



***The Future of Research and Development***  
*[Focus on the life science industry]*



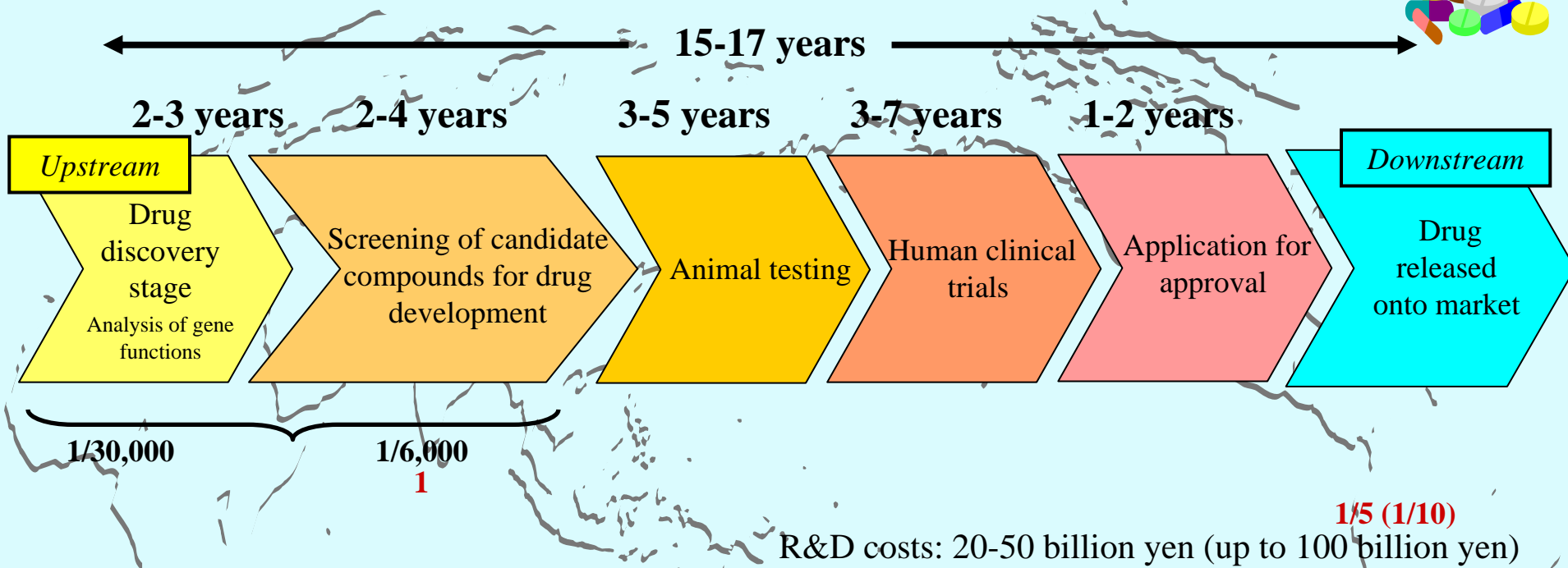
January 11, 2008

Otemachi Sankei Plaza

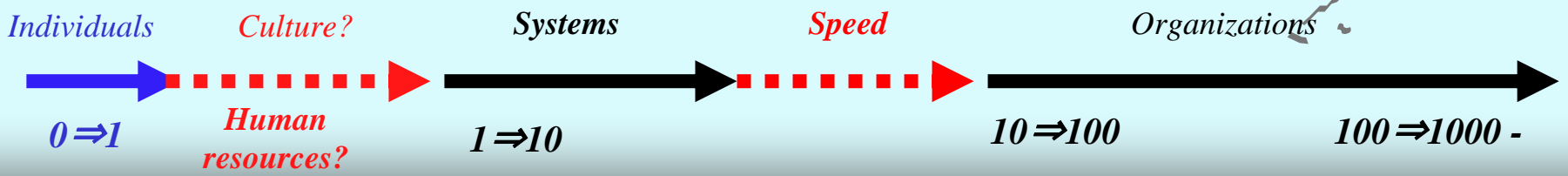
Hiroshi Akimoto, Managing Director

Takeda Pharmaceutical Co. Ltd.

# R&D, intellectual property and human resources in the life science industry



*Upstream: Gene, research tool and screening patents*  
*Midstream: Substance, formula, application and pharmaceutical patents*  
*Downstream: Combined usage and combination patents, design trademarks*  
*After release: Reexamination period, LCM patents*



# Top 20 Global R&D Spenders, 2006

RANK 2006	RANK 2005	COMPANY	R&D SPENDING			HEADQUARTERS LOCATION	INDUSTRY
			2006, IN MILLIONS	CHANGE FROM 2005	AS A % OF SALES		
1	3	Toyota	\$7,691	9.6%	3.7%	Japan	Auto
2	2	Pfizer	\$7,599	4.7%	15.7%	North America	Health Care
3	1	Ford	\$7,200	-10.0%	4.5%	North America	Auto
4	7	Johnson & Johnson	\$7,125	10.3%	13.4%	North America	Health Care
5	4	DaimlerChrysler	\$6,678	-5.6%	3.5%	Europe	Auto
6	5	General Motors	\$6,600	-1.5%	3.2%	North America	Auto
7	8	Microsoft	\$6,584	6.5%	14.9%	North America	Software and Internet
8	10	GlaxoSmithKline	\$6,351	10.2%	14.9%	Europe	Health Care
9	6	Siemens	\$6,294	-2.5%	5.8%	Europe	Industrials
10	9	IBM	\$6,107	4.5%	6.7%	North America	Computing and Electronics
11	11	Samsung	\$5,924	2.8%	6.7%	Rest of World	Computing and Electronics
12	12	Intel	\$5,873	14.1%	16.6%	North America	Computing and Electronics
13	14	Sanofi-Aventis	\$5,571	9.5%	15.6%	Europe	Health Care
14	16	Novartis	\$5,349	10.9%	14.8%	Europe	Health Care
15	13	Volkswagen	\$5,312	4.0%	4.0%	Europe	Auto
16	19	Roche Holding	\$5,262	16.2%	15.7%	Europe	Health Care
17	15	Matsushita	\$4,992	2.4%	6.3%	Japan	Computing and Electronics
18	17	Nokia	\$4,892	1.9%	9.5%	Europe	Computing and Electronics
19	22	Merck	\$4,783	24.3%*	21.1%	North America	Health Care
20	20	Honda	\$4,765	8.1%	5.0%	Japan	Auto
			<b>\$120,950 TOTAL**</b>	<b>5.0% AVG.</b>	<b>6.9% AVG.</b>		

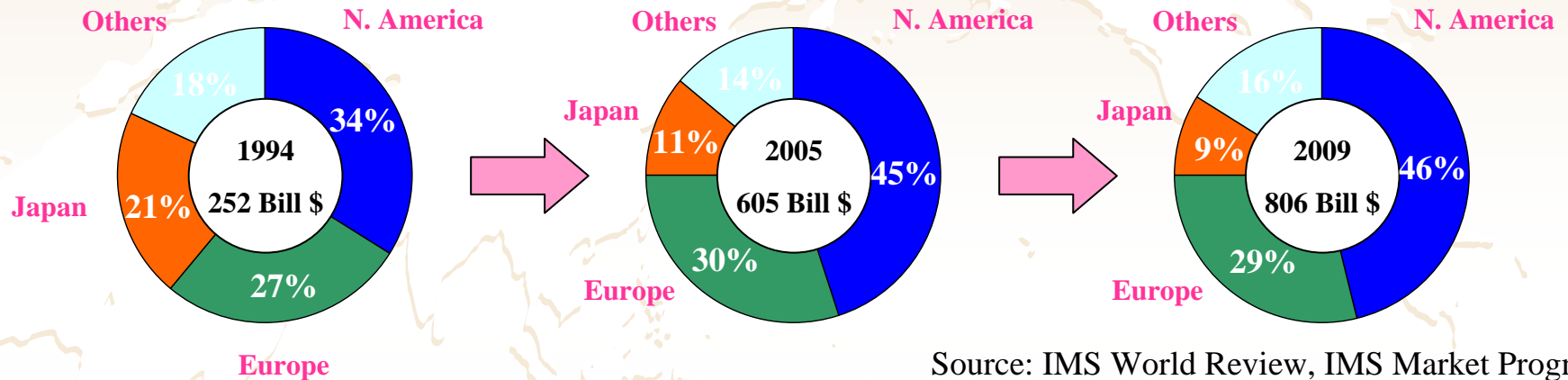
Source: Booz Allen Hamilton

\* Includes substantial acquired research.

\*\* Sums do not add up to total due to rounding.

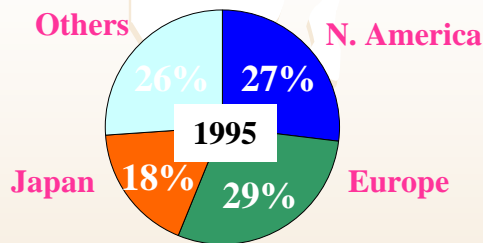
# The global pharmaceutical market – now and in the future

Japan's share of the global market is on the decline and is set to dip below 10%.



Source: IMS World Review, IMS Market Prognosis

## Share of regional GDP



Source: *Main Economic Indicators of Selected Countries*, Ministry of Internal Affairs and Communications Statistics Bureau (1995 shares estimated based on relevant data)

## Issues

- Strengthening R&D capabilities first and foremost to fulfill role as core industry under *Innovation 25*
- Determining how to help control increases in medical costs and maintain and improve QOL in an aging society



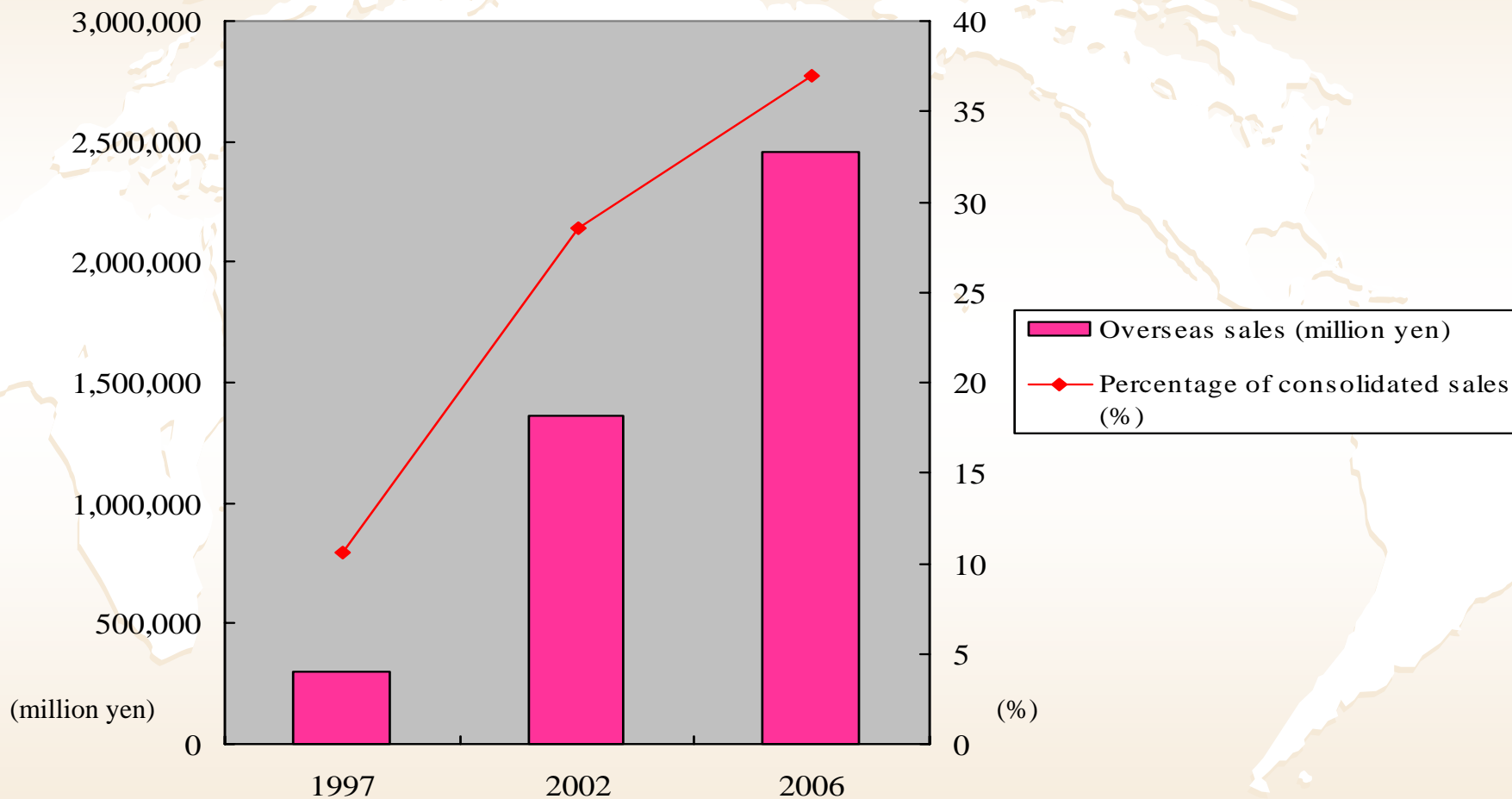
**Developing groundbreaking new drugs**

## *Presence of pharmaceutical industry in overseas markets*

<b>Fiscal year</b>	<b>Overseas sales (million yen)</b>	<b>Percentage of consolidated sales (%)</b>
1997	297,249 <b>13 companies</b>	10.6
2002	1,360,367 <b>30 companies</b>	28.5
2006	2,454,792 <b>Top 19 companies</b>	37

Sources: For 1997 and 2002 figures, *Data Book 2004*, Japan Pharmaceutical Manufacturers Association (JPMA)  
For 2006 figures, *International Drug Bulletin* June 11, 2007 issue

# *Presence of pharmaceutical industry in overseas markets*



Sources: For 1997 and 2002 figures, *Data Book 2004*, Japan Pharmaceutical Manufacturers Association (JPMA)  
For 2006 figures, *International Drug Bulletin* June 11, 2007 issue

# Worldwide ranking of drugs originating from Japan

Position	Brand	Manufacturer	Worldwide sales (million \$)
13	Takepron (ulcers)	Takeda	4,170
19	Actos (diabetes)	Takeda	3,275
26	Blopress (antihypertensive)	Takeda	2,842
29	Cravit (antibiotic)	Daiichi/Sankyo	2,740
31	Pariet (ulcers)	Eisai	2,703
34	Aricept (Alzheimer's)	Eisai	2,483
40	Harnal (prostatic hyperplasia)	Astellas	2,284
42	Crestor (hyperlipidemia)	Shionogi	2,212
49	Mevalotin (hyperlipidemia)	Daiichi/Sankyo	1,983
50	Leuplin (prostate cancer)	Takeda	1,981
51	Abilify (schizophrenia)	Otsuka	1,972
58	Epogin (renal anemia)	Chugai	1,827
71	Prograf (immunosuppressant)	Astellas	1,474
78	Olmotec (antihypertensive)	Daiichi/Sankyo	1,392
	Items originating from Japan	(14 items)	33,338
	Items with sales of 1,300 million dollars or more	(85 items)	230,781
	Japan's share	(16.5 %)	14.4 %

Jan. 11, 2008

7



## **- Attitudes and underlying feelings amongst life science researchers**

[Attitude] Want to invent groundbreaking drugs and make a contribution to the company and society as a whole

[Underlying feelings] Want to see more credit given to inventors for their achievements (contributions)

## **- Attitudes, underlying feelings and preferences within the life science (pharmaceutical) industry**

[Attitudes towards inventors]

- Want inventors to play a prominent role and develop as many hit products as possible in the interests of corporate development
- Companies also want to back up such activities

[Underlying feelings within industry]

- With such intense global competition just to stay afloat, companies can't afford to fight it out over lawsuits involving employee inventions
- Inventors and companies should work together to survive within a difficult R&D environment

[Preferences regarding jurisdiction over final decisions on the value of inventions]

- Want recognition of the fact that companies face different risks to other industries in view of the rapidly growing array of obstacles making it difficult for drug-discovery pharmaceutical companies to sustain their business models (development periods, development costs, probability of success, etc.)
- Want balance between inventor rewards and the company's contribution in bringing the product to market to be taken into account
- Want values to be calculated appropriately, taking into account the new Article 35 of the Patent Act when applying the former Article 35



# *What next !? Emerging technologies ??*

**Genomic drug  
discovery**

**Genetic drug  
discovery**

**Biologics**  
Antibodies, vaccines

**New drug  
development**

**Nucleic medicine**

**Collaboration  
between engineering,  
medicine and  
pharmacology**

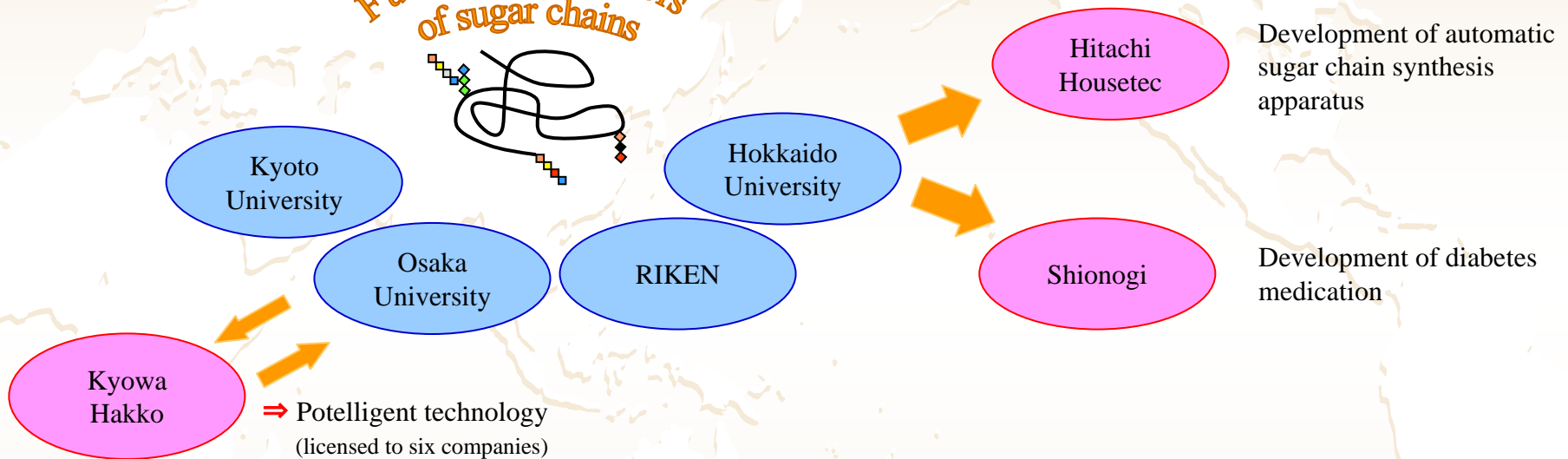
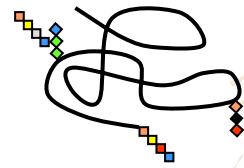
**Regenerative  
medicine**

# *The secret to collaboration between industry, academia and government based on successful examples ~ Academic-led collaboration ~*

Progress is being made with collaboration spearheaded by universities and research institutes in the Japan-dominated field of sugar chain research.

Plan to support development of new industries harnessing the functions of sugar chains (2002-)

*Functional analysis  
of sugar chains*



Osaka University-Kyowa Hakko: Development of next-generation antibody drugs through sugar chain regulation  
Integration and development of Osaka University's sugar chain modification technology and Kyowa Hakko's increased antibody activity technology proposed by Osaka University

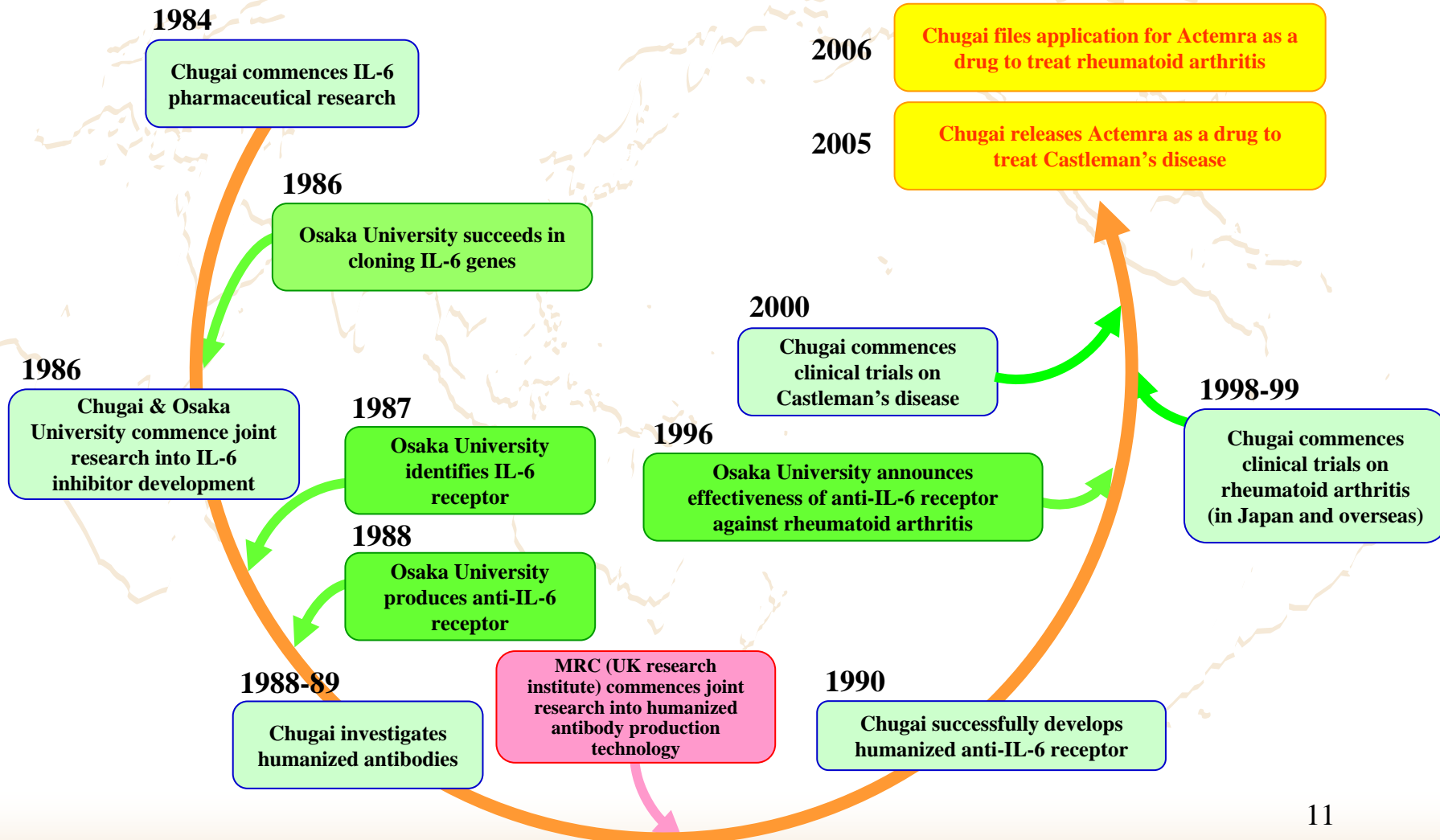
Hokkaido University-Hitachi Hometec-Shionogi: Establishment of a center for future drug discovery and medical innovation

Application of Hokkaido University's automatic sugar chain synthesis technology for the purpose of drug discovery and subsequent commercialization proposed to partner companies

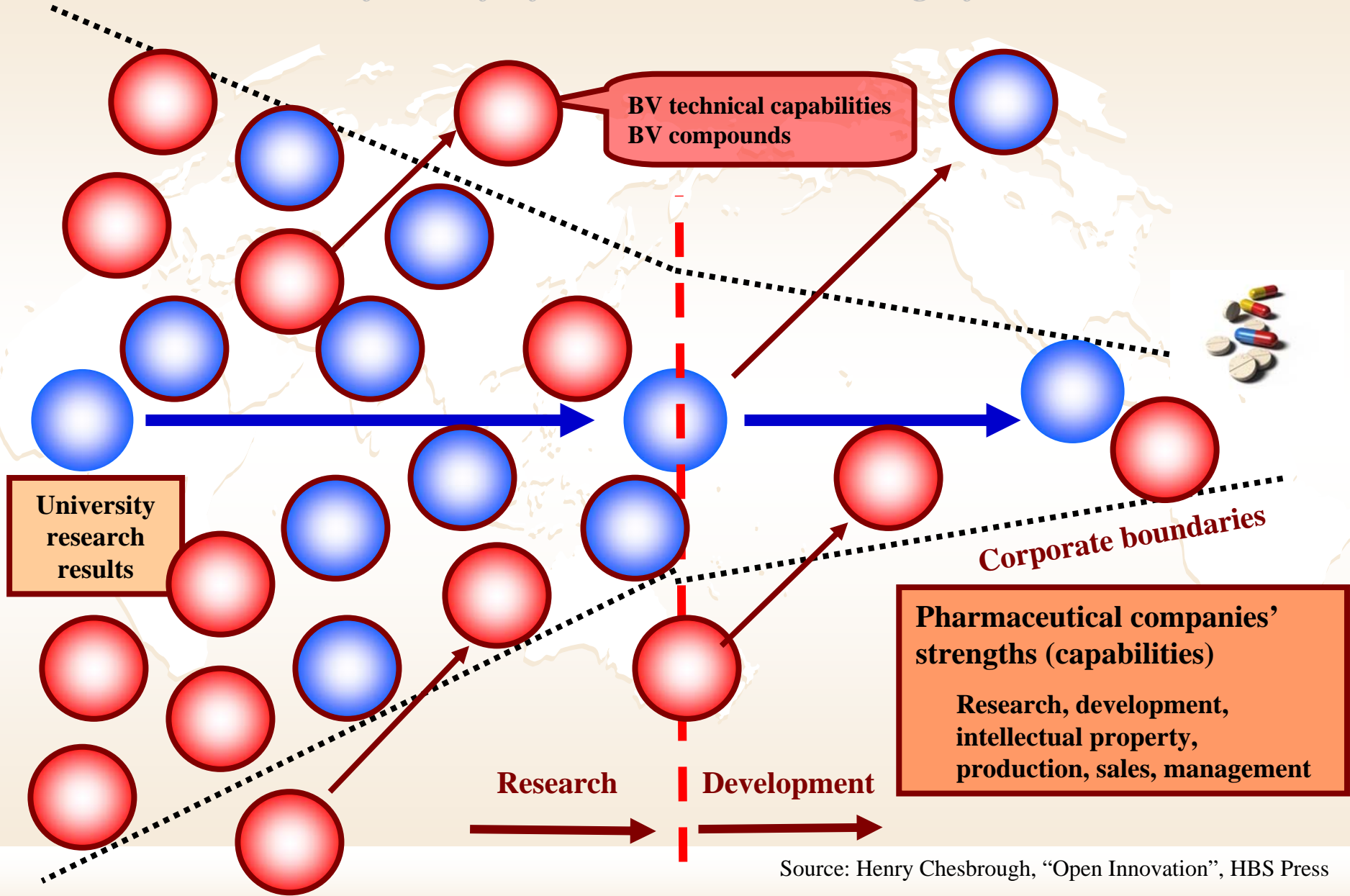
*Need to actively disseminate information to link "seeds" and "needs"*

# *The secret to collaboration between industry, academia and government based on successful examples ~ Industry-led collaboration ~*

**Actemra, Japan's first IL-6 inhibiting antibody drug, was developed over the course of two decades based on an effective combination of Osaka University's research results and Chugai Pharmaceutical's technical capabilities.**

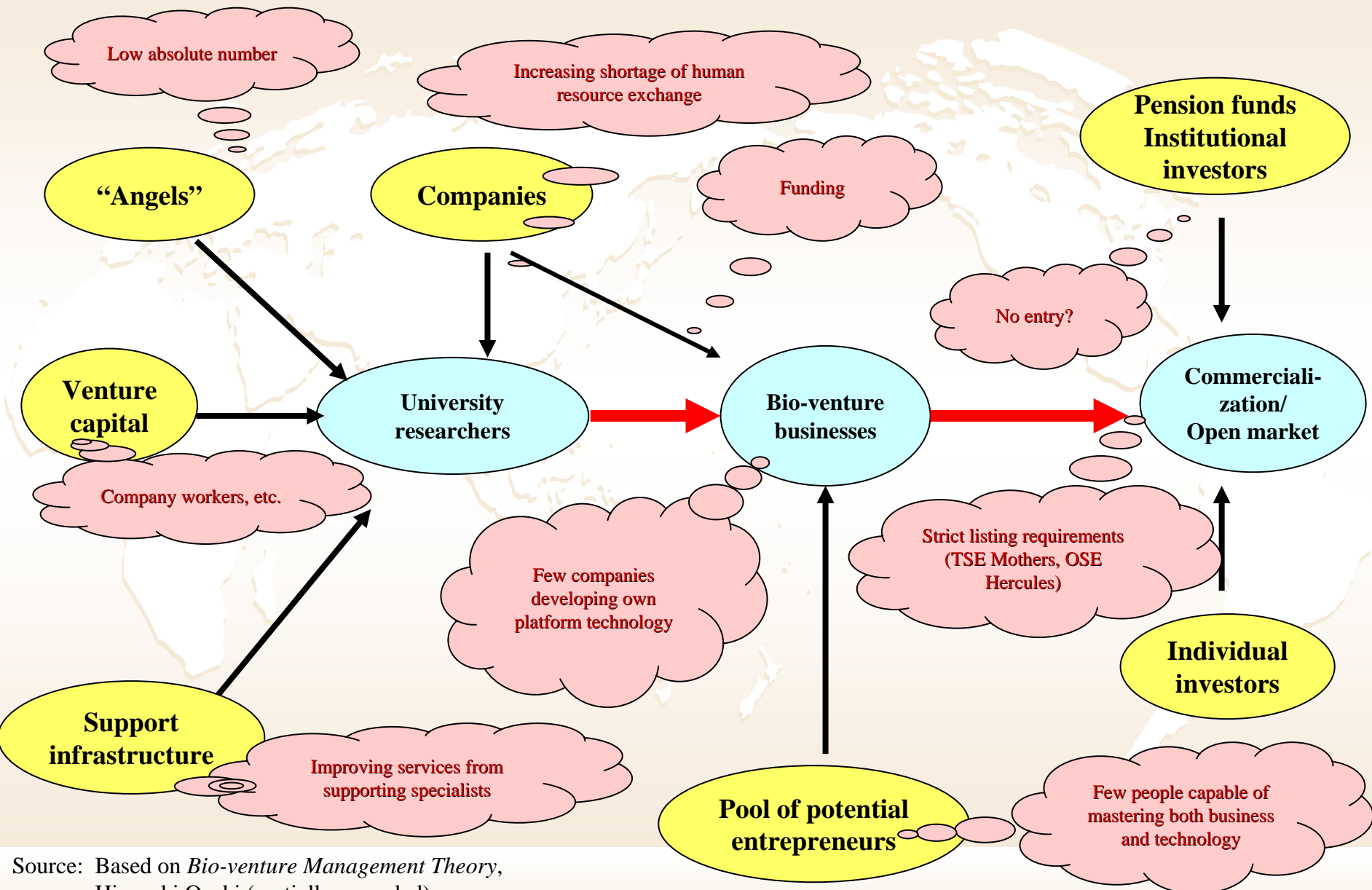


# Collaboration between industry, academia and government in the field of life sciences and its significance



Source: Henry Chesbrough, "Open Innovation", HBS Press

# The collaborative relationship between industry, academia and government in the field of life sciences

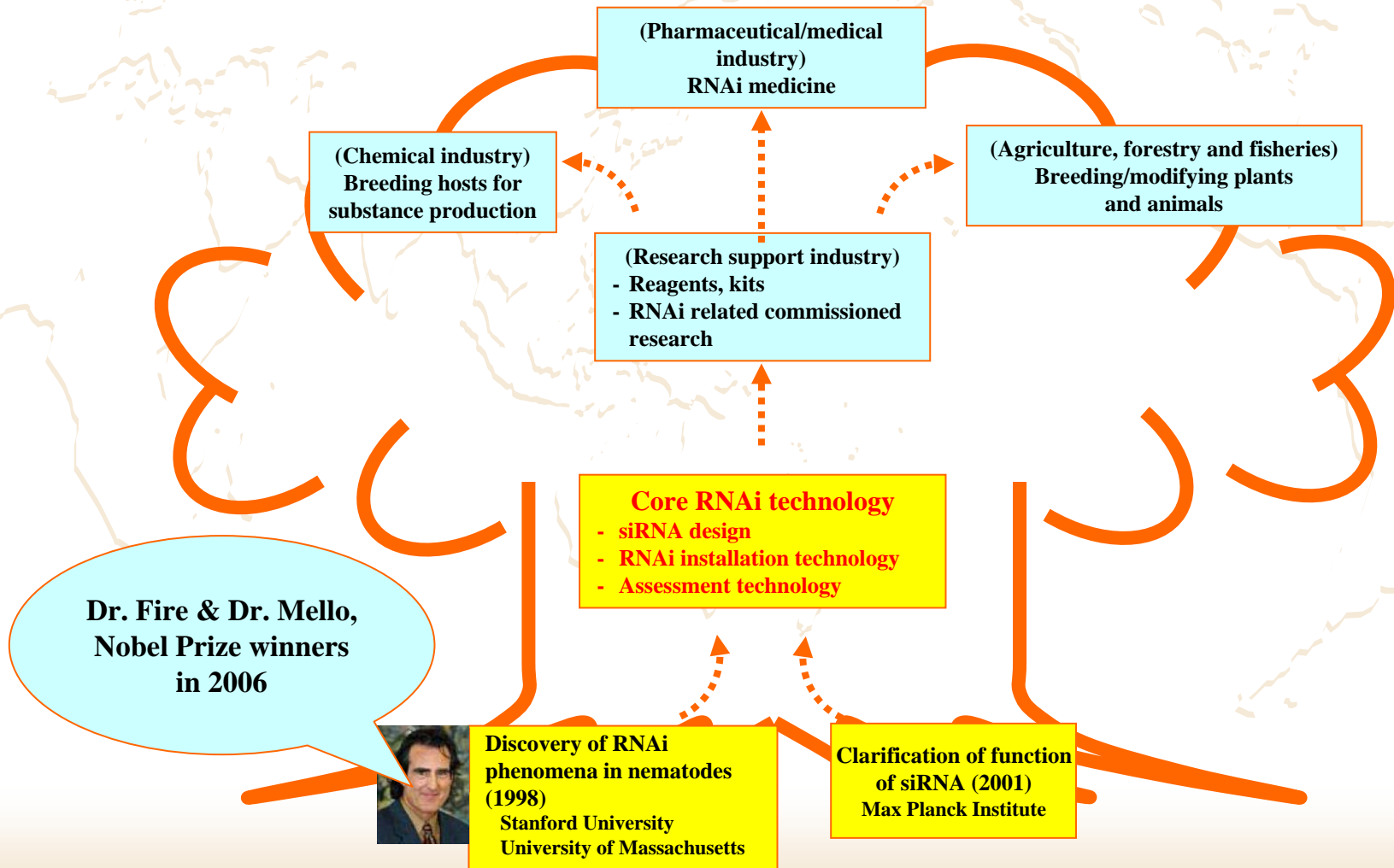


Source: Based on *Bio-venture Management Theory*,  
Hiroyuki Ozaki (partially amended)

# E.g. Core RNAi\* technology and its scope of application

There are high hopes for the application of RNAi technology in the medical, chemical, agricultural, forestry and fisheries industries and other bio industries. Extensive work is currently underway on the development of core technology for the practical application of RNAi.

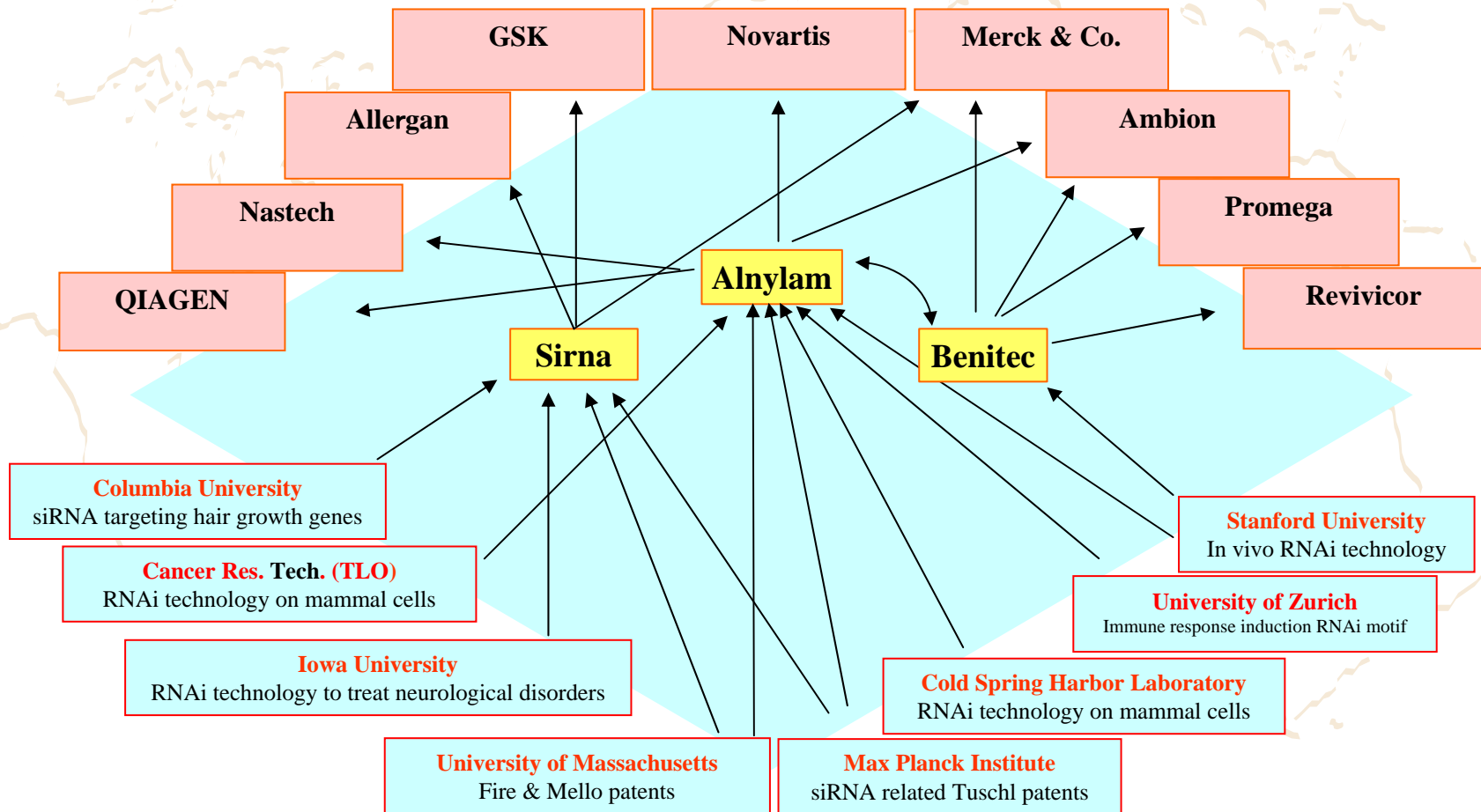
\* RNAi (RNA interference): Technology that uses short RNA duplexes to inhibit the expression of specific genes





# Collaboration on core RNAi technology between industry and academia (and government)

Originating from a number of pioneering US universities, including the University of Massachusetts, the Max Planck Institute and Stanford University, a robust framework of professional innovation has been built up through venture businesses into several mega pharmaceutical companies, as outlets for industrialization.





# What does collaboration between industry, academia and government in the field of life sciences entail?

## Life science companies

- Production of new drugs
- Breeding/modifying plants and animals
- Development of research support technology and tools

## Universities/ research institutes

- TLO Law (1998)
- Japanese Bayh-Dole Act (1999)
- Comprehensive intellectual property strategy (2002)

## Government/ industrial policy

- Clarification of disease mechanisms
- Discovery of target molecules
- Development of assessment technology
- Development of new models
- Basic research tools

Basic research that is beyond the capabilities of companies is handled by universities and research institutes based on a range of policies (**soil**) aimed at promoting collaboration between industry and academia. Research results (**seeds**) are then nurtured by companies in order to produce drugs and other products (**fruit**).