Large Molecule Bioanalytical Service in WuXi AppTec Lab Testing Division
Global Bioanalytical Services

**Capacity**
- Largest bioanalytical lab: >300 staff (~100 are large molecule) in China (Shanghai, Suzhou and Nanjing) and global operations in US (Plainsboro, NJ)
- Size: > 30,000 Sq.Ft. globally (1/3 is large molecule BA)
- Passed GLP inspection and certification by OECD(Belgium) health authorities
- Passed US FDA BE inspection and EMA inspection
- Passed Chinese FDA provincial inspections
- Submitted data accepted by worldwide health authorities, US FDA, China CFDA, EMA, PMDA, Health Canada, Australia TGA

**Compliance**
- Supported over 2000 global/China clinical trials collectively
- Over 100 active clients, including preferred vendor status with 6 of the top 20 global Pharmaceutical companies

**Collaboration**

Full Immunochemistry-based Bioanalytical Services

**Preclinical**
- Pharmacokinetics (PK) bioanalytical services
- Toxicokinetics (TK) bioanalytical services
- Immunogenicity (ADA) bioanalytical services

**Clinical**
- Pharmacokinetics (PK) bioanalytical services
- Immunogenicity (ADA) bioanalytical services
  - Screening Assays
  - Confirmatory Assays
- Neutralizing Antibody (NAb) Assays
- Pharmacodynamics (PD) and exploratory biomarker bioanalytical services
- Clinical kits for clinical trial support

Large Molecule Bioanalytical Coverage (GLP)

**Capabilities**
- Reagent Generation
  - ADA polyclonal positive control
  - Anti-id monoclonal antibody for PK/TK methods
- Method Development
- Method Transfer
- Method Validation (GLP)
- Sample Analysis (GLP)
- Fully validated LIMS system with audit trail for sample and data management

**Technology Platforms**
- ELISA
- Electrochemiluminescence (ECL)
- Radioimmunochemistry (RIA)
- Luminex
- Flow Cytometry
- Gyros
  - Automation – Tecan and Hamilton
  - Cell-based functional Assays
  - AlphaLISA

- Reagent Generation
- Assay Development / Transfer
- Assay Validation
- Sample Analysis
- Pre-Tox
- Tox
- Clinical

- ELISA
- RIA
- MSD
- Gyros
- Luminex
- Automation
- LC/MS
- MSD
- Ligand / mAb / pAb Affinity purification
Global Large Molecule Service Platforms (GLP)

**Key Capabilities**

- 70 Validated Biomarker Assays
- LM Products Supported
- Track Record of Experience

<table>
<thead>
<tr>
<th>Product type</th>
<th>Program</th>
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<tbody>
<tr>
<td>Antibody</td>
<td>&gt;30</td>
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<tr>
<td>Recombinant protein</td>
<td>&gt;10</td>
</tr>
<tr>
<td>Peptide (including conjugated)</td>
<td>&gt;10</td>
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<tr>
<td>Fusion protein</td>
<td>&gt;10</td>
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<tr>
<td>ADC</td>
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<tr>
<td>Other</td>
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<table>
<thead>
<tr>
<th>Assay Type</th>
<th>Validated</th>
<th>Study</th>
<th>Sample</th>
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<tbody>
<tr>
<td>PK</td>
<td>51</td>
<td>&gt;100</td>
<td>&gt;100,000</td>
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<tr>
<td>ADA</td>
<td>26</td>
<td>&gt;70</td>
<td>&gt;50,000</td>
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<tr>
<td>Nab</td>
<td>11</td>
<td>&gt;30</td>
<td>&gt;500</td>
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<tr>
<td>Biomarker</td>
<td>75</td>
<td>&gt;250</td>
<td>&gt;130,000</td>
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<tr>
<td>Total</td>
<td>135</td>
<td>&gt;450</td>
<td>&gt;280,000</td>
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</tbody>
</table>

- Fully validated PK and ADA methods for 6 top mAb innovators
  - PK: ELISA
    - One assay approach
  - ADA: ECL (MSD) bridging assay
    - Bioanalytical similarity assessment between innovator and biosimilar
    - One assay or parallel methods for innovator and biosimilar
- Ligand-binding (LBA) and cell-based NAb assays under development
  - LBA NAB:
    - High sensitivity
    - High drug tolerance with BEAD (Bead Extraction and Acid Dissociation)
  - Cell-based Assay:
    - Functional assay
    - Preferred method for determination of NAb activity by regulatory agencies

**In House Biosimilar Full Assay Development**

**Highlights**

- GLP validation of bioanalytical method (including PK, ADA and Nab assays) for top 6 mAb biosimilars (as listed)
- Easy access to proprietary validated method for biosimilar clients
- Platform based GLP biologics MD/MV capability
- Opportunity for further biological product development
- One-stop solution with WuXi biologics division to serve global clients

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Pharma</th>
<th>Target</th>
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<tbody>
<tr>
<td>Humira</td>
<td>Abbott</td>
<td>TNFa (fully human)</td>
</tr>
<tr>
<td>RITUXIMAB</td>
<td>Janssen</td>
<td>CD20 (chimeric)</td>
</tr>
<tr>
<td>Avastin (Bevacizumab)</td>
<td>Roche</td>
<td>VEGF (humanized)</td>
</tr>
<tr>
<td>Remicade (Infliximab)</td>
<td>Janssen</td>
<td>TNFa (chimeric)</td>
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<tr>
<td>Herceptin (Trastuzumab)</td>
<td>Roche</td>
<td>Her2/neu (humanized)</td>
</tr>
<tr>
<td>Erbitux (Cetuximab)</td>
<td>Merck</td>
<td>EGFR (chimeric)</td>
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GLP Laboratory Operation

Sample Management
- Clinical Lab located in Free Trade Zone
- Global sample receiving capability
- Expedited customs clearance (9-yr experience)
- Dedicated sample/reference management (7/24)
- Centralized temperature monitoring/alarming (phone, email, text messaging @ 7/24)
- Short and long term storage available
- Nearly 80 freezer units/rooms at -20°C or -80°C

Data Management
- Validated Watson LIMS (over 200 accounts)
- UPS and backup power systems
- Secure electronic data transfer
- Daily dual incremental backup from instruments to dedicated hard disk server in two cities
- Weekly dual full backup from disk server to tape server in two cities
- Periodic restoration test
- New server facility completed & migration in planning

Quality Assurance Unit

Structure
- QA team at each site: Shanghai (14) and Suzhou (10), US (6)

Function
- Perform in-process audits on GLP studies, study data and report audit
- 5 days average TAT from QA receipt of a submission (table or report) to QA release of the submission
- Facility Audit and Vendor Audit

Inspection History (no critical finding to impact study)

- Passed OECD, CFDA audits
- Passed FDA, OECD and CFDA audits
- Passed CFDA, OECD audit

2009
2011
2013
2015

2010
2012
2014

Passed CFDA audit
Passed CFDA audit
Passed EMA, CFDA audits