AURIGENE
PHARMACEUTICAL SERVICES

Small Molecules
Discovery Services

- Discovery Chemistry
- Discovery Biology
- Niche Modalities
- Technology Platforms

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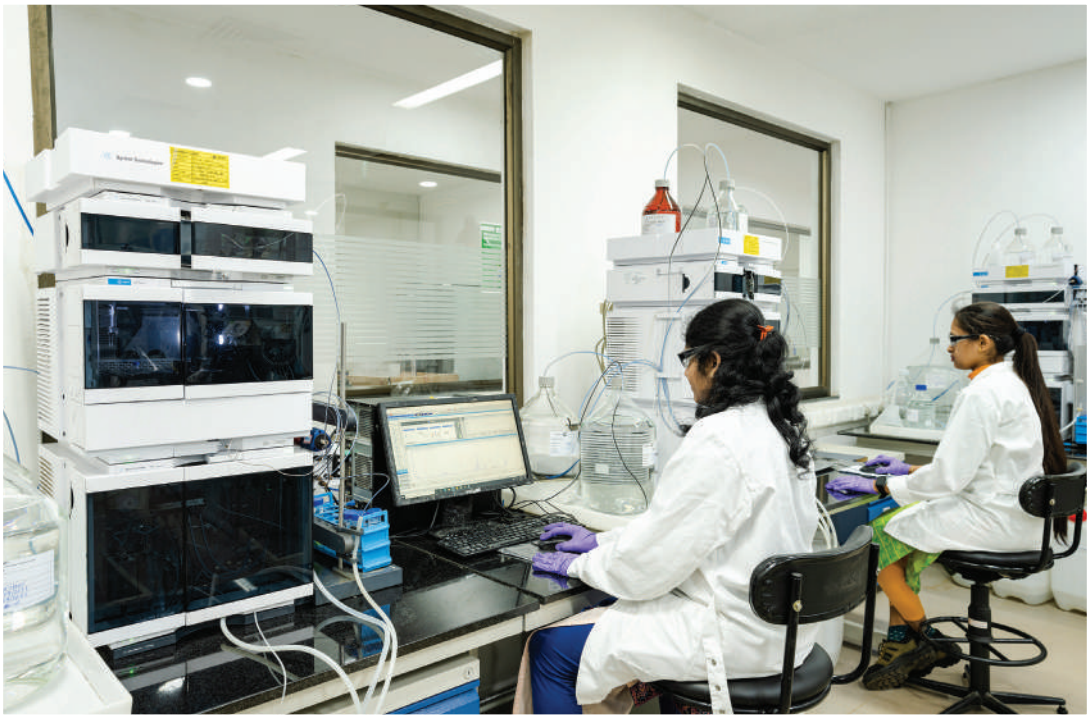
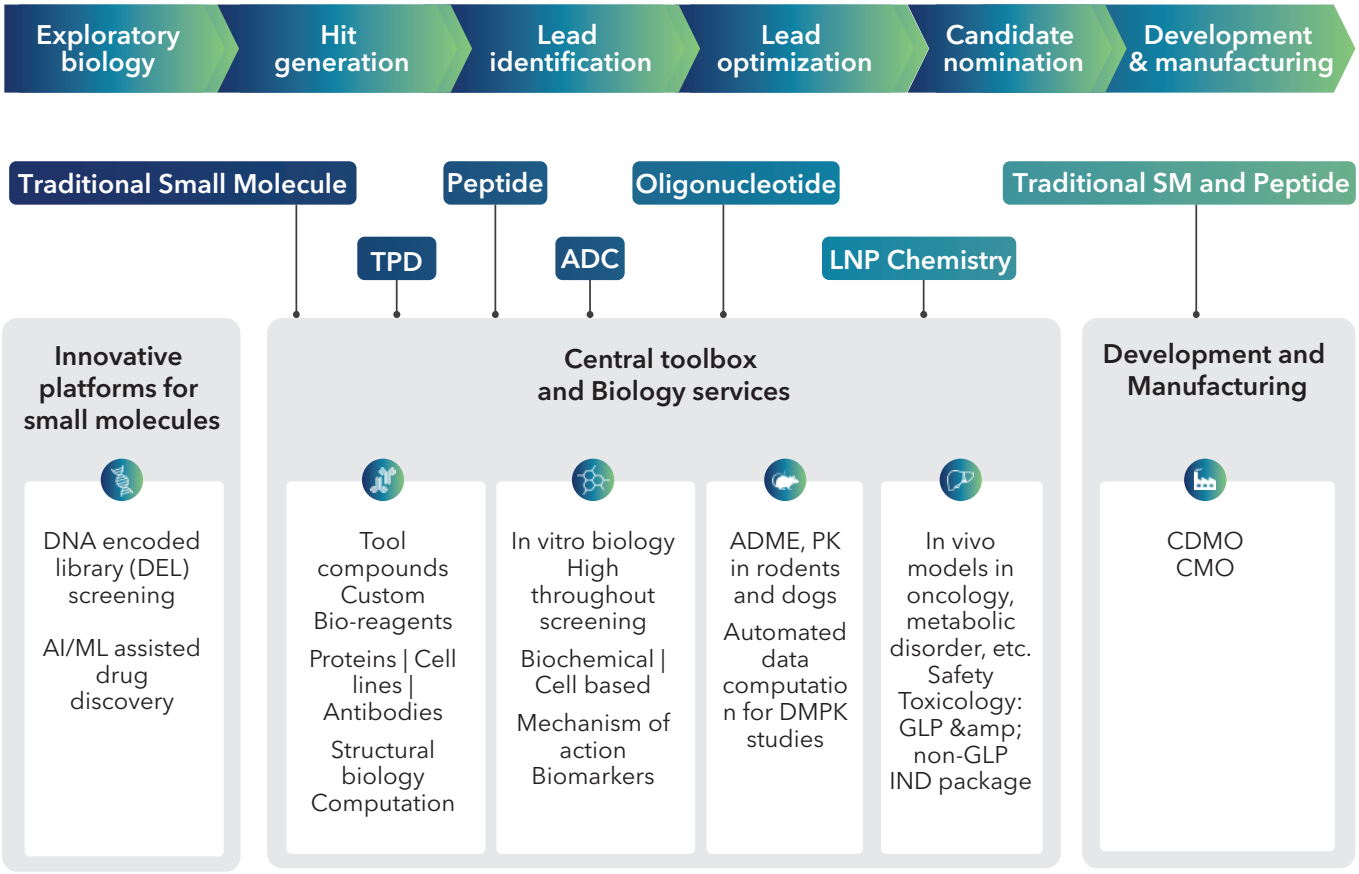


Aurigene Pharmaceutical Services

Your trusted CRO/CDMO partner for end-to-end services across drug discovery, development, and manufacturing.

With a legacy of 25 years, Aurigene offers integrated and standalone services in drug discovery space for chemistry and biology to innovative pharma and biotech companies. As per customer needs, we are flexible in our approach and offer a variety of business models, including FTE and FFS modes of collaboration, integrated projects, stand-alone chemistry or biology projects, and mix-and-match programs. Our track record and experience in discovery services have helped our clients accelerate their drug discovery programs. Our highly qualified and experienced team of scientists is supported by state-of-the-art infrastructure in Bangalore and Hyderabad to help advance our client molecules through the different phases of pre-clinical discovery (i.e., target identification to hit, hit to lead, lead optimization, and pre-clinical stage).

Integrated end-to-end Discovery services



Integrated Drug Discovery Services

Technology Platforms

- AI-assisted Drug Discovery (AIDD)
- Computer-Aided Drug Design (CADD) and Informatics
- DNA Encoded Libraries (DEL)

Discovery Chemistry

- Medicinal Chemistry
- Analytical Chemistry
- Custom Library Synthesis
- Custom Peptide Synthesis
- PROTAC Synthesis and Screening
- Oligonucleotide Synthesis
- Lipid synthesis

Discovery Biology

- *In vitro* Biology
- DMPK
- *In vivo* Pharmacology
- Toxicology
- Microbiology

Technology Platforms

AI-assisted Drug Discovery

Enabling and Accelerating Candidate Nomination

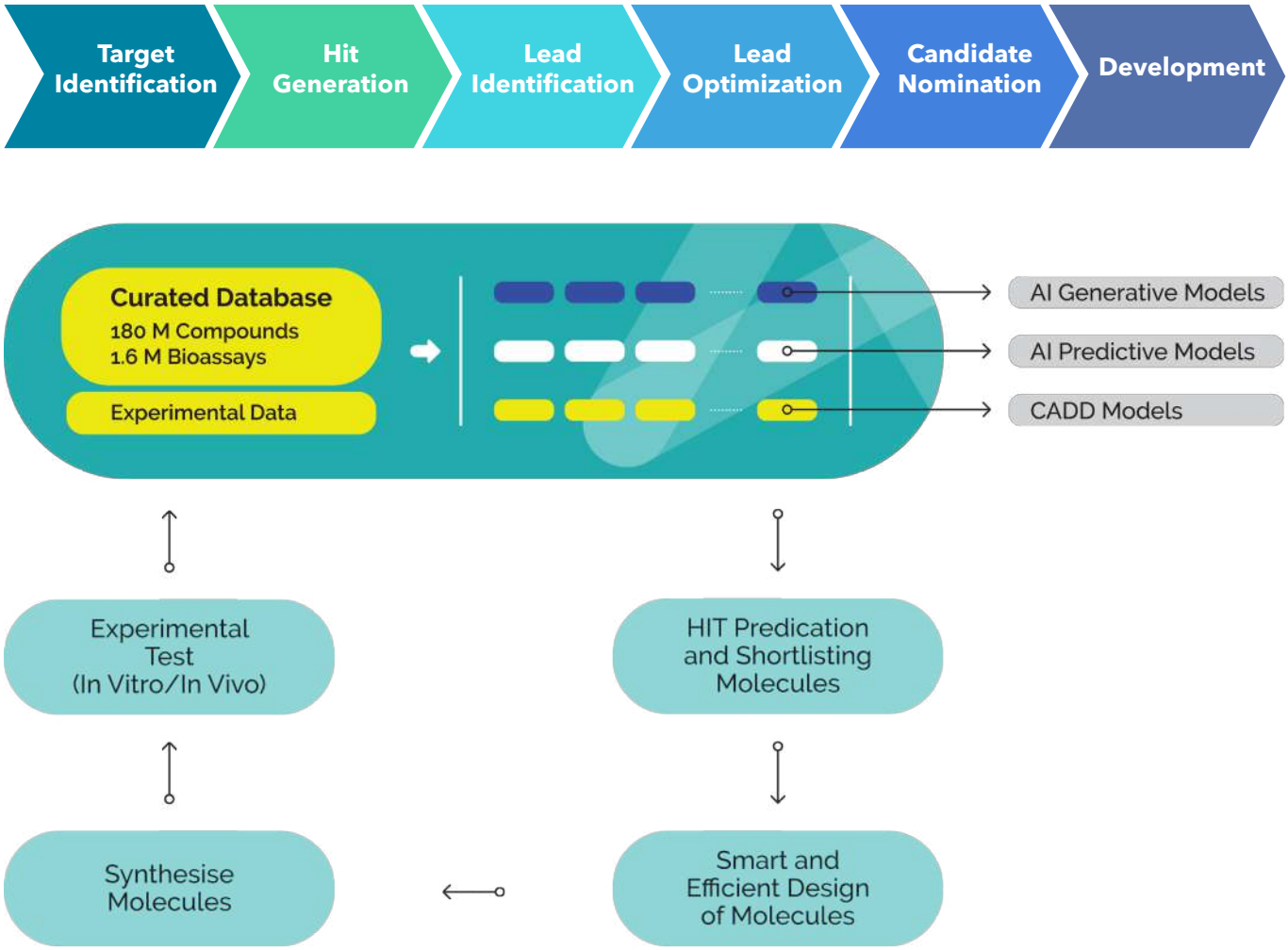
- Aurigene.AI: An AI-assisted drug discovery platform
- Aurimine: A virtual database comprising of 12+ billion compounds

AURIGENE.AI™

Key Capabilities

- Aurigene.AI consists of a **meticulously curated compound database,** which is ever-expanding using both in-house and public domain information.
- This database currently consists of **180 million compounds, and 1.6 million validated bioassay data points** and serves as a training data for the Aurigene.AI platform.
- This evolving platform consists of several **top-tier AI algorithms - 4 predictive, 11 generative and 8 CADD models.**
- This **modular platform enables** our scientific experts to cherry-pick the right set of AI models for a given application. The model output can help prioritize the chemical designs with appropriate properties, thereby leading to increased probability of success.
- We are well equipped to quickly synthesize and run a variety of experimental assessments both ***in vitro and in vivo***. The data output can be used for training the AI models to further improve the chemical design.
- The accuracy and reliability of the data output from Aurigene.AI results from an iterative DMTA cycle followed by training the AI models with generated data in real-time.

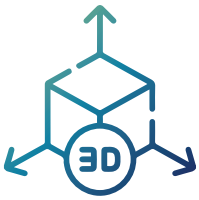
Aurigene.AI Platform Architecture:



Top 5 reasons to partner with Aurigene.AI

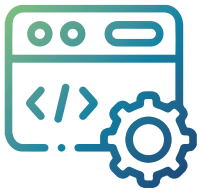
1. Interpretable AI platform
2. Enables "fail fast and iterate faster" model
3. Scientific experts can cherry-pick the right set of AI models for a given application
4. Customizable and ever-expanding data base and algorithms
5. An end-to-end solution combining AI with Aurigene's core expertise in synthesizing and experimentally testing the molecules

Computer-Aided Drug Design (CADD) and Informatics



3-D virtual reality facility

High-end software for simulation and modelling (Schrödinger and MolSoft)



Team lead by domain expert in CADD and informatics

CADD facility rigorously supports discovery projects, starting from target identification to clinical positioning of the clinical candidate. We have proven track record of successful collaborations across small molecule, PROTAC and peptide drug discovery projects.

Techniques and Tools

Virtual Screening:

- Access to **50 billion virtual compound library**
- Performs multiple applications including hit scouting and hit-to-lead optimization
- Used to decide which compounds to screen, which libraries to synthesize, and which compounds to finalize
- Both, **structure-based and ligand-based design approaches** are used

Tools and Software:

- Equipped with a state-of-the-art **"Nanome" interactive virtual reality platform**
- Supplemented by the acclaimed **"Schrödinger and MolSoft" commercial suite** to carry out all modeling studies
- Open-source CADD-related software **(e.g. KNIME, Cytoscape, Datawarrior, Cresset, Nanome, Python and Docker)** used to enrich modeling and simulation-related work

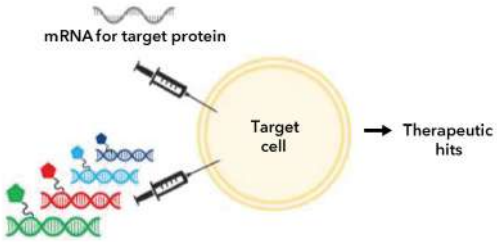
DNA Encoded Libraries (DEL)

Vipergen X AURIGENE PHARMACEUTICAL SERVICES

High fidelity DEL screening technologies

DELs in Cells

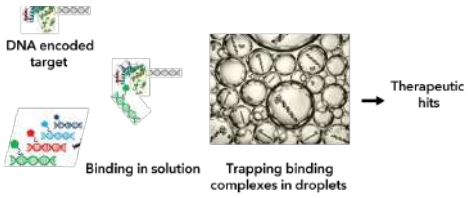
Provide the target amino acid sequence - we'll screen in a living cell



- High success rate
- Low attrition rate
- Physiologically relevant conditions
- Broad target space
- Short TAT
- No purified target protein needed
- Molecular glue screening enabled by multiplexing capability

Binder Trap Enrichment

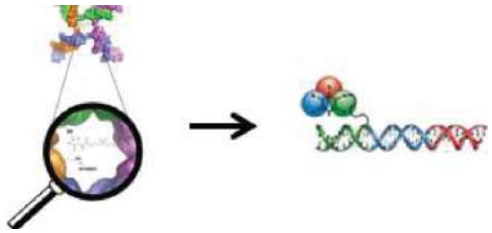
Provide the target protein - we'll screen in a homogenous assay



- Solution based (homogenous assay)
- No matrix binders
- No target denaturation by immobilization
- Low false positive rate
- Multiplexing (unique capability)

Yoctoreactor

High fidelity DNA Encoded Libraries



- Chemical diversity by building blocks
- Physicochemical properties kept in check
- 100% match between code and compound
- Purification after each synthesis step (unique capability)
- Low false positive rate

Novel offerings:

- **DELs in Cells – Express:** Only six weeks from project initiation to delivery of resynthesized hits
- **DELs in Cells** – Molecular Glue Direct:
  Unique multiplexing technology used to directly discover molecular glues

Discovery Chemistry

Medicinal Chemistry

Expertise in wide range of medicinal chemistry services: small molecules heterocyclic / carbocyclic/ asymmetric chemistry, carbohydrates, peptides, PROTACs, molecular glues, oligonucleotides, phosphoramidites and lipids

Specialized synthetic needs | Heterocyclic chemistry | Transition metal-mediated reactions | Click chemistry | Handling of gaseous reagents | Labelling | Synthesis of probes | Payloads and linkers | Conjugation | Synthesis of macrocycles | Electro organic chemistry | Photo redox reactions | Chiral resolution | Compound management

Chemistry services

- Mix and match programs (Chemistry + CADD, Chemistry + DMPK, Chemistry + *In vitro* Biology etc.)
- Collective experience of >200 years, together with experience in handling complex synthetic chemistry problems
- In-house collection of >50000 chemicals to jumpstart projects
- Best-in-class medicinal chemistry services across various platforms
- Flexible business models (FTE, FFS, Risk-sharing IDD etc.)

Analytical Chemistry

Two decades of analytical R&D experience in purification, characterization, discovery, development, biologics, drug substance and drug product analysis

Development and verification | Purification | Supercritical Fluid Chromatography (SFC) Characterization | Solubility studies | Stability studies

Purification:

Preparative High-Performance Liquid Chromatography (HPLC), Supercritical Fluid Chromatography (SFC), Mass Directed Purification (MDP), Chiral purification

Characterization:

Identification, Physiochemical, Structure elucidation, Impurity profiling and characterization

Impurities:

Genotoxicity impurities, Nitrosamine impurities

Stability studies:

Drug substance, Impartial stability studies, Hold time stability studies, Intermediate, Drug substance and drug product

Analytical instruments:

Supercritical Fluid Chromatography (SFC), Differential Scanning Calorimeter (DSC), High-Performance Liquid Chromatography (HPLC), Ultra-Performance Liquid Chromatography (UPLC), LC-MS/MS, LC-MS-Tof, GC-HS, GC-MS, ICP-MS, Nuclear Magnetic Resonance (NMR), UV-VIS Spectrophotometer, FT-IR Spectrophotometer, Polarimeter, Thermo gravimetric analyzer

Custom Library Synthesis

Rapid synthesis of focused, mid-size compound libraries with high purities, using wide range of in-house available building blocks.

Capability for design and execution with quick access to inventory | Parallel synthesis, work up and purification | Mass directed purification systems for faster TAT

Capabilities:

- Standard transformations like amidations, reductive aminations, alkylations, C-C, C-O and C-N bond transformations etc.
- Heterocyclic chemistry including the synthesis of almost any 5 or 6 membered ring analogues.
- Scaffold synthesis in multigram scale for parallel diversification.
- Protection and deprotection strategies, customized for acid-mediated, neutral or base-mediated post-library works.
- Routine transition metal-mediated reactions including Suzuki, Stille, Heck etc have been executed in focused libraries.
- >80% success rate in many critical transformation like C-C, C-N bond and amide couplings

Custom Peptide Synthesis

End-to-end peptide synthesis services, from discovery to manufacturing,
with core competencies ranging from simple linear peptides to most complex forms.

**Improving peptide druggability | Peptide modification |
Backbone and side-chain modification | Cyclization | Derivatization and conjugation |
High throughput synthesis | Microwave peptide synthesizer**

Peptide Modification

Backbone modification

- N-alkylated amino acids
- D-amino acids
- Depsipeptides
- Peptidomimetics

Cyclization

- Lactam
- Stapled
- Click
- Di-sulfide
- Thioether

Conjugation/ derivatization

- Maleimide
- Lactam
- Click
- Ester

- PEG
- Lipid
- PMD
- Oligo
- Bio-isosteres
- Florescent probes

Capacity

Synthesis:

- Manual and automated synthesis
- Automated microwave peptide synthesizer

Analysis:

- LC-MS
- Analytical HPLCs
- Salt content (TFA, Acetate)
- Peptide content (By elemental analysis)

Purification:

- Flash chromatography
- Reverse phase purification
- Ion exchange chromatography
- Salt exchange technologies
- Preparative HPLC
- Lyophilizer

PROTAC Synthesis and Screening

Synthesis of PROTACs and molecular glues for targeted protein degradation for various therapeutic indications.

Targeted protein degradation | Integrated drug discovery | Molecular glues | Expertise in purification of PROTACs | In-house partial PROTAC library

PROTAC synthesis

- Synthesis of common E3-Ligase ligands (CRBN, VHL, cIAP and MDM-2)
- Novel flexible or rigid linkers for various discovery needs
- Synthesis of molecular glues and monovalent protein degraders
- In-house library of >500 partial PROTACs and linkers for rapid target engagement
- Flexible business models including stand-alone and various integrated services
- Stand-alone biology support including *in vitro* and *in vivo* profiling

Molecular Glues

- Synthesis and profiling of molecular glues provides a unique advantage in offering standalone, semi-integrated and fully integrated discovery programs

PROTAC screening

- Target binding studies and ternary complex formation (HiBiT, Nano-BRET, SPR etc.)
- TR-FRET assays for biochemistry (Envision XCite)
- Cell-based assays for evaluating target degradation (WB, Automated)
- Preliminary ADME studies (e.g., permeability, solubility, microsomal stability)
- PK studies in rodents (terminal) and in dogs (non-terminal studies)

Oligonucleotide Synthesis

Capabilities to perform oligonucleotide synthesis, post-synthesis modifications, characterization, and biological evaluation.

Synthesis between 10 - 60 mer oligonucleotide | Milli gram to gram scale synthesis with in-house custom synthesis of phosphoramidites | Post synthesis modification with click chemistry, amide coupling, thiol mediated C-S and S-S bonds | Purification with ion exchange and reverse phase HPLC | Expertise in nucleosides, sugar and base modifications

Synthesis and purification

- Scale: 1100- µmol (11000- mg)
- Size: 10 to 60- mer
- 2'- F, 2'- OMe, 2'- O – MOE, LNA and all standard modifications
- Anion/cation exchange purification
- Reverse phase HPLC
- Size exclusion
- Desalting

Analysis

- UV quantification
- Purity and identity analysis using LC-MS (TOF) and mass deconvolution
- HPLC with different mobile and stationary phase for purity assessment

Biology

- *In vitro* IC50, Kd and binding assessment and *in vivo* activities evaluation with wide range of cells. Efficacy experiment in oncology and inflammation model
- Toxicology studies with ASO

Conjugation

- Acid-amine coupling
- Alkyne-azide coupling
- Thiol-maleimide coupling
- S-S and C-S bond formation

Lipids

Lipid nanocarriers for delivery applications

Lipid nanoparticles | In-house custom synthesis of lipids | Conjugation of drugs to the polymers | Polymeric lipid-nanoparticle synthesis using various techniques

- 10 mg to 10 g scale of lipid-polymer synthesis having molecular weight up to 5000 Da. All kind of controlled polymerization techniques are internalized by our chemist.
- Lipid-polymer based, lipid-PEG based amphiphilic lipid polymers
- Various chain lengths of PEG polymers to attachment of drug molecules
- Conjugation of hydrophobic drugs to the hydrophilic PEG polymers
- Linear and branched lipids
- Lipid – polymers characterization using

  GPC – size exclusion chromatography (RI detector)

  Multi- Angle Laser Light Scattering (MALS)

  HRMS and MALDI-TOF

  1H, 13C & 31P– NMR

Discovery Biology

In vitro Biology

Our *in vitro* biology team is highly skilled in wide range of therapeutic areas and target classes, like GPCRs, ion channels, proteases, other hydrolytic enzymes, membrane receptors etc.

Assay Capability Range

Functional Assay

- Cell Viability
- Apoptosis
- Invasion
- Migration
- Cell Senescence
- Cell Cycle Analysis
- Necroptosis Assay
- Pyroptosis Assay

Specialized Assays

- Target engagement assays via Nano-BRET/ CESTA
- 3D cells co-culture
- Spheroid culture
- Organoid culture
- Stem cell-derived functional cells –Hepatocytes, Cardiac etc.

Immunological Assays

- Dendritic cell
- T-cell cytotoxicity
- Treg –Immune suppression
- Immune cell profiling
- Mixed lymphocyte

Biomarker Assay

- Cytokine modulation
- Target gene expression
- Phosphorylation of signaling intermediates
- Cytokine-induced transcription factor phosphorylation

Screening: Medium to high throughput screening in different assay platforms, liquid handling platform for 384 well format.

Readout platforms: We offer diverse readout platforms such as Luminescence, Fluorescence (FRET, TR-FRET), Fluorescence Polarization (FP), AlphaLISA, AlphaScreen, Absorbance, UV to NIR, Flow cytometry, Western blot, qPCR etc.

Drug Metabolism and Pharmacokinetics (DMPK)

Customized and innovative solutions for standalone DMPK and integrated drug discovery services with quick turnaround times

- Expertise in integrated drug discovery and standalone DMPK services
- Highly qualified scientists with successful track record
- Validated protocols and customized study designs catering to client/project requirements
- State-of-the-art *in vitro* ADME and tissue culture labs
- AAALAC and OLAW accredited animal facility for *in vivo* PK studies in rats, mice and dogs
- GLP and Non-GLP bioanalytical labs with high-end LC-MS/MS instruments

DMPK Capabilities

- *In vitro* ADME studies: Capable of high-throughput screening with best in industry turnaround times
- *In vivo* PK studies: Established surgical models, microsampling, discrete or cassette designs, PK in various matrices for different therapeutic indications
- Bioanalysis of small molecules, PROTACs, therapeutic peptides and biomarkers. Highly sensitive bioanalysis methods for low dose PK studies
- Automated compound management and data handling systems

Broad-panel of *in vitro* ADME studies

- **Physiochemical properties:** Solubility and chemical stability at different pH, SIF and SGF to replace with solubility and chemical stability at different pH and matrices

  Solubility: Kinetic, thermodynamic

  HT logD and ChromLogD
- **Permeability:** Caco-2 bi-directional permeability, efflux ratio, MDCK, MDCK-LE, MDCK-MDR1, MDCK-BCRP permeability, PAMPA
- **Distribution:** Plasma protein, *in vitro* tissue binding, blood to plasma partition, brain to plasma partition
- **Metabolism:** Microsomal clearance, S9, phase I/phase II, hepatocyte clearance, plasma/whole blood stability, CYP phenotyping
- **Drug-Drug interactions:** CYP TDI, kobs, CYP induction, P-gp and BCRP inhibition and substrate identification

In vivo Pharmacology

Wide array of therapeutic areas and target specific models

Oncology | Inflammation and auto-immune disorders | Pain | Metabolic disorders

Oncology

- A549-Lung cancer, NSCLC
- H929 -Multiple myeloma
- MCF-7-Breast cancer
- 22RV1 -Prostate cancer
- Additional model in development stages
- CT-26-Colon cancer
- Colo-205 Colon cancer
- SKOV-03 Ovarian cancer
- MOLM-13 Acute myeloid leukemia

Inflammation and auto-immune disorders

Acute efficacy models

- LPS-induced systemic inflammation (Plasma TNF-α)
- LPS-induced systemic inflammation (Plasma IL-17)
- LPS-induced paw edema
- Carrageenan-induced paw edema
- Acute Arthus reaction
- The SCF-induced systemic histamine release model
- Mouse passive cutaneous anaphylaxis model
- TNF + Zvad induced hypothermia

Arthritis

- Collagen-Induced Arthritis
- Adjuvant-Induced Arthritis (Prophylactic)
- Medial meniscus Induced tear osteo arthritic model

Dermatology

- DNFB-induced contact dermatitis
- Oxazolone-induced contact dermatitis
- Imiquimod-induced psoriasis model
- IL-23-induced dermatitis model

Colitis

- Dextran Sulphate Sodium induced colitis
- Trinitrobezene sulphonic acid-induced colitis

Others

- Unilateral ureteral obstruction model for kidney fibrosis
- Hamster ear sebaceous gland model for anti acne evaluation
- Ovalbumin/LPS induced neutrophilic asthma model
- MOG-induced EAE model in C57BL/6J mice

Toxicology

Offering full range of exploratory and GLP toxicology studies for 20+ years

Preclinical safety assessment | Genetic toxicology | Animal toxicology

General Toxicology

- Exploratory Non-GLP toxicology
- GLP definitive toxicology
- Reproductive and developmental toxicity
- Customized toxicity

Safety Pharmacology

- Functional Observational Battery (FOB) study (Modified Irwin's test)

Genetic Toxicology

- Bacterial reverse mutation test (OECD 471)
- *In vitro* chromosomal aberration test using human blood lymphocytes (OECD 473)
- *In vitro* micronucleus test using human blood lymphocytes (OECD 487)
- Mammalian cell gene mutation assay (OECD 490)

Toxicokinetics

- Single or multiple-dose PK: rodents (GLP)
- Tissue distribution in rodents using in-situ perfusion techniques

Key Highlights:

AAALAC and OLAW accredited animal facility

Support for standalone to integrated services to IND filings

Submissions to the US FDA, MHRA, EMA and DCGI

State-of-the-art facilities equipped with GLP compliant instruments

Expert team of General and Genetic Toxicologists

Microbiology

Capabilities for anti-bacterial and anti-fungal *in vitro* assays along with murine infection models

Integrated Drug Discovery | BSL-2 compliant facility | US FDA audited

We offer wide range of

anti-bacterial and anti-fungal services to meet your scientific needs

Capabilities:

Antibiotic Susceptibility Testing:

Minimum Inhibitory Concentration (MIC), Minimum Bactericidal Concentration (MBC), Broth micro-dilution, broth macro-dilution, disk diffusion and agar dilution tests conducted in accordance with CLSI guidelines with IBSC approvals.

In vitro Assays:

Time Kill Kinetics, Post-antibiotic effect, Post antibiotic sub-MIC effect against strains of Staphylococcus aureus, Enterococcus faecalis, Pseudomonas aeruginosa, Escherichia coli, Enterobacter spp., Klebsiella pneumoniae, Acinetobacter spp. etc.

Murine Infection Models:

Systemic infection, respiratory tract infection, thigh infection model and organ burden model in CD1 or BALB/c mice with IAEC approved experimental protocols.

Accelerating Drug Innovation!

Discovery | Development | Manufacturing

Commitment to Sustainability and Social Responsibility

Driving Public Health, Innovation and Environmental Stewardship

Being committed to environmental stewardship

Making our products accessible and affordable to patients

Contributing to a fairer and more socially inclusive world

Enhancing trust with our stakeholders

Accreditations and awards

Aurigene as a wholly owned subsidiary of Dr. Reddy's Laboratories adopts the ESG goals of our parent company. Dr. Reddy's has been committed to sustainability for over two decades and has been honored with numerous accreditations and awards.

Dow Jones Sustainability Indexes

Retained the position on the DJSI (Dow Jones Sustainability Index)

Greenco Summit 2019

Environment Excellence Award from CII

Bloomberg Gender-Equality Index

First Indian company featured in the Bloomberg Gender-Equality Index (GEI).

GOLD 2023 ecovadis Sustainability Rating

Awarded Gold Medal by Ecovadis, a global sustainability ratings agency placing us in the top 5% of companies worldwide

Thank You

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https://www.aurigeneservices.com/

To place an inquiry please visit
https://www.aurigeneservices.com/form/contact

Mail us at
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