



Acceleration of Product Creation

June 29, 2011

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Chief Product Creation Officer

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- Risks and uncertainties include general industry and market conditions, and general domestic and international economic conditions such as interest rate and currency exchange fluctuations. Risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, technological advances and patents attained by competitors; challenges inherent in new product development, including completion of clinical trials; claims and concerns about product safety and efficacy; obtaining regulatory approvals; domestic and foreign healthcare reforms; trends toward managed care and healthcare cost containment; and governmental laws and regulations affecting domestic and foreign operations.
- Also, for products that are approved, there are manufacturing and marketing risks and uncertainties, which include, but are not limited to, inability to build production capacity to meet demand, unavailability of raw materials, and failure to gain market acceptance.
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Eisai Product Creation Systems (EPCS)

Transformation from Research & Development to Eisai Product Creation Systems



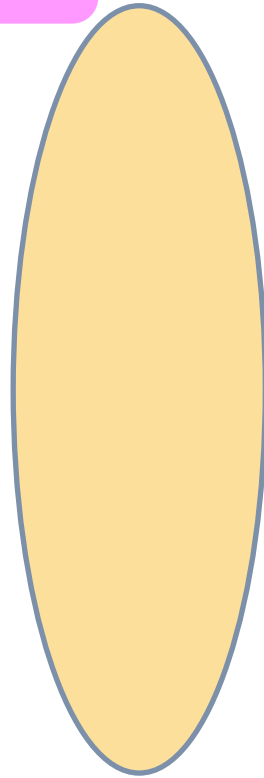
since July 1st, 2009

- ***Realizing venture-like productivity by autonomous unit management***
- ***Shortening development time by integrating cutting-edge technologies***
- ***Realizing innovation through organic collaboration between units***

“Timely deliver good medicines to patients who are waiting for new remedies to treat and cure their diseases”



Realizing innovation, which is ‘to shorten development timeline’ through organic inter-unit collaboration by autonomous management



Enhancement of global clinical development and global submission

Practical Example

Regulatory submissions for Halaven in JP, EU and US were achieved simultaneously on March 30, 2010 and resulted in obtaining approvals in all of those regions within 13 months. Also obtained approvals in Singapore and Switzerland and subsequently submitted in other countries including Asian countries

Practical Examples

Apply biomarker for all phases of drug development to assess pharmacological activity in the early stage and to shorten development timeline by targeting patient population, who are expected to show efficacy

Contribute to oncology and Alzheimer disease projects through development of biomarker and imaging marker

Commence Phase I study as early as possible with simple formulation

Achieve POC as early as possible allocating necessary resources by strategic partnering

Shorten clinical development timeline through running multiple studies in parallel and simultaneously

Minimize data analysis time by leveraging data

Pursuit of Open Innovation by integration of internal and external knowledge

Practical Examples

Establish Open Innovation Group in Neuroscience PCU to promote research collaboration with external institutes

Introduce innovative technologies from bio-ventures in oncology area and realize personalized medicine based on oncogene

Utilize diversity oriented synthesis (DOS) libraries

Concentration of resources on in-house original NMEs with high probability of success

Practical Example

Invest in new indications for Halaven, perampanel, lenvatinib, farletuzumab and E5501, which are expected to be launched during the

perampanel

Partial onset seizures:

Submission: in process in U.S. and accepted in EU
Approx. 1 year and a half ahead of schedule

lenvatinib

Thyroid cancer: initiated phase III

Dacogen

Acute myelogenous leukemia

(AML) for adult: submission being
processed in U.S.

Halaven

Minimized drug lag by simultaneous
submissions in U.S., Europe, and Japan
for 3rd line breast cancer

Approved in November 2010 in U.S.,
February 2011 in Singapore,
March 2011 in E.U.,
and April 2011 in Japan

Submitted CTA in March 2011 in China
*CTA: Clinical Trial Application

farletuzumab

Platinum sensitive ovarian cancer:
phase III

Number of patients enrolled
ahead of schedule



Acceleration of Biomarker Research

1. Biomarkers enable **early confirmation of efficacy and safety, and stratification of patient who may be effective** in discovery stage and early clinical stages
2. Biomarkers enhance **speed and success rate of clinical development** by stratifying patient who may be effective before the clinical study and confirming efficacy & safety with accuracy and speed
3. Biomarkers development **realizes personalized medicine** and provides additional benefits to patients and their families

Biomarkers can **accelerate overall process of product creation**

Phase II Study of Lenvatinib in Advanced Radioiodine-



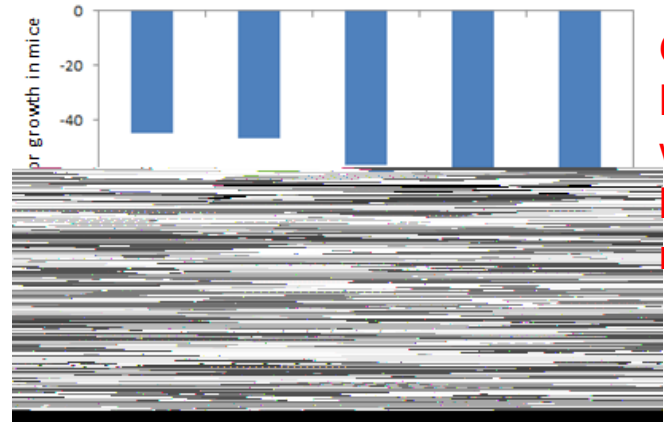
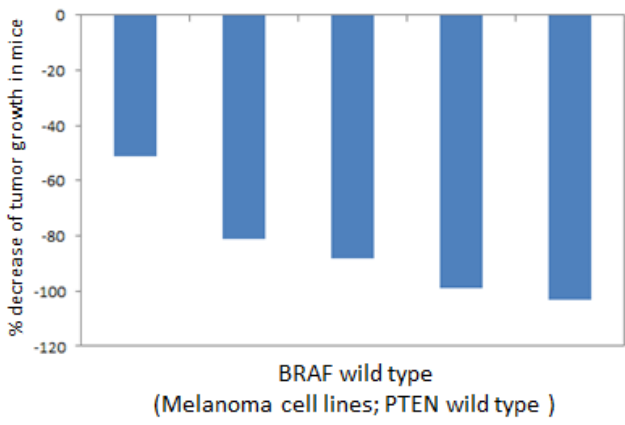
Phase II Study of lenvatinib in DTC Genetic Biomarkers Analysis



Ras mutational significantly extend duration of probability of progression free survival



Anti-tumor activity of lenvatinib in preclinical melanoma models



Genetic biomarker:
BRAF wild-type melanoma was the most sensitive to lenvatinib in a preclinical model.

Maximum tumor shrinkage effect of lenvatinib to melanoma of Phase I study

Phase II study is ongoing that stratify patients based on gene mutations

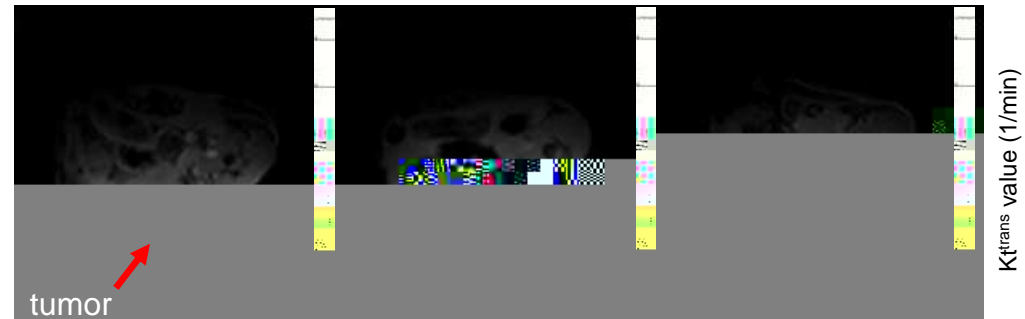
Predictive biomarkers among proto-oncogene wild type melanoma are being validated
Those biomarkers will be tested in an ongoing phase II study

Day 1

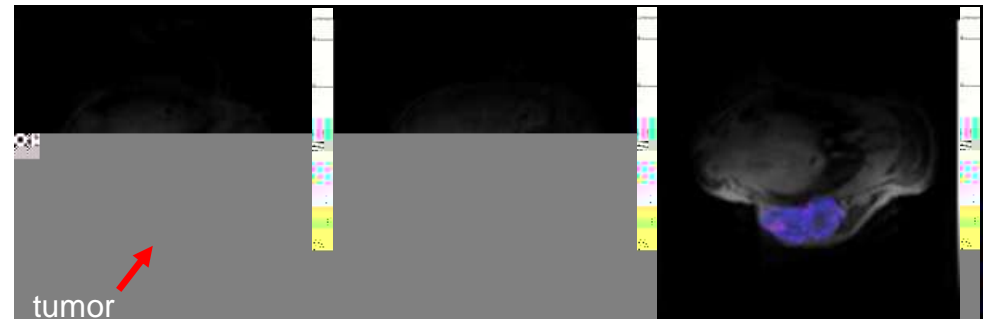
Day 5

Day 14

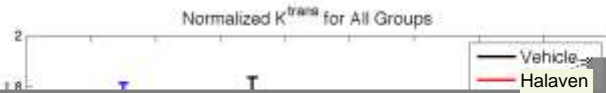
Halaven treated



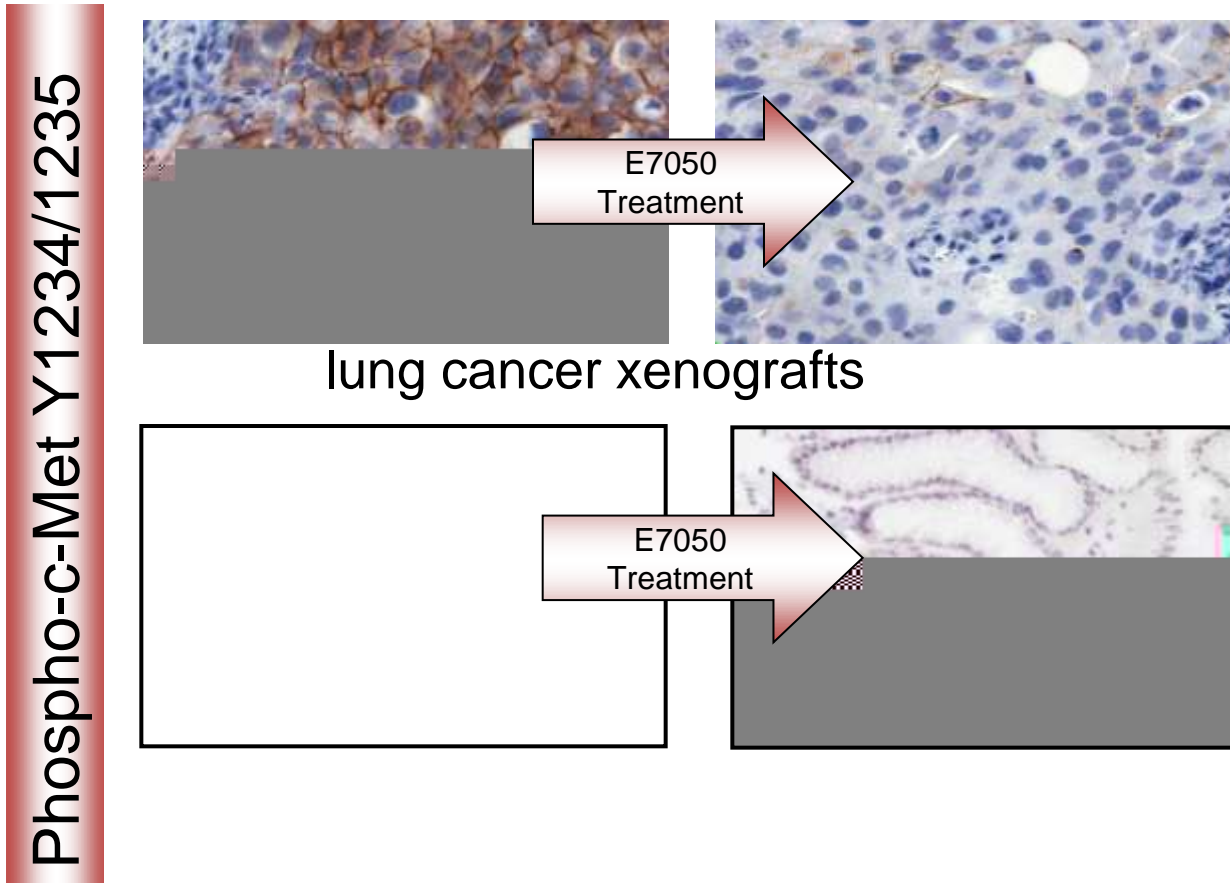
Paclitaxel treated



In xenograft mouse model of aggressive human breast cancer cell line (MX-1), Halaven appeared to decrease vascular permeability



Example of Bridging Between Preclinical and Clinical Data via Biomarkers



Confirmation of Aricept Pharmacology Effect in Preclinical Imaging



- Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) may be utilized to study disease model progression, proof of pharmacology, and efficacy to aid in the discovery of Alzheimer's therapies
- Measures of metabolic activity blood flow, plaque burden, pharmacokinetic response, and receptor occupancy can all be quantified with preclinical imaging studies
- A study was conducted to measure the effect of Aricept on AD transgenic mice

Focusing on Patients from Research to Clinical Practice



“Biomarker research should accelerate product creation and enhance success rate of Eisai drug development”



Progress of Accelerating Oncology Portfolio

June 29th, 2011

Takashi Owa

Oncology Product Creation Unit

- Professor Hirata, †

Halaven EMBRACE Study Update

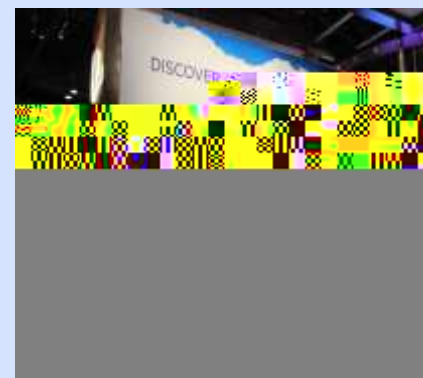
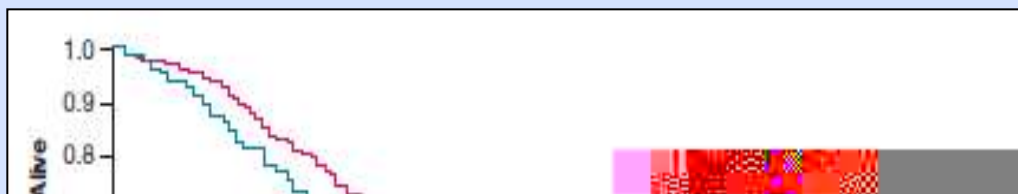


- Reconfirmed overall survival benefit-

- Presented the latest analysis of overall survival (OS) of EMBRACE Study at San Antonio Breast Cancer Symposium in December 2010
 - Reconfirmed Halaven's overall survival benefit
 - Safety profile has not been changed since the last analysis

Halaven-treated patients actually survived a median of 2.7 months longer than those in the TPC arm

	OS Median
Halaven arm	13.2 months
TPC arm	10.5 months
P=0.014	



Halaven booth at ASCO

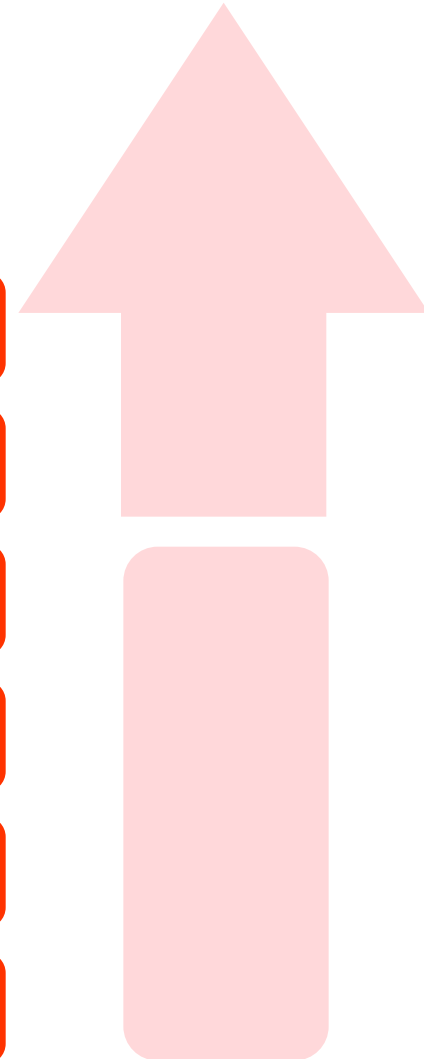


NSCLC

Sarcoma

BC 2nd line

BC 3rd line



Comparison of Neuropathy-Inducing Effects of Eribulin, Paclitaxel, and Ixabepilone in Mice



Sciatic nerve morphology in mice

A: Vehicle

B: MTD* of Eribulin

C: MTD of Paclitaxel

D: MTD of Ixabepilone



Eribulin at its MTD induced some mild pathology, but it was less frequent than with Paclitaxel or Ixabepilone, more closely resembling vehicle-treated mice

A phase II study is ongoing to compare eribulin and Ixabepilone in causing or exacerbating in patients with advanced breast cancer

Kinome dendrograms

Lenvatinib(E7080)

sunitinib*

sorafenib*

Prior VEGFR-
targeted
therapy N=17
(%)

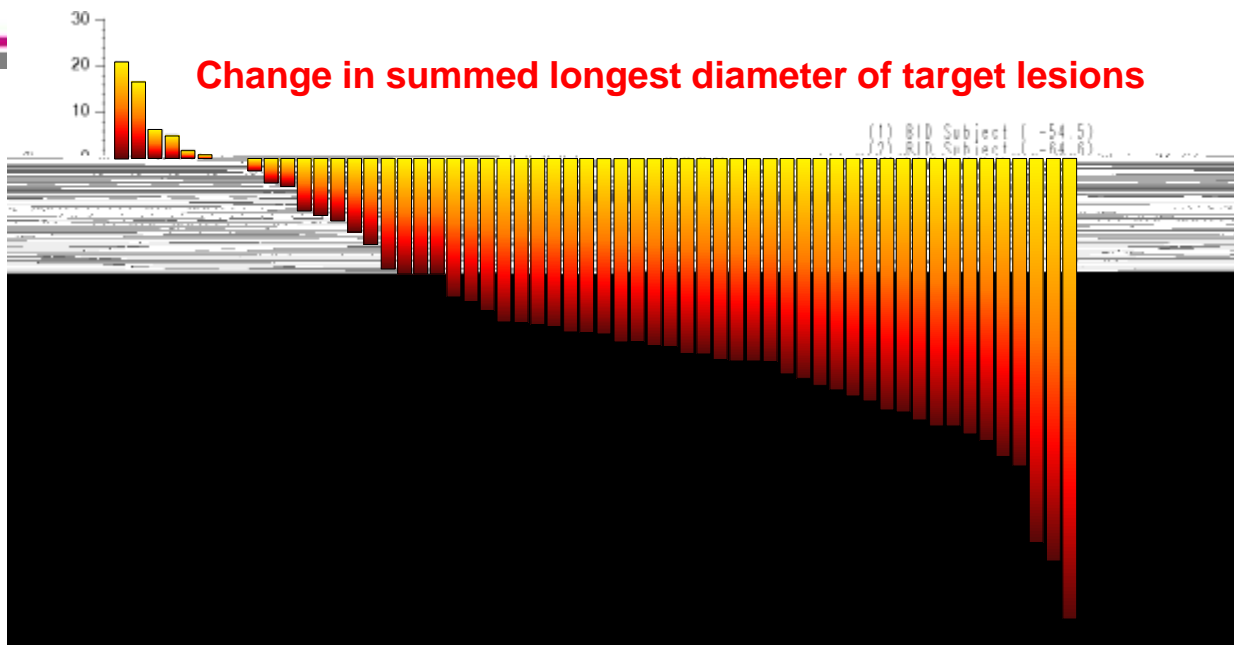
No prior
VEGFR-
targeted
therapy
N=41 (%)

Overall
N=58 (%)

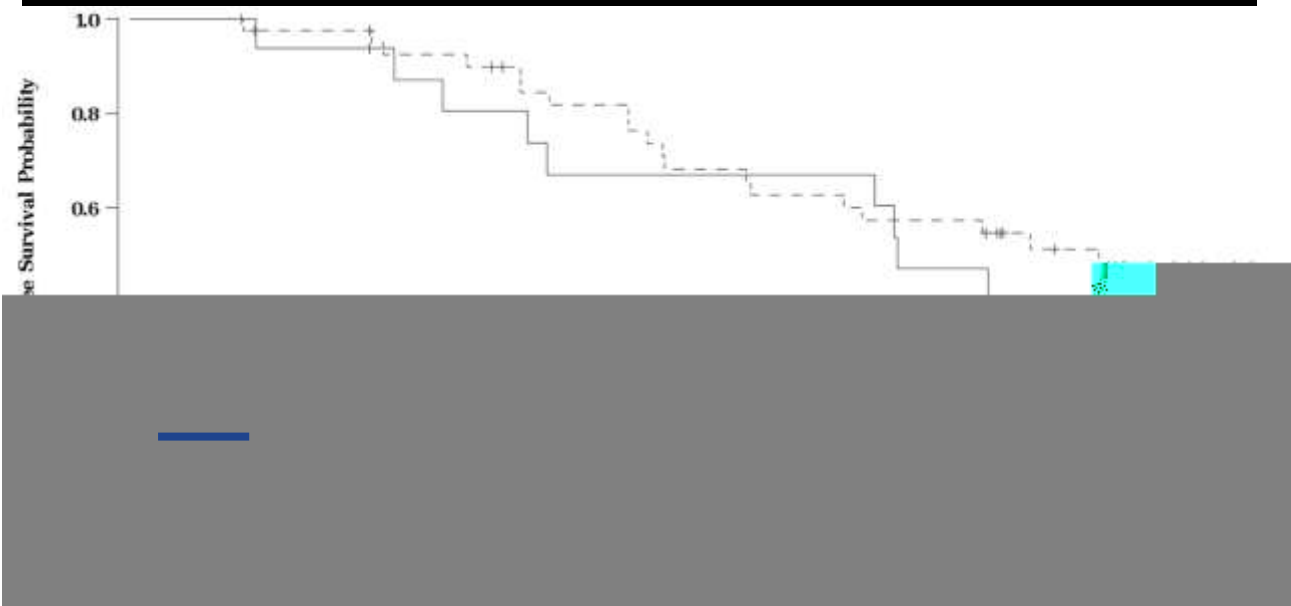
Lenvatinib: Activity in DTC Phase II Trial (Investigator Assessment at 14 month minimum follow-up)



Waterfall plot



**Progression Free
Survival**



Acceleration of Clinical Studies for lenvatinib



Eisai Regimen



Open Innovation



Epigenetic edge

By Chris Gallo

- **EZH2 overexpression in numerous solid tumors, correlated with poor prognosis of breast cancer, prostate cancer, NSCLC, etc.**
- **EZH2 Y641 activating mutations in some lymphomas (DLBCL and FL)**

PRC2

Polycomb Repressive Complex 2



Target gene
Transcription

Oncology PCU Pipeline Portfolio



PRE-CLINICAL
(CS/CI STAGE)

Phase I

Phase II

Phase III

SUBMISSION

eribulin(E7389)

(microtubule

dynamics

Inhibitor)

Liposomal formulation

Cytotoxics

Eisai's biologics Product Creation Unit developing biological-based products through proprietary technologies and development know-how

**June 29, 2011
Nicholas Nicolaides
President, Morphotek PCU**

Morphotek Business Model

leveraging technology and partnerships to develop novel biological-based agents for human healthcare

Lead clinical products

Farletuzumab (MORAb-003) - oncology

- Ph3 1st relapsed platinum-sensitive ovarian cancer
- Ph2 platinum-resistant ovarian cancer
- Ph2 1st line NSCLC adenocarcinoma

Amatuximab (MORAb-009) - oncology

- Ph2 1st line mesothelioma

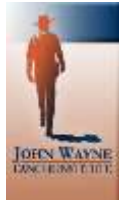
MORAb-004 - oncology

- Ph2 metastatic chemorefractory colorectal cancer
- Ph2 metastatic sarcoma
- Ph2 melanoma

Product pipeline

- MORAb-022, Ph1, inflammatory disease
- MORAb-028, Ph1, metastatic melanoma
- MORAb-047, PC, infectious disease
- MORAb-048, PC, infectious disease
- MORAb-050, PC, pan-cancer
- MORAb-066, PC, pan-cancer
- KANAb-071, PC, immunology area
- MORAb-075, PC, pan-cancer

Targets/technology collaborations



Technology for discovery/products



Tumor targeting peptide

MORAb-003 (farletuzumab)

First-in-class humanized IgG₁ monoclonal antibody to Folate Receptor Alpha (FRA)

FRA over-expressed in ovarian (OC), breast, colon, NSCLC, renal and other cancers

FRA over-expression in normal cells results in transformation independent of folate

Global randomized-controlled, double-blinded Ph3 study ongoing in 1st relapse PS OC

Ph2 randomized-controlled, double-blinded study in PR OC ongoing

Clinical studies in other cancer indications being pursued 1st line NSCLC initiated

Granted orphan status by FDA in 2006; by EMA in 2008

PS = platinum-sensitive

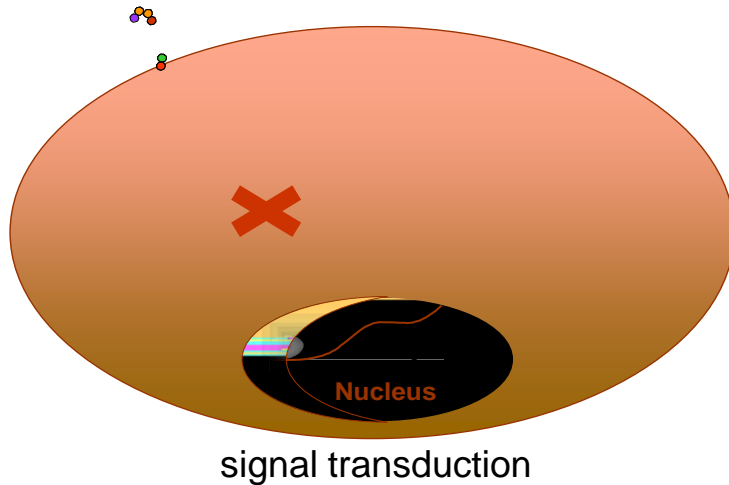
PR = platinum-resistant

OC = ovarian cancer

Farletuzumab differentiated mechanism of action

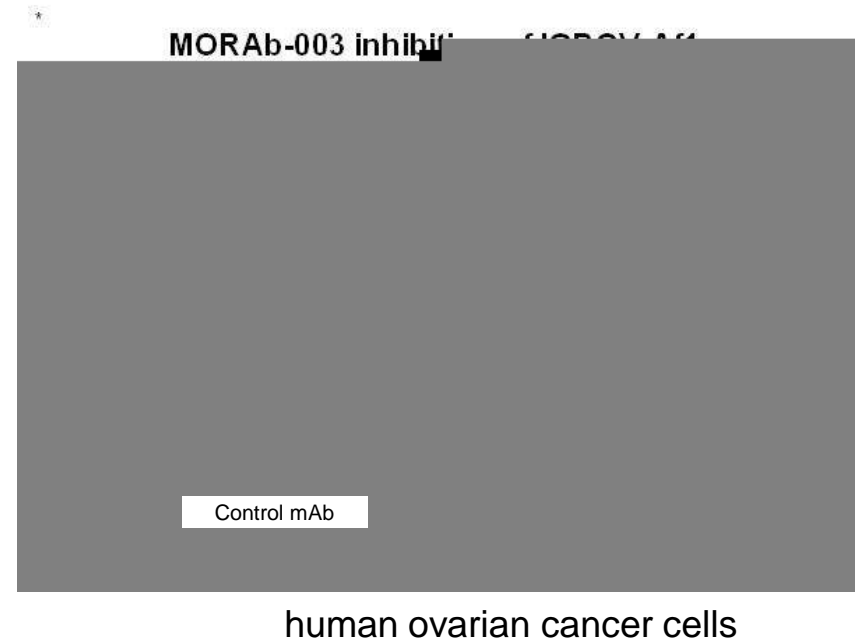
Biology of folate receptor alpha (FRA)

cellular pathway of transformation



Activity of farletuzumab (MORAb-003)

xenograft studies with FRA-expressing tumors



-mediated signal transduction and immune-effector function
Has no effect on folate biology; ADCC = antibody dependent cellular cytotoxicity; CDC = complement dependent cytotoxicity

Farletuzumab clinical observations

- *70% of OC patients in Ph1 study with advanced disease had stabilization*
- *Ph2 study, 90% patient benefit observed in PS OC patients in combo with SOC vs 45%*
- *Ph2 study, 20% of patients had 2nd remission greater than first (occurs < 5% with SOC)*
 - *Currently have several patients with 1st remission <12 mos that are now >3 yrs disease free*
- *No severe adverse events observed from long-term farletuzumab treatment (3+ yrs)*
- *Support by FDA for single pivotal study in 1st relapse PS ovarian cancer (FAR-131)*
- *Effect on PR ovarian cancer in combination with weekly taxane observed experimentally*
- *Pursuing supporting study in PR ovarian cancer (FAR-122)*

Farletuzumab pivotal trials in platinum-sensitive and resistant ovarian cancer



- *Carboplatin/taxane + farletuzumab (1.25 mg/m² or 2.5 mg/m²) or placebo*
- *Improvement in PFS in 1st relapse ovarian cancer patients vs 1st line SOC alone*
- *Trial design supported by FDA under Special Protocol Assessment, EMA and PMDA*
- *70% of trial enrolled from sites in 30 countries; targeting completion FY2011*
- *BLA filing in FY2012*



- *Weekly taxane + farletuzumab or placebo*
- *Patients with platinum-resistant disease*
- *Improvement in overall survival vs weekly taxane therapy alone*
- *62% of trial enrolled from sites in 8 countries; targeting completion FY2012*

MORAb-004: mAb to endosialin

Mechanisms of activity of MORAb-004 on tumor cells and cells of the microenvironment

Tumor Microenvironment Activity

Endosialin is expressed on tumor pericytes and fibroblasts to support tumor growth and maintenance



Tumor Cell Activity

A mechanism of plexikon resistance in melanoma has been up regulation of PDGFR- and signaling

Effects on tumor growth and vascularization in human-endosialin knock-in mice treated with MORAb-004



Suppression of endosialin pathway leads to blockade of PDGFR- mediated signaling and growth in mesenchymal-derived cells



MORAb-004: mAb to endosialin

A first-in-class mAb to endosialin and tumor pericyte cells

Endosialin is expressed on tumor pericytes and tumor cells of mesenchymal origin **not** endothelial cells (VegF target)



Suppressed vascularization in vitro via MORAb-004

Human endosialin knock-in mice with human tumor xenograft cells analyzed at day 14.



Human endosialin knock-in mice with metastatic melanoma cells analyzed at day 19



Technology Platforms

Maintain cutting edge novel targeting platforms

- *Morphotek has 18 mAb programs in development from existing technologies*
- *New mAb technologies are maturing to support product development of competitors*
- *One of EPCS goals is to stay at the cutting edge of targeted therapy technologies to improve success rate of development and efficacy of new drugs for patients needs*
- *Examples of new Ab technologies:*
 - *Antibody fragments*
 - *Antibody drug conjugates for oncology*
 - *Targeted peptide-conjugates for oncology*
- *Morphotek exclusively acquired a tumor targeting peptide platform and clinical assets from TransMolecular in March 2011*

TM Tumor Targeting Peptide

Tumor Targeted Chemotherapies

Therapeutic agent/companion diagnostic



Summary

- *18 products in development (preclinical to Ph3 pivotal studies)*
- *Farletuzumab is our most advanced and is positioned for completion of a global Ph3 study in OC and regulatory filing in US, EU and Japan in FY2012*
- *Expanding farletuzumab into new indications involving FRA+ cancers*
- *MORAb-004 has completed a Ph1 study and shown activity in various cancers*
- *MORAb-*



H3 Biomedicine Inc.

- Our Approach and Value -

June 29, 2011

Hiroyuki Kato

Officer, Executive Director, Product Creation HQs

h3c
human health care

Concept of H3* Biomedicine

- Commitment to Focused Medicine -

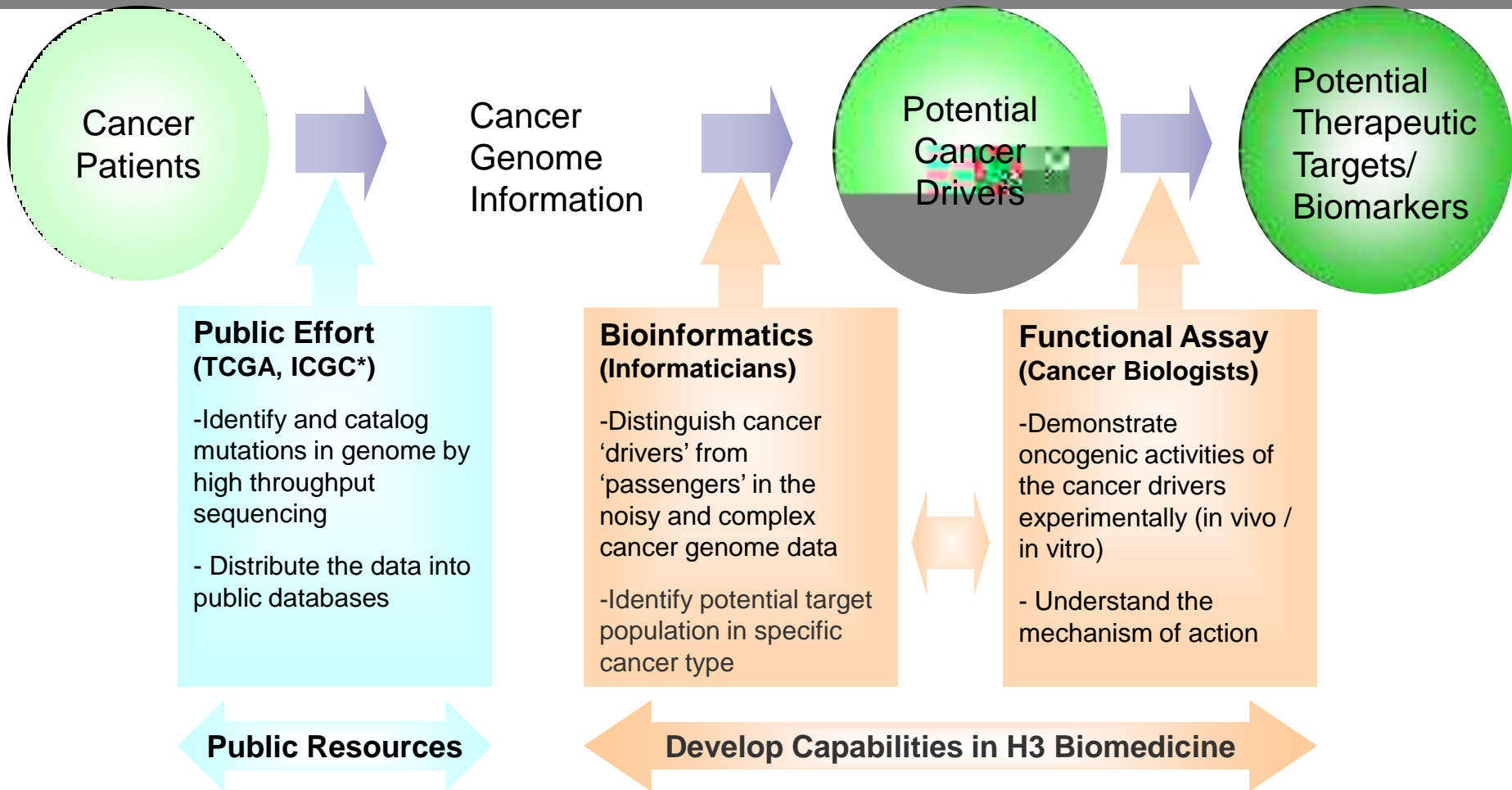


Functional
Collaborations
With Eisai

"Disciplined" Approach



Prospective Utilization of Cancer Genomics



H3 Biomedicine will use genomic information of cancer patients prospectively to discover novel targets and biomarkers rather than just using the information retrospectively to interpret clinical outcomes

Diversity-Oriented Synthesis (DOS)

- Power of Modern Synthetic Chemistry -

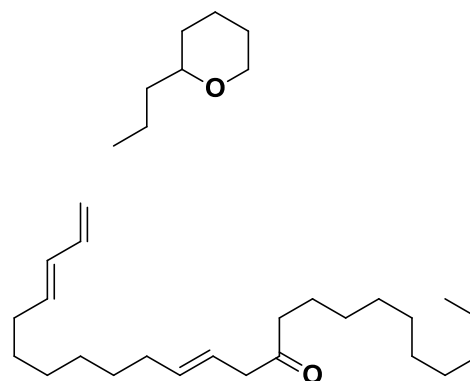
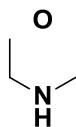


Commercial

DOS

Natural products

Structural complexity

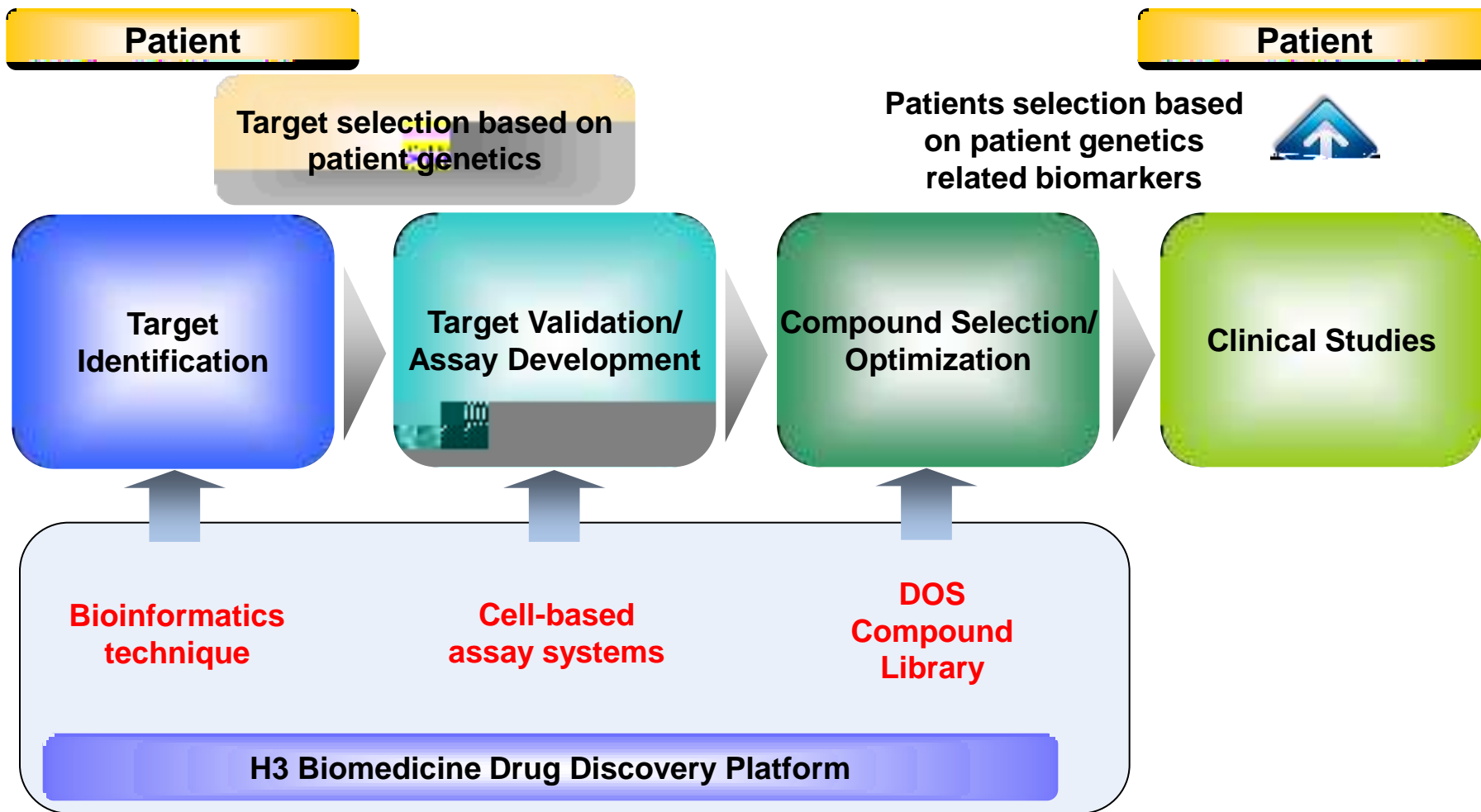


Ease of synthesis

- Striking a balance between structural complexity and ease of synthesis
- Accessing skeletal and stereochemical diversity

Create unique compound libraries to challenge difficult targets

Research Strategies of H3 Biomedicine



Knowledge of Scientific Founders / Eisai's Scientific Excellence / Strong Leadership

Value Creation of Focused Medicine

- Through "Disciplined" Approach -



Evidence-based value proposition to patients, providers and payers based on the high efficacy rate to specific target populations

Time and cost savings by small-sized and cost-effective clinical studies realized by efficient stratification strategy based on patient genetics (i.e., biomarkers) and a high response rate

Rational combination with the existing drugs by investigating the genetic features of resistance mechanism of those drugs

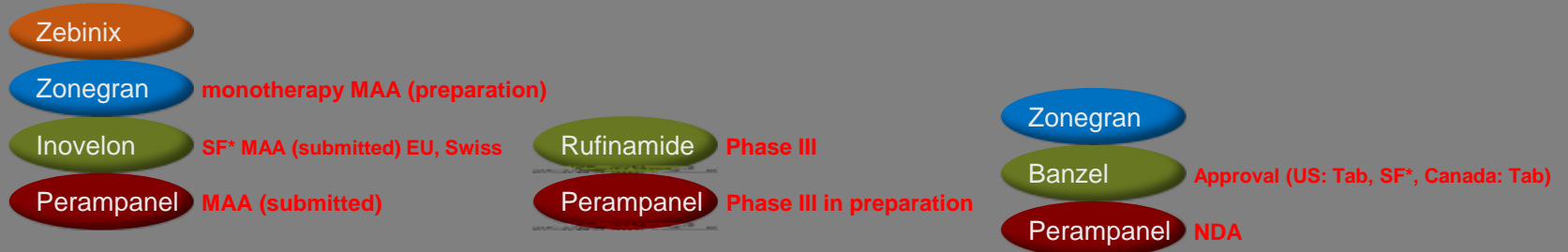


Accelerated Progress in Neuroscience Portfolio

June 29, 2011
Lynn D. Kramer
Neuroscience PCU

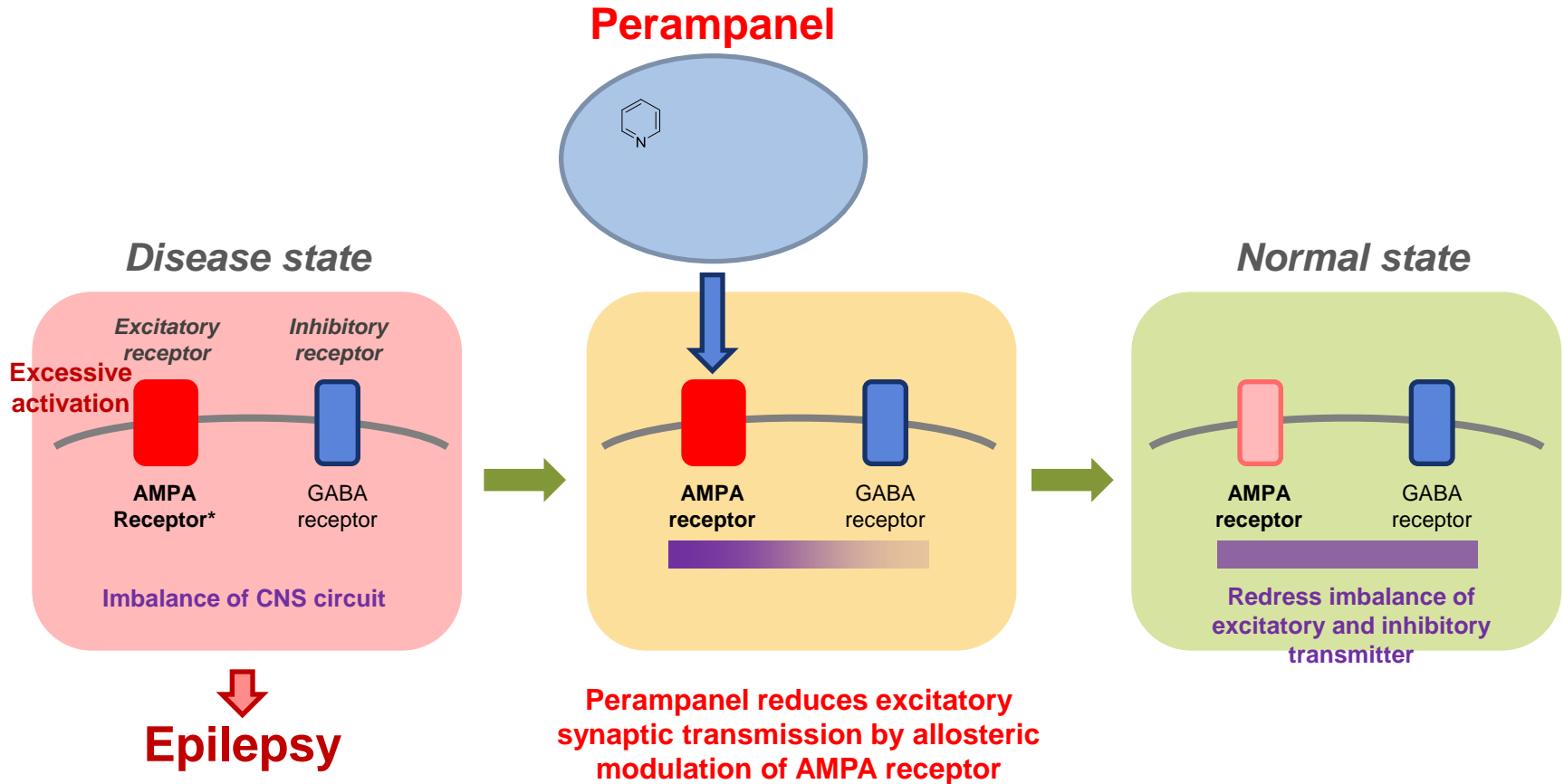
Global Epilepsy Franchise

Rich product family for treatment of refractory epilepsy



Perampanel: Mechanism of Action

A highly selective non-competitive AMPA-type glutamate receptor antagonist



AMPA receptor: -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor

AMPA receptors are responsible for the bulk of fast excitatory synaptic transmission throughout the CNS and their modulation is the ultimate mechanism that underlies much of the plasticity of excitatory transmission that is expressed in the brain.

Perampanel: Successful NDA*/MAA



Achieved submissions 18 months early!

Significant timeline acceleration has been achieved with multiple strategic approaches

Innovative operations

PK-PD confirmation of Phase II study results

Simultaneous initiation for multiple Phase III studies

Global standardization and utilization of operational processes

Full utilization of data management center in India

Careful real-time data review using standardized processes to identify study site understanding

EPCS model strengthens study outcomes

Enhanced motivation by project ownership under EPCS framework

Strong support by leadership members in Neuroscience

Reliable technical support by Core Function Units (CFUs)

Knowledge obtained through other epilepsy products

Banzel (Inovelon), Zonégren and Zebinix



These approaches are standardized in the operation and are being applied to future Product Creation including other indications

Perampanel: Successful NDA/MAA

First-in-class of AMPA Antagonist



Mechanism of action

- **A highly selective non-competitive AMPA receptor antagonist**
- **First-in-class**
 - Has benefit as addition to existing mechanisms of anti-epilepsy drugs

Efficacy

Perampanel: Efficacy Results

Epilepsy Phase III studies



Study number							
Clinical dose							
<u>Primary</u> Outcome (FDA) Percent Change in Seizure Frequency (Ancova) ¹	0.4197	0.0026	< 0.0001	0.0261	0.0158	TBP*	TBP*
Log transformation	0.2542	0.0037	< 0.0001	0.0044	0.01842 ²	TBP*	TBP*
<u>Primary</u> Outcome (EMA) Responder Rate ¹	0.4863	0.0132	0.0003	0.07603 ³	0.09143 ³	TBP*	TBP*
<u>Secondary</u> Outcome Measure (Both) Complex Partial + Generalized Seizures ¹	0.6506	0.0070	0.0005	0.0020	0.00812	TBP*	TBP*
<u>Secondary</u> Outcome Measure (Both) Dose response analysis of seizure frequency	< 0.0001			0.0262		TBP*	

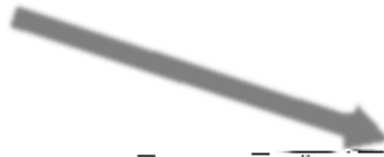
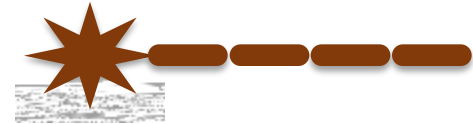
¹ Full ITT includes all treated with any post-baseline diary data

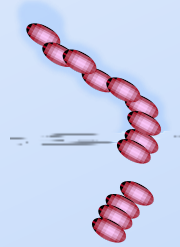
² If limited to North America only

³ If limited to North America only

* TBP: To be presented at IEC2011 in August/September (Rome, Italy)

p-value < 0.005 < 0.05 0.05 - 0.10 > 0.10







Exploratory Research by Open Innovation

Collaboration with both broad vision & project specific



Novel MoA/Compounds

University
College London

Biomarkers
Proteostasis
Neuroinflammation
Neurovascular
-mitochondria

Neuroscience
Discovery
Research

Neuroscience
Clinical
Research

Project Specific

Aestus
Therapeutics

Psychiatric disease

BioArctic

Anti-protofibrils mAb

IMMD Inc.

Virtual screening

John's Hopkins
University
Brain Science
Institute

GCP2 inhibitor

Technology/Platform

National
Institute
of Radiological
Science
(NIRS)

Brain PET imaging

National Institute
of Advanced
Industrial Science
And Technology
(AIST)

Novel animal model

Keio University

Age-related
neurodegenerative
70 disorders



E5501

Best in Class Among
Thrombopoietin (TPO) Agonists

June 29, 2011

Yasunobu Kai

President, Frontier PCU

- *ITP: Treatment for thrombocytopenia of chronic idiopathic thrombocytopenic purpura*
 - *Most advanced program among E5501 development*
- *Promising data obtained in Studies 003/004*
 - *POC achieved*
 - *Key differentiation point identified*
- *Successfully completed the end of phase II meeting with FDA/EMA*
 - *Phase III pivotal studies are being planned*
China site will be included for the studies

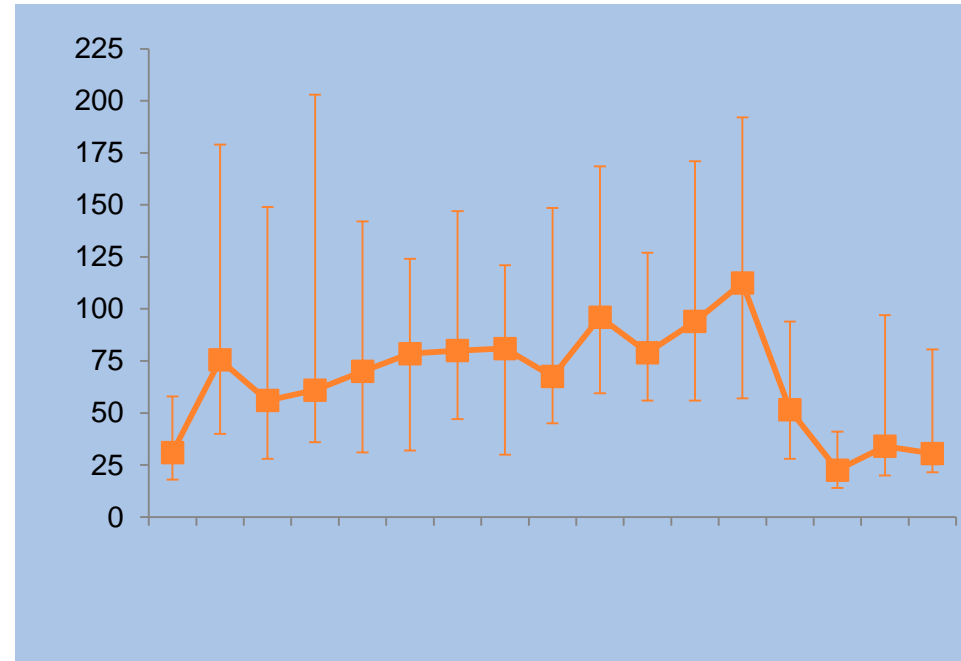


E5501-ITP: Key messages from phase II studies



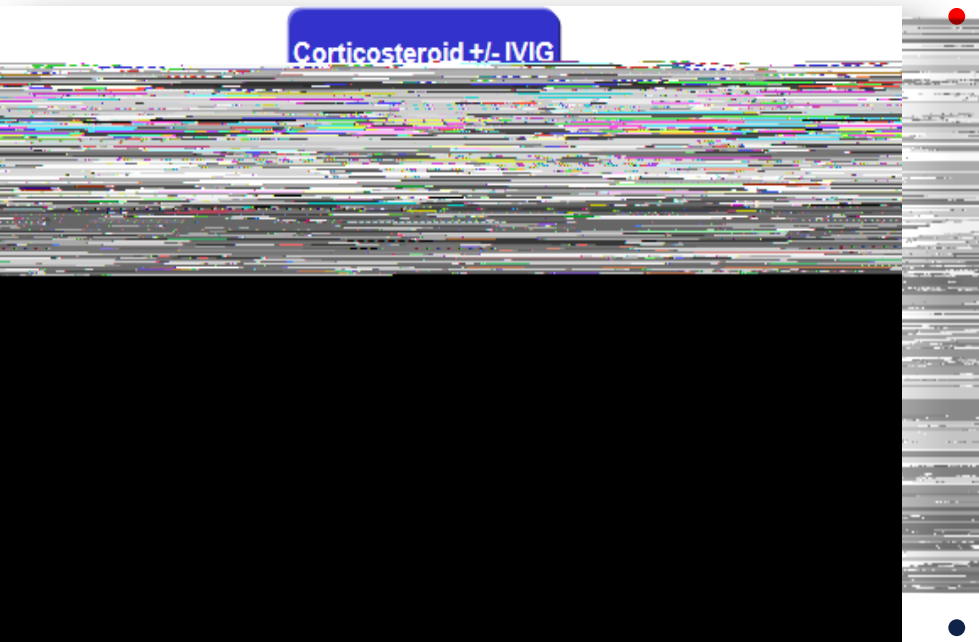
1. Dose-dependent responses and early on-set (Day 7) were shown and maintained (through Day 28)

2. Significant short and long-term platelet responses were observed



3. E5501 was well tolerated and demonstrated a favorable safety profile over the extended 6-month treatment period

Targeting 2nd/3rd line therapy for chronic ITP



Corticosteroid +/- IVIG

- Best in class among TPO agonist
 - Early on-set of the efficacy
 - No significant hepatic toxicity and drug-drug interaction
 - No significant food effect
 - Orally administrative



- Potentially replacement for other standard of care

ITP

Treatment for thrombocytopenia of chronic idiopathic thrombocytopenic purpura

- POC achieved
- Phase III being planned for targeting 2nd/3rd line therapies for chronic ITP
- Most advanced program among the planned programs

aTLD

Treatment for thrombocytopenia with chronic liver disease patients who will undergo elective surgical or diagnostic procedures

- POC study on-going
- Topline results expected within FY2011

E5501

cTLD

Treatment for thrombocytopenia of patients with chronic liver diseases requiring antiviral therapy with INF - both initiation and maintenance

- POC study will be initiated 2QFY2011
- Accelerated clinical development in China/Asia with huge market potential
- Planning for hepatitis B in China

CIT

Treatment of the patients associated with chemotherapy induced thrombocytopenia

- POC study design under discussion



Accelerating Product Creation in East Asia Region

Acceleration of clinical development in East Asia by JAC PCU(Japan/Asia Clinical Research PCU)



- High incidence of hepatitis virus infection in the Asia/Pacific region
 - About 78% of the patients with Hepatitis B (HBV) infection (350M) in the world, i.e., 275M live in the Asia/Pacific region



Liver disease franchise



Fulfill Asian-specific unmet medical needs with multiple treatment

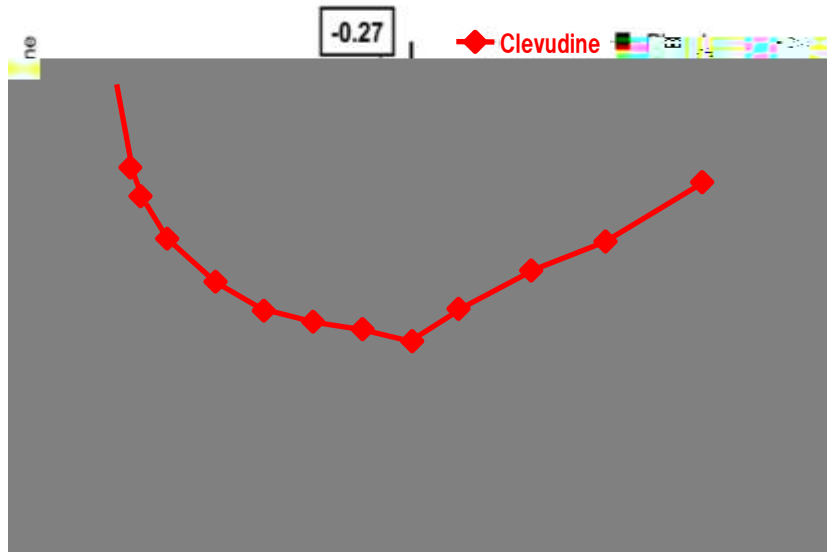
Clevudine (Treatment for Hepatitis B)



Anti-virus agent for treatment of hepatitis caused by the hepatitis B virus based on DNA polymerase inhibition

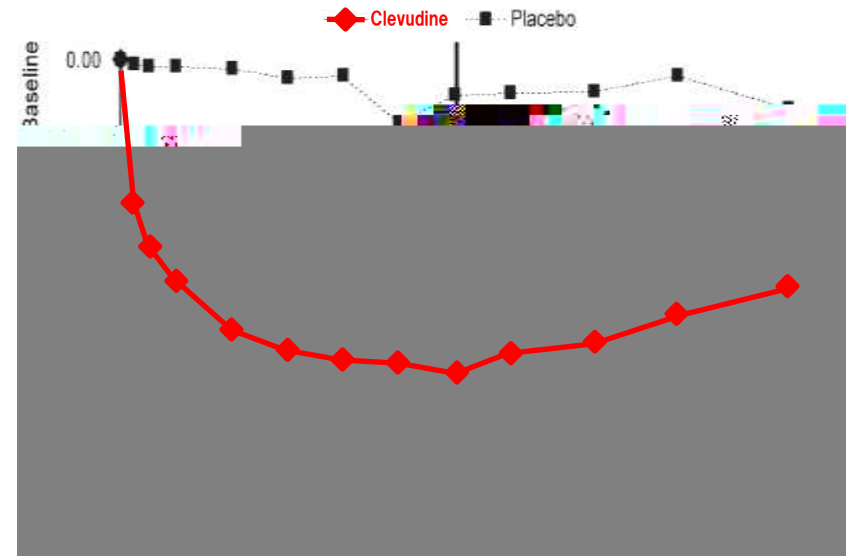
- In-licensed from Bukwang Pharm (South Korea)
- Powerful and sustained virus suppression (Korea Phase II)

Korea Study 301: HBeAg (+)



Yoo BC, Lee HS. Hepatology 2007;45:1172-78

Korea Study 302: HBeAg (-)



Yoo BC, Lee HS. Hepatology 2007;46:1041-48

- Positive results of Phase III conducted by Eisai were obtained in China
IDL (Import Drug License) was submitted in Dec 2010; targeting approval in FY2011

Liver disease franchise NDA submission plans



Submitted

FY2012

Beyond FY2014

Lenvatinib (E7080)

Clevudine
(Hepatitis B)

China: IDL

**Expected response from
authority in FY2011**