Syngene

Putting Science to Work

Innovate I Integrate I Customize I Accelerate


Syngene

Contents

Who We Are?

24+ Years of Unparalleled Experience In

A Global CRO

- Integrated discovery, development and manufacturing service provider
- Small & large molecules, ADCs, Oligonucleotides

Track Record

- Collaborations and partnerships to deliver numerous clinical candidates
- Delivery history for integrated CMC programs towards FIH and beyond

Facilities and Team

- 1.3 Mn Sq.ft. World-class R&D & manufacturing infrastructure
- ~3500 scientists including Ph.D / MS

Novel Molecule Discovery & Development Services

IP Position

- No internal programs / products
- IP is always client owned
- No transgression of IP / data confidentiality

Quality Focus

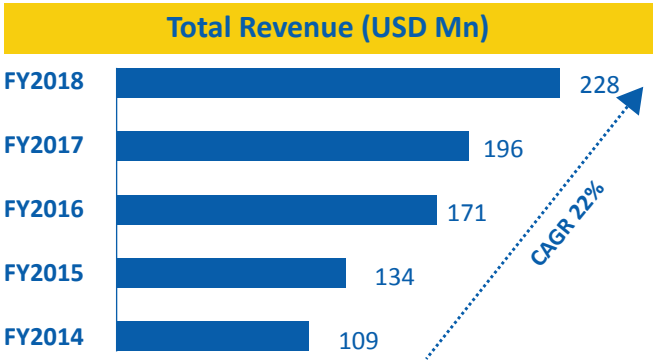
- Quality driven organization
- Excellent track record of compliance with various global regulators

World-class Infrastructure

- Audited successfully by US FDA, EMA, AAALAC, PMDA and major life sciences partners

Where Are We Today?

STRONG TRACK RECORD OF GROWTH



Extend Existing Client Association

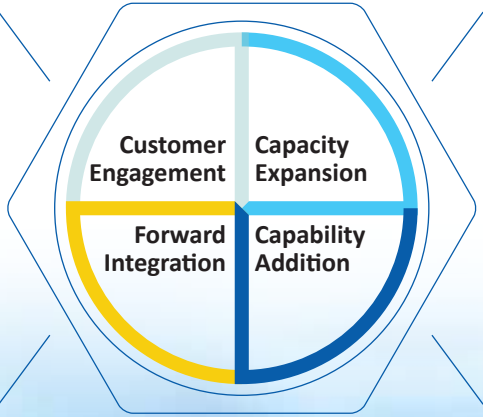
- High service integration
- Dedicated R&D centers

Engage New Clients

- Customized service offerings to suit requirement

"Follow the Molecule"

- Evolving from a CRO to a CRAMs Player



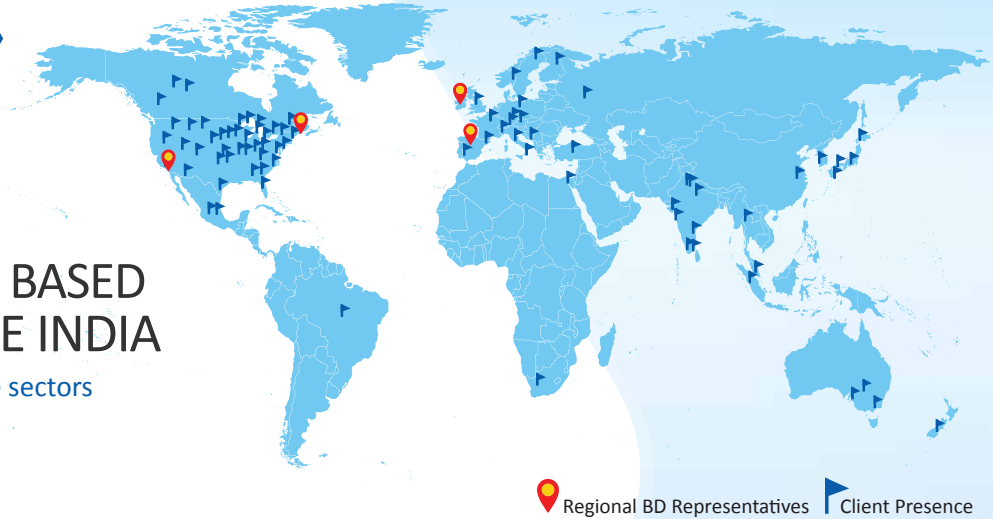
Capacity Expansion

- Consistent expansion
- FTE services, Manufacturing, Formulation, Biologics, Stability

Capability Additions

- New capabilities across multiple domains including allied sectors
- Stability, Analytical & Bio-analytical services, Oligos, Viral Testing, Bioinformatics

Global Presence



95% CLIENTS BASED OUTSIDE INDIA

316 global clients across multiple sectors including 8 out of top 10 global pharma companies

- Pharmaceuticals
- Biotechnology
- Nutrition
- Agrochemicals
- Animal Health
- Speciality Chemicals
- Consumer Goods
- Academic and Nonprofit Organizations

Our Services Spectrum

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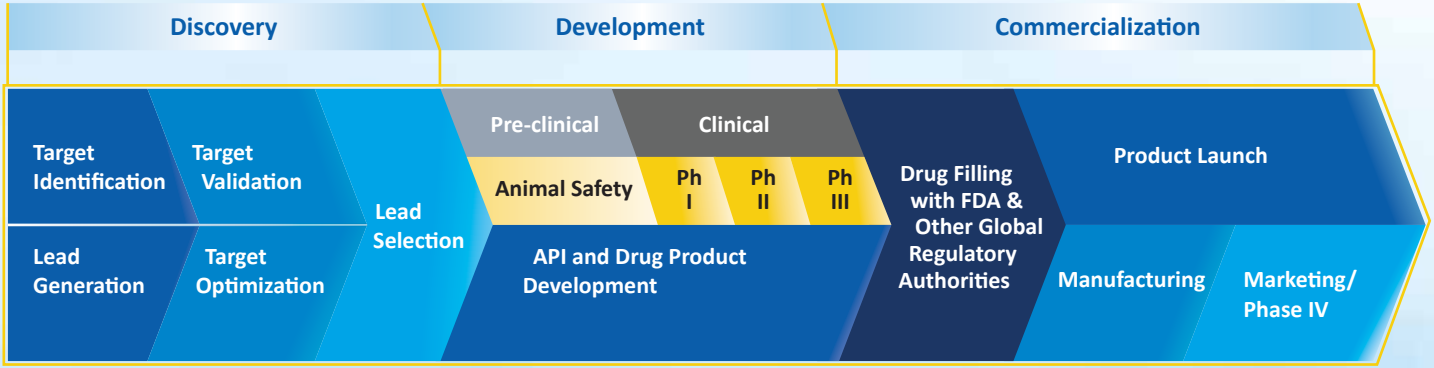
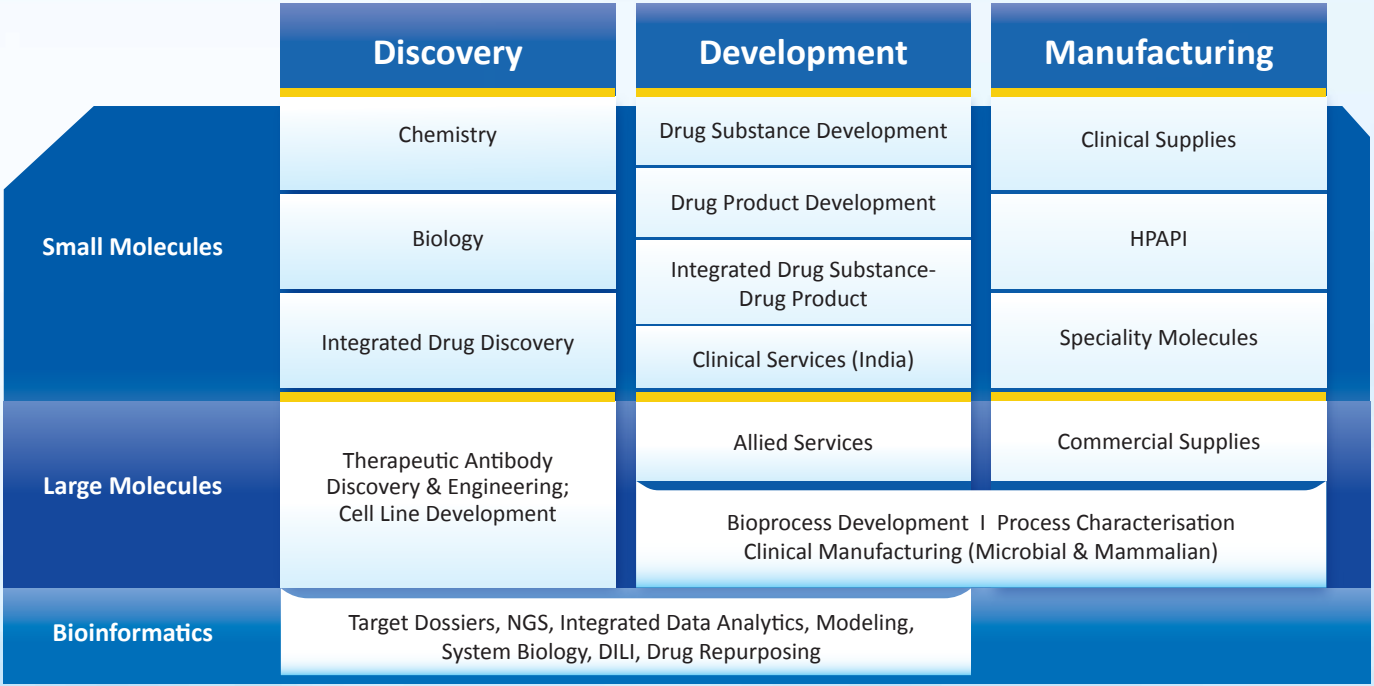


Providing multiple points of engagement for a client to associate with Syngene across the DDC* continuum

** Discovery, Development, Commercialization*

Advancing Your Molecule



Wide spectrum of services across a range of molecules including Antibody Drug Conjugates and Oilgonucleoties.

Dedicated R&D Centers

Exclusive and customized centers of excellence with dedicated infrastructure and scientific teams to suit the requirements of individual clients

Bristol-Myers Squibb	Baxter	AMGEN	HERBALIFE
Largest R&D center in Asia for BMS setup in 2009. Contract extended till 2026.	Dedicated R&D center in India for Baxter setup in 2013.	Exclusive R&D center for Amgen Inc. setup in India in 2016.	Herbalife's 1st Nutrition Research and Development Lab setup in India in 2016.
Dedicated Center of research excellence with world class facilities.	State-of-the-art facility supporting R&D of medical products and devices worldwide.	State-of-the-art dedicated center supporting variety of discovery and development projects for biotechnology and small molecule medicines.	Dedicated center spanning 3,000 sq.ft. and houses cGMP formulation lab to support product testing, sampling and end-product development.
~500 scientists supporting novel molecule research in small and large molecules.	Engages multidisciplinary team of ~150 scientists.	Engages a multidisciplinary team of 185 scientists.	Focus on product development, sensory evaluation and testing, scientific content writing, project management, formulation development, analytical service, stability study and other related services.
Produced nine drug candidates for further study and advanced new compounds for first-in-human studies.	R&D activities centered on product and analytical development, preclinical evaluation in parenteral nutrition and renal therapy.	Focus on medicinal and process chemistry, biologics, bioprocess, drug metabolism, pharmacokinetics, bioanalytical research and pharmaceutical development.	

Why Syngene?

Ability to adapt to industry-specific expertise

- Significant expertise in offering services to diverse industries

Ability to attract experienced scientific talent pool

- Scientific talent pool with relevant expertise and experience

Syngene

World-class offerings at par with global standards

- World-class infrastructure, quality systems, scientific standards and productivity

Customization of resources with flexibility

- Customized, dedicated resources with the flexibility to up or down regulate

Variabilization of resources

- Converting fixed R&D, manufacturing costs to variable costs

Our Discovery Solutions

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Discovery Biology

Discovery Chemistry

Safety Assessment

Bio-Informatics

Discovery Biology

Assay Biology
- All Target Class Assays
- Biochemical, Binding, Functional
- Phenotypic Screens, Primary Cell Assays, High Content Imaging
- Compound Management
- HTS, 384 Format

ADME & PK
- ADME assays
- In vivo PK
- Bioanalysis
- High throughput

Protein Sciences
- Expression- Bacteria, Yeast, Insect, Mammalian
- Large Scale Production
- Purification
- Gene to Structure
- Crystallography

Antibody Discovery
- Tools, Surrogate, Therapeutic
- Hybridoma
- Single B Cell Cloning
- NGS
- Phage/Yeast Display
- Tg Mice with Human Igs

70,000 Sq.ft. Labs, State-of-the-art Infrastructure, ~350 Scientists

Target Identification & Validation

Assay Development & Screening

Lead Identification & Optimization

Pre-clinical Development

In vivo Pharmacology
- Target Engagement and Disease Models in Oncology, Metabolic Disorders, Pain, Inflammation, Auto Immune Diseases, Neurology
- PK-PD, Histopath, Biomarkers

Cell Line Engineering
- Adherent/Suspension
- Stable/Transient
- Characterization & Validation
- Stability & Cell banking
- KI, KO Cell Lines

Genomics & Translational Biology
- PDX
- Biomarkers
- NGS
- Immuno-oncology Studies

Discovery Chemistry

Integrated Drug Discovery

- Seamless co-ordination between Chemistry, Biology, DMPK and Animal studies Bioinformatics

Medicinal Chemistry

- SAR analysis and analoging
- Hit to lead and lead optimization
- Candidate selection
- IP scoping and patent coverage
- Pro-drug and drug targeting
- Irreversible and bivalent ligands

Synthetic Chemistry

- Small-scale synthesis support
- Heterocycles, complex organic compounds
- Natural product synthesis
- Small scale GMP synthesis
- Impurities and metabolite synthesis
- Route scouting and early process R&D
- Flow chemistry

CADD

- SBDD, FBDD, Ligand based designs
- Virtual screening and hit analysis

600 Highly Trained **Scientists**

>100,000 Sq.Ft. of State-of-the-art Lab Space

Nucleoside and Carbohydrates

- Multistep synthesis of nucleosides
- Nucleoside Phosphoramidates
- Nucleoside and Carbocyclic Nucleoside Libraries
- Complex Oligosaccharides (Up to Heptasaccharides)

Library Synthesis

- Focussed library
- Diverse screening library
- Fragment library
- Macrocyclic library
- Bb collection synthesis

ADC and Toxin Synthesis

- Antibody Discovery and Engineering
- Linker Synthesis and Conjugation
- Toxin Synthesis and Payload development

Organic Electronic Materials

- Multifunctional polyaromatics
- Heteroaromatics and Bicyclic compounds
- Transition metal complexes (eg. Ir, Rh, Co, Pd, Pt, Zn)

Peptide Synthesis

- Linear peptides (50 Mer)
- Conformationally constrained
- Stapled peptides
- Biotin, Fluorescein in-tagged peptides

Safety Assessment

- AAALAC accredited
- GLP certified animal facility
- FDA inspected large molecule bio-analytical facility

Bio Assays of Biologics

Pathology Services

Analytical & Bioanalytical Capabilities (Small and Large Molecule)

Exploratory & GLP Toxicology

- Discovery Toxicity Studies
  - Single dose/MTD studies
  - Acute toxicity (six pack studies)
  - 4 day toxicity studies
  - 7/14 day toxicity studies
  - Mini Ames
  - Discovery Micronucleus test
- IND and NDA Enabling Studies
  - 7/14 day dose range finding study
  - 28 day toxicity study with Toxicokinetics and recovery
  - Battery of Genetic Toxicology studies: Ames and Chromosomal Aberration, Micronucleus test (In vivo & In vitro)
  - 3 month Sub-chronic Toxicity study in rats
  - 6 month Chronic Toxicity study in rats
  - Reproduction Tox studies (seg-I, II and III)

Xybion Online Data Capture with SEND Capability

Bioinformatics

Capabilities

- **Mechanistic Hepatotoxicity Prediction**
  - Patented *In vitro In silico* platform
  - Cross species comparison
  - *In vitro* screening services
- **NGS and Multi-Omics Analysis**
  - Genomics, Transcriptomics. Protemics, Metabolomics, Metagenomics
  - MOA, Gene signatures, Biomarker discovery, Patient stratification analysis
- **Target Intelligence**
  - Pharmacogenomic target dossiers
  - Knowledge base creation and curation
- **Systems Modeling (QSP)**
  - Clinical trial simulations
  - Disease, Toxicity, Efficacy models
- **Drug Repurposing**
  - Drug centric, Disease centric, Target centric
  - Gene signatures, Target pathways, Machine learning
  - Complete solution – *In silico, In vitro, In vivo*
- **Integrated Drug Discovery**
  - Cheminformatics, Molecular modeling
  - AI platform for Multi-objective optimization
  - Data mining, Visualization, Machine learning
  - Small molecule and Biologics

Highlights

- Highly experienced team with cross functional expertise in biology, drug discovery and bioinformatics
- Experience in developing custom bioinformatics solutions
- Patented technology to predict liver toxicity during lead optimization stage
- AI design and decision support for pharma R&D
- Cloud-based/on-prem solutions

Our Development Solutions

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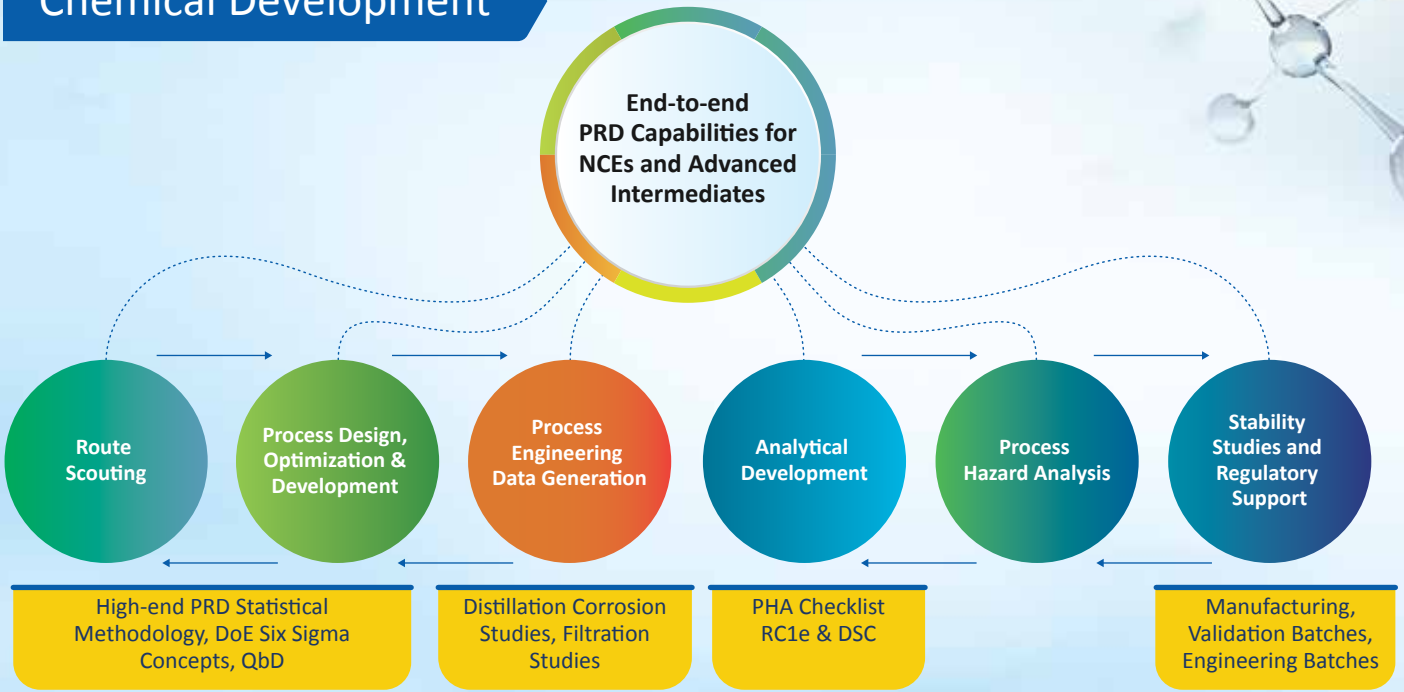
Chemical Development

Formulation Development

Stability Studies

Oligonucleotides Drug Substance Development & Manufacturing

Chemical Development



Highlights

- 125+ fume hoods in multiple suites
- Capacity up to 20L liquid handling
- High potent lab
- OEL - micro gram 0.1 µg/ m^3-8h
- Dedicated process engineering and safety lab
- Automated lab scale jacketed reactors (-70 To 180 °c)
- Flow chemistry
- Oligonucleotide lab

Chemical Manufacturing

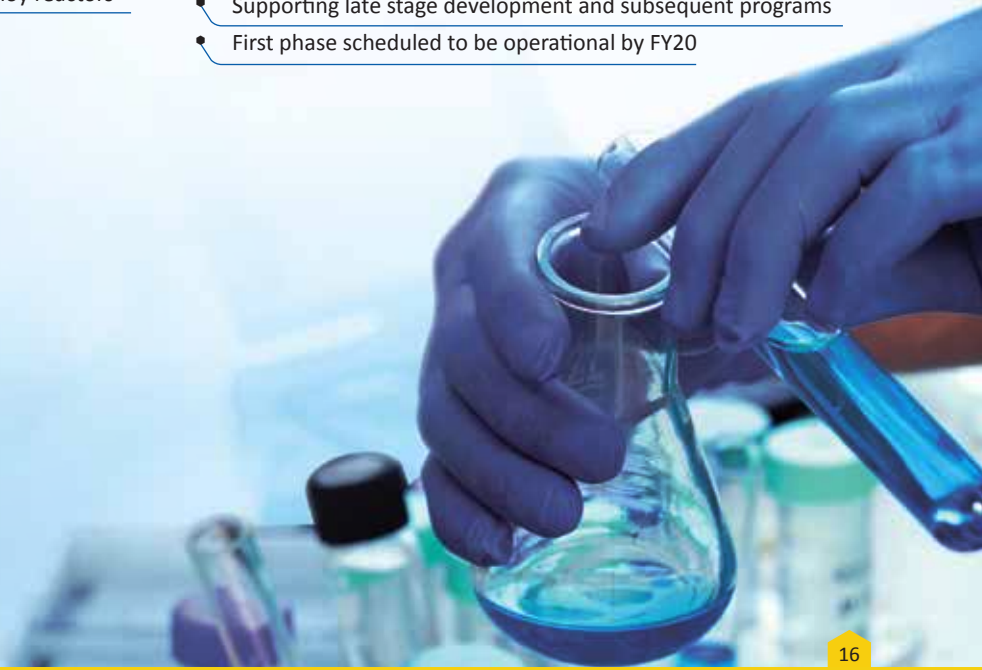
Capabilities

Manufacturing of Regulatory Starting Materials, APIs and HPAPI

- USFDA and PMDA inspected manufacturing facilities
- Dedicated Hydrogenation suites with hastelloy reactors
- Wide range of reactors (60L To 8KL)
- Total reactor volume (71KL)
- Temperature range (-80 To 140° C)
- Multi-purpose production facilities

Capacity Expansion

- Upcoming commercial manufacturing facility with total reactor volume upto 240KL
- Spread across 40 acres in the SEZ area at Mangalore, India
- Equipped to manufacture NCEs & novel advanced intermediates
- Supporting late stage development and subsequent programs
- First phase scheduled to be operational by FY20



Formulation Development

Capabilities

- Salt and Polymorph Screening, Preformulation Studies and Preclinical Formulation Development
- Formulation Development – Oral Solids, Liquids, Injectables, Semisolids
- Integrated CMC Development Services – from Lead to FIH
- NDDS Including Modified Release Formulation Development
- Enabling formulation approaches - Spray-Dried Dispersion (SDD), Hot Melt Extrusion (HME) and Nanosuspensions
- Ready to use and Lyophillized injectable product development, including suspensions
- Analytical method development and validation
- Scale up and technology transfer
- Registration batches
- Small scale commercial supply
  - Niche and Orphan drugs
  - 1kg to 120 Kg batch size
- OEL: ≥ 1 µg /m3
- Multiple formulation technologies available, including
  - High Shear Granulation, Roller Compaction, Fluid Bed Granulation, Spray Drying, Extrusion and Spheronization
  - Wurster Coating, Accela-Cota®
  - Blister & Bottle Packaging
  - Bilayer Tablets

Highlights

- Complex formulation development creating IP
- Delivered 12 integrated CMC projects in last 3 years
- Can handle low volume commercial batches for oral solid dosage forms

Stability Studies

Capabilities

- End-to-end offerings including
  - License application
  - Centralized logistics team to handle all inbound and outbound shipments fast clearance being In SEZ
  - Statistical analysis
- Studies at different phases – FIH, NDA/ ANDA and Commercial
- 4000m³ of multiple walk-in chambers with all climatic zones as per ICH guidelines
- Dedicated chamber space and stability chambers can be provided based on requirement

Highlights

- 72,000 Sq.Ft. state-of-the-art facility
- Well-equipped analytical laboratories which can be dedicated
- Quality systems audited by the US FDA and approved for conducting studies on commercial products
- Backup chambers available as part of business continuity plan
- Biometric Access Control System for individual chambers apart from Overall Facility Access Control
- Stability studies for Pharma, Animal Health, FMCG, Generics and OTC Products

Oligonucleotides Drug Substance Development and Manufacturing

Salient Features

- Process development and cGMP supplies of Therapeutic Oligonucleotides
  - Antisense, siRNA, miRNA, Exon Skipping and Oligo Conjugates
- Tox to clinical supply – grams to Kg scale
- Platform analytical methods, method development, qualification and validation
- cGMP facility of 1,500 sq.ft with 4 dedicated suites (Suites 1,2 & 3:ISO 8 | Suite 4:ISO 7)
- Equipped with AKTA OP100 & 400, AKTA Process, Uniflux 30 supported by other automated and semi-automated equipment
- Successful completion of projects for process development, optimization and material supply for feasibility as well as Phase-I studies

Our Clinical Development Solutions

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BA/BE Studies

Clinical Trial Management

Central Laboratory Services

Clinical Data Management & Biometrics

Clinical Development Solutions

Capabilities

BA/BE Studies to Support Development of Generic Drugs

- Over 150+ validated methods available as per USFDA guidelines
- Total Mass Specs: 10 [API 4000s and API 6500s]
- State-of-the-art instrumentation [with qualification]
- Analysis of drug(s)and/or metabolite(s) in biological specimen [e.g. blood, plasma, serum etc.] to support TK,PK, early phase clinical development, BA/BE and TDM studies
- Team of 40 qualified and experienced researchers with experience in method development, validation and regulated Bioanalysis for a wide range of chemically diverse drug molecules

Clinical Trial Management (Phase I-III Trials) of Novel Drugs and Biosimilars

- One of the most experienced Indian CROs in conducting patient-based trials
- Over 100 clinical trials conducted for registering products in US, Europe, India and ROW countries
- Deep experience in Oncology, Diabetes and Auto-immune disorders
- Full service solutions, incl. Clinical Supplies Management, Central Lab and CDM & Biometrics

- **Central Laboratory Services Encompassing Clinical/Safety Lab and Bioanalytical Services for Small Molecules & Biologics**
  - CAP accredited Central lab offering clinical testing services exclusively for Phase I-IV clinical trials and BA/BE studies
  - GLP-certified, FDA-inspected bioanalytical lab offering PK, ADA and NAb assays
  - 21CFR-11 compliant laboratory information management system with customizable project management and reporting capabilities
  - Supported over 100 NDAs/BLAs submitted to US FDA, EMA and PMDA
  - r HbA1c

- **Clinical Data Management and Biometrics**
  - Stand alone or integrated data management for Phase I-IV studies
  - Statistics and SAS programming for Clinical and non- clinical development programs
  - **Data Acquisition:**
    - Web based through in-house eCRF - Oracle clinical/ Inform
    - Paper CRF based data capture – Oracle

Regulatory Track Record

- **Audited by major life sciences Co's & Regulatory agencies from North America and Europe**
- **Certifications/Accreditations: ISO 9001:2008, 14001, OHSAS 18001, AAALAC, GLP**
- **HPU & Bioanalytical labs are inspected by:**
  - US-FDA - 7 audits
  - EMA - 3 audits
  - Thai FDA for GLP - 2 audits
  - ANVISA -Brazil - 2 audits

Our Biologics Development & Manufacturing

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Large Molecules

Viral Clearance Studies

Antibody Drug Conjugates (ADCs)

Our Biologics Development & Manufacturing

Capabilities

Bio-therapeutic Discovery

- Protein Engineering & Expression
- Analytical & Functional Characterization
- Antibody Development

Biologics Development

- Cell Line & Process Development
  - Freedom CHO-S Expression
  - Upstream process: Multi-reactor system for DOEs, Shake flasks and 1-50L Bioreactors, perfusion (ATF)
  - Primary Recovery: Depth & Polymeric Filtration & Centrifugation
  - Purification: High Throughput Screening (HTS) and Column Chromatography (IEX, Affinity, HIC, Mixed-mode)
- Analytical Development, Qualification, Validation and Product Characterization
  - Routine Testing –HPLC/UPLC (RP, SE, IE, Pro-A), Electrophoresis, Capillary Electrophoresis (CE-SDS, cIEF), ELISA, Process Residuals (HCP, DNA, rProA)
  - Product Characterization –Mass Spectrometry, LC-MS (Glycan and product variants), MALDI-TOF, MS/MS (Ion-trap), CD, Fluorescence, SPR (Biacore), PAMAS (sub-vis)
  - Stability Studies –Exploratory, Freeze-thaw, Real-time, Accelerated and Stress (forced degradation)
  - Bioassays – cell based, Non-cell based, ***In vivo***, Proliferation, Inhibition, Reporter Gene, Effector Function, Secondary Signaling
- Tox, Early Clinical Supplies

cGMP Manufacturing

- New biologics manufacturing plant for mammalian products (3 X 2000L)
- 3 x 2000L Single-Use bioreactors 100→500→2,000L trains
- Two upstream suites allow parallel operations
- Downstream train with post-viral segregation
- Intended for clinical and commercial manufacturing for global markets

Highlights

- 8 Novel Biologics supplied for Clinical Trials Phase I to US, EU, Australia, Singapore & India
- Worked with >30 Clients globally, >150 GMP runs
- High Yield Processes Developed: Antibody process with Harvest Titre 4 g/L and *E. Coli* process with Expression 5 g/L
- Competitive execution timelines
  - mAb development from MCB to GMP Drug Substance (DS) supply in 13 Months
  - *E. Coli* Product from Lab-scale Tech Transfer to GMP Drug Substance (DS) supply in 6 Months
  - mAB development from Transfection to GMP Drug Substance (DS) supply in 16 Months
- Allied Capabilities (Including Viral Clearance Studies, Immunogenicity Assays and Antibody Drug Conjugates) under one roof

Viral Clearance Studies

Salient Features

- Cell Based *In vitro* testing of unprocessed bulk harvest (CHO Derived)
- 28 Days *In vitro* adventitious virus detection & retrovirus detection by Cell based assay
- Viral clearance for cell culture processes for phase 1 and commercial
- GMP/GLP compliant systems to meet global regulatory expectations
- Segregated labs for Cell culture, Virology, PCR
- Dedicated suites for running client process
- Dedicated cell bank area for the storage of analytical cell lines
- Safe working practices for personnel and environment through EHS policies

Antibody Drug Conjugates

Salient Features

- **Conjugation**
  - Variety of chemistries available
  - Pilot facility for Contained Conjugation & ADC Processing
- **Linker**
  - Client Proprietary or In-licensed Linker
  - Developed Novel Patentable Linkers
  - Development and Manufacturing capability in-house
- **Antibody (Discovery & Development)**
  - Hybridoma/Phage Display
  - Recombinant Abs/Fragments
  - Functional Evaluation (*In vivo*, *In vitro*)
  - Process Development
  - cGMP Manufacturing
- **Payloads**
  - Payload Experience: Duocarmycin, MMAF, DM1, DM4, PBD dimer, Tubulysin, SN38
  - HPAPI facility for development and cGMP manufacturing

Contact Us

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