1 and MHC1 on tumor cells
- Profile of immune responses against immune checkpoint inhibitors



Standardized immune cell phenotyping of all our syngeneic models is performed via flow cytometry investigating the frequency of CD4⁺ T cells, CD8⁺ T cells, T regs, MDSCs, and macrophages

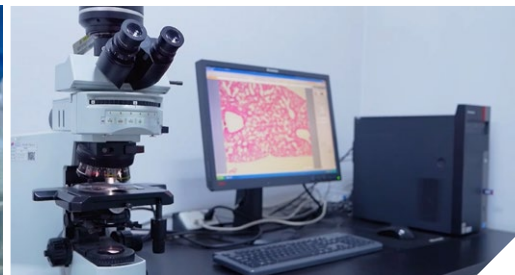
350+ Clinically Relevant Patient-Derived Xenograft (PDX) Models

Enhancing clinical outcome predictions for new cancer drugs

We support our clients' model selection process by providing:

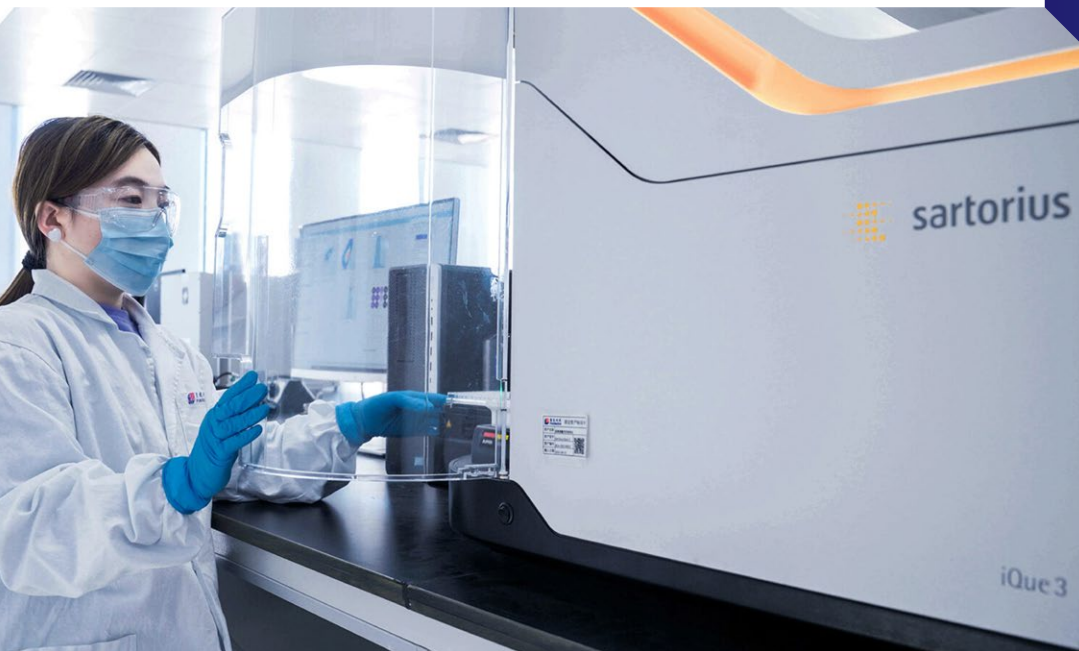
- Patient treatment history
- PDX sample archive for testing of presence of target and markers
- PDX database of gene expression and mutation data
- PDX organoid platform for *in vitro* efficacy testing

The use of PDX models allows for the translation of benchtop findings to clinical applications as they maintain the characteristics of the original tumor and allow testing on a patient-by-patient basis in an animal.



Humanized Models

The human-like immune system of **humanized mouse** models enables our clients to study the immune-modulating effects of their drug candidates on human immune responses



Pharmaron offers mouse models with a stable humanized immune system constituted through the adoptive transfer of human CD34+ stem cells. The stem cells stably engraft the bone marrow and develop into various types of blood cells for over one year.

Identify novel therapeutic targets by uncovering genes that drive drug treatment resistance.

Knocking in or out clusters of genes or single genes in cancer cells before drug exposure in mice allows for the assessment of gene alterations after treatment.

The Power of *in vivo* CRISPR Screening

Library Screening: Enables the simultaneous analysis of thousands of oncogenes at endogenous, physiological condition in animal studies.

Human Relevance: Screens are conducted using human tumor cells, ensuring highly translatable findings.

Physiological Context: The *in vivo* environment provides more realistic conditions than *in vitro* screens, enabling the evaluation of gene alteration compensation while accounting for interactions with blood vessels, immune cells, and surrounding tissues.

Genetically Engineered Tumor Models

Advanced drug testing in genetically engineered tumor models to support our client's drug development strategies

In-house generated transgenic cell lines are created via CRISPR/Cas9 or virus-based engineering tailored to the specific requirement of our clients. Tumor cells are subcutaneously implanted into host mice for drug efficacy testing.

We offer a number of genetically engineered cell line tumor models, including:

- Ba/F3 cell-based target-specific tumor models
- Genetically edited engineered human tumor cell lines and tumors models
- Tumor cell lines expressing immune-relevant antigens



Finding next-generation drug candidates to treat patients with drug resistant cancer

Pharmaron's approach to developing new drug-resistant mouse models involves long-term treatment of cell cultures with standard-of-care medication. The potency of next-generation drug candidates is assessed through the testing of drugs *in vivo* on tumors implanted subcutaneously. RNA sequencing data is made available to our clients.

In addition to studying newly created drug-resistant cell lines, we can also conduct drug resistance studies on:

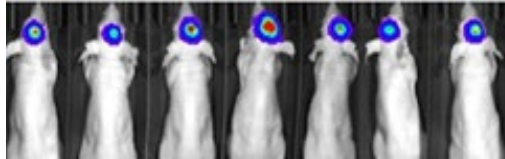
- Genetically engineered tumor models with mutations rendering tumors resistant
- Tumor models with known drug resistances: we help identify suitable models from our collection of more than 2,300 tumor cell lines
- Drug resistant PDX models can be identified via PDX organoids screening

Various methods are utilized to gain understanding of the underlying mechanism of resistance, which includes:

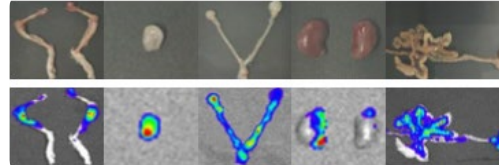
- Characterization of the cell morphology via cell painting
- Proteome analysis via RPPA (Reverse Phase Protein Array)
- Transcriptome analysis via RNA sequencing

Pathways involved in drug resistance are identified by our bioinformatics team through machine-learning algorithms.

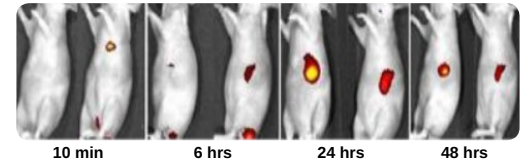
Visualization of tumor progression and drug dissemination with cutting-edge imaging technologies



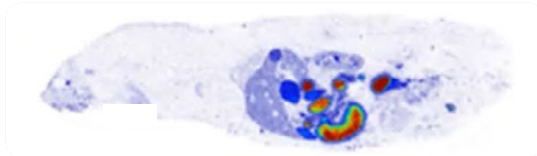
A luciferase-expressing glioblastoma model viewed by one of our seven IVIS imaging systems



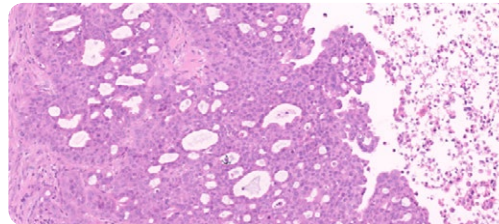
ex vivo imaging of luciferase-expressing tumor cells in organs



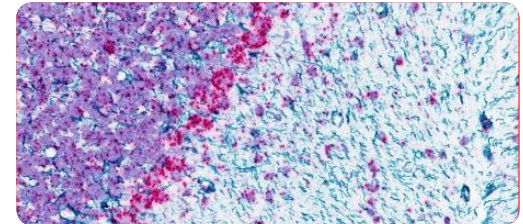
Kinetic dissemination of fluorescent probes



Dissemination of radiolabeled small molecules in the rodent body



Histopathologic analysis of tissue



Multiplex staining on tissue samples

Biomarkers help our clients understand and monitor how a drug affects the target, the disease, and the animal

Any *in vivo* samples can be analyzed including

- Blood / plasma
- Tissue
- Cerebrospinal fluid
- Urine / feces
- Other body fluids

- Is the intended target hit?
- How does the drug affect the body, the tumor, and the immune system?
- Which blood parameters are changed?
- What is the drug exposure?

Quantification of biomarkers with our comprehensive suite of state-of-the-art technologies

- Genomic and individual gene level
- Proteomic and individual protein level
- Flow cytometry / cell sorting
- Histology / immunohistochemistry / immunocytochemistry
- Hematology
- Blood chemistry
- Small and large molecule bioanalysis



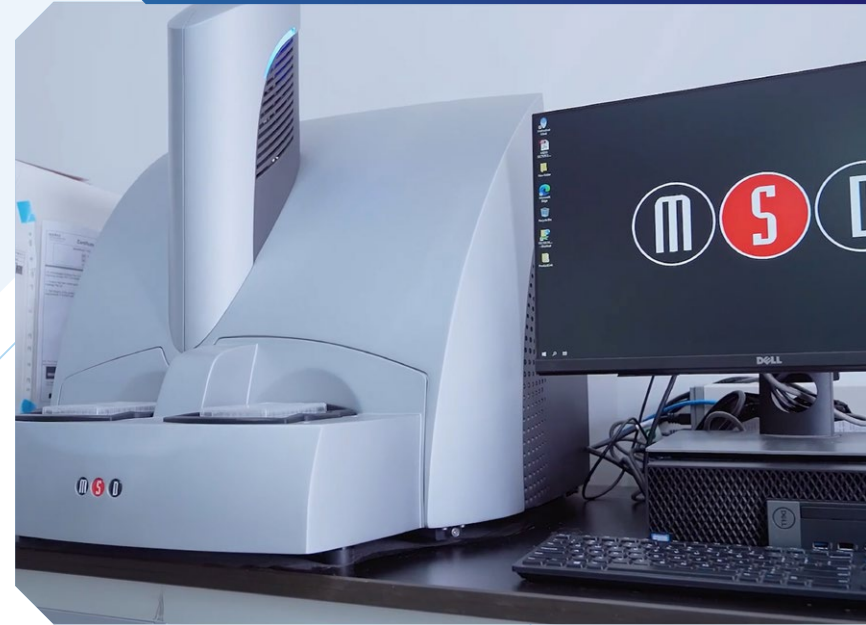
Empowering immune-related research with in-depth immune response profiling

We assist our clients in comprehending the impact of their drug on the immune system by examining:

- Inflammation markers
- Immune cell frequency
- Immune cell location
- Immune cell function and activation status
- Gene and protein expression profiles

Pharmaron uses state-of-the-art methods and advanced technologies for in-depth understanding of the immune response:

- Multicolor flow cytometry and cell sorting (70+ markers established)
- *Ex vivo* functional immune cell assays
- Multiplex IHC and RNA in-site hybridization
- Multiplex cytokine/chemokine profiling
- High content imaging
- Next-generation sequencing and qPCR
- Automated Western blotting



A state-of-the-art platform to discover new therapeutics leveraging radiotherapy

Finding next-generation drug candidates to treat patients with drug resistant cancer.

Our *in vivo* pharmacology team uses a radiation therapy platform designed specifically for small animal research. This technology allows us to measure the effects of radiotherapy and radiosensitizing drugs with high accuracy, providing critical insights into their therapeutic potential.

Targeted irradiation is conducted with a X-Rad225 unit from Precision, USA.

- Suitable for cell culture and small animal irradiation
- Collimators to adjust radiation beam size and shape
- Turntables allow increased throughput and automated treatment
- Capabilities for BLI and x-ray imaging

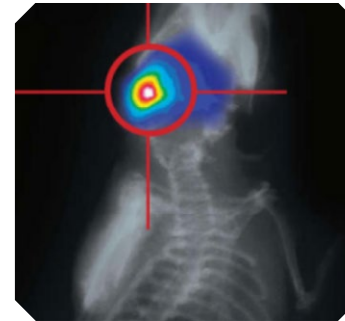


Image-guided radiation



Our clients benefit from studies conducted at our AAALAC accredited facilities:

- **High standards** for rigorous animal care and ethical research practices.
- **Studies conducted** with meeting or exceeding regulatory requirements
- **High quality** via standard operation procedures that lead to more reliable research outcomes.
- **Reduced risk** associated with animal welfare concerns, legal issues, or public relations challenges.



- 7,400 sqft of vivarium
- 3 facilities (1x Beijing, 2x Ningbo)
- Capacity: 17,000 animals in Beijing, 100,000 animals in Ningbo

Animal welfare is important to us

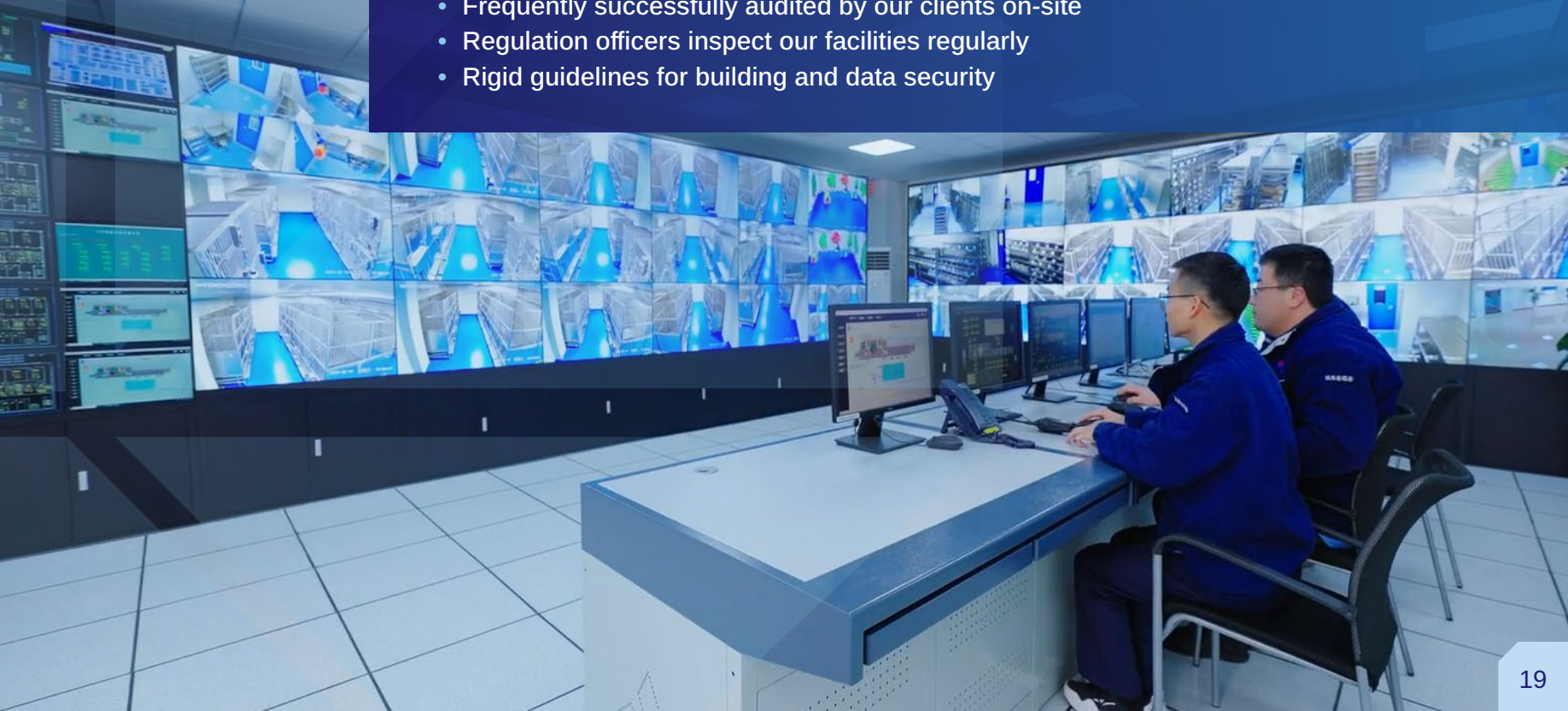
Our IACUC (Internal Animal Care and Use Committee) team guides humane research practices following the 3R principles.

- **Animal replacement:** Replacing animals is achieved by compound testing in predictive *in vitro* models
 - 2D cell panel screening
 - 3D co-culture testing
 - PDX-derived organoid testing
 - Identification of predictive biomarkers
- **Animal reduction:** Thorough characterization of our animal models helps selecting the right animal model for your study goals. Non-invasive imaging technologies and isolation of samples from live mice (e.g., blood, CSF) enables repeated measurements on the same animal.
- **Refinement:** Our SOPs for surgeries are honed over many years to minimize suffering of the animals.



Pharmaron's Vigilant Scrutiny: Mitigating Risks in Your Drug Discovery Program

- Frequently successfully audited by our clients on-site
- Regulation officers inspect our facilities regularly
- Rigid guidelines for building and data security



Driven by Science to Help Our Partners Succeed

Discuss your research needs with a scientifically trained representative near you.

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