KriSan Biotech

KriSan Biotech Co., Ltd.

International
CDMO Expert
in
GMP Drug Substance

KriSan Biotech

Innovation·Focus·Profession

- Established in August, 2015.
- Accredited Contract Development and Manufacturing Organization

  Pharmaceutical Research Company (approved by Taiwan MOEA)

  Small Molecule, Complex Drug Substance,

  Peptide, Oligonucleotide.
- Six GMP production lines.
- Taiwan FDA GMP certificate for pilot plant (2019.03.11).
- Japanese Accreditation of Foreign Manufacturers (AFM) certificate.

Southern Taiwan
Science Park
3F, 4F, 5F

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Drug Substance Contract Service

PIC/S GMP and ICH Compliance

- Research
- Preclinical Study
- IND Application
- Phase I
- Phase II
- Phase III
- NDA Application
- Exclusive Launch

Research (Chemistry)

Development (Control)

GMP (Manufacturing)

Process and Analysis R&D

Validation and Stability Test

CMC Documentation

Authority Inspection

Technical Transfer Service

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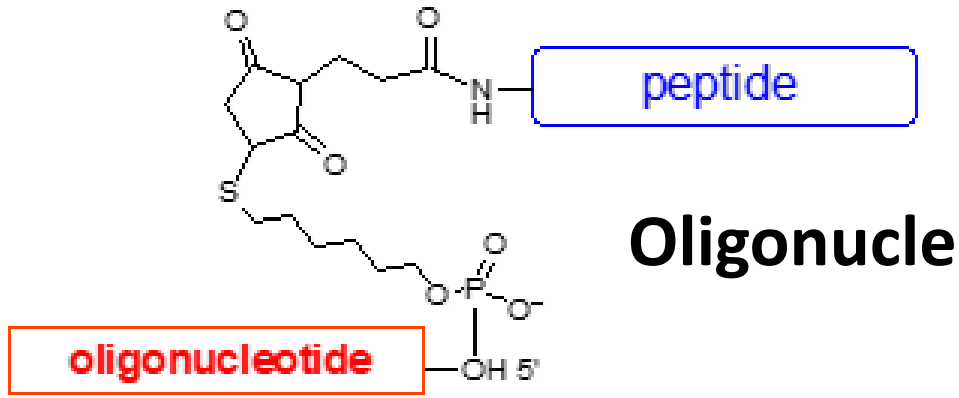
Provide GMP Adjuvant Molecules

- **Type 1:** Oligonucleotides (start from Feb. 2022)
- **Type 2:** Antigenic Epitope Peptides
- **Type 3:** Customized synthetic molecules (Conjugate)
- **Type 4:** Natural Products (Purification)



Thiol-Maleimide linkage

Oligonucleotide---Peptide Conjugate

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Drug Substance Supply from Preclinical

1. Disease Selection	2. Gene function	3. Target to Lead	4. Lead to Candidate	5. Approval for human (IND)	6. Phase I 20 -100 volunteers Safety and tolerability in healthy volunteers	7. Phase II 100 to 300 patients Efficacy Safety	8. Phase III 1000 to 2000 patients International multicenter trials different patient populations Pproof of efficacy, safety and value	9. File to Launch (NDA)	10. Life cycle

Appropriate GMP and GMP

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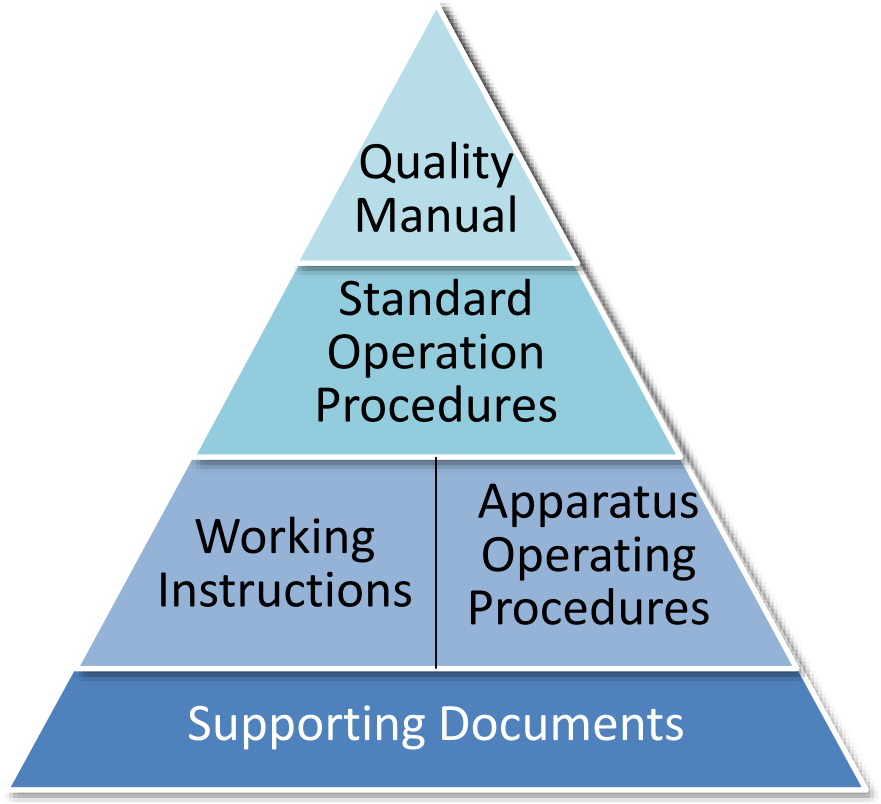
Quality Management System



- Personnel Qualification
- Equipment and Facilities
- Material Management
- Production and In-process Control
- Labelling Control
- Storage and Distribution
- Laboratory Control
- Change Control
- Non-Conformance Event Management & CAPA
- Documentation and Records
- Contractor and Consultant
- Internal Audit
- Complaints and Recalls

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Quality Control & Quality Assurance

Quality Control

- **Raw & Starting Materials**
  - Method Development / Validation
  - Sample Testing
  - Establish Specification
- **Standard**
  - API, intermediate, Impurity Ref. Std. Qualification
- **In Process Control**
  - IPC Method Development /Validation
  - IPC Sample Testing
  - Key Intermediates Testing
- **API**
  - API Method Development / Validation
  - Cleaning Method Development / Validation
  - Cleaning Sample Testing
  - API Testing / COA Issuance
  - Establish Specification
- **Stability**
  - Stability Study Conditions:
    -20 ℃, 5 ℃, 25 ℃, 30 ℃, 40 ℃

Quality Assurance

- Product Release
- Change Control
- Investigation & Deviation Management
- CAPA Program Management
- Complaint Handling
- Document Control
- Review & Approval of GMP Documentations
- Internal Audits
- Handling Customer Audits and Regulatory Inspections
- Vendor Audits
- Training Coordination/ GMP Training

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Achievements since 2015.08~~

- **45** Customers：

  USA、Japan、European、Singapore、Middle East and Taiwan

- **88** Products Delivered：

  Small Molecule：**64 Products**。

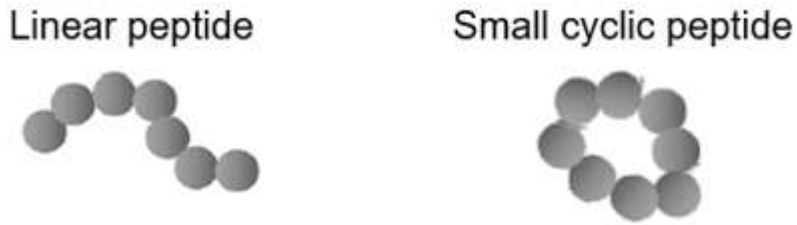
  Complex Drug Substance：**14 Products**。

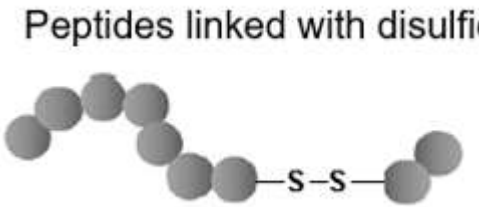
  Peptide：**8 Products**。

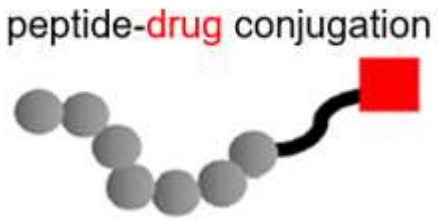
  Oligonucleotide：**2 Products**。

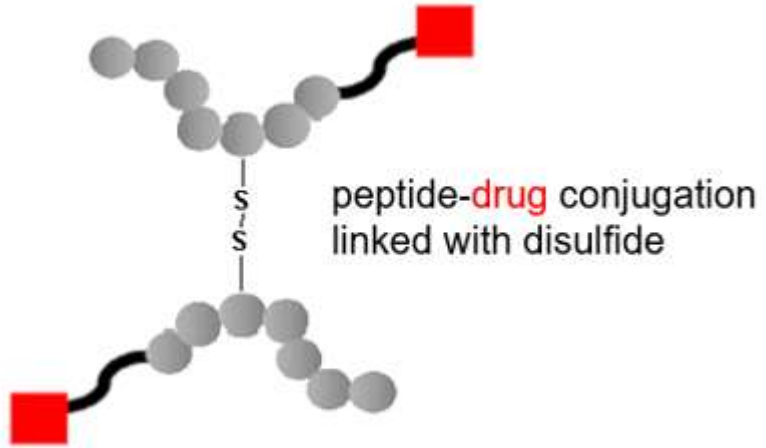
- **11** Clinical Phase Products：

  1 Phase III，6 Phase II，4 Phase I









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Oligonucleotide

- Analytical Method Evaluation
- Stability Studies: **36 months**

  Long-Term: -20°C

  Accelerated: 5 ± 3 °C

AKTA Oligo 100

1 µmol to 9 mmol

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Analytical Instrument

Chemical Property Determination	Physical Property / Spectroscopic Analysis	Stability Study
➢ HPLC / UPLC - UV - PDA - Refractive Index - Fluorescence ➢ GC / Headspace GC ➢ Auto-titration ➢ Total Organic Carbon	➢ DSC ➢ TGA ➢ Polarimeter ➢ Particle Size Analyzer ➢ Karl Fisher - Volumetric - Coulometric - Thermoprep (oven) ➢ Melting Point ➢ FT-IR ➢ UV-Vis ➢ ICP-MS / / Microwave digestion ➢ Vacuum Oven ➢ Conductivity Meter	➢ Stability Chamber -20 °C 5 °C 25°C / 60%RH 30°C / 65%RH 40°C / 75%RH ➢ Suntest **Outsourcing** ➢ Dynamic Vapor Sorption (DVS) ➢ NMR ➢ Mass (LC-MS, GC-MS, MS-MS) ➢ X-Ray diffraction ➢ Microbiological Examination ➢ Specific Microorganisms

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GMP Manufacturing Equipment

Line No.	API Batch	Equipment	Temeperature ℃	Glove Box Filter Dryer (Hastelloy C276)	Status
1	1 kg	10 L and 30 L Reactor (Glass)	-60 to 150	10 L	Qualified
2	3 kg	20 L and 60 L Reactor (Glass)	-25 to 150	10 L	Qualified
3	4 kg	30 L and 63 L Reactor (Glass)	-25 to 150	10 L	Qualified
4	100 g · Oligonucleotide · Peptide · Complex Drug Substance **Preparation** **Purification**	**Oligonucleotide Synthesizer** (AKTA Oligo 100) **DAC Column Purification** (HPLC Grade Column Ø 150* 450 mm)	NA	NA	Synthesizer (2022.02) DAC Column (Qualified)
5	10 L · Oligonucleotide · Peptide · Complex Drug Substance **Purification** **Lyophilization**	**Plate type lyophilizer** (0.67 m^2 effective shelf area vacuum < 0.01 mbar) **Semiauto-Ultrafiltration** (filtration area from 0.5 to 5 m^2)	-70 to 80	NA	Qualified
11	10 kg	250 L and 160 L Reactor (Glass-lined)	-25 to 150	40 L	Qualified

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From Research to GMP Production

GMP Production Capability

- 10L to 250 L, Glass-lined Reactor (1 to 10 kg/batch)
- Glove Box Operation (Nitrogen)
- DAC Column (∅150*450 mm, 100 mL/load)
- TFF-Ultrafiltration Equipment (100 L)
- Lyophilization Equipment (10 L, 5 Trays)
- Peptide Synthesis (Solid Phase Synthesis, 20 L)
- Oligo100 Synthesizer (1 μmol to 9 mmol, 0.009 to 80 g for 30 mers)

Acknowledgement

Key relationship in Science and novel Biotech