

**NOVEL BIOLOGICS** FOR BETTER LIFE

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Investor Relations | October 2020



# Contents

Investor Relations

ALTEOGEN Inc.

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4. Biosimilar (ALT-L9)
5. Hyaluronidase (ALT-B4)
  - Herceptin SC Biosimilar (ALT-LS2)

Established 13<sup>th</sup> of May, 2008

CEO Soon Jae Park

Headquarter Daejeon

IPO KOSDAQ: 196170 (2014)

Subsidiary ▶ Ceres F&D Inc.  
(KGMP Certified/cGMP planned)

- Teicoplanin
- Tacrolimus
- Everolimus



▶ LS Meditech Corp.  
- Drug Distribution Company

### History

- May 2008 Company Establishment
- June 2010 CEO Soon Jae Park inaugurated
- December 2014 KOSDAQ Market listed
- June 2018 A subsidiary company was established (Ceres F&D Inc. )



# ALTEOGEN's Business Domains

Platform Provider for Biobetter Drugs

## Biobetter Platforms

Long-acting  
Biobetter

- Technology to increase half-life

Antibody-Drug  
Conjugate (ADC)

- Novel anti-cancer drug

## Prioritized Biosimilars

Biosimilars

- Differentiated Biosimilar technology

## Enabling Technology

Hyaluronidase

- Novel human hyaluronidase for Mab SC use
- Dermal and Ophthalmology use

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Platform Provider for Biobetter Drugs

2008~

Long-acting  
Biobetter

- long-acting **hGH**, and **GLP-NexP-FGF19**

2011~

Antibody-Drug  
Conjugate (ADC)

2014~

Biosimilars

2018~

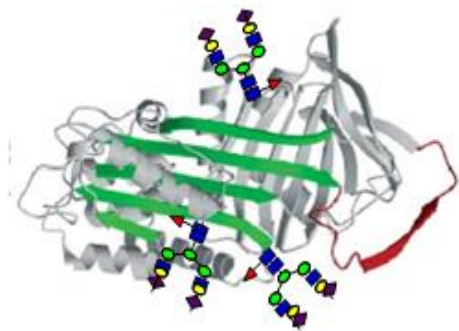
Hyaluronidase





# Development of NexP™ Fusion Technology – Long acting Biobetter

## A1AT (Alpha 1 Anti Trypsin)



### ► Specification

- Abundant in human blood (1.5~3.5 g/L)
- Long *in-vivo* half life (4.5~6.0 days)

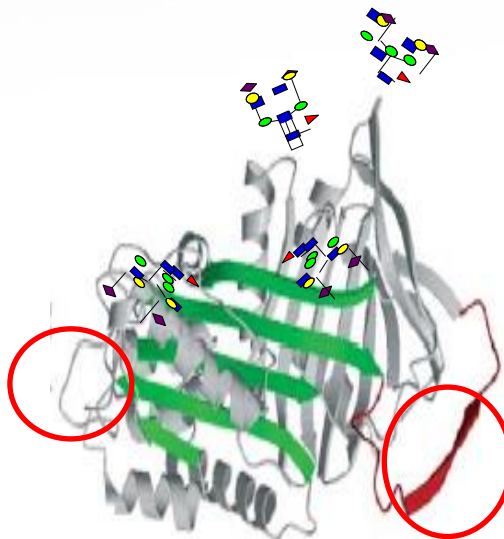
### ► Function

- Serine protease inhibitor
- Have been used for Emphysema

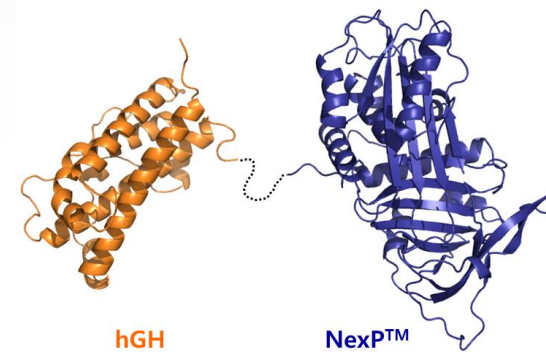
### ► As a long-acting carrier

- No side effect and immunogenicity in case of high dosage in long period
- Long *in-vivo* half life

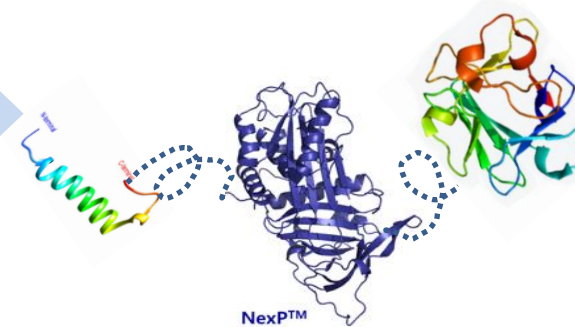
## Protein Engineering



NexP Carrier



ALT-P1 (long acting hGH)



ALT-F2 (NASH treatment)

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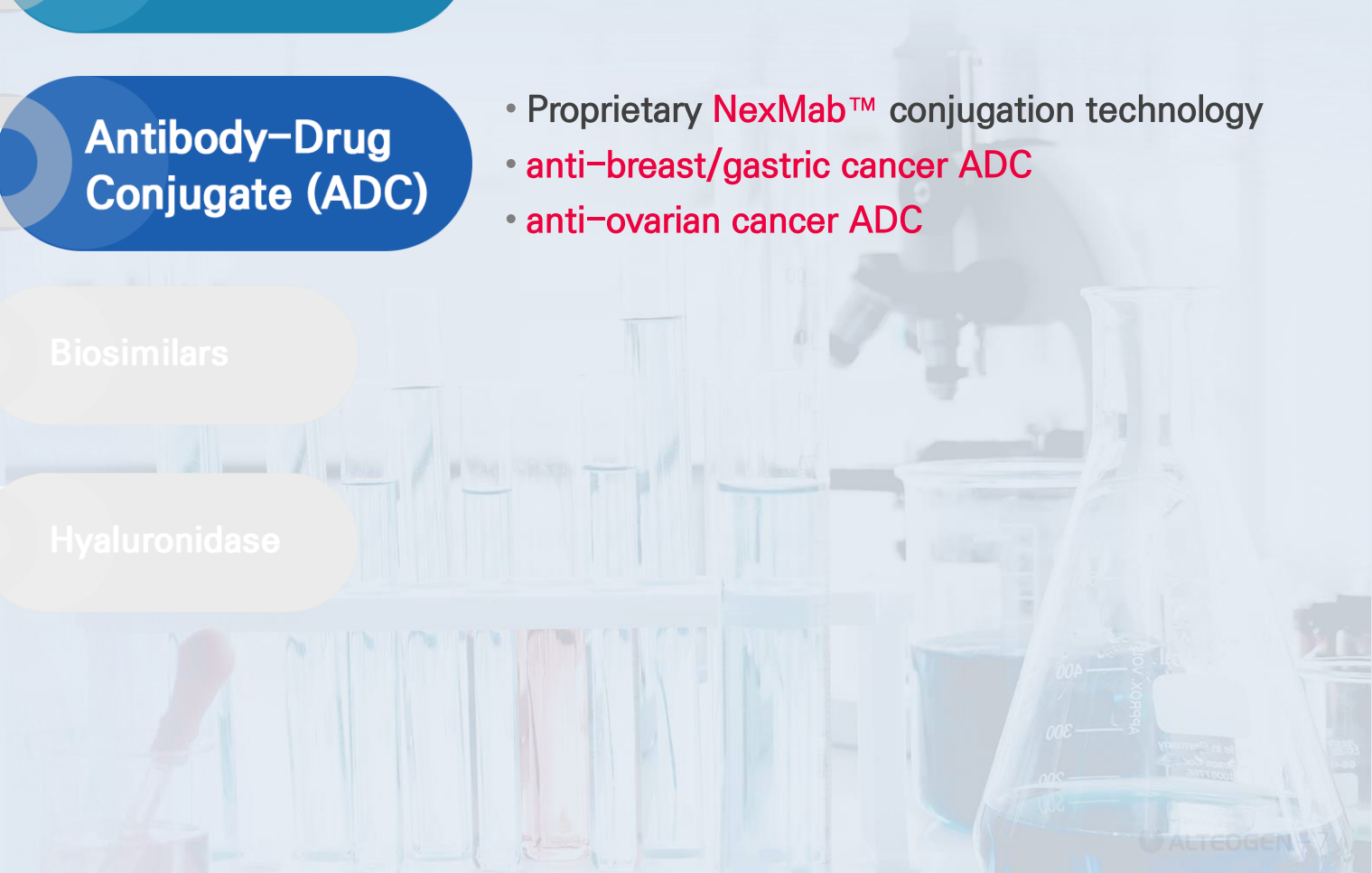
- Proprietary **NexMab™** conjugation technology
- **anti-breast/gastric cancer ADC**
- **anti-ovarian cancer ADC**

2014~

Biosimilars

2018~

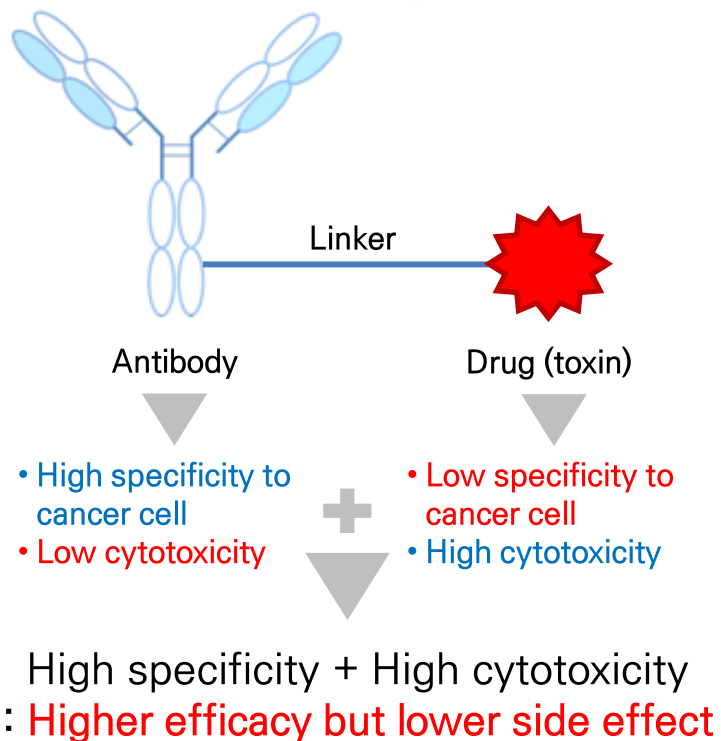
Hyaluronidase



## Novel therapeutic anti –cancer antibody technology, ADC

### ■ Concept of ADC technology

#### Antibody–Drug Conjugate (ADC)



### ■ Mode of action of ADC

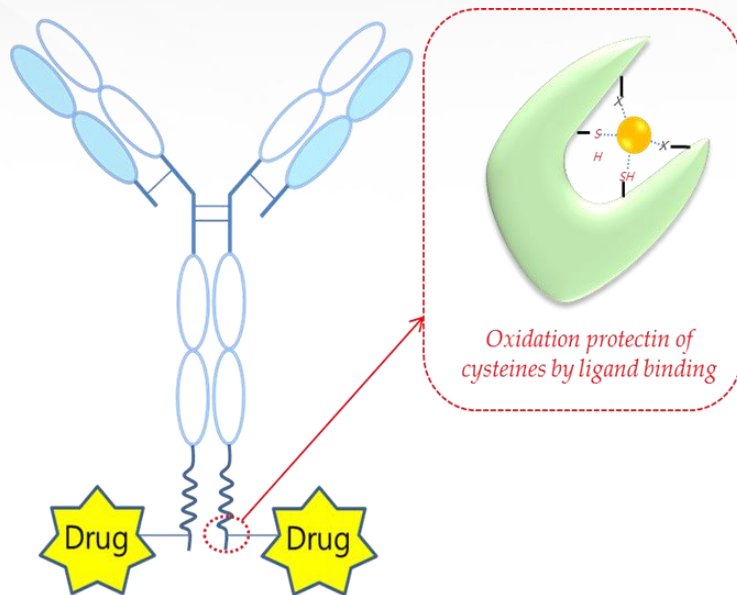
1. Antibody delivers the drug to the specific target antigen
2. Internalization of ADC
3. Drug released from ADC inside target cells
4. Drug kill the target cells





# NexMab™ : Proprietary site-selective ADC conjugation technology

## Alteogen's NexMab™ technology



Site-specific conjugation to C-terminus of Fc

High productivity and homogeneity

Simple conjugation process

High in vivo stability and low toxicity

*Simple and efficient  
site-specific conjugation technology*

Patent  
Registered

- USA(2017)
- EU (2020)
- Korea (2015)
- Russia (2016)
- Japan (2016)
- Mexico (2018)
- China (2018)
- Australia (2016)

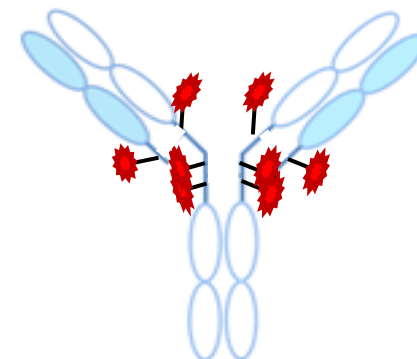
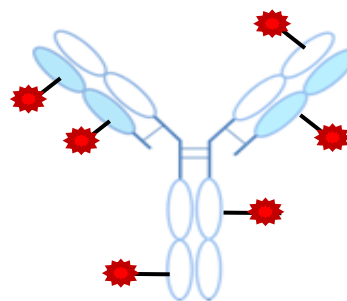
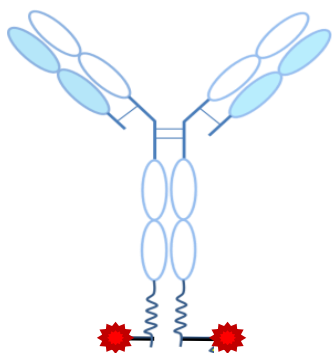
Patent  
Filed

Canada, Brazil

## ALT-P7: Anti-breast/anti-gastric cancer ADC

### Comparison of ALT-P7 with other HER2-targeted ADC

ADC	ALT-P7 (HM2-MMAE)	T-DM1 (Trastuzumab emtansine)	DS-8201 (Trastuzumab deruxtecan)
Company	Alteogen	Genentech (Roche)	Daiichi-Sankyo AstraZeneca
Linker	cleavable	non-cleavable	cleavable
Payload	MMAE	DM-1	DXd
DAR	2	3.5	~8
dosage	4.5 mpk (RP2D)	3.6 mpk	5.4 mpk



# ALT-P7: Anti-breast/anti-gastric cancer ADC

## ALT-P7 Phase 1 Summary

Characteristics (Total, n=27)	cohort1 (0.3mg/kg) (n=4)	cohort2 (0.6mg/kg) (n=3)	cohort3 (1.2mg/kg) (n=3)	cohort4 (2.4mg/kg) (n=3)	cohort5 (3.6mg/kg) (n=3)	cohort6 (4.8mg/kg) (n=5)	cohort7 (4.2mg/kg) (n=3)	cohort8 (4.5mg/kg) (n=3)
Age, years (median, SD)	53.23(±14.08)	60.3(±4.62)	49.3(±8.08)	44.3(±12.58)	57.3(±14.19)	63.4(±10.16)	45.0(±2.65)	45.3(±7.64)
<65years (n)	4	3	3	3	2	3	3	3
≥65years (n)	0	0	0	0	1	2	0	0
<b>Her2 Expression</b>								
IHC2+/FISH+ (n, %)	2(50%)	1(33%)	1(33%)	2(67%)	0	1(20%)	0	1(33%)
IHC3+ (n, %)	2(50%)	2(67%)	2(67%)	1(33%)	3(100%)	4(80%)	3(100%)	2(67%)
<b>ER/PR Expression</b>								
+/+			1	1	1	1	2	2
+/-	1			1	1	1		
-/+			1			1		
-/-	3	3	1	1	1	2	1	1
<b>Previous anti-HER2 therapy</b>								
Trastuzumab (n, %)	4(100%)	3(100%)	3(100%)	3(100%)	3(100%)	5(100%)	3(100%)	3(100%)
T-DM1 (n, %)	4(100%)	3(100%)	3(100%)	2(67%)	3(100%)	5(100%)	3(100%)	2(67%)
Pertuzumab (n, %)	2(50%)	1(33%)	2(67%)	1(33%)	3(100%)	1(20%)	1(50%)	3(100%)
Lapatinib (n, %)	4(100%)	1(33%)	2(67%)	1(33%)	2(67%)	3(60%)	3(100%)	1(33%)
Margetuximab (n, %)	0	0	1(33%)	0	0	0	1(50%)	0
Pozotinib (n, %)	0	1(33%)	0	0	0	1(20%)	1(50%)	0
DS-8201 (n, %)	0	0	0	0	0	0	0	1(33%)

MTD and RP2D of ALT-P7 was determined to be 4.5 mg/kg in HER2+ metastatic breast cancer

- The most common grade  $\frac{3}{4}$  TRAE was neutropenia (n=4)  
⇒ Other TRAEs were myalgia, fatigue, sensory neuropathy, and rash.
- The subject who has been receiving ALT-P7 for the longest time has been maintained without cancer progression for more than 600 days.

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- Proprietary **NexMab™** conjugation technology
- **anti-breast/gastric cancer ADC**
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2014~

Biosimilars

- **Eylea®** biosimilar development  
(proprietary formulation/fermentation patents)

2018~

Hyaluronidase

# ALT-L9 : Eylea® Biosimilar



Ingredient

Aflibercept

Developer

Regeneron, Bayer

Indications

- Wet Age-related Macular Degeneration (wAMD)
- Diabetic Macular Edema (DME)
- Macular Edema Following Retinal Vein Occlusion (RVO)
- Myopic CNV

Patents  
Expiration

- Substance Patent: 2024~2025
- Formulation Patent: 2027~2030

Molecule  
Structure

Fc fused VEGF Receptors

▶ 2019 : US\$ 8B

▶ 2025 : > US\$ 10B Expected

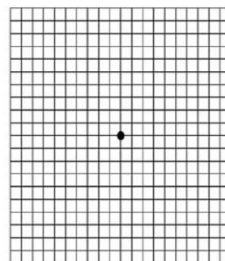
Drusen (deposits) causing  
macula degeneration  
(dry AMD)

8.7% of  
World population  
(WHO)

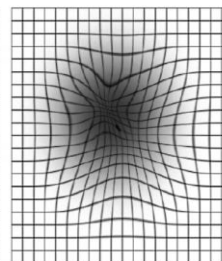
Abnormal new blood vessels  
cause rapid and severe loss of  
central vision (wet AMD)

~ 10–15% develop  
wAMD

Progression to reduced vision and blindness



Normal  
Vision



wAMD  
Vision

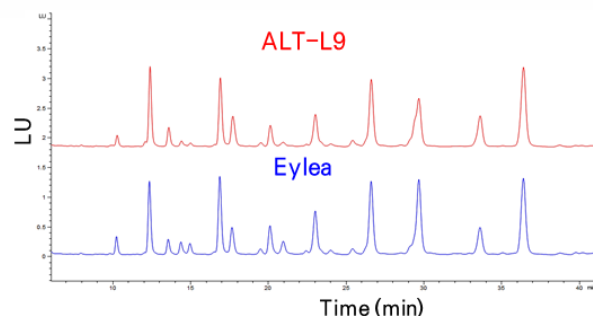
Leading cause of blindness  
in patients over 60 years old



# ALT-L9 : Competitive Edge

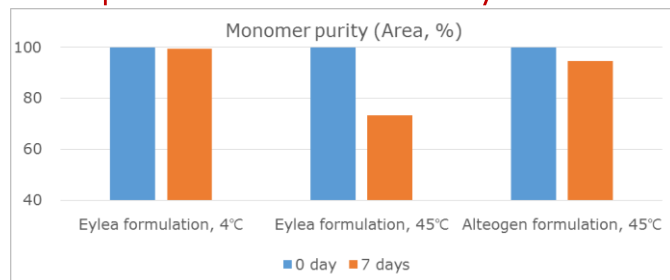
## 01 Alteogen uses the same Cell Line which has been used by originator

- ✓ Cell line may affect the carbohydrate pattern and similarity in biosimilar products
- ✓ ALT-L9 has an excellent similarity in Glycan Profile comparing to Eylea®



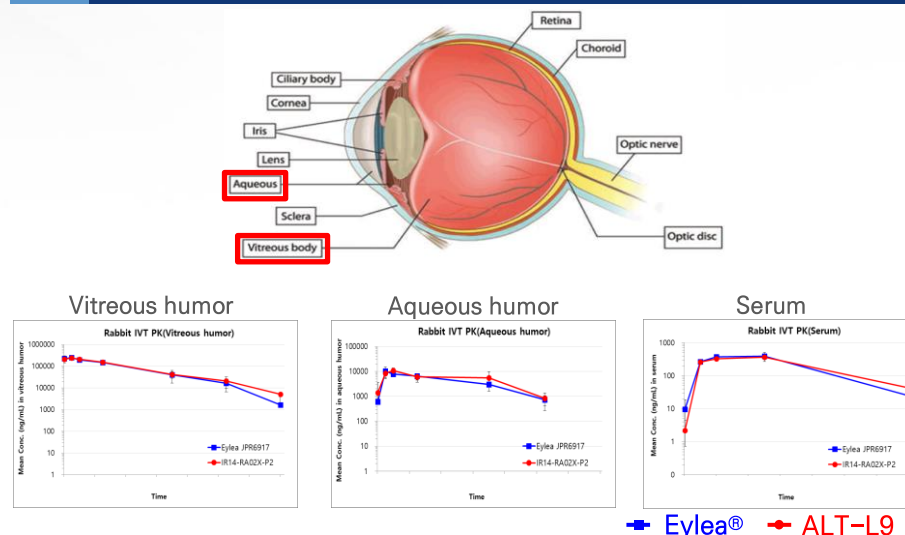
## 03 Alteogen developed a unique formulation

### ► Improved thermal Stability



- ✓ The formulation patent of the originator expires in 2027–2030
- ✓ Patent is registered in Korea, US, Russia, and Japan and filed in
- ✓ 8 additional countries including EU

## 02 High level of similarity in PK profile in animal studies



## 04 Alteogen obtained Process Patent

### ► Fermentation of fusion protein

- Other Eylea® biosimilar developing companies who produce Aflibercept under fed-batch fermentation mode may infringe Alteogen's fermentation patent.
- ✓ Alteogen is in position to block other companies' attempt to develop Eylea® biosimilar
- ✓ Registered in Korea and Australia

## ALT-L9 : Business Model

Completed Phase 1  
Study in  
4 sites in Korea

safety, efficacy,  
PK



Global Phase 3  
planned

efficacy, similarity,  
immunogenicity

First to be launched when the substance patent expires

2024

Korea/ Japan/ ROW

2025

EU

2028

US

After launching in 2025 (Total Market US\$10B Expected),  
Market Share Target: >30% in Eylea biosimilar Market

**ALT-L9 Annual Sales of \$500M ~ \$800M Expected**

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2014~

Biosimilars

- **Eylea®** biosimilar development  
(proprietary formulation/fermentation patents)

2018~

Hyaluronidase

- Novel human hyaluronidase for **Mab SC use**  
⇒ **Herceptin® SC** biosimilar development
- Hyaluronidase for **Dermal and Ophthalmology**

## Routes of administration of biologics



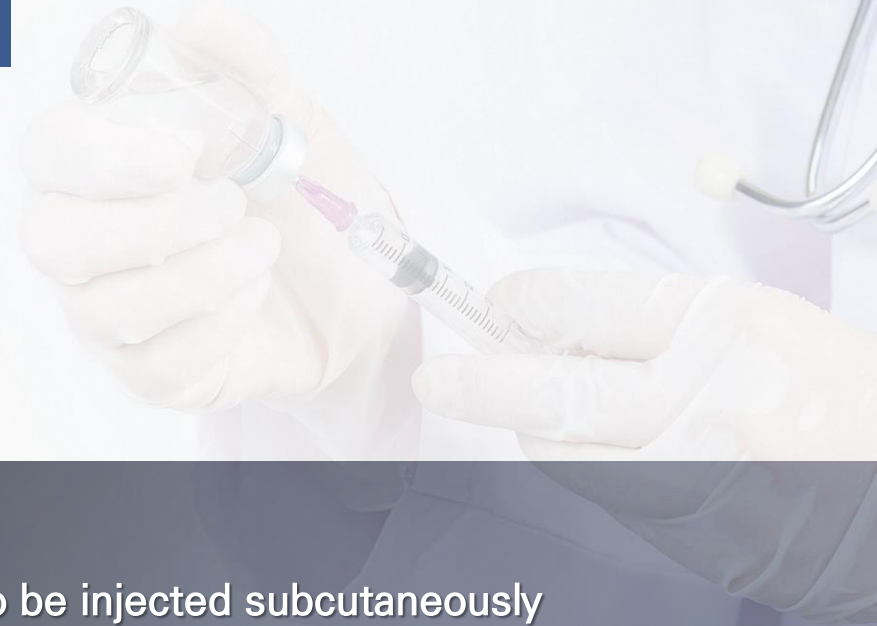
### *iv infusion*

- ▶ Discomforts for patients, side-effect
- ▶ Time/cost efficiency is low



### *sc injection*

- ▶ Short injection time
- ▶ Allows self-injection



- ▶ Current trend of switching to SC formulation
- ▶ Need Hyaluronidase when the large volume is to be injected subcutaneously

## Subcutaneous injection of antibody using Human Hyaluronidase



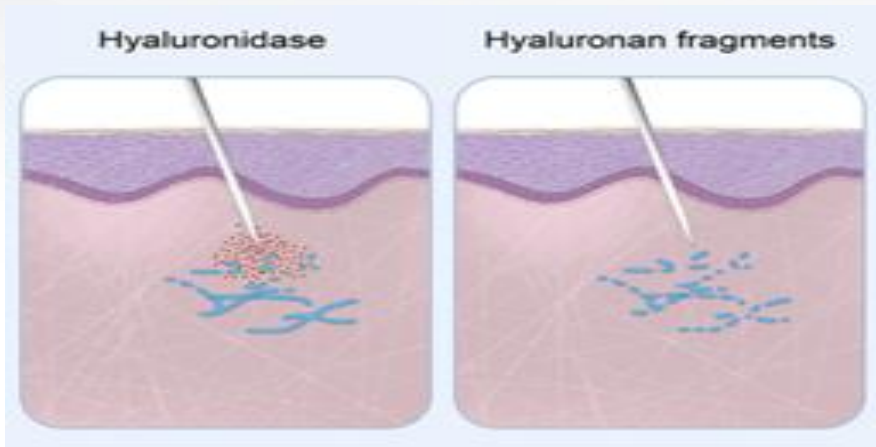
(Source: British Journal of Cancer(2013) 109, 1556–1561)

- Need Hyaluronidase when the large volume is to be injected subcutaneously



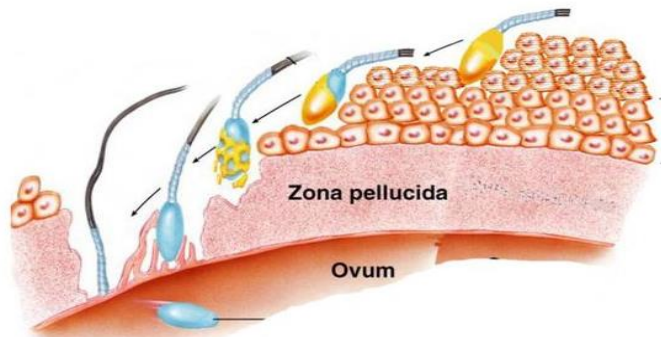
# Hyaluronidase

- Enzyme hydrolyzing **hyaluronan** in the extracellular matrix

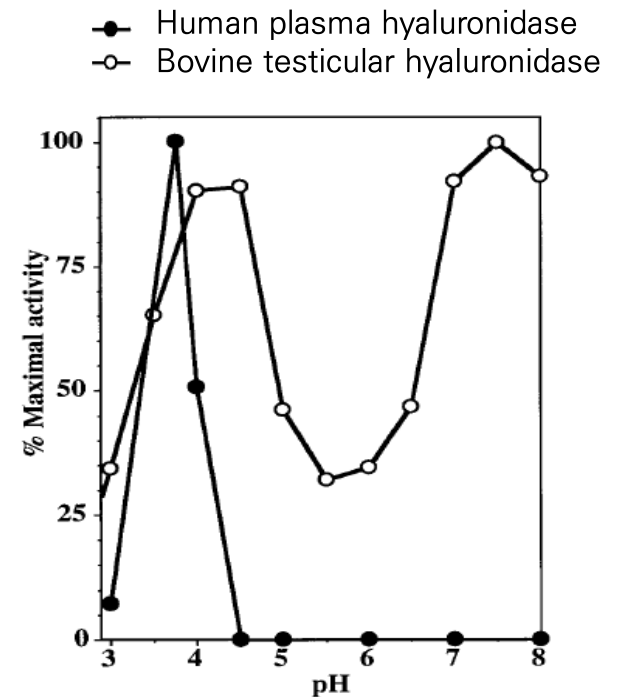


## ► Five Human Hyaluronidases

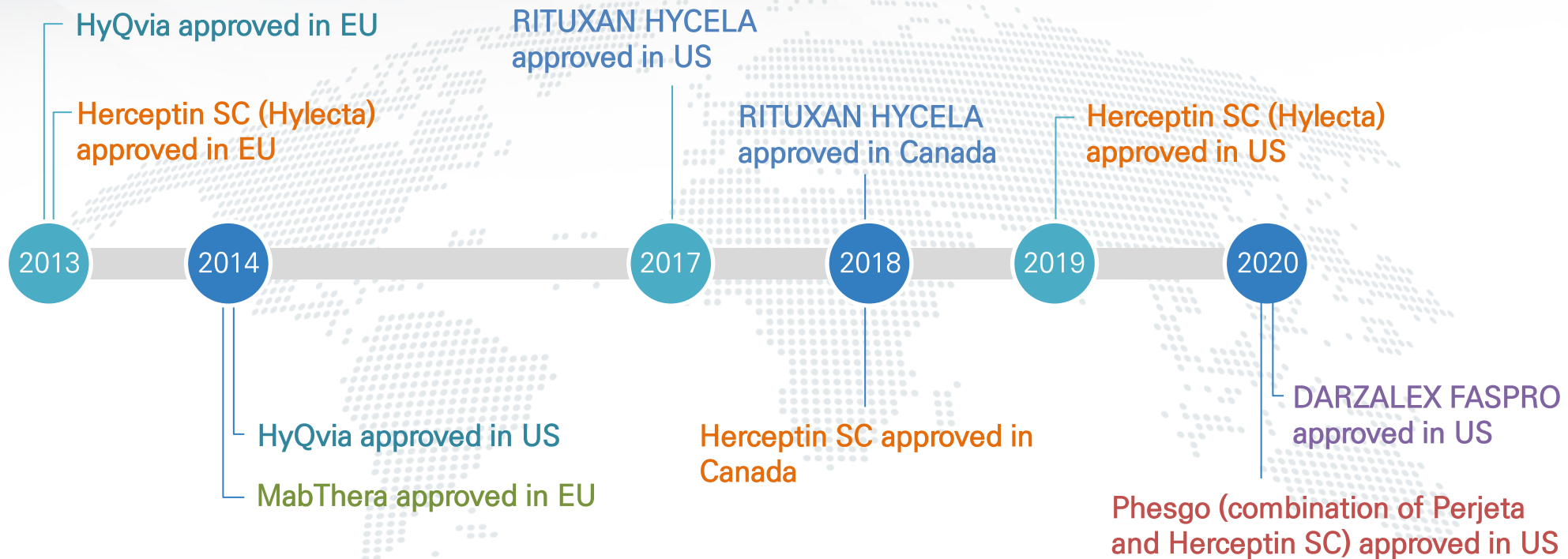
- Hyal1, Hyal2, Hyal3, and Hyal4: Optimum at pH 3
- PH20: Also active at pH 7~8



PH20 aids in penetrating the layer of cumulus cells

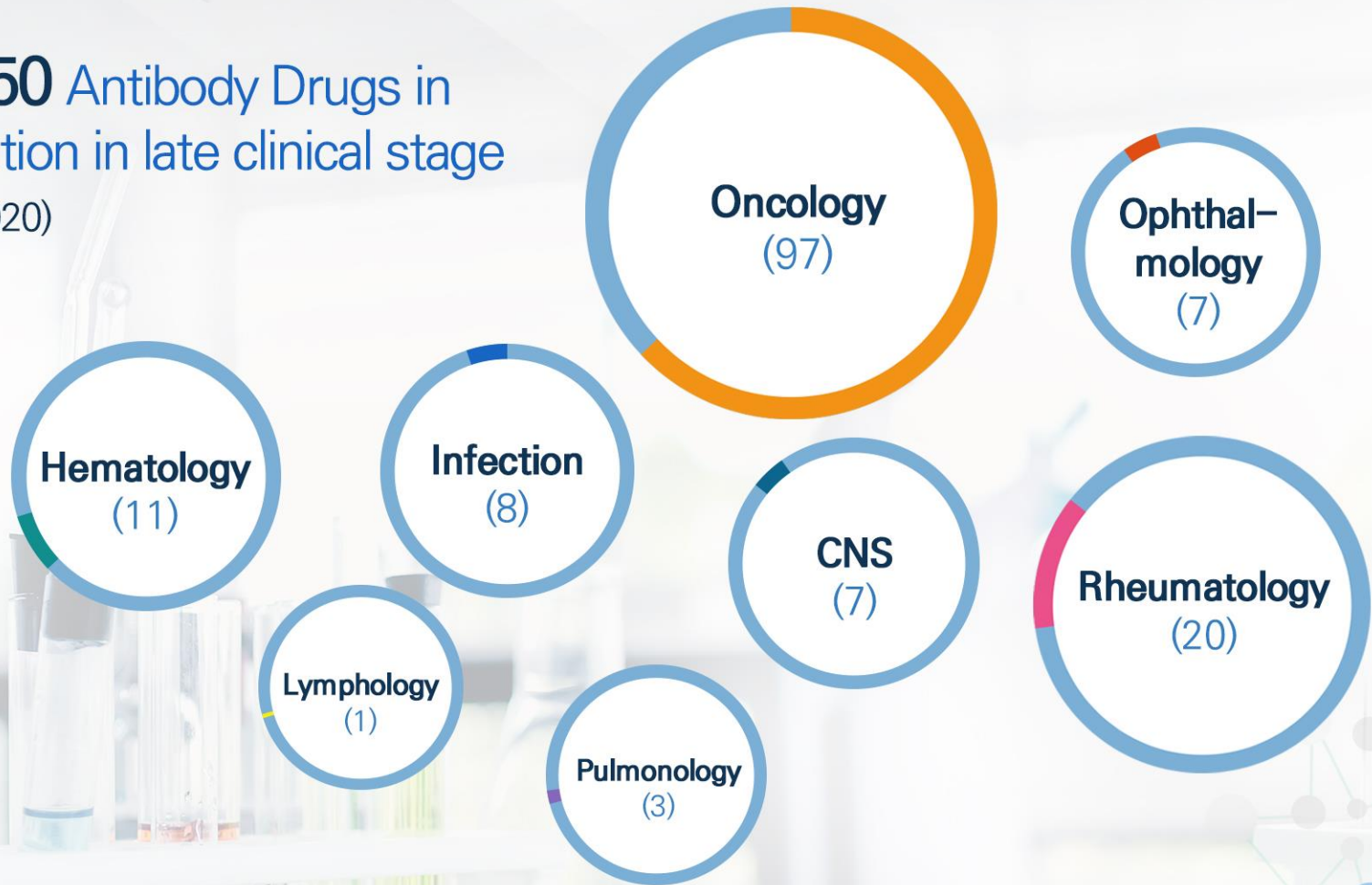


## Development of SC formulation with Hyaluronidase



\* At present clinical trials of Mab sc products are actively conducted by global Pharma/Biotech companies

└ **About 150** Antibody Drugs in  
IV formulation in late clinical stage  
(As of July 2020)



About 610 novel antibody drugs in early to late clinical stages

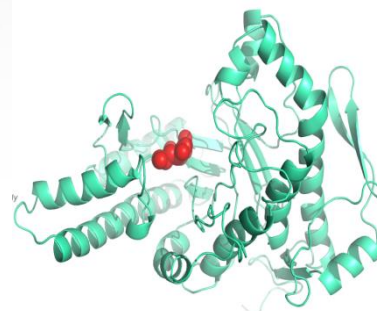
# ALT-B4 : Novel Hyaluronidase Hybrozyme™ Technology

## Novel Human Hyaluronidase

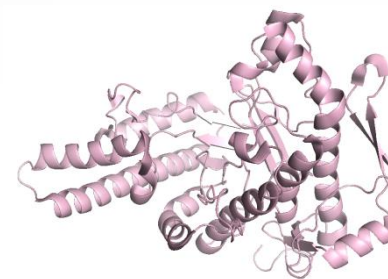
- ▶ Allows conversion of IV formulation of biologics to SC formulation
- ▶ Same mode of action (MoA), but enhanced enzymatic activity and thermal stability (aggregation temperature)

### [ Improved technology compared to competitor's ]

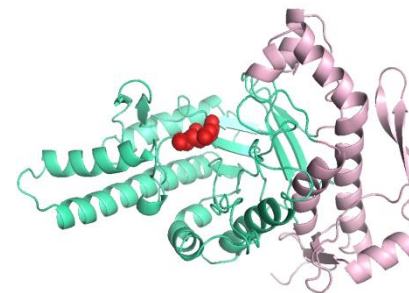
- Enhanced thermal stability and protein stability
- High Productivity
- Lower immunogenicity compared to wildtype pH20 determined by *In vitro analysis*
- Completed PCT filing



PH20











Hyal



ALT-B4



## ALT-B4 : *In vivo* Study – Bleb Size measurement with mini pig

ALT-B4 (2ml/min)	0h	1h	2h	24h
0 U Buffer only				
2000 U				

\* Experiments were performed by our partner company with six, 1-yr old male mini pigs



## ALT-B4 : Business Model



### Licensing-Out to global company for SC formulations

2019.12.02

Entered Non-exclusive License Agreement with a Top 10 Global Pharmaceutical Company (Total \$1.373B)

2020.06.24

Entered Non-exclusive License Agreement with a Top 10 Global Pharmaceutical Company (Total \$3.865B)

Current

In discussion with multiple global Pharmaceutical companies

\* Alteogen will provide ALT-B4 Drug Substance globally

Novel and Biosimilar mAb: 2024 ~\$329B  
Conversion from IV to SC : \$\$\$\$ Potential Market

# ALT-B4 : Business Model (Standalone)

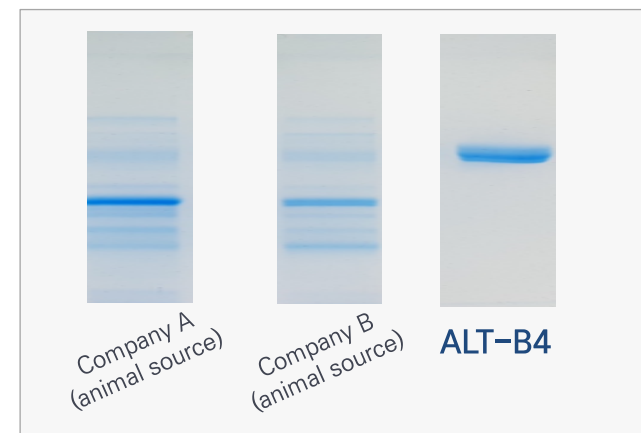
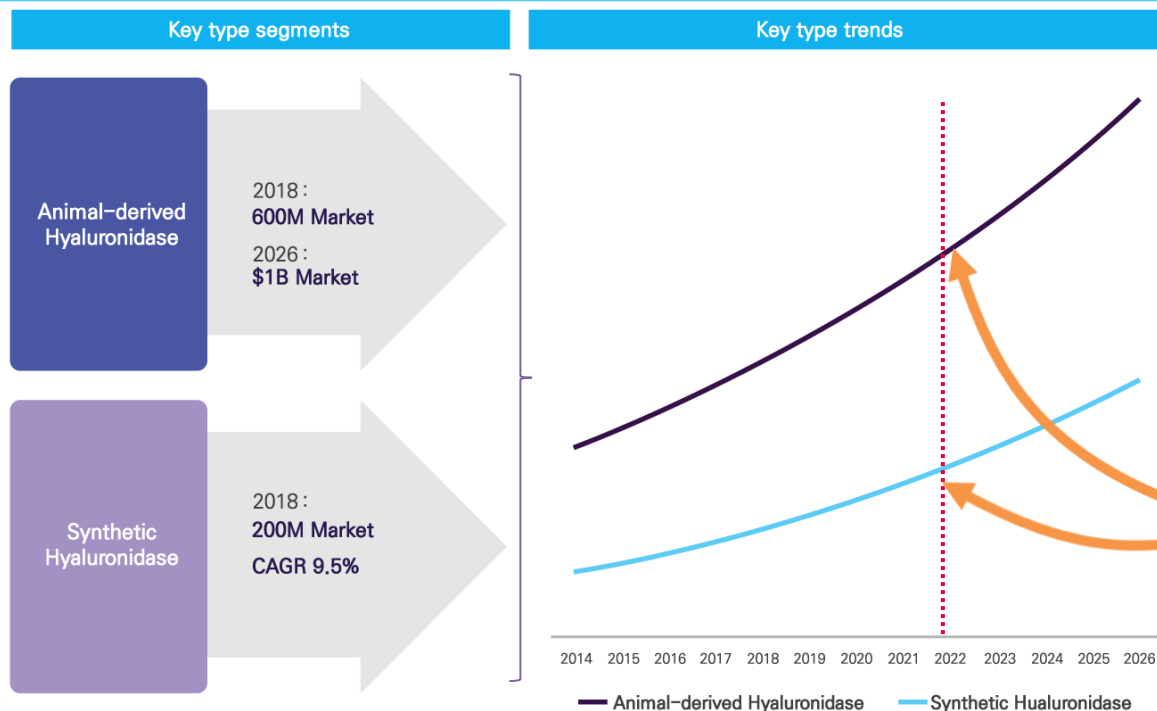
## • ALT-B4 : Approval of standalone product for global market

- ✓ Replacing animal-derived Hyaluronidase
- ✓ Starting with Korea-launch in 2021, it will be exported globally

### Indications

• Dermatology • Ophthalmology • Plastic Surgery • Reduce Pain

### Hyaluronidase market: Type movement analysis



- 2022 \$1B Market
- 2026 \$2B Market (Ceres F&D Export)
- ✓ Aim Market Share > 30%

# Biosimilar Market Analysis and Strategy

Business Environment

Switched to **Red Ocean** from **Blue Ocean**

Herceptin iv Biosimilar : 6 Products approved in EU as of September 2020

Universalization of biosimilar development technology:  
Rapid rise of Chinese and Indian companies

Original companies' patent extension strategies: differentiated with biobetter products

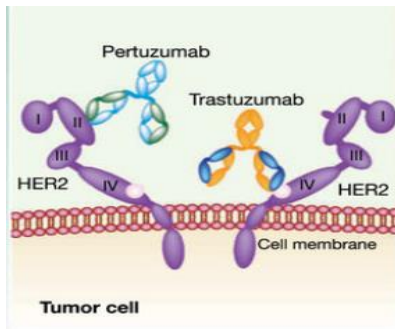
An attractive field, given the cost and probability of success in new drug development

**Need differentiated Biosimilar Strategy**

# Development of differentiated biosimilar using ALT-B4 (1)

- Roche's HER2 targeted anti-cancer drug development strategy

## Herceptin iv



- 2019 Herceptin sales: ~ US\$ 7B
- 2019 Perjeta sales: ~ US\$ 3B

**Herceptin HYLECTA™**  
trastuzumab and hyaluronidase-oysk  
INJECTION FOR SUBCUTANEOUS USE | 600 mg/10,000 units

Herceptin sc



Perjeta iv

**PHESGO™**  
pertuzumab/trastuzumab/hyaluronidase-zzxf  
SUBCUTANEOUS INJECTION / 1,200 mg/600 mg/30,000 units  
600 mg/600 mg/20,000 units

(Herceptin + Perjeta) sc

Alteogen is the only company to develop **Herceptin sc** and **Perjeta sc** using ALT-B4

## Development of differentiated biosimilar using ALT-B4 (2)

- Alteogen can develop **Blockbuster sc Biosimilar** using ALT-B4  
→ establish differentiated biosimilar strategy



Rituxan® sc Biosimilar (US\$ 7.0 B)



Opdivo® sc Biosimilar (US\$ 7.9 B)



Remicade® sc New drug (US\$ 4.5B )

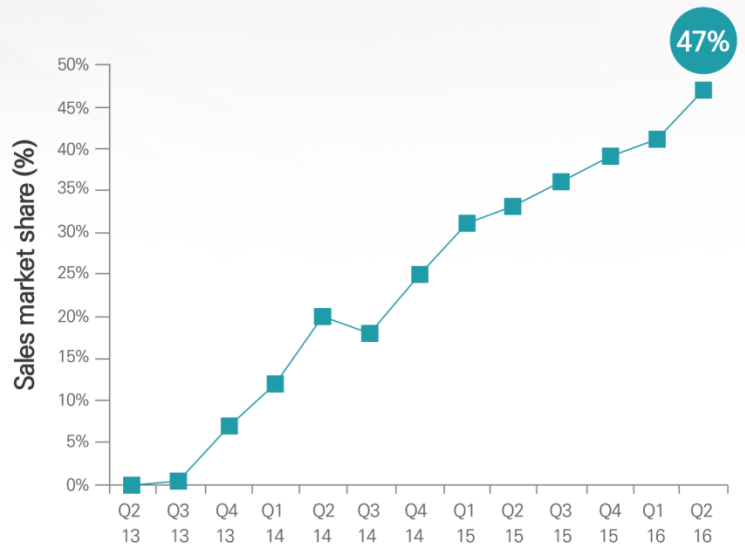


Darzalex® sc Biosimilar (US\$ > 3B)



# ALT-LS2 : Herceptin SC biosimilar

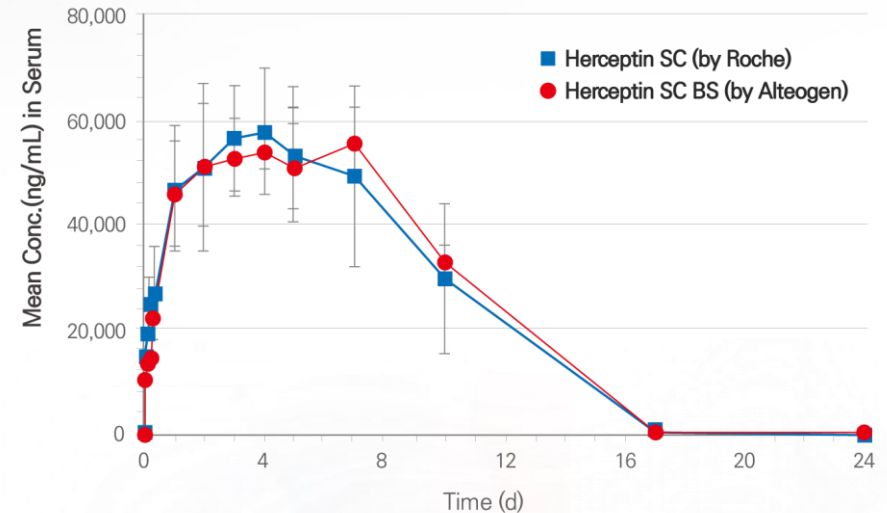
## Herceptin SC in Europe



(자료: Roche, 대신증권 Research&Strategy본부)

- Rapid rise of Herceptin sc in Market
  - Future Market Share over 50%
  - US FDA approval in 2019
- Convenient for patients
  - Total cost is less than iv injection
- Competitive Market for Herceptin iv Biosimilar
  - Limitation on iv biosimilar products

## PK Profiles



- ✓ Roche's Formulation Patent Expires in 2030
- ✓ Formulation Patent Filed (2019)

The first and only  
Herceptin SC biosimilar in the world  
**Aim > US\$ 1B annual sales revenue**

# | Alteogen's Strategy as Platform Provider



# ALTEOGEN

- ALT-B4 (Hyaluronidase) for sc injection
  - ▶ Collaboration with Global Partners
- ALT-B4 for stand alone
  - ▶ Global marketing
- ALT-L9 (Eylea Biosimilar)
  - ▶ Entering Global Market
- ALT-P7 (Cancer) / ALT-P1 (GHD) / ALT-F2 (NASH)
  - ▶ Novel drugs based on ADC/  
long-acting technologies



[ Establishing own  
manufacturing facility ]



**Thank you  
for your attention!**



[www.alteogen.com](http://www.alteogen.com)