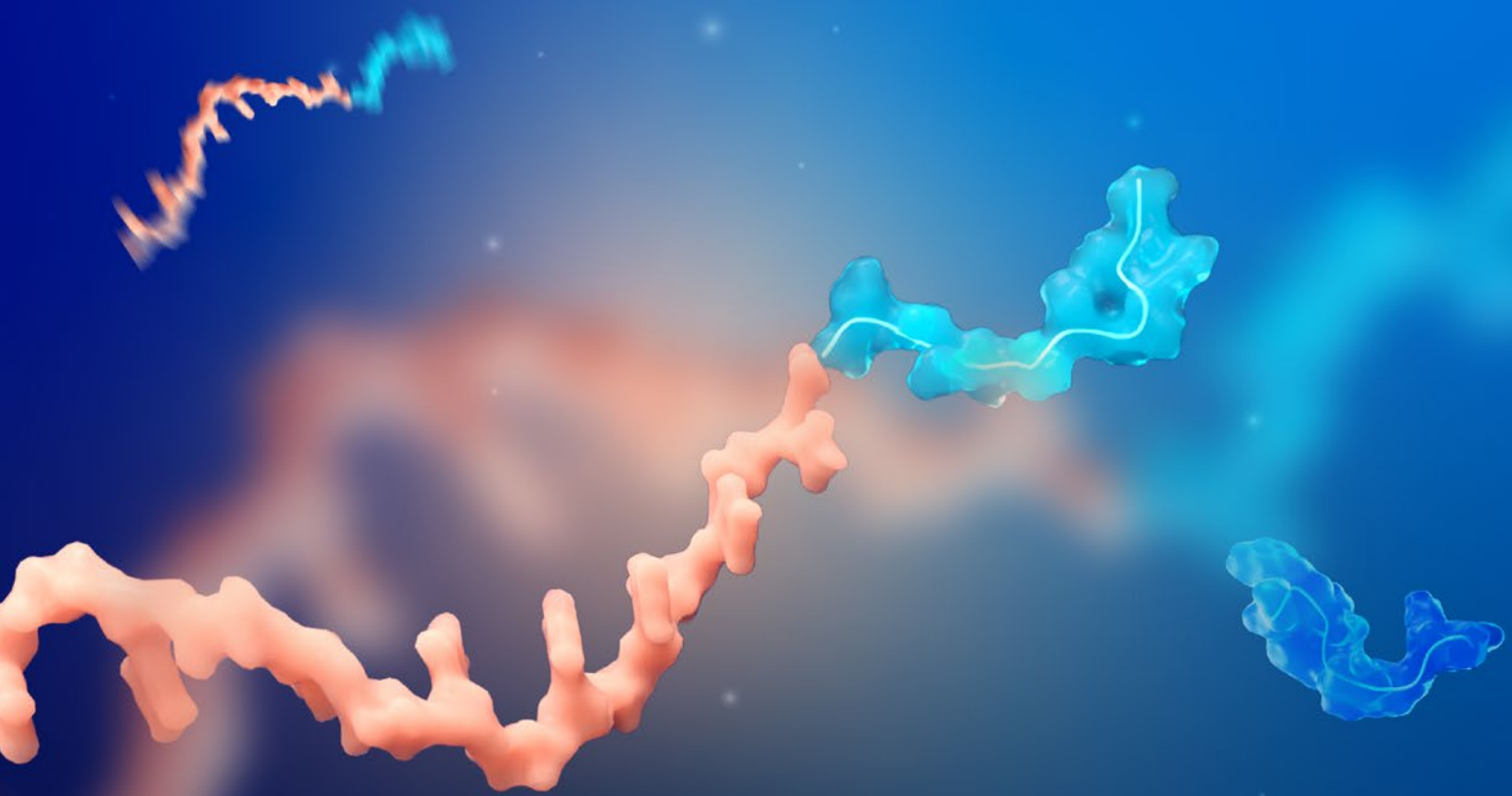
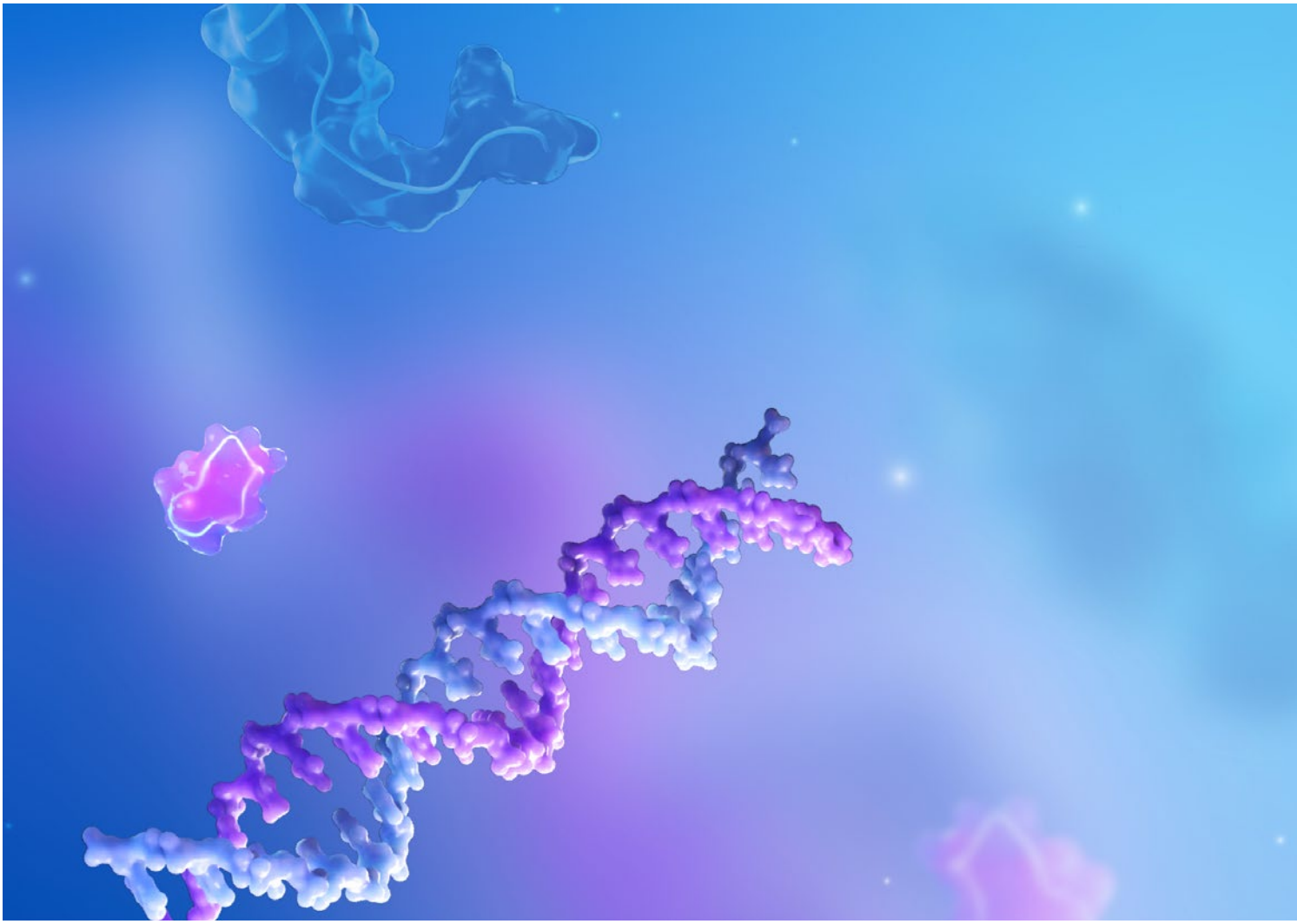
STA 合全药业 | 药明康德 WuXi AppTec

WuXi TIDES

End-to-End CRDMO Platform

for Oligonucleotide and Peptide Therapeutics





About Us

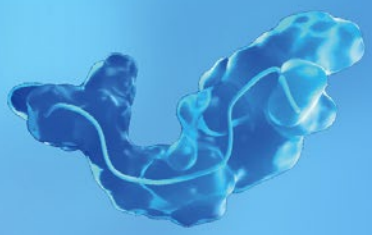
WuXi TIDES, a leading Contract Research and Development Manufacturing Organization (CRDMO) platform, is an integral part of WuXi STA, a subsidiary of WuXi AppTec. WuXi TIDES offers our worldwide partners efficient, flexible, and high-quality solutions for the drug development of oligonucleotides, peptides and related synthetic conjugates ("TIDES" drugs). We greatly simplify the TIDES drug development by providing all discovery, CMC development and the entire manufacturing supply chain under one roof.

With over 1,000 scientists from 10 R&D and manufacturing sites, we offer discovery compound screening and synthesis, process development and manufacturing of novel monomers, linkers and ligands, oligonucleotides, peptides and complex synthetic conjugates at any scale. Beyond chemistry, we offer formulation development, manufacturing, labeling and distribution services in a variety of injectable dosage forms and filling formats including the Lipid Nanoparticle (LNP) drug delivery platform. Our comprehensive analytical method development, validation and testing platform will support your needs in TIDES drug development from discovery through clinical to commercial. Moreover, our Regulatory Affairs CMC team is experienced in preparing CMC dossiers to support global filings for TIDES new drug applications.

Enabler of Innovation | Trusted Partner | Global Contributor

End-to-End CRDMO Platform for Oligonucleotide and Peptide Therapeutics

Oligonucleotide Chemistry Platform
from Discovery to Commerical



Monomer/Ligand
- Amidite
- mRNA NTP
- GalNAc
- Linker, Spacer, CPG

Oligonucleotide
- DNA
- ASO
- PMO
- siRNA
- sgRNA
- Aptamer
- microRNA
- gRNA
- Degenerate
- Oligonucleotide Pools

Conjugate
- Oligo-Peptide
- Oligo-Toxin
- Oligo-Lipid
- Dye Labeled Oligonucleotide

Peptide Chemistry Platform
from Discovery to Commerical

Unnatural Amino Acid
- Catalog Product
- Custom Synthesis

Peptide
- Long linear Peptide
- Cyclic Peptide
- Modified Peptide
- PEGylated Peptide
- Peptidomimetics

Conjugate
- PPMO
- Oligo-Peptide
- Peptide-Toxin, etc.

Oligonucleotide and Peptide CMC Platform

	PRECLINICAL	PHASE I	PHASE II	PHASE III	COMMERCIAL
API	PROCESS R&D AND MANUFACTURING (Monomer, Ligand, Oligonucleotide, Peptide, Conjugate)				
Drug Product	PRE-FORMULATION, FORMULATION DEVELOPMENT & MANUFACTURING (Oral, Injectable, LNP Delivery Technology)				
Analytical	ANALYTICAL DEVELOPMENT, QUALITY CONTROL AND STABILITY STUDIES				
Regulatory Affairs CMC	CMC DOSSIER PREPARATION TO SUPPORT GLOBAL REGULATORY FILING				

WuXi TIDES R&D and Manufacturing Network

Discovery Site

Shanghai, China
discovery oligonucleotide & peptide, preformulation and formulation development

Tianjin, China
discovery oligonucleotide, amidite, GalNAc

Chengdu, Sichuan, China
discovery peptide, unnatural amino acid

Wuhan, Hubei, China
discovery peptide

API Development and Manufacturing Site

Changzhou, Jiangsu, China
API process development and manufacturing

Taixing, Jiangsu, China
API process development and manufacturing
(Operational in 2023)

Singapore
API process development and manufacturing
(Operational in 2026)

Formulation Development and Manufacturing Site

Wuxi City, Jiangsu, China
formulation development and manufacturing

Middletown, DE, USA
formulation development and manufacturing
(Operational in 2026)

Couvet Neuchâtel, Switzerland
Drug Product Manufacturing

O Oligonucleotide
P Peptide

Maintaining the Highest Global Standards

WuXi STA has an ingrained quality culture and follows the same quality and EHS system across all sites globally, with proven track record of inspections from all major regulatory agencies and our global customers.

10 successful US FDA inspections
2013 - 2023

4 successful EU EMA inspections
2019, 2021, 2022

48 successful China NMPA inspections
2015 - 2023

6 successful Japan PMDA inspections
2019 - 2022

4 successful South Korea MFDS inspections
2022

5 successful SwissMedic inspections
2018 - 2022

300+ Client audits
every year

Why WuXi TIDES

- ***Scalability***
  From discovery to development and commercialization all within WuXi STA with readily available large R&D and manufacturing capacity

- ***Conjugation Chemistry***
  Seamless collaboration among oligonucleotide, peptide and small molecule teams

- ***New Technology***
  Oligonucleotide: Biocatalysis for gRNA synthesis, Thin Film Evaporation (TFE)
  Peptide: Reactor-in-series (with PAT data collection) , continues flow chromatography, Tangential Flow Filtration (TFF)/precipitation

- ***Global Quality Standard***
  One quality system across all sites approved by major regulatory agencies around the world

- ***Comprehensive Analytical Platform***
  Method development and validation, IPC and release testing, characterization, stability

- ***Integrated CMC***
  API process R&D and manufacturing, formulation development and manufacturing, analytical, CMC dossier preparation and clinical supply services

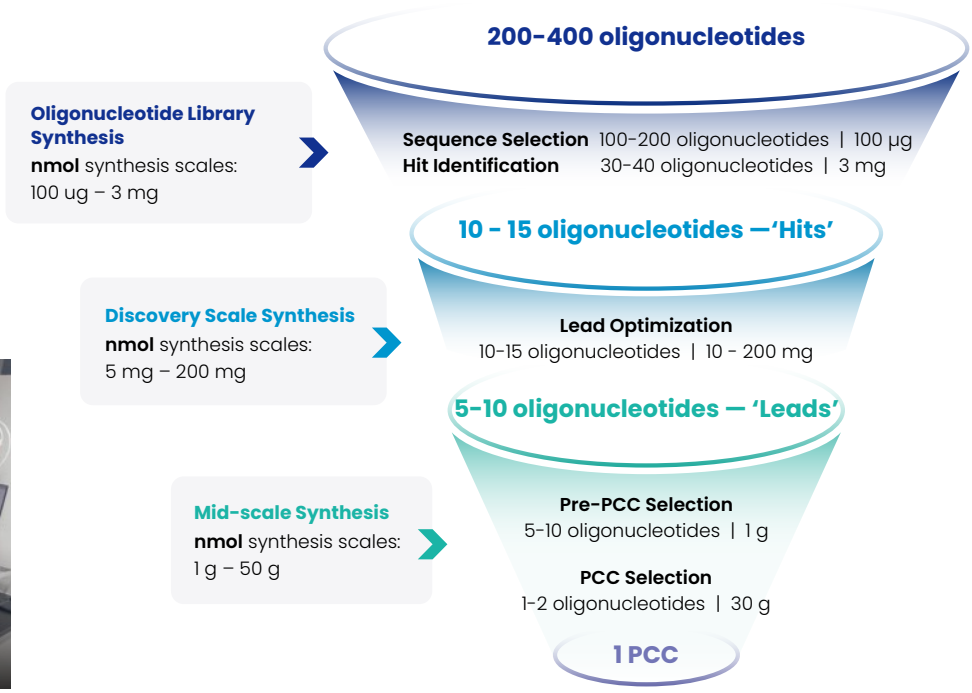
Oligonucleotide Discovery Services

Experience with Modified Oligonucleotides

- ASO with all chiral phosphorothioates
- RNA with 3′/5′-GalNAc
- Custom 3'/5' and internal GalNAc conjugation
- Custom amidite modification and synthesis
- Linker synthesis (cleavable and noncleavable)
- Lipidation
- PEGylation (~40 kD), etc.


192-channel synthesizer

In-silico Sequence Design



0.1 mg-50+ g Synthesis Capability

Produce 100,000+ Oligonucleotides Per Year

Up to 130-nt Long Oligonucleotides

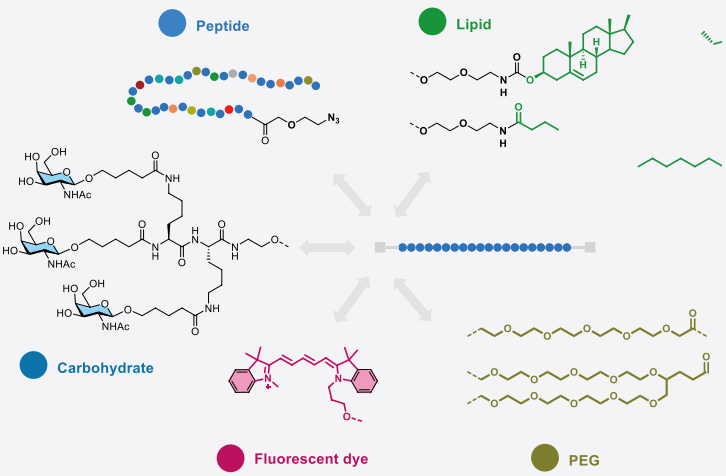
Access to 300+ Modifications & Conjugations

Comprehensive
Extensive experience in various modalities

Diversity
Large variety of linkers/conjugation strategies

Flexibility
Custom-tailored solution according to your application

Linker Chemistry	Topology
Amide coupling	3′- or 5′-conjugation
Thiol-maleimide addition	Base/backbone conjugation
Click chemistry:	Complex dual conjugation:
CuAAC | SPAAC	3′,5′- | 3′,3′- | 5′,5′-
Broad selection of spacers	Multi-valency:
Custom-tailored linkers	Mono- | di- | tri- | tetra



Peptide Discovery Services

High-Throughput Peptide Discovery Synthesis
mg to kg scale
High quality – Over 98% Success rate
High purity – Up to 99.9% Purity
Fast delivery – 2 weeks turnaround time for most peptides under 30 AA at mg scale

Customized Peptide Synthesis
Up to 200 AA modified peptide with ligation
Up to 70 AA modified peptide with SPPS only
Modification: Dye/Biotin | PEG | Isotope labelling
Peptidomimetics | Peptoid | PNA
Cyclic peptides: Thioether | Disulfide | Biocyclic | Lactam | RCM | Lactone | Click

Our quick turnaround time and greater than 98% success rate ensures that our customers advance their projects quickly and efficiently. Most peptides under 40 amino acids are completed within 2 weeks from order placement with MS and HPLC/UPLC analytics data. Flexible deliverables include on-resin, crude, as well as purified powder at desired purity up to 99%.


Biotage Syro II

Automatic Synthesis and Purification Platform

Automated solid-phase (Fmoc) synthesis provides efficient and reliable custom sequences up to 160 AA with over 80% purity. Our platform is equipped with a wide range of instruments to fit project requirements with a greater than 95% success rate.

2,500+
Unnatural amino acid catalog products

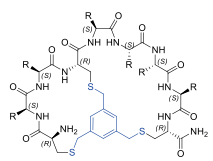
Broad range of instruments
- CEM liberty blue
- Biotage Syro II
- CSBio automatic synthesizer
- Gilson Prep-HPLC
- Agilent UPLC
- Symphony X

Served 300+ customers and deliverd
20,000+ peptides every year

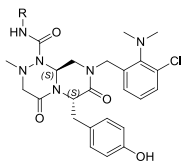
Peptide Drug Conjugate (PDC) Platform

With our Integrated HPAPI capabilities, large linker library, and comprehensive chemistry platforms, we support Peptide Drug Conjugate (PDC) development from discovery to commercial.

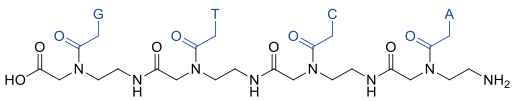
Thio-ether bicyclization



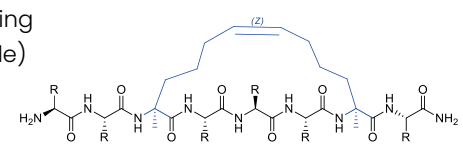
Peptidomimetics



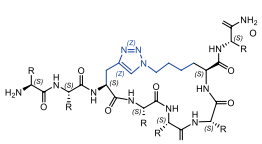
PNA Length up to 30



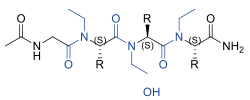
RCM monocyclic peptide (Double RCM ring also achievable)



Click chemistry



Peptoid



Oligonucleotide API Process Development and Manufacturing

We have 27 lines that cover a variety of Oligonucleotide types including ASO, siRNA, Aptamer, Oligonucleotide conjugates, PMO and PPMO.

- Utilize various modified monomers (2'-H, 2'-OH, 2'-F, 2'-OMe, 2'-OMOE, LNA, cEt, LNA, Vinyl-phosphate, Spacer, etc.)
- Chiral oligo synthesis
- Modification at 3'-end or 5'-end with GalNAc, triphosphate, cholesterol, saccharides, peptides, maleimide, etc.

Our team supports oligonucleotide production from lab scale to commercial scale with more than 20 small- to mid-scale production lines and 4 large scale production lines up to 6.0 mol per synthesis run.

Morpholino Oligonucleotide (PMO) Development and Manufacturing

We have developed high loading solid-phase PMO synthesis process that can achieve >50% yield, >75% crude purity, >90% final product purity with <0.045 EU/mg endotoxin.

Our chemistry knowhow enables various PMO 5' modifications with improved cleavage & de-protection process. Our optimized process offers freedom to operate without IP concerns.

We have customized PMO synthesis reactors up to 100L to support large-scale production. Our team has successfully completed kilogram scale PMO development and manufacturing projects.

Recent Experience

- Completed 100 batches of 900mmol DNA production (>400kg delivery in total) including PPQ enabling studies and PPQ campaign in 9 months.
- Completed 3 x1.6mol ASO production in 2 months
- 20+ ongoing siRNA projects with modifications at 5'-end or 3'-end such as GalNAc and cholesterol modifications, including 11 integrated API/DP projects.

4 large-scale oligonucleotide production lines
27 lines at various scales

Oligoprocess™
Changzhou, Jiangsu, China

Peptide API Process Development and Manufacturing

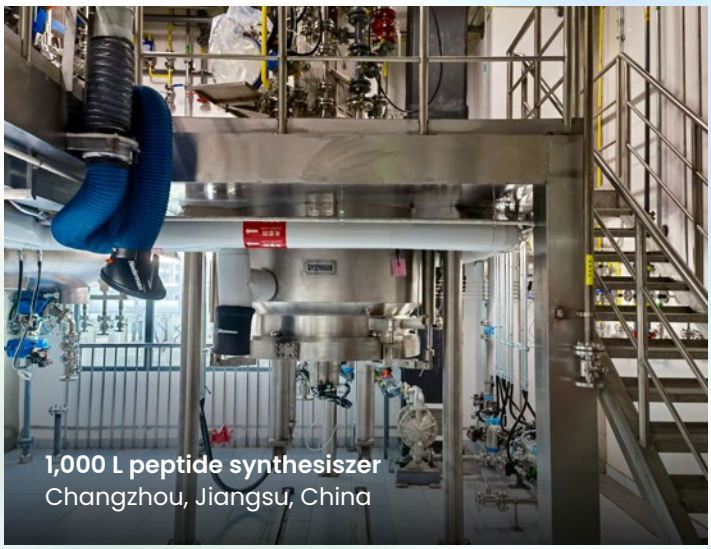
Same as oligonucleotide, our peptide platform is also in Changzhou site with industry-leading capabilities and capacities, covering a wide range of peptides and their conjugates.

- Long linear peptides
- Cyclic/Bicyclic peptides
- Modified peptides
- PEGylated peptides
- Peptidomimetics
- Branched peptides

We have built extensive experience with peptide-based conjugates including PPMO, Oligo-Peptide, Peptide-Toxin, Peptide–Antibody etc.

In Changzhou, we currently have 10,490 L total reactor volume, with reactors up to 2,000 L.

The Taixing site will open in 2023. New 3,000 L reactor will be installed and the total reactor volume will increase to 20,000 L.



1,000 L peptide synthesiszer
Changzhou, Jiangsu, China

Successfully supported a new peptide drug approved and now providing commercial API manufacturing

Our dedicated oligonucleotide and peptide analytical team has more than 150+ scientists, supported by more than 400 co-located analytical scientists from the process analytical and QC team to ensure the capacity required.

A full suite of state-of-the-art analytical instruments, including two-dimensional UPLC coupled with high-resolution MS for sequence and impurity analysis, enables the safety assurance and reproducibility required for regulatory submissions.

General Required Tests for Oligonucleotide and Peptide

- Purity and assay
- Microbiology safety including endotoxin and bioburden
- Stability study

	Oligonucleotide	Peptide
Unique Capabilities	• Identity by MW and sequencing with 2D UPLC coupled Q-TOF, MALDI-TOF and TOF HRMS • Backbone composition identification by 31P NMP • Purity by QTOF HRMS and quadrupole LC-MS	• Amino acid analysis and enantiomeric purity • Identity by peptide mapping • Identity by MW and sequencing with 2D UPLC coupled Q-TOF, MALDI-TOF and TOF HRMS

Comprehensive Analytical Testing

Formulation Development and Manufacturing Platform

Drug Product Overview

- Pre-formulation
- Formulation development
- Clinical & commercial manufacturing

Sterile Parenteral Formulation Manufacturing Platform

- Disposable bags
- Mixing-filtration-filing with sterile
- Containers in a fully isolated system
- Wholly automated, robotic operation
- 12 million units per year
- High potency (HP) injectable drug manufacturing
  (Can handle OEB5 compound; OEL: 10 ng/m^3)

Dosage Forms

- Injection, Solution
- Injection, Emulsion
- Injection, Sterile Powder (Lyophilized)
- Injection, Liposome

Filling Capacity

- Vial, prefilled syringe, cartridge

Lipid Nanoparticle (LNP) Platform

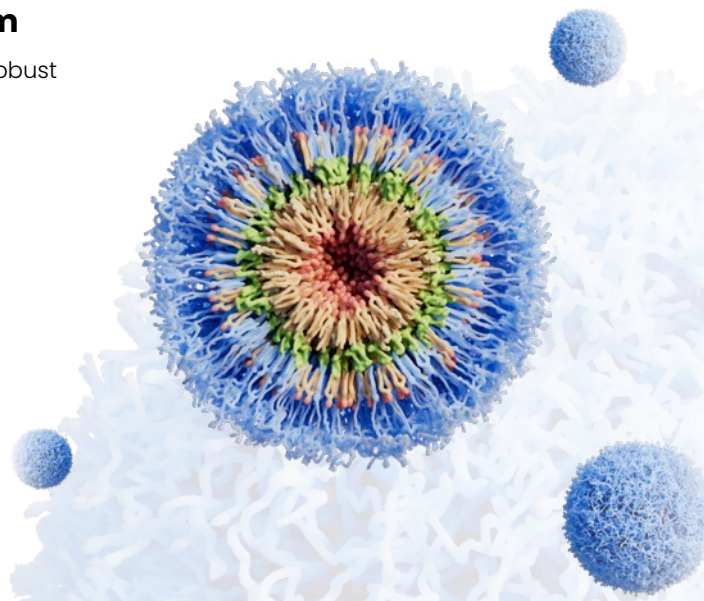
- Novel multi-channel mixing n-port provides robust scalability and reproducibility
- Novel lipid design and synthesis at any scale

Research & Development

- Robust scalability and reproducibility (start from 5 mL)
- Small particle size (80~100 nm) and narrow PDI (< 0.10)
- Optimized ultrafiltration and sterile filtration process

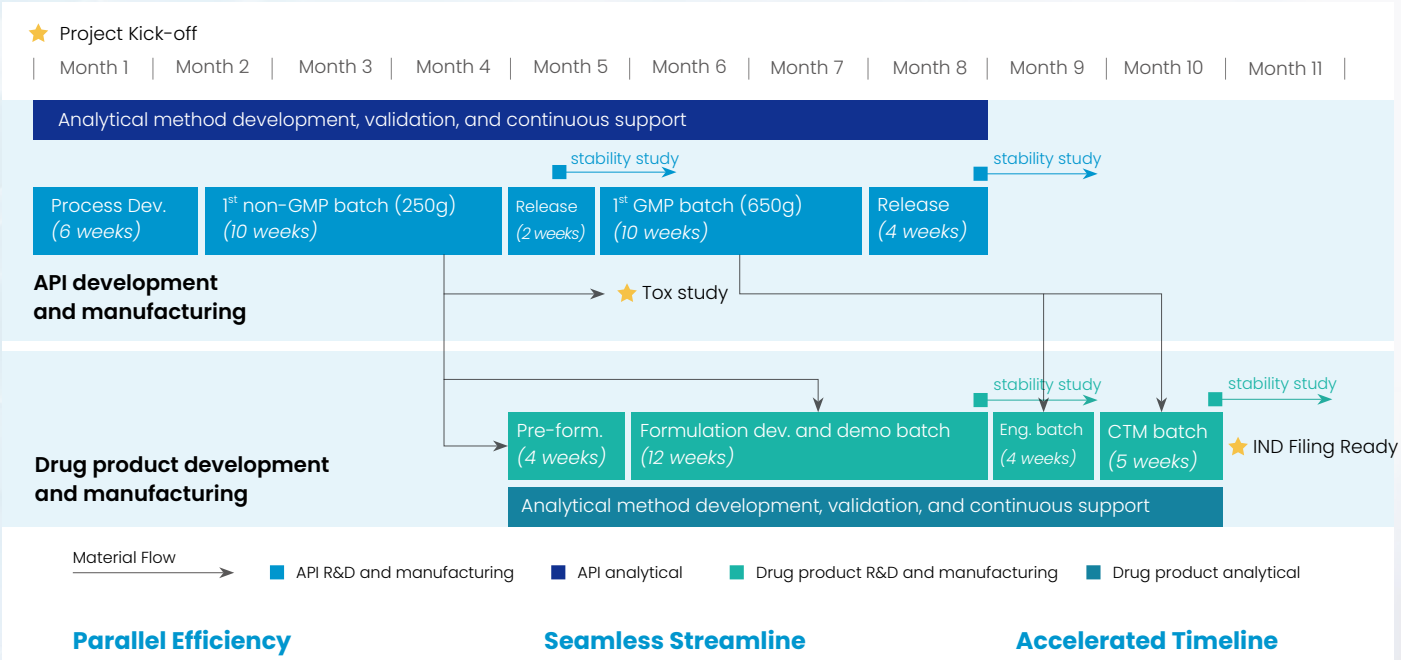
GMP Manufacturing

- Modular designed
- Flexible scale, 10 L - 50 L per sub-batch



Case Study

Accelerated Timeline to IND for siRNA Based Therapeutics

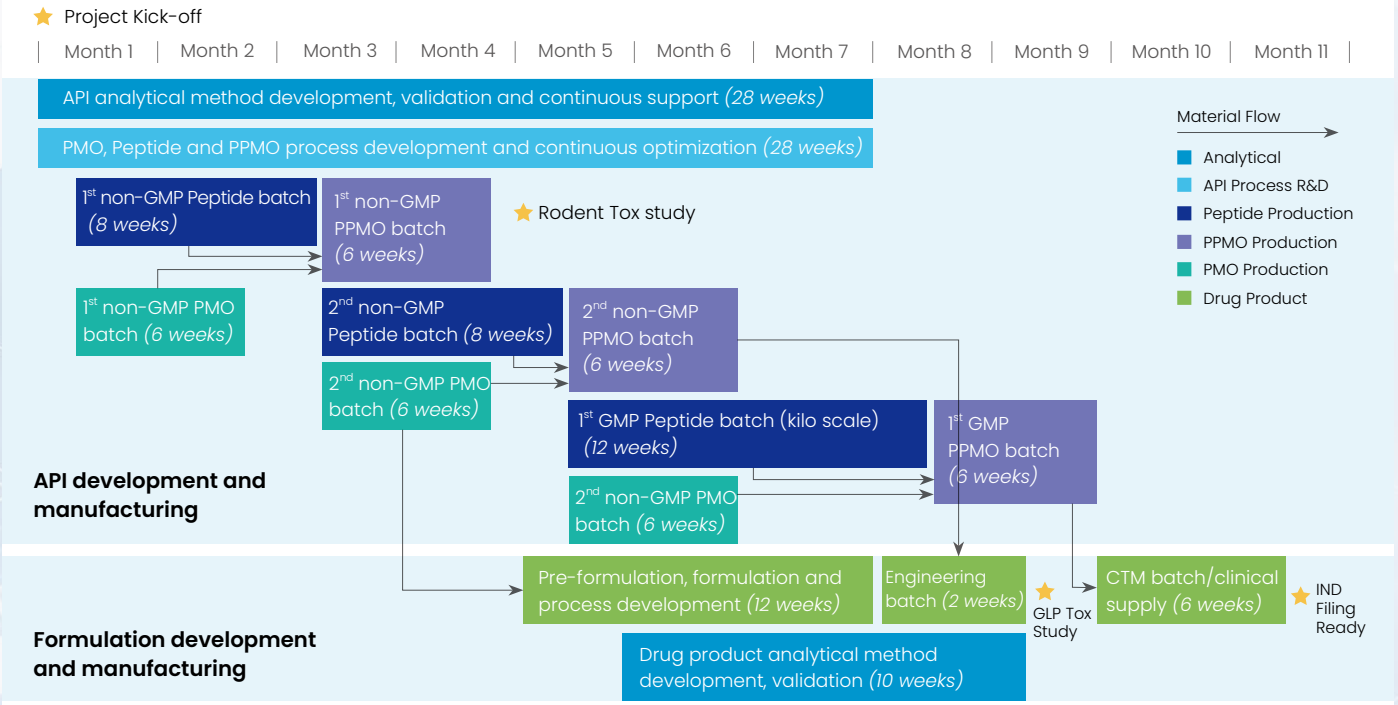


Parallel Efficiency
API, DP, analytical and QC team works closely in parallel

Seamless Streamline
From API to DP, manufacturing continues with no pause

Accelerated Timeline
Clinical supply and IND filing ready in 10 months

Accelerated Timeline to IND for PPMO Based Therapeutics

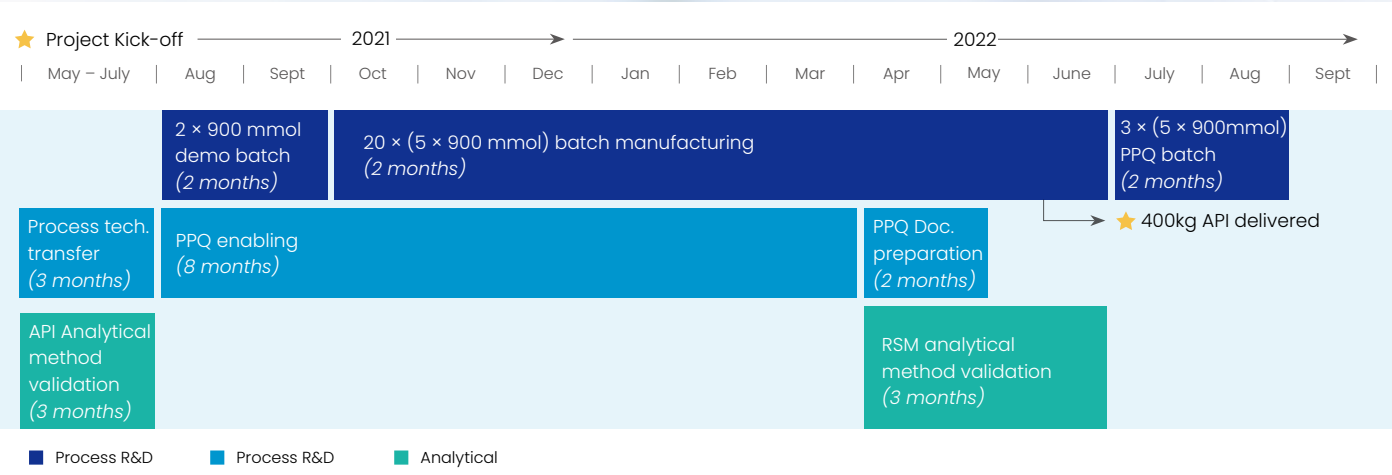


Seamless collaboration with in-parallel activities among 6 teams

Integrated CMC approach enables IND filing in 11 months

Peptide Phosphorodiamidate Morpholino Oligomers (**PPMO**)

Tech. Transfer and Commercial Manufacturing of CpG ODN



Quality and Speed

Successfully completed tech transfer, PPQ enabling, PPQ campaign, and commercial production (>400kg delivery) in one year

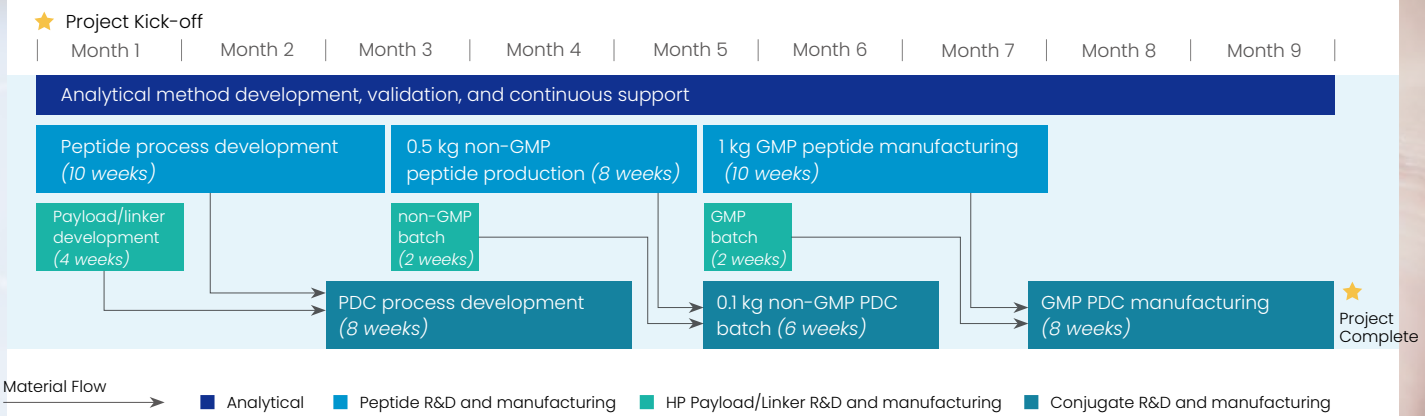
Continuous Improvement

Reduced commercial production cycle time by 50%

Robust Supply Chain

Established robust supply chain covering all raw materials, reagents, solvents, etc. used in oligonucleotide commercial production

PDC Drug R&D and Manufacturing in 9 Months



PDC
Peptide Drug Conjugate

- Seamless collaboration with in-parallel activities among 4 workstreams
- Integrated small molecule and peptide R&D and manufacturing saves 4–6 months

Regulatory Affairs CMC Platform

376

CMC submission packages written to support global IND and NDA filings from 2019 to 2022

Streamlined CMC writing integrated as part of the project team

Project Initiation
Provide RA consultation for phase and modality appropriate, country specific project scope and strategy

Project Execution
Provide filing template, collect data once testing completed. Finish section writing along different phases and perform timely data review with clients to mitigate potential risks

Project Completion
Complete submission-ready CMC dossiers

Phase appropriate RA CMC filing strategies tailored to oligonucleotide and peptide drug characteristics

Adopt principles of ICH Q3 (impurities) and Q6 (specifications) to oligonucleotide and peptide based on our experience with O&P IND and NDA

10+ Global ESG Recognitions

2nd
Place in the entire global CXO industry (2022)

MSCI ESG RATINGS AA
CCC B BB BBB A AA AAA

Member of
Dow Jones Sustainability Indices
Powered by the S&P Global CSA

CDP DISCLOSURE INSIGHT ACTION
Top 1
in global CXO industry

ESG INDUSTRY TOP RATED

ESG REGIONAL TOP RATED

SILVER 2022 ecovadis Sustainability Rating

Passed 85+ Client EHS Audits since 2016

- Conducting formal process safety evaluations prior to manufacture
- Providing thorough health and safety training programs for both employees and contractors
- Conducting toxicological and risk assessments for all new introduced processes
- Working with our suppliers and customers to minimize environmental impacts across the entire production and supply value chain
- Reducing our overall usage of water, energy, waste production, and emissions
- To enhance our delivery of EHS policies, we have created several bespoke groups to drive forward a culture of corporate citizenship, including; EHS committee; process safety management committee; general manager representative; and a standalone EHS department

Our promises to health, safety and environmental care

Shanghai Waigaoqiao, China

API Manufacturing Development
Formulation Development and Manufacturing

90 Delin Road Waigaoqiao Free Trade Zone, Shanghai, 200131, China
Tel: +86 (21) 5046-1111

Shanghai Jinshan, China

API Process Development & Manufacturing

9 Yuegong Road Jinshan District, Shanghai 201507 China
Tel: +86 (21) 6725 6015

Changzhou, Jiangsu, China

API Process Development & Manufacturing
(small molecule, oligonucleotide, peptide)

589 North Yulong Road XinBei District, Changzhou, 213127, China
Tel: +86 (519) 8128-7118

Wuxi City, Jiangsu, China

Formulation Development & Manufacturing

8 Xinrui Road Xinwu District Wuxi, Jiangsu 214028 China
Tel: +86 (510) 8051 1666

Taixing #1, Jiangsu, China (start operation in 2023)

API Process Development & Manufacturing
(small molecule, oligonucleotide, peptide)

29 Shugang Road Taixing Economic Development Zone

Taixing #2, Jiangsu, China

API Manufacturing

Changshu, Jiangsu, China

API Manufacturing

Tianjin, China

Discovery oligonucleotide, amidite, GalNAc

168 Nanhai Road Tianjin Economic-Technological Development Area (TEDA), Tianjin, 300457, China
Tel: +86 (22) 5998-7288

Chengdu, Sichuan, China

Unnatural amino acid synthesis

No.388 Haifa Road, Chengdu Cross-Strait Science & Technology Industrial Development Park, Wenjiang District, Chengdu, Sichuan, 611130, China
Tel: +86 (28) 6495-6666

Wuhan, Hubei, China

Peptide discovery

666 Gaoxin Road East Lake High-tech Development Zone Wuhan, China
Tel: +86 (27) 6539-0001

San Diego, CA, USA

API Process Development & Manufacturing
Drug Product Manufacturing

6114 Nancy Ridge Drive San Diego, CA 92121 USA
Tel: +1 (609) 606 6504

Middletown, DE, USA (start operation in 2026)

API & Drug product manufacturing

1091 Industrial Drive, Middletown DE 1970, USA

Couvet, Neuchâtel, Switzerland

Drug Product Manufacturing

Rue du Pré-Jorat 14, Convent, CH-2108 Switzerland
Tel: +41 32 864 7136

Singapore (start operation in 2026)

R&D and Manufacturing

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