

### Safe Harbor Statement

# This presentation contains certain forward-looking statements.

These forward-looking statements may be identified by words such as 'believes', 'expects', 'anticipates', 'projects', 'intends', 'should', 'seeks', 'estimates', 'future' or similar expressions or by discussion of, among other things, strategy, goals, plans or intentions. Various factors may cause actual results to differ materially in the future from those reflected in forward-looking statements contained in this presentation, among others:

- 1. pricing and product initiatives of competitors;
- 2. legislative and regulatory developments and economic conditions;
- 3. delay or inability in obtaining regulatory approvals or bringing products to market;
- 4. fluctuations in currency exchange rates and general financial market conditions;
- uncertainties in the discovery, development or marketing of new products or new uses of existing products, including without limitation negative results of clinical trials or research projects, unexpected side-effects of pipeline or marketed products;

- 6. increased government pricing pressures;
- 7. interruptions in production
- 8. loss of or inability to obtain adequate protection for intellectual property rights;
- 9. litigation;
- 10. loss of key executives or other employees; and
- 11. adverse publicity and news coverage.

TTY Biopharm cautions that this foregoing list of factors is not exhaustive. There may also be other risks that management is unable to predict at this time that may cause actual results to differ materially from those in forward-looking statements.

You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date on which they are made. TTY Biopharm undertakes no obligation to update publicly or revise any forward-looking statements. Any statements regarding earnings growth is not a profit forecast and should not be interpreted to mean that TTY Biopharm's earnings or earnings per share for this year or any subsequent period will necessarily match or exceed published earnings or earnings per share forecasts of TTY Biopharm Company Limited.



### **Our Mission**

We have been striving to extend liposomal & microsphere depot platform technologies for treatment of various diseases.

Our Target is to improve health and quality of life through innovative, cost-effective therapeutics and specialty drugs.

Our focus is on the **"Unmet Medical Needs"** in challenging diseases throughout the world, such as <u>Cancer</u>, <u>CNS</u>, <u>Autoimmune</u>, <u>Diabetes Mellitus</u> & <u>Infectious Diseases</u>.

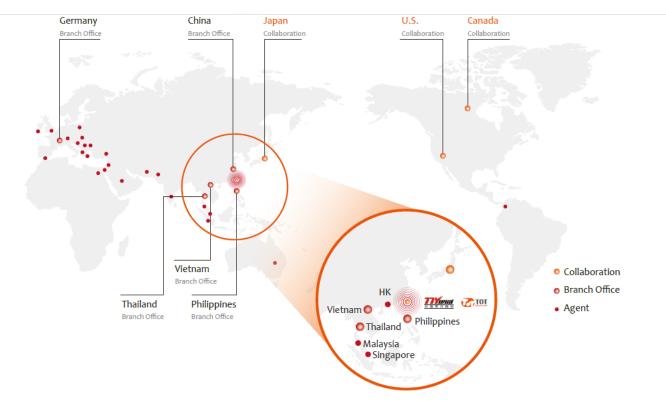


# Agenda

**Company Overview Product Strategy Product Pipeline** Manufacture Facilities Successful Product Categories In Progress Status **Biotech Success** 



# **Company Overview**



- Founded in 1960, restructured in 1996
- Traded in the Taiwan TPEx

(2001, Code: 4105);

Shares outstanding: 248 Million Shares

(December, 2017)

■ TTY Biopharm consolidated sales as of

2017- NTD 4.08 Billion, USD 138 Million

■ Headquarters: Taipei, Taiwan

Number of employees: 520





#### 台灣東洋 TTY Biopharm

- New Drugs & Super Generics
- Market cap US\$856mn.

ROE 2011-2016: 19.5%.

**ROE 2017: 24.5% (above industry average 11.13%).** 

Targets for 28%-35% in 2018-2020.

#### 殷漢 EnhanX (67%)

- R&D / New Drug Development
- Clinical Trials & Marketing

#### 東生華製藥 TSH (56.48%)

- New Drug Development & Marketing of Chronic Diseases (CV/GI/Immune)
- (listed), Market cap US\$76mn

#### 智擎生技 PharmaEngine (17.92%)

- New Drug Development
- (listed), Market cap US\$628mn

#### 創益生技 CY Biotech (27.54%)

- Probiotics & Obesity Diseases
- (listed), Market cap US\$37mn

#### 榮港生技 WorldCo (100%)

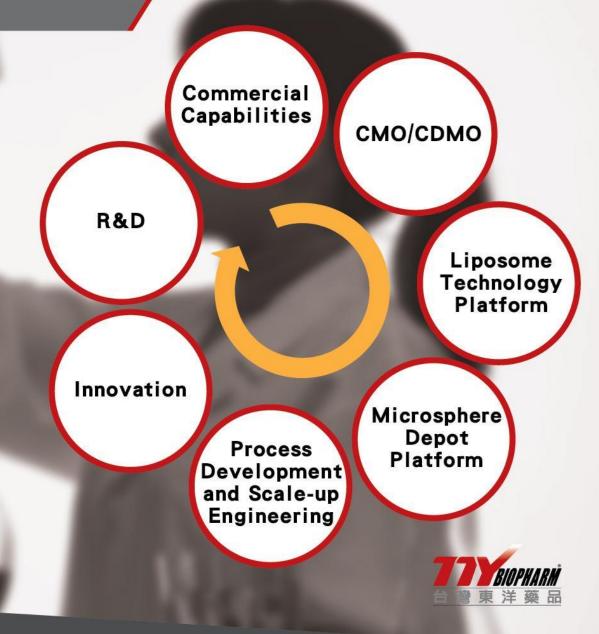
- New Drug Development (liver/ID/CNS)
- Marketing

#### ATB泰/ATB菲/越辦事處 40%/87%/100%

New Drug Development & Marketing



# **TTY Core Competences**



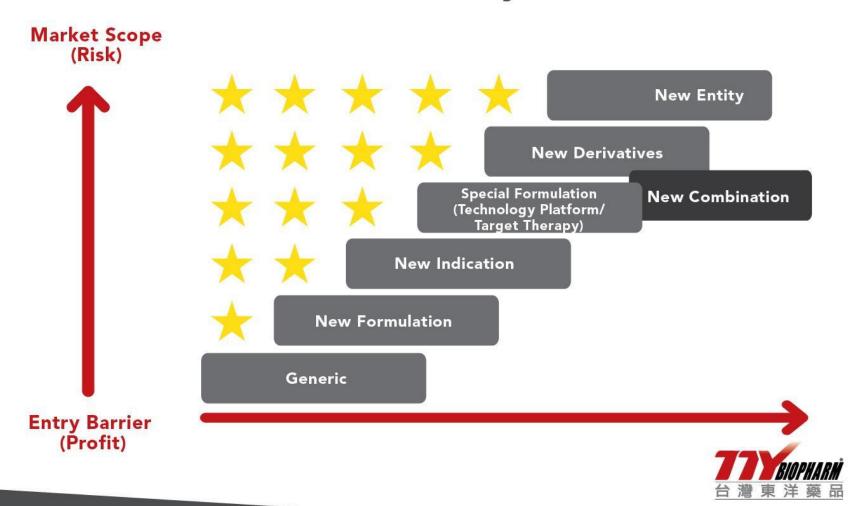
# Agenda

**Company Overview Product Strategy** Product Pipeline Manufacture Facilities Successful Product Categories In Progress Status **Biotech Success** 



# **Product Strategy**

### **Trends for Pharmaceutical Industry**



# Agenda

Company Overview

**Product Strategy** 

**Product Pipeline** 

Manufacture Facilities

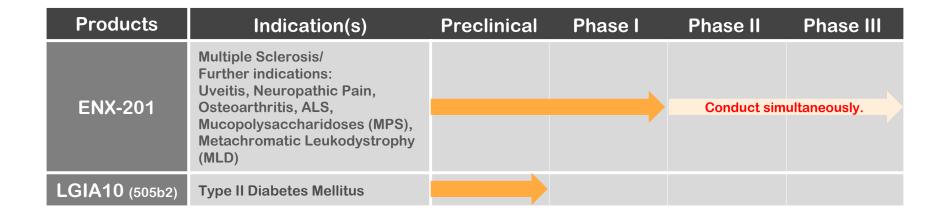
Successful Product Categories

In Progress Status

**Biotech Success** 



# New Drug Pipeline



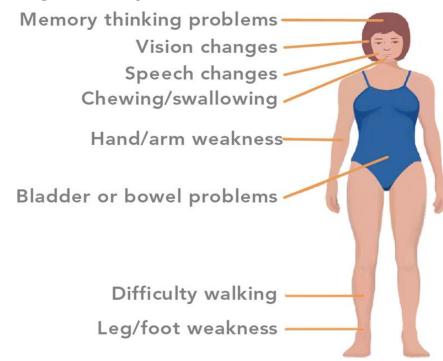


Products	World Market USD/M (est.	) Core Technology	Advantages
ENX-201	1,700	Liposome Technology	Penetrating Blood-Brain- Barrier (BBB) capability
LGIA10	910	Microsphere Formulation	Worldwide Manufacturing Patent Microsphere Deport Platform



# MS: a chronic, autoimmune & neurodegenerative disorder Body's own defensive system attacks myelin

- Inflammatory damage in the brain and spinal cord
- Loss of myelin and axons (scars at multiple sites)
- Neurologic disability



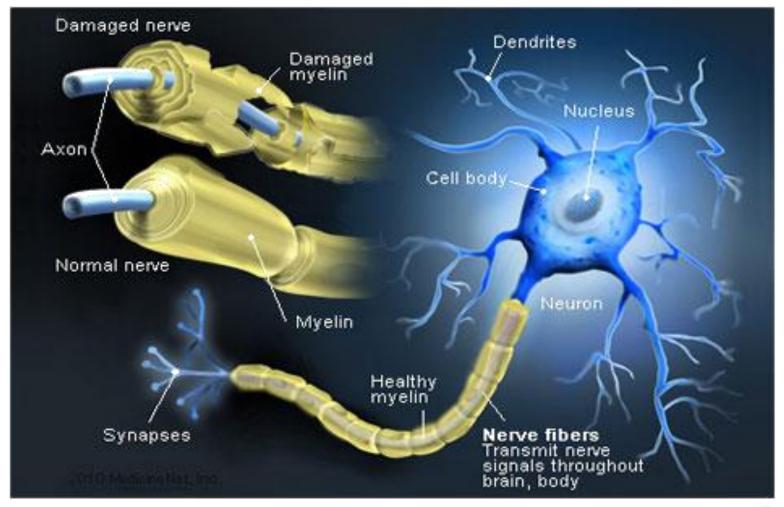
#### Whole body:

Itching

Fatigue
Coordination
Dizziness/poor balance
Muscle tightness
or stiffness
Numbness/tingling
Pain
Burning

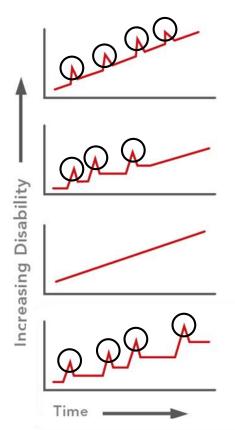


### Introduction of MS's MoA





#### Four Classifications of MS



#### PRMS Progressive Relapsing MS

Steady decline since onset with super-imposed attacks.

#### **SPMS** Secondary Progressive MS

Initial RRMS that suddenly begins to decline without periods of remission and relapses.

#### **PPMS** Primary Progressive MS

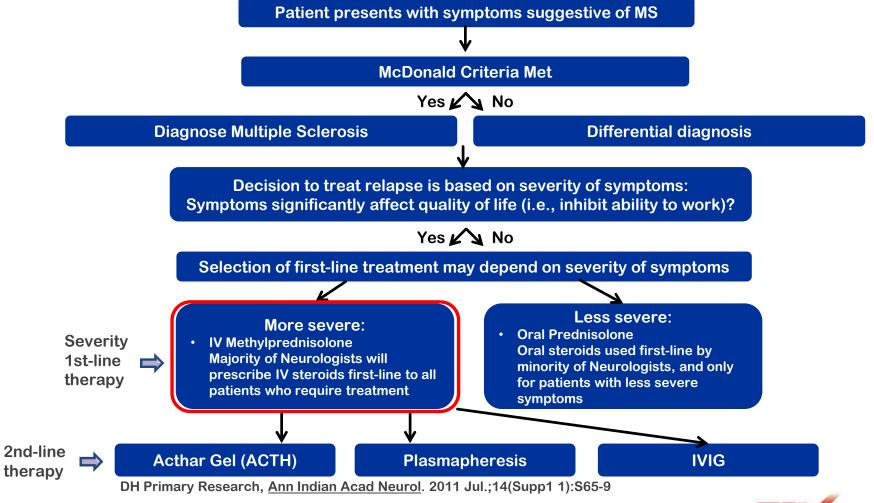
Gradual progression of the disease from its onset with no relapses or remissions

#### RRMS Relapsing/Remitting MS 85%~90% patients

Unpredictable attacks which may or may not leave permanent deficits followed by periods of remission

Either one of the four classifications occurs in acute is the target patient pool of ENX-201. 不管屬於哪一個發病類型,只要是急性復發,就是ENX-201的target 病患。



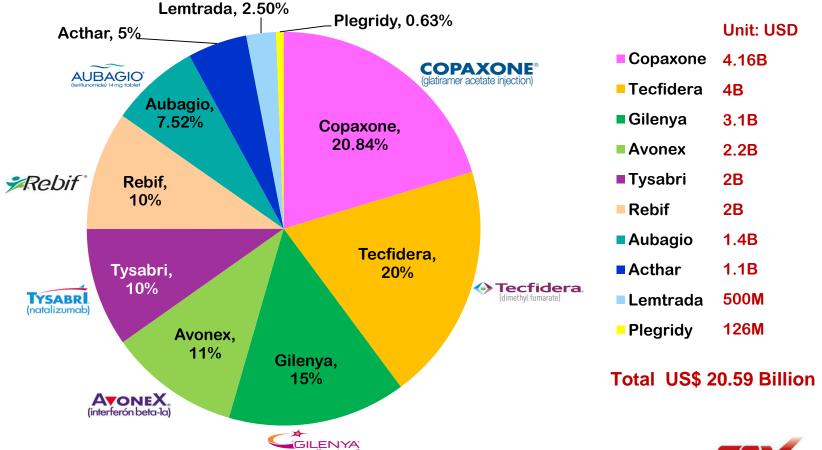




# World distribution of multiple sclerosis: greater prevalence in higher northern and southern latitudes



Major existing choices for MS treatments (2016 Sales & Market Share in Value)





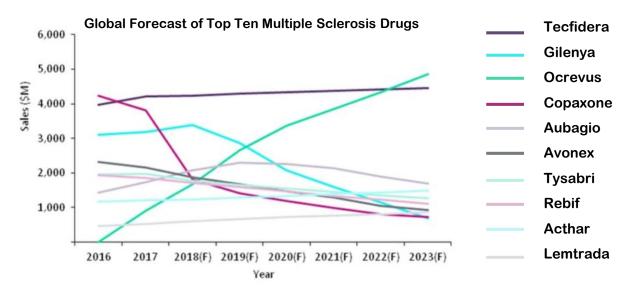


### Potential Global Market Size

#### Global estimation

MS treatment market rising from \$20.59 billion to \$27.38 billion from 2016 to 2026 (approx.), at a Compound Annual Growth Rate (CAGR) of 2.89%.

Global existing MS treatment market value										
2016 2017 2018 2019 2020 2021 2022 2023 2024 2025 2026										2026
20.59B	21.19B	21.80B	22.43B	23.08B	23.74B	24.43B	25.14B	25.32B	25.30B	27.38B

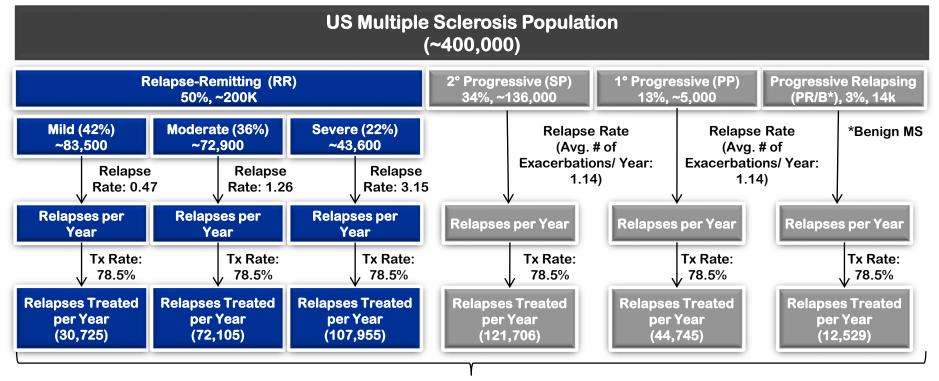


A treatment costs USD\$50,000~65,000.

Source: GlobalData, Pharma Intelligence Center, Drugs Database (Accessed February 23, 2018)



### Patients Distribution in US Market

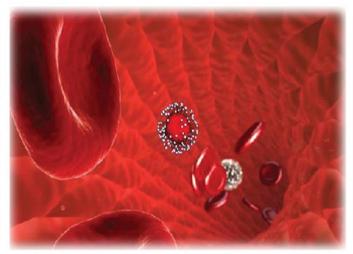


Minimum, Target, and Ideal Penetration Rates based on Use as First-Line or Second-Line Treatment from Physician Survey

Relapses Treated with ENX-201 at Peak Under Minimum, Target, and Ideal 1st-Line/2nd-Line Penetration Scenarios

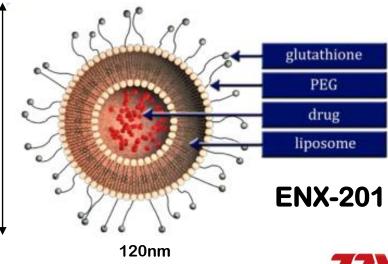


### Introduction of the Product



Targeting Liposomal Methylprednisolone Injection (glutathione PEGylated liposomal methylprednisolone) is being developed for patients suffering from acute and chronic neuro-inflammatory diseases, with an initial focus on patients with acute MS relapses.



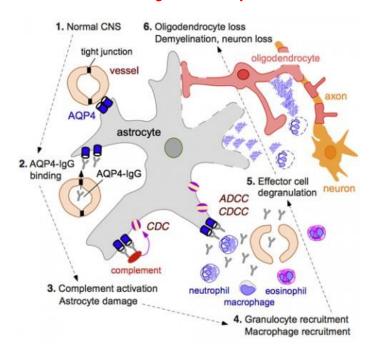




### Introduction of the Product

#### **ENX-201's potential indications**

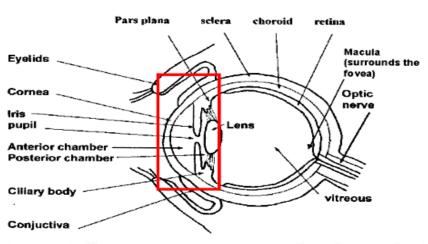
#### **Neuromyelitis Optica**



Source: http://www.msdiscovery.org/news/news\_synthesis/

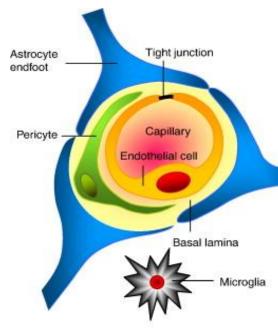
8147-neuromyelitis-optica-part-2-pathogenesis Source: https://www.uveitis.net/patient/anterior.php

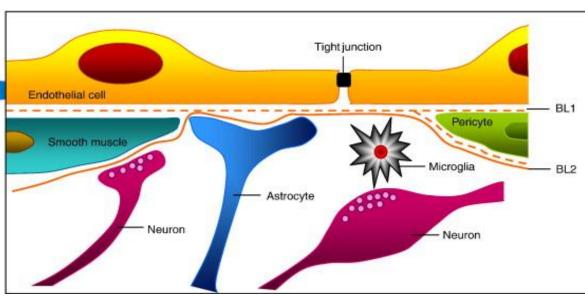
#### **Uveitis**



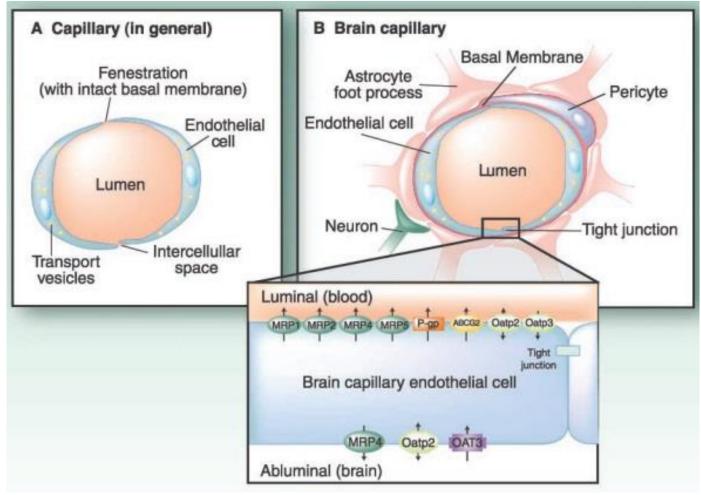
Neuro-inflammation is associated with a wide range of CNS diseases, including multiple sclerosis (MS), optic neuritis, non-infectious uveitis, acute disseminated encephalomyelitis (ADEM), neuromyelitis optica (NMO), as well as neuropathic pain, amyotrophic lateral sclerosis (ALS) and Parkinson's disease.



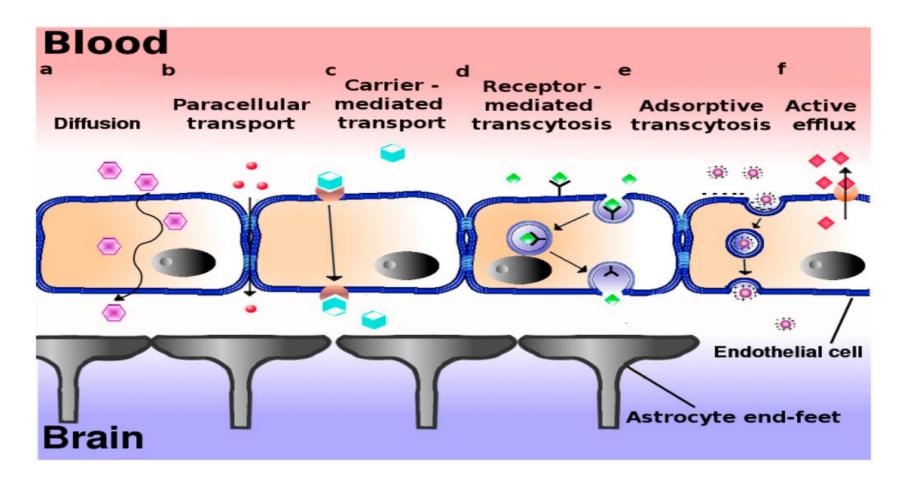












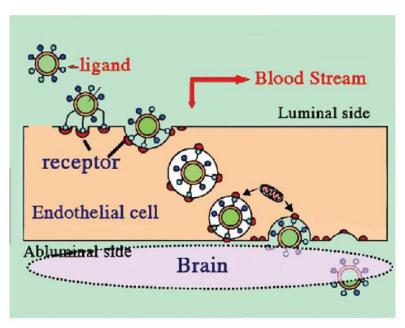


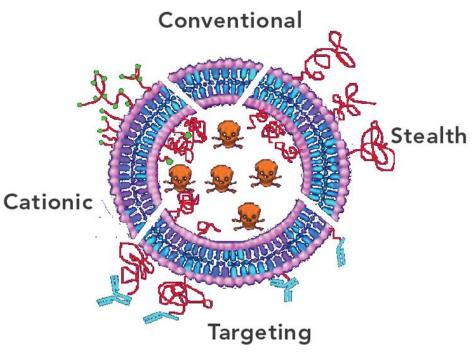
NO.	TARGETING LIGANDS	NOTE
1	Transferrin	MBP-426, MBP-Y003
2	Melanotransferrin	
3	Insulin	
4	LDL	
5	Angiopeps	
6	Leptin	
7	Thiamine	
8	Glutathione	2B3-101, <b>ENX-201</b>
9	Synthetic Opioid Peptides	
10	RVG Peptide	
11	Tetanus Toxin, Tet1 and G23	
12	Diphteria Toxin	
13	TAT peptide	



### **ENX-201 Introduction**

#### Effective drug delivery to across the blood-brain barrier (BBB)

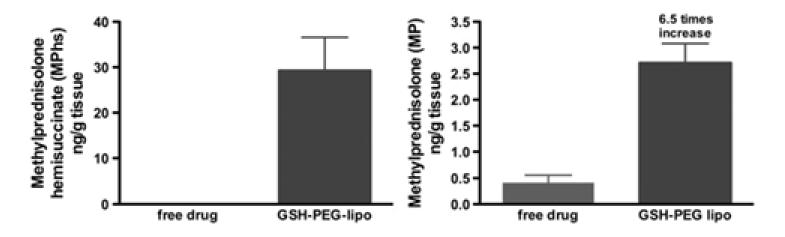






## **Preclinical Study**

在大鼠實驗的結果顯示,在注射8小時後,在腦中MP的量,ENX-201超過非微脂體的MP6倍以上。



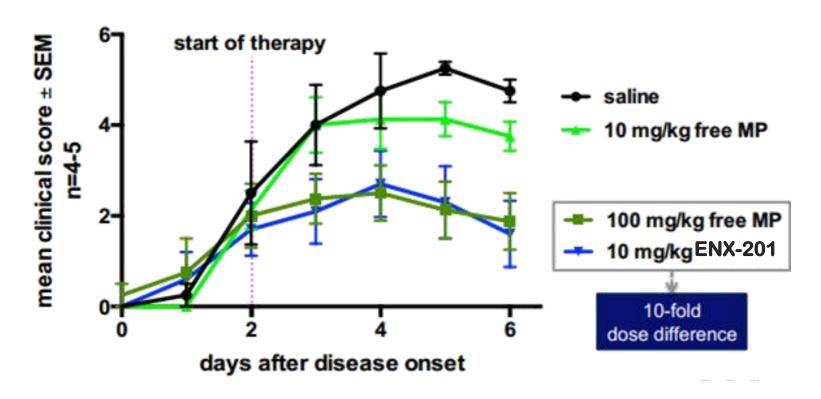
**Fig. 3.** Brain uptake of methylprednisolone hemisuccinate (left) and methylprednisolone (right). Rats (n=4/group) received 1 bolus i.v. administration of 10 mg/kg glutathione pegylated liposomal methylprednisolone (GSH-PEG lipo) or free methylprednisolone (free MPhs, 10 mg/kg). Brain uptake was determined 8 h after administration.



# **Preclinical Study**

ENX-201: 藥效驗證試驗

**EAE-MOG** mouse model of MS

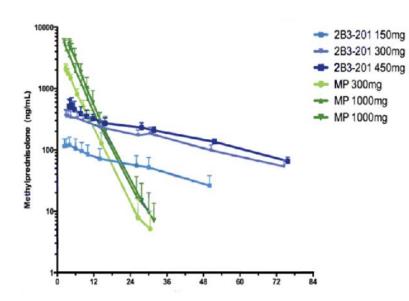




## Phase I Study (Solution)

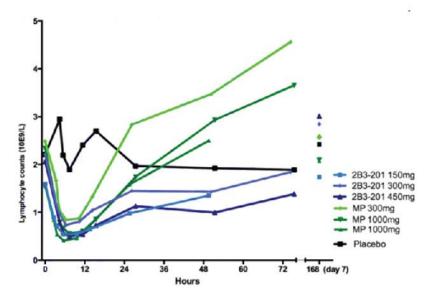
# Phase I dose-escalation results Pharmacokinetics

- Long circulation half-life of ENX-201 (23~28 hrs) vs. MP (2.5 hrs)
- Reduced high peak exposure



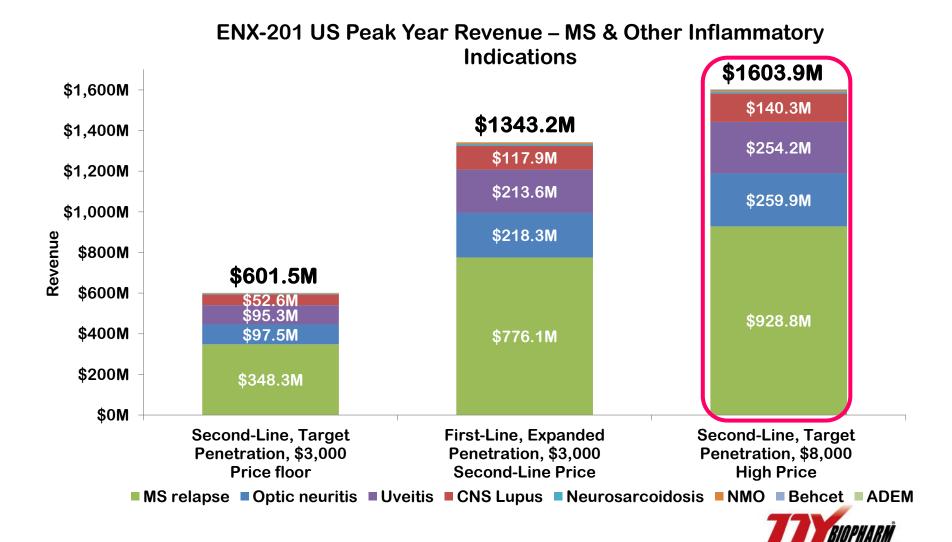
#### Phase I dose-escalation results Effect on lymphocytes

- Rapid and sustained immunosuppressive effect
- Lymphocyte count crossed baseline within 7 days in all groups





#### **Potential Market Size**



## **ENX-201 Development Strategies**

### ENX-201's strengths

- ENX-201 is a pegylated liposome which glutathione is attached on its lipid, while methylprednisolone as the main substance is encapsulated inside.
- Compared with the standard of care, i.e., a free methylprednisolone, ENX-201 is an one-shot intravenous injection which brings home-care convenience and better tolerance to patients suffering acute multiple sclerosis relapses.



# **ENX-201 Pipeline**

ENX-201: Liposomal Methylprednisolone Injection (glutathione PEGylated liposomal methylprednisolone)

	20	)14	- 20	16	201	17		20	18		20	19		20	20		20	21		20	22	
Phase I																						
Phase I bridging study (lyophilized injection)																						
Scientific advice from FDA & EMA																						
Phase II/III in MS relapses (vs placebo)																						
Phase II/III in MS relapses (vs MP)																7	X				<b>→</b>	
US NDA indication #1																,						
EU MAA indication #1																						



# Multiple Indications to Go (Pipeline)

	Indications to Develop	Market Potential Size	Competitors				
1	Multiple Sclerosis (多發性硬化症)	>21.5B	Teva (2014) Biogen EMDSerono Novartis				
2	Uveitis (葡萄膜炎) (眼睛發炎)	>0.531B	Humira (2016)				
3	Neuropathic Pain (神經性疼痛)	>5.7B	Pfizer (2011)				
4	Osteoarthritis (骨關節炎)	>5.335B	Anika (2014)				
5	ALS (漸凍人一肌萎縮性脊髓側索硬化症)	>25M (a negative CAGR of 16.10%)	Biogen Idec Inc. Avanir Pharmaceuticals Inc. Isis Pharmaceuticals Inc. Sanofi Bristol-Meyers Squibb Co.				
6	Mucopolysaccharidoses (MPS, 黏多醣症)	>300M	Vimizim				
7	Metachromatic leukodystrophy (MLD, 異染性腦白質失養症)	1B	Shire Plc Nuo Therapeutics GlaxoSmithKline Plc Zymenex A/S RegenxBio Inc. Novartis AG				

**Unit: USD/Billion** 



# **ENX-201 Management Team**















































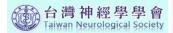
# **ENX-201 Scientific Advisory Board**

蔡清標 Taipei,Taiwan













Olaf Stuve (Texas, USA)

> UTSouthwestern Medical Center







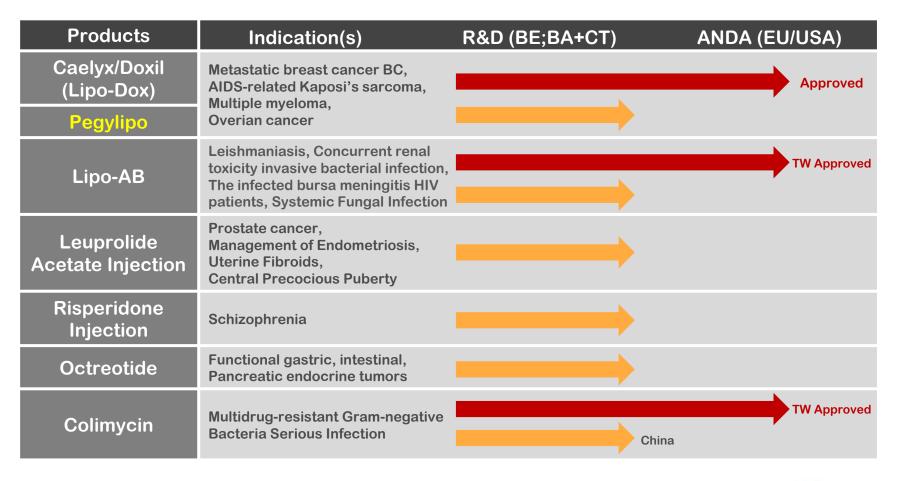
Frederik Barkhof (Amsterdam, Netherlands)

\*UCL





# Super Generics Pipeline

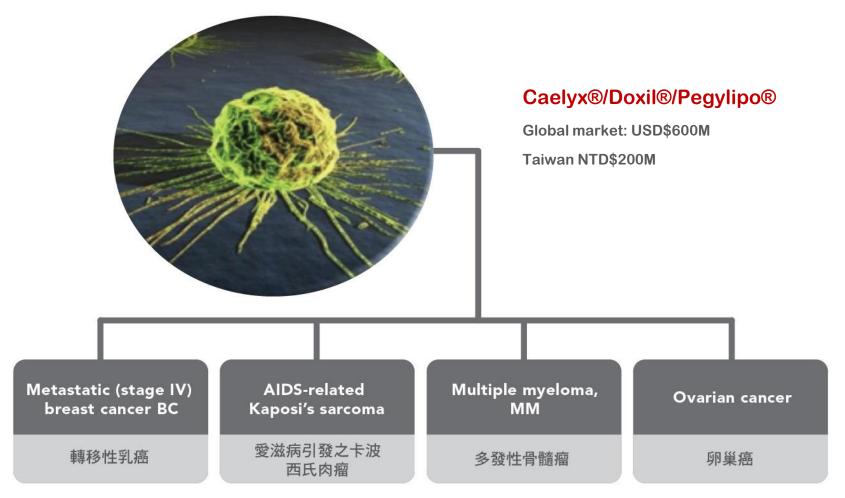




Products	World Market USD/M (est.	) Core Technology	Advantages
Caelyx/Doxil (Lipo-Dox) Pegylipo	600	Pegylated Liposome Technology	Worldwide Manufacturing Patent
Lipo-AB	440	Liposome Technology	Worldwide Manufacturing Patent
Leuprolide Acetate Injection	1,240	Lupron Depot Microsphere Formulation	Worldwide Manufacturing Patent
Risperidone Injection	960	Microsphere Formulation	Worldwide Manufacturing Patent
Octreotide	1,500	Microsphere Formulation	PLGA, Star Polymers Synthesized by TTY.
Colimycin	150	Formulation	First Choice Irreplaceable Options, TWNIH



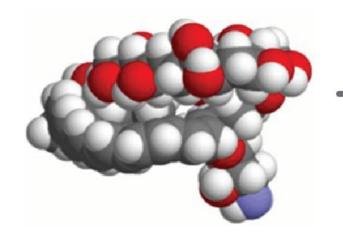
# Specialty- Caelyx®/Doxil®/Pegylipo®



Source: Thomson Reuters Mar./2017



# **Specialty-Lipo-AB**



### Lipo-AB

Global market: USD\$440M

**Target: worldwide 35~50%** 

#### Leishmaniasis

利時曼氏病 又稱 Kala-azar 黑熱病 Concurrent renal toxicity invasive bacterial infection

骨髓移植併發腎毒侵入性 細菌威染 The infected bursa meningitis HIV patients

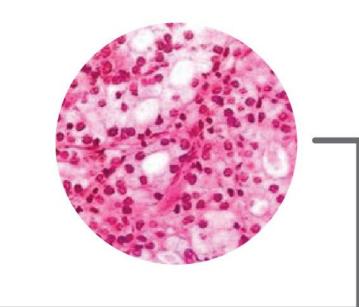
愛滋病患者腦膜炎

Systemic fungal infection

腎功能不全之菌種咸染病患



# **Specialty-Leuprolide**



### **Leuprolide Acetate Injection**

Global market: USD\$1,240M

**Target: worldwide 20~35%** 

**Prostate Cancer** 

前列腺癌

Management of Endometriosis

子宮內膜異位症

**Uterine Fibroids** 

子宮肌瘤

Central Precocious Puberty

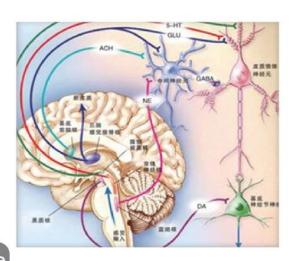
中樞性性早熟



# **Specialty- Risperidone Injection**

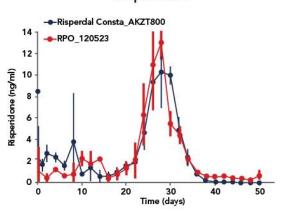
### **Risperidone Injection**

Global market: USD\$960M

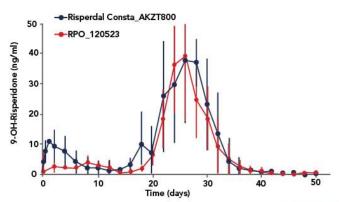


### Beagle in vivo release

Risperidone



#### 9-OH-Risperidone





# **Specialty-Octreotide**



### Indications:

- Acromegaly
- Severe diarrhea/flushing episodes associated with metastatic carcinoid tumors
- Profuse watery diarrhea associated with VIP-secreting tumors

### Synthesized by TTY

### TTY synthetic star polymers as a carrier!!

Polymer	Lot	MW(K Da)	PI
Poly(lactide-co-glycolide) star, glucose core LA:GA=1:1	TTY#783053	53	1.67



### Introduction of Octreotide

### **Symptoms-**

- Acromegaly
- Metastatic Carcinoid tumors
- VIP-secreting tumors







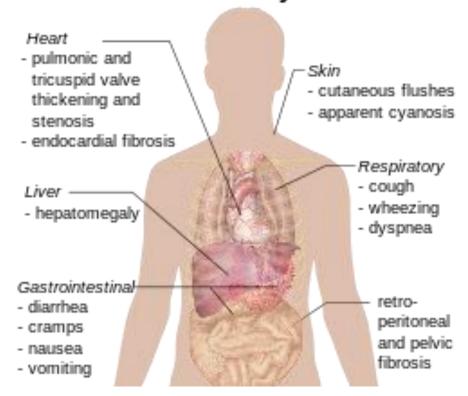


Day 4



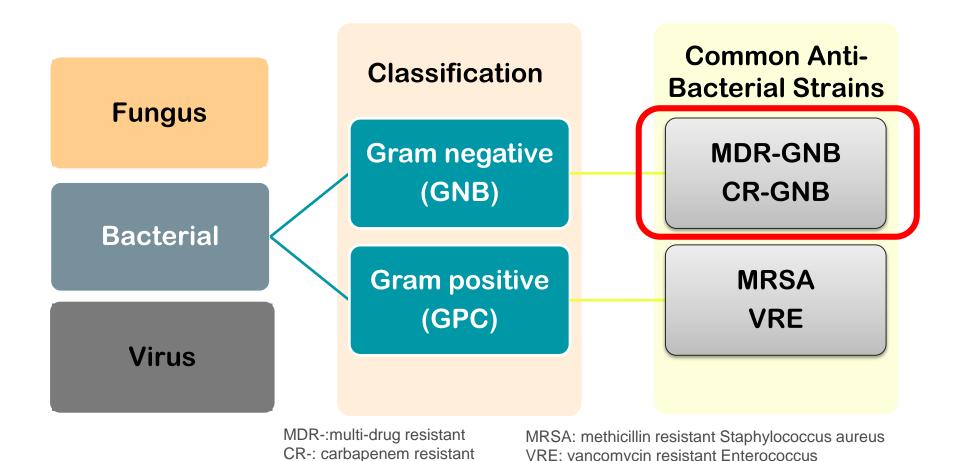
Day 21

### Carcinoid syndrome





# Colimycin

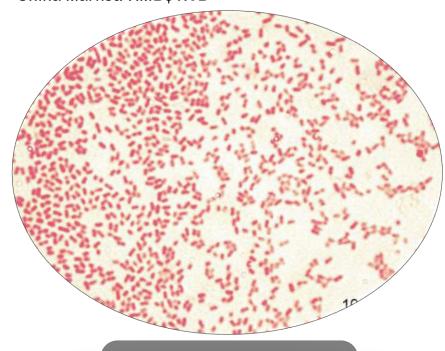


VRE: vancomycin resistant Enterococcus

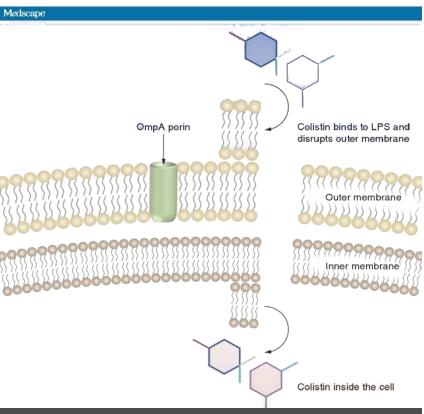
## Colimycin

### Colimycin

Global Market: US\$150M China Market: RMB\$1.0B



Multidrug-resistant Gram-negative Bacteria Serious Infection



Source: Expert Rev Anti Infect Ther. 2012;10(8):917-934

From Y\_tambe's file, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=49535



# Agenda

**Company Overview Product Strategy Product Pipeline Manufacture Facilities** Successful Product Categories In Progress Status **Biotech Success** 



### **Manufacture Facilities**

- The only PIC/S GMP certified manufacture sites for high potency oncology, 2008/2013/2016 EMA, 2010/2014 Japan, 2013/2016 US FDA, 2013 Brazil, Australia
- High standard Validation of
  - Equipment qualification/ Laboratory instruments qualification/ HVAC system/ Water system/ Compressed air system/ Nitrogen system/ Cleaning/ Analytical method/ Process/ Computer/ Logistic
- Individual flow management
  - Air flow/ Man flow/ Material flow/ Product flow/ Waste flow
  - To prevent cross contamination and environmental pollution

**HVAC System** 

**Work Safety** 



**Environmental Protection** 







# **Chungli Factory**



2008 **EMEA Arabian** Official

继续机机

2009 **EMEA** Official



2010 2011 Jordan Germany Official **Brazil** 





2012 **Japan** Official



2013 **US FDA** Japan Official



2014

**EMA** 

**Turkey** 

MOH



2015 Korea Kazakhstan









2016 **US FDA** 







# **Lioudu Factory**



Comply with PIC/S GMP and Taiwan FDA inspection for

non-cytotoxic or non-hormone







# Agenda

100

**Company Overview** 

**Product Strategy** 

**Product Pipeline** 

Manufacture Facilities

**Successful Product Categories** 

In Progress Status

**Biotech Success** 



# Oncology/Successful Products for Global

### TTY has successfully registered 47 oncology product licenses in 9 countries.

Country	UFur	Oxalip	Lipo-Dox	Irino	Asadin	Gemmis	Tynen	Epicin	Thado	Anazo	Folina	Sulfin	Algycon	Colimycin	Maxtam	Total
Thailand	1	1	1	1	1				1		1	1	1	1	1	11
Philippines			1	1	1			1		1		1	1			7
Vietnam	1	1	1	2	1		2		1							9
Hong Kong	1	1		1		2	2	3								10
Malaysia	1		1		1		1		1		1					6
Singapore				1												1
India	1															1
Sri Lanka										1						1
Guatemala			1													1
Total	5	3	5	6	4	2	5	4	3	2	2	2	2	1	1	47

TTY's CMO partner holds the licenses of TTY brand drug- Doxil in US and Caelyx in EU. 國際代工合作廠商擁有Lipo-Dox在美國(Doxil)及歐洲(Caelyx)之藥證。



## **Successful Oncology Products**

**Asadin** (伸定注射劑)



**TS-1** (愛斯萬膠囊)



**Epicin** (益彼欣注射液)



**Tynen** (汰能注射劑)



Anazo (安納柔膜衣錠)



**Gemmis** 

(建仕注射液)



Zobonic

(抑骨凍晶靜脈 注射劑)



lvic

(癌微可膜衣錠)



**UFUR** (友復膠囊)



Pexeda Inj. (派癌休注射劑)



Lipo-Dox

(力得微脂體 注射劑)



**Painkyl** 

(平舒疼口頰溶片)



**Oxalip** 





Thado

(賽得膠囊)



Irino

(益立諾)



Lonsurf

(朗斯弗膜衣錠)



Megest

(麥格斯口服 懸液劑)



Otril

(嘔速停靜脈 注射劑)



**Folina** 

(芙琳亞錠)





## **Successful Products of Intensive Care**

Brosym C+S (博益欣)







(克痢黴素注射劑)



#### Cubicin

(救必辛注射劑)



### **Flusine**

(弗路欣錠)



#### **Exacin**

(依克沙)



#### Maxtam

(抑酉每靈注射劑)



### Agrippal

(安爾保流感疫苗)





## **Successful Healthcare Products**

Algitab (艾胃逆服)



Cepiro (希比洛靜脈乾粉注射劑)



Alginos (胃逆舒)



METACIN (西腹黴素注射劑)



BIO-CAL PLUS (滋骨咀嚼錠)



Sulfin (速復利錠)





# R&D Investment 研究及臨床

Year Subject	2013	2014	2015	2016	2017
Revenue (NTD,000)	2,307,540	2,384,220	2,738,956	3,344,262	3,672,040
R&D Expense (NTD,000)	289,530	283,470	236,398	230,192	219,126
Total Staff	484	494	450	508	520
R&D Manpower	111	105	97	105	98
R&D Expense/ Revenue	12.55%	11.89%	8.63%	6.88%	5.97%
R&D Total Staff	22.93%	21.26%	21.56%	20.67%	18.85%



# Agenda

**Company Overview** 

**Product Strategy** 

**Product Pipeline** 

Manufacture Facilities

Successful Product Categories

In Progress Status

**Financial Disclosure** 



# Financial Performance (Parent Company Only)

#### **NTD** in Thousands

Item	2013		2014		2015		2016		2017	
	Amount	%								
Net Sales	2,292,163	100%	2,384,207	100%	2,738,956	100%	3,344,262	100%	3,672,040	100%
<b>Gross Profit</b>	1,404,003	61%	1,411,875	59%	1,777,941	65%	2,217,286	66%	2,347,809	64%
Operating Expenses	-1,121,548	-49%	-1,144,400	-48%	-1,035,412	-38%	-1,063,104	-32%	-1,135,595	-31%
Operating Profit	282,455	12%	267,475	11%	742,529	27%	1,154,182	34%	1,212,214	33%
Non-Operating Income and Expenses	413,685	18%	596,585	25%	705,211	26%	277,855	9%	351,484	10%
Income before Tax	696,140	30%	864,060	36%	1,447,740	53%	1,432,037	43%	1,563,698	43%
Net Income	587,440	26%	779,645	33%	1,211,018	44%	1,193,324	36%	1,344,731	37%
EPS	2.52		3.14		4.87		4.80		5.41	



# Financial Performance (Consolidated)

#### **NTD** in Thousands

Item	2015		2016		2017		1H/2018	
	Amount	%	Amount	%	Amount	%	Amount	%
Net Sales	3,195,218	100%	3,760,717	100%	4,078,760	100%	2,037,817	100%
<b>Gross Profit</b>	2,183,144	68%	2,559,220	68%	2,668,845	65%	1,342,746	66%
Operating Expenses	-1,393,357	-44%	-1,379,533	-36%	-1,411,855	34%	807,347	40%
Operating Profit	789,787	24%	1,179,687	32%	1,256,990	31%	535,399	26%
Non-Operating Income and Expenses	735,808	23%	332,372	8%	338,077	8%	376,541	19%
Income before Tax	1,525,595	47%	1,512,059	40%	1,595,067	39%	911,940	45%
Net Income (Consolidated)	1,246,592	38%	1,254,724	33%	1,368,314	33%	756,782	37%
Net Income (TTY)	1,211,018	37%	1,193,324	31%	1,344,731	32%	751,061	37%
EPS	4.87		4.80		5.41		3.02	



# **Dividend Payout**

Year Item	2013	2014	2015	2016	2017
Yield Rate (%)	1.91	2.39	3.86	3.42	4.52
P/E	41.65	33.23	18.61	23.16	18.39
Cash Dividend	2.00	2.50	3.50	3.80	4.50
Cash Payout Ratio	79.4%	79.6%	71.9%	79.2%	83.2%
Stock Dividend	0.67	-	-	-	-
Total Dividend	2.67	2.50	3.50	3.80	4.50



# Gov't Funds & Ins. Co.'s Holdings

Holdings Institution	April	2015	April/	2016	April/	2017	April/2018		
	Shares	Holdings (%)	Shares	Holdings (%)	Shares	Holdings (%)	Shares	Holdings (%)	
Insurance Company	4,880,800	1.96%	11,339,000	4.56%	18,169,000	7.31%	33,474,000	13.46%	
Government Funds	817,021	0.33%	21,177,843	8.52%	14,904,000	5.99%	10,088,843	4.06%	
Total	5,697,821	2.29%	32,516,843	13.08%	33,073,000	13.30%	43,562,843	17.52%	

