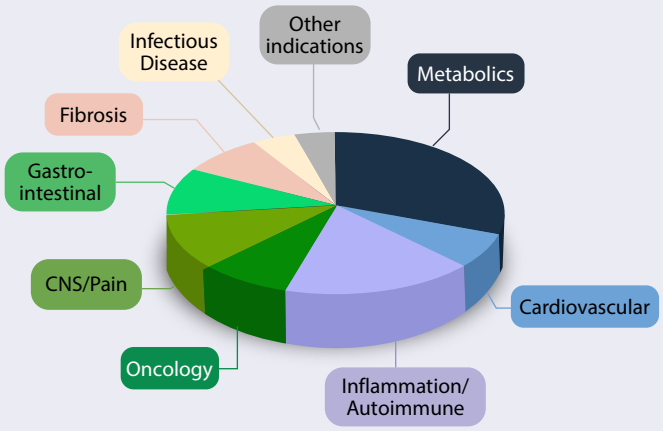
eurofins | Advinus

GLOBALLY TRUSTED & TESTED INTEGRATED DRUG DISCOVERY PARTNER

Integrated Drug Discovery Experience

- Over a decade of experience in drug discovery, with 35+ discovery programs
- Integrated Chemistry & Biology experience across therapeutic area and target classes
- Past success in multi-year discovery alliances with Merck, J&J, Takeda, Novartis, Celgene, DNDi & others
- Provide services to start-ups, universities, small & large biotechnology companies

Diverse Indications



Diverse Target Classes

Target Class	No. of Programs
Enzymes	12
Kinases	9
GPCRs	8
Nuclear Receptors	2
Transporters	1
Ion Channels	1
Polypeptide Hormone	1
Epigenetic	1
Target class unknown	1

Extensive experience in multiple therapeutic areas to develop assays, animal models, and engaging different target types

Comprehensive experience for pre-clinical development

Pre-clinical Development

- DS Process Development

Safety Assessment

- IND filing studies
- Single-dose studies
- Genetic toxicology
- Safety pharmacology
- Repeat dose studies

Bioanalytical services

Medicinal Chemistry

Strategic support with execution

Hit Identification	Hit to Lead	Lead Optimization	Candidate Nomination
Knowledge-based approach: Design and synthesis of multiple (4-7) novel and diverse chemotypes	Focused NCEs from each chemotype for rapid SAR determination	Compounds with optimized potency and selectivity	Scale-up of compound(s) for IND enabling studies
CADD approach	Enhancing potency, selectivity and improving drug-like properties	Optimization of potency in pharmaco -dynamic or target engagement assay	Desirable safety margin in non-GLP safety assessment (14 day repeated rat toxicokinetic and cardiovascular study)
Molecular docking, Homology modeling & Fragment based drug discovery, Pharmacophore modeling and core hopping	Early assessment of ADME properties	Favorable /agreed upon ADMET/PK properties	
	Prioritization of chemotypes (minimum 2) to identify leads	Meeting desired mutually agreed ED50 criteria	
These approaches can be applied in parallel	Filing of provisional patent application	Minimizing off-target activity	
		Selection of optimized lead(s) for further progression towards candidate	

Electronic Resources

- SciFinder: Unlimited access to scientists
- ChemAxon tools (Marvin) for Calculating Physiochemical Properties

Ease of knowledge transfer as the teams are on same campus

Molecular Modeling & Computational Chemistry

From de novo design to structural or guided parameter assessment

Target Validation

- Homology Modeling & Bioinformatics
- Binding Site Identification & Analysis
- Protein Crystal Structure Refinement Analysis
- Molecular Dynamics

Hit Identification

- Library Enumeration
- Structure-Based Virtual Screening
- Ligand-Based Virtual Screening
- De Novo Design
- Molecular Dynamics

Lead Generation

- Structure-Based Design
- 2D Ligand-Based Design
- 3D Ligand-Based Design
- Fragment-Based Discovery

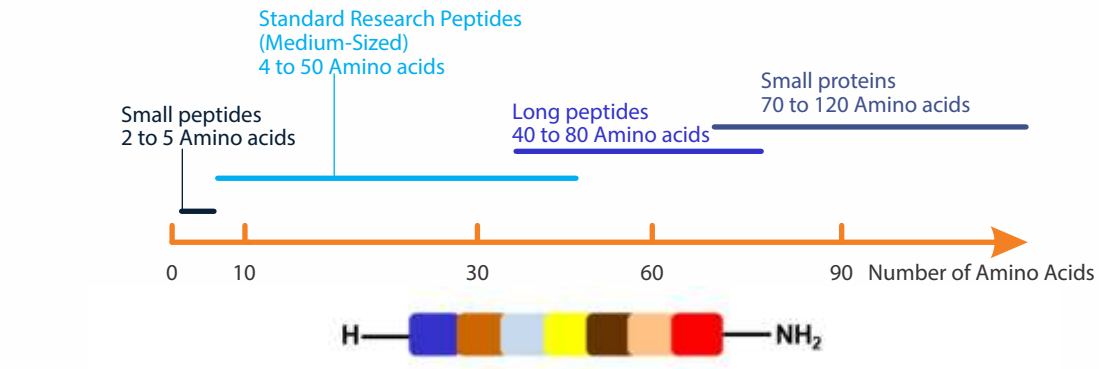
Lead Optimization

- Molecular docking
- Protein flexibility
- Fragment docking
- Scoring functions
- Scaffold hopping
- Combinatorial docking
- Properties profiling
- Off-target screening

Solid Phase Peptide Synthesis Capabilities

Skilled team capable of taking care of your requirements in Peptide chemistry

- Linear and Cyclic Peptide
- Branched, Lactam and Stapled Peptide
- Biotinylated, Fluorescent labelled and Conjugated Peptide
- Oligonucleotide-Peptide Conjugates (OPC) by native chemical ligation and click chemistry



Discovery Biology

In Vitro Biology

Molecular and Cell Biology

- Stable cell line generation
- Cloning and Over-expression
- Protein purification and Characterization
- Biomarker studies
- PBMCs derived from Blood
- Flow cytometry and FACS
- Immunological techniques

In Vitro Assays

- Enzyme assays: Inhibition, activation, kinetic analyses
- Functional Assays: Cell signaling (Gs, Gi, Gq, GTPγS), substrate uptake, ion flux, glycolysis, glycogenesis, mechanism of action and PD marker studies
- Ligand binding assays
- **OECD *In vitro* Assays:**
  In vitro Phototoxicity
  In Vitro Dermal Absorption (Franz cell) assay imported using human skin IVPT, IVRT – under method development Antimicrobial Assay (MIC, MBC, Checkerboard)

Assays in number of different detection modes ex. Radiometric, luminescence, fluorescence, TR-FRET

In Vivo Pharmacology

- **Oncology Models:** Syngeneic (ex. lung, breast, colon cancer) & Xenograft (ex. NSG/ NOD/ BALB/c Nude mice)
- **Inflammation and Autoimmune Disease:** Acute, respiratory , skin, joint inflammation, inflammatory bowel diseases, Systemic lupus erythematosus, Multiple sclerosis
- **Fibrosis:** Lung , kidney and liver fibrosis/NASH
- **Pain Models:** Acute, chronic, neuropathic pain, inflammatory, post-surgical pain models
- **Gastro-Intestinal Diseases:** GI motility studies, ulcer models, LPS induced diarrhea, DSS/TNBS induced colitis, isolated fundus strips etc.
- **CNS Models:** Parkinson's disease, depression, cognition, cerebral ischemia, anti-epileptic activity
- **Metabolic disease:** *In vivo* metabolic and cardiovascular profile and *ex vivo* studies
- **Ocular Pharmacology:** Atropine induced Dry eye Rabbit model Alkali induced corneal injury & assessment of corneal wound regeneration in Rabbits Steroid induced Glaucoma model in rats – Also offered in GLP Pupillometry assay in rat Uveitis in Rabbits Eye

Comprehensive pharmacodynamics and efficacy studies in several therapeutic areas

ADME / DMPK

Capability to develop fit for purpose ADME and *in vivo* pharmacokinetic studies

Absorption

- Permeability across Caco-2 cells, MDCK cells *(in vitro)*
- IV & PO PK – Absolute bioavailability in rodents and non-rodents for screening lead like molecules
- PK assessment of different formulations

Distribution

- Plasma protein binding *(in vitro)*
- Blood to plasma partitioning *(in vitro)*
- Volume of distribution from IV PK data
- Tissue levels

Metabolism

- Microsomal Stability in Tox species and Human *(in vitro)*
- Efflux transporter substrate identification.
- Metabolism by human CYPs *(in vitro)*
- Inhibition of human CYPs *(in vitro)*
- Induction of human CYPs *(in vitro)*
- Metabolite structure identification
- Metabolites in bile

Excretion

- Excretion in urine and faeces
- 14C ADME studies – mass balance and tissue distribution
- Excretion in bile

Infrastructure

Synthesis Labs – 7-10 FTE Pods

- Biotage/ Combiflash purification systems with ELSD
- Microwave initiator
- Lyophilizers
- Mini-Block parallel synthesis system/Radleys multi-experiment work station

Purification Labs

- Mass-Directed Auto Purification system (MDAP)
- Purification of chiral compounds by Prep SFC
- Automated Multiple Prep-HPLCs equipped with PDA and ELSD detectors

Analytical Capabilities

- 400 MHz NMR with multi nuclear probe
- UPLC-MS
- Multiple HPLC/UPLC
- GC-HS; Gas Chromatography-Head Space
- FTIR
- DSC and polarimeter
- Method development for chiral compounds by SFC (Acquity UPC2)

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