



*Fueling life sciences through  
transformative transactions*

## BIOPHARMA PARTNERING IN JAPAN

December 2017

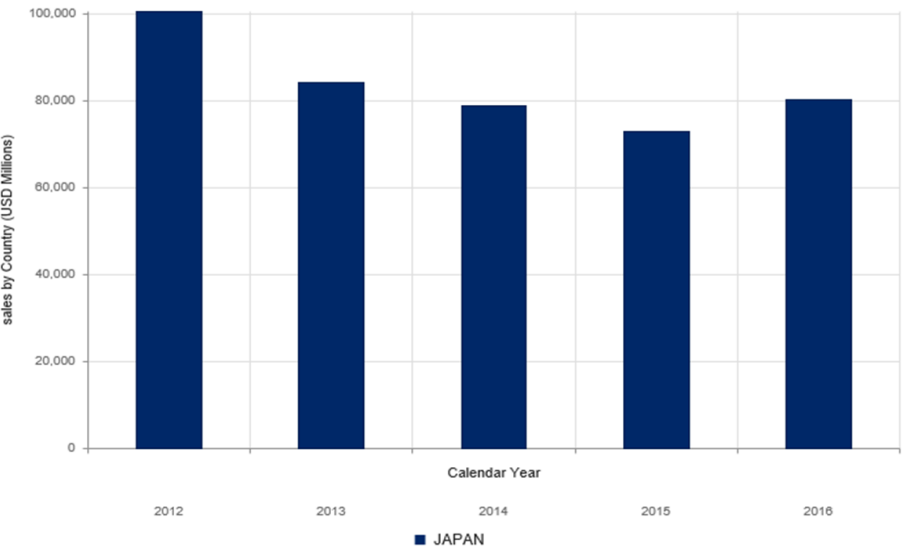
# AGENDA

- 1 The Japan Pharmaceutical Industry
- 2 Japan Biopharma and the Public Markets
- 3 Deal Trends in Japan
- 4 How Locust Walk Can Assist

# THE JAPAN PHARMACEUTICAL INDUSTRY

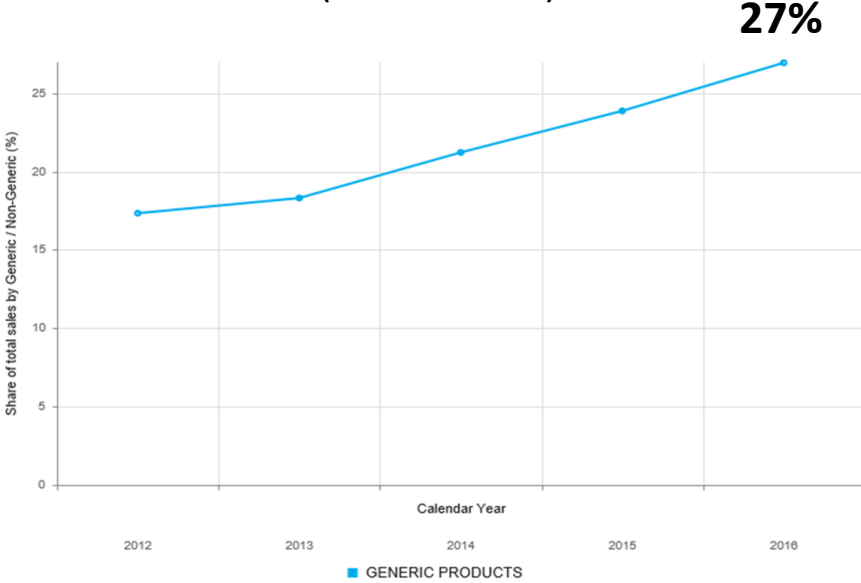
The Japan ethical pharmaceutical market is ~\$80B; generics continue to gain market share but still represent a fraction of total sales

**Total pharmaceutical sales in Japan**  
(2012 – 2016)



Source: IMS Health Analytics Link; IMSAudited






**Generic share as a % of total market**  
(2012 – 2016)



Source: IMS Health Analytics Link; SalesbyVolumn

Source: IMS Health Analytics

# Takeda remains the top domestic pharma company with a market value of nearly \$50 billion

Company	Market Cap (\$B)*	Total Sales in FY2016 (\$B)	Therapeutic areas of interest	Mkt cap/sales
 Takeda	43.4	15.4	GI, Oncology, CNS, Cell Therapy	2.8x
 CHUGAI	29.2	4.4	Oncology, Autoimmune, Bone & Joint, Renal, Regenerative & Gene Therapy	<b>6.6x</b> ←
 astellas	26.5	11.6	Oncology, Urology & Renal, Immunology	2.3x
 Otsuka	24.4	10.6	GI, CV, Ophthalmology, Dermatology (Japan only)	2.3x
 SHIONOGI	18.2	3.0	Pain, CNS, Infectious Disease, Metabolic Disorders	<b>6.1x</b> ←
 Daiichi-Sankyo	17.2	8.5	Oncology, Cardiovascular, CNS	2.0x
 ONO	12.4	2.2	Oncology, Diabetes, Orthopedic	5.6x
 Mitsubishi Tanabe Pharma	12.1	3.8	CNS, Autoimmune & Inflammatory, Diabetes & Kidney, Vaccine, Regenerative Medicine, Biologics	3.2x
 KYOWA KIRIN	10.6	3.0	Nephrology, Immunology/Allergy, Oncology, CNS	3.5x

Source: company documents; IMS Health Analytics; Bloomberg; 1 USD= 112 JPY

\* As of Dec 4, 2017

# Foreign pharmaceutical companies are growing in Japan, with Pfizer in the #1 position in terms of sales; 11 of top 20 companies are foreign






## Japan Market Sales

Units: USD million

2016 Ranking		2015	2016	YOY %
1	Pfizer	4,160	4,280	3%
2	Daiichi Sankyo	3,212	3,542	10%
3	Chugai	3,147	3,479	11%
4	Takeda	3,149	3,308	5%
5	Gilead	1,531	2,855	<b>86%</b>
6	AstraZeneca	2,169	2,446	13%
7	Mitsubishi Tanabe	2,384	2,348	-2%
8	MSD	2,280	2,295	1%
9	Bayer Yakuhin	1,868	2,142	15%
10	Otsuka	1,987	2,135	7%
11	Novartis	2,073	2,107	2%
12	Eli Lilly Japan	1,788	2,104	18%
13	GSK	1,819	1,914	5%
14	Astellas	1,834	1,912	4%
15	Nippon Boehringer	1,718	1,899	11%
16	Ono	991	1,727	<b>74%</b>
17	KHK	1,529	1,626	6%
18	Sanofi Japan	1,925	1,476	<b>-23%</b>
19	Janssen	1,142	1,382	21%
20	Shionogi	1,225	1,237	1%

Source: IMS Health Analytics

## Foreign pharmaceutical companies performance in Japan vs ROW (2016)

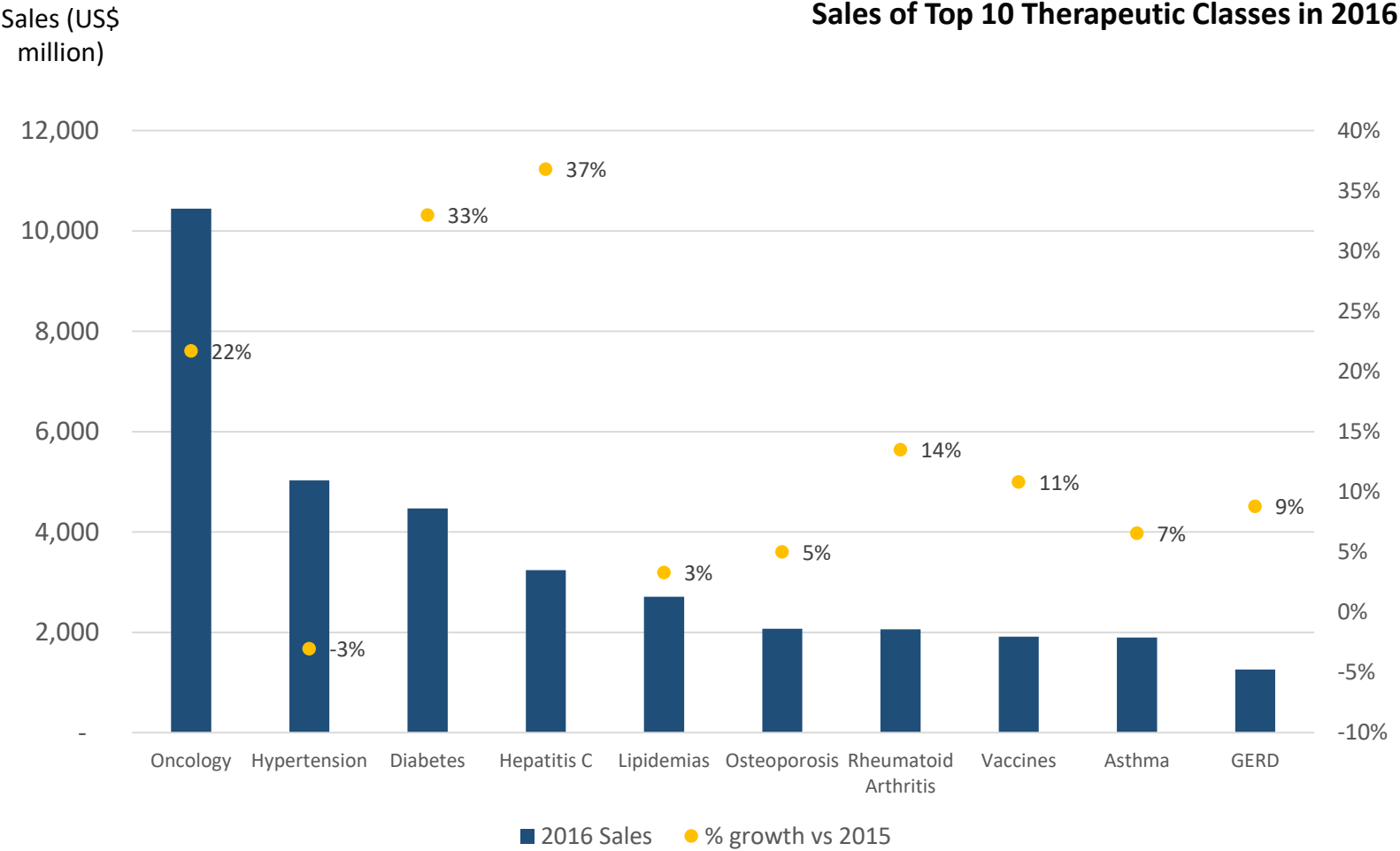
Company	Global Ranking	Japan Ranking	GAP (+/-)
 Bayer	16	9	+7
 CHUGAI Roche	6	3	+3
 Boehringer Ingelheim	17	15	+2
 Pfizer	1	1	-
 GILEAD	5	5	-
 MSD	7	8	-1
 gsk GlaxoSmithKline	8	13	-5
 NOVARTIS	2	11	-9
 SANOFI	3	18	-15
 Johnson & Johnson	4	19	-15
 abbvie	10	25	-15

Japan **Over Performing** vs. Global

Japan Performance **on Par** w/Global

Japan **Under Performing** vs. Global

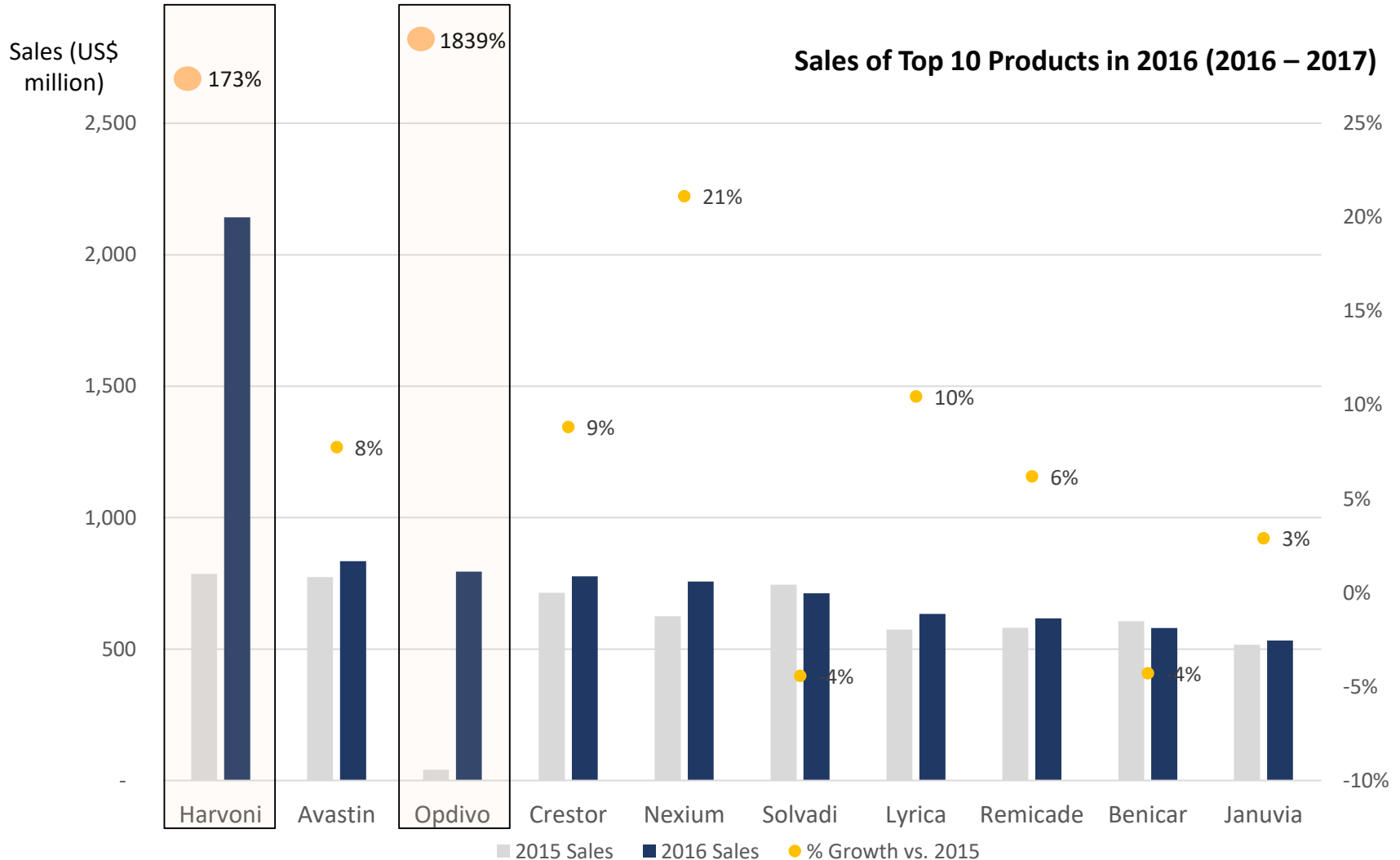
# Oncology is largest therapeutic area in Japan with sales >\$10 billion in 2016 fueled by launch of PD-1 inhibitor class (Opdivo®)



Source: IMS Health Analytics



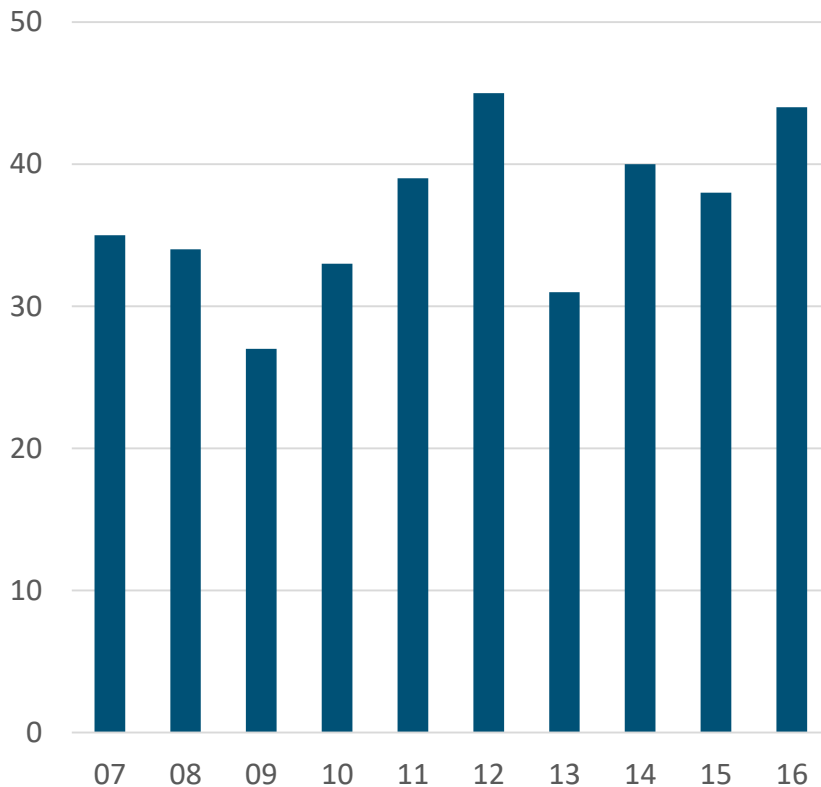
# Sales of Opdivo® and Harmoni® grew +1839% and +173% in 2016



Source: IMS Health Analytics

~ 40 NCEs have been approved each year during the past 10 years; 4 regenerative medicine products have been approved to date

# of novel drugs approved in Japan (2007 – 2016)<sup>1</sup>



Regenerative medicine products approved<sup>2</sup>

Brand	Description
JACC® (J-TEC)	Autologous cultured cartilage
JACE® (J-TEC)	Autologous cultured epidermis
TEMCELL® HS (JCR Pharma)	Mesenchymal stem cells; acute graft-versus-host disease
HEARTSHEET® (Terumo)	Severe heart failure

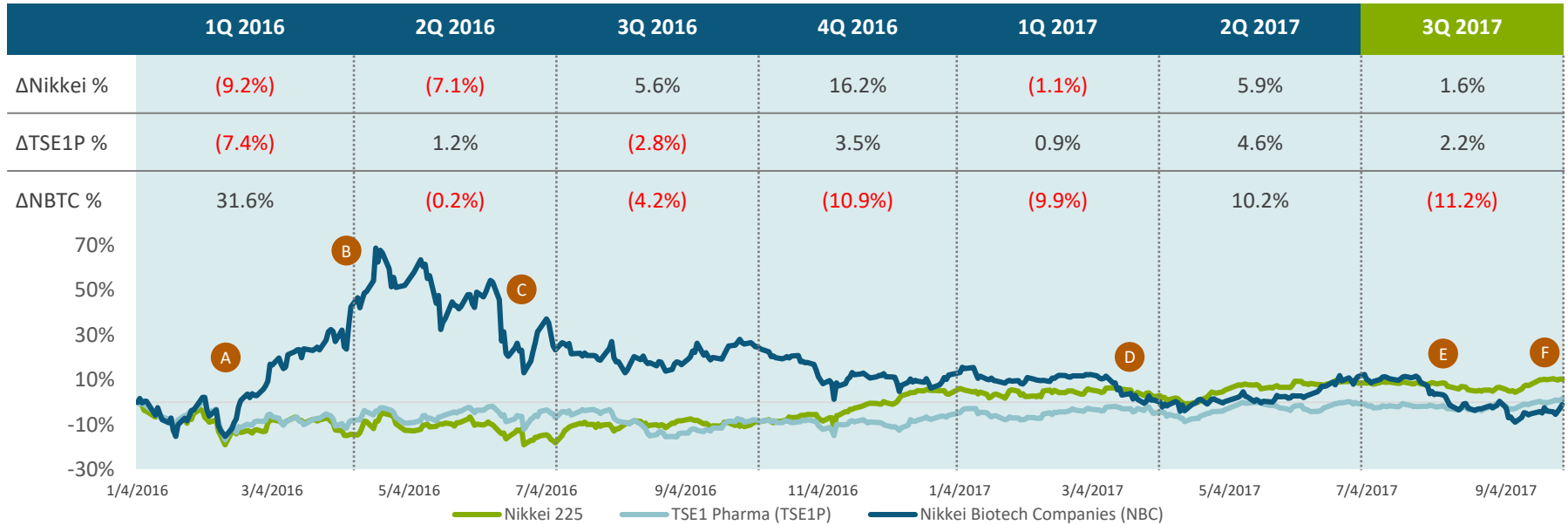
Source: <sup>1</sup>JPMA Data Book 2017

<sup>2</sup> <https://www.pmda.go.jp/review-services/drug-reviews/review-information/ctp/0008.html>

# JAPAN BIOPHARMA & THE PUBLIC MARKETS

The Japanese biotech market is slightly down since the beginning of 2017, and lags behind the broader Nikkei 225 index

### 3Q 2017 and Historical Performance of Key Market Indices



Key Event	
A	Japanese biotech shares begin steep rise in March 2016 driven by gains in stocks such as PeptiDream, Sosei, and AnGes MG
B	Sosei's affiliate Heptares and Allergan announced \$3.3B partnership agreement with \$125M upfront on April 7
C	Drop in shares traded on MOTHERS* market due to UK "Brexit" vote, followed by brief recovery
D	Solasia Pharma listed on the MOTHERS stock market at 185 JPY on 3/24
E	With no event impacting the NBC stock index, the price has been hovering near low levels for the year
F	<b>Sept 30, 2017: NBC closes -13% since the beginning of 2017</b>

SOURCE: Locust Walk analytics, Nikkei BioTech Online, Yahoo Finance; \*MOTHERS (Market of high growth and emerging stocks: stock market at Tokyo Stock Exchange)

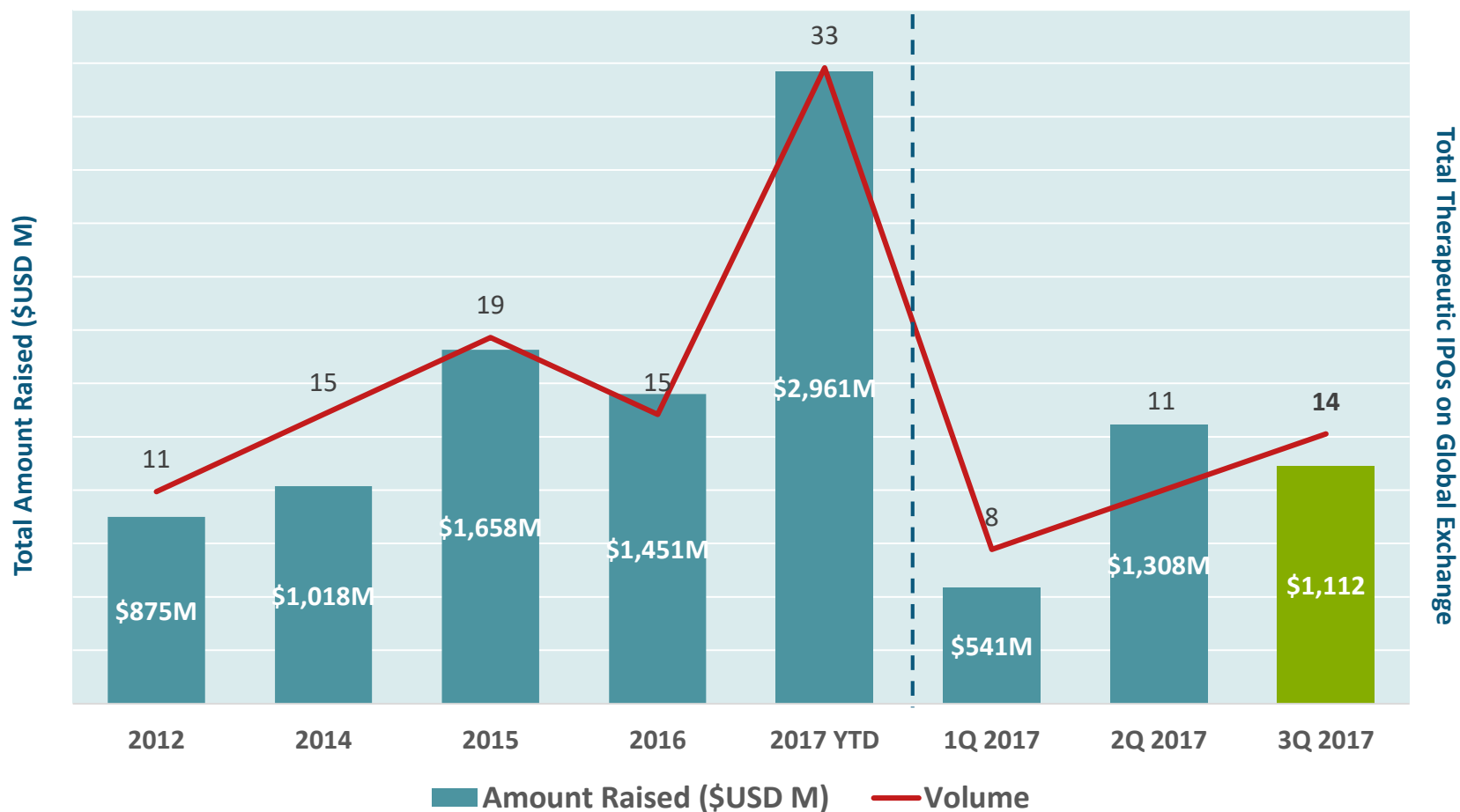
Since 2014, there have been **only 7 IPOs** of biopharma companies in Japan, and **only 1 IPO** thus far in 2017 raising \$32M

Listing Date	Company	Market	Amount raised at IPO (JPY & USD)	Market Cap at IPO (JPY & USD)	Market Cap today (12/4)	% Change since IPO
Mar 2017	Solasia Pharma	Mothers	3.6B \$32M	19.7B \$179M	39.6B \$352M	<b>101%</b>
Mar 2016	Pheonix Bio	Mothers	700M \$6M	6.6B \$60M	3.4B \$30M	<b>-49%</b>
Oct 2015	BrightPath Biotherapeutics	Mothers	2.9B \$26M	13.2B \$120M	24.8B \$220M	<b>88%</b>
Jun 2015	Healios	Mothers	7.3B \$66M	58.4B \$531M	72.1B \$639M	<b>23%</b>
Apr 2015	SanBio	Mothers	8.0B \$72M	74.6B \$678M	139.7B \$1.2B	<b>87%</b>
Sep 2014	Ribomic	Mothers	2.8B \$25M	22.1B \$201M	7.8B \$69M	<b>-64%</b>
Feb 2014	Acucela Inc.	Mothers F	16.6B \$151M	81.9B \$744M	21.0B \$186M	<b>-74%</b>

SOURCE: Locust Walk analytics, Mitsubishi UFJ, Google Finance

Japan IPO market is dwarfed by China where **33 biopharmas** have gone public with \$3B raised through 3Q 2017

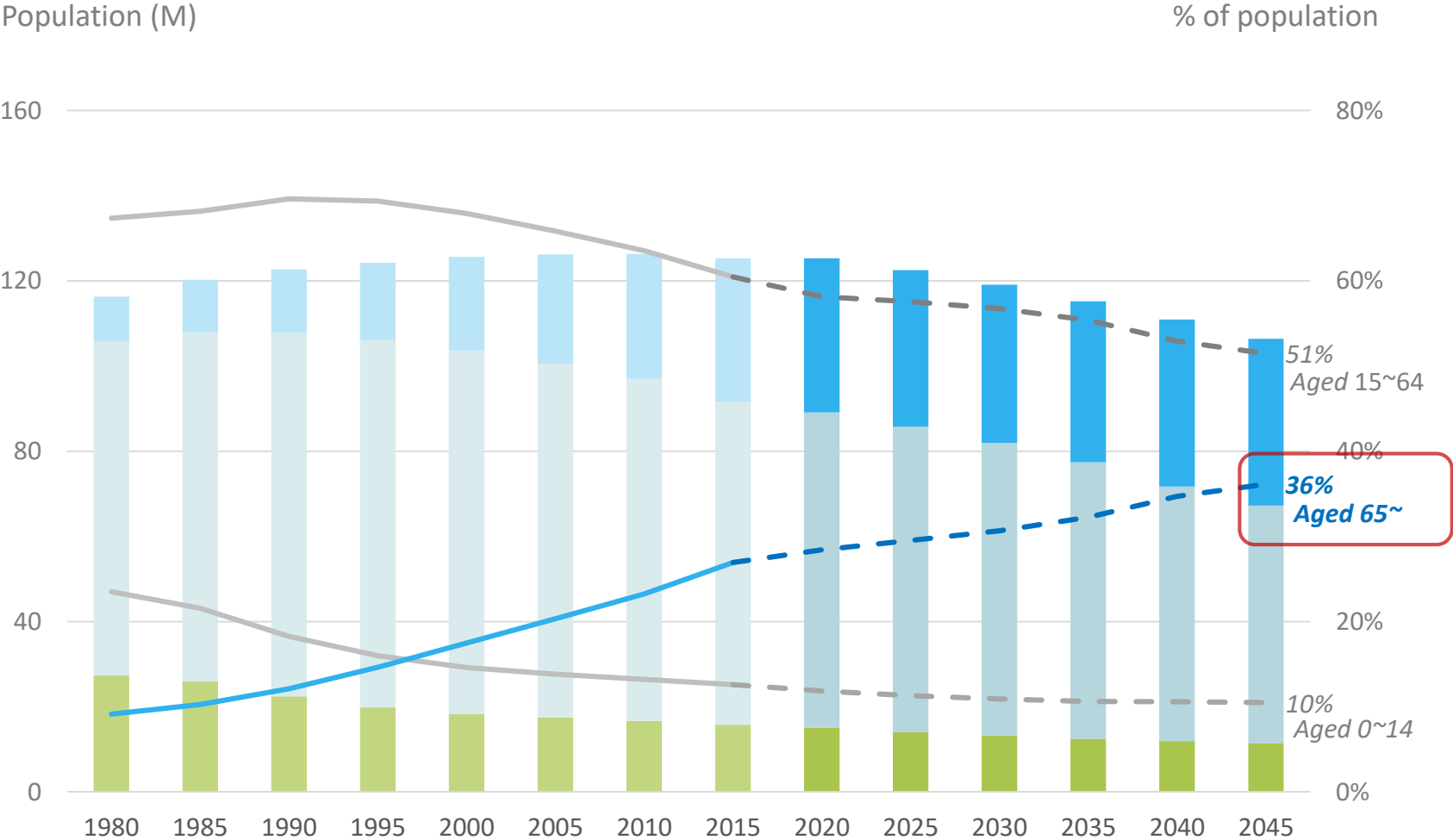
Number of China Biopharma IPOs and Aggregate Total Raised By Quarter



SOURCE: Locust Walk analytics ; Eastmoney

## DEAL TRENDS IN JAPAN

# The Japanese population is rapidly shrinking - an estimated 35% of the population will become over 65 years old by 2045



SOURCE: Locust Walk Analysis based on Vital Statistics (2015), Ministry of Health, Labour and Welfare and the 2017 estimation, National Institute of Population and Social Security Research



# Japanese pharmaceutical companies are facing unprecedented pressure to develop and launch new drugs

Universal health care insurance system



Rapidly aging society with shrinking working generation

- ✓ Reimbursement pricing reform
  - ▶ Government working on changing drug price revision schedule from *once every other year* to *once every year*
- ✓ Increasing share of generics
- ✓ “SAKIGAKE Designation System” to promote R&D in Japan aiming at early practical application for innovative pharmaceutical products

**Challenge**

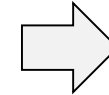
Holding down government spending on health care

Reducing Japanese pharmaceutical companies' dependency on long-term listed drugs by stimulating the development of novel drugs

# Other key trends should result in Japan pharmaceutical companies becoming more active in-licensing assets from the west

## Changes to Pricing Regs in Apr '18

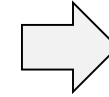
- Changes will seek to reduce # of drugs with “Price Maintenance Premium”; novel drugs likely continue to qualify



Critical for companies in Japan to develop & launch **novel** products

## Regenerative Medicine

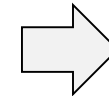
- Government continuing to support development of cell-based therapies; lots of action at the PMDA



Expect **increasing number of cell-based therapies** in next 5-10 years

## Under developed biotech sector

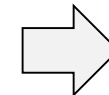
- Due to lack of private and public funding, the Japan biotech sector lags the west and increasingly China



Domestic Japanese companies must continue to **look outside Japan** for novel pipeline

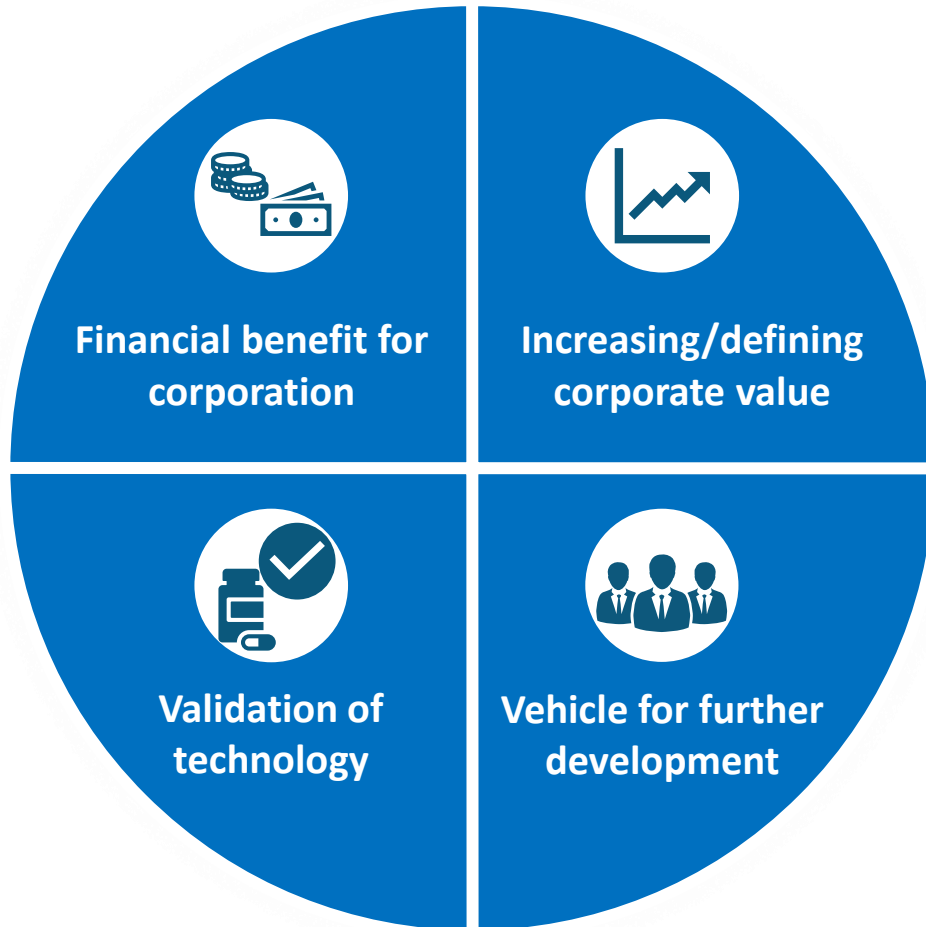
## No 505b(2) pathway

- While the US has an expedited regulatory pathway for novel formulations, Japan does not



Japan patients **may not be able to access** novel formulations available outside Japan

# For western biopharma, there are a variety of benefits from out-licensing to Japan



## Benefits from out-licensing to Japan

- **Financial benefit**
  - Non-dilutive financing
  - Cash for next projects to generate new cash in-flow
- **Increasing / defining corporate value**
  - Increase value of corporation through affirmation of asset's potential, possibly resulting in further fund-raising
- **Validate technology**
  - Confirms confidence in asset from a Japan partner following rigorous due diligence and communications with the Japanese regulatory agency
- **Vehicle for future development**
  - Potential for shared cost of development
  - Intellectual input and contribution from partner through co-development

## In 2017 YTD, Takeda's \$340M licensing deal with Tesaro, including \$100M upfront in cash, has been the largest Japanese deal in value

Licensee	Licensor	Date	Stage	Upfront (\$M)	Deal Size (\$M)	Subject
Nanocarrier	VBL Therapeutics	11/2017	Phase 3	15	115	VB-111, an innovative gene therapy for cancer with success Phase 2 data
Ono	Karyopharm	10/2017	Phase 3	22.3	193	Selinexor and KPT-8602, oncology products
Asahi Kasei	Bone Therapeutics	09/2017	Phase 3	2	11	PREOB®, an autologous bone cell therapy product
Takeda	Tesaro	07/2017	Marketed	100	340	Niraparib, a PARP inhibitor for tumor
Ono	Array Biopharma	05/2017	Phase 3	31.6	187	Binimetinib, a MEK inhibitor and Encorafenib, a BRAF inhibitor
ASKA	Pieris	02/2017	Phase 2	2.75	80	PRS080, an anti-hepcidin anticalin for CKD related anemia
Takeda	Exelixis	01/2017	Approved	50	145	Cabozantinib; a tyrosine kinase inhibitor for oncology indications
Sato	Novan	01/2017	Phase 3	11	35	SB204, a topical product for acne vulgaris
Millennium (Takeda)	Maverick	01/2017	Discovery		125	T-cell engagement platform for cancer
Daiichi Sankyo	Kite	01/2017	BLA filed	50	250	Chimeric antigen receptor (CAR) and T cell receptor (TCR) products for oncology indications

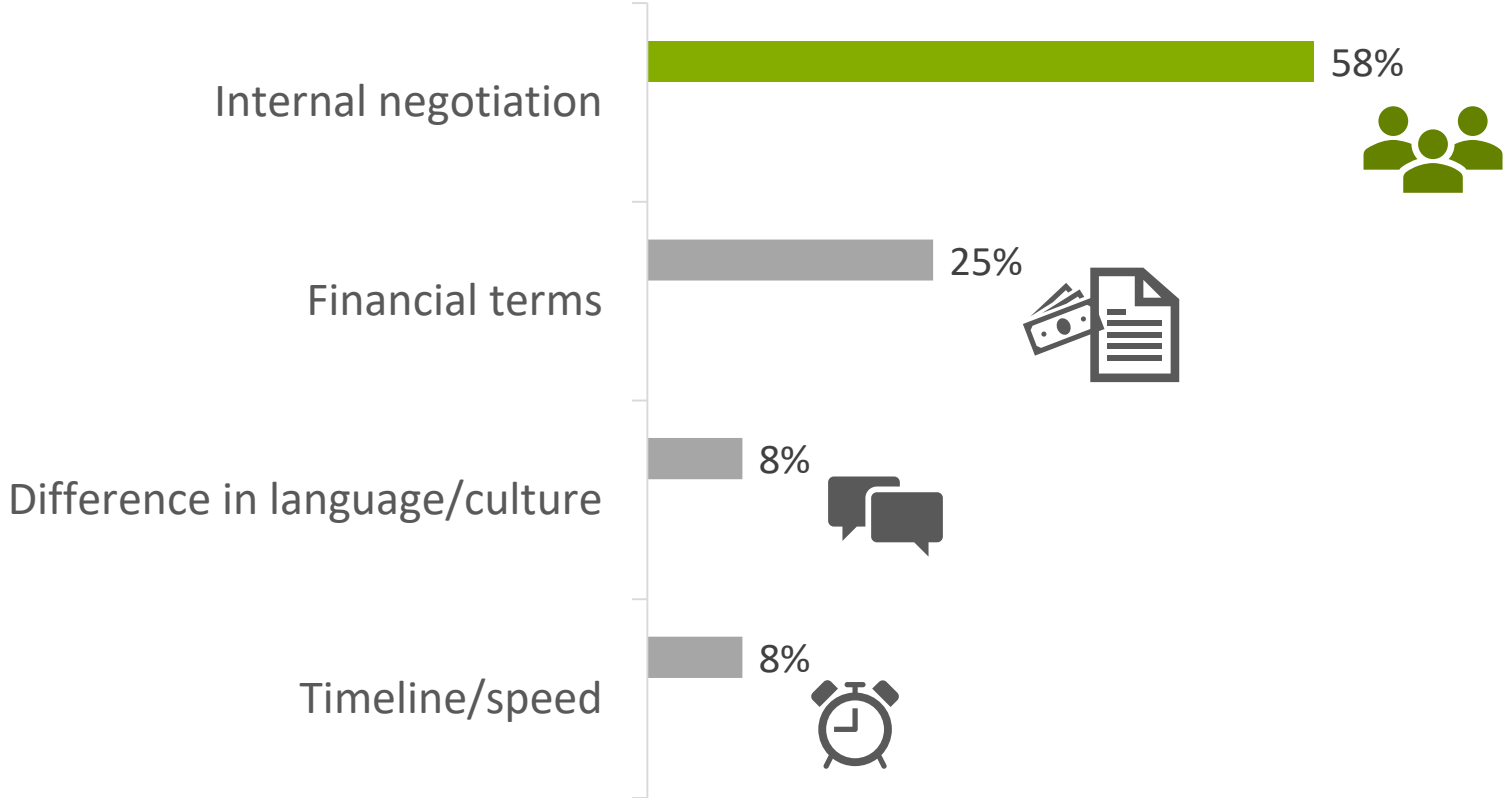
SOURCE: Locust Walk analytics, BioSciDB, Global Data

## Five large M&As by Japanese pharma have been announced thus far in 2017 including Takeda's \$5.2B acquisition of Ariad Pharmaceutical

Seller	Buyer	Date	TA	Deal Size (\$M)
NeuroDerm	Mitsubishi Tanabe Pharma	07/2017	Central Nervous System	1,100
Ogeda	Astellas	04/2017	Endocrinological & Metabolic	533
PCT (Caladrius Biosciences)	Hitachi Chemical	03/2017	Cell Therapy	80
Neurovance	Otsuka	03/2017	Psychiatric	100
Ariad	Takeda	01/2017	Oncology	5,200

SOURCE: Locust Walk analytics, BioSciDB, Global Data

We recently asked BD execs at Japan pharma, “What are the biggest barriers for Japanese companies to get deals done with western companies?”



## Key thoughts to keep in mind when talking with Japanese pharmaceutical companies about a possible collaboration

- Know the key decision-making people at all levels
- Understand the culture
- Communicate in simple and plain English
- Consider having someone local on the ground to help facilitate discussions in “real time” and in Japanese

## HOW LOCUST WALK CAN ASSIST



# Locust Walk's Japan team is fully-dedicated to our clients' strategic interests throughout Asia

## MD, SVP, VPs

### Steve Engen\*

Managing Director, Head of Asian Practice Tokyo

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## Joining LW on January 1st

### Hayato Watanabe

Vice President | Tokyo

We are uniquely positioned as a fully integrated advisor



### Commercial Assessments

- Qualitative KOL market research
- Quantitative physician market research
- NHI pricing analysis
- Secondary desk research

### Outreach to Japanese biopharma

- Build strategic contact log
- Initial outreach to senior executives
- Management presentation
- Due diligence support

### Negotiations & Contracts

- Term sheets from multiple parties
- Build competitive tension
- Guidance letters
- Definitive agreement negotiations and deal close

### Regulatory Pathway

- Preliminary meeting(s) with PMDA
- Formal meeting(s) with PMDA

**We operate in Japan...speak the language...have the senior contacts**

# Execution of Japan partnership for a novel oral testosterone in less than 2 months

## Situation Assessment

**TesoRx**

**ASKA Pharmaceutical Co., Ltd.**

- TesoRx Pharma LLC is a private biopharmaceutical company focused on the development innovative therapeutics in the urology and oncology fields using proprietary delivery system technology.
- TesoRx is a long-standing client of Locust Walk. In 2014, Locust Walk successfully negotiated an \$85M transaction between TesoRx and the Aspen Group.
- TesoRx was interested in licensing Japan rights to their novel oral testosterone product, THG-1001, for the treatment of male hypogonadism. TesoRx initiated discussions with Japanese companies, including ASKA Pharmaceutical (Tokyo, Japan), a leading company in the hormone therapy field in Japan.
- In November 2016, TesoRx engaged Locust Walk to assist in expediting a transaction for THG-1001 in Japan. They were keen to leverage the Locust Walk network in Japan and its relationships with senior officers at ASKA.

## Key Activities

- Identified the strongest potential partners in Japan for THG-1001, focusing on companies in the urology and hormone therapeutic areas. Leveraged Locust Walk contact network to conduct outreach to potential Japanese partner companies.
- Conduct face-to face meetings with Japanese companies and TesoRx in Japan. Locust Walk managed the competitive deal process and continued to negotiate deal terms with ASKA.
- Met regularly with top executives at ASKA to understand the key issues inside ASKA that could impact transactability.
- Led final negotiations with ASKA regarding deal structure and economics. Worked between TesoRx and ASKA to overcome challenges and hurdles, many unique to the Japan pharmaceutical environment.

## Successful Outcome

- TesoRx engaged Locust Walk in November 2016 to drive its in-house process of securing a Japan partnership to the most beneficial conclusion. Our combined efforts led to TesoRx and ASKA consummating an partnering arrangement for Japan rights to THG-1001 on December 30, **less than 2 months after Locust Walk was engaged by TesoRx.**
- Under the terms of the partnership, ASKA will pay upfront and license fees and milestones to TesoRx. ASKA will also share in the development costs and pay royalties to TesoRx on sales for THG-1001 in Japan.

Locust Walk looks forward to working with you as a trusted advisor to help you succeed in Japan

### **Opportunity**

- 3rd largest pharmaceutical market: \$80B
- Pharmaceutical companies seeking in-licensing opportunities

### **Challenge**

- Difficulty of communication: language, time zone, culture...
- Unique epidemiology and market: need to understand “Japan”

### **Solution**

- Locust Walk Japan’s team together have >50 years experience working in the Japan pharmaceutical industry
- Let us help you build the story for your asset and create value through cross-border collaborations

# Thank you for listening!

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