Current R&D Status of Daiichi Sankyo

Mizuho Investment Conference
December 8th, 2008

Kazunori Hirokawa
Executive Officer,
Head of R&D Division

Daiichi-Sankyo

Concept of Therapeutic Areas

R&D Core Disease Areas

Areas where R&D investment is focused on for development as our future growth drivers

- Thrombotic Disorders
- Malignant Neoplasm
- Diabetes Mellitus
- Autoimmune Disorders / RA

Franchise Areas

Areas on which current revenue is based and should be maintained and expanded

- Hypertension
- Hyperlipidemia / Atherosclerosis
- Bacterial Infections

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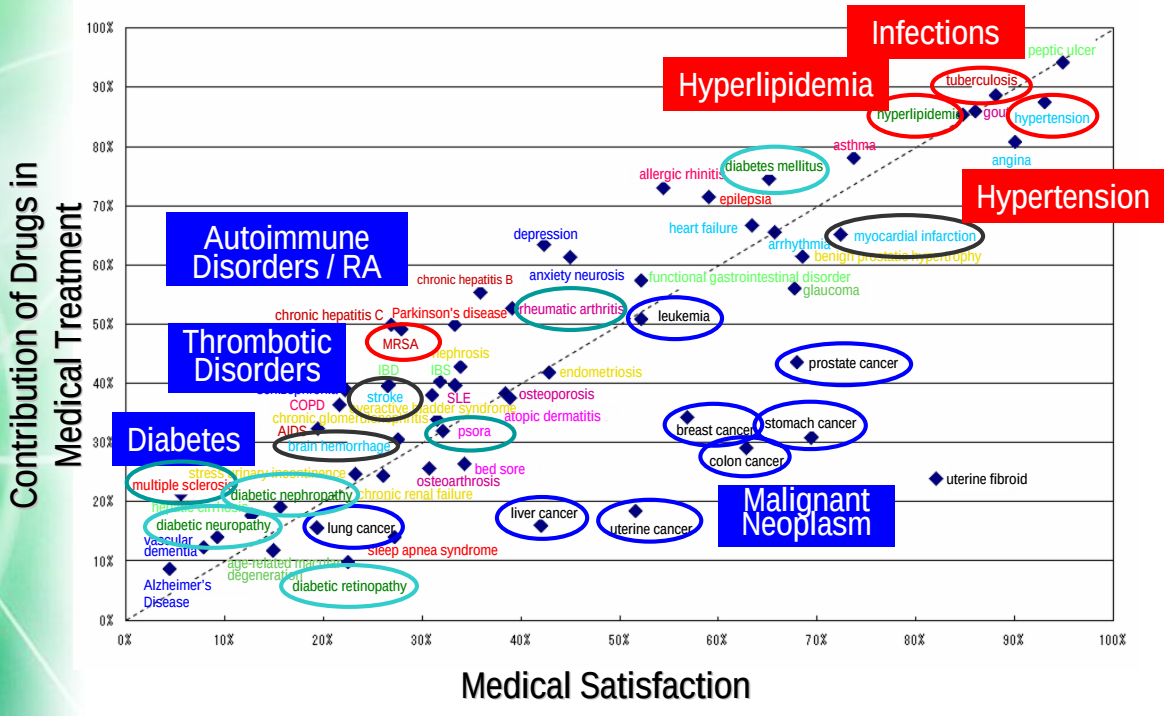
Medical Satisfaction and Contribution of Drugs



Japan Human Health Sciences Foundation;
Investigation of Japan's Fundamental Technology Report - View of medical treatment needs in 2015 (2005)

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Development Pipeline

	Phase 1	Phase 2	Phase 3	Application
Cardiovascular diseases	CS-8080 DB-772d	Olmetec/diuretic Combo (#)	DU-176b Prasugrel (ACS-MM) CS-8635 Olmetec additional indication (#) <Diabetic nephropathy> Olmetec/Calblock Combo (#)	Prasugrel (ACS-PCI)
Glucose metabolic disorders	CS-1036 (#)		Rivoglitazone	
Infectious diseases			Levofloxacin inj (#) CS-8958	Levofloxacin high-dose (#)
Malignant neoplasm	CS-7017 U3-1287	CS-1008 Nimotuzumab (#) ARQ 197		
Immunological allergic diseases	CS-0777	SUN 13834		
Bone / joint diseases			Denosumab (#) Loxonin gel (#)	
Others		Human ghrelin	Memantine hydrochloride (#) Silodosin	Feron/Ribavirin combination therapy (#)
Total	6	6	12	3

Change from October

New : ARQ 197
Change of stage :
DU-176b Ph2 ---> Ph3
CS-8958 Ph2 ---> Ph3
Sevikar (EU) Application ---> Approval

- Only the most advanced stages are described for the projects under global development
- Projects with highest priority are underlined (blue)

: Developed only in JPN

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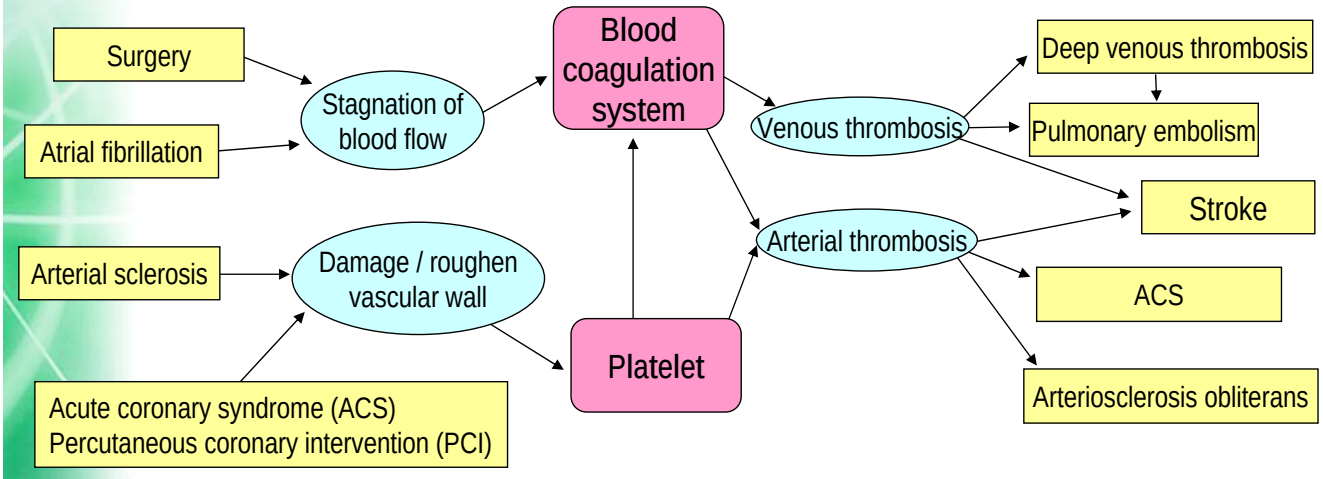
Targets for Thrombotic Disorders

- Blood clots formed through various causes can result in emboli in the heart, lungs, or brain, and may lead to fatal conditions
- The blood coagulation system and platelet are the two primary targets



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To Become a Leader in Thrombotic Disorders

	Arterial thrombosis	Venous thrombosis
Target	Platelet	Blood coagulation system
Drugs currently used	Anti-platelet	Anticoagulant
	Acetylsalicylic acid Ticlopidine Clopidogrel	Low-molecular weight heparin Warfarin Argatroban
Daiichi Sankyo's Pipeline	Prasugrel	DU-176b
	• Higher IPA* • Rapid onset of IPA • More consistent IPA * IPA: inhibition of platelet aggregation	Target Profile • Efficacy not inferior to Warfarin • Wide therapeutic range and lower incidence of bleeding • No hepatotoxicity

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Anti-platelet: Prasugrel

Best-in-class

Thrombotic Disorders

ACS-PCI* (TRITON TIMI-38)

* ACS: acute coronary syndrome
PCI: percutaneous coronary intervention

US Dec-2007

- New Drug Application (NDA) filing in US

Sep 26, 2008

- The U.S. Food and Drug Administration (FDA) did not complete its review by PDUFA goal date, and continues to review prasugrel NDA

Europe Feb-2008

- Marketing Authorization Application (MAA) filing in Europe

As of Dec-2008

- Review by the European Medicines Agency (EMEA) underway

ACS-MM** (TRILOGY ACS)

** MM: medically managed
(without a planned artery-opening procedure)

Jun-2008 Phase 3 study

- Double-blind, parallel-arm, active control study
- To evaluate safety and efficacy of prasugrel against clopidogrel
  Reducing the risk of cardiovascular death, heart attack, or stroke
- About 10,000 patients in more than 800 hospitals in 35 countries
- Duke Clinical Research Institute (Dr. Magnus Ohman)

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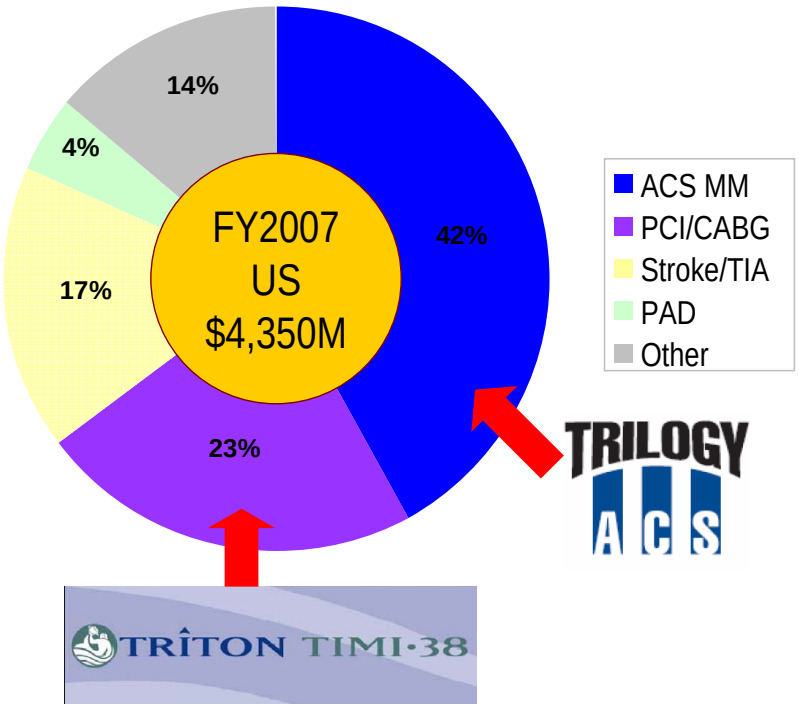
Anti-platelet: Prasugrel

Thrombotic Disorders

Clopidogrel's Source of Business Fiscal Year 2007 (company analysis)



Source: IMS NPA Mar 2008 MAT Plavix Sales + NDTI (physician audit)

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Oral Factor Xa Inhibitor: DU-176b

Best-in-class

Thrombotic Disorders

Completed strict dose-finding studies and started phase 3 studies

Target Indication / Development Stage	Phase 2b completed		Phase 3
Prevention of thromboembolic events in patients with non-valvular atrial fibrillation (AF)	US/EU	Results presented at American Society of Hematology in Dec-08	Started in November
	JP	Completed	
Prevention of venous thromboembolism (VTE)	US/EU	Results presented at European Society of Cardiology in Sep-08 <Prevention of venous thromboembolism in patients after total hip replacement surgery>	Planned
	JP	Results presented at Asian-Pacific Society of Thrombosis and Hemostasis in Sep-08 <Prevention of venous thromboembolism in patients after total knee replacement surgery>	

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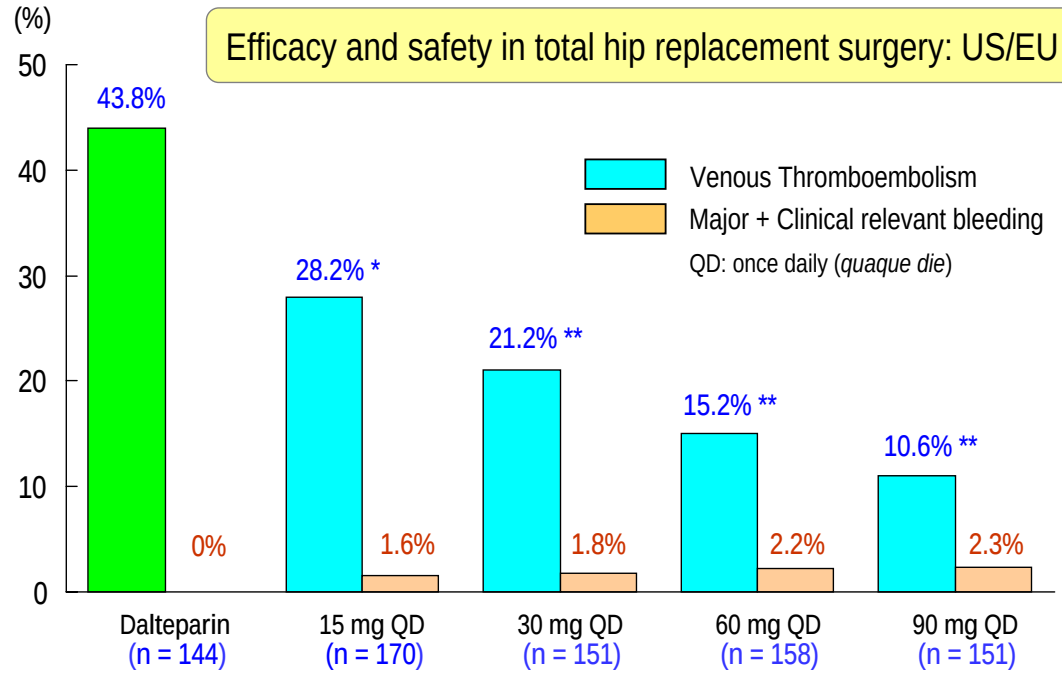
Oral Factor Xa Inhibitor: DU-176b

Thrombotic Disorders

Efficacy and safety in total hip replacement surgery: US/EU



* *P* = 0.005 (vs. Dalteparin) ** *P* < 0.001 (vs. Dalteparin)

Dose-dependency in VTE incidence; *P* < 0.001 (Cochran-Armitage)

No increase in major or clinically relevant bleeding

European Society of Cardiology (September 2, 2008, Munich)

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Protocol of Ph2b Studies in AF (US/EU)

Thrombotic Disorders

- Primary objective
  - Evaluate safety of DU-176b compared to Warfarin
- Patient population
  - Patients with non-valvular atrial fibrillation
- Design
  - Randomized, double-blind, active-controlled, DU-176b and open−label warfarin study
- Treatment period
  - 3 months treatment
- Number of patients
  - 1,143

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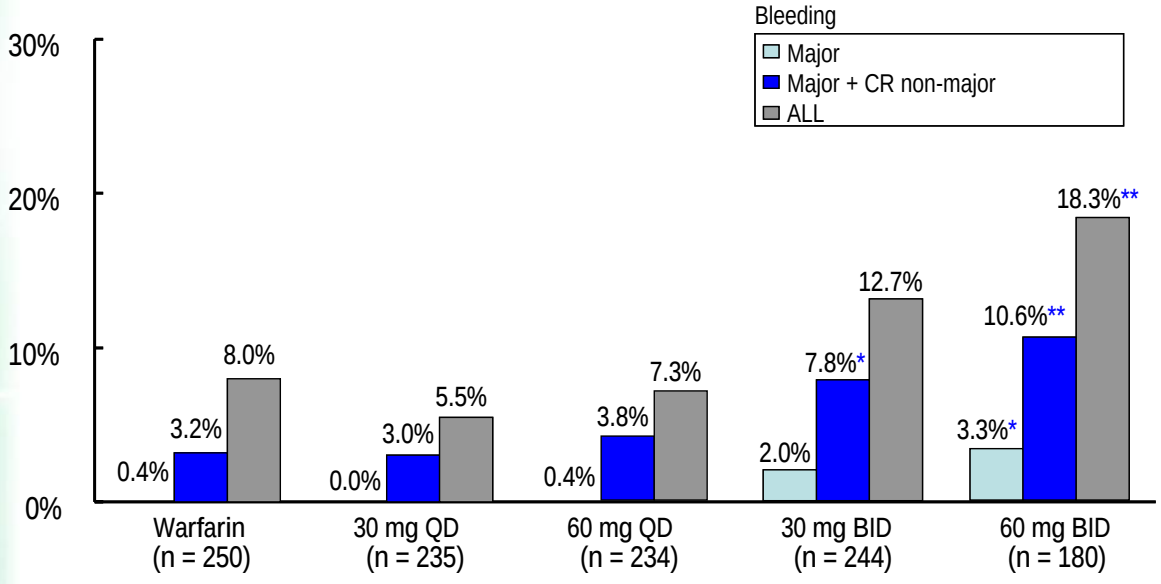
Oral Factor Xa Inhibitor: DU-176b

Thrombotic Disorders

Safety in atrial fibrillation: US/EU



* p<0.05 ** p<0.01 (to Warfarin)

DU-176b 30 mg qd and 60 mg qd dose regimens had a safety profile similar to warfarin in patients with AF.

American Society of Hematology (December 7, 2008, SF)

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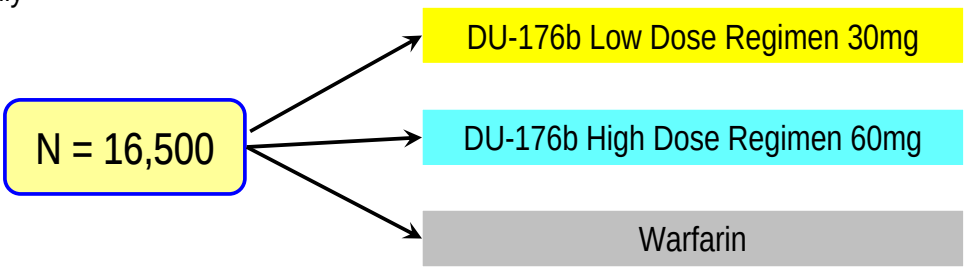
ENGAGE-AF TIMI 48 (DU-176b Ph3)

Thrombotic Disorders

Effective Anticoagulation With Factor Xa Next Generation in Atrial Fibrillation

- Randomized, double-blind, double-dummy, parallel group, multi-center, multi-national study
- To evaluate efficacy and safety of DU-176b versus Warfarin in subjects with atrial fibrillation
- Once daily



Primary endpoint = Stroke and Systemic Embolic Events (SEE)
Secondary endpoint = Stroke, SEE, and All-Cause Mortality
Safety Endpoint = Major Bleeding

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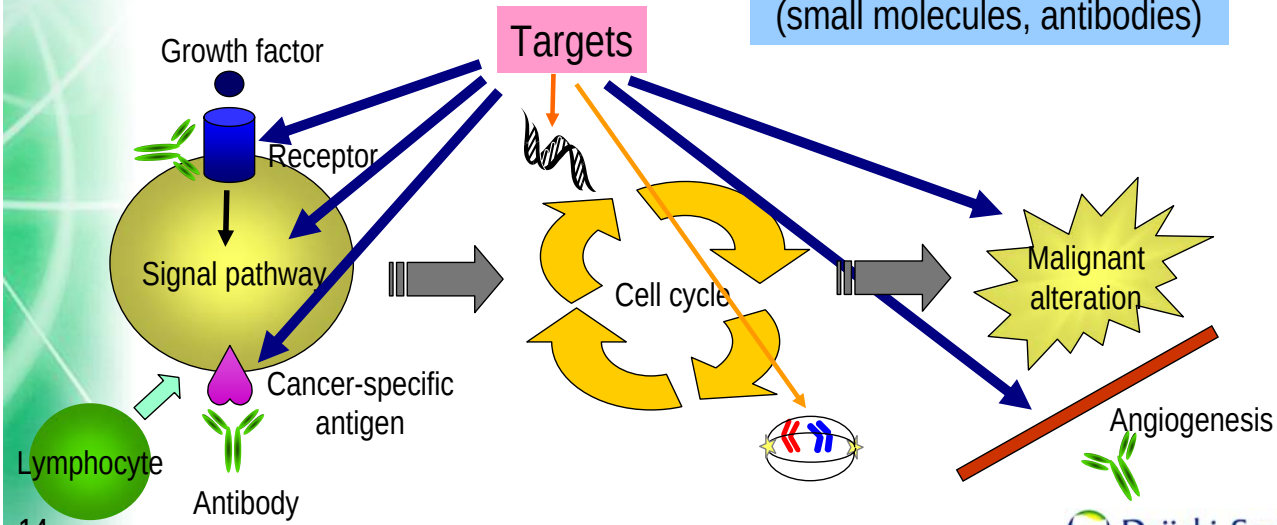
Targets for Malignant Neoplasm

Malignant Neoplasm

Chemotherapeutic agents inhibiting cell division functions → Targets specifically seen in cancer cells and environment surrounding cancer tissues

Molecularly targeted drugs (small molecules, antibodies)



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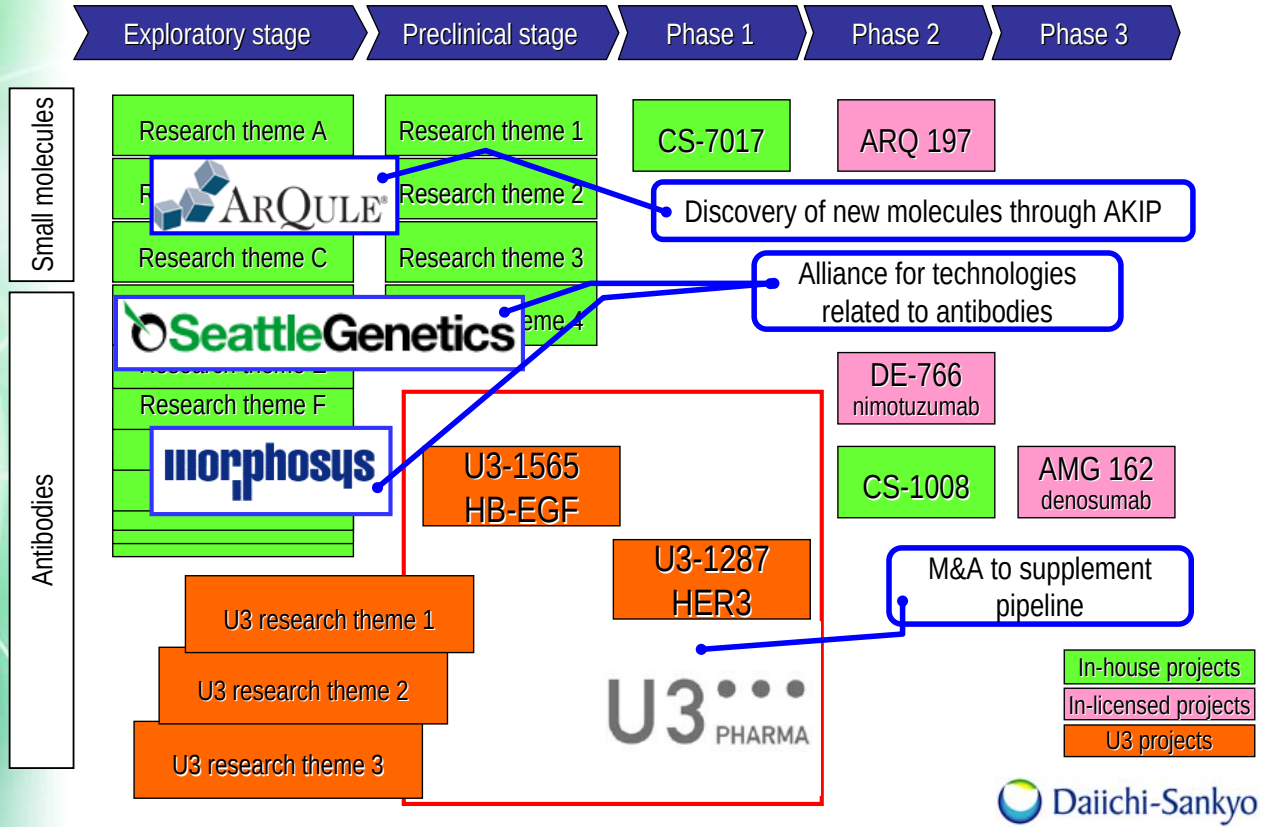
Malignant Neoplasm Pipeline

Malignant Neoplasm



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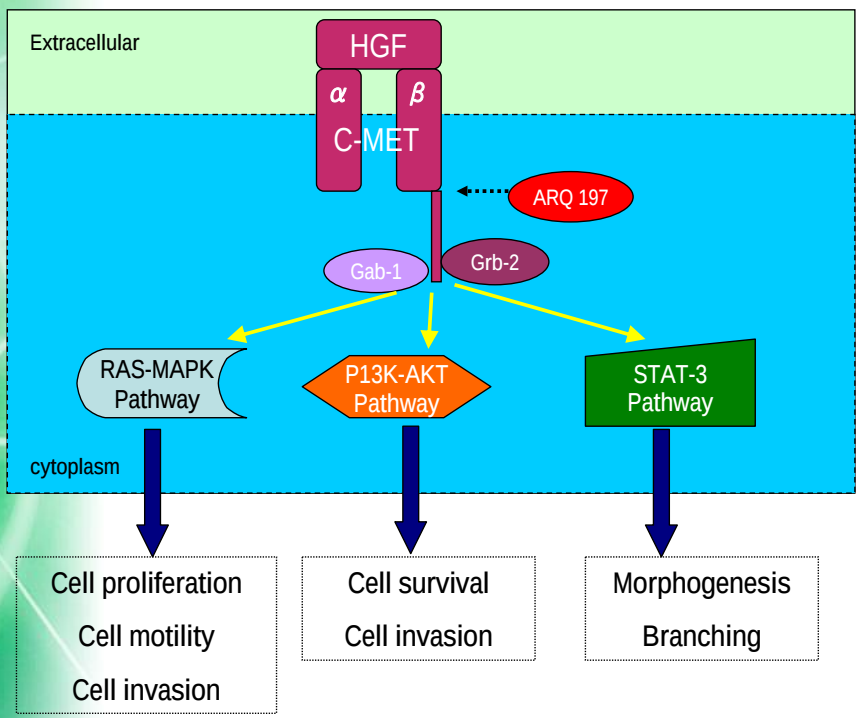
c-Met inhibitor: ARQ 197 (small molecules)

First-in-class / Best-in-class

Malignant Neoplasm



- c-Met: receptor for tyrosine kinase of hepatocyte growth factor (HGF)
  - Multiple roles in intracellular signal transductions such as cancer cell motility, proliferation, angiogenesis, invasion, and apoptosis induction
- Variation of c-Met
  - Gastric, Pediatric Hepatoma, Head and Neck cancer
- High expression of c-Met
  - Colon, Hepatoma, Pancreatic, Prostate, Breast cancer, etc
- c-Met inhibitors are suggested to be used as anti-cancer agent by
  - Relationship between variation or high expression of c-Met and carcinogenesis

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Antibodies: AMG 162 (Denosumab Anti-RANKL)

First-in-class

Malignant Neoplasm

Fully human monoclonal antibody that specifically targets the receptor activator of nuclear factor kappa B ligand (RANKL), an essential regulator of the cells that break down bone

- Multinational Phase 3 studies, including in Japan, are in progress for bone metastases of cancer
- Phase 2 study in US for rheumatoid arthritis completed (by Amgen)
- Promising results from studies for postmenopausal osteoporosis
  FREEDOM (presented by Amgen: at American Society for Bone and Mineral Research in September)

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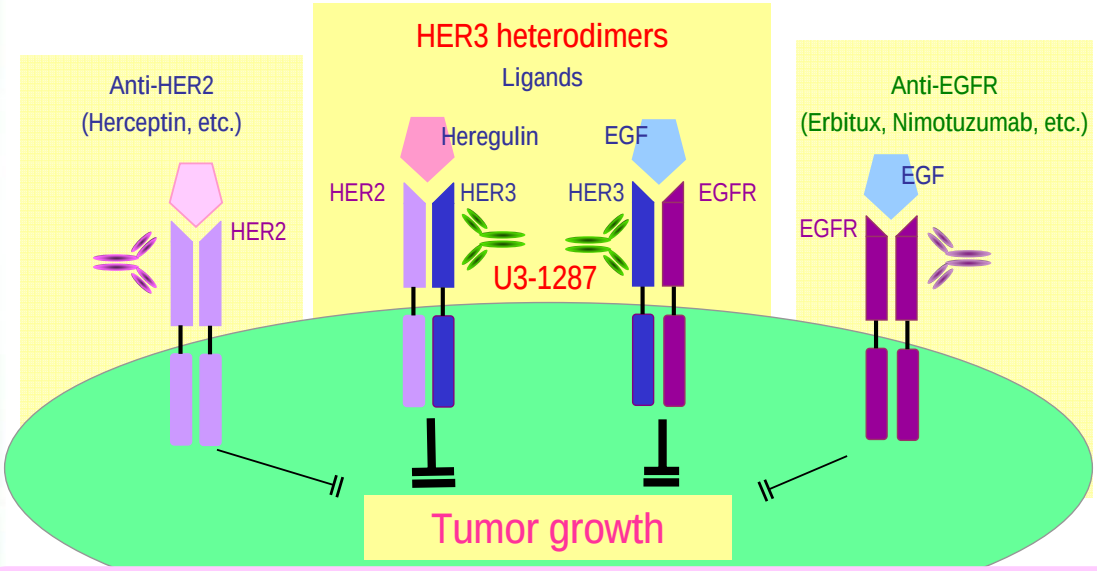
Antibodies: U3-1287 (Anti-HER3)

First-in-class

Malignant Neoplasm



HER3: the third member of the EGFR family

- Expression upregulated in several cancer cells
  - breast, gastrointestinal, lung, pancreas, prostate, skin tumors, etc.
- HER3 heterodimers have relatively higher mitogenic potential than HER2 homodimers or EGFR homodimers

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Anti-influenza agent: CS-8958

Best-in-class

- Anti-infectious agent; Neuraminidase inhibitor
- Inhaler formulation; Dry powder inhaler and nebulizer
- Long acting
- Target indication; Treatment and Prophylaxis of influenza
- Treatment: Single administration for treatment
  Prophylaxis: Once weekly (possibility)
- Self Development in Japan
  - Phase 2 completed, POC confirmed
  - Phase 3 on-going
- Collaboration with Biota for out-licensing in US/EU

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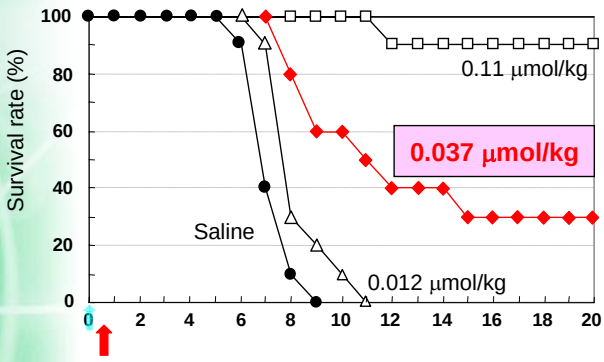
Anti-influenza agent: CS-8958

Lifeprolonging effect of single CS-8958 treatment is same as Oseltamivir repeated treatment

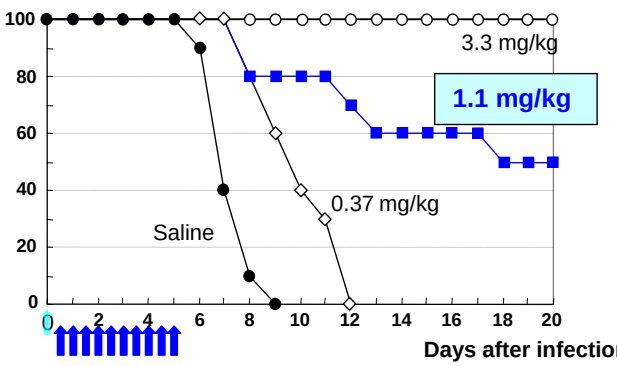
Non-clinical Data Summary
- Pharmacology -

CS-8958



Single administration（per nasal）

Oseltamivir Carboxylate*



10 times administration（per oral）

*) **Tamiflu active metabolite**

Minimum effective dose for significant life prolongation compared with saline arm

CS-8958 single: 0.037 μmol/kg = 18 μg/kg → 1.1 mg/body

Oseltamivir repeat: 1.1 mg/kg (for mouse) **→ 66 mg/body** (in human terms)

Mouse: BALB/c, ♀, 6w, N = 10
Infection: A/PR/8/34, 100pfu, *i.n.*
Treatment: CS-8958 single
Oseltamivir twice/day 5 days

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Anti-influenza agent: CS-8958

Inhibitory activity of Neuraminidase from Tamiflu-resistant strain (IC50, nM)

Non-clinical Data Summary
- Pharmacology -

Influenza Virus			R-125489	Zanamivir	Oseltamivir Carboxylate
A/H1N1	A/Yokohama/67/2006	wt	3.03	2.70	2.28
		H274Y	5.62	3.05	755
		R/wt ratio	1.9	1.1	330
A/H3N2	A/Kawasaki/IMS22A-955/2003 A/Kawasaki/IMS22B-955/2003	wt	15.4	8.29	1.25
		R292K	10.6	11.2	10400
		R/wt ratio	0.69	1.4	8400
	A/Yokohama/IMS9A-2029/2003 A/Yokohama/IMS9B-2050/2003	wt	19.2	10.7	1.78
		E119V	13.2	7.71	140
		R/wt ratio	0.69	0.72	79
	A/Kawasaki/MS31A-1030/2002 A/Kawasaki/MS31B-1206/2002	wt	13.4	7.82	1.18
		R292K	37.3	13.5	37.2
		R/wt ratio	2.8	1.7	32

wt: Wild type strain
cf.R292K: AA changing point (Resistant st.)
R/wt ratio: IC_{50} activity ratio

R-125489: CS-8958 active metabolite
Zanamivir: Relenza
Oseltamivir Carboxylate: Tamiflu active metabolite

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Daiichi Sankyo R&D Strategy Vision Statement

As a **Global Pharma Innovator**, Daiichi Sankyo R&D will discover and develop value added first-in-class and best-in-class therapies expanding on our legacy of quality and innovation to improve patient health and raise global standards for disease treatment and prevention

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Corporate Mission, Vision

To Enrich the Quality of Life around the World
through the Development of Innovative Pharmaceuticals

Global Pharma Innovator

To Become a World-class Pharmaceutical Innovator

Expanding our Global Reach	Fulfilling Unmet Medical Needs	Creating an Innovative Business Model
Global	**Pharma**	**Innovator**
Establish our own operations in key areas and strengthen our presence worldwide	Focus on pharmaceuticals and continuously develop novel therapies	Achieve scientific and technological innovations; create an innovative business model

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