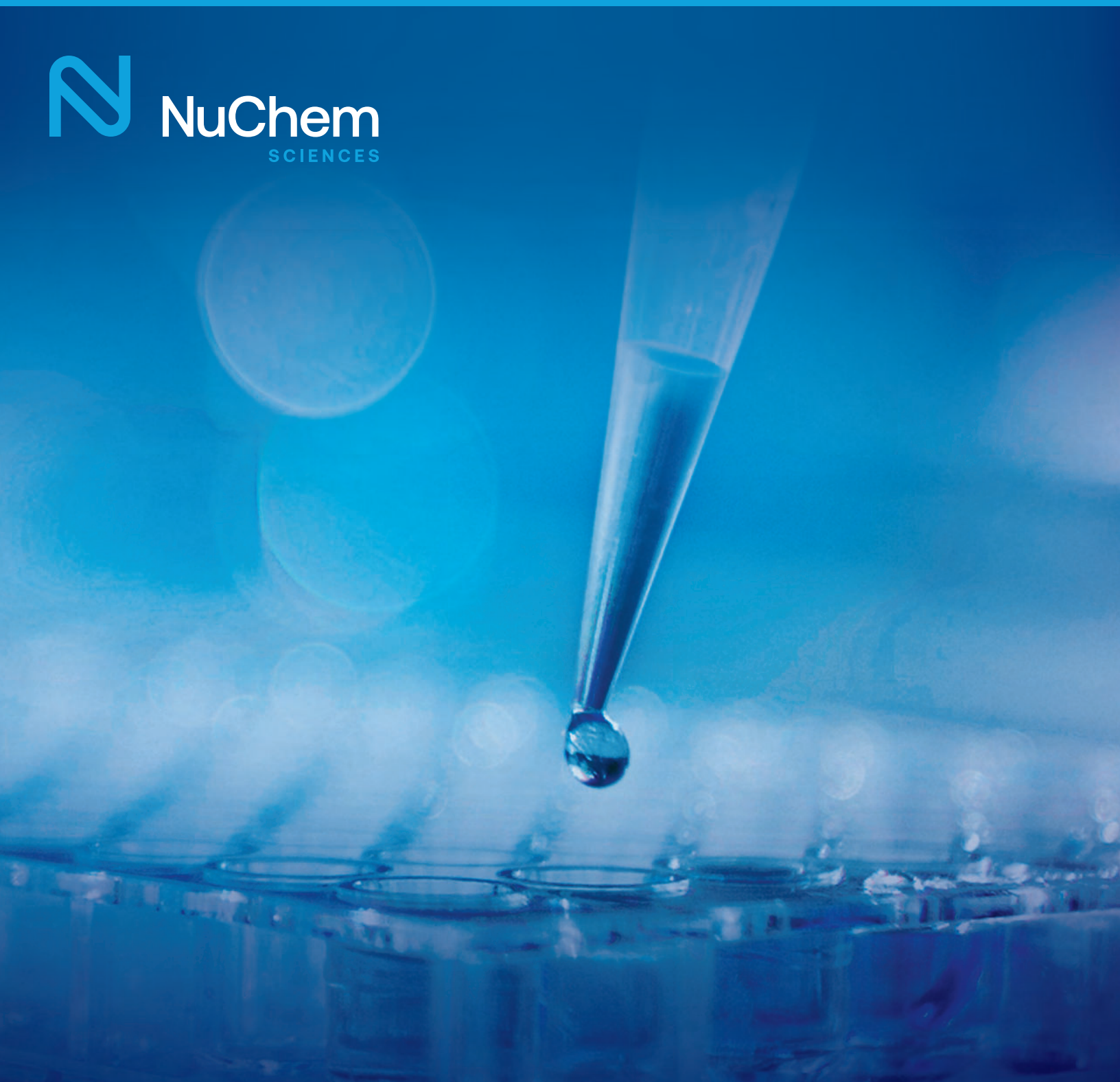
NuChem
SCIENCES



Transform Ideas Through Science

With an unparalleled knowledge base and a truly unique collaborative process, NuChem propels the dream of a potential breakthrough into a workable reality.

Transform Ideas Through Science

The CRO for Integrated & Co-located Services in Canada.

Understanding your needs & challenges.

Since our launch in 2011, we have established a diverse customer base of biotech, pharma and academic research laboratories within North America. Our senior team members have extensive experience in drug discovery project management. This expertise was developed while working in a broad range of therapeutic areas including inflammation, diabetes, bone, obesity, infectious diseases, cancer and pain.

Drug Discovery is our passion.

Our scientific team consists of experienced researchers recruited from former pharmaceutical companies in Montreal including AstraZeneca and Merck. We have also drawn from the strong academic pool of young scientists produced by Canadian and international universities to create a dynamic mix of youth and experience.

Why work with NuChem?

Reliability

Trust expert guidance

When faced with critical decisions, you need a trustworthy team that's known for reliability. Give your projects expert guidance through the development process with the capabilities of the NuChem team, backed by more than 10 years of project collaborations with diverse customers from biotech, pharma and academic research laboratories within North America & Europe. Benefit from the extensive know-how our leadership team provides from decades of experience in drug discovery, developing marketed drugs and multiple clinical candidates.

Adaptability

Rely on partnership at any stage of the development process

Wherever you are in your drug discovery process, our flexible team collaboration options meet your evolving project needs. Use the services you require. Whether you require synthetic and medicinal chemistry, computational chemistry, *in vitro* biology, *in vivo* pharmacology, structural biology or specialized services, you can count on our team for superior execution.

Expertise

Have a powerhouse team at your disposal

Set your projects up for success with our experienced, knowledgeable team. Our scientists are highly experienced in the pharma and CRO arena and have proven track records of delivering high-quality data with maximal speed. Whether you need help with target validation, hit finding, hit to lead, lead optimization, chemical development, or anything else on the drug discovery path, the NuChem team can provide unparalleled capabilities for your projects.

Collaboration

Turn our experience into your advantage

To help your team learn and grow as your company evolves, collaborative work is essential. However, getting the maximum value out of collaborative work requires a certain mindset. With our team, you benefit from our ability to manage communication and logistics for project success. When working collaboratively, our team shares knowledge so our experience becomes your advantage.

Co-located services in Canada

We have more than 300 employees deployed at six sites located throughout Montreal & Quebec City.

OmegaChem
A Division of NuChem Sciences

(Acquired in 2021)

Strike force in chemistry with scale-up facilities and capabilities.

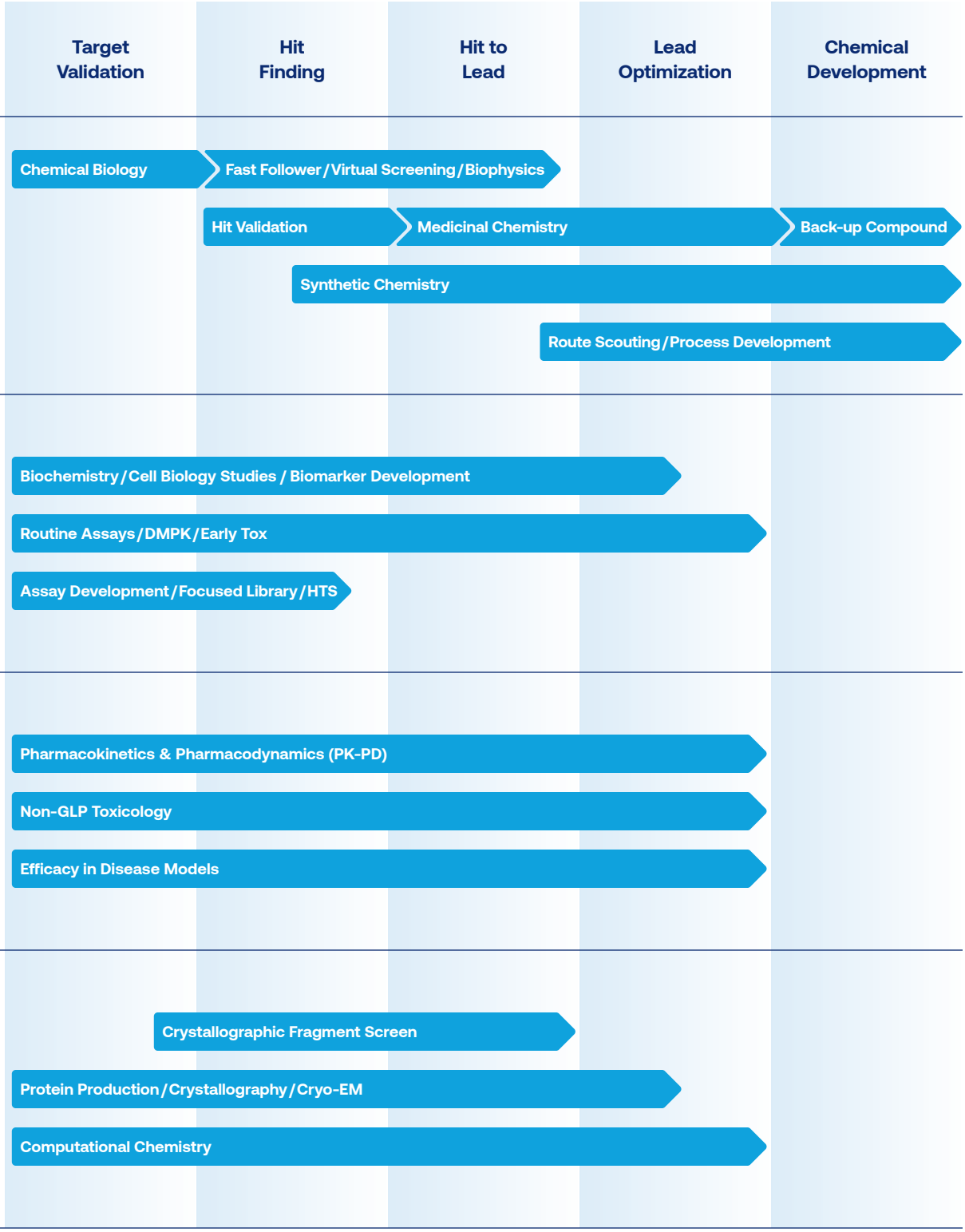
Inixium
A Division of NuChem Sciences

(Acquired in 2022)

Structural biology facilities and capabilities (crystallography and protein production & characterization)

Integrated Drug Discovery

A new era brings a new reality. Together with our customers **We are Pharma™**.



Chemistry

Leveraging all data sources combined with perfect Chemistry execution and discovery experience gives your project the edge: **Lead the Pack™**.

in vitro Biology

Biochemistry and Cell Biology working together to answer key questions and go **Beyond the Kit™**.

in vivo Pharmacology

Study the biological effects of a compound in living organisms to **Understand your Drug Profile** through data you can trust.

Structural Biology

Crystallography and protein production are key to understanding how drugs interact with proteins. The basis of our **Target Insight™** approach.

Medicinal & Synthetic Chemistry

Our custom solutions propel your project to the edge: **Lead the Pack™**.

Hit Finding

This is the genesis of the discovery path... The stage that starts it all. The seed for new proprietary chemical matter, from which great potential value is created.

Medicinal Chemistry Scientific Consulting

- Prior art review - freedom to operate analysis
- Design of novel proprietary chemical matter
- Map out the initial synthetic plan

Computational Chemistry

- Prior analysis and Go/No-Go assessment of the relevance of in silico to the project
- Model preparation from available X-Ray or via homology modeling
- Targeted virtual screening
- Identification of synthetically feasible or commercially available hits

Synthetic Chemistry

- Unlock the chemistry and make the compounds
- Get new compounds screened to validate the design

Hit to Lead

Transformation of top initial hits to the actual value as early lead compounds. Enable all stakeholders to nominate to Lead Optimization and reach the next level.

Medicinal & Synthetic Chemistry

- Provide scientific leadership and management
- Design cores, analogs, and focused libraries
- Work with biology to generate, analyze, and compile data
- Collaborate with **Computational Chemistry** to establish SAR
- Collaborate with **Biochemistry & Cellular Biology** for *in vitro* assays

Lead Optimization

An all-hands-on-deck effort with the desired profile of the development candidate in sight. Careful selection of the right series to push forward with potential backup compounds identified.

Medicinal & Synthetic Chemistry

- Provide scientific project leadership and management
- Design cores, analogs, and focused libraries
- Rapid candidate selection
- Plan backup compounds
- Collaborate with **Cellular Biology** for *in vitro* assays
- Define **Pharmacology** and **ADME-PK**

Chemical Development

Making it real: enabling the chemistry to generate the material needed for key studies to convert a development candidate into a clinical compound.

Route Scouting/Process development

- Thorough evaluation to determine deficiencies in the original synthetic route
- Exhaustive retrosynthetic analysis of the target compound to provide a thoughtfully different approach
- Establishing a new route that is safe, scalable, environmentally friendly, and cost-effective
- Execution of the new approach and timely delivery of the requested material that meets the client's specifications;
- Possibility to produce a non-GMP batch (up to 1 kg) of advanced synthetic intermediate or API

Tech Transfer to CMO

- Generation of detailed report/technical transfer package suitable for a commercial scale CMO
- Assisting in the implementation of the new process at the alternative facility

Process Chemistry

We work with you to establish chemistry and **Revisit Possible™**.

Route Scouting & Process Development

Our process chemistry group is composed of highly skilled and creative organic chemistry scientists who have significant experience in synthetic chemistry and process development of drug candidates, intermediate compounds, and building blocks.

Our services include the following:

- Thorough evaluation to determine deficiencies in the original synthetic route
- Exhaustive retrosynthetic analysis of the target compound to provide a thoughtfully different approach
- Establishing a new route which is safe, scalable, environmentally friendly, and cost effective
- Execution of the new approach and timely delivery of the requested material that meets client's specifications
- Ability to produce multi-kilogram batches of non-GMP advanced synthetic intermediates or APIs
- Identification of impurities and their synthesis when required

Cutting-Edge Technologies

NuChem process chemistry team experienced chemists exploit the potential of cutting-edge technologies to work more efficiently. Our **flow chemistry** systems offer precise control and high-throughput reactions, while our **photochemistry** and **electrochemistry** capabilities allow for unique synthetic pathways. Our state-of-the-art **cooling systems** provide optimal conditions for even the most temperature-sensitive reactions. Experience the benefits of large scale chemical synthesis with NuChem's innovative technologies.

Scalability

Our process chemistry team uses state-of-the-art chemistry methodologies and creative design of synthetic routes to develop processes suitable for the larger-scale manufacturing of drug candidates. We have the capability to prepare complex, challenging molecules in house, accommodating **multi-kilogram requirements as needed**.

Our scalable equipment includes the following:

- Glass reactors up to 50 L (temperatures from -78 °C)
- Hastelloy reactors up to 7.5 L (pressure up to 200 psi) with heating/cooling systems,
- Process safety assessment (Thermal Screening Unit),
- CombiFlash Torrent System for large scale purification,
- Preparative SFC for complex purification up to 400 mL/min & 1 kg scale

Technology Transfer to CMO

To ensure the smoothest possible transition, NuChem follows a proven transfer process.

Our transfer process includes the following:

- A detailed report/technical transfer package suitable for a commercial scale CMO
- Detailed analytical conditions to ensure proper reaction monitoring and identification of product and impurities
- Assistance with implementation of the new process at the alternative facility

OmegaChem

A Division of NuChem Sciences

35 years of bringing drug discovery to the next level. Together.

OmegaChem is a Canadian manufacturing company that specializes in fine chemicals by offering innovative products and services to the pharmaceutical industry. Its mission is to develop, manufacture, and distribute high value-added organic synthesis intermediates to its customers.

Computational Chemistry

As an integral part of the team, we catalyze your project by **Challenging Ideas™**.

Cheminformatics

Data Management

- Databases clean-up and preparation
- Cross format data (*e.g.* from TXT to SDF)
- 2D-to-3D chemical structures
- Data clustering and filtering

Property Calculation

- Physicochemical and thermochemical descriptors calculation (*i.e.* LogP, TPSA, molecular weight, acidity/basicity, ...)
- CNS MPO and BBB scores calculations

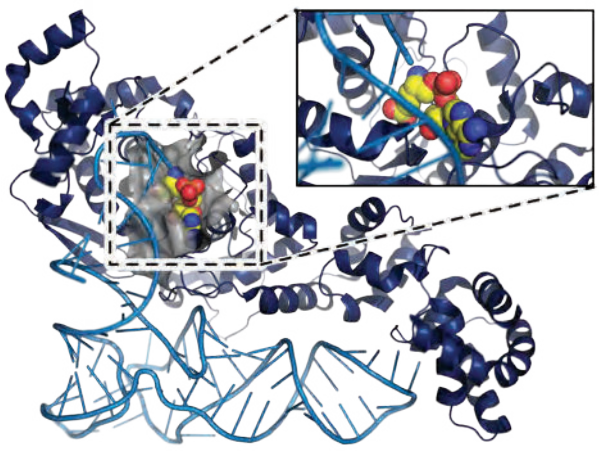
Quantum Mechanics

- Ligand conformation analysis and energy evaluation
- Molecular orbital calculation and analysis (HOMO, LUMO, reactivity indices, charge, and NBO)
- Interaction analysis
- Organic reaction and transition state analysis
- Potential energy surface (reaction mechanism) exploration

Protein Motions in Drug Discovery

Molecular Dynamics

- Simulation of free and bound protein
- Identification of principal motions
- Analysis of the protein function and drug molecule's mechanism.
- Binding site identification and analysis
- Ligand binding refinement
- Clustering (RMSD), interaction (Occupancy), motion (RMSF, PCA) and correlation analysis



Protein/Ligand Protein/ Protein Interactions

Building a Docking Model

- Assessment of available structures (crystallographic data and AlphaFold model)
- Generation of homology models
- Docking protocol creation and validation

Virtual Screening

- Selection of suitable candidates for virtual screening from large library of commercial compounds
- Generation of combinatorial libraries based on current synthetic approaches
- Selection based on desired parameters

Structure Activity Relationship (SAR)

- Qualitative model elaboration
- QSAR model elaboration

New Chemical Matter

- IP landscape analysis
- Scaffold modification/replacement
- *De Novo* scaffold design

Protein/Protein Model

- Protein surface (contacts, hydrophilic-hydrophobic hot-spots, electrostatic, surface area and pocket volume) analysis
- Antibody interaction analysis
- Protein/protein docking

Special Platform

Protacs

- Protacs development through end ligands
- Linker design and optimization

Illimited Computational Power

- Internal servers for day-to-day computing
- On demand external server with state-of-the-art security for:
  - Docking
  - Virtual screening
  - Molecular dynamics

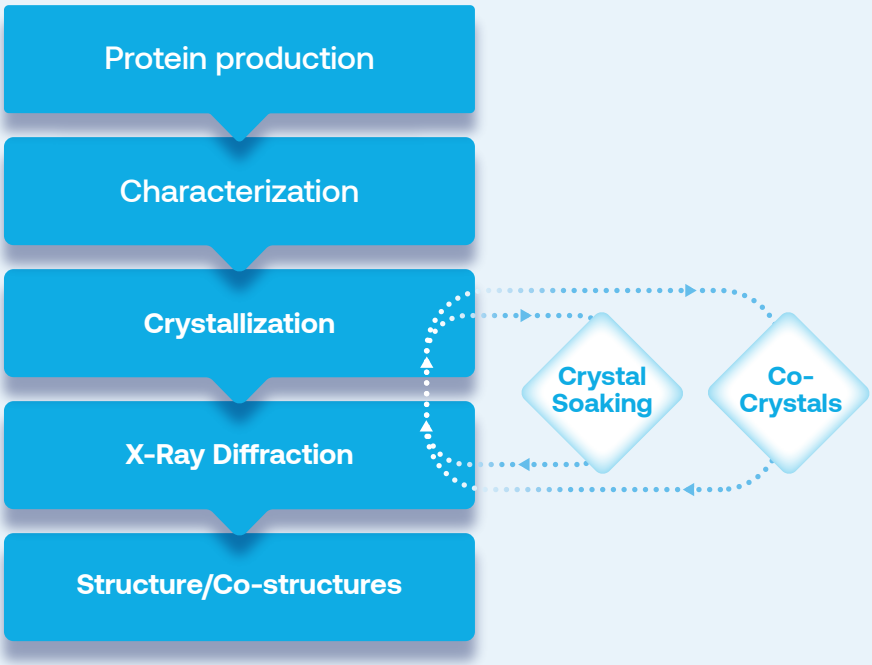
Structural Biology

The basis of our **Target Insight™** approach.

Target Identification	Hit Finding	Hit to Lead	Lead Optimization	Chemical Development
	Target Production Assay Development & HTS			
	Fragment Screening (AS-MS, X-ray)			
	System Characterization (ITC, TSA, DLS)			
	SAR Analysis			
	Rational Drug Design			

IniXium
A Division of
NuChem Sciences

IniXium was created in 2014 as a contract research organization (CRO) providing crucial knowledge-based expertise in structural biology, and more specifically in crystallography and protein production, to the biotech and pharmaceutical industry worldwide. IniXium culture of excellence purpose is to speed-up the drug discovery process by using X-ray crystallography as a core technology.



Our Services

- Target production and characterization
- Gene to structure projects
- Fragment-screening campaign
- Protein crystallization
- Cryo-EM
- Structure determination of complexes

Our Core Technologies

- Large scale protein production in E. coli, mammalian, and insect cells
- Protein purification
- Biophysical characterization
  - DLS plate reader
  - Automated ITC
  - Fast TSA
- High throughput fragment screening by X-ray crystallography
- Automated crystallization with robotic nanoliter drop maker
- Rapid and automated solution maker
- Visible and UV automated crystal imaging system for rapid analysis of crystallization experiments
- Regular access to synchroton (ALS, APS, CLS) for diffraction analysis
- Regular access to high end electron microscopes for Cryo-EM (McGill)

in vitro Biology

Biochemistry and cell biology working together to answer key questions and go **Beyond the Kit™**.

Facilities

- Multiple PCR and qPCR machines
- Robot pipetting station
- LC-MS/MS
- Multimode plate readers
- Bright field and fluorescent microscopes
- Western blot imager (in-cell & in-gel)
- Capillary electrophoresis (protein simple system)
- Cell culture facility (BSL2)
- Biology and chemistry all under the same roof

in vitro ADME

- **Bioanalytics**
- **Chemical Stability & Solubility**
  SGF/SIF & plasma stability
- **Absorption/Permeability**
  Pampa
  MDCK (transcellular absorption)
  Caco-2 (Bi-direction & efflux transporters)
- **Protein Binding**
  Albumin, plasma, brain tissue, whole blood
  Blood to plasma ratio
- **Metabolism**
  Metabolic stability, hepatic intrinsic clearance
  Oxidation and conjugation pathways
- **Elimination**
  Excreta analysis of metabolites and parent compound
- **Data Analysis and Report Production**
  Summary report for discovery lead selection
  Detailed report for IND filing

Biochemical Assays

- **Enzyme Assays**
  Recombinant
  Whole cell
  Cell lysate
- **Detection Assays**
  Fluorescence polarization, TR-FRET (HTRF), ADPGlo, AlphaScreen, LanthaScreen
- **Mechanism of Action**
  Enzyme kinetics
  Activity & binding assays
  Mechanism profiling to help understand SAR
- **Protein-Protein Interactions**
  Competitive inhibition and binding assays, SPR, ITC, TSA

Expert Consulting

- Strategic biology planning for preclinical development
- Expert unbiased reviews of current discovery projects
- Problem-solving and troubleshooting of issues in screening and assay development
- Oversight and management of outsourcing to other CROs
- Due diligence and asset evaluation

Screening

- Assay internalization & adaption from other CROs, institutes, or your own labs
- Customized assays – we make it and run it
- Up to 384-well format for enzyme- and cell-based assays
- Robotic automation for liquid handling (screening libraries in 384-well format)

Biomarker Development

- Testing services to support the unique needs of any inical development program
- Metabolic biomarkers with LC-MS/MS
- Related biomarkers in body fluid or tissues
- Access to FACS and MSD platform

Cellular Assays

- **Primary Cells/Tissues**
  Primary neuronal cell culture from mouse & rat brain
  Primary splenocyte culture
  Primary peripheral blood mononuclear cells (PBMCs)
  Monocyte, macrophage, and microglia primary cultures
- **Established Cell lines**
  (Human and animal cell lines)
- **Cell Line Development**
- **Cell Viability & Death**
- **Reporter Assays**
- **AlphaLISA**
- **HTRF, BRET assays**
- **Protein post-translational modifications**
- **DNA Methylation**
- **Accessible to FACS service**
- **Protein & Gene Expression**
  Reporter gene assays
  Western blot
  Capillary electrophoresis (protein simple system)
  PCR & qPCR
  ELISA, MSD
- **Assays Toward Different Target Classes**
  GPCRs (CAMP, calcium mobilization), PDEs, Kinases, Proteases, tRNA transferases and others...
- **Microscopy & Cell Imaging**
  Phase-contrast (bright field) microscopy
  Fluorescent microscopy
  ImageJ analysis software

DMPK

Drug Metabolism and PharmacoKinetics

Bridge the gap between *in vitro* and *in vivo* data sources with critical insights that give candidate selection the **Leading Edge™**.

Drug Discovery Screening for Lead Compound Selection

After target validation and hit identification, the chemical and enzymatic stability of new chemical entities should be performed to identify the most stable compounds during the intestinal transit and absorption while having minimal degradation by first-pass metabolism.

ADME screening services (full package or tailored studies) help you to select compounds with the best chance of giving an ideal pharmacokinetic profile.

Absorption

The **PAMPA** assay is rapid and produce data quickly for screening purpose.

The **MDCK** affords permeability data with a good correlation with the Caco-2 assay with a shorter culture time (5-day *vs* 21-day for the Caco-2).

The **Caco-2** monolayer is the best *in vitro* model for the prediction of *in vivo* absorption and the most relevant *in vitro* model for the prediction of absorption and first-pass metabolism.

Ideal Candidates with Drug-Like Properties

- Comply with Lipinsky's rule of 5
- Permeability > $3x10^{-6}$ cm/sec
- *in vitro* microsomal stability $T_{1/2}$ > 45-min
- *in vivo* bioavailability > 35%, and half-life > 2 h

Chemical & Metabolic Stability

A good lead candidate is a compound with no undesirable functional group or no chemical reactivity. To screen out those structures, a compound is incubated:

- with GSH (chemical reactivity)
- with GSH and glutathione S-transferase (GST) to select the most stable compounds.

NuChem scientists can determine the metabolic clearance, biotransformation and elimination pathways *in vitro* of your lead candidates to ensure that a good exposure (AUC) is achievable *in vivo*.

Bioanalytics

- **PharmacoKinetic (PK) Studies**
  LC-MS/MS method development
  Plasma or whole blood
  CSF or tissue homogenates
  Different administration routes (IP, PO, etc.)
  Phoenix WinNonlin software

in vitro ADME

- **Chemical Stability & Solubility**
  SGF/SIF & plasma stability
- **Absorption/Permeability**
  Pampa
  MDCK (transcellular absorption)
  Caco-2 (Bi-direction & efflux transporters)
- **Protein Binding**
  Albumin, plasma, brain tissue, whole blood
  Blood to plasma ratio
- **Metabolism**
  Metabolic stability, hepatic intrinsic clearance
  Oxidation and conjugation pathways
- **Elimination**
  Excreta analysis of metabolites and parent compound
- **Data Analysis and Report Production**
  Summary report for discovery lead selection
  Detailed report for IND filing

in vivo Pharmacology

Keeping the target in sight with the desired *in vivo* efficacy. Decisions guided by the **Target Insight™** approach.

Facilities

- Conveniently located in the State-of-the-Art Montreal biotechnology hub-adMare Bioinnovation/NeoMed institute
- Vivarium is CCAC accredited
- IVIS imaging system
- Housing and procedure suites
- Cell culture lab
- BSL-2 hoods
- Behavior testing suites
- Specialized equipment:
  - **Biological safety cabinets** for immune-deficient rodent manipulations
  - **Automated Dynamic Weight Bearing (DWB)** system for rodent arthritic joint pain measurements and activity measurements
  - **Plethysmometer** for precise paw volume measurements in inflammation, pain and arthritis models
  - **Tail-immersion** water bath for pain measurements
  - **Video camera** system for capturing rodent behavior and pain reactions
  - **Digital and manual calipers** for tumor volume and paw/knee thickness measurements
  - **Perfusion system** for rodent cardiac perfusion
  - Automated **glucometer** for blood glucose level measurements
  - Necropsy suites with required equipment

Support

- Bioanalytical (DMPK)
- Biomarkers (cell biology)
- Histology

Capabilities

- Expertise with most drug administration routes in rodents
  - **Systemic**: oral gavage (p.o.), intravenous (i.v.), intra-peritoneal (i.p.), subcutaneous (s.c.), intra-muscular (i.m.), intra-nasal (i.n.), intra-dermal (i.d.), intra-plantar (s.c. or i.d.), intra-rectal (i.r.)
  - **Local**: intra-articular (i.a.), intra-thecal (i.t.)
- Expertise in blood collections
  - **In-life**: jugular vein, saphenous vein, tail vein, tail-snip
  - **Terminal**: intra-cardiac, abdominal aorta, abdominal vena cava
- Clinical sign observations, food consumption, body weight
- Behavior and pain assessments (DWB, vide o recording, plethysmometer)
- Stool evaluation for Hemoccult examination
- Tumor cell culture, cell inoculation and tumor volume measurements
- In-life stool and urine collections
- Brain & CSF collections
- Tissue/organ sample collections
- Formulation support (pilot formulation for new molecules)

Disease Models

- Oncology (CDX, Orthotopic, Syngeneic)
- Rheumatoid arthritis (CIA, CAIA, TNF)
- Osteoarthritis (MIA)
- Acute and inflammatory pain (tail-flick, carrageenan, formalin, capsaicin)
- Obesity/Diabetes (DIO, Db/Db, STZ)
- Inflammatory bowel disease (DSS)
- Fibrosis (Bleomycin, CCL4, ALD, NFALD)
- Systemic inflammation (LPS)
- On demand pilot models

Pharmacokinetic (PK) studies

Non-GLP toxicology studies

Transform Ideas Through Science

Medicinal & Synthetic Chemistry

Process Chemistry

Computational Chemistry

Structural Biology

***in vitro* Biology**

DMPK
Drug Metabolism and PharmacoKinetics

***in vivo* Pharmacology**

Project Management

Speciality Services

Leverage 3rd Party Services

NuChem SCIENCES

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