Peptide Drug Development  SR-DDS BIOTECH

Since 1997

IPO on July 22, 2015 (KOSDAQ)
Peptide?

biologically occurring short chains of amino acid monomers linked by peptide (amide) bonds

Generally, composition of <50 amino acids is classified as peptide while >50 amino acids is accepted as protein.

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**Amino Acids**

<table>
<thead>
<tr>
<th>Peptide</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>: Hormones</td>
<td>: Enzyme, Antibody</td>
</tr>
<tr>
<td>insulin</td>
<td></td>
</tr>
</tbody>
</table>

**MW**

<table>
<thead>
<tr>
<th>Small molecule</th>
<th>Peptide</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amino Acids</strong></td>
<td>5</td>
<td>50</td>
</tr>
<tr>
<td><strong>MW</strong></td>
<td>500</td>
<td>5,000</td>
</tr>
</tbody>
</table>

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**Chemical Synthesis**

manufacturing

Recombinant (biologics)

microorganism, cell culture

generic ↔ biosimilar
Market Trend of Peptide Drug

Peptide Drug - Biological amino acid polymer

Better Safety & Efficacy but,

- Low stability
- Low oral bioavailability

→ Injections & frequent dosing

Development of Long-Acting Form to maximize efficacy & compliances

Big Market Potential of Long-Acting form

[Prostate Cancer]
Leuprolide
- monthly
  - 1989
- Lupron Depot®
  - Global No. 1
- $1.88B
  - 2016

[Acromegaly]
Octreotide
- monthly
  - 1998
- Sandostatin® LAR
  - Global No. 1
- $1.65B
  - 2016

[Diabetes]
GLP-1 analog
- 2005 Twice-daily Byetta® (exenatide)
- 2009 Once-daily Victoza® (liraglutide)
- once weekly
  - 2012 Bydureon® (exenatide)
  - 2014 Tanzeum® (albiglutide)
  - 2014 Trulicity® (dulaglutide)

1989
1998
2005
2009
2012
2014
2016
Market Trend of Peptide Drug

Type2 Diabetes market forecast by class in the US, Japan, and 5EU

$23.3B (2014) → $42.3B (2023)

Marketed & late-stage pipeline (Ph3) products

### Peptide/Protein (injection): 58% market share
- FDC (GLP-1 + long-acting insulins) → $0 → $3.1B
- GLP-1 agonists (~1-week) → $4.1B → $8.6B
- Long-acting insulins (Basal, Daily) → $6.1B → $8.9B
- Fast-acting/pre-mix insulins → $3.3B → $4.1B

### Small Molecule (oral)
- FDC (DPP-4 + SGLT-2 inhibitors)
- etc.
- SGLT-2 inhibitors
- DPP-4 inhibitors → $7.8B → $9.6B

*FDC: Fixed Dose Combination*
Chapter 2

Platform of Technology

Long-Acting Technology Roadmap

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**SR-DDS (Sustained Release)**
- Oil / Suspension
- In situ forming Gel

*LAR (Long-Acting Release)
- *Microsphere (Depot)*
  - Emulsion Type
    - Takeda, Alkermes
  - Spray Drying Type
    - Peptron

**Modification**
- PEGylation
- Fatty acid Linkage

**Carrier Protein Linkage**
- Conjugation (external)
- Fusion Protein

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**Depot/LAR Platform of Technology**

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**Peptide**
**Protein**

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- No change of API; better to have 100% efficacy
- Easier to make Longer acting-form (monthly form)
- Possible to bypass stability/safety study of API

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- Modified API; Efficacy may not be guaranteed
- Max 1-week (monthly form on development)
- New drug \( \rightarrow \) requires full clinical trials
Platform of Technology

Sustained Release Depot Formulation

Drug

Carrier: Biodegradable Polymer

Biodegradation of Carrier
→ Sustained Release of Drug
Platform of Technology

Manufacturing

[Ultrasonic Spray Drying]

API + Solvent

Carrier + Solvent

Ultrasonic nozzle

Spray-Dryer

Homogeneous, size controllable & Good reproducibility

★ Microsphere

API

Peptide
> Small molecule
> Protein

Carrier

Bio-degradable Polymer:
PLGA, PLA > PGA

Solvent

Class 3 solvent:
glacial acetic acid (Non toxic)
**Platform of Technology**

**Process Comparison**

**Spray Drying type**
- Spray drying of Exenatide and PLGA in single clear solution
- Residual solvent removal
- Recovery & Drying

**Emulsion type**
- Exenatide & sucrose in water
- PLGA in organic phase
- High-speed mixing
- Primary emulsion
- Polymeric Precipitant (silicon oil)
- Embryonic microparticles
- Hardening Washing
- Recovery
High production yield and reproducibility

Continuous process / easy to Scale-up

Non-toxic solvent


Lab-scale GMP Compliant cGMP for Regulated Market

Platform of Technology

Achievements of Unique Tech & Equipment
Platform of Technology
Better Features for Convenience

01 Syringeability of suspension
- Injection force: < 20 N
- 27G - 30G needle applicable

02 Resuspendability of reconstitution
- Less than 10 seconds

03 Sedimentation Time after reconstitution
- Over 2 minutes

Size comparison
(a) 21 gauge (b) 27 gauge (c) 31 gauge (d) 33 gauge
LUPHERE® DEPOT (SR-Leuprolide, 1-month)
for Prostate cancer

The First Marketed product from Peptron
License out to Daewoong → commercial sales & marketing

- Generic of Lupron Depot® (Takeda)
- Similar efficacy & safety with original confirmed through successful Phase IV study
- Experienced from R&D to commercialization
- Setting up key technologies for product development
# Drug Development Pipeline

## SR peptide drug pipeline by developing stages

<table>
<thead>
<tr>
<th>Category</th>
<th>Stage</th>
<th>Description</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SR-Generic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>SR 1</td>
<td>(SR 1 month) generic of Lupron Depot® (Takeda)</td>
<td>Approved/Marketed</td>
</tr>
<tr>
<td>Acromegaly</td>
<td>SR 1</td>
<td>(SR 1 month) generic of Sandostatin LAR® (Novartis)</td>
<td>L/O to DAEWOONG → Royalty 5% of net sales</td>
</tr>
<tr>
<td><strong>New-SR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes: GLP-1 class</td>
<td>Ph2</td>
<td>(SR 2 weeks) Ph2 finished in Korea</td>
<td>SR-1 site (KGMP/on-going)</td>
</tr>
<tr>
<td>GLP-1 class</td>
<td>Global</td>
<td>(SR 1 month) Global Ph2 preparing</td>
<td>Clinical study sample and commercial product for Korea</td>
</tr>
<tr>
<td>Insulin</td>
<td></td>
<td>(SR 1 week) Preclinical / Animal study</td>
<td>SR-2 site (cGMP/Planned)</td>
</tr>
<tr>
<td>Prostate cancer: Goserelin</td>
<td></td>
<td>Formulation candidate</td>
<td>Ph 3 and commercial for US/EU</td>
</tr>
<tr>
<td><strong>Drug Repositioning</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson’s: GLP-1 class</td>
<td>Ph2</td>
<td>(SR 2 weeks) Ph2 IND approved</td>
<td>Acquired Exclusive patent license from NIH</td>
</tr>
<tr>
<td><strong>New Peptide Drug</strong></td>
<td></td>
<td></td>
<td>CRADA with NIA, NIH</td>
</tr>
<tr>
<td>SR development collaboration</td>
<td></td>
<td></td>
<td>SR formulation feasibility test</td>
</tr>
</tbody>
</table>
Osong SR-1 site
- Manufacturing of clinical sample and R&D on site
- Osong High Tech Medical Cluster 18-5 block
- Area: 10,912 m²

Drug Development Pipeline

Osong SR-1 manufacturing site

<table>
<thead>
<tr>
<th>Procedure</th>
<th>2Q 2017</th>
<th>3Q 2017</th>
<th>4Q 2017</th>
<th>1Q 2018</th>
<th>2Q 2018</th>
<th>3Q 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Construction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Installation &amp; Piping</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>DQ / IQ / OQ</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PQ / APV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PV batch production</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Drug Development Pipeline

Parkinson’s Disease

Limitation of current options (Levodopa)

- Short duration of efficacy and only symptom release
- First line standard treatment option but has withdrawal syndrome

Source: Neurological benefits of GLP-1 receptor activation, NIA, NIH, 2012 (Review Article)
At Johns Hopkins Bayview Medical Center

Drug Development Pipeline

Peptron & NIH(NIA)

US NIH firstly confirmed possibility of neurodegenerative disease treatment with brain GLP-1 receptor agonist

- Acquired Exclusive patent license of usage for neurodegenerative diseases from NIH in 2014
- Collaborative Research and Development Agreement (CRADA) with NIH for neurodegenerative disease in 2014
- Drug-Repositioning → additional indications (Alzheimer’s, TBI, etc.)
Drug Development Pipeline

Global R&D overview - PD

About 50 New products are in development pipeline globally in Phase 2 or later stages

- Pipeline : 3
  - Filed
  - Annual sales(2022) : $ 308 mil
  - Rasagiline Mesylate (Takeda)
  - Neupro (New Bridge Pharmaceuticals)
  - Inbrija (Acorda Therapeutics)

- Pipeline : 15
  - Ph III
  - Annual sales(2022) : $ 459 mil
  - Tozadenant (Acorda Therapeutics)
  - PF-06649751 (Pfizer)
  - APL-130277 (Sumitomo Dainippon Pharma)

- Pipeline : 62
  - Ph II
  - Annual sales(2022) : $ 363 mil
  - ND0612H (NeuroDerm)
  - Ongentys (Ono Pharmaceutical)
  - NTCell (Otsuka Holdings)

Excluding Generics, Source : Evaluate Pharma
Drug Development Pipeline

Mechanism of Neurological Effects of GLP-1

Ref. Cell Transplant 2017 Sep;26(9):1560-1571
• Difference of off medication scores in MDS-UPDRS part3 are -3.5 points at 60 weeks and -4.3 points at 48 weeks comparison with control and exenatide treated group

• Compared with placebo, exenatide treatment is associated with positive and persistent effects on off-medication motor scores as measured by MDS-UPDRS part 3.

• GLP-1 receptor agonists have a useful role in the treatment of Parkinson’s disease.
**Drug Development Pipeline**

**Why Exenatide for PD treatment?**

1. Proof of concept study shown possibility of disease modifying effect with 12 months treatment (Aviles-Olmos et al, 2013) – Byetta (daily Exenatide)

2. Similar outcomes with treatment duration as 48 weeks shown in another study (Athauda et al, 2017) – Bydureon (weekly exenatide)

3. Proven safety for exenatide after commercialization in 2005 (Byetta, AZ)

4. Can across through Blood Brain Barrier (BBB)

First in Class & New option for unmet medical needs of PD
Company Overview

History

Continuous development of high potential sustained release type peptide drugs with proven peptide synthesis and SR DDS technology

1997
- Establishment of Peptron, Inc.

1998
- Start peptide custom synthesis business for research use
- Established the company affiliated R&D institute named as Peptron Biochemistry Research institute

1999
- Certified as venture company

2001
- Certified as a Technology Innovative small sized Business (INNO-BIZ)
- Acquired certification of ISO 9001 for peptide synthesis

2003
- Signed license-out agreement with Daewoong Pharmaceutical Co, Ltd. on the technology transfer for prostate cancer treatment
- AchievedExporting Peptides to over 25 Nations in Worldwide

2004
- Selected as “Advanced Technology Center (ATC)"

2005
- Launched an Anti-cancer agent (Prostate cancer) (Daewoong Pharmaceutical Co, Ltd., Luphere Depot inj.)
- Assigned as the Special District R&D Project by The Ministry of Science and Technology

2007
- Acquired Certification of NET for “Manufacture Process Technology of Slow Release Microsphere injectable Formulation, using Ultrasonic Spray Drying”

2009
- Approval of Phase 1 clinical trial for type 2 diabetes (PT302)

2011
- License out agreement of Diabetes treatment drug with Yuhan corporation
- KFDA Approval of Phase II clinical trial for the Sustained Release Anti-diabetic Drug
- Agreement on Neurodegenerative Disease exclusive license-in and Cooperative Research and Development Agreement (CRADA) with NIH
- Approval of phase 2 clinical trial for Parkinson’s disease
## Financial Statement

### Consolidated Financial Position statement

<table>
<thead>
<tr>
<th>Year</th>
<th>2017 3Q</th>
<th>2016 FY</th>
<th>2015 FY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accounting Standard</td>
<td>K-IFRS</td>
<td>K-IFRS</td>
<td>K-IFRS</td>
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<tr>
<td>Current Asset</td>
<td>33,477</td>
<td>49,107</td>
<td>14,843</td>
</tr>
<tr>
<td>Long Term Asset</td>
<td>21,181</td>
<td>8,795</td>
<td>6,813</td>
</tr>
<tr>
<td>Total Asset</td>
<td>54,658</td>
<td>57,902</td>
<td>21,656</td>
</tr>
<tr>
<td>Current Liabilities</td>
<td>1,344</td>
<td>924</td>
<td>2,912</td>
</tr>
<tr>
<td>Long term Liabilities</td>
<td>3,257</td>
<td>3,769</td>
<td>1,517</td>
</tr>
<tr>
<td>Total Liabilities</td>
<td>4,601</td>
<td>4,693</td>
<td>4,429</td>
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<tr>
<td>Capital</td>
<td>3,785</td>
<td>3,695</td>
<td>3,250</td>
</tr>
<tr>
<td>paid-in capital in excess of par value</td>
<td>71,538</td>
<td>71,628</td>
<td>32,565</td>
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<tr>
<td>Other capital surplus</td>
<td>278</td>
<td>278</td>
<td>278</td>
</tr>
<tr>
<td>Earned Surplus</td>
<td>(25,544)</td>
<td>(22,392)</td>
<td>(18,866)</td>
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<tr>
<td>Total Equity</td>
<td>50,057</td>
<td>53,209</td>
<td>17,227</td>
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<tr>
<td>Liabilities and Equity</td>
<td>54,658</td>
<td>57,902</td>
<td>21,656</td>
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### Consolidated Income statement

<table>
<thead>
<tr>
<th></th>
<th>3Q 2017</th>
<th>3Q 2016</th>
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</thead>
<tbody>
<tr>
<td>Revenue</td>
<td>640</td>
<td>1,732</td>
</tr>
<tr>
<td>Cost, Expenses, and Others</td>
<td>292</td>
<td>1,008</td>
</tr>
<tr>
<td>Gross Profit</td>
<td>348</td>
<td>724</td>
</tr>
<tr>
<td>Selling and Administrative Expenses</td>
<td>1,350</td>
<td>4,101</td>
</tr>
<tr>
<td>Operating Profit</td>
<td>(1,002)</td>
<td>(3,377)</td>
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<tr>
<td>Other Income</td>
<td>23</td>
<td>77</td>
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<td>Other Expenses</td>
<td>12</td>
<td>462</td>
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<td>Financial Income</td>
<td>125</td>
<td>423</td>
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<tr>
<td>Financial Expenses</td>
<td>0</td>
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<tr>
<td>Income before taxes</td>
<td>(866)</td>
<td>(3,338)</td>
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<tr>
<td>Income Taxes</td>
<td>0</td>
<td>(41)</td>
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<tr>
<td>Net Income</td>
<td>(866)</td>
<td>(3,297)</td>
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</table>
Better compliance and beyond,
COZY CURE