Henlius
HLX02 (Trastuzumab) EU GMP Status Update

April, 2020
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Mission & Vision

**Mission**

“To improve patients’ lives by timely providing them with quality and affordable protein therapeutics through technical innovation and operation excellence.”

**Vision**

“Be the most trusted and admired biotech company providing innovative and affordable medicines to all patients.”

- Reliable Quality
- Affordable Innovation
- Biosimilars + Bio-innovatives + Combo
- Quality Focus • Global Footprints

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HLX02 (Trastuzumumab) EU GMP Approval
1.1 Henlius HLX02 (Trastuzumab) of Xuhui Facility Received Official EU GMP Approval

GMP Certificate
- Certified product: HLX02 (trastuzumab for injection) (lyophilized powder)
- Certification body: Chief Pharmaceutical Inspector (a health regulatory body in Poland)
- Certification scope: drug substance, cell bank preparation, storage and management, lyophilized drug product line in Xuhui facility
- Valid period: 3 years

Applicable Regions
- According to the GMP mutual recognition system of EU member states, the Company’s Xuhui Facility has met the GMP standards of the EU
- EU GMP certification can be mutually recognized and shared among nearly 30 member states
- Inspection results can be shared with nations such as U.S. and Canada which signed Mutual Recognition Agreement (MRA)

Global Impact
- “EU Guidelines for Biosimilars” (CHMP/47/04) took effect in 2005, which is the world’s first guiding principle for biosimilar research and evaluation
- EU GMP certification is one of the world’s most authoritative and stringent certifications, it has a significant global influence and is considered as a “PASS” for drugs to access global markets
EU MAA Application for HLX02 (Trastuzumab) Accepted in June, 2019

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trastuzumab</th>
</tr>
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</table>
| Originator Drug | Herceptin® (Genentech & Roche)  
USA: Approved in 1998  
EU: Approved in 2000  
China: Approved in 2002 |
| HLX02 | Recombinant Anti-HER2 Humanized Monoclonal Antibody Powder for Concentrate for Infusion  
Biological Product for Treatment  
International Multicenter phase III clinical Trials |
| Indications | Metastatic breast cancer, early-stage breast cancer, metastatic gastric cancer |

HLX02 Registration Application Process

- CTA Approval: 2017.05-09
- MAA Accepted by EMA: 2019.06
- EMA GCP Inspection: 2019.10-2020.01
- EMA GMP Inspection: 2019.12
- Pass GCP Inspection: 2020.03
- Pass GMP Inspection: 2020.04

EMA SA Meeting: 2016.06
1.3 Henlius Established Strict Quality System Based on Global Standards since Inception

Quality Management System

Drug Production

- Quality Assurance
- Label/Packaging Control
- Quality Control
- Supply Chain Management
- Production Management

Based on “Good Manufacturing Practice” (revised in 2010), Henlius established drug quality management system using global standards and ensured production of high quality drugs.

175 staff in quality management team, with a ratio of 7:10 compared with staff in production and operation team.

# of quality and production staff

- 2015: 59 (Quality), 50 (Production)
- 2016: 73 (Quality), 89 (Production)
- 2017: 101 (Quality), 120 (Production)
- 2018: 116 (Quality), 153 (Production)
- 2019: 175 (Quality), 250 (Production)
### Successful Inspection Results with High Standard Quality System

<table>
<thead>
<tr>
<th>Inspection Org</th>
<th>External Expert</th>
<th>Fosun Group</th>
<th>Business Partners</th>
<th>NMPA</th>
<th>SFDA</th>
<th>Foreign Drug Regulatory Agencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inspection #</td>
<td><strong>30</strong></td>
<td><strong>9</strong></td>
<td><strong>3</strong></td>
<td><strong>4</strong></td>
<td><strong>20</strong></td>
<td><strong>1</strong></td>
</tr>
<tr>
<td>Inspection Reason</td>
<td>Continuous improvement of quality system</td>
<td>Routine Inspection</td>
<td>DD/Quality audit</td>
<td>NDA Inspection</td>
<td>- IND Inspection</td>
<td>- GMP Certification</td>
</tr>
</tbody>
</table>
| Inspection Scope    | All Quality Systems | All Quality Systems | All Quality Systems | All Quality Systems | All Quality Systems | All Quality Systems |}

- Conducted multiple inspections / audits with the help of domestic and foreign regulators
- Invited domestic and foreign experts for mock audit / consultation, (e.g. UK, Poland, US)
- Completed more than 1,600 quality system improvements
## A Significant Value for Facilities with EMA/FDA GMP Certification Has Been Demonstrated by Previous Deals

<table>
<thead>
<tr>
<th>Acquirer</th>
<th>Owner of Manufacturing Facility</th>
<th>Facility Information</th>
<th>Acquisition Time</th>
<th>Deal Value (USD)</th>
</tr>
</thead>
</table>
| FUJIFILM          | Biogen                          | Deal Location: Denmark  
- 6 X 15,000L Bioreactors  
- Certification: EMA | 2019              | ~$890M           |
| Catalent          | COOK                            | Deal Location: USA  
- 2 X 2,500L Bioreactors  
- 1 X 600L Bioreactor  
- Multiple 100L Bioreactors  
- Certification: FDA | 2017              | ~$950M           |
| AGC               | CMC biologics                   | Deal Location: USA/Denmark  
- 1 X 2,000L Bioreactor  
- 2 X 1,500L Bioreactors  
- 5 X 3,000L Bioreactors  
- Certification: FDA/EMA | 2016              | ~$510M           |
Globalization Strategy
### Quality Attributes

#### Methods

- **HLX**
- **Originator**

### Functional Characterization

- **FcRn binding**
  - SPR
- **FcyR binding**
  - SPR
- **Target binding**
  - Cell based or ELISA binding assay
- **Anti-proliferation potency**
  - Cell based assay
- **C1q binding**
  - ELISA
- **CDC potency**
  - Cell based CDC assay
- **ADCC potency**
  - Cell based ADCC assay
- **Apoptosis**
  - Cell based apoptosis assay

### Others

- **Stress stability**
  - 40°C
  - R-PM-UPLC-MS/CEX/SEC

### Clinical Data

- **PK in Cynomolgus Monkey**
- **Toxicology - Single Dose**
- **Toxicology - Multiple Doses**
- **Immunogenicity Study in Monkeys**

### Structural Characterization and Biosimilarity Data Package

#### Category

- **Physicochemical Characterization**
  - **Primary structure**
    - Amino acid sequence
  - **Higher order structure**
    - Secondary and tertiary structure
  - **General charge heterogeneity and modifications**
  - **Charge heterogeneity**
  - **Size heterogeneity**
    - LMW, HMW and monomer

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**2.1 Advance with High Quality Standard**

- **China’s first** biosimilar with global multi-center Phase 3 clinical trial (2017-2019)
- **China’s first** trastuzumab developed based on “Guiding Principles of Biosimilars” with NDA accepted by NMPA (2019.04)
- **China’s first** domestic mAb biosimilar to file NDA (2019.06) in EU as well as the first “Chinese” trastuzumab to receive EU GMP certificate (2020.04)
Our Partner Accord Will Commercialize HLX02 for EU While Henlius Will Be Responsible for China Market

### Henlius/Accord Transaction Regarding HLX02
- Henlius grants Accord exclusive license to commercialize HLX02 in Territory (53 countries in Europe, 17 in Middle-East North Africa, and some CIS countries) including but not limited to sales, import, distribution, and other commercialization activities
- Henlius will receive milestone payments (not exceeding USD 40.5 million) and royalties
- Through its global R&D, manufacture and sales network, Accord will accelerate the expansion of overseas market

### About Accord
- Accord is a global pharmaceutical company primarily engaged in the business of developing, manufacturing and marketing generic products and biosimilars in North America, Europe, Australia, South Africa, and other regions
- Ranked top three in Europe for sales of generics, and No.1 for sales of generics in oncology
- + 8,500 generic products on market, covering more than 85 countries with a strong portfolio of products in areas including cancer, heart disease, mental illness, and diabetes
- Products manufactured under International Standards in plants approved by USFDA, MHRA, EMA, TGA, MCC, ANVISA, etc
- Committed to providing high quality and affordable products and services to patients, with the goal of becoming the world's leading healthcare provider

### Key terms

<table>
<thead>
<tr>
<th>Licensee</th>
<th>Accord Healthcare Limited</th>
</tr>
</thead>
<tbody>
<tr>
<td>License</td>
<td>Shanghai Henlius Biotech Inc.</td>
</tr>
<tr>
<td>Effective Date</td>
<td>2018-06</td>
</tr>
<tr>
<td>Product</td>
<td>HLX02 (Trastuzumab)</td>
</tr>
<tr>
<td>Territory</td>
<td>Europe, Middle-East North Africa, Commonwealth of Independent States (&quot;CIS&quot;)</td>
</tr>
<tr>
<td>License granted to Accord</td>
<td>Exclusive rights for the commercialization of the Product and exclusive supply</td>
</tr>
</tbody>
</table>
| Milestone Payments | • Upfront on the effective date: USD 8 million  
  • Upon EMA’s acceptance of the MAA submission: USD 5 million  
  • On Day 105 of the centralized procedure: USD 5 million  
  • Upon EMA’s approval of the MAA: USD 5 million |
| Royalties | 13.5%-25% of the net sales |

Data source: Company announcement
2.3 EU GMP Approval Is an Important Step for Us to Establish Strong Global Commercialization with Our Strategic Partners

- Exclusive licensing and commercial rights of rituximab (HLX01) in Colombia, Peru, Ecuador and Venezuela
- Exclusive commercial rights of PD-1 (HLX10) in Philippines, Indonesia, Malaysia, Singapore, Thailand, Laos, Myanmar, Cambodia, Brunei and Vietnam
- Exclusive commercial rights of trastuzumab (HLX02) for over 70 jurisdictions and regions in Europe, MENA, North Africa and CIS

Jointly advance product commercialization of HLX01/03 in the PRC with Fosun Pharma
- Exclusive commercial rights of rituximab (HLX01) and adalimumab (HLX03) in the PRC

Benefit from Fosun Pharma:
- Decades of market experience and know-how in a changing Chinese healthcare industry
- Superior market access ability, providing comprehensive coverage for product portfolio
- Extensive sales network covering both higher and lower tier markets, penetrating deeply nationwide

Self-managed sales team is in charge of China sales of HLX02 (trastuzumab) and following products
- 100+ clinical study sites, 5+ years of clinical trial experience and access to a comprehensive KOL and physician network
- Assemble a sales team of 400-500 staff during the year

Note: as of March 31, 2020
Review and Outlook
3.1 Henlius Is Committed to Helping Domestic and Overseas Patients with Global Quality

- Successful launch of HLX02 is a key focus of 2020, will become an engine and a cornerstone of Henlius commercialization

- **Enhance manufacturing capacity:**
  - Accelerate capacity optimization and maximization, as well as build brand image of “Made by Henlius, International Quality”
  - Strategic planning of long-term domestic and overseas biopharmaceutical manufacturing base

- **Business development:**
  - Achieve synergy with Fosun Pharma via strategic partnership on product development
  - Actively seek domestic and overseas BD opportunities, including product license-out, joint-venture, and etc.

- **Innovation of commercialization model:**
  - Win-Win strategy of multiple-party cooperation: actively collaborate with multiple partners such as PhIRDA, building a domestic biosimilar ecosystem together, demonstrating “the most reliable” value of Henlius

- **Optimize commercial operation:**
  - Sales team management
  - Market penetration
  - Access (pricing strategy, payment plan etc)

- **Organization model based on talent + ability + culture:**
  - Best talent
  - Highly efficient team
  - Strong focus on Compliance
### Recent Progress Strengthens Our Confidence to Achieve Full Year Target

<table>
<thead>
<tr>
<th>Major Milestones</th>
<th>Current Status</th>
<th>Guidance</th>
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<tbody>
<tr>
<td><strong>Products/Development</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HLX02 EMA MAA approval</td>
<td>GCP, GMP approved</td>
<td>HLX02 approved in EU in 2H20</td>
</tr>
<tr>
<td>HLX02 China NDA approval</td>
<td>On progress as scheduled</td>
<td>HLX02 China approval and launch in mid-2020</td>
</tr>
<tr>
<td>Other products</td>
<td>On progress as scheduled</td>
<td></td>
</tr>
<tr>
<td><strong>Manufacturing</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HLX01 2,000L sNDA approved</td>
<td>Approved on April 14, 2020 (see previous announcement)</td>
<td>End of April/ early May</td>
</tr>
<tr>
<td>Songjiang Plant One pilot production</td>
<td>Pilot production started in early April 2020</td>
<td>2Q20</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td></td>
<td></td>
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<tr>
<td>STAR board (A share) listing</td>
<td>Kick-off on March 30, 2020 (see previous announcement)</td>
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Reliable Quality | Affordable Innovation