

For Massachusetts Biotech Council

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Japan/Asia Partnering

4 Mergers Create a New Paradigm

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Background of Tanaka

- Born-raised in Los Angeles of parents from Japan.
- Former Accenture international management consultant, Los Angeles office, 11 years.
- Exclusive consultant to help organize-chair BIO's 1st partnering conference in Tokyo in '94 & assisted in creating BIO-Asia Partnering Conference in Tokyo.
- Assisted US-Canada-UK clients to sign 20 alliances in Japan and Korea. Deal #21 now in global license term sheet negotiations.
- Organized for clients over 2,500 alliance development meetings in Japan, Korea, Taiwan & China.

Japan: Biggest Change in 50 Years

- Past 2 years: *Astellas/Yamanouchi+Fujisawa; Daiichi + Sankyo; Dainippon+Sumitomo; Mitsubishi+Tanabe.*
- **Takeda** remains #1; & **Eisai** continues independently.
- Many have licensed-in 50% their clinical pipeline.
- In Japan, dev-reg-sales tedious, slow, with thin profit.
- **Above new top 6 firms** seek global rights for indications where they have a related sales force or plan one.
- 30+ smaller Japan firms focused on 1-3 indications and for only Japan turf, can sub-license to Korea + Taiwan.
- Oncology players shrink to 14; many more in CNS; diabetes; immuno-allergy; pain; urology; age-related.

Re-ranking Top Japan Partners

- Takeda
- Astellas
- Daiichi Sankyo
- Mitsubishi Tanabe
- Eisai
- Dainippon Sumitomo
- Otsuka
- Shionogi
- Ono
- Kyowa Hakko
- Another 30+ active companies

Takeda

- Founded 1781; #1 Rx domestic leader many decades.
- Global HQ-Lic at Osaka; sales \$11.2B; #16 global rank.
- Sales ¥: Japan 30.5%; N. America 54%; EU 13.4%.
- Outside Japan: No. America R&D, sales & VC; EU R&D, sales & manufacturing.
- Franchise: metabolic-CV-oncology; **emerging: urology-CNS**; others: bone-joint, GI, allergy, COPD.
- In-license at late-Preclinical if MOA IP + major market.
- A multi-national based in Japan; aim to be a global top 10 player. takeda.co.jp

Astellas Pharma

- 2005 merger of #2 Yamanouchi + #5 Fujisawa.
- Global HQ at Tokyo; sales \$7.8B; global rank #18-19.
- Sales ¥: Japan 54%, EU 24%, N. Amer 19%, Asia 3%.
- N. America/IL: sales; manufacturing; trials; & VC fund.
- EU HQ in UK: sales in Germany; development + manufacturing in Netherlands & Ireland.
- Asia 7 subsidiaries: Korea; Taiwan; China; Philippines; Thailand; Indonesia; & Hong Kong.
- Bus dev focus: urology; immunology & inflammatory; diabetes; CNS; infectious viral diseases; & cancer.
- Global rights where they have strong sales franchises.
- Goal to become global top 10. astellas.com

Daiichi Sankyo

- Merged 2005; Sankyo was #3 & Daiichi #6.
- Global HQ at Tokyo; global sales \$6.9B; Japan #3 sales.
- Sales ¥: Japan 65%; USA 19%; EU 14%; other 4%.
- Sales staff: Japan 2,300; USA 1,500; EU 800 in 10 countries; China-Korea-Taiwan-Thailand-others 450.
- Priority R&D: Thrombosis; diabetes II; cancer; autoimmune disease/rheumatoid arthritis.
- Others: CV; bone/joint; infectious diseases.
- License-in at preclinical or later, case-by-case.
- R&D staff: Japan 2,200; USA 270; EU 130; China 35.
- daiichisankyo.com

Mitsubishi Tanabe

- Yesterday's merger of Mitsubishi Pharma + Tanabe.
- HQ Osaka, Bus Dev HQ Tokyo; combined sales \$3.5B.
- Earlier merged 4 companies: Mitsubishi Chemical Rx Research, Tokyo Tanabe, Green Cross & Yoshitomi.
- Sales-force: Japan; USA, UK, Germany, France, Italy.
- Investment sub in Boston, a MBC member.
- R&D pipeline: cardiovascular/metabolics; immunology/inflammation; respiratory; CNS; hepatic; & urology.
- Global development: renal diseases; diabetes-related; and cerebral diseases.
- Strategically establishing-expanding: China & Asia.

Eisai

- Global HQ at Tokyo; started 1941.
- Total sales \$5.7B, inventor of “Aricept” for Alzheimers.
- Sales ¥: US 45%, 1st time more than Japan; Japan 44%; EU 8%; Asia 3%.
- Sales staff: Japan 1,200; US 865; EU 475; Asia 940.
- Aricept sales \$2.2B in 70+ countries: US 63%; Japan 20%; EU 14%; Asia 3%.
- R&D, sales & manufacturing in US, in 9 EU countries & Japan, plus sales-manufacturing in 9 Asian countries.
- Bus Dev focus: neurology; GI; cancer; & acute care.
- Acquired Pennsylvania mAb oncology firm Morphotek.
- eisai.co.jp

Dainippon Sumitomo

- Merger in 2005 of 2 medium-large companies.
- HQ Osaka; global sales \$2.2B; domestic sales in CV-metabolic; CNS; oncology-infection; GI; inflammation-allergy.
- Japan sales force 1,470.
- R&D staff 1,230.
- Overseas base: NJ; London; Beijing-Shanghai-Suzhou.
- Bus Dev focus: CNS including USA; Diabetes II; CV; inflammation, immunology & allergy.
- In-license & out-license. ds-pharma.co.jp

Another 30+ in Japan

- Another 30+ domestic firms actively license-in/-out; closely-held; decades dedicated in 1-2 indications.
- Focusing on niche markets passed-over by top 6.
- Smaller firms seek Phase IIa data to in-license.
- Sales-force throughout Japan; sub-license experience to Korea & Taiwan.
- Population of Japan 127 million, Korea 48 million, & Taiwan 21 million.
- They are members of *Japan Pharmaceutical Manufacturers Association*, jpma.or.jp/english, with links to Japan regulatory basic description.

Japan Partnering Paradigm

- Priority indications: oncology (not skin but digestive, breast, lung, etc); diabetes II; CNS; RA-OA; allergy; pain; age-related; more conservative safety than USA.
- Top 6 consider **late-Preclinical** stage for big global drug, strong MOA IP, case-by-case; & next 30, Phase IIa.
- Global rights for their expanding sales-forces.
- License Term Sheet discussion reached in 3 quarters.
- Their culture is to develop people-relationships.
- Alliance creation managed by Japan HQ License dept.
- Long-term, detail-oriented, conscientious partner.
- Baseball analogy: *seller "pitches," buyer "bats."*

C H I N A

- 1.3 billion population.
- Growing upper-middle income population.
- Non-stop, daily flights SFO/LAX to Beijing.
- “Coming-out” celebration at Olympics.

China: Country Highlights

- 1.3B pop: **urban 500M**, 167% of total USA; rural 800M.
- Land: equal size to all Europe, 400% pop. of USA.
- 31 regions governed by Beijing.
- 8,000 yrs human settlements, 4,000 yrs written history.
- Discovered paper-making; typesetting; gun powder; compass; etc.
- National language: Mandarin, Cantonese only SE China.
- Admitted to W.T.O.; upgrading various infrastructures.
- Getting PhDs, MBAs in English-speaking countries.
- Beijing: 14.6M, HQ State FDA, Olympics 8-08-'08.
- Shanghai: 17M, "financial-commercial NYC" of China, highly entrepreneurial-quick, World Expo 2010.

China: Rx Market Environment

- **3rd biggest country Rx market** in 12 years, 2020.
- 1.45B population in 22 years, 2030, with age 60+ of **350M**.
- Current life expectancy 71.9 years.
- **HBV; malignant cancers; blood brain vessel; respiratory; heart; GI; metabolic; neurological; & reproductive.**
- Current Rx are off-patent generics & traditional medicines.
- **75M people** in Eastern cities today can afford US Rx prices.
- Liver transplants by Shanghai's top 5 hospitals of ~500/year.
- Improving national healthcare past 50 years, per 1,000 pop:
 - hospital bed 0.15 to 2.30
 - MDs 0.67 to 1.48
 - nurses 0.06 to 1.00
 - medical workers 0.93 to 3.40

China: Rx Industry Overview

- In year 2000, 6,000 Rx+OTC manufacturers; now 4,000, further slimming & privatizing.
- Multi-national subsidiaries investing in R&D centers with low cost, young Chinese scientists.
- ICH GCP experience at a few CROs & major hospitals.
- Establishing international IP laws & infrastructure.
- Rx infringers easier to track-down than DVD-CD pirates.
- Domestic firms applying for DDS/improvement **patents**.
- Some domestic R&D start-ups led by USA-trained, entrepreneurial Chinese CEOs - future NCEs license-in to USA; hundreds of such start-ups in Shanghai, Beijing & Shenzhen.

China's Door is Opening

- Multi-national subs are changing the landscape.
- Last January, private Shanghai Fosun Pharmaceutical sent 7 to *BIO-Asia Partnering Conference* in Tokyo, BioEurope & BIO-Boston in 2007.
- Privatized new management teams are under age 45.
- Fosun Licensing director, U of Texas PhD + Purdue MBA.
- China's leading Rx tech transfer center invited Tanaka to speak at their 10th annual conference in Beijing.
- Shanghai government in contact with Tanaka desiring *international Rx partnering conferences* in Shanghai.
- The more publicity re China's regulatory issues, the more focus on fixing - positive progress.

Dealing with China Issues

- Patent infringement - creatively design putting licensee at joint diligence-risk for any infringement.
- Market & pricing - understand through interview of potential partners, market research firms, CROs, VCs, and your network at multi-national and R&D firms.
- Sales reporting for royalty determination - understand how actual sales are reported as a base for royalty fees.
- Cash payments - specify payment schedule & penalties.
- Design shared risks-rewards for your partner and your company.

Recap: EAST ASIA Partnering

- **Japan:** most experienced, richest & top 6 firms have global interests; another 30+ interest by indication for East Asia.
- **China:** growing desire by non-govt cos.; studying how to license-in approved or P3 for China; begun to attend *BIO-Asia Partnering Conference* in Tokyo, bio.org/bioasia; Tanaka speaks at top China domestic Rx business conference.
- **Korea:** keen interest in many indications, approved or P3 drugs; 48M population; only Korea rights.
- **Taiwan:** interest like Korea; Mandarin language & some ties to China distributors makes them a possible Taiwan-China partner; 21M population.
- **Southeast Asia:** a new 500M regional population to join Rx partnering in the next decade.

Overall Strategy Consideration

- 1 Japan's top 6, amongst the world's top 30, increasingly seek-pay for global rights where they have sales-force.
- 2 Many domestic Japan firms have intangible advantages in their own different, unique culture of dev-reg-sales.
- 3 You may receive signing-milestone income from first carving out Japan-Korea-Taiwan to a Japan partner.
- 4 Hold onto **China** rights because including China now adds little value; to most Japan licensees, not having China now, is not a deal-breaker.
- 5 License China in a few years when China's market is more ripe, your drug is further developed, and partner then at a higher value with an eager player.

Thank you

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tanakaintl.com