Research and Development at Daiichi Sankyo

GLENN GORMLEY MD PhD
Global Head, Research & Development
Senior Executive Officer
Agenda of R&D Day

1. Research and Development Overview (Glenn Gormley)

2. Research Overview (Masahiko Ohtsuki)

3. Biologics Overview (Junichi Koga)

4. Development Overview (Mahmoud Ghazzi)

5. Closing (Glenn Gormley)
R&D Challenge: More Competitive External environment

- Declining number of approved NMEs
- Escalating R&D costs
- Growing share of biologics among approved NMEs
R&D Challenge: More Competitive External environment

- Declining number of approved NMEs
- Escalating R&D costs
- Growing share of biologics among approved NMEs

R&D response to Challenges: Increase Productivity

- increase output at lower cost
- Accelerate development timelines
- Maximize the value of each R&D unit
Global R&D 5 Year Business Plan

Drivers of success
- Leadership
- Innovation
- Efficiency
- Empowerment
- Smart Risk taking

Productivity (Output)
Costs (Input)

2013 2014 2015 2016 2017
Global R&D 5 Year Business Plan
Key success factors

- Shorten R&D Timelines
- Focus on Personalized Medicine
- Enhance Leadership and Decision-Making
- Enhance Portfolio Management & Resource Planning
- Develop and Acquire global Talent
- Develop Global R&D IT Strategy
Productivity gains at Daiichi Sankyo

Number of Projects Entering Phase 1 development

- R&D Integration
- Restructuring Of Discovery
- R&D 5YBP

![Diagram showing productivity gains over years with numbers of projects entering Phase 1 development from 2007 to 2017.](image)
Priority Areas at R&D Stages

- **Research**
  - Early Development
  - Late Development
  - LCM Market

**Research to POC**

- **Priority TAs**
  - CV-M
  - Oncology
  - Frontier

**Priority Areas**

- Thrombosis
- Hypertension
- Pain
- CV-M
- Oncology
- Pain
## Major R&D Pipeline

**Therapeutic area**

### Cardiovascular-Metabolics
- **Phase 1**
  - **DS-1040** (Acute ischemic stroke / TAFIα inhibitor)
  - **U3-1565 (US/JP)** (Anti-HB-EGF antibody)
  - **DS-7423 (US/JP)** (PI3K / mTOR inhibitor)
  - **DS-3078 (US/EU)** (mTOR inhibitor)
  - **DS-3032 (US)** (MDM2 inhibitor)
  - **PLX7486 (US)** (Fms / Trk inhibitor)
  - **DS-8895 (JP)** (Anti-EPHA2 antibody)
  - **DS-8273 (US)** (Anti-DR5 antibody)
  - **PLX8394 (US)** (BRAF inhibitor)
  - **DS-6051 (US)** (NTRK / ROS1 inhibitor)

### Phase 2
- **CS-3150 (JP)** (Hypertensive / DM nephropathy / MR antagonist)
- **DS-8500 (JP)** (Diabetes / GPR119 agonist)
- **Patritumab (US/EU)** (U3-1287 / anti-HER3 antibody)
- **Vemurafenib (US/EU)** (PLX4032 / BRAF inhibitor)
- **PLX3397 (US)** (Fms / Kit/Fit3-ITD inhibitor)

### Phase 3
- **Prasugrel (JP)** (CS-747 / ischemic stroke / anti-platelet agent)
- **Prasugrel (US)** (CS-747 / sickle Cell Disease / anti-platelet agent)
- **Tivantinib (US/EU)** (ARQ 197 / HCC / Met inhibitor)
- **Denosumab (JP)** (AMG 162 / breast cancer adjuvant / anti-RANKL antibody)
- **Nimotuzumab (JP)** (DE-766 / gastric cancer / anti-EGFR antibody)
- **Vemurafenib (US)** (PLX4032 / melanoma adjuvant / BRAF inhibitor)
- **Quizartinib (US/EU)** (AC220 / AML / FLT3 inhibitor)

### Others
- **PLX5622** (Rheumatoid arthritis / FMS kinase inhibitor)
- **DS-1093** (Anemia of chronic kidney disease / HIF-PH inhibitor)
- **DS-3801** (Chronic obstipation / GPR 38 agonist)
- **DS-1971** (Chronic pain)
- **Mirogabalin (JP)** (DS-5565 / chronic pain / α2δ ligand)
- **SUN13837 (US/EU)** (Spinal cord injury / modulator of bFGF signaling system)
- **Laninamivir (US/EU)** (CS-8958 / anti-influenza / out-licensing with Biota)
- **Iofiforminol (JP)** (GE-145 / X-ray contrast media / angiography)
- **Mirogabalin (US/EU)** (DS-5565 / Fibromyalgia / α2δ ligand)
- **Levofloxacin (JP)** (DR-3355 / anti-infection / New quinolone)
- **Denosumab (JP)** (AMG 162 / rheumatoid arthritis / anti-RANKL anti-body)
- **Hydromorphone (JP)** (DS-7113 / narcotic analgesic / opioid μ-receptor regulator)
- **CHS-0214 (JP)** (Etanercept BS / rheumatoid arthritis / TNFα inhibitor)
- **CL-108 (US)** (Acute pain / opioid μ-receptor regulator)

**As of December 2014**

Underline: Change from FY2014 2Q Financial Announcement

**Application**
- **Edoxaban (US/EU/Others)** (DU-176b / AF / oral factor Xa inhibitor)
- **Edoxaban (US/EU/Others)** (DU-176b / VTE / oral factor Xa inhibitor)
Targets for Approval and Launch

**Japan**
- FY2014: Edoxaban AF, Edoxaban VTE, Prasugrel CAD, Denosumab GCTB
- FY2015: Levofloxacin Injection
- FY2016: Denosumab BC adj., Etanercept BS RA, Prasugrel CVA
- FY2017: Denosumab RA
- > FY2018: Oncology
  - Tivantinib
  - DE-766
  - Patritumab
  - Quizartinib
  - PLX3397
  - Vemurafenib (LCM)

**US**
- FY2015: CL108 Acute Pain
- > FY2018: CV-M (CVM)
  - CS-3150
  - DS-8500
  - Prasugrel (LCM)
  - Edoxaban (LCM)

**Western Europe**
- FY2015: Edoxaban AF, Edoxaban VTE
- > FY2018: Others
  - Mirogabalin
  - SUN13837
  - DS-7113
  - GE-145
  - Denosumab (LCM)

**Others**
- FY2015: Edoxaban AF&VTE (China・LTAM etc.)
Decision Making Body for Global R&D Projects

Global Executive Meeting of Research And Development

Chief Medical Advisor
Regional Development Heads
GH of Global PM
GH of RD Planning
GH of Research
GH of Biologics
GH of Development

Corporate Strategy
GH of BD&L
Function Committee Chairs
GH of IP
GH of Clinical Safety and PV
GH of Pharmaceutical Technology

PJ Team Leaders

GEMRAD
Daiichi Sankyo’s Decision Making System:

Simple: One decision making body for all teams in early phase development
Fast: Monthly meetings
Aligned: All stakeholders represented at TR-GEMRAD and empowered

Translation Research Phase

Pre-clinical Ph 1 Ph 2a

GOAL: Positive POC

Decision-Making Body

TR-GEMRAD

Project Team

Early development - Project Team
Daiichi Sankyo’s Decision Making System:

Simple: One decision making body for all teams in late phase development
Fast: Monthly meetings
Aligned: All stakeholders represented at GEMRAD and empowered

GOAL: NDA approval

Late Development Phase
Ph 2b  Ph 3  LCM

Decision-Making Body

Integrated Project Team

Daiichi Sankyo’s Decision Making System:
Translational Research Concept:

Confirm POM*/POC quickly

In Translational research phase:

- Test key elements of Target Product Profile quickly
- Take smart risks to establish Proof of Concept
- Ensure continuous feedback loop to maximize learning

*POM: Proof of Mechanism
Global Sites for competitive theme creation

Discovery Engine

- DS Tokyo R&D Labs: Oncology, CVM, Frontier
- Venture Science Lab: Aging Process, Neurodegenerative Diseases
- ASUBIO: Neurologic disease, Inflammation, Cell Regeneration
- Plexxikon: SBDD Platform, Oncology
- RCI: Inflammation, Infection
- U3 Pharma: Oncology
Venture Science Laboratories (VSL) in-house Venture model

- Deliver innovative FIC products in a biotech-like lab
- Develop therapeutics and diagnostics for neurodegenerative diseases such as Alzheimer’s disease through research collaboration with UCSF-IND (Institute for Neurodegenerative Diseases)

UCSF-IND

- World class academia laboratories focusing on neurodegenerative diseases led by Dr. Stanley B. Prusiner, recipient of Nobel Prize for research on prions in 1997
Priority Areas at Research to POC

Research to POC

Priority TAs
- CV-M
- Oncology
- Frontier

Early Development
- Thrombosis
- Hypertension
- Pain

Late Development
- CV-M
- Oncology
- Pain

LCM Market
- Thrombosis
- Hypertension
- Pain
Mission for Global Research of Daiichi Sankyo

- Challenge high unmet medical needs by novel science and technologies
- Create a Competitive Pipeline and Deliver Innovative Products Quickly and Consistently to Patients

**Approach in Priority Area**

- **CV-M**: Utilizing past experience and strength and challenge to new approaches
- **Oncology**: Actively utilize open innovation and create strong franchise
- **Frontier**: Targeting First-In-Class drug discovery through new approach, Discovery Focus
Total care of thrombotic diseases

**Anti-platelet**
Oral P2Y$_{12}$ antagonist
PCI, stroke

**Anti-coagulant**
Oral Factor Xa inhibitor
AF, VTE, DVT-OS

prasugrel
edoxaban

**Fibrinolysis enhancer**
TAFIa inhibitor
Acute ischemic stroke

**DS-1040**

PCI: Percutaneous Coronary Intervention
AF: Atrial Fibrillation
VTE: Venous Thromboembolism
DVT-OS: Deep Vein Thrombosis after orthopedic surgery
DS-1040
TAFIa inhibitor brings safer thrombolysis

◆ UMN in Acute Ischemic Stroke
  ● SOC for blood reflow: rt-PA (alteplase)
    • Very limited eligible patient
    • Strict applied condition including narrow therapeutic time window due to increasing intracranial hemorrhage (ICH) risk

◆ TAFIa inhibitor brings safer thrombolysis
  ● TAFIa inhibitor would recruit plasminogen and tPA to fibrin surface followed by promoting thrombolytic effect of tPA/plasmin
    • Expected low ICH risk by localizing thrombolysis around the fibrin
Open Innovation is the key for success

Daiichi Sankyo

- Strong Medicinal Chemistry
- Unique Compound Library
- Experienced Pharmaceutical Science

Academia

- Innovative Target
- Academic Network
- Scientific Excellence
- Clinical Insight

+ New Business Model

Discovery of Innovative Drug
Open innovation at Daiichi Sankyo

- Traditional
- Competitive
- Comprehensive
- Networking
- Compound-based
- Academia/Industry/Financier
DS-3032: Mdm2 inhibitor for cancer

Mechanism of Action: Inhibition of MDM2-p53 interaction
Indication: Leukemia, solid tumor
Collaborator: UCSF (Frank McCormick), Rigel

Cancer Cells
mutated p53
50%
wild-type p53
50%

p53 activation
Mdm2 Inhibitor
Mdm2
Overexpression / Activation
Tumor suppression

Traditionally known
WT genotype
p53 gene sequencing

DS identified
WT phenotype
Gene signature
Select patients
**IDH1 mutant inhibitor:** cancer drug with much lower adverse effect

Mechanism of Action: Selective inhibition of IDH1 mutant

Indication: Leukemia, solid tumor (glioma etc)

Collaborator: National Cancer Center

IDH1 mutant inhibitor:
cancer drug with much lower adverse effect

**Comprehensive**

- **IDH1/2**: exist in normal cells
- **IDH1mut**: exit in specific tumor cells

**Mechanism of Action:**
Selective inhibition of IDH1 mutant

**Indication:**
Leukemia, solid tumor (glioma etc)

**Collaborator:**
National Cancer Center

**IDH1 mutant inhibitor:**
cancer drug with much lower adverse effect
IDH1 mutant inhibitor is effective in leukemia model

• Administration of IDH1 mutant inhibitor decreases 2HG level and AML cells

(National Cancer Center, Daiichi Sankyo 2014)
TaNeDS
“Take a New challenge for Drug discovery”

Multi-Entrance

- Multi ENTRANCE
  From preliminary ideas to strengthening IP
- Multi EXIT
  From contract-based research to supported collaboration to establish a venture

Multi-Exit

- collaborative research on drug creation
- further investigations into discovered results
- fostering intellectual property or technologies from a business viewpoint
- utilization of OiDE projects

Research stages

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Access to a variety of academia: Alliance with Virtici/Celdara Medical (VCM)

- Partnership for novel drug target identification research
- VCM gathers many collaboration proposals from their wide range academia network in US
- DS selects research projects and conduct drug discovery research

1. collaboration proposal
2. triaged candidate based on DS wish list
3. selected candidate
4. contract with academia
Library compounds exchange with Astellas: For better drug candidates

Daiichi Sankyo  Astellas

0.4 million Compounds for HTS

0.4 million Compounds for HTS

Share compounds

Possibility of obtaining hit compounds
Diversity of hit compounds

Better drug candidates
Designed compound library for high quality hit: Pharma Space Library

- Novel fragments
- Conversion of reactive functional group etc
- Bioactive fragments
- ligand-protein interaction substructures
- Novel structures
- Combination
- Novell fragments
- Conversion of ring system etc
- Drug-like fragments
- Substructures common to bioactive compounds
- Bioactive compounds
Synergistic combination between academia and Daiichi Sankyo

Academia (novel drug target) → free offer!

Daiichi Sankyo (Pharma Space Library)

Library Screening → Hit compound

Publication → Compound for clinical trial → Clinical development

first stage collaboration

second stage collaboration

- compound optimization
- patent filing
- milestone/royalty payment
Biologics Overview

Junichi Koga
Global Head of Biologics
Strategy

1st wave
- Conventional full body Antibodies

2nd wave
- ADCC
- ADC
- Bispecific
- Protein scaffold

3rd wave
- Peptides
- Nucleic acids
- Cell Therapy etc.

Expansion of
- Therapeutic area
- Target molecules

COG reduction
- Enhanced efficacy

Business value, opportunities

*ADCC: Antibody Dependent Cellular Cytotoxicity
**ADC: Antibody Drug Conjugate
Stepwise approach for biologics business

**Preparatory**
- Master Cell Bank development

**“Jump-in” JPN/Asia**
- Establish in-house mfg* facility

**Launch in-house mfg* BS**
- Expand in-house mfg* facility

**Portfolio expansion**

- * manufacturing

**Biosimilar**
- JPN/Asia early entry to BS arena via alliance
- Launch of in-house BS globally

**Innovative**
- Innovative products/pipeline expansion

Profit maximization through full implementation of biologics business
Bio-Research engine creates RD candidates effectively.

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As of Mar 2014

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<td>(New entry)</td>
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EPHA2 is known to be highly expressed in multiple tumors (gastric, breast, lung, ovarian, colorectal cancer etc.)

- Potent ADCC activity
- It is effective even in the tumors with KRAS active mutation in preclinical models
One of the 2nd wave technologies, ADCC enhancement technology, was applied.

DS-8895a is effective in EPHA2 positive preclinical tumor models including gastric, breast, lung, and ovarian cancer.

Phase 1 study is ongoing.
Antibody Drug Conjugate

- Strong Warhead (Drug)
- Functional Linker
- Appropriate target molecules and Ab

- Enhance anti-tumor activity of Antibody
- Deliver enough amount of drug to the target tumor

Provide ADCs which combine the features of Strong Anti-tumor Effect and Excellent Safety
DS original technology of ADC

- Targeting to tumor specific Ags* prone to efficiently internalize
- Stable in blood, specific drug release by endolysosomal enzymes
- Unique and strong payload: Topoisomerase I inhibitor

* Antigens

Potential to be a global standard Payload/Linker system
B7-H3 ADC showed potent efficacy

**A375 (melanoma)**

B7-H3: 1.6x10^5/cell

**Injection**

10 mg/kg, qw x 3, i.v.

**Estimated tumor volume (mm³)**

- Untreated
- Anti-B7-H3 mAb
- ADC
Most advanced Abs mfg plant based on Single Use Bioreactor (SUB)

◆ Concept
  ● Compliant with JP, US, EP GMP
  ● Single Use - Facility Integration
  ● Multiproduct facility

◆ Facility / Equipment
  ● 2,000L SUB* x 2 x 2 lines
  ● Two purification lines
  ● Start of operation : Feb, 2012

*Single Use Bioreactor
What is process development?

Our challenge!!

Host

Vector

Screening procedure

media

*Mab* manufacturing process

* Monoclonal antibody
Contribution to consortium* led by METI※

* Manufacturing Technology Research Association of Biologics (MAB)

- 4 Univ., 1 Research Inst., 2 NPO※ and 25 companies
- DS is the only pharmaceutical company in MAB
  - To establish upstream techs
  - To identify the requirements from user’s view point

※ METI : Ministry of Economy, Trade and Industry
NPO : Non-profitable organization
### Duchenne-type and Becker-type Muscular Dystrophy

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<th>Type</th>
<th>Duchenne</th>
<th>Becker</th>
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<td>Cause</td>
<td>Dystrophin protein</td>
<td>incomplete expression (quality, quantity)</td>
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<td>Deficient</td>
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<tr>
<td>Mutation</td>
<td>Out-of-frame</td>
<td>In-frame</td>
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ENA® Oligonucleotide-induced exon skipping would save Duchenne type patients by changing to Becker type.
ENA® Oligonucleotides

ENA: 2′-O,4′-C-Ethylene-bridged Nucleic Acids

- High affinity
- Highly resistant to nucleases
- In vivo antisense activity was observed in diabetic mice model*

*Koizumi et al., Oligonucleotides, 16: 253-262 (2006)

ENA is a registered trademark of Daiichi Sankyo.
Concept of ENA® Oligonucleotide-induced exon skipping

- Exon 44 deletion
  - out-of-frame mutation (Duchenne type)

- Exon 45 skipping by ENA oligonucleotide

Exon 44 & exon 45 deletion → mRNA splicing modulation to in-frame mutation

- Incomplete but functional dystrophin protein (Becker type)
DS has interest in research and development for Orphan Disease, in order to achieve this we have structured a new business model.

**New business model for open development**

- **Investment business establishment**
  - Innovation Network Corporation of Japan

- **Advice for R&D**
  - Kobe Gakuin Univ Prof. Matsuo
  - Hyogo College of Medicine Prof. Takeshima

- **Drug for DMD**
  - Orphan Disease Treatment Institute Co., Ltd.

- **Investment**
  - Daiichi Sankyo

- **R&D execution**
  - Mitsubishi UFJ capital

* Duchenne Muscular Dystrophy*
Global Development at Daiichi Sankyo

Mahmoud Ghazzi, MD PhD
Global Head of Development
Daiichi-Sankyo Global Development governance and structure is designed to deliver quality new medicines, efficiently and quickly.

**Governance**

- **GEMRAD**
  - Decision making body (Project)

- **GRDC**
  - Decision making body (Non-Project)

**Structure (Matrix)**

- **Global Functional Cmts**
  - Clinical
  - Regulatory
  - Project M.
  - TMCP
  - BioStat
  - Clin. Ops

*Not a complete list, for illustration only*
An Example of DS Development Capability: Edoxaban Phase 3 Global Program


Edoxaban project enrolled over 30,000 patients in phase 3 trials and was submitted to JP, US, EU, Switzerland, Brazil, Taiwan and South Korea
Targets for Approval and Launch

**Japan**
- FY2014: Edoxaban AF, Edoxaban VTE, Prasugrel CAD, Denosumab GCTB
- FY2015: Levofloxacin Injection
- FY2016: Denosumab BC adj., Prasugrel CVA
- FY2017: Denosumab RA, Etanercept BS RA, Prasugrel CVA
- FY2018: Oncology (Tivantinib, DE-766, Patritumab, Quizartinib, PLX3397, Vemurafinib)
- Others: Mirogabalin, SUN13837, DS-8500, Prasugrel (LCM), Denosumab (LCM)

**US**
- FY2014: Edoxaban AF, Edoxaban VTE
- FY2015: CL-108 Acute Pain
- Others: CS-3150, DS-8500, Prasugrel (LCM), Edoxaban (LCM)

**Western Europe**
- FY2014: Edoxaban AF, Edoxaban VTE
- Others: Mirogabalin, SUN13837, DS-7113, GE-145, Denosumab (LCM)

**Others**
- FY2014: Edoxaban AF & VTE (China・LTAM etc.)
- Others: Mirogabalin, SUN13837, DS-7113, GE-145, Denosumab (LCM)
Late Stage Development Update

- Edoxaban for Atrial Fibrillation and Venus Thrombo-Embolism
- Mirogabalin (DS-5565) for Neuropathic Pain and Fibromyalgia
- CL-108 for Pain management
- Quizartinib a FLT3 inhibitor for Acute Myeloid Leukemia
- PLX3397 a CSF1R/KIT/FLT3 inhibitor for Pigmented Villonodular Synovitis (PVNS)
Late Stage Pipeline: Edoxaban
Edoxaban: Competitive advantage

- Oral, highly selective, direct, and reversible Factor Xa inhibitor
- Unique combination of both once-daily convenience and superior safety for atrial fibrillation and VTE
- The only NOAC with three approved major indications in Japan: AF, VTE and DVT-OS

AF: Atrial Fibrillation; VTE: Venous Thromboembolism; DVT-OS: Deep Vein Thrombosis - Orthopedic Surgery
### Target Indications

| Prevention of stroke and systemic embolic events in patients with atrial fibrillation | **Japan:**
| **Approved in Sep 2014** |
| **US:**
| **Filed in Jan 2014,**
**Advisory committee (AF indication) in Oct 2014**
**PDUFA date in Jan 2015** |
| **EU:**
| **Filed in Jan 2014** |
| **Other:**
| **Filed in Switzerland, Brazil, Taiwan and South Korea** |
| Treatment and prevention of recurrence of venous thromboembolic event in patients with DVT/PE* | **Japan:**
| **Launch in Jul 2011** |
| **AF:** Atrial Fibrillation
| **DVT:** Deep Vein Thrombosis
| **PE:** Pulmonary Embolism
Commitment to Edoxaban Life Cycle Management:

◆ Generating supportive data related to AF and VTE
  - Safety of edoxaban in patients with AF undergoing planned electrical cardioversion (On-going)
  - Safety of edoxaban in patients with AF following PCI with stenting (under evaluation)
  - VTE in patients with cancer for whom long term treatment with LMWH is intended (under evaluation)

◆ Reversal agent programs (Multiple)
  - Perosphere, PER977 (small molecule)
  - Portola, Andexanet Alfa (recombinant proteins)
  - CSL Behring, Beriplex®/Kcentra® (4-factor prothrombin complex concentrate)

◆ Pediatric Development
Late Stage Pipeline:
Mirogabalin

- Phase 2 (U201) Study Results
- Broad Global Development Strategy
Mode of Action

- In neuropathic pain, neurons respond to stimuli with excessive Ca\(^{2+}\) influx and release of neurotransmitters
- Mirogabalin binding to presynaptic α2δ subunits inhibits Ca\(^{2+}\) influx and neurotransmitter release
**U201 Phase 2 Study Results**

**ADPS Change from Baseline at Week 5**

Mirogabalin

<table>
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<th>PGB 5 mg/day</th>
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<td>-2.04</td>
<td>-2.32</td>
<td>-2.66</td>
<td>-2.79</td>
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* *p<0.05, **p<0.01 vs placebo (LOCF); †p< 0.05 vs pregabalin (LOCF), ADPS (average daily pain score)*

*(Vinik et al, Diabetes Care, Sep 2014)*

59
Mirogabalin: Broad Global Development Strategy

◆ Development program in three indications
  - Focus on Fibromyalgia (FM) in West and future consideration for Japan
    *(Fibromyalgia: a chronic condition of widespread pain, debilitating fatigue, sleep disturbance, and joint stiffness)*
  - Focus on Peripheral Neuropathic Pain (DPNP and PHN) indication in Japan and Asia

◆ Program Status: Phase 3
  - Fibromyalgia: on-going, FPI: Nov. 2014
  - Broad Neuropathic Pain: FPI: Jan. 2015

DPNP: Diabetic peripheral neuropathic pain; PHN: Post herpetic neuralgia
Late Stage Pipeline: Quizartinib (Ambit AC 220)
**Quizartinib (AC220):**
**Ph3 for Acute Myeloid Leukemia (AML)**

**Target Indication:**
Relapsed or refractory FLT3-ITD positive AML patients.

**Mechanism of Action:**
Potent and selective inhibitor of FLT3, a validated target in AML

**Unmet Medical Need:**
- AML accounts for ~36% of all new leukemia cases
- Five-year survival 23%
- No new treatments approved in the last 30 years.
- Fast Track review granted

FLT3 receptor tyrosine kinase. *Litzow, Blood 2005*

Fröbling. S. et al., 2002
Quizartinib: Effect in FLT3-ITD(+) AML

Response Rate for FLT3 Inhibitors Observed in Clinical Trials of AML

Ambit Presentation & Knapper, S., 2011
Late Stage Pipeline
Hydrocodone combination CL-108
CL-108: Hydrocodone combination
Pain relief with less Opioid-Induced Nausea and Vomiting

Novel, fixed-dose, bi-layered tablet provides anti-emetic activity prior to hydrocodone effect

- Exclusive license for commercialization in US from Charleston Laboratories Inc.*
- Indication: Opioid Induced Nausea and Vomiting (OINV)
- Ph3 studies: treatment of moderate to severe acute pain as well as the reduction of OINV
- NDA: Targeted for FY2015

* Charleston Laboratories, Inc., privately held and located in Jupiter, Florida, is a specialty pharmaceutical company focused on the research and development of novel pain products
Late Stage Pipeline:
PLX3397: Pigmented Villonodular Synovitis (PVNS)
PLX3397: for the treatment of Pigmented Villonodular Synovitis (PVNS)

◆ **PVNS:**
A painful and motion limiting joint disease characterized by inflammation and overgrowth of the joint lining.

◆ **MOA:**
PLX3397 targets the CSF1 Receptor blocking tumor-produced cytokines action on CSF1.

◆ **Unmet Medical Need:**
No systemic therapies available.

◆ **Clinical Study Status:**
- Phase 1 ongoing, and preliminary data presented at ASCO June 2014
- Phase 3 in planning

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Efficacy Evaluation by Tumor Volume Score (TVS)

79% overall response rate

Tap, ASCO 2014
Global Development Summary

Daiichi-Sankyo development is a global and capable organization with proven record of delivery of large scale projects.

There is an exciting list of phase 3 projects with a mix of best-in-class and first-in-class mechanisms.
Closing Remarks – Our Culture
DS R&D Culture

People
- Smart risk taking
- Venture Spirit

Productivity
- Rapid Decisions
- Empowerment

Projects
- FIC Focus
- Personalized Medicines