ASYMCHEM



CENTER OF SYNTHETIC BIOLOGY TECHNOLOGY



www.asymchem.com

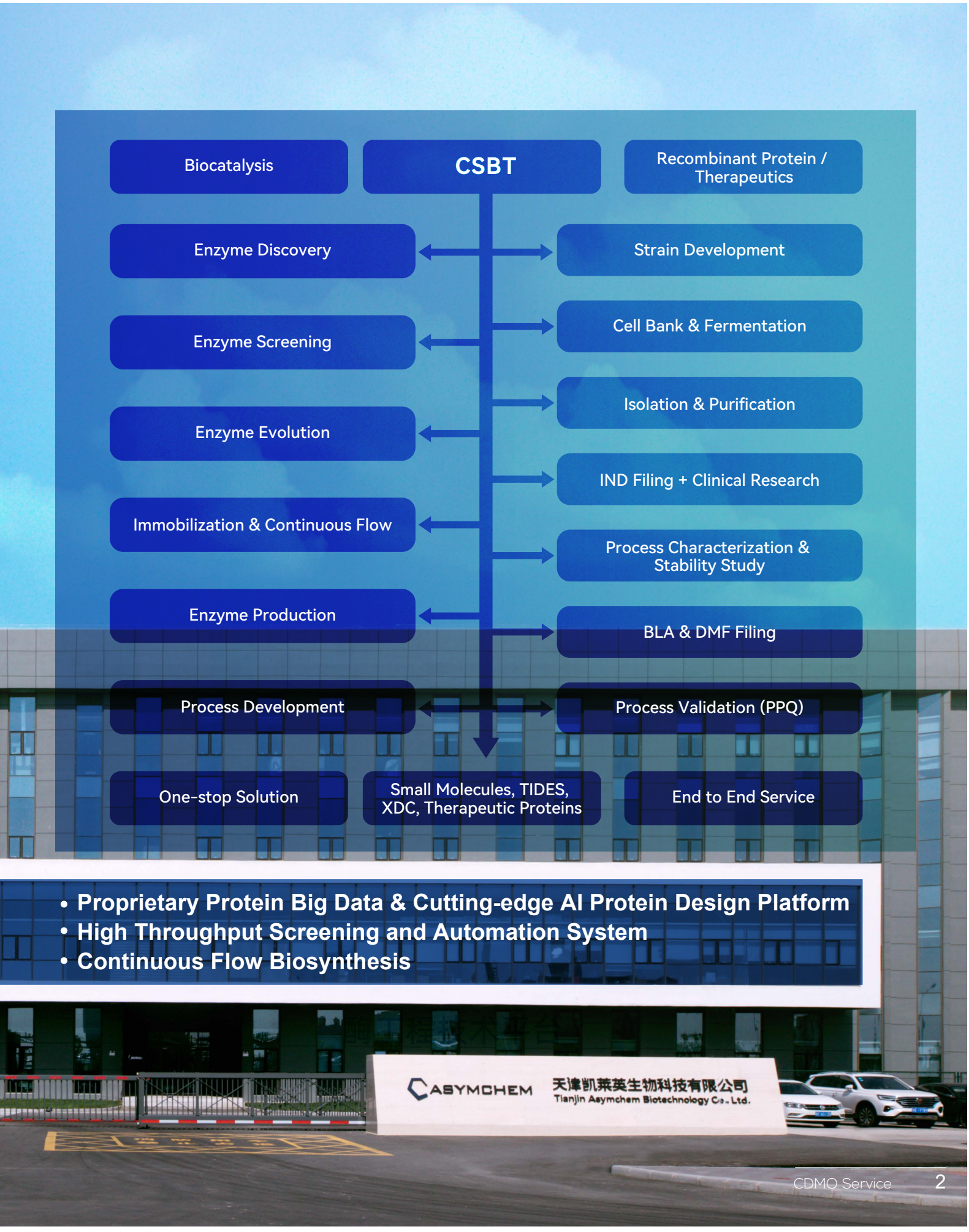
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Synthetic Biology Technology One-Stop Service

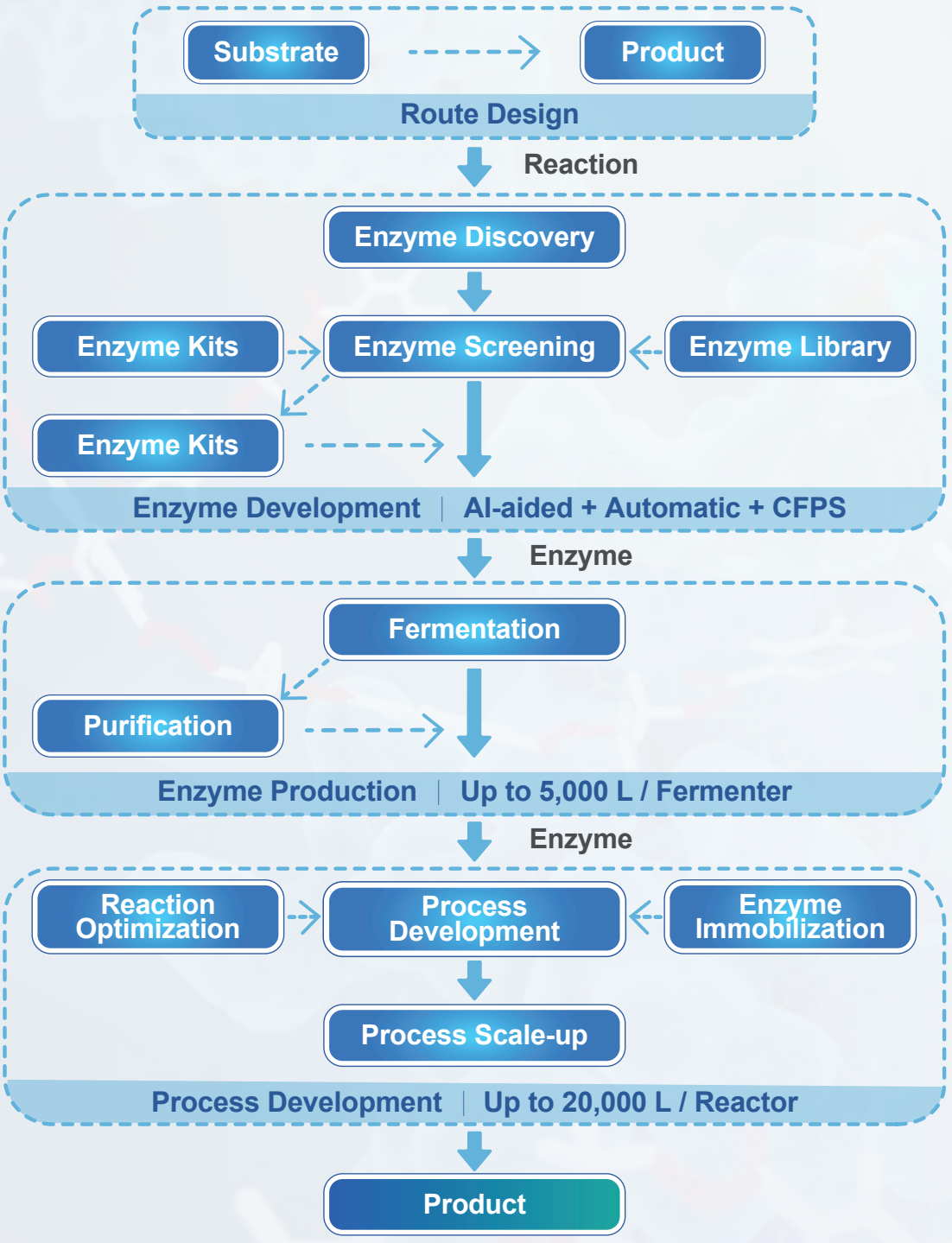
From R&D to Commercial

15+	350	350+	15,300m²	17,000m²
Years of Experience	Scientists Ph.D. 30, M.S. 200	Patents	R&D Center	Production Facility



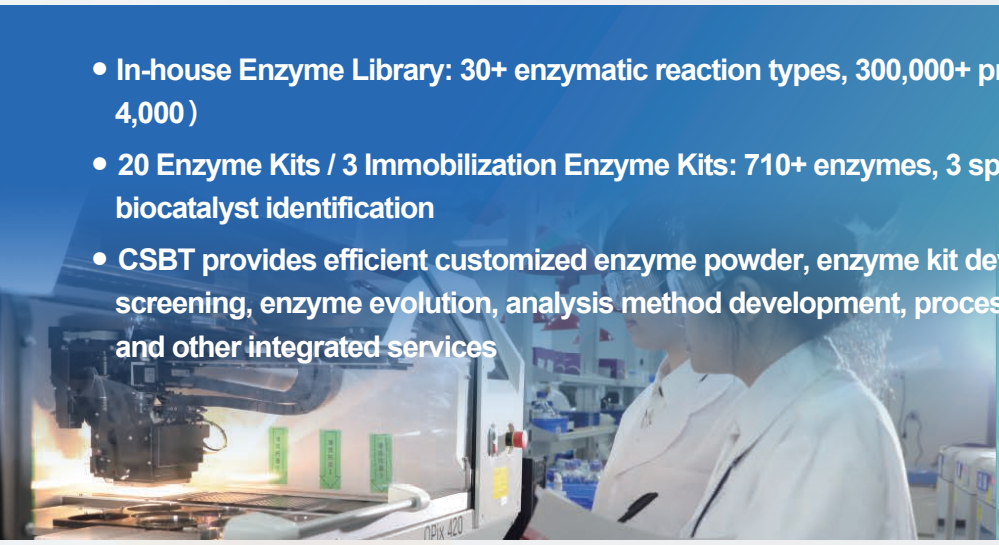

Biocatalysis
CSBT
Recombinant Protein / Therapeutics
Enzyme Discovery
Strain Development
Enzyme Screening
Cell Bank & Fermentation
Enzyme Evolution
Isolation & Purification
IND Filing + Clinical Research
Immobilization & Continuous Flow
Process Characterization & Stability Study
Enzyme Production
BLA & DMF Filing
Process Development
Process Validation (PPQ)
One-stop Solution
Small Molecules, TIDES, XDC, Therapeutic Proteins
End to End Service
• Proprietary Protein Big Data & Cutting-edge AI Protein Design Platform
• High Throughput Screening and Automation System
• Continuous Flow Biosynthesis
ASYMCHEM
天津凯莱英生物科技有限公司
Tianjin Asymchem Biotechnology Co., Ltd.

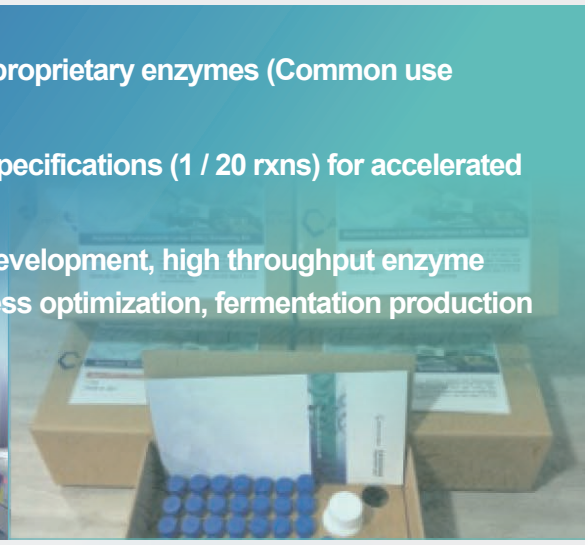
From Concept to Product

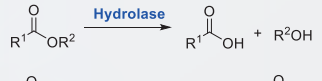


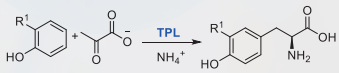
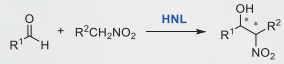
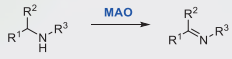
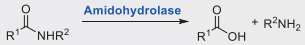
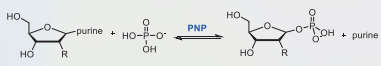
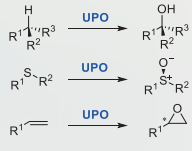
Enzyme Library & Kits

- **In-house Enzyme Library: 30+ enzymatic reaction types, 300,000+ proprietary enzymes (Common use 4,000)**
- **20 Enzyme Kits / 3 Immobilization Enzyme Kits: 710+ enzymes, 3 specifications (1 / 20 rxns) for accelerated biocatalyst identification**
- **CSBT provides efficient customized enzyme powder, enzyme kit development, high throughput enzyme screening, enzyme evolution, analysis method development, process optimization, fermentation production and other integrated services**





Enzyme	Reaction Equation
Ketoreductase	
Transaminase	
Hydrolase (Lipase & Esterase)	
Amino Acid Dehydrogenase	
Nitrilase	
Ene Reductases	
Baeyer-Villiger Monooxygenase	
Proline Hydroxylase	
Imine Reductase	

Enzyme	Reaction Equation
Phenylalanine Ammonia Lyase	
Tyrosine Phenol-lyase	
Hydroxynitrile Lyase	
Monoamine Oxidase	
Amidohydrolase (Amidase & Acylase)	
Styrene Monooxygenase	
Purine Nucleoside Phosphorylase	
Unspecific Peroxygenases	

Enzyme Evolution

- **Big Data**
  - Machine-learning powered directed evolution
  - Proprietary evaluation algorithms (score function)
  - Multi-site mutations by a single prediction

- **Structure Modeling**
  - High throughput structure prediction
  - Catalytic transition state modeling
  - Dynamic structure in buffer and organic co-solvents
- **In-house DNA Synthesis & Sequencing**
  - Comprehensive IP protection

Improved Enzyme → **Mutant Library Construction**

Precise identification of key residues

Activity, Selectivity, Stability, Expression & Solubility Improvement

High Throughput Screening

- **Cell-Free Protein Synthesis (CFPS)**
  - Efficient: 3 step to get protein (traditional >10 steps)
  - Fast: 2-3 times faster than traditional methods

- **Automation**
  - Dedicated automation platform
  - Operating 24/7



- **High Throughput Screening**
  - Microfluidic system for reaction screening
  - Screening > 300,000 reactions per week

Enzyme Production Capacity

- High cell density fermentation
- 1.5 L × 32 Multi-Parallel Bioreactors, high throughput and continuous fermentation
- Automatic intelligent and data-driven production system ensures process stability
- GMP compliant equipment chain to meet the needs of different scale production
- Separate upstream and downstream production areas
- Scalable separation and purification technology platform
- Comprehensive quality management system
- Provide high quality gram to ton products

17,000 m^2
Production Plant

15,000 **kg/year**
Production Capacity

Production Line	5 L × 16	50 L × 6	500 L × 4	5000 L × 3











Process Development

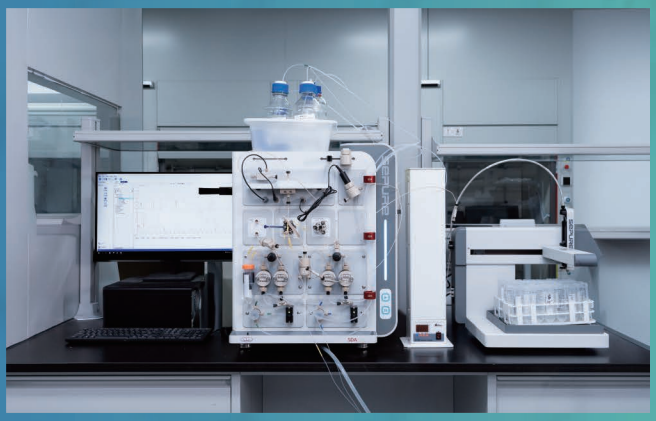
Reaction Optimization & Work-up Development | **Validation** | **Commercial Production**

- Optimization and development of biotransformation process (Batch & Flow)
- Oxygen / pH self-control program
- By-product removal program
- Membrane filtration (continuous / batch operation)
- Efficient solid-liquid separation technology and equipment

- 200+ projects biotransformation production
- 2,000+ batches
- Single batch maximum size: 20,000 L



Reaction Optimization & Work-up Development



Process Verification



Production



Immobilization & Flow

Enzyme Immobilization & Continuous Flow Synthesis

Commercially Available Carriers

100+ Polymer Beads

Hydrophobic adsorption
Affinity adsorption
Covalent binding

In-house Modified Carriers

200+ Polymer Beads

Customized for precise targeting
Higher performance
Wide versatility

Enzyme Immobilization & Continuous Flow Synthesis

- Customized development of enzyme immobilization continuous flow process
- High throughput screening platform, process development completed in 3 weeks
- 150+ enzyme immobilization solutions
- Covering ~20 classes of enzymatic reaction



Enzyme Immobilization (Batch)

- Enzyme cost reduction by ≥70%
- Simplified product separation process
- Significantly increase yield and reduce production costs

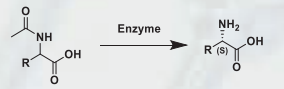
Continuous Flow Synthesis

- 50+ cases
- Production capacity improved by 20~1500 folds, 0.5-30 kg/L/d
- Instant & online separation of the product
- Easy for amplification

Tons Scale Production

- 10 T+ commercial production
- In-house design of reactor and centralized control system
- Rapid and accurate process control
- Minimized waste generation

>>Case Study: Biosynthesis of Small Molecule Intermediates in Flow Mode



*** 10 mt scale production**

1st

3000 L Batch Tank
Low Production Capacity
STY: 0.051 kg/L/d

2nd

1*40 L PBR using Commercial resin
Space Time Yield: 2.4 kg/L/d
Enzyme Cost: Saved by 80%

3rd

1*40 L PBR using Asymchem Designed Resin
Space Time Yield: 5.5 kg/L/d
Enzyme Cost: Saved by 85%

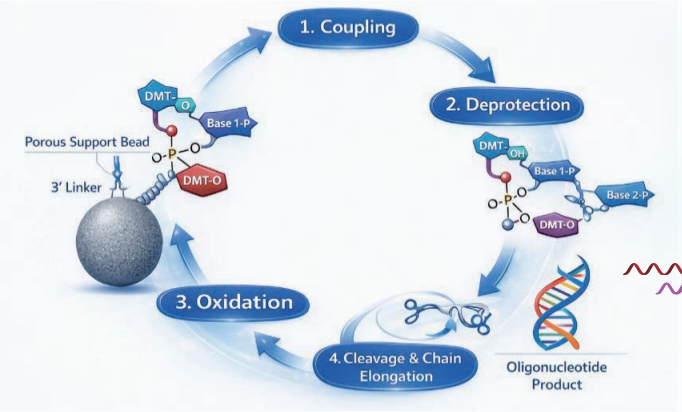
4th

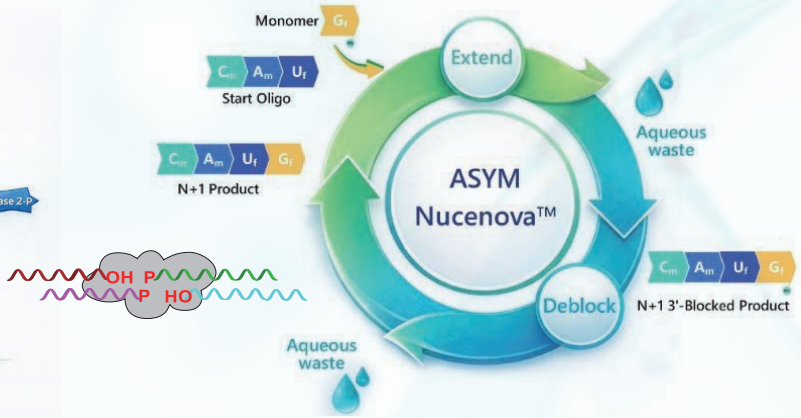
1*40 L Improved PBR using Asymchem Designed Resin
Space Time Yield: 12.6 kg/L/d
Enzyme Cost: Saved by 90%

An Integrated View of Oligonucleotide Synthesis Technologies

Nucleic Acid Synthesis Platforms

From Solid-Phase to Enzymatic Solutions





Solid-Phase (Current baseline)

Robust chemical platform for high-quality oligonucleotide production

- High cost, high PMI, limited scalability
- Approaching inherent technical constraints

Chemoenzymatic (Core platform)

Hybrid enzymatic platform for efficient oligonucleotide synthesis

- ↓ Cost, ↓ PMI, ↑ Scalability vs. Solid-phase
- Chemical efficiency + enzymatic precision
- Ideal for current manufacturing needs

De Novo Enzymatic (Future direction)

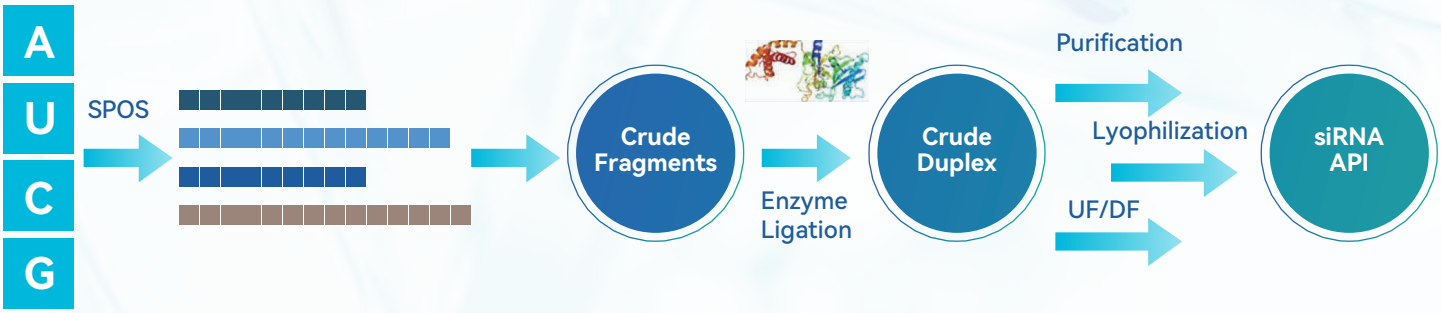
Fully enzymatic platform for template-free synthesis

- Further ↓ Cost & ↓ PMI
- Complementary to hybrid approach

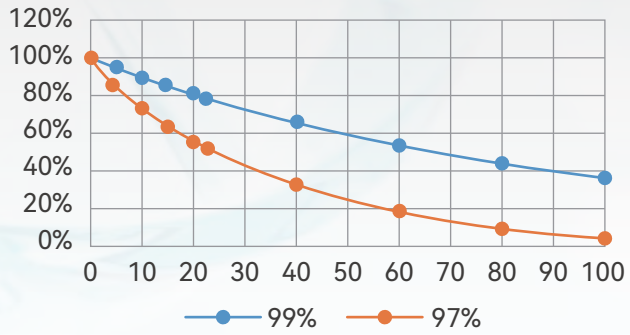
>>Oligo manufacturing is evolving from single-method chemistry toward integrated chemical and biological solutions.

Chemoenzymatic Oligonucleotide Manufacturing in Practice

Chemoenzymatic Synthesis of Oligonucleotides



SPOS



Crude fragment purity > 90%
Yield > 85%

Enzymatic Ligation



Conv. of enzymatic ligation > 99%
No misligation-induced impurity

Work-up

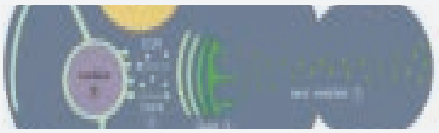
- Chromatographic purification process Denaturing purity ≥ 95%
- Chromatographic-free process Denaturing purity ≥ 90%

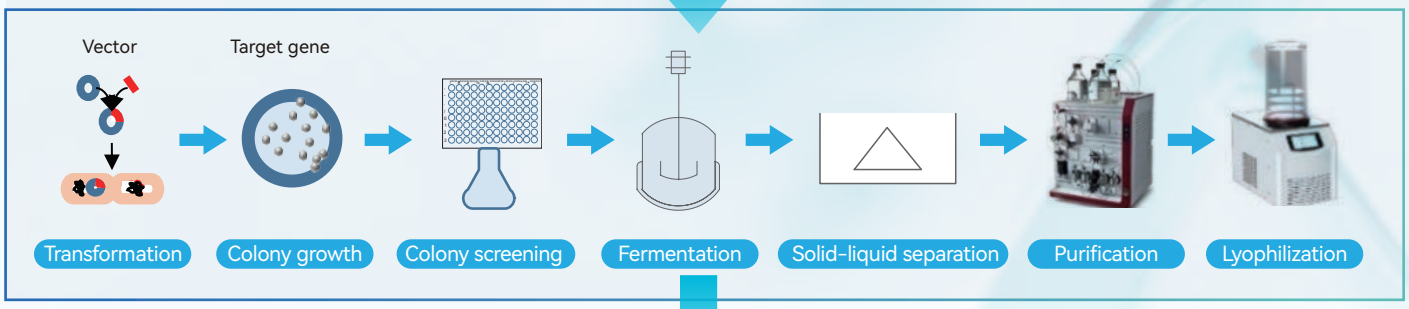
>>High-conversion enzymatic ligation enables efficient assembly of high-purity oligonucleotides from well-designed fragments.

Peptide Biosynthesis

E. coli	*B. subtilis*	Yeast







Enzymatic synthesis of UAAs:

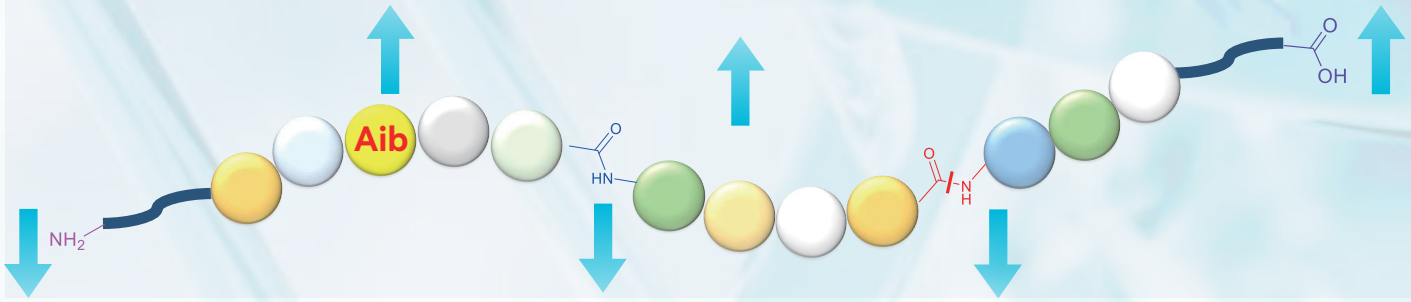
- Developed 10 types and >1500 enzymes for synthesizing > 120 UAAs;
- Proved scalability at 100 kg scale.

Peptide biosynthesis:

- Fermentation titer >15 g/L, purity >98%, isolated yield >60%;
- Fermentation capacity up to 1.3 ton per year.

C-terminal functionalization:

- Demonstrated universality across >10 different peptides without affecting the side-chain COOH and OH groups.



N-terminal acetylation:

- Asymchem's enzymes catalyze acetylation on 19 AAs but inert toward side chains.

Ligation:

- >1000 enzymes with Asymchem's IP;
- AI powdered peptide ligation;
- Purified enzyme yield > 2 g/L; g to kg; loading 0.001 wt;
- Reaction scale g to kg, API up to 60mer; 10 V;
- Advantages: no racemization; greener solvent; high yield (>35%) and purity (>97%); superior impurity profile; reduced PMI > 30%.

Degradation:

- TEV protease, Kex2 protease, Carboxypeptidase B, Trypsin, SUMO protease, SplB protease.

- **Comprehensive expression library: 300+ promoters, 200+ signal peptides, 70+ fusion tags, 100+ terminators, 90+ chaperones**
- **High-efficiency strain development capability: gene editing, high-throughput screening, rational & irrational strain engineering**

>> *E. coli*

- Recombinant strain & process development in 6 months.
- Over 20 peptides expressed on this platform, with GLP-1 precursor scaled up to 5000 L GMP-compliant fermentation.
- Single & multi-copy strategies: fermentation titer >15 g/L, isolation yield ~60%, outputting 20–30 kg peptide per 5000 L batch and an annual capacity of 1–2 tons.
- AI assisted tool enzyme engineering: improving enzyme robustness, stability and activity while reducing non-specific digestion.
- PoC for site-specific incorporation of unnatural amino acids (UAAs) including Aib and Boc-lysine via genetic code expansion.

>> Yeast

- Recombinant strain & process development in 6-8 months
- High-efficiency GLP-1 secretory expression strain: 500 L scale with multi grams per liter, ~85% isolation yield and ≥97% purity.

>> *B. subtilis*

- Peptide expression PoC achieved in 2 months (product identity verified by mass spectrometry)
- Lipopeptide, titer >6 g/L

Lab to Commercial Protein Expression & Purification Services

- Gene Synthesis & Expression Vector Construction
- High Throughput Protein Expression Screening
- Efficient Expression Systems:
  E. coli, S. cerevisiae, P. pastoris, B. subtilis
- GMP Cell Bank Establishment
- Strain Preservation & Secured Storage

- Growth Media Design & Screening
- Fermentation Development & Scale-up
- Shake flask to production scale up in shortest time
- Expertise to handle & trouble shoot difficult proteins
- Dedicated 50 L, 500 L, 5000 L production line to enable GMP compliant protein(s)



- Competent quality control and quality assurance system
- Process verification
- BLA Filing
- DMF Filing

- Sample production for clinical & preclinical study
- Analytical method development / transfer/ pre-validation
- Physicochemical characterization
- Stability study
- Product release testing
- Analytical trouble shooting

- Purification process design and resin screening
- Isolation & purification process development across various platforms
- Scalable, GMP compliant purification process equipment(s)
- Endotoxin/ HCP/ HCD control systems

Diverse Products: Enzyme(s), Fusion Protein, Nanobody, Peptide Antibiotics, Polypeptide, Growth Factor(s), Cytokines, etc.

>>Strain Development

Expression Element Library

Promoters	Fusion Tags	Expression Plasmids	Chaperone Protein	Signal Peptides	Hosts	Terminator
300+	70+	100+	90+	200+	50+	100+

High Throughput Screening

Recombinant Protein/ Peptide Strain Screening → ***E.coli*** → ***S. cerevisiae / P. pastoris*** → ***B. subtilis…***

Gene Editing | **Transcription & Translation Regulation** | **DNA Assembly**

Efficient Expression Systems

- ***E.coli:*** Low cost, high titer
- ***Yeast:*** High titer, post-translational modification
- ***Bacillus subtilis*** and other expression systems

Flexible and Efficient Delivery Cycle

- **3~4 weeks** High throughput codon screening
- **3~4 weeks** Element library/expression condition high throughput screening
- **2 weeks** per round of host cell modification

Excellent Strain Stability

- High batch to batch stability
- Plasmid loss rate <10%

Case Study: Trypsin Expression Optimization

- Conventional Expression Element
- Host
- Optimized Codon

→

- High Throughput Optimization of the TIR
- Expression Element Combination Optimization

→

- Protein Modification Improves Stability
- Gene Copy Number Regulation
- Host Cell Modification
- Molecular Chaperone Co-expression

→ **3 Months Yield Improved by 30 Folds**



>>Cell Bank Establishment & Fermentation Process Development

Cell Bank Establishment

- Primary cell bank（PCB）
- Master cell bank（MCB）
- Working cell bank（WCB）
- Cell Characterization and Testing
- Cell Bank Security and Storage Management System

Fermentation Process Development

- Growth Medium design & screening
- HTP fermentation process development by 24×1.5 L multi-parallel bioreactor systems
- High density fermentation process development
- Optimization of fermentation process based on QbD design concept & DOE platform
- Seamlessly scaled up fermentation processes based on platform technologies
- Robust process development in 6 weeks

Fermentation Process Scale-up

- Dedicated production lines for 50L, 500L, and 5000L fermentation, alongside matching downstream processing (DSP) equipment
- Fully compliant with GMP quality management system
- Highly experienced and trained production team ensuring on-time and high-quality delivery

Case Study: Recombinant Protein Fermentation Process Development

Original Process

- High Plasmid Loss Rate
- Low Protein Expression

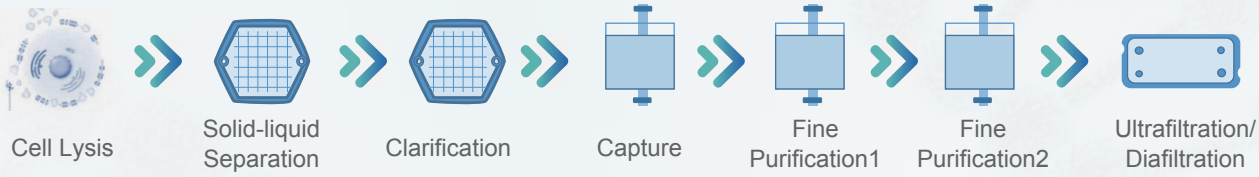
Host Engineering & Optimization

HTP Fermentation Process Optimization

- **Plasmid Retention Rate: Improved from 30% to >90%**
- **Yield:Improved from 200mg/L to 800 mg/L**

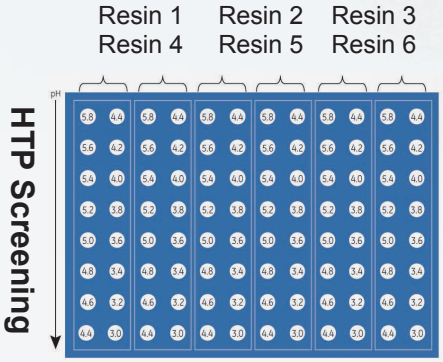


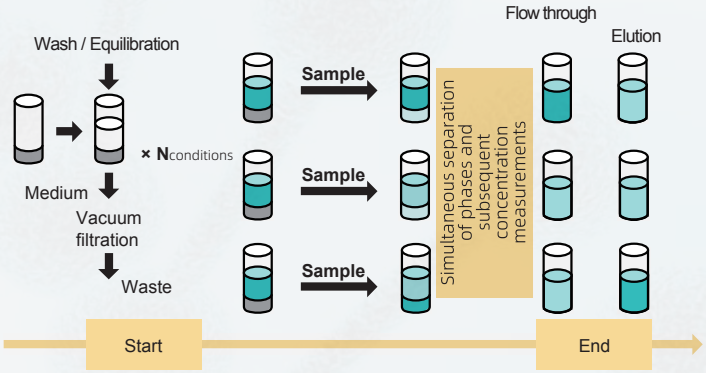
>>Separation & Purification Process Development



- HTP Resins Screening Platform
- Rapid Evaluation of Purification Process Parameters
- Diverse Isolation & Purification Techniques: Affinity Chromatography, Size-exclusion Chromatography, Ion Exchange Chromatography and Hydrophobic Interaction Chromatography

Case Study: Recombinant Protein Isolation & Purification Process Development





- HTP Technology
- **2.5 weeks** Chromatographic Column Amplification Purification Process

- 3 Steps Chromatography, the Product SEC_HPLC **≥ 99%**, HPLC **≥ 99%**
- 3 Steps Chromatography, Yield **≥ 70%**
- Endotoxin **< 0.1 EU/mg**
- HCP ≤ 10ng/mg, HCD ≤ 1ng/mg

>> Nanobody (Injection) Project Case

DS Process Difficulties:
High Plasmid Loss Rate, Low Yield, Low Endotoxin Level Required

High Plasmid Loss Rate
Original engineering strain: plasmid loss rate ＞70%

Low Yield.
E.Coli low expression, yield 40 mg/L

High Endotoxin Level
Original purification route: high endotoxin level, 10 EU/mg



Optimized Expression System
Host & expression plasmid optimization: plasmid loss rate ＜10%

Fermentation Process Optimization
Asymchem HTP fermentation platform, screening the optimal process, yield improved by 400%

Develop Specific Purification Route
Composite packing purification technology & Chromatographic membranes, endotoxin levels ＜ 0.1 EU/mg

Recombinant Protein / Therapeutics Production Capacity

- Powered by state of the art R&D and GMP grade facility, including BSL-2 capability, CSBT has the richest experience and expertise to accelerate design, develop, demonstrate and deliver recombinant protein of interest.
- Our research and production platforms, ranging from 5 L through 5000 L scale, enable seamless scale up both in production & purification with our key attribute to handle complex downstream processing & purification.
- Automatic intelligent and data-driven production system ensures process stability
- Consistent supply of high quality product.
- Can achieve low endotoxin limits <0.1 EU/mg, HCP or HCD levels as desired.

17,000 m^2
Production Plant

50 L / 500 L / 5000 L GMP
Production Line

The Production Needs of Enzymes, Recombinant Proteins, Peptides, Biobased Small Molecules and Other Biological Products Can Be Met



Comprehensive Analysis Platforms

One-Stop Analysis Services



Physicochemical & Biochemical Platform

- ID (HPLC/SDS-PAGE/HRMS/WB)
- Conc. (UV/BCA/Bradford/Lowry)
- Purity (HPLC-UV/CAD/ELSD/FLD/RID)
- Heterogeneity (SEC/IEX/iCIEF)
- HCP (ELISA)
- HCD and DNA Fragment Size (qPCR)
- Residual Solvents (GC/HS-GC)
- Elemental Impurities (ICP-MS)
- Enzyme Activity (HPLC/Spectrometer)
- High Throughput Screening (Echo MS)

Structural Characterization & Impurity Analysis Platform

- Nucleic Acid Analysis
  (Oligonucleotide Intact mass analysis, Mapping, Modification,Impurities)
- Protein/Peptide Analysis
  (MW, Peptide Map, Sequence coverage, PTM, N/C-Terminal Sequence, Disulfide bond, Glycosylation site, Protein Absorption Coefficient, Amino Acid Composition, Amino Acid Absolute Quantification)
- Structural Characterization
  (FTIR/UV-Vis/LC-MS/NMR/MALLS/CD)

Bioassay & Microbiology Platform

- Microbial Limit
- Endotoxin
- Sterility
- Environment Monitoring
- PCB/MCB/WCB Testing
- Binding ELISA
- Cell Proliferation
- Cell Inhibition
- Cytotoxicity
- Luciferase Reporter Assay

Release Testing Platform

- Raw Material Testing
- In-Process Production Testing
- Product Release Testing
- Reference Material Management
- Stability Studies
- Cleaning Testing
- Method Verification / Validation / Transfer



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