



# WuXi AppTec Discovery Services

**Enabling unbounded possibilities**

## Our Footprint — China



### Shanghai R&D Headquarters

Library, Custom synthesis, Medicinal chemistry, Peptide, Isotope labeling, Special technology, Oncology and immunology, GEMM and rare disease models, biomarker services, DEL, In vitro and in vivo pharmacology, Infectious Diseases

3000+ employees 45000+ m<sup>2</sup>



### Shanghai HDB

Medicinal chemistry, Catalog, Target Validation, Hit to Lead & Lead Discovery, DMPK/Safety, Efficacy PK/PD Disease Model, Assay & Biology

340+ employees 13000+m<sup>2</sup>



### Chengdu Healthcare Industrial Park

Custom synthesis, Medicinal chemistry

2000+ employees 90000+ m<sup>2</sup>



### Wuhan Chemistry and Drug Discovery

Custom synthesis, Catalog, Peptide, CMC, Fluorine Chemistry

2500+ employees 42000+ m<sup>2</sup>



### Tianjin Chemistry and Drug Discovery

Custom synthesis, Library, Discovery Process Chemistry, Oligonucleotide, Special technology

4000+ employees 79400+ m<sup>2</sup>



### Nantong Small Molecule R&D

Synthesis, Medicinal Chemistry, Oncology and immunology, GEMM and rare disease models, In vitro and in vivo pharmacology, Infectious Diseases, Lung diseases

1000+ employees 30000+ m<sup>2</sup>



### Suzhou Drug Safety Evaluation

Oncology and immunology, Antibody production, Protein production, X-Ray Crystallography, Large animal disease models

290+ employees 3300+m<sup>2</sup>

## Discovery Services

Delivering comprehensive end-to-end solutions for creating, identifying, and supporting preclinical candidates, from discovery to development, with our integrated chemistry and biology research platform

Target

Hit

Lead

Candidate

IND

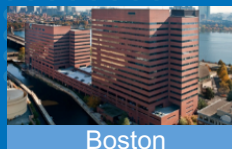
## Our Footprint - Global



Munich

### Germany Munich

Protein production, FBDD,  
Crystallography, Biophysics, DEL  
1600+ m<sup>2</sup>



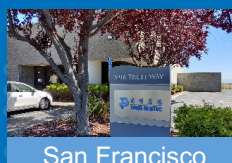
Boston

**U.S.**  
**Boston Office**  
DEL teaching lab



Cambridge

### U.K. Cambridge Office



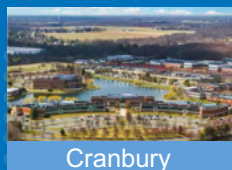
San Francisco

**U.S.**  
**San Francisco Bay Area Site**  
Chemistry



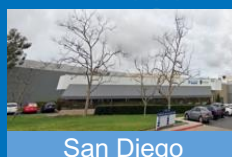
Tel Aviv

### Israel Tel Aviv Office



Cranbury

**U.S.**  
**Cranbury New Jersey Site**



San Diego

**U.S.**  
**San Diego Preclinical R&D**  
*In vivo* pharmacology, Oncology and immunology, Target Discovery, Assay and screening, Infectious diseases  
3400+ m<sup>2</sup>

## Our History

2001

Chemistry Service

2002

Chemistry Analysis Service

2008

Biology Platform

2014

Oncology & Immunology Service Separated

2016

Acquired Crelux

2017

Acquired HD Biosciences

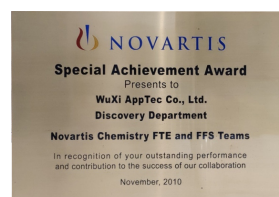
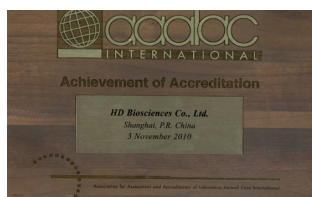
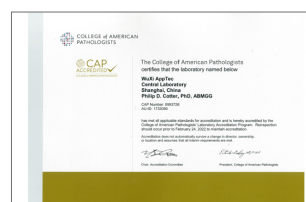
2018

DEL Platform

2020

HitS Established

## Commitment to Excellence



>13,000 scientists across integrated chemistry and biology platform.

CAP-certified pathology and FACS for clinical biomarker services

The largest synthetic team with 21+ years of experience in route design and synthesis

AAALAC-accredited SPF animal facility

Successfully supported numerous IND-enabling FDA- and CFDA-filings

The world's leading integrated tumor model online database with mobile APP

# Integrated Chemistry and Biology Research Platform

From Discovery to Candidate Selection and Beyond

## Enabling Discovery

Gene therapy

AAV, shRNA

Cells & Proteins

Molecular biology, cell lines, protein engineering/production

*In vitro* Hit Finding

DEL, HTS, ASMS, FBDD

Structural biology

X-ray crystallography, Cryo-EM

*In silico* drug discovery

Virtual screening, computer-aided drug design, machine learning

## Creating Therapies

Chemistry

Synthetic, medicinal, analytical, early discovery process

*In vitro* pharmacology

*In vitro* assays, efficacy, MOA, SAR support

*In vivo* pharmacology

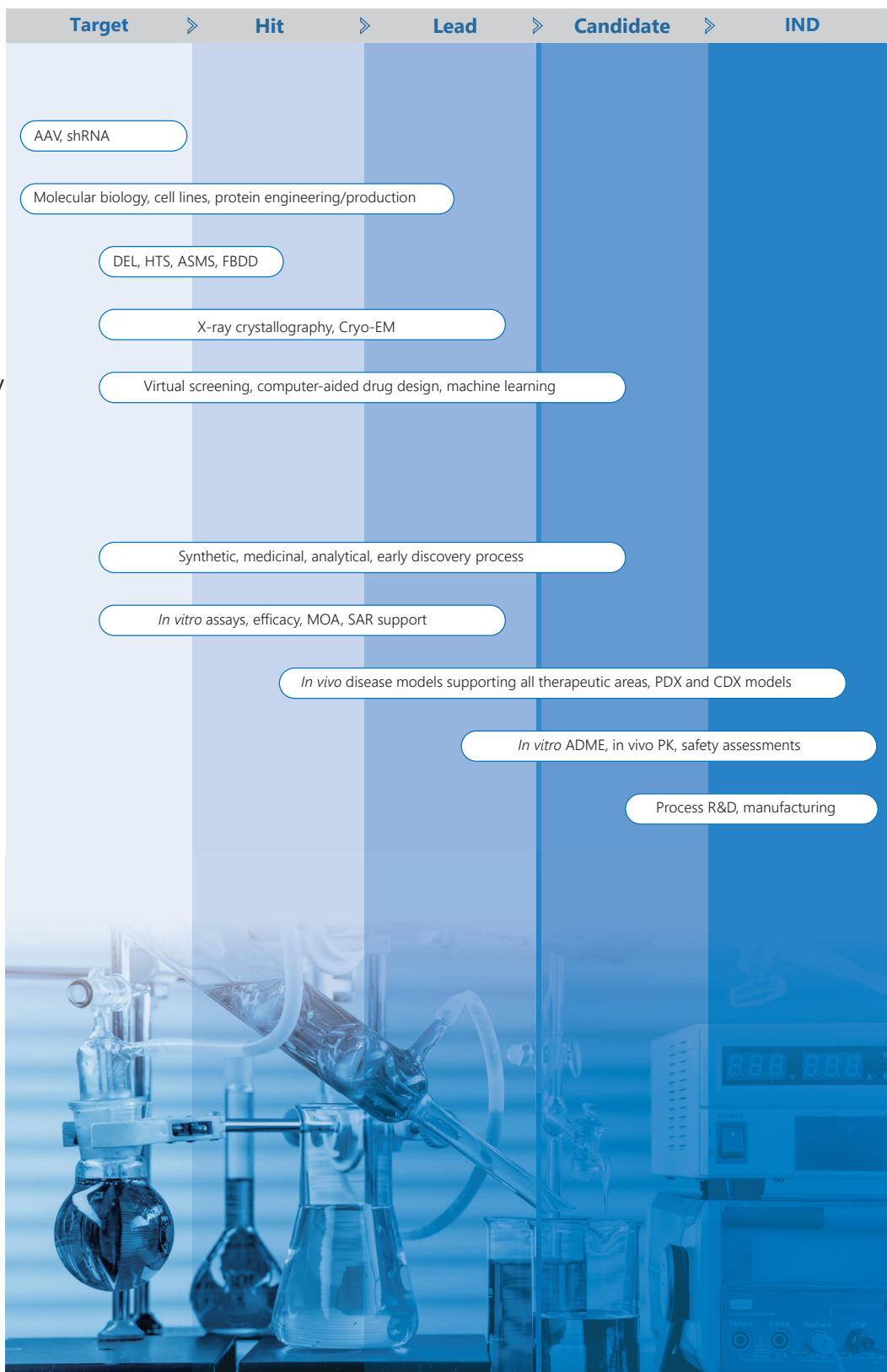
*In vivo* disease models supporting all therapeutic areas, PDX and CDX models

DMPK & Toxicology

*In vitro* ADME, *in vivo* PK, safety assessments

API & DP

Process R&D, manufacturing



## ■ Gene Therapy Platform

Platform with **innovative technology** and **know-how**

Comprehensive options from **cellular, tissue, and in vivo studies**

Comprehensive platforms and service types in **target validation** and **target identification**

Well-established **efficacy evaluation platform** for rare diseases



### AAV platform

- Large collection of AAV vectors
- Established delivery routes for AAV serotypes
- Providing diverse clients with AAV technology for target gene OEX, KD in all therapeutic areas



### shRNA

- Inducible KD and OEX

Target

Hit

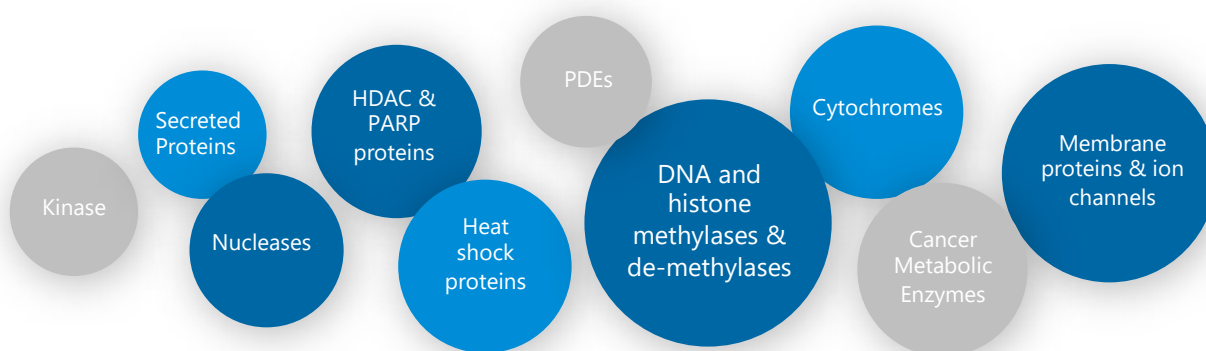
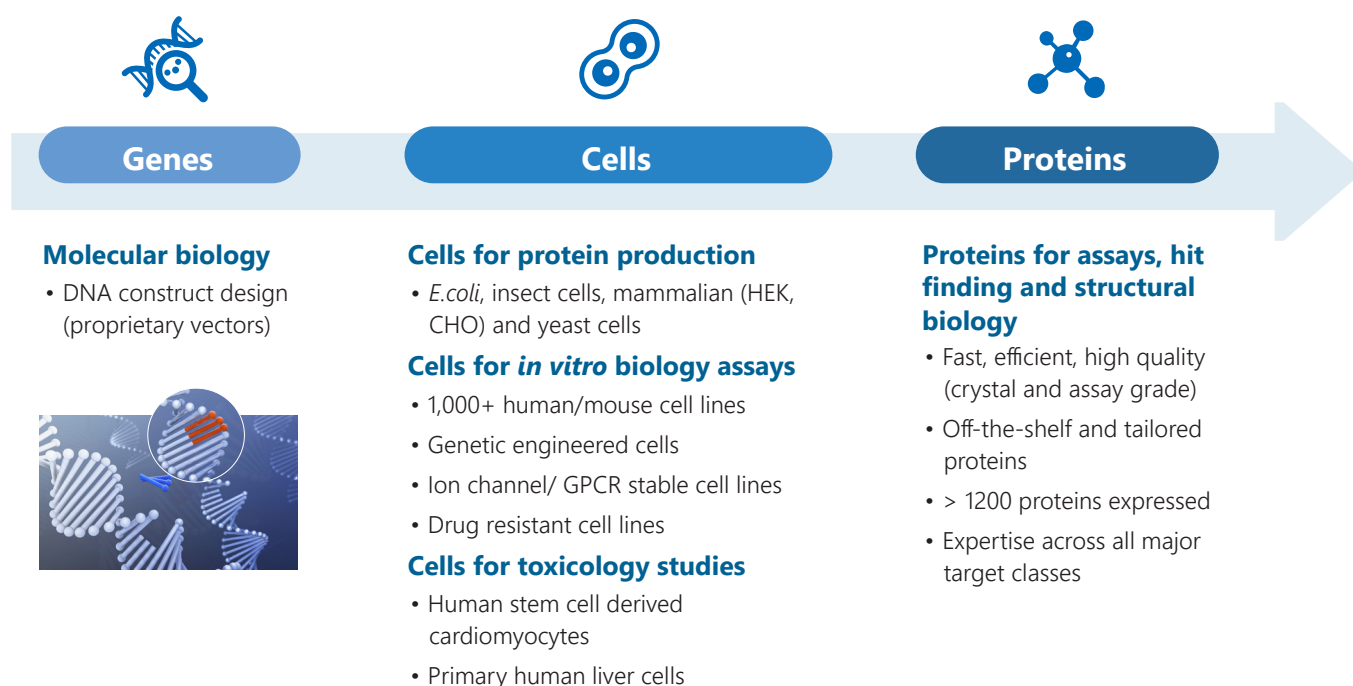
Lead

Candidate

IND

## Cells and Proteins

- Enhanced expression tools available for **diverse systems**
- Conscientious **assay** specific protein engineering
- Comprehensive coverage of **target classes** and **therapeutic modalities**



Target

Hit

Lead

Candidate

IND

## **In vitro Hit Finding Platform**



### **DNA-Encoded Library (DEL)**

- > 90 billion compounds
- Nanomolar binding hits in several target classes
- 3,500+m<sup>2</sup> lab designed for library production & screening
- Flexible business model (DELopen, DELight, DELpro)

### **Affinity Selection Mass Spectrometry (ASMS) Screening**

- SEC-plate/LCMS and 2D-HPLC-MS
- High sensitivity, resolution and accuracy
- Very high throughput

### **High throughput Screening (HTS)**

- ~300K compounds
- 384 + 1536 screening format
- Unique WuXi Library (no IP restrictions) or client library

### **Fragment-based Drug Discovery (FBDD)**

- >3,500-member novel fragment library
- Fragment Screening by SPR, NMR or DSF
- Biophysical hit confirmation and validation with fragment complex structures, biophysics and biochemistry

- Hundreds of successful hit finding campaigns
- Fully integrated with medicinal chemistry, in vitro biology and ADME for lead optimization
- Mosaic compound management system, and Spot-file data analysis system provide strong support for data processing
- Comprehensive bioassay platform and ability to assay development

Target

Hit

Lead

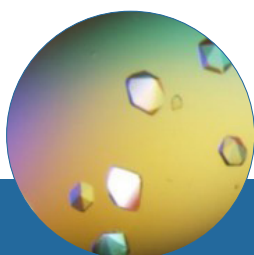
Candidate

IND

## ■ Structural Biology

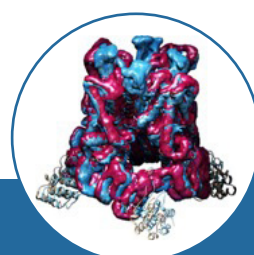
### Providing insights and data to support hit finding through to lead optimization

- Multiple drug discovery programs leading to launched products supported with structural biology data
- Comprehensive coverage of target classes and therapeutic modalities
- Integrated services to provide data and support for in silico hit finding, FBDD, SAR and medicinal chemistry design



#### X-ray crystallography

- **XPRESS:** established conditions for > 250 drug targets crystallized
- **XPEDITE:** crystallization of targets based on published conditions; 35+ protein targets per year
- **XPERT:** de novo structure generation, challenging targets (e.g., multi-subunit complexes, membrane proteins); > 10 de novo structures per year



#### Cryo-EM

- Supported clients to achieve <3.5 Å Cryo-EM structures
- Comprehensive structure characterization of protein complexes and membrane proteins
- Comprehensive structure characterization of target APO form and in complex with multiple compounds
- Reconstruction of antigen-antibody complex to determine conformational epitope

Target

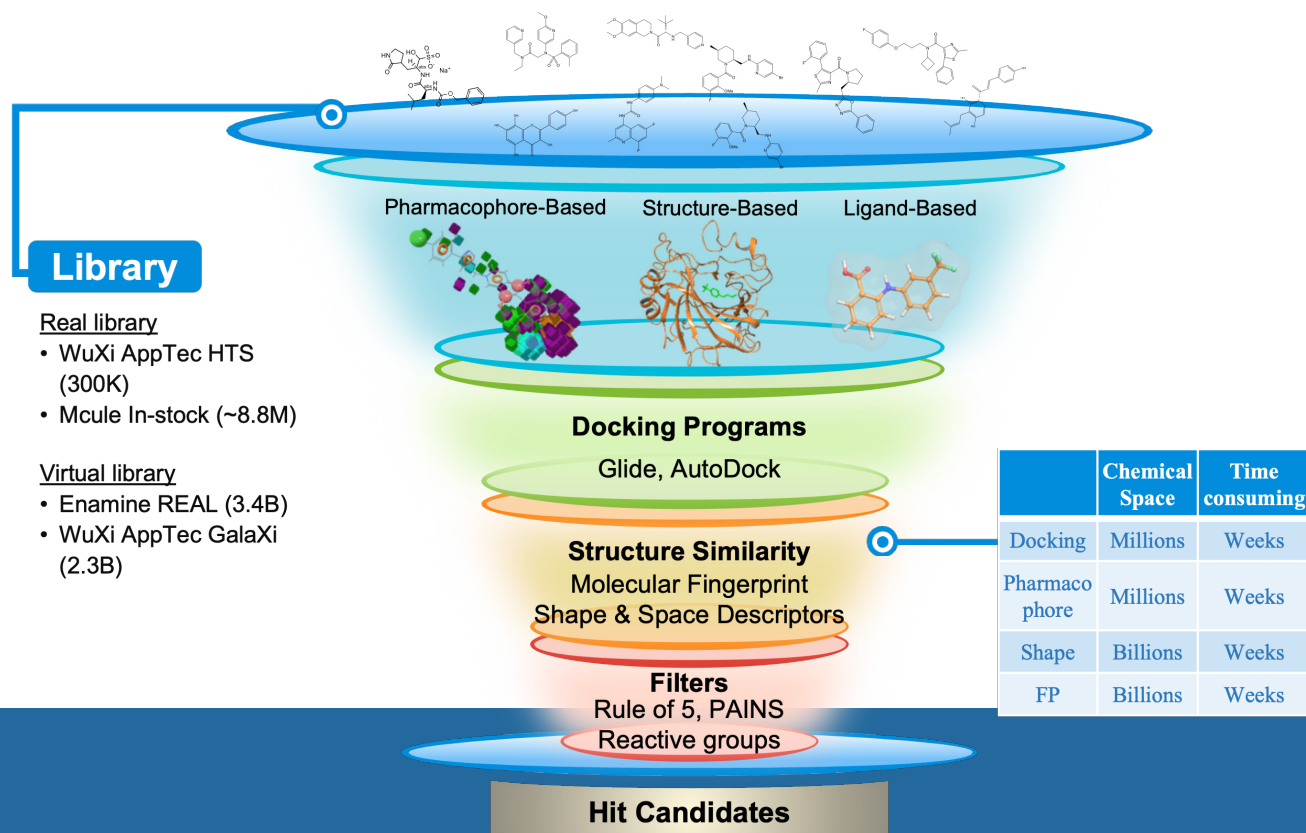
Hit

Lead

Candidate

IND

## Virtual Screening



- Searching against large chemical space (from millions to billions)
- Efficient screening with high successful rate of activity
- Compounds from WuXi AppTec GalaXi virtual library can be shipped in 4-6 weeks with successful rate of 60% - 80%
- Integrated services to provide rational starting point for hit identification, lead optimization and medicinal chemistry design
- Reducing real laboratory experiments and accelerating the drug discovery process in a more efficient and economical way

Target

Hit

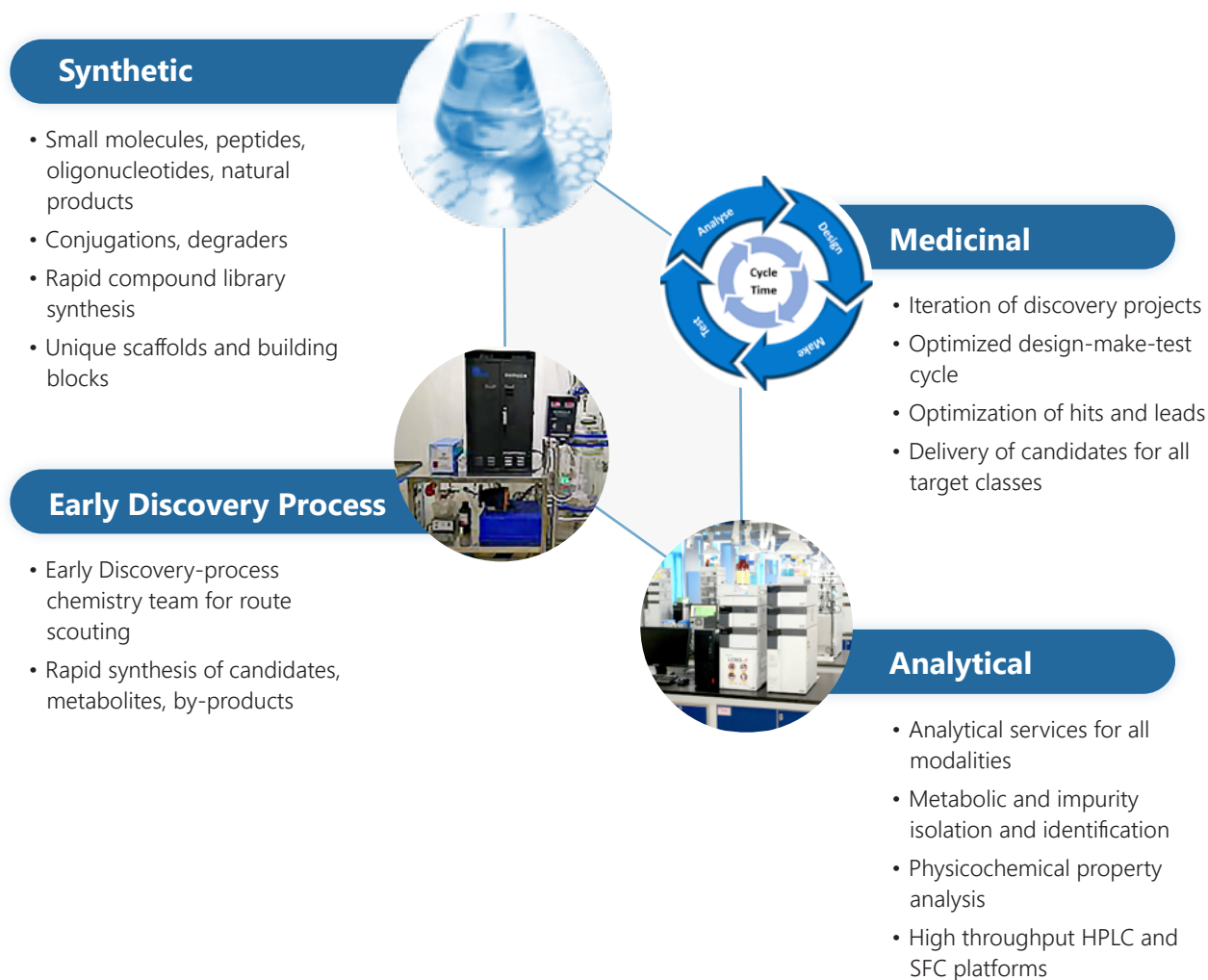
Lead

Candidate

IND

## Chemistry

- **Flexible business models: Long or short term FTE, FFS, project management, and fully integrated programs**
- **Delivered 26 preclinical candidates (PCCs) in 2021**
- **Deliver >280,000 compounds in 2021**
- **Dedicated analytic team is equipped with best-in-class automated instruments to provide extensive analytical and purification services in chiral separation, high-throughput purification, physicochemical property determination, impurity isolation and identification.**



Target

Hit

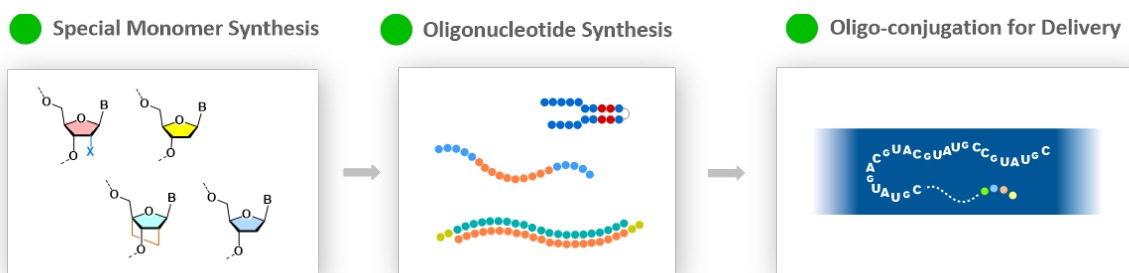
Lead

Candidate

IND

## Oligo Capability

- Dedicated synthetic and analytical teams with oligonucleotide expertise
- One-stop service to provide RNAi sequence design, monomer synthesis, oligo synthesis and conjugation, formulation, and biological evaluations
- State-of-the-art Facilities for oligonucleotide synthesis, purification, and analysis



01

### Oligo Synthesis — From Library to Mid-scales

To meet research needs throughout discovery process of oligonucleotide therapeutics.

02

### Capable of a Broad Range of Oligo Therapeutics

siRNA, ASO, saRNA, miRNA, aptamer, chimeric oligo, DNA, long RNA, PMO, PNA, etc.; 4-nt to 100 nt

03

### Offering an Extensive Selection of Rare modifications

Incorporation of linkers, spacers, dyes, PS bond, and modified bases and sugars (e.g. bridged nucleic acids – such as LNA, acyclic nucleic acid – such as UNA, GNA)

04

### Providing a Comprehensive Collection of Oligo-conjugation

Carbohydrate (e.g. GalNAc, Glucose), peptide (e.g. CPP), lipid (e.g. cholesterol), PEG, Fluorophores (e.g. Cy5), small molecules (e.g. PROTAC), proteins, etc.

05

### *In vitro* bioassays, *in vitro* toxicity testing, and *in vivo* efficacy

State-of-the-art assays using cell lines or primary human cells; off-target and immunotoxicity assays; animal models for *in vivo* PoC

Target

Hit

Lead

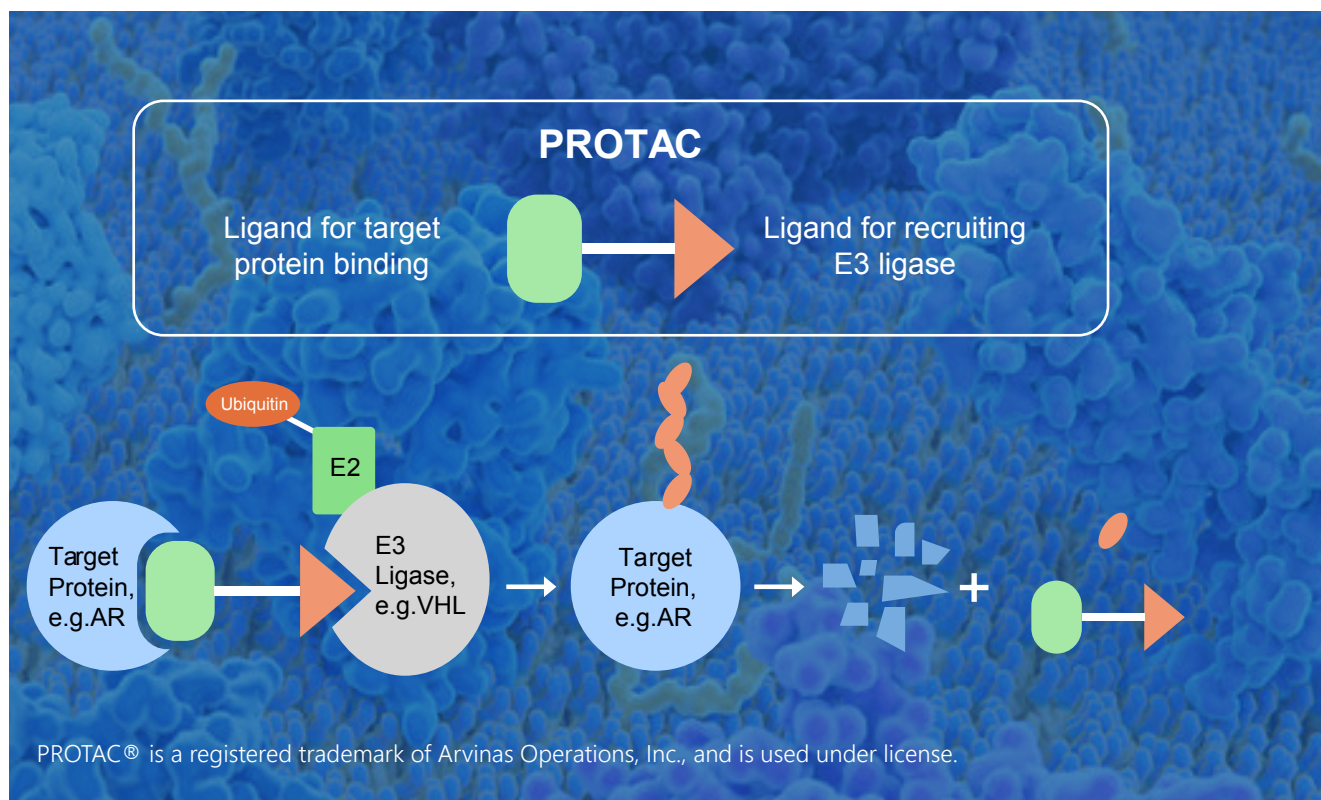
Candidate

IND

**PROTAC® Capability**

- **800+ FTE** chemists, with considerable experiences in the linkers, E3 ligase ligand and target protein ligand synthesis since 2016
- **80+** clients/collaborations
- Dedicated analytical team has solid experiences to handle purification of various compounds, up to **500k-700k** each year.

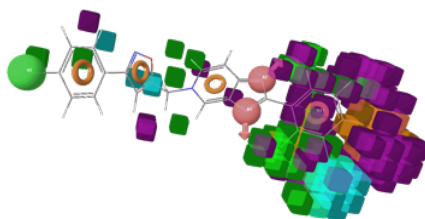
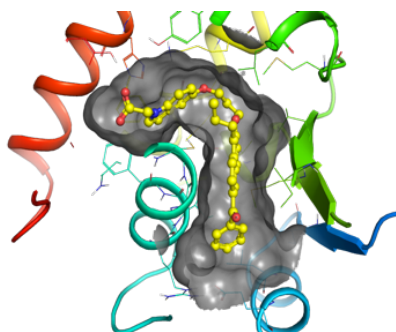
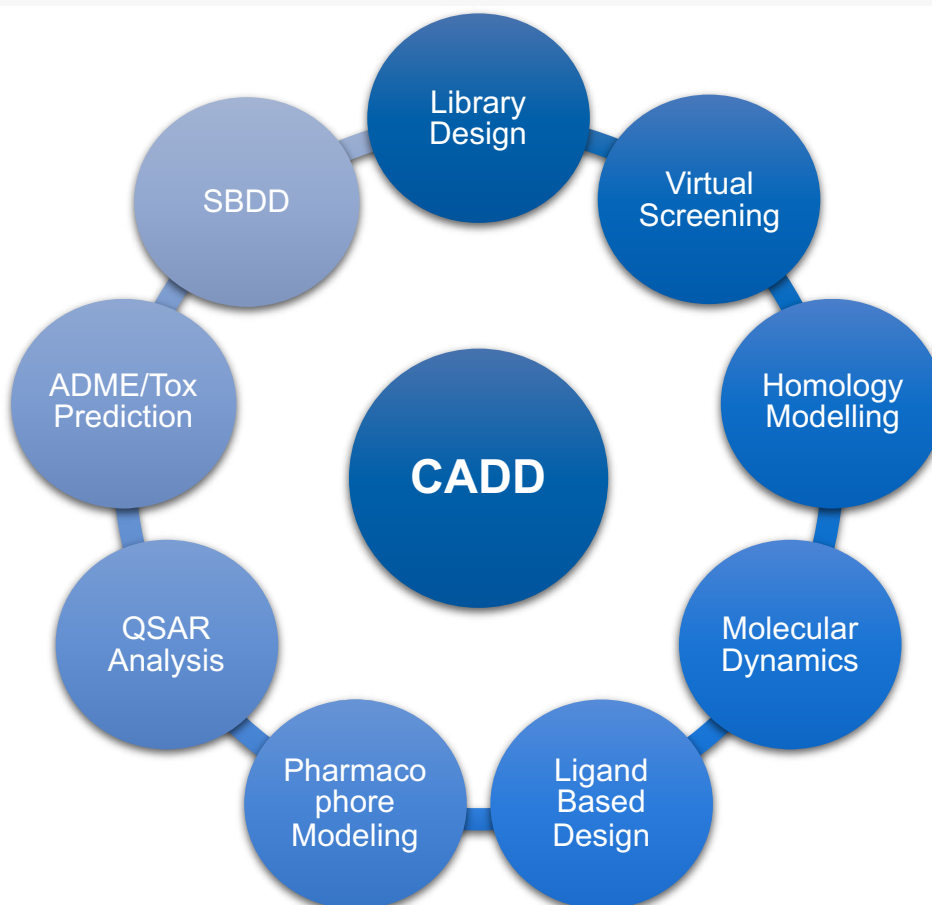
- Novel chemical modalities and screening methods like DEL and fragment screening
- >200 methods of Prep-HPLC and chiral-SFC for purification
- Efficient in-vitro/ in-vivo testing by WuXi AppTec DMPK
- 10 types, >1,000 of versatile linkers were successfully synthesized
- Novel linker synthesis by high productivity, quality, speed, and reliability PROTAC Platform
- >100 novel E3 ligase ligands
- >60 series of target protein ligands coupled with various linkers
- Computational design tools for linker design
- State-of-the-art biophysical and biochemical methods



## Computational Chemistry

### Cutting edge computational chemistry capabilities

- Comprehensive software suite
- Deep experience in the application of computational tools to all aspects of drug discovery
- Hit identification with virtual screening and pharmacophore development
- High-throughput virtual library screening with on-the-fly enumeration
- Make-on-demand libraries



SCHRÖDINGER.

**GalaXi™**  
Powered by 

Target

Hit

Lead

Candidate

IND

## ***In vitro* Pharmacology**

- **Thousands of** assays off-the-shelf, **millions of** data points generated to support hit ID, lead finding and candidate selection
- **Expertise in** all major disease areas and target classes
- **State-of-art facilities** with high end technology, instrumentation and comprehensive service platforms

### **Target classes:**

- Enzymes
- Ion channels
- GPCR/receptors
- Transporters
- NHRs
- Protein-protein interactions

### **Enzyme/ biochemical assays**

- TR-FRET, FP, ADP-Glo, Z-Lyte, ELISA, abs
- End-point assay & continuous assays
- Compound profiling (IC<sub>50</sub>, Ki), inhibitor characterization

### **Biophysical assays**

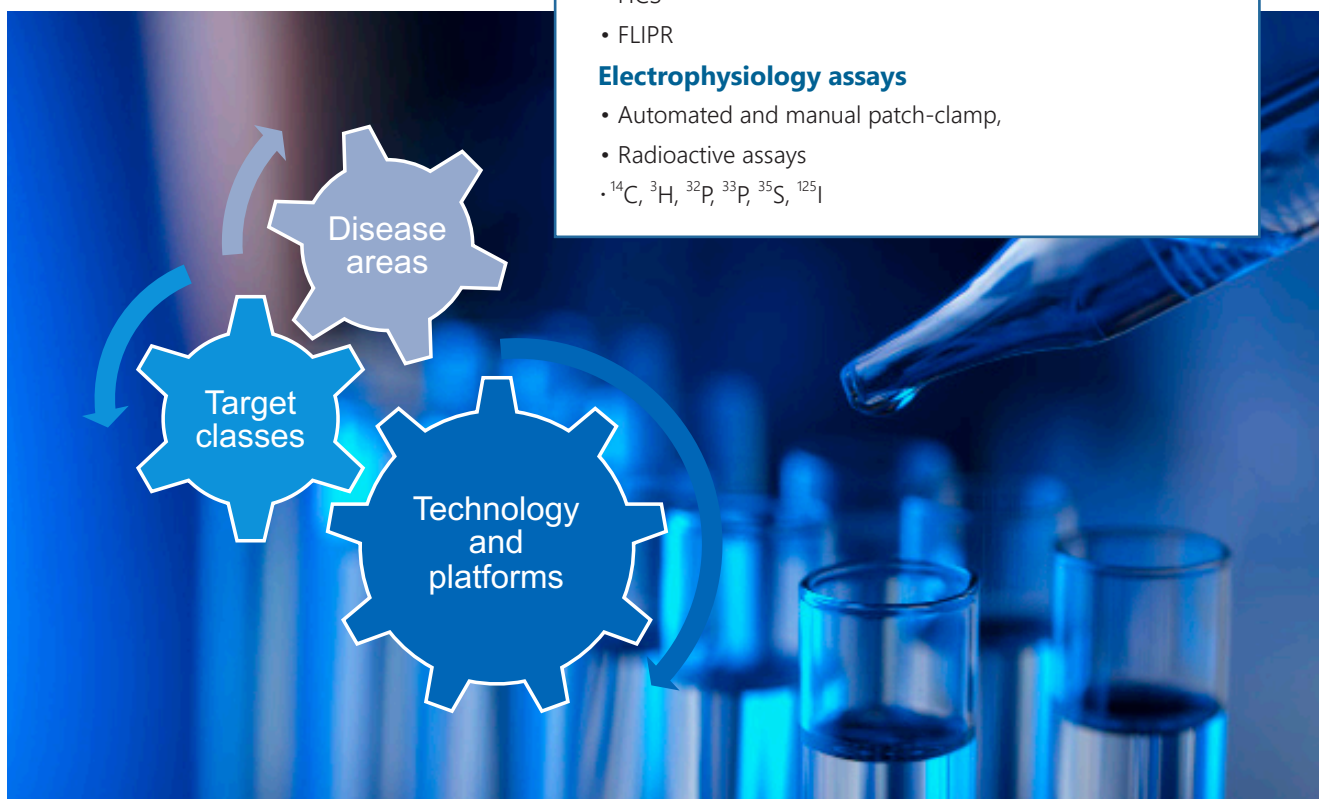
- SPR, LC-MS, MST, DSF/Nano-DSF, ITC, Alpha screen, DBS SwitchSENSE

### **Cell-based assays**

- Target-based mechanistic assays, cell functions assays
- HCS
- FLIPR

### **Electrophysiology assays**

- Automated and manual patch-clamp,
- Radioactive assays
- <sup>14</sup>C, <sup>3</sup>H, <sup>32</sup>P, <sup>33</sup>P, <sup>35</sup>S, <sup>125</sup>I



Target

Hit

Lead

Candidate

IND

## In vivo Pharmacology

- **Large and expanding infrastructure**
  - AAALAC-accredited animal facility
  - IVC-cages capacity in SPF barrier
- **Growing number of available animal models**
  - **1000+** tumor models, **1300+** PDX models, **280+** CDX models.
  - Gene KO/KI animals
- Exploration in **new technologies** including patient-derived organoids and single cell RNAseq etc..
- **Integrated with** in vitro biology, DMPK and toxicology studies to provide datasets and evidence for IND-enabling



### Oncology & Immuno-oncology

All major cancer types



### Neuroscience

Parkinson's | Alzheimer's | Pain | Epilepsy/  
seizure | Brain stroke | TBI



### Cardiovascular and metabolic diseases

Heart failure & stroke | Hypertension | AF  
Obesity & diabetes | NASH & liver fibrosis |  
Kidney failure | Hyperuricemia



### Infectious diseases

HDI | AAV/HBV | HBV | RSV | Influenza | HSV  
| EV71 | HCMV



### Immunology and inflammation

Rheumatoid arthritis | IBD | MS | SLE |  
Psoriasis | ACD



### Lung, Kidney, GI Diseases

COPD | Asthma | PAH | Lung Fibrosis | ALI |  
Nephropathy | Acute kidney injuries | kidney  
fibrosis | Gastric ulcer | IBS

Target

Hit

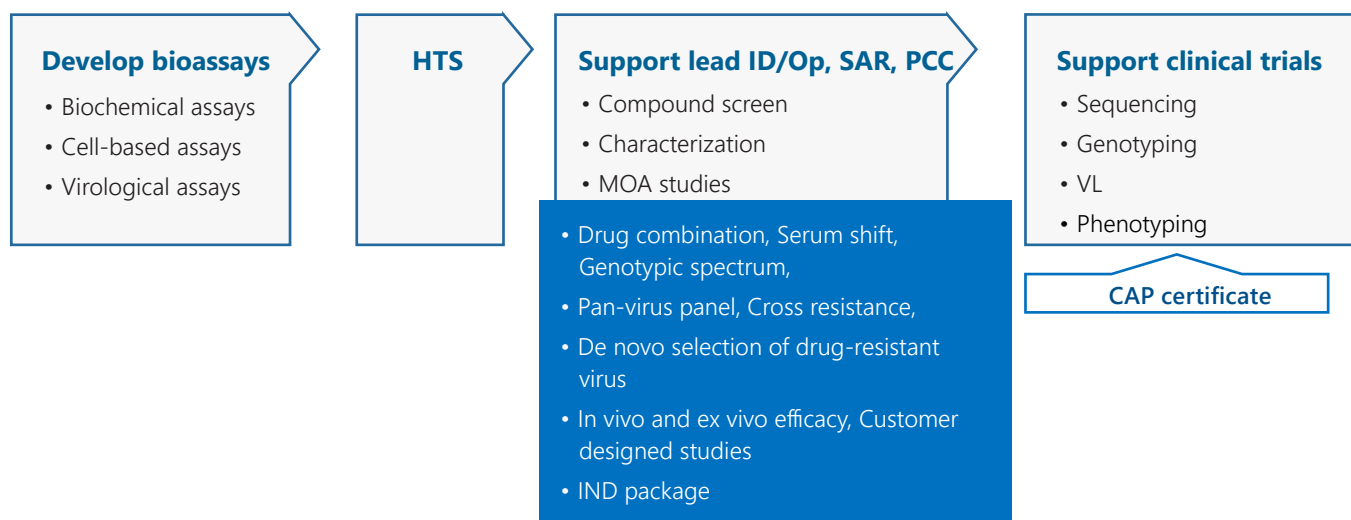
Lead

Candidate

IND

## Infectious Diseases

- **A comprehensive virology platform**
- Integrated drug discovery services **from assay setup to clinical trial support**
- The outstanding infrastructure and instrumentation allow us to conduct high quality researches both in vitro and in vivo for our clients.



Target

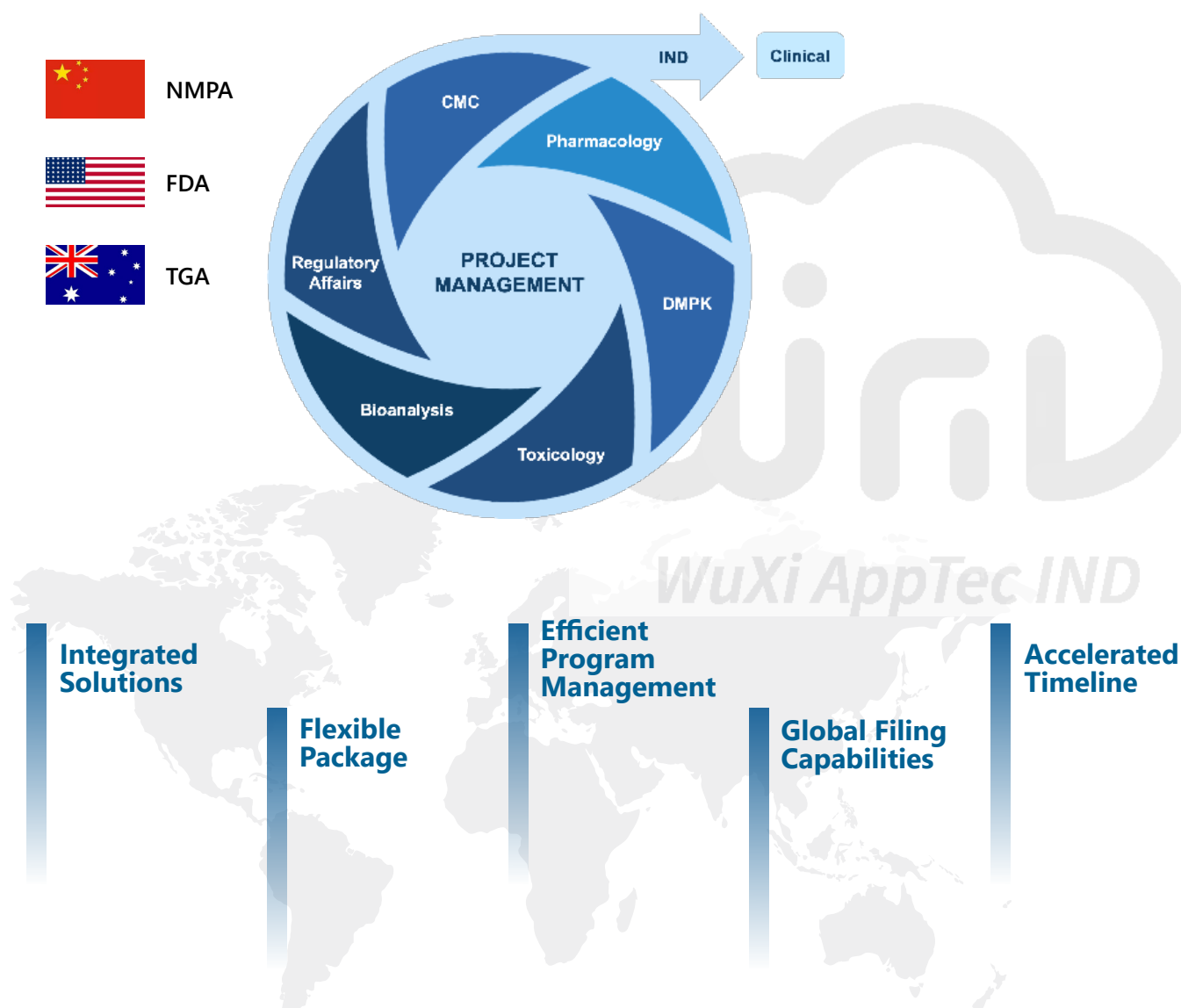
Hit

Lead

Candidate

IND

## WuXi IND Submission (WIND)



### WuXi IND and Beyond

Integrated Services and Solutions from Discovery to Successful IND and Beyond

### Essential Elements for

#### Successful IND

Integrate CMC, Pharmacology, DMPK, Toxicology and Bioanalysis services into a complete "package"

### Time save

Accelerate IND process through the integrated platform and seamless connection of researches.

### Meeting the highest

**Global Regulatory Standards**

Target

Hit

Lead

Candidate

IND

## Contact

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