Asymchem

Green Chemistry is the Future

www.asymchem.com     Stock Code: 002821.SZ
Our mission is helping clients to speed up the drug development and achieve their excellence by providing fully integrated quality services from discovery to commercialization.
IP Protection

Asymchem is a pure CDMO

All IP developed as a service by Asymchem, is the Property of the Client
Company Overview
Capacity and Capabilities on R & D and Manufacture
Innovation and Collaboration
Technology Platforms
Compliance
Company Introduction

- Established in 1998
- Listed in Shenzhen Stock Market with a Market Cap. of $3 B.
- Sales revenue > $275 M in 2018

Sales by Region

<table>
<thead>
<tr>
<th>Region</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>117.5</td>
<td>136.2</td>
<td>166.7</td>
<td>214.7</td>
<td>275.8</td>
</tr>
<tr>
<td>US</td>
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<tr>
<td>EU</td>
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<tr>
<td>Others</td>
<td></td>
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</tbody>
</table>

Revenue in USD Millions
Green Chemistry is the Future

20 Years

3500+ Employees 1500+ Scientists 8 Manufacturing Sites 30+ Successful Inspections USFDA/NMPA/TGA/MFDS 400+ Global Clients 600+ On-going Clinical Projects 30+ On-going Commercial Projects

Your Preferred Partner From Preclinical to Commercial

CMC+Clinical Research
Small Molecules/Biologics/Chemical Macromolecules

API Drug Product Clinical Research Analytical Service IND/NDA-NMPA/FDA
Our Performance

In the Past 20 years, Asymchem has been recognized as the most valuable/strategic partner by both major pharma and leading biotech companies.
R&D Capabilities

- Process Chemistry Research
- Process Chemistry Development
- Safety Assessment
- Full DoE Design
- Crystallization Study and Salt Selection
- Formulation Development
- Analytical Research and Development
- Biotransformation
- Flow Chemistry
- High Pressure Reactions
- Cryogenic Reactions
- High Potency API Development
- Peptides/Oligonucleotide/Glycans

R&D Capacity

- > 1500 research scientists
- > 50% hold an MSc or above
- > 550 hoods for chemical development
Analytical Service for APIs and Formulation

Analytical Services

- Analytical Method Development and Validation
- Stability Testing
- Force degradation studies
- Stability testing to support clinical studies
- Stability testing under ICH guidelines
- API Reference Standard Qualification and Maintenance
- Spectroscopic Structure Confirmation
- Release Testing
- Identification Product and Pathway
- Cleaning Validation
- Physical Property Characterization
- Microbiology Testing
- Endotoxin/aseptic/potency/positive bacteria testing

Major Analytical Equipment

- HPLC, GC, ICS-1500/5000, UPLC, SFC
- LC-MS, LC-MS/MS, LC-TOF, ICP-MS
- GC-MS, HS GC-MS
- NMR(300, 400, 500MHz), ICP-OES, XRD, FTIR, UV-vis, OR
- pKa logP/D test, HS KF-V20, KF-C20, TOC, Melting Point Detector
- TGA, DSC, DVS, PSA, Potentiometric Titrator
- Stability chambers

Full in-house release of APIs and Formulation
World-class Manufacturing Facilities

2,357m³ in total
1,669m³ cGMP
687m³ cGMP-like

Single quality system across all manufacturing sites
## Total Manufacturing Capacity – By Site

<table>
<thead>
<tr>
<th>Site</th>
<th>Capacities</th>
<th>Vessel sizes</th>
<th>Working Parameters</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cGMP</td>
<td>cGMP-like</td>
<td>Working Temperature</td>
<td>Working Pressure</td>
</tr>
<tr>
<td>TJ1</td>
<td>11.55m³</td>
<td>--</td>
<td>5L~3,000L</td>
<td>-20°C ~ 110°C -0.1~7MPa</td>
</tr>
<tr>
<td>TJ2</td>
<td>125.60m³</td>
<td>--</td>
<td>5L~8,000L</td>
<td>-90°C ~ 120°C -0.09~0.02MPa</td>
</tr>
<tr>
<td>TJ3</td>
<td>106.0m³</td>
<td>--</td>
<td>500L~8,000L</td>
<td>-110°C ~ 200°C -0.1~7MPa cGMP manufacturing, formulation</td>
</tr>
<tr>
<td>FX1</td>
<td>350.78m³</td>
<td>276.8m³</td>
<td>80L~12,500L</td>
<td>-90°C ~ 130°C -0.1~0.02MPa RSM &amp; Carbapenems</td>
</tr>
<tr>
<td>FX2</td>
<td>--</td>
<td>191.5m³</td>
<td>500L~12,500L</td>
<td>-90°C ~ 130°C 0.1~0.02MPa Non-cGMP Back Integration</td>
</tr>
<tr>
<td>DH1</td>
<td>747.4m³</td>
<td>214.5m³</td>
<td>200L~20,000L</td>
<td>-90°C ~ 200°C 0.1MPa~7MPa cGMP manufacturing, RSMs, high-pressure chemistry</td>
</tr>
<tr>
<td>DH2</td>
<td>328.5m³</td>
<td>--</td>
<td>3,000L~20,000L</td>
<td>-90°C ~ 110°C 0.1MPa Carbapenem manufacturing</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,669.83 m³</strong></td>
<td><strong>687.3 m³</strong></td>
<td><strong>--</strong></td>
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</tr>
</tbody>
</table>

- HP, API, high-pressure chemistry
- All aspects of chemical manufacturing & development
- cGMP manufacturing, formulation
- RSM & Carbapenems
- Non-cGMP Back Integration
- Carbapenem manufacturing
**Analytical service**
- Analytical method development, transfer and validation.
- Cleaning method development and validation.
- Microbiological method development and validation.
- Stability study as ICH requirement.

**Formulation and process development**
- Oral immediate release and sustained release formulation rapid development
- Conventional parenteral formulations and non-biological complex drug formulation rapid development
- Robust process development and optimization
- QbD based solutions for process scale-up from laboratory to pilot and commercial scales
- Technology transfer from one site to the other site

**Production and registration support**
- Dossier filling for IND, NDA (ANDA) application in compliance of NMPA and US regulatory requirement.
- Clinical sample manufacture to meet different phase requirement.
- Commercial product production in compliance with cGMP.
Oral Solid Dosage Form Production lines

◆ OSD Lab Plant 1 (R&D, pilot batches)
◆ OSD Plant 2 (Commercial batches)
◆ OSD Plant 3 (Imported equipment’s- USA, Europe.)

Processing capabilities

◆ Clinical Phase 1:
  500 to 30,000 units per batch
◆ Clinical Phase 2:
  2000 to 150,000 units per batch
◆ Commercial:
  5-80kg and above based on requirement
## GMP Manufacturing of Injections

### Processing capabilities

<table>
<thead>
<tr>
<th>Workshop</th>
<th>Injection Type</th>
<th>Spec.</th>
<th>Batch Size</th>
<th>Annual Capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>INJ-1 (ampoule) Terminal sterilization</td>
<td>Solution INJ.</td>
<td>1-20ml</td>
<td>20,000 to 66,000</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>Freeze Drying</td>
<td>2-50ml</td>
<td>20,000 to 45,000</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>10,000 to 29,000</td>
<td></td>
</tr>
<tr>
<td>INJ-2 (vial) Non-terminal sterilization</td>
<td>Solution INJ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Freeze Drying</td>
<td>2-30ml</td>
<td>12,000 to 24,000</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>1,000 to 3,000</td>
<td></td>
</tr>
<tr>
<td>INJ-3 (miniKUfill-Vial) Non-terminal sterilization</td>
<td>Solution INJ.</td>
<td>2-30ml</td>
<td>12,000 to 24,000</td>
<td></td>
</tr>
</tbody>
</table>
Confidential

Project Management – On Time, In Scope, In Budget

Our Internal project manager will be your key contact for all Asymchem solutions

Client

Asymchem PM

Transparent, Real-Time Communication

R&D

Manufacturing

QA

QC

Sourcing

Logistics

RA

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10+ High quality Papers Published:
72 patents authorized in China
16 international invention patents

Extensive cooperation with the Scripps Research Institute was established since 2014.

Flow Chemistry

Photochemistry

Electrochemistry

Biotransformation

Non-Noble Metal Catalysis
• Modular radical cross-coupling with sulfones enables access to sp3-rich (fluoro)alkylated scaffolds, Science, 2018, 4, 75-80
• Scalable and safe synthetic organic electroreduction inspired by Li-ion battery chemistry, Science, 2019, Vol. 363, Issue 6429, pp. 838-845
• Decarboxylative alkenylation, Nature, 2017, 545,213-218
• Scalable and sustainable electrochemical allylic C–H oxidation, Nature, 2016, 533, 78-81
Global Level Consultant Team

Board of Scientific Advisory (BSA) comprises distinguished scientists from industry and academia including Nobel Prize winners and National Academy of Science members.

1. **Professor K. Barry Sharpless**
   - Professor at the Scripps Research Institute, the winner of the 2001 Nobel Prize in Chemistry

2. **Professor Jin-Quan Yu**
   - Professor at the Scripps Research Institute, expert in C-H activation chemistry, 2016 MacArthur Award Winner, Academician of AAAS (American Academy of Arts and Sciences)

3. **Professor Phil Baran**
   - Professor at the Scripps Research Institute, USA MacArthur Award Winner, member of the National Academy of Science

4. **Professor Stephen L. Buchwald**
   - Associate Head of the Chemistry Department at MIT, Member of the National Academy of Science

5. **Professor Nicholas Turner**
   - Professor at the University of Manchester - a Leading Global Expert for Making Better Enzymes

6. **Professor Timothy F. Jamison**
   - Professor at MIT - Leading Global Expert for Flow Chemistry
Global Level Consultant Team

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Dr. Stephane Caron
Executive Director of Chemical Process R&D at Pfizer, Member of American Chemical Society

Dr. Tony Zhang
CEO of Tyligand Bioscience, >25 years’ Experience in Eli Lilly as Senior Research Fellow.

Dr. Martin Eastgate
Director of Chemical and Synthetic Development at BMS, >14 years’ Experience in the Pharmaceutical Industry

Dr. Seble Wagaw
Senior Director at AbbVie, Head of Organic Chemistry Process Research and Development

Dr. Scott A. May
Research Fellow, Small Molecule Design and Development, Eli Lilly

Dr. Patricia A. Aired
President of Patricia Aired Consulting, LLC, Expert in the Operations and Development of Biomolecules
Global Level Consultant Team

Board of Strategy Development & Scientific Advisors

于明德
Mingde Yu
President of Chinese Pharmaceutical Enterprises Association and China Pharmaceutical Enterprises Association, engages in management of drug production and circulation.

朱宝泉
Prof. Baoquan Zhu
Ph.D., President, Researcher, Doctoral supervisor of School of Pharmacy in Shanghai Jiaotong University, engages in screening of new antibiotics, bacteria identification, separation and purification.

周德敏
Prof. Demin Zhou
Ph.D. in pharmaceutical chemistry, professor of chemical biology, “Changjiang Scholar”, Chief Scientist of Ministry of Science and Technology “973” Project, President of Peking University School of Pharmaceutical Sciences, Director of State Key Laboratory of Natural and Biomimetic drug.

张自然
Dr. Ziran Zhang
President of Chinese Pharmaceutical Enterprises Association and China Pharmaceutical Enterprises Association, engages in management of drug production and circulation.

朱建伟
Prof. Jianwei Zhu
Ph.D., distinguished expert of the “Thousand Talents Plan”, Professor of Shanghai Jiaotong University. Committed to the R&D and industrialization of biotech drugs.

金克文
Dr. Kewen Jin
Partner of Sija Jianxin Fund and president of The BayHelix Group, once served as consultant of many transnational pharmaceutical companies, investment fund companies, two domestic leading life science industrial parks, etc.
Technology Platform - Flow Chemistry

- >90 Highly-experienced scientists & engineers
- >400 reactions scaled to multi-kilogram scale
- Validation and scale-up to ton-scales at US FDA-inspected cGMP Site
- Extensive use of PAT, in-line extraction & filtration to provide genuine, end-to-end solution
- Commercial supply of products made by Flow Chemistry technologies.
Technology Platform - Flow Chemistry

Scale up to 4,000 KG

- Electrochemical Reaction
- Diazomethane reaction
- Dibal-H reaction
- high-temperature reaction
- low-temperature reaction
- Curtius rearrangement reaction
- Continuous catalytic hydrogenation reaction
- Continuous reaction with high energy reagents (TMSN₃, NaN₃, H₂O₂, TBHP, etc.)

Scale up to 40,000 KG

- Continuous Ozonolysis / Ozonation reaction
- Continuous Nitration reaction

Process development of Flow Chemistry, from 0 to 1

01. Assessment of flow reaction feasibility
02. Process definition/optimization
03. Validation and scale up
04. Prototype design (new tech platforms)
05. Tech-package generation
06. Technology transfer to production
07. Continuous improvement through accumulation of knowledge
08. Fully-optimized process at lab, kilo, and commercial scale

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- Assessment of flow reaction feasibility
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- Process definition/optimization
- Validation and scale up
- Prototype design (new tech platforms)
- Tech-package generation
- Technology transfer to production
- Flow reaction feasibility assessment
Technology Platform - Biotransformation

Integrated Service for Biotransformation

Enzyme Engineering:
- Enzyme discovery / development / evolution / immobilization
- Multiple enzyme screening kits

Bioorganic Chemistry:
- High throughput screening of enzyme libraries
- Development of scalable biotransformation processes

Enzyme Production:
- Fermentation at scales up to 5,000L
- Purified enzyme solutions suitable for direct use

Experienced Team:
4 Ph.Ds and 46 Masters, Totally 110 scientists and engineers
Asymchem Enzyme Library

By leveraging our expertise on enzyme discovery and engineering, Asymchem has established an Enzyme Library containing > 900 Enzymes. Asymchem has clear FTO for all these enzymes in the library. Stocks are maintained and replenished continually.
Well-developed systems to eliminate contamination vectors such as pressurization, primary decontamination stations within suites & qualification of facilities & processing equipment

Ongoing performance monitoring
Dust testing of isolators & air monitoring

Rigorous training for handling potent compounds
OEB 5 compounds safely handled

Facilities independently tested by ISS

Outstanding track-record of containment control
Dedicated facilities with isolators suitable for OEB 5 compounds
US FDA-inspected facility - can handle all aspects of the development & manufacture of HPAPIs
DoE (Design of Experiment) is the core part of Process Validation Enabling work and is vitally important for NDA filling. Asymchem can provide the full DoE work as a package.

### Service Scope
- Condition Screening
- Process Optimization & Development
- RSM Justification
- Specification Study
- CPP/KPP/CIPC Study

### Capabilities
- > 80 Successful DoE projects have been either delivered or in progress, demonstrating a proven track record in executing projects efficiently.

### Objective
- Optimized manufacturing process
- Process Validation Enabling
- NDA Filing

- The DoE team consists of >35 scientists covering experiment design, conduct and data analysis.
- Multi-disciplinary teams working together to make most efficient use of resources and timely completion of studies.
DoE Application in Asymchem

DoE Software

Parallel Reactor

EasyMax 102

RC 1

Experiment Design

Condition Screening

Process Development

PV Enabling Work

Process Validation

Optimal Condition

Parallel Reactor

Jacket Cylinder Reactor

React-NIR

DynoChem

Simulation Software
Crystallization Development

- Pre-clinical
  - New salt, co-crystal, polymorph screening
  - Polymorph conversion, solubility evaluation
  - Crystal form stability evaluation
  - Candidate salt/form evaluation and confirmation
  - Crystallization process design & optimization

- Clinical Phase I
  - Salt/polymorph Clinical evaluation
  - Full screening of polymorphism and advantage form
  - Crystal properties design & screening

- Clinical Phase II
  - Crystallization process optimization & scale-up
  - Crystal properties optimization

- Clinical Phase III
  - Crystal structure analysis
  - Patent applications
Core Services of Crystallization R&D

**Solid Form Screening**
- Salt & Polymorph/Cocrystal Screening
  - High throughput screening
- Crystal form Evaluation
  - Solubility and hygroscopicity
  - Crystal form Stability
  - Thermodynamic stability
  - Polymorph conversion
- Crystal structure analysis
  - Cultivation of a single crystal
  - Structural analysis & refinement
- Process design & Optimization

**API and Formulation R&D**
- Purification R&D
  - High purity, less key impurities
- Crystal Size Distribution Optimization
  - Improve Mobility and Controlled-released
- Crystal Thermodynamic R&D
  - Solubility and Metastable zone width
- Crystal Habit Design & Evaluation
  - Formulation requirements
- Process Optimization and scale up

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**Technology Platform – Crystallization Study**

- Process Design & Optimization
- Process scale up

- Crystal characterization
- Polymorph conversion
- Crystalline product
- Solubility and MSZW
- Desired Habit & CSD
- Support of formulation

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Peptide, ADC Warhead, Oligonucleotide, Glycans

Client Peptide / ADC Warhead
- >120 experienced process chemists/analysts/engineers
- Solid-Phase / Liquid-phase peptide synthesis
- Preparation of peptide fragments via SPPS, cleavage from resin, final coupling via LPPS.
- IND enabling / (A) NDA filling
- Lab /Kilo production / Commercial production
- ADC Warhead CDMO Service: MMAE/MMAF, PBD, Doxorubicin, Camptothecin, and etc. as toxin

Glycans
- Cyclodextrin derivatives, commercial available
- Dextrin derivatives and others

Nucleotide and Oligonucleotide
- Modification and synthesis of nucleotide monomers
- Lab/Kilo production / Commercial production
- Solid-Phase / Liquid-Phase synthesis
- High throughout synthesis
Capacity of Peptide Manufacturing

**Production Space**
- 300 m² R&D Lab;
- 300 m² HiPo and 1000 m² Grade D Area, all production in USFDA-inspected facilities
- Operations supported and monitored by a dedicated QA/QC group

**Lab/Pilot Solid-Phase**
- Automatic Peptide synthesizer (6-channel), Experienced using a number of solid-phase supports and coupling reagent.
- Experience of assembling up to >40 amino acids with further investments in the technology planned.

**Commercial Solid-Phase**
- Reactor sizes for solid-phase synthesis – 20~200 L, Up to ~2 Kg/batch scale,
- 4 Grade D production suites with independent air condition system

- 20~200 L SPPS Reactor
- OEB5 Isolator
- Freeze Dryer
- Nano-filtration
The Compliance
Quality Assurance Overview

Audits
- TGA 2015/2017
- NMPA 2012/2015/2016/2017/2018
- MFDS (SKR) 2017

100+ Clients / Authorities audits each year
200+ Clients on site visit each year
- Totally enclosed secondary wastewater treatment facility with odor removing equipment and online monitoring
- Regenerative Thermal Oxidizer achieving VOCs removal rate $\geq 99.5\%$ and heat recovery rate $\geq 95\%$

- Asymchem is one of the first batch companies elected as a “Green Factory” by the Ministry of Industry and Information Technology of China
- Continuous breakthroughs in green technology have been achieved, generating improvements in production efficiency & significant reductions in waste generation
- Passed PSCI (Pharmaceutical Supply Chain Initiative) EHS Audit
- Advanced in-house Process Safety Lab, process hazard assessment (PHA)/facility and major process HAZOP, and safety training prior to production
- DCS (Distributed Control System) and SIS (safety instrumented system) installed to mitigate risks
- Engineering controls (with priority), administrative controls and PPE to eliminate occupational exposure
We are proud of the advancements we have made over the past 20 years and will continue to improve and innovate so that we can better serve you.

Customer Focus

Quality & Compliance

Continuous Improvement

Expansion Plans
Thanks for your time!

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