INTRODUCTION
R&D MEETING 2016

Yoshihiko Hatanaka
President and CEO
Astellas Pharma Inc.
December 8, 2016

ACHIEVING SUSTAINABLE GROWTH

Strategic Priorities –Strategic Plan 2015-2017

Maximizing the Product Value

Creating Innovation
- Enhancing Capabilities to Deliver Innovative Medicines
- Advancing into New Opportunities

Pursuing Operational Excellence

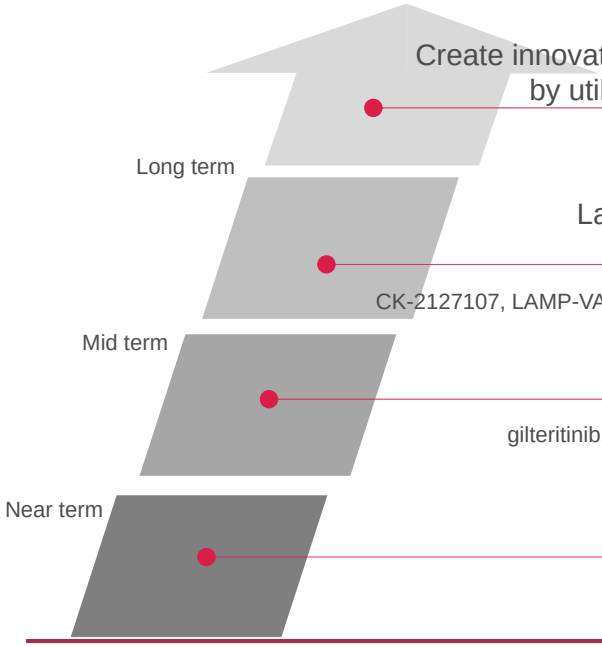
Achievements since FY2015

Launch	Development progress	Acquisition	Research collaboration
Repatha (evolocumab) injection 140 mg/mL	6 approvals for NDA/sNDAs*1 8 NDA/sNDAs*1 8 Phase 3 entries	OCATA THERAPEUTICS, GANYMED Pharmaceuticals AG *2	Multiple collaborations in focused research area

*1 NDA/sNDA in each region of US, EMEA and Japan
*2 Transaction announced, completion pending

CREATE INNOVATION WITH EVOLVING FOCUS

Turn innovative science
into value for patients
on the forefront of healthcare change



Long term

Create innovative treatments for broad range diseases by utilizing new technology/modality platforms

New technologies/modalities

Next-generation vaccines, cell therapy

Mid term

Launch products in new therapeutic areas and realize new technologies/modalities

Current pre-POC projects, new technologies/modalities

CK-2127107, LAMP-VAX DNA vaccine, immuno-oncology, RPE cell program

Near term

Launch and grow later stage products in existing therapeutic areas

Post-POC projects

gilteritinib, IMAB362, enfortumab vedotin, ASP8273, roxadustat

Maximize product value

Launched products

XTANDI, overactive bladder treatments

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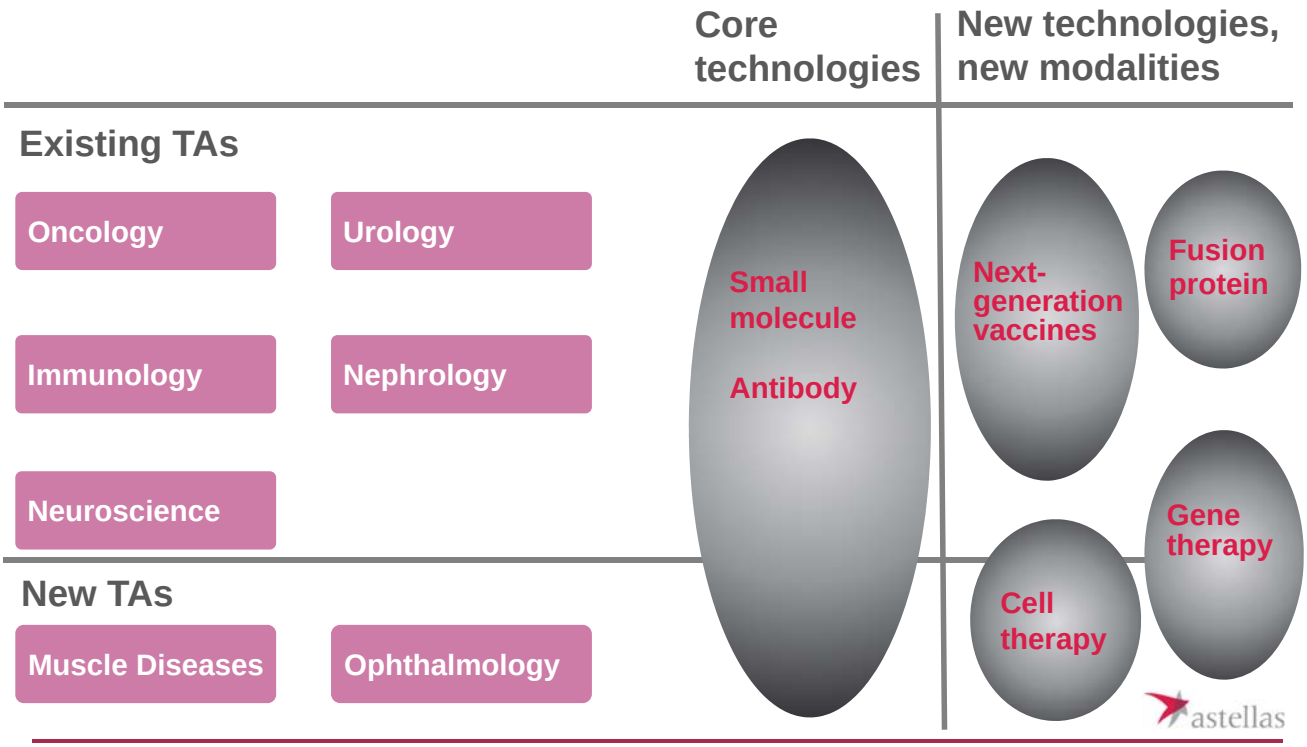
CURRENT FOCUS AREAS



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DEVELOPMENT
R&D MEETING 2016

Sef Kurstjens, M.D., Ph.D.
Chief Medical Officer
Astellas Pharma, Inc.
December 8, 2016

DEVELOPMENT PURPOSE

Turn innovative science into value for patients by

characterizing the therapeutic potential of our products.

OUR CORPORATE STRATEGY DRIVES ALL DEVELOPMENT PRIORITIES

Astellas Strategy

Maximize the Product Value	Create Innovation	Pursue Operational Excellence

STRATEGIC PRIORITY: MAXIMIZE THE PRODUCT VALUE

Astellas Strategy

Maximize the Product Value	Create Innovation	Pursue Operational Excellence

Development Priorities

- Expand current indications, explore future indications, evaluate new formulations: enzalutamide
- Meet pediatric regulatory requirements: mirabegron; solifenacin
- Evaluate combination therapy in underserved patient populations: mirabegron + solifenacin

STRATEGIC PRIORITY: CREATE INNOVATION

Astellas Strategy

Maximize the Product Value	**Create Innovation**	Pursue Operational Excellence

Development Priorities

- Assess full treatment paradigm: gilteritinib
- Recognize competitive environment: ASP8273
- Explore opportunities in treatment-resistant patients: enfortumab vedotin (ASG-22ME)
- Explore new approaches in areas of unmet needs: IMAB362*
- Take flexible licensing approach for novel assets: roxadustat, ASP0113
- Leverage Japan expertise: Amgen Astellas joint venture

*Transaction announced, completion pending

STRATEGIC PRIORITY: PURSUE OPERATIONAL EXCELLENCE

Astellas Strategy

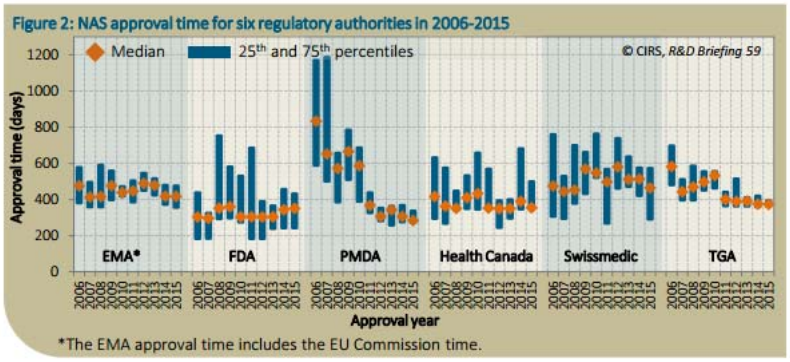
Maximize the Product Value	Create Innovation	**Pursue Operational Excellence**

Development Priorities

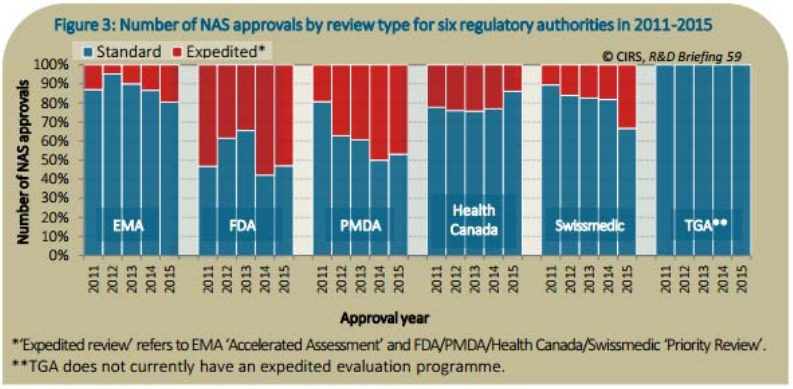
- Build speed and efficiency into pre-POC activities, in light of historical attrition rates in early-stage development
- Leverage global reach and balance internal and external capabilities to execute late stage studies

ASTELLAS STRATEGY ALIGNS WITH EVOLUTION OF EXTERNAL REGULATORY ENVIRONMENT

More consistent approval time across regulatory authorities



Increasing use of expedited review for novel compounds in areas of high unmet medical need



Source: Bujar M, McAuslane N, Liberti L. 2016. R&D Briefing 59: The impact of the evolving regulatory environment on the approval of new medicines across six major authorities 2006-2015. Centre for Innovation in Regulatory Science.

STRATEGIC FOCUS WILL ENABLE EFFECTIVE AND EFFICIENT DELIVERY OF OUR EXPANDING PIPELINE

Phase 1

- enfortumab vedotin (ASG-22ME)
- ASG-15ME
- ASP5878
- AGS67E
- ASP4132
- gilteritinib (NSCLC)
- AGS62P1
- ASP2205
- ASP6282
- YM311/FG-2216 (JP)
- ASP7398
- ASP6294
- ASP8302
- ASP5094
- ASP3662
- ASP4345
- ASP4070
- ASP7266
- ASP0892
- ASP1807/CC8464

Phase 2

- enzalutamide (Breast cancer, HCC)
- AGS-16C3F (Renal cell carcinoma)
- blinatumomab (AMG 103) (Acute lymphoblastic leukemia, JP)
- YM311/FG-2216 (Renal anemia, EU)
- ASP8232 (Diabetic nephropathy)
- bleselumab (ASKP1240) (rFSGS)
- peficitinib (ASP015K) (Rheumatoid arthritis, US/EU)
- ASP7962 (Osteoarthritis)
- ASP8062 (Fibromyalgia)
- ASP0819 (Fibromyalgia)
- ASP1707 (Endometriosis, rheumatoid arthritis)
- ASP7373 (H5N1 influenza, JP)
- CK-2127107 (SMA, COPD)
- RPE cell program (Dry AMD etc.)

Phase 3

- enzalutamide (M0 CRPC, M0 BCR: US/EU/Asia, M1 HSPC, TNBC: US/EU/JP/Asia)
- degarelix (3-month, JP)
- gilteritinib (ASP2215) (AML, US/EU/JP/Asia)
- ASP8273 (NSCLC, US/EU/JP/Asia)
- solifenacin (Pediatric NDO, US/EU)
- solifenacin/mirabegron (Concomitant use, US/EU/Asia)
- mirabegron (Pediatric NDO, EU)
- roxadustat (ASP1517/FG-4592) (Anemia associated with CKD, EU/JP)
- ASP0113/VCL-CB01 (CMV-HCT, US/EU/JP)
- peficitinib (ASP015K) (Rheumatoid arthritis, JP/Asia)
- romosozumab (AMG 785) (Osteoporosis, JP)
- fidaxomicin (Infectious enteritis: JP, pediatric: EU)
- ipragliflozin/sitagliptin (Fixed dose combination, JP)
- ipragliflozin (Type 1 diabetes, JP)
- linaclotide (Chronic constipation, JP)

Filed

- enzalutamide (Tablet, EU/JP)
- quetiapine (BP-D, JP)
- ASP7374 (Seasonal influenza, JP)
- linaclotide (ASP0456) (IBS-C, JP)

THERAPEUTIC AREA:

- Oncology
- Urology, Nephrology
- Immunology, Neuroscience
- Others

● New molecular/biological entity

Outline of the projects are shown. Please refer to pipeline list for details including target disease.

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NSCLC: Non-small cell lung cancer, HCC: Hepatocellular carcinoma, CMV: Cytomegalovirus, SOT: Solid organ transplant, rFSGS: Recurrence of focal segmental glomerulosclerosis, PDPN: Painful diabetic peripheral neuropathy, SMA: Spinal muscular atrophy, COPD: Chronic obstructive pulmonary disease, AMD: Age-related macular degeneration, M0 CRPC: Non-metastatic castration-resistant prostate cancer, M0 BCR: Non-metastatic biochemical recurrence, M1 HSPC: Metastatic hormone sensitive prostate cancer, TNBC: Triple-negative breast cancer, AML: Acute myeloid leukemia, NDO: Neurogenic detrusor overactivity, CKD: Chronic kidney disease, HCT: Hematopoietic cell transplant, BP-D: Bipolar disorder depressive episodes, IBS-C: Irritable bowel syndrome with constipation

DEVELOPMENT PORTFOLIO HIGHLIGHTS

R&D meeting 2016

Bernie Zeiher, M.D.
President, Development
Astellas Pharma Inc.
December 8, 2016

AGENDA

I Establishing a Leadership Position in Oncology

II Potential for Gilteritinib in Acute Myeloid Leukemia (AML)

III Advancing Other Late-Stage Oncology Programs

IV Update on Other Late-Stage Programs

ESTABLISHING A LEADERSHIP POSITION IN ONCOLOGY

ESTABLISHING A LEADERSHIP POSITION IN ONCOLOGY

2007	2009	2010	2016
Agensys Acquisition	**Enzalutamide Licensure**	**OSI Pharmaceuticals Acquisition**	**Ganymed AG Pharmaceuticals Acquisition***
Added large-molecules and Antibody Drug Conjugates (ADCs) to development portfolio	Gained rights to a leading prostate cancer therapy, with potential applicability in other tumor types	Established expertise in lung cancer; added on-market infrastructure	Added novel pipeline of Ideal Monoclonal Antibodies (IMABs), including late-stage asset IMAB362

Established strategic collaborations with world-class research institutions,
such as Dana Farber Cancer Institute and MD Anderson Cancer Center, among others

*Transaction announced; completion pending

DEVELOPMENT STRATEGY IN ONCOLOGY

- Demonstrate impressive efficacy and safety in treatment-resistant populations and areas of highest unmet need
- Expand into earlier stages of disease and/or other tumor types if appropriate
- Utilize precision / targeted approaches if appropriate
- Consider combinations or immuno-oncology (I/O) approaches

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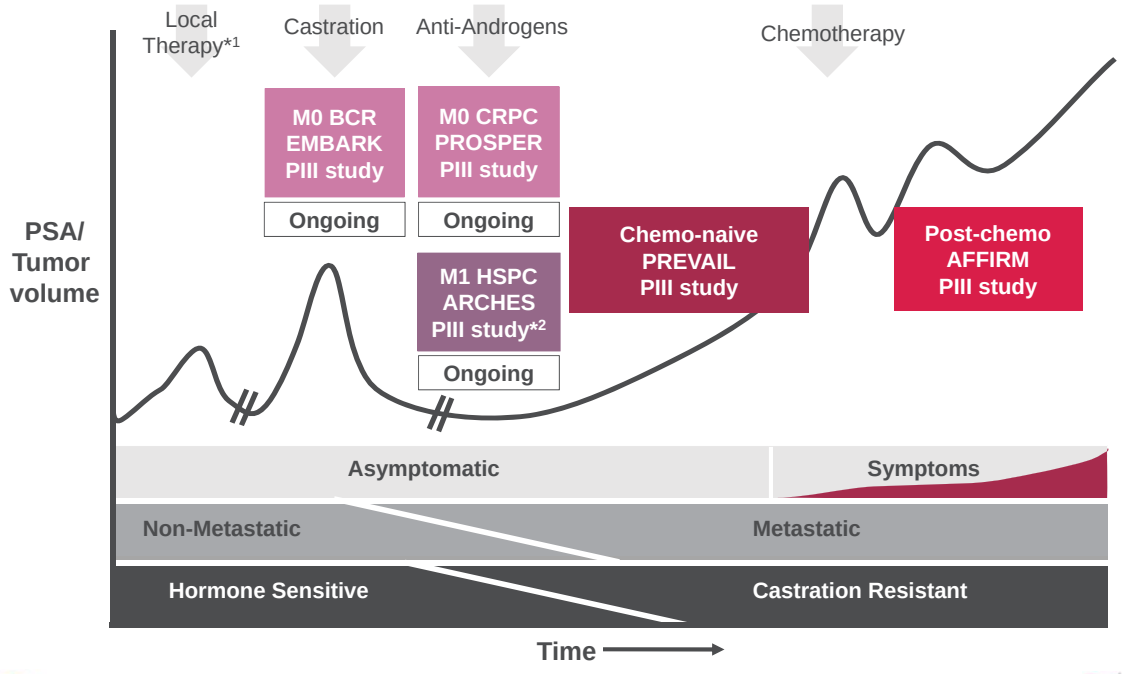
FULLY EXPLORING THE THERAPEUTIC POTENTIAL OF ENZALUTAMIDE IN PROSTATE CANCER



Pfizer

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Mulders *et al*., EAU2012; Modified by Astellas
*1 Radiotherapy, prostatectomy
*2 Metastatic at the time of diagnosis

PSA: Prostate-specifc antigen, M0 CRPC: Non-metastatic castration-resistant prostate cancer
M0 BCR: Non-metastatic biochemical recurrence prostate cancer,
M1 HSPC: Metastatic hormone sensitive prostate cancer

EVALUATING ENZALUTAMIDE IN OTHER SOLID TUMOR TYPES

Phase 3 Development Program: Triple Negative Breast Cancer
Precision medicine approach

Phase 2 Development Program: Breast Cancer sub-types
ER/PR+, AR+/Her-2+

Phase 2 Development Program: Hepatocellular Carcinoma

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ASTELLAS' ONCOLOGY PIPELINE

	Project	Target Cancer	Characteristics	P1	P2	P3	Filed
Small molecule	**enzalutamide**	Prostate cancer (M0 CRPC, M0 BCR, M1 HSPC), Breast cancer, Hepatocellular carcinoma	Androgen receptor inhibitor	PC, TNBC			
				BC, HCC			
	degarelix	Prostate cancer	GnRH antagonist	3-month: JP			
	gilteritinib	Acute myeloid leukemia, Non-small cell lung cancer	FLT3/AXL inhibitor	AML			
				NSCLC			
	ASP8273	Non-small cell lung cancer	Mutant-selective irreversible EGFR inhibitor				
	ASP5878	Solid tumors	FGFR inhibitor				
	ASP4132	Advanced cancer					
Antibody	**IMAB362***	Gastroesphageal adenocarcinoma	Ideal Monoclonal Antibody (target: CLDN18.2)				
	AGS-16C3F	Renal cell carcinoma	Antibody utilizing ADC (target: ENPP3)				
	blinatumomab	Acute lymphoblastic leukemia	Anti-CD19 BiTE				
	enfortumab vedotin (ASG-22ME)	Urothelial cancer Solid tumors	Antibody utilizing ADC (target: Nectin-4)				
	ASG-15ME	Urothelial cancer	Antibody utilizing ADC (target: SLITRK6)				
	AGS67E	Lymphoid malignancy	Antibody utilizing ADC (target: CD37)				
	AGS62P1	Acute myeloid leukemia	Antibody utilizing ADC (target: FLT3)				

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*Transaction announced; completion pending

ASTELLAS' ONCOLOGY PIPELINE

	Project	Target Cancer	Characteristics	P1	P2	P3	Filed
Small molecule	**enzalutamide**	Prostate cancer (M0 CRPC, M0 BCR, M1 HSPC), Breast cancer, Hepatocellular carcinoma	Androgen receptor inhibitor	PC, TNBC / BC, HCC			
Small molecule	**degarelix**	Prostate cancer	GnRH antagonist	3-month: JP			
Small molecule	**gilteritinib**	Acute myeloid leukemia, Non-small cell lung cancer	FLT3/AXL inhibitor	AML / NSCLC			
Small molecule	**ASP8273**	Non-small cell lung cancer	Mutant-selective irreversible EGFR inhibitor				
Small molecule	**ASP5878**	Solid tumors	FGFR inhibitor				
Small molecule	**ASP4132**	Advanced cancer					
Antibody	**IMAB362***	Gastroesphageal adenocarcinoma	Ideal Monoclonal Antibody (target: CLDN18.2)				
Antibody	**AGS-16C3F**	Renal cell carcinoma	Antibody utilizing ADC (target: ENPP3)				
Antibody	**blinatumomab**	Acute lymphoblastic leukemia	Anti-CD19 BiTE				
Antibody	**enfortumab vedotin (ASG-22ME)**	Urothelial cancer, Solid tumors,	Antibody utilizing ADC (target: Nectin-4)				
Antibody	**ASG-15ME**	Urothelial cancer	Antibody utilizing ADC (target: SLITRK6)				
Antibody	**AGS67E**	Lymphoid malignancy	Antibody utilizing ADC (target: CD37)				
Antibody	**AGS62P1**	Acute myeloid leukemia	Antibody utilizing ADC (target: FLT3)				

*Transaction announced; completion pending

POTENTIAL FOR GILTERITINIB IN AML

ACUTE MYELOID LEUKEMIA AND GILTERITINIB

Jessica K. Altman, M.D.
Director, Acute Leukemia Program
Robert H. Lurie Comprehensive Cancer Center
Associate Professor of Medicine
Feinberg School of Medicine, Northwestern University, Chicago, IL
December 8, 2016

AGENDA

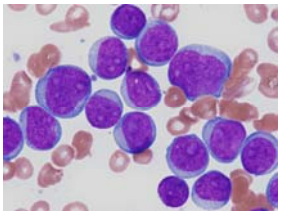
I Current treatment landscape in AML and unmet medical needs

II Characteristics of gilteritinib

III Expectation for gilteritinib as a clinical physician

CASE

- “Deb” (alias), 52-year-old female, presented to her primary care physician with a week of fever of 103° F, generally feeling unwell;
- Because of the persistent symptoms, a complete blood count (CBC) is drawn revealing white blood cells (WBC) of 196,000/uL, Hemoglobin (Hgb) of 5.7 g/dL, and platelet (PLT) count of 80,000/uL;
- She is instructed to go to the Emergency Room (ER) for urgent evaluation. At the ER, her exam is notable only for scattered bruises and mild gingival hyperplasia;
- She undergoes bone marrow evaluation and is diagnosed with AML with Normal karyotype (NK) and a FLT3 ITD



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ACUTE MYELOID LEUKEMIA (AML) INTRODUCTION

- Estimated new cases/deaths (US) 2016: 19,950/10,430
- ~25% will survive 5 years
- Median age: 67 years
- Heterogeneity in genetics, clinical manifestations, and outcome
- New targeted agents promising

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SEER data available at: http://seer.cancer.gov/statfacts/html/amyl.html

APPROACH TO NEWLY DIAGNOSED PATIENT

- History and physical (organomegaly, extramedullary disease)
- CBC with differential, chemistry panel including uric acid
- Smear review
- PT, PTT, fibrinogen (Disseminated intravascular coagulation (DIC) panel)
- Bone marrow aspirate and biopsy
  - Morphology and flow cytometry
  - Cytogenetics – prognosis, treatment, role of transplant
  - Molecular studies – prognosis, role of transplant, targeted treatment (had been restricted to trials but not for long)
- Risk assessment and transplant planning
- Discussion of fertility

TOWARDS A RECLASSIFICATION OF CYTOGENETIC (AND MOLECULAR) RISK GROUPS

Very favorable	t(15;17) with any abn
Favorable	inv(16) lacking c-KIT; t(8;21) lacking del(9q) or complex karyotype or c-KIT; Mutated NPM1 without FLT3-ITD (normal karyotype); Mutated CEBPα+ (double mutation) (normal karyotype)
Intermediate	Normal or +8 or +21 or others
Unfavorable	-5/del(5q), -7/del(7q), inv(3) or t(3;3), t(v;11)(v;q23), 17p, t(6;9), t(9;22), complex karyotypes with $\geq$ 3 abn; inv(16) or t(8;21) with c-KIT; normal karyotype with FLT3+; monosomal karyotype

Continued modification with the recognition of new prognostic markers

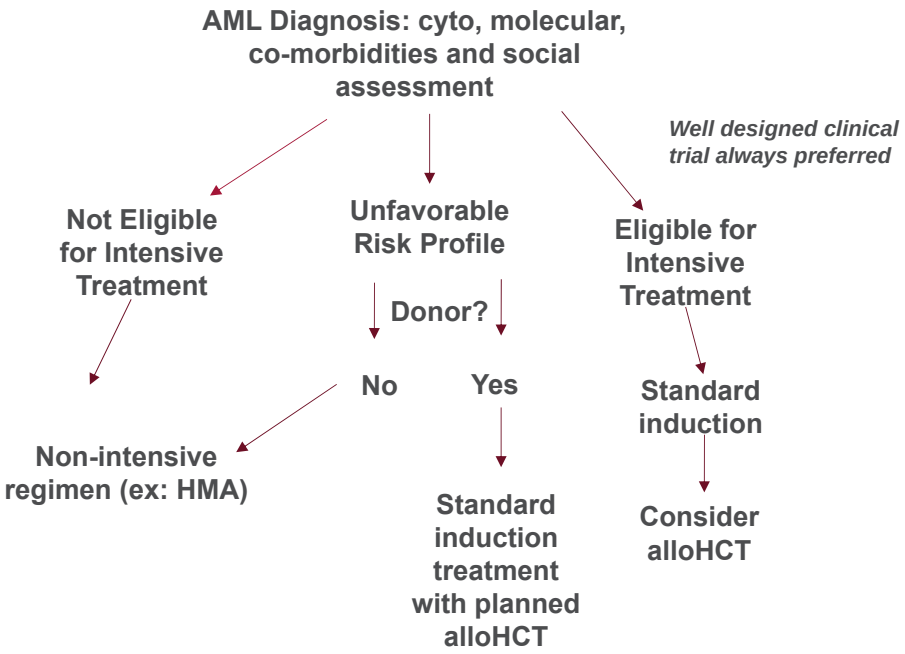
Adapted from Slovak Blood 2000 and Dohner Blood 2010

TREATING AML IN YOUNGER ADULTS

- Induction: dauno 90 mg/m^2/d x 3d (or ida) + ara-C 100 mg/m^2/d x 7d continuous infusion;
- Consol: multiple cycles (3-4) of HIDAC in younger pts fav-risk, NK *FLT3-/NPM1+, or biallelic CEBPα+;* 3-4 for CBF
- Allogeneic HCT for intermed- and high-risk (consider alternative donor if no sib); including *FLT3 ITD +*
- No maintenance
- Relapse: Re-induction chemo then allogeneic transplantation

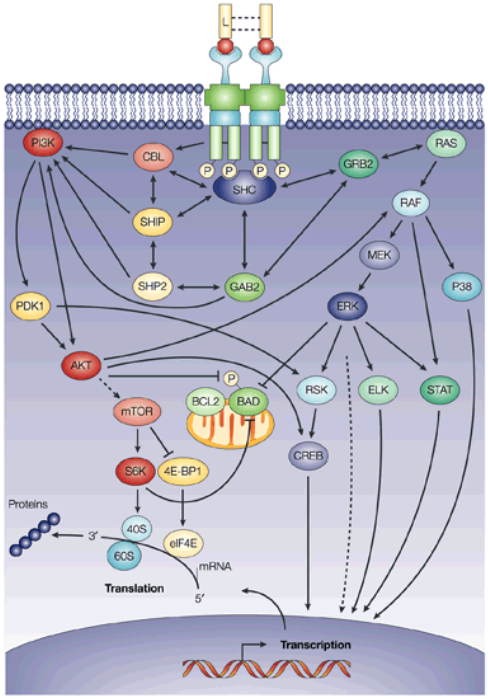
Paschka et al. J Clin Oncol, 2006; Schlenk et al. N Engl J Med, 2008; Green et al. J Clin Oncol, 2010; Dohner et al. Blood, 2010

A GENERAL APPROACH TO THE OLDER ADULT WITH AML



In part adapted from: Ossenkoppele and Löwenberg *Blood* 2015 125:767-774

FLT3 AS A TARGET IN AML



Stirewalt DL, et al. 2003;3:650-665

- Promotes proliferation and blocks differentiation
- Activating mutations present in ~30% of AML (ITD and activation loop)
- Patients with FLT3/ITD mutations have a worse prognosis – increased relapsed rate, lower OS
- Associated w leukocytosis and high percentage of bone marrow blasts, de-novo AML
- *FLT3* inhibitors in development; single agent and combination studies

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Kottaridis PD, et al. *Blood.* 2001;98(6):1752-1759;
Frohiling S, et al. *Blood.* 2002;100(13):4372-4380.

FLT3 INHIBITOR DEVELOPMENT

Table 1. Most frequently used FLT3 inhibitors

Name of the drug	*Kinase inhibitory profile*	*Disease under evaluation*	*Notes*
Sorafenib (Nexavar)	*CRAF* and *BRAF* *KIT, FLT3, VEGFR-2, VEGFR-3* and *PDGFR-ß* *RAF/MEK/ERK* pathway[47]	AML Hepatocellular carcinoma Renal cell carcinoma Thyroid carcinoma	Most of these kinases are involved in angiogenesis.
Quizartinib (AC220)	*FLT3/STK1* *CSF1R/FMS* *SCFR/KIT* *PDGFRs*	AML	It is the most potent *in vitro* FLT3 inhibitor.[16]
Midostaurin (PKC412)	*FLT3* *KIT, PDGF-Rß, VEGFR-2* *PKC*	AML MDS Aggressive systemic mastocytosis and mast cell leukemia[81]	Inhibits FLT3 at very low doses, generally in the nanomolar range.[48]
Lestaurtinib (CEP701)	*FLT3* *JAK2* *TRK A/TRK B/TRK C*	AML and MPN[82,83]	—
Crenolanib (CP868596)	*FLT3*-ITD *FLT3*-D835 *PDGFR-α* *PDGFR-β*	AML GIST Glioma	—
Gilteritinib (ASP2215)	*FLT3* *AXL* *ALK*	AML	—

Abbreviations: FLT3 = FMS-like tyrosine kinase 3; GIST = gastrointestinal stromal tumor; ITD = internal tandem duplications; MDS = myelodysplastic syndrome; MPN = myeloproliferative neoplasms.

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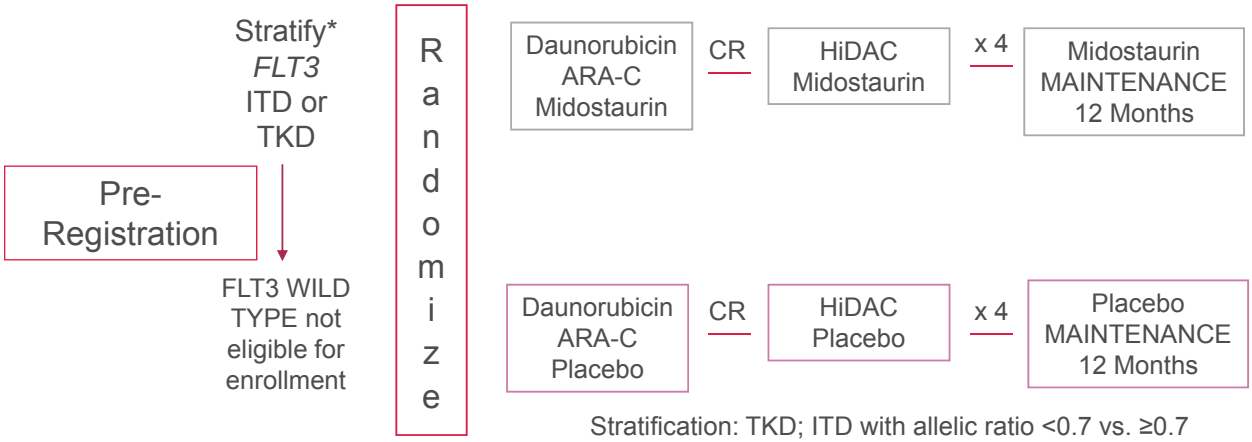
Antar A et al; Bone Marrow Transplantation (2016) 1-8.

PHASE 3 RATIFY TRIAL SCHEMA



Stratification: TKD; ITD with allelic ratio <0.7 vs. ≥0.7

Prospective Phase 3, double-blinded randomized study of induction and consolidation +/- midostaurin (PKC412) in newly diagnosed adults <60 years old with FLT3 mutated AML

Stone R, et al. 2015 ASH Annual Meeting and Exposition. Oral Abstract #6

RATIFY TRIAL RESULTS

- *FLT3* centrally (48 hr)
- CR by day 60 in midostaurin arm 59% vs. 53% in placebo arm (NS)
- Median OS: Midostaurin 74.7 months; placebo 25.6 mo (p = 0.0074)
- Midostaurin improves OS when added to standard chemotherapy with maintenance in newly diagnosed patients aged 18-60 years old with ITD and TKD *FLT3* mutant AML

Stone R, et al. 2015 ASH Annual Meeting and Exposition. Oral Abstract #6

"DEB'S" TREATMENT

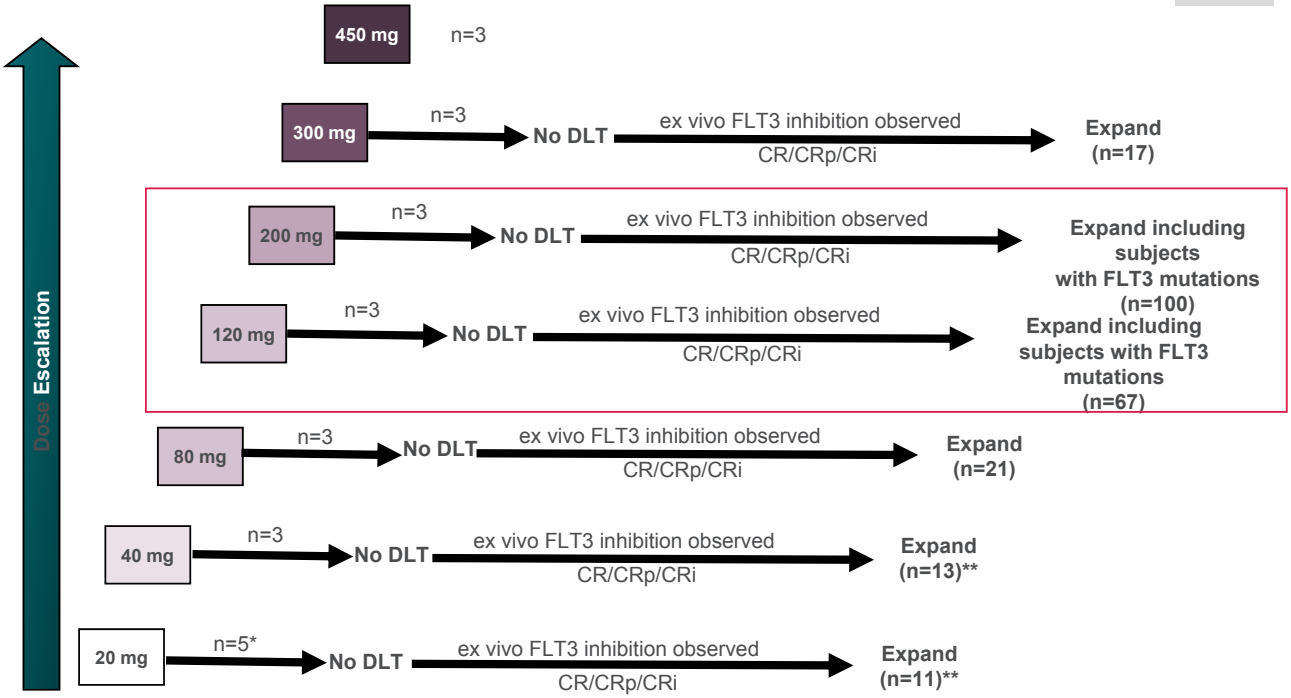
- Enrolled on C10603: *A Phase 3 Randomized, Double-Blind Study of Induction (Daunorubicin/Cytarabine) and Consolidation (High-Dose Cytarabine) Chemotherapy + Midostaurin (PKC412) or Placebo in Newly Diagnosed Patients < 60 Years of Age with FLT3 Mutated AML*
- Attained aplastic marrow at day 14 and then entered CR ~ day 28
- Matched sibling donor allogeneic stem cell transplant in CR1
- (Deb's disease recurred ~ day 100 and was treated off study w 5-aza and sorafenib)

GILTERITINIB: A HIGHLY SELECTIVE FLT3/AXL INHIBITOR

- **Activating mutations of *FLT3* occur in ~30% of AML cases[1]**
  - Internal tandem duplications (ITD) in the juxtamembrane domain confer a poor prognosis[1,2]
  - Point mutations (especially D835) in the tyrosine kinase domain induce resistance to FLT3 inhibitors[3]
- **Gilteritinib (ASP2215) is a highly potent, selective FLT3/AXL inhibitor that has demonstrated consistent and sustained inhibition of FLT3 in vitro[4-6]**
- **CHRYSALIS is a first-in-human, pharmacodynamic-driven, open-label Phase 1/2 trial (NCT02014558) of once-daily oral gilteritinib in relapsed/refractory (R/R) AML**
  - Adults with R/R AML irrespective of FLT3 mutation status were enrolled from 28 sites across the US and Europe
  - Primary end points were safety, tolerability, and pharmacokinetic profile
  - The key secondary end point was antileukemic activity; pharmacodynamic effects were an exploratory end point
  - Data locked June 2016

[1]Levis M. *Hematology Am Soc Hematol Educ Program.* 2013;2013:220-226; [2]Grunwald and Levis. *Int J Hematol.* 2013; 97(6):683-694. [3]Smith CC, et al. *Nature*. 2012; 485(7397):260-263. [4]Mori M, et al. *J Clin Oncol.* 2014;32(5s suppl): Abstract 7070. [5]Perl, A et al. *Haematologica.* 2015;100(Suppl 1); [6]Levis et al. *J Clin Oncol*. 2015;33(Suppl). AML, acute myeloid leukemia; FLT3, fms-like tyrosine kinase 3.

CHRYSALIS STUDY DESIGN AND COHORT ACCRUAL



* Three evaluable subjects
** Enrollment stopped early for low response rate

CR indicates complete remission; CRi, complete remission with incomplete hematologic recovery; CRp, complete remission with incomplete platelet recovery; DLT, dose limiting toxicity; FLT3, fms-like tyrosine kinase 3.

PATIENT DISPOSITION

All Enrolled Patients (N=265)

Patients continuing treatment* **31 (12%)**

- All patients continuing treatment harbored the FLT3-ITD mutation

Treatment discontinuations **234 (88%)**

Progressive disease	75 (28%)
Lack of response	44 (17%)
Death	29 (11%)
Adverse events	34 (13%)
Subject withdrawal	17 (6%)
Other	25 (9%)
Never received drug	8 (3%)
Lost to follow-up	2 (1%)

37 patients (14%) underwent transplantation

- 13 (5%) resumed treatment after transplant

***As of November 2015**

DEMOGRAPHICS AND BASELINE CHARACTERISTICS

	Safety Population (N=252)
Median age, years (range)	62 (21–90)
Sex, n (%)	
Male	129 (51)
Female	123 (49)
FLT3 Mutation*, n (%)	191 (76)
FLT3-ITD only	162 (64)
FLT3-ITD and FLT3-D835	16 (6)
FLT3-D835 only	13 (5)
Prior AML lines of therapy, n (%)	
1	75 (30)
2	66 (26)
≥3	111 (44)
Prior stem cell transplant, n (%)	
0	179 (71)
1	67 (27)
≥2	6 (2)
Prior TKI therapy†, n (%)	63 (25)

Safety population is defined as any subject who received at least one dose of study drug.
*3 patients had mutations other than only FLT3-ITD, both FLT3-1TD and FLT3-D835, and only FLT3-D835 mutations.
†Sorafenib was the most commonly used prior TKI (n=54).

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D835, missense mutation at aspartic acid residue 835; FLT3, fms-like tyrosine kinase 3; ITD, internal tandem duplication; TKI, tyrosine kinase inhibitor.

INCIDENCE OF ADVERSE EVENTS (SAFETY POPULATION; N=252)

Treatment-Emergent Adverse Events Occurring in ≥20% of Patients		
	All Grades, n (%)	Grade ≥3, n (%)
Anemia	86 (34)	62 (25)
Febrile neutropenia	98 (39)	98 (39)
Constipation	57 (23)	0
Diarrhea	92 (37)	13 (5)
Nausea	54 (21)	5 (2)
Fatigue	83 (33)	15 (6)
Peripheral edema	67 (27)	3 (1)
Pyrexia	65 (26)	13 (5)
Elevated AST	66 (26)	15 (6)
Cough	54 (21)	0
Dyspnea	59 (23)	12 (5)

AST, aspartate aminotransferase.

- Maximum tolerated dose of gilteritinib was 300 mg/day; 2 of 3 patients in the 450 mg/day dose escalation cohort experienced dose limiting toxicities (diarrhea and elevated AST)
- Most common treatment-related AEs: diarrhea, fatigue, elevated ALT and AST; most were generally <Grade 3
- Overall, 11 patients (4%) had a maximum post-baseline QTcF interval >500 ms
- Seven deaths were deemed possibly related to treatment (pulmonary embolism, respiratory failure, hemoptysis, intracranial bleed, ventricular fibrillation, septic shock, neutropenia; n=1 each)

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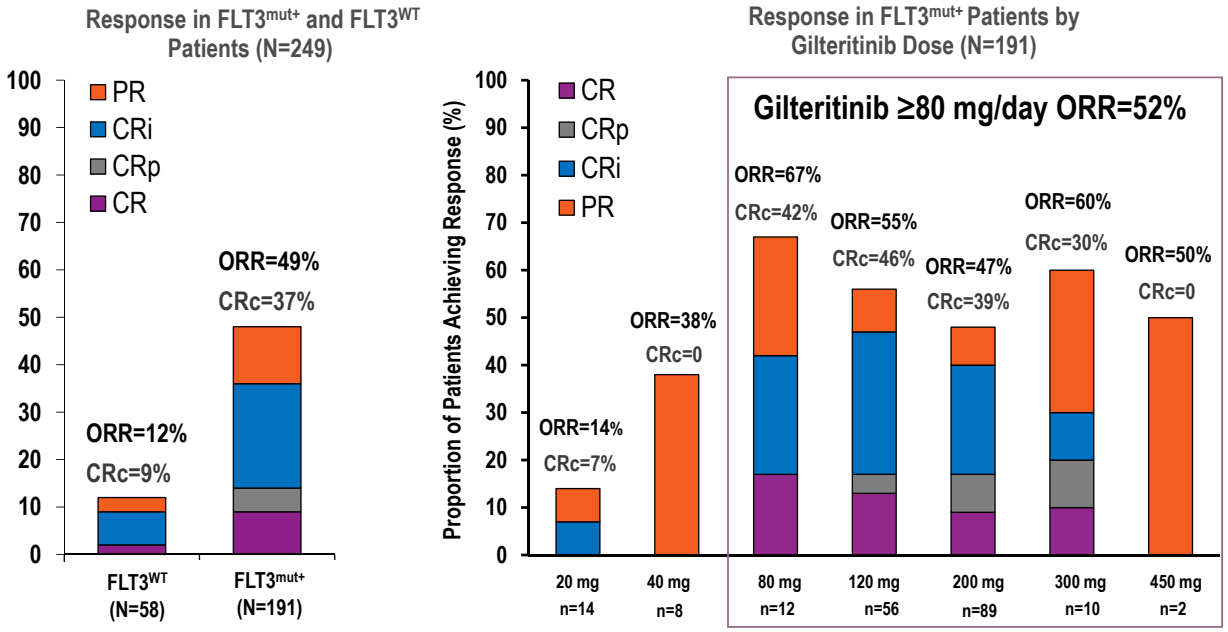
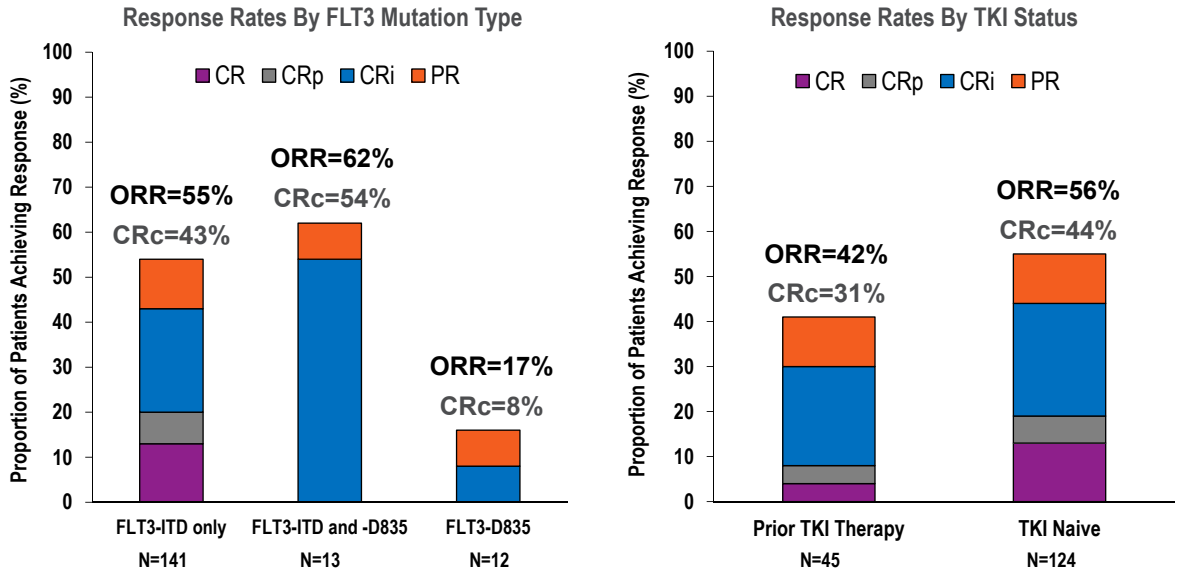
ANTILEUKEMIC ACTIVITY OF GILTERITINIB



CRc included patients who achieved complete remission, complete remission with incomplete hematologic recovery, and complete remission with incomplete platelet recovery
ORR included patients in CRc plus patients who achieved PR.

CR, complete remission; CRc, composite remission (CRc=CR+CRi+CRp;); CRi, complete remission with incomplete hematologic recovery; CRp, complete remission with incomplete platelet recovery; ORR, overall response rate (ORR=CRc+PR); PR, partial remission.

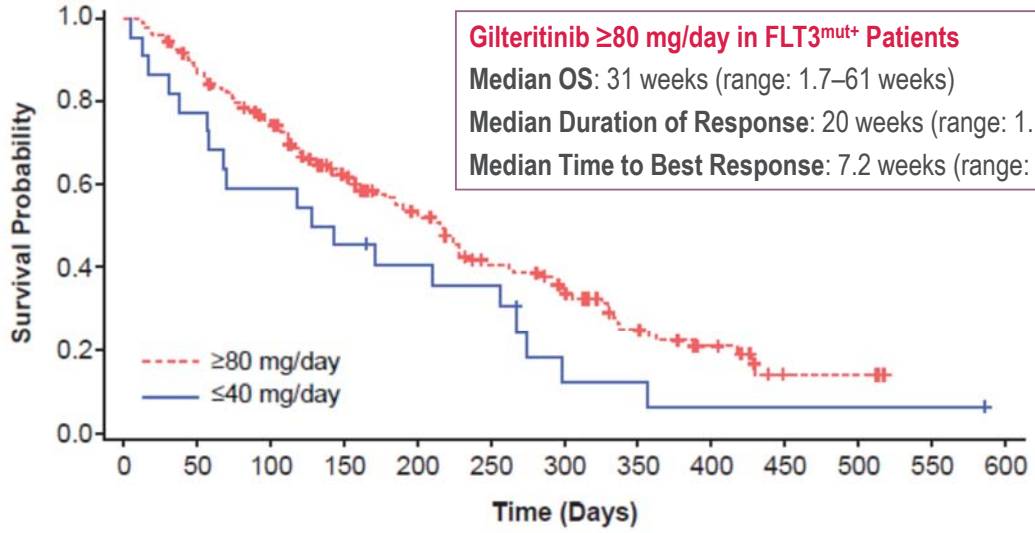
ANTILEUKEMIC RESPONSE TO ≥80 MG/DAY GILTERITINIB IN FLT3MUT+ PATIENTS BY MUTATION TYPE AND TKI STATUS



CRc included patients who achieved complete remission, complete remission with incomplete hematologic recovery, and complete remission with incomplete platelet recovery
ORR included patients in CRc plus patients who achieved PR.

CR, complete remission; CRc, composite remission (CRc=CR+CRi+CRp;); CRi, complete remission with incomplete hematologic recovery; CRp, complete remission with incomplete platelet recovery; ORR, overall response rate (ORR=CRc+PR); PR, partial remission.

OVERALL SURVIVAL IN FLT3^{MUT+} PATIENTS TREATED WITH GILTERITINIB (N=191)



Gilteritinib ≥80 mg/day in FLT3^{mut+} Patients

Median OS: 31 weeks (range: 1.7–61 weeks)

Median Duration of Response: 20 weeks (range: 1.1–55 weeks)

Median Time to Best Response: 7.2 weeks (range: 3.7– 52 weeks)

Subjects at risk

≤40 mg/day	22	17	13	10	8	7	2	2	1	1	1	1
≥80 mg/day	169	147	120	82	64	42	30	18	9	3	3	

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OS, overall survival.

CONCLUSIONS

- Gilteritinib was well tolerated across a wide range of doses and displayed a long half-life that was supportive of once-daily administration
- As a single agent, gilteritinib demonstrated strong antileukemic activity in heavily pretreated FLT3^{mut+} R/R AML patients regardless of prior TKI therapy
- Doses of 80 mg/day and higher were associated with more potent target inhibition, higher response rates, and longer survival
- Response rates were similar in patients harboring both FLT3-ITD and D835 mutations and in patients with FLT3-ITD mutations alone
- Higher response rates were observed among FLT3^{mut+} (49%) patients compared with FLT3 wild-type (12%) patients, suggesting FLT3 kinase selectivity of gilteritinib
- The Chrysalis study confirms that FLT3 is a high-value target in R/R AML
- An ongoing Phase 3 trial of gilteritinib in R/R AML (Admiral Study; NCT02421939) will further validate safety and antileukemic activity of gilteritinib

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DEVELOPMENT PORTFOLIO HIGHLIGHTS_CONTINUED

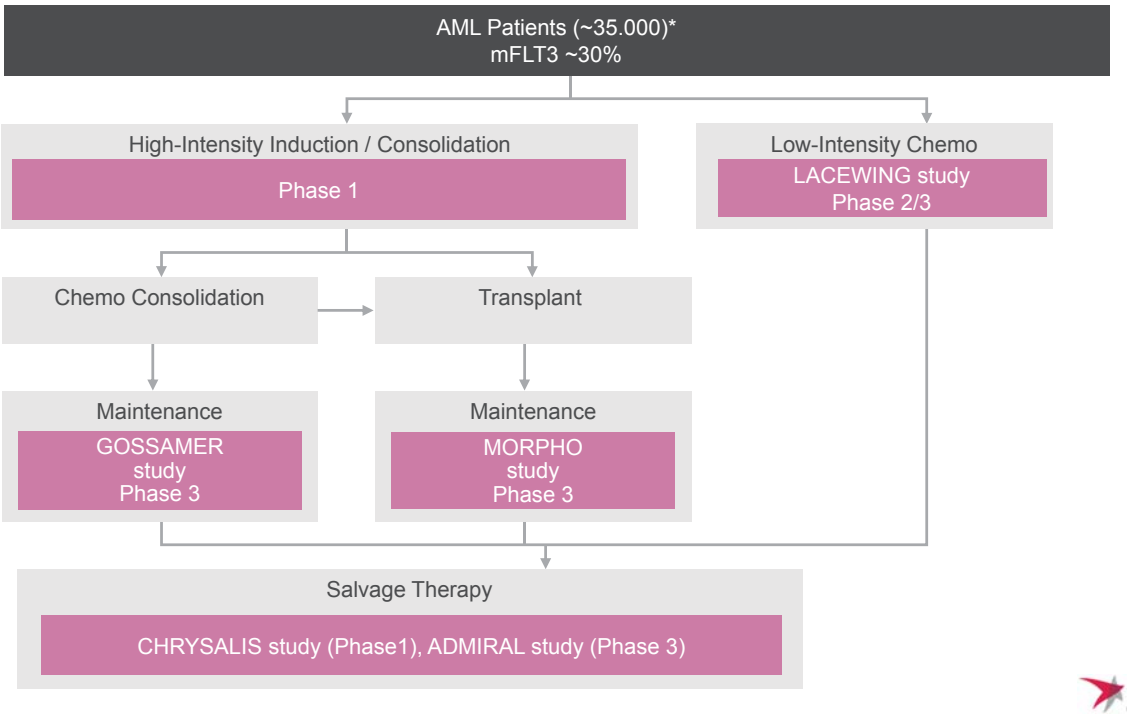
R&D meeting 2016

Bernie Zeiher, M.D.
President, Development
Astellas Pharma Inc.
December 8, 2016

POTENTIAL FOR GILTERITINIB

CONTINUED

GILTERITINIB: TREATMENT ALGORITHM AND DEVELOPMENT PROGRAM



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ADVANCING OTHER LATE-STAGE ONCOLOGY PROGRAMS

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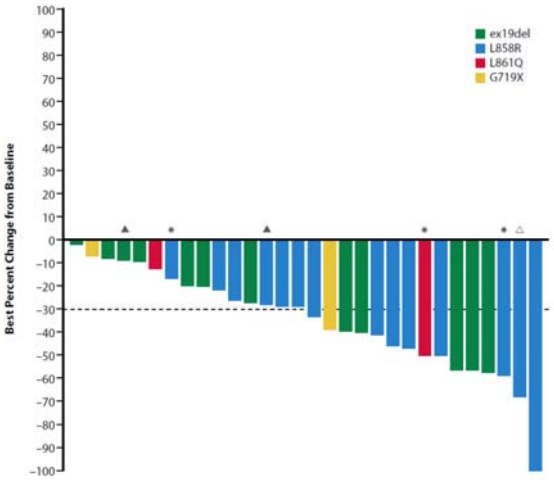
ASP8273: JAPANESE PHASE 2 DATA FOR NSCLC FIRST LINE TREATMENT PRESENTED AT 17TH WORLD CONFERENCE ON LUNG CANCER

Best percentage change from baseline in target-lesion size



Waterfall plot shows investigator-assessed tumour response. Thirty subjects had evaluable target lesion data.
*Denotes patients with de novo T790M mutation; △patient who experienced progressive disease; ▲patients who discontinued due to progressive disease.

Treatment-related adverse events occurring in >=15% of the ASP8273 300 mg population

	ASP8273 300 mg (N=31)				
Treatment-Related Adverse Events, n (%)[a]	Grade 1	Grade 2	Grade 3	Grade 4	Overall
Diarrhoea	14 (45)	5 (16)	2 (6)	0	21 (68)
Peripheral sensory neuropathy	11 (36)	1 (3)	0	0	12 (39)
Elevated ALT	6 (19)	3 (10)	2 (6)	0	11 (35)
Hyponatraemia[b]	3 (10)	–	6 (19)	1 (3)	10 (32)
Nausea	7 (23)	3 (10)	0	0	10 (32)
Dry mouth	6 (19)	2 (6)	0	0	8 (26)
Elevated AST	5 (16)	2 (6)	1 (3)	0	8 (26)
Decreased appetite	5 (16)	1 (3)	1 (3)	0	7 (23)
Dry skin	5 (16)	2 (6)	0	0	7 (23)
Stomatitis	5 (16)	1 (3)	0	0	6 (19)
Dysgeusia	3 (10)	2 (6)	0	0	5 (16)
Malaise	4 (13)	1 (3)	0	0	5 (16)
Rash	4 (13)	1 (3)	0	0	5 (16)
Vomiting	5 (16)	0	0	0	5 (16)

[a]TRAE occurring in ≥15% of subjects;
[b]No classification of Grade 2 hyponatremia within the NCI-CTCAE.
Date of data cut off: 23 February 2016.

Nishio *et al*., WCLC2016
NSCLC, Non-small cell lung cancer; ALT, alanine aminotransferase; AST, aspartate aminotransferase;
NCI-CTCAE, national cancer institute common terminology criteria for adverse events; TRAE, treatment-related adverse events.

ENFORTUMAB VEDOTIN (ASG-22ME): TARGET AND MECHANISM OF ACTION

Target

Nectin-4 is a type I transmembrane protein that belongs to the Nectin family of adhesion molecules

Normal tissue:

- Variable, mostly weak or moderate, expression was detected by IHC in transitional epithelium of bladder, skin (epidermis, sweat glands and hair follicles),salivary gland (ducts), esophagus, breast, and stomach

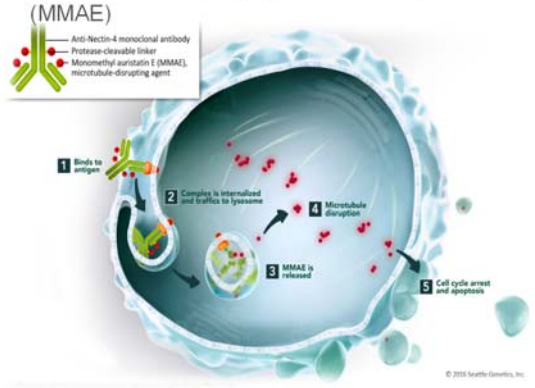
Malignant tissue:

- Highly expressed in bladder cancer with more moderate expression in breast, pancreatic, lung and ovarian cancer tissue microarrays (TMA)
- 83% (434/524) of bladder cancers on TMA were positive, 60% with strong or moderate staining

Antibody Drug Conjugate (ADC)

Enfortumab vedotin is an antibody drug conjugate (ADC) with the following components:

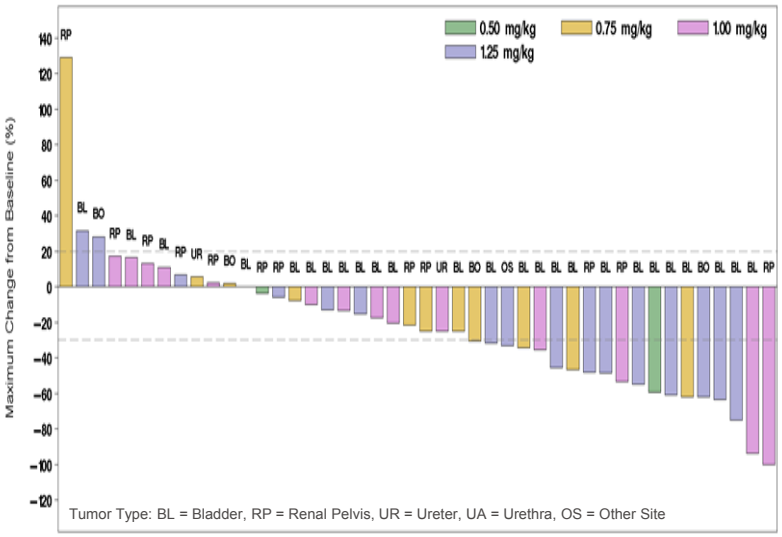
- Fully human monoclonal antibody IgG1k directed against Nectin-4
- Protease-cleavable linker
- Microtubule-disrupting agent monomethylauristatin-E (MMAE)



Morrison *et al*., Mol. Cancer Ther. 0570.215.epub. 2016.

ENFORTUMAB VEDOTIN: PHASE 1 IN METASTATIC UROTHELIAL CARCINOMA SUBJECTS

Waterfall Plot of Maximum Change from Baseline in Phase 1 Metastatic Urothelial Carcinoma Subjects



*Evaluable Subjects are defined as subjects having at least one post-baseline radiographic assessment; Response assessed per RECIST 1.1 Response rate includes unconfirmed response, study is enrolling.

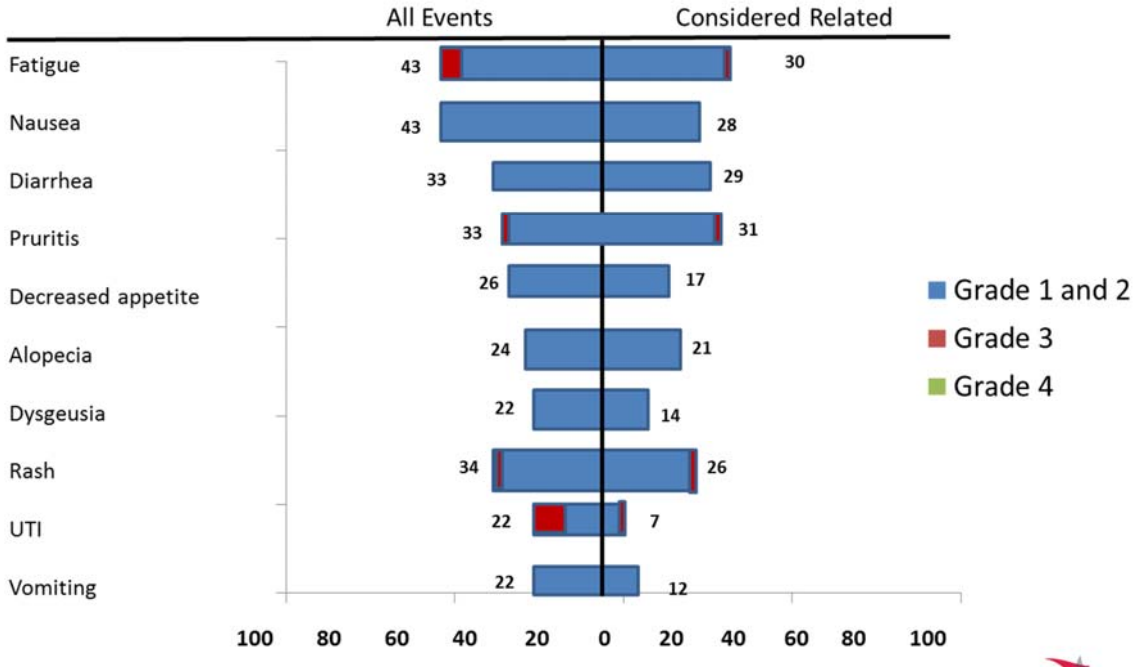
Overall Response in Evaluable Subjects* with mUC

Best Overall Response, N (%)	1.25 mg/kg (n=17)	Total (N=49)
ORR (CR+PR)	**10 (59)**	**18 (37)**
95% CI	32.9, 81.6	23.4, 51.7
DCR (CR+PR+SD)	14 (82)	37 (76)
95% CI	56.6, 96.2	61.1, 86.7
ORR Subcategories, N (%)		
Subject with liver metastasis	1/1 (100)	5/12 (42)
Prior taxanes	4/6 (67)	8/20 (40)
Prior CPI	**4/7 (57)**	**6/16 (38)**

Rosenberg *et al*., ESMO2016
CI: Confidence intervals, DCR: Disease Control Rate

ENFORTUMAB VEDOTIN: SAFETY DATA IN PHASE 1 STUDY

Treatment-Emergent Adverse Events (TEAE)* ≥ 20% N=58



*No events were Grade 4 in severity

Rosenberg *et al*., ESMO2016

ENFORTUMAB VEDOTIN: NEXT STEPS

Consult with regulatory agencies and pursue registrational-directed development plan in patients who have been exposed to check point inhibitor (CPI) therapy

Continue Phase 1 expansion cohorts in other Nectin 4 expressing solid tumors, including NSCLC and ovarian

GANYMED: LEVERAGING ACQUISITIONS TO ACQUIRE NEW PLATFORMS AND TARGET NEW TUMOR TYPES

Strategic acquisition*

Would expand oncology pipeline

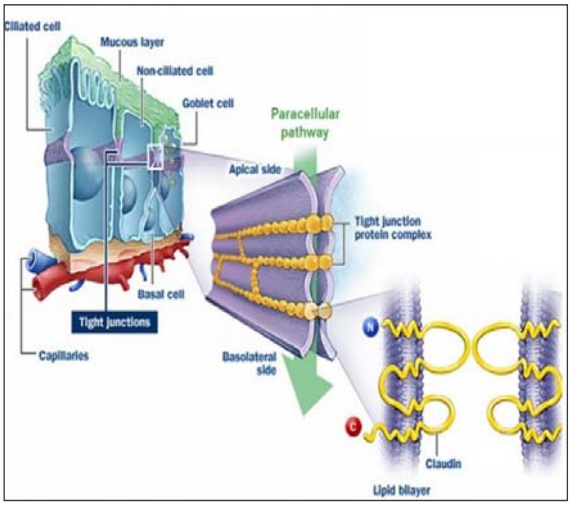
Includes IMAB362, the late-stage first-in-class antibody against CLDN18.2

Received orphan drug designation in the U.S. and EU for gastric and pancreatic cancers

*Transaction announced; completion pending

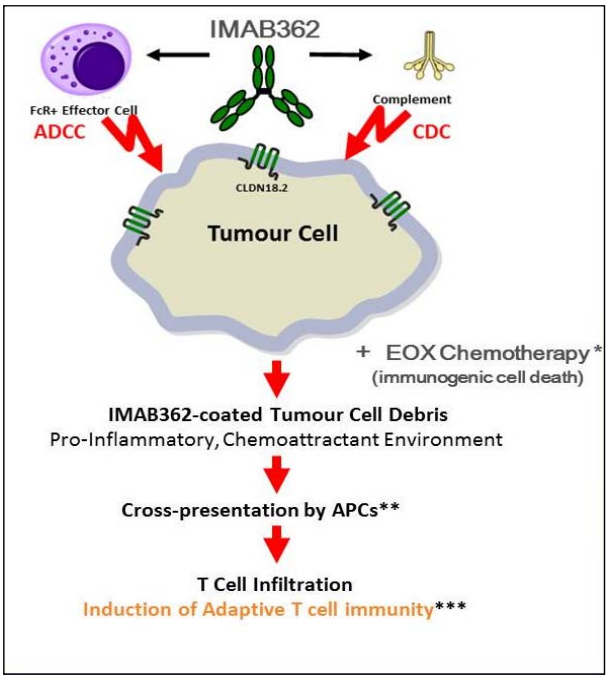
IMAB362: THE TARGET OF CLAUDIN18.2

- Member of the claudin family
- Major structural component of tight junctions
  - Seals intercellular space in epithelial sheets
- Broadly express in various cancer types
  - ~70-90% biliary duct, pancreatic, gastric and mucinous ovarian cancer
  - ~10% ovarian cancer and NSCLC
- Not expressed in any healthy tissues, except for stomach mucosa, with limited accessibility to the antibody



Al-Batran *et al*., ASCO2016

IMAB362: MECHANISM OF ACTION

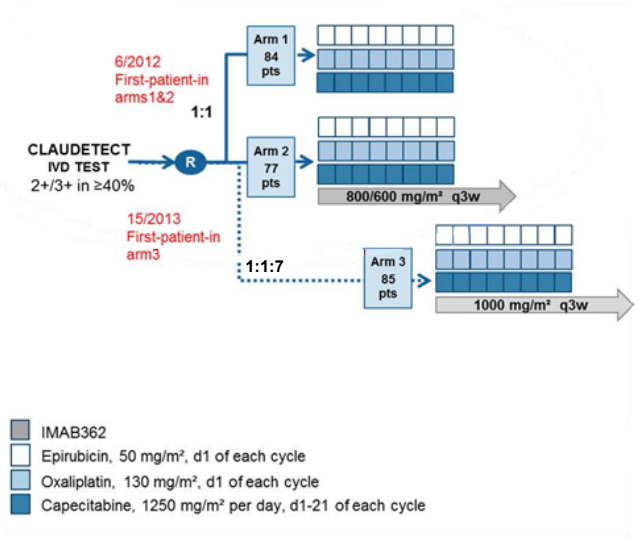


*Kroemer et al, 2013. EOX: Epirubicine, Oxaliplatin, Capecitabine;
**Rogers, Veeramani and Weiner, 2014;
***Biachini and Gianni, 2014

- Chimeric IgG1 backbone antibody
- Highly specific for Claudin18.2
- Modes of action:
  - Antibody-dependent cellular cytotoxicity (ADCC)
  - Complement-dependent cytotoxicity (CDC)
  - In combination with chemotherapy:
    - enhances T-cell infiltration
    - induces pro-inflammatory cytokines

Al-Batran *et al*., ASCO2016

IMAB362: DESIGN OF PHASE 2 FAST STUDY



Target patients

- Gastric, esophageal or the gastroesophageal junction adenocarcinoma
- CLDN18.2: 2+/3+ intensity in ≥ 40% tumor cells (centrally measured with analytically validated, CE marked IVD Kit)
- 1st line, no prior CTx for advanced disease
- Locally advanced or metastatic disease

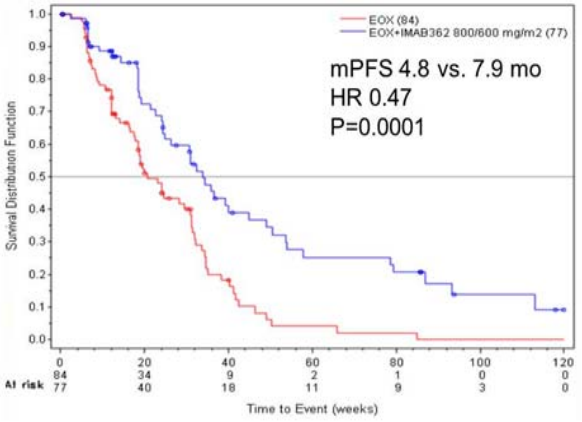
Design

- Randomized Phase 2 trial, open-label
- Arm 1, Arm 2 randomized 1:1
- Added exploratory Arm 3, started after 80% of arms 1&2 had been recruited, 1:1:7 randomization for catch up
- At randomization: Stratification according (i) CLDN18.2 positivity, (ii) measurability of disease
- Primary endpoint: Progression-free survival (PFS), Key secondary endpoint: Overall survival (OS)

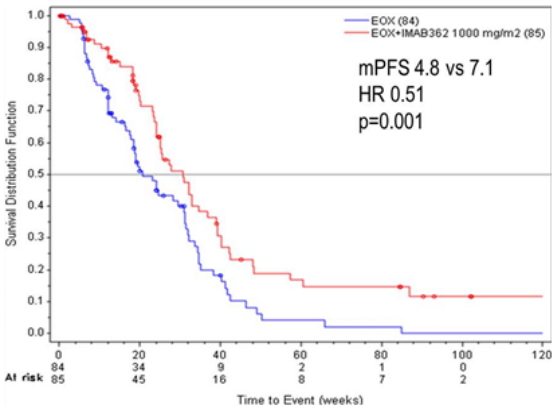
Al-Batran *et al*., ASCO2016

IMAB362: PFS IN FAST STUDY TOTAL POPULATION (2+/3+ CLDN18.2 STAINING IN ≥ 40% OF TUMOR CELLS)

PFS* (primary endpoint): Arm 2 vs. Arm 1



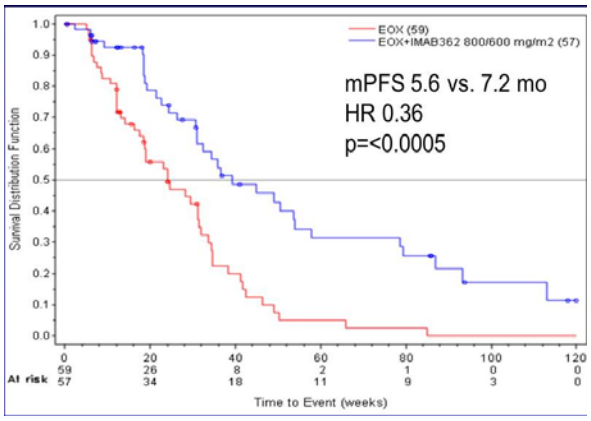
PFS (exploratory): Arm 3 vs. Arm 1



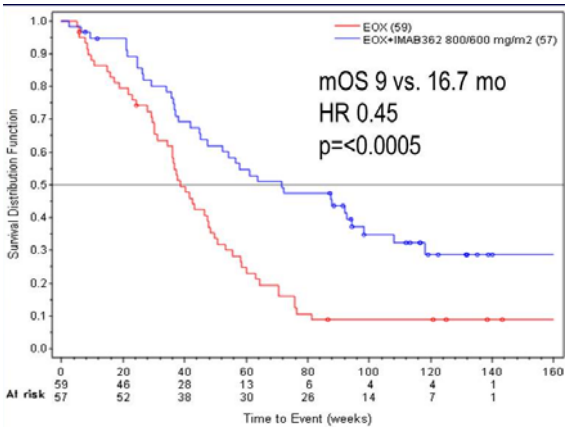
*Based on central imaging assessment in patients with 2+/3+ CLDN18.2 staining in ≥40% of tumor cells (total population);
Updated data presented by Al-Batran *et al*., ASCO2016

IMAB362: PFS AND OS IN PATIENTS WITH 2+/3+ CLDN18.2 STAINING IN ≥ 70% OF TUMOR CELLS (HIGH EXPRESSOR SUBGROUP) IN FAST STUDY

PFS



OS



Al-Batran *et al.*, ASCO2016

IMAB362: SELECTED ADVERSE EVENTS (NCI-CTC CRITERIA) IN FAST STUDY

Adverse Event/ treatment arm	EOX		EOX+IMAB362	
	G1/2	G3/4	G1/2	G3/4
Anemia	24 (28.6)	6 (7.1)	29 (37.7)	9 (11.7)
Leukopenia	10 (11.9)	5 (6)	8 (10.4)	6 (7.8)
Neutropenia	18 (21.4)	**18 (21.4)**	18 (23.4)	**25 (32.5)**
Thrombocytopenia	7 (8.3)	3 (3.6)	12 (15.6)	0
Diarrhea	29 (34.5)	3 (3.6)	12 (15.6(	3 (3.9)
Nausea	52 (61.9)	3 (3.6)	56 (72.7)	5 (6.5)
Vomiting	**29 (34.5)**	**3 (3.6)**	**43 (55.8)**	**8 (10.4)**
Asthenia	17 (20.2)	2 (2.4)	11 (14.3)	2 (2.6)
Fatigue	14 (16.7)	3 (3.6)	20 (26)	5 (6.5)
Infections	9 (10.7)	2 (2.4)	11 (14.3)	0

Al-Batran *et al.*, ASCO2016

UPCOMING ONCOLOGY CATALYSTS

FY2016-2017

IMAB362
- Closing of Ganymed acquisition*

Enzalutamide
- Readout of P2 ER/PR
- Readout of P2 Her2+

ASP8273
- Final results for P1/2

Gilteritinib
- FPI in GOSSAMER and MORPHO P3 Maintenance Trials

Enfortumab Vedotin
- Regulatory discussions
- Initiate study in CPI treated patients

FY2018-2020

Enzalutamide
- Data readout for PROSPER

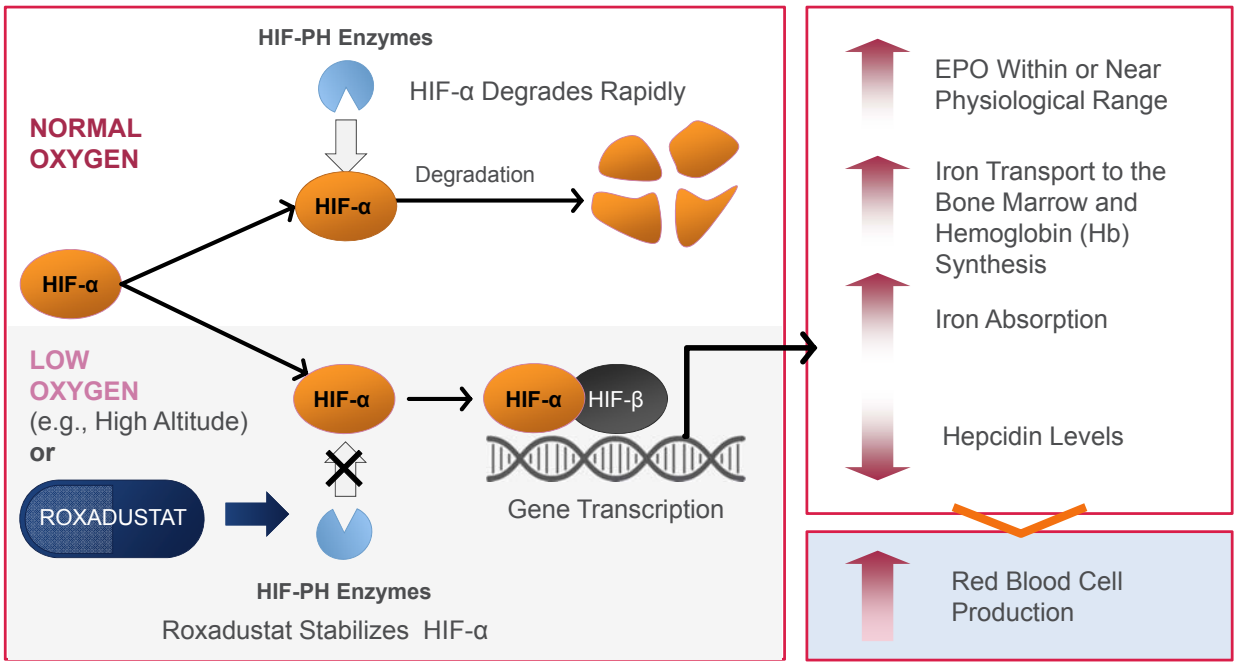
Gilteritinib
- Data readout for ADMIRAL

ASP8273
- Data readout of P3

Note: All dates are approximate. Timing to be based on study progress, event rates and interim analysis triggers
*Transaction announced; completion pending

UPDATE ON OTHER LATE-STAGE PROGRAMS

ROXADUSTAT: ACTIVATES A NATURAL PATHWAY TO INCREASE RED BLOOD CELL PRODUCTION



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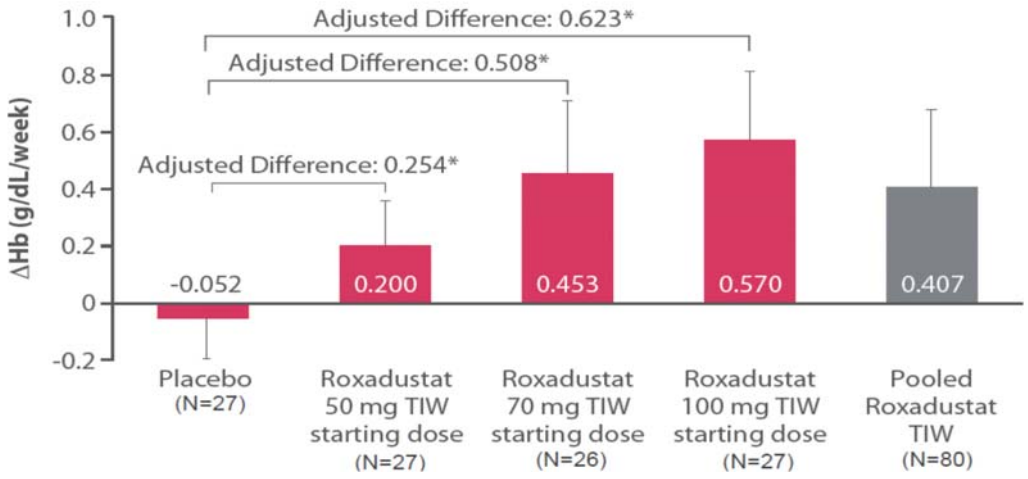
HIF-PH - hypoxia-inducible factor prolyl hydroxylase

ROXADUSTAT: RESULTS FROM NON-DIALYSIS PHASE 2 STUDY IN JAPAN

Primary endpoint Mean change in Hb from baseline during the fixed-dose period



*P<0.001. Rate of rise was calculated as the slope of a linear regression for each patient using all Hb data collected during the fixed-dose period.
Error bars represent standard deviation

Safety Roxadustat was well tolerated and had an adverse event profile similar to that observed in previous studies

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Akizawa *et al*., American Society of Nephrology Kidney Week2016
dL: deciliters, g: grams, Hb: hemoglobin, mg: milligrams, TIW: three times weekly

ROXADUSTAT: ROBUST PHASE 3 PROGRAM TO SUPPORT FILING AND REIMBURSEMENT IN EUROPE AND JAPAN

	Dialysis	Non-dialysis
Global	HIMALAYAS: FibroGen Incident dialysis, vs epoetin alfa	DOLOMITES, vs darbepoetin astellas
	SIERRAS: FibroGen Stable dialysis, vs epoetin alfa	ALPS, vs placebo astellas **Enrollment completed**
	PYRENEES: astellas Stable dialysis, vs epoetin alfa or darbepoetin **Enrollment completed**	ANDES, vs placebo FibroGen
Japan astellas	HD: Conversion, vs darbepoetin	Conversion, vs darbepoetin
	HD: Conversion, long-term **Enrollment completed**	
	HD: Correction	Correction
	PD	

For additional anemia indications

Phase 3 study to start for anemia in myelodysplastic syndromes (MDS)

✓ US FDA has approved an IND for anemia in MDS

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HD: Hemodialysis, PD: Peritoneal dialysis
Note: Company logo in the table shows the sponsor of studies

SOLIFENACIN/MIRABEGRON: OBTAINED TOP LINE RESULTS FROM PHASE 3 STUDY SYNERGY 2

Phase 3 program

BESIDE

- Achieved primary endpoints, demonstrating that solifenacin with mirabegron as add-on therapy was superior to solifenacin monotherapy

SYNERGY

- Did not meet one of primary endpoints (p=0.052), but improvements for a number of efficacy endpoints indicative of additive effects.

SYNERGY 2

- Double-blind, active-controlled (vs monotherapies), long term study (n=1,829)

Safety in SYNERGY 2

- All treatments were well tolerated.
- The safety profile was as expected based on that of the monotherapies with the frequency of TEAEs (one of the primary endpoints) in the combination group somewhat higher compared to the S5 mg and M50 mg groups.

Efficacy in SYNERGY 2

- Combination S5+M50 mg was statistically significantly superior to the M50 mg and S5 mg groups for the primary efficacy endpoints (change in incontinence episodes and change in micturitions per 24 hours).
- Efficacy was maintained during the 1-year treatment period for all primary and key secondary efficacy endpoints.

Plan to discuss next steps with health authorities based on results from Phase 3 studies

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S5+M50 mg: solifenacin 5 mg + mirabegron 50 mg, S5 mg: solifenacin 5 mg, M50 mg: mirabegron 50 mg TEAEs: treatment emergent adverse events

UPDATES FOR LATE STAGE PROJECTS

ASP0113

ASP0113

- Target: Cytomegalovirus (CMV) reactivation in hematopoietic cell transplant recipients
- Designed to elicit both T-cell and antibody immune responses against CMV

Progress

- **Phase 3 study enrollment completed**
- Top line results are expected in FY2017

Romosozumab

Romosozumab

- Target; Osteoporosis
- Romosozumab is studied for its potential to increase BMD, improve bone structure and strength and reduce the risk of fractures.

Progress

- **We plan to file in Japan later this month.**

Other P2/P3 programs

Immunology

- Peficitinib (ASP015K): Phase 3 for rheumatoid arthritis ongoing in Japan
- Bleselumab (ASKP1240): Initiated Phase 2 with Kyowa Hakko Kirin for recurrence of focal segmental glomerulosclerosis in de novo kidney transplant recipients

Neuroscience

- ASP7962 for osteoarthritis
- ASP8062 and ASP0819 for fibromyalgia

OUR CONTINUED EFFORT

Turn innovative science into value for patients by

characterizing the therapeutic potential of our products.

APPENDIX

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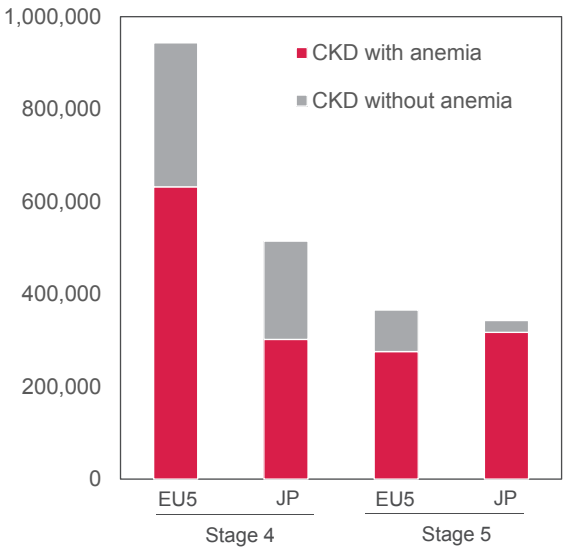
ROXADUSTAT: ANEMIA IN CHRONIC KIDNEY DISEASE

Relevance of anemia of CKD

- Hb decrease = capacity for oxygen transport to tissue decrease
- Negative impact on physical functioning, performance and well-being, including weakness, fatigue, poor concentration, dizziness and dyspnea
- Stage 4 & 5 CKD patients typically managed by nephrologists to correct and manage anemia
- Currently available anemia of CKD treatment requires oral/intravenous iron, erythropoiesis stimulating agents (ESAs) with or without iron, and RBC transfusion depending on the severity of the anemia

Patient numbers*



FIBROGEN

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*Patient number in 2015

MARKETING STRATEGY IN ONCOLOGY THERAPEUTIC AREA

R&D MEETING 2016

Peter Sandor M.D., MBA
Vice President
Head of Oncology Therapeutic Area,
Marketing Strategy
December 8, 2016

AGENDA

I Oncology marketing strategy and capabilities

II Potential patient impact in priority cancer types

ADVANCING SCIENCE TO TRANSFORM LIVES OF CANCER PATIENTS

Mission

We dedicate our collective strengths to develop and deliver paradigm changing treatment options for cancer patients globally

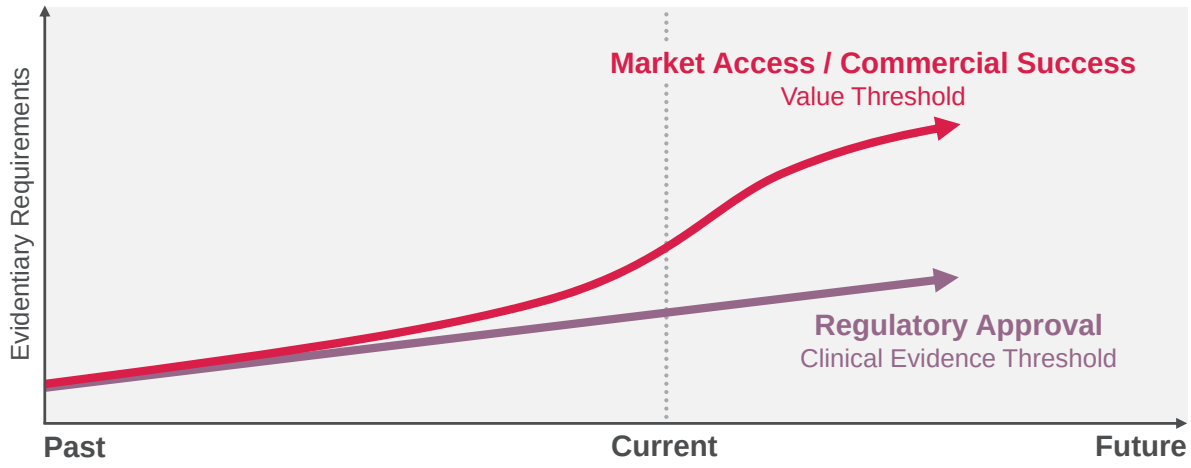
Strategy

- Drive organic innovation and capture external opportunities
- Deep understanding of customer needs
- Define value based strategy and clear differentiation
- Build Global Marketing excellence
- Develop strong launch capabilities

THERE IS AN INCREASING GAP BETWEEN REGULATORY APPROVAL VS. COMMERCIAL SUCCESS

New Product Evidentiary Requirements

Illustrative



To secure market access and reimbursement, new products must prove they deliver value to all key stakeholders in the Healthcare System

ONCOLOGY MARKETING - KEY HIGHLIGHTS AND PRIORITIES

Drive Growth

Execute XTANDI strategy

- Earlier M1 CRPC use
- Strong case for value
- New indications in PC

Business Development

- Integration of Ganymed
- Continue to amend pipeline

Progress Pipeline

Launch preparation

- Enzalutamide BC
- Gilteritinib in r/r AML
- ASP8273 in NSCLC
- Enfortumab vedotin in Bladder cancer

Select and progress the most differentiated assets

- Strong scientific evidence and value proposition
- Well defined Life Cycle Plan

Commercial Excellence

- Global launch excellence
- One global voice – strengthen marketing capabilities and center of excellence
- Early value and access decisions – established global function
- Start with the patient - understand and focus on their needs

PC: Prostate cancer, BC: Breast cancer, M1 CRPC: Metastatic castration-resistant prostate cancer,
r/r AML: Relapsed or refractory acute myeloid leukemia, NSCLC: Non-small cell lung cancer

SELECTED ONCOLOGY PIPELINE OPPORTUNITIES

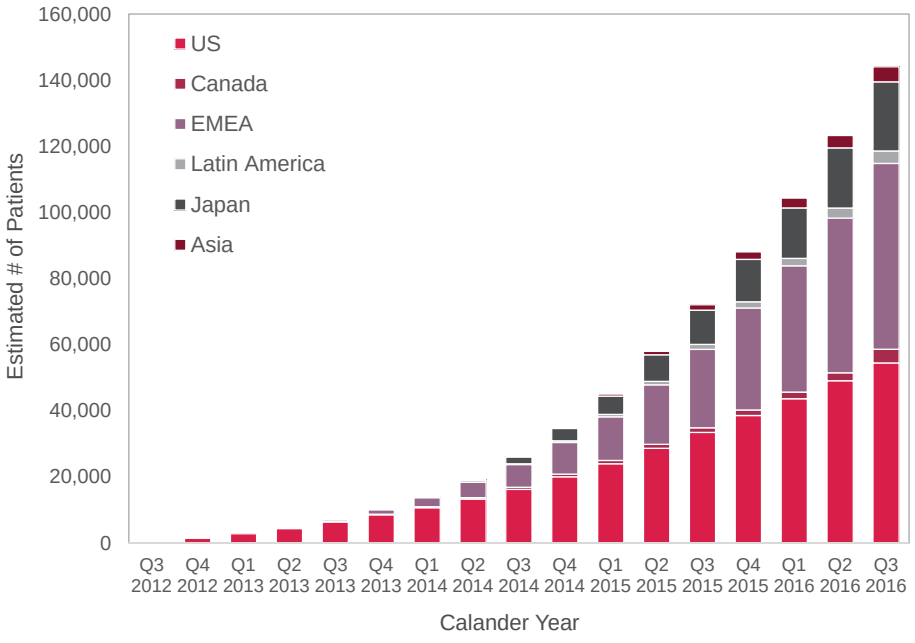
	Project	Patient Population	Dev Phase	Patient Number
Small molecule	**Enzalutamide**	Prostate cancer (M0 CRPC, M0 BCR, M1 HSPC), Breast cancer, Hepatocellular carcinoma	Phase 3 Phase 2	● ● ●
	Gilteritinib	Acute myeloid leukemia, Non-small cell lung cancer	Phase 3 Phase 2	● ● ○
	ASP8273	Non-small cell lung cancer	Phase 3	● ● ●
Antibody	**IMAB362***	Gastroesophageal adenocarcinoma	Phase 2	● ● ●
	Enfortumab vedotin (ASG-22ME)	Urothelial cancer, Solid tumors	Phase 1	● ● ○
	ASG-15ME	Urothelial cancer	Phase 1	● ● ○

● ● ● > 50.000 Patients ● ● ○ 20.000 - 50.000 Patients ● ○ ○ < 20.000 Patients

*Transaction of Ganymed announced; completion pending
M0 CRPC: Non-metastatic castration-resistant prostate cancer, M0 BCR: Non-metastatic biochemical recurrence,
M1 HSPC: Metastatic hormone sensitive prostate cancer

XTANDI: MORE THAN 140,000 PATIENTS HAVE BEEN TREATED WITH XTANDI SINCE IT'S LAUNCH IN SEPT. 2012

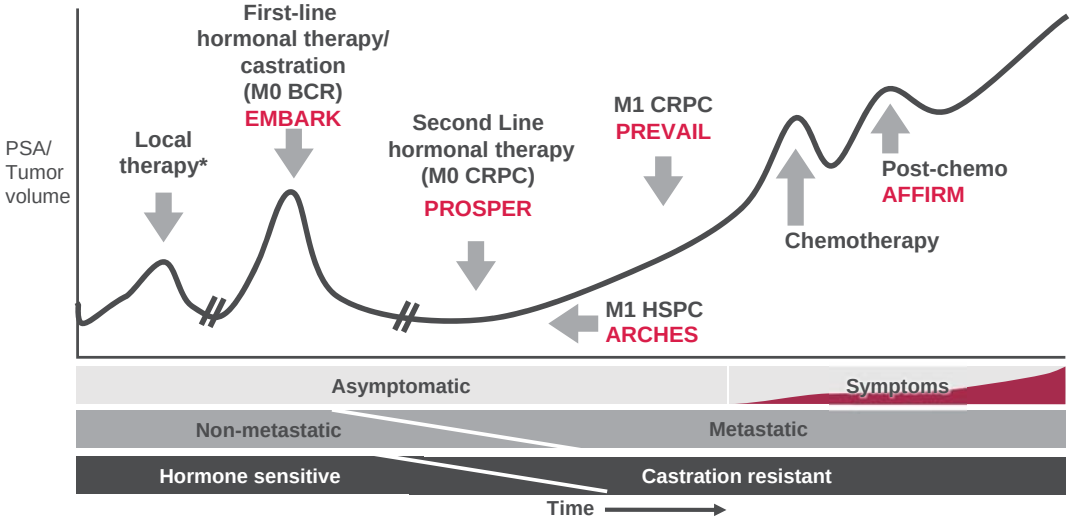
XTANDI: Cumulative Patients Treated Since Launch



- Launched in 65 countries
- Strong Y-o-Y growth
- Strengthening market position
- #1 prescribed novel hormone therapy in uro-oncology

Assumes 8 month avg. duration on therapy
Source: Internal sales volumes

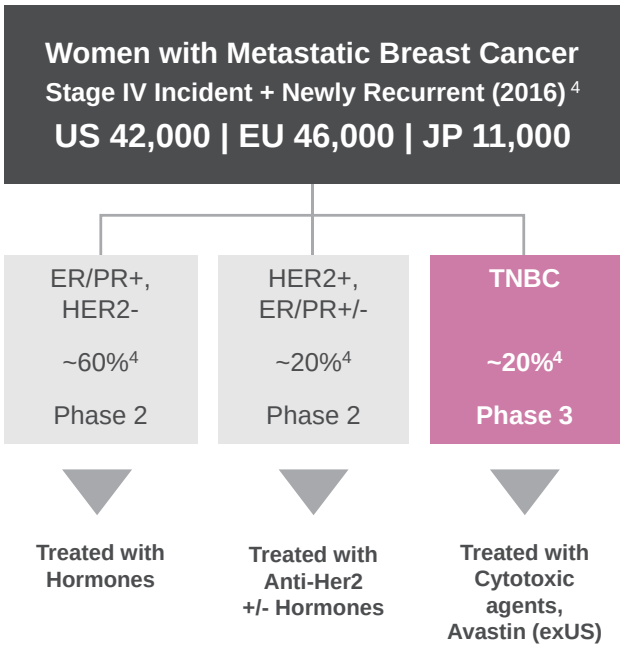
ENZALUTAMIDE: ~575,000 PROSTATE CANCER PATIENTS DIAGNOSED THROUGH THE DISEASE CONTINUUM IN THE G7 MARKETS IN 2015



Treating Physicians

*For example, surgery and radiotherapy.
Source: Kohli M, Tindall DJ. Mayo Clin Proc. 2010;85:77-86; CancerMPact; Epiphany; CancerImpact 2015
G7: U.S., EU5 and Japan.

ENZALUTAMIDE: THE CURRENT DEVELOPMENT PROGRAM IS INVESTIGATING ENZALUTAMIDE IN 3 BIOLOGICAL BREAST CANCER SUBTYPES

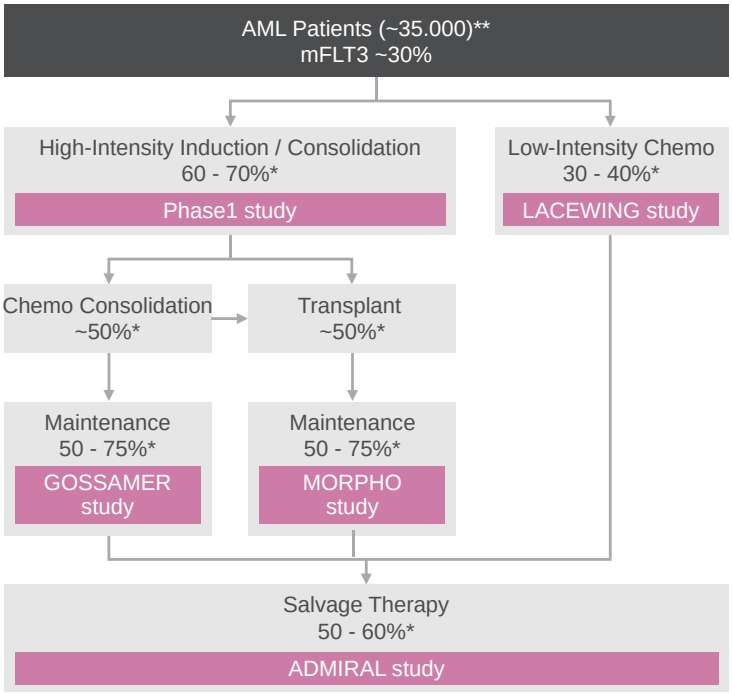


TRIPLE NEGATIVE BREAST CANCER

- Worst prognosis of all Breast Cancer biologic subtypes[2]
- Patients diagnosed with TNBC tend to be younger (median age 55-years vs 61 years)[1,3]
- ~ 50% of patients test positive to our proprietary diagnostics, which may correlate with enzalutamide responsiveness
- New drugs (PARPS and PD-1s) may enter the market, but expected to demonstrate a benefit in a portion of patients and will leave considerable unmet need

Source:1. Ovcaricek et al., Radiol Oncol. 2011, 2. Schnitt, Mod. Pathol. 2010, 3. Collins et al, Mod. Pathol. 2011 4. Denotes the % this subtype represents of the total breast cancer population. Kantar CancerMPact, 2016
ER: Estrogen receptor, PR: Progesterone receptor, HER2: Human epidermal growth factor receptor 2, TNBC: Triple-negative breast cancer

GILTERITINIB: DEVELOPMENT SEEKS TO ADDRESS KEY PATIENT NEEDS ACROSS FLT3^{MUT} AML

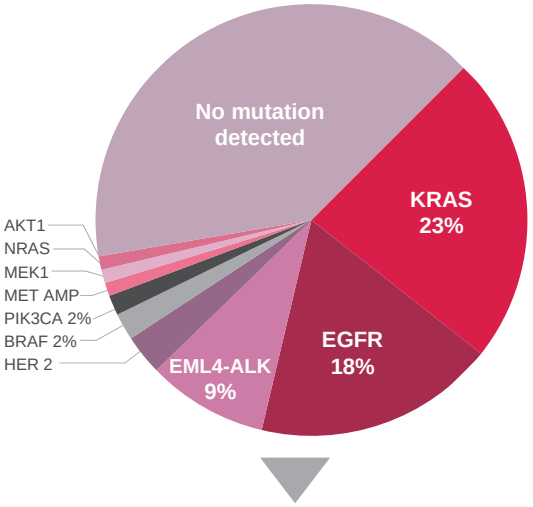


CRITICAL UNMET NEED ADDRESSED BY THE BROAD DEVELOPMENT PROGRAM

- First launch in r/r AML
- Extend indication step by step into earlier lines of treatment
- Create value for FLT3 AML patients

*Source: 2016 ClearView Market Research, 2016 ZS Market Research; **Incidence in U.S., EU5, JP, Cancer Impact 2015
FLT3: FMS-like tyrosine kinase 3, r/r AML: Relapsed or refractory acute myeloid leukemia

ASP8273: EGFR MUTATIONS ARE FREQUENTLY FOUND IN NON-SMALL CELL LUNG CANCER (NSCLC)



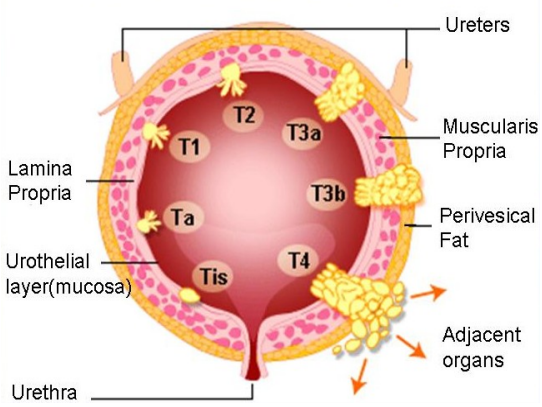
Annual Incidence, EGFRm+[3]	US	44,400
	EU5	42,900
	Japan	22,700

- Most commonly diagnosed cancer worldwide[1]
- Accounted for 13% of the global cancer burden with an estimated 1.59 million lung cancer deaths in 2012[1]
- Frequency of the EGFR mutations is 10-20% in Caucasians and 30-40% of East Asian NSCLC cases[2]
- T790M mutations are the primary resistance mechanism for 50%-60% of patients progressing on EGFR TKI's (erlotinib, gefitinib, afatinib)[2]
- EGFR T790M mutations are found in ~5% of TKI-naïve NSCLC[2]
- EGFR TKIs remain the preferred treatment of 1st and 2nd lineT790M patients after the launch of PD1/PDL1

Source: 1. UpToDate, MedScape, Ferlay et al., 2014; Robert Koch Institute, 2014; United Nations Population Division, 2013;
2. Midha A. Am J Cancer Res. 2015;5:2892-911, Cancer Genome Atlas Research Network. Nature. 20120;489:519-25, 3. Kantar Cancer Impact 2015
EGFR: Epidermal growth factor receptor

ENFORTUMAB VEDOTIN: UROTHELIAL CANCER IS THE FIFTH MOST COMMON TUMOR TYPE

Bladder Cancer Overview



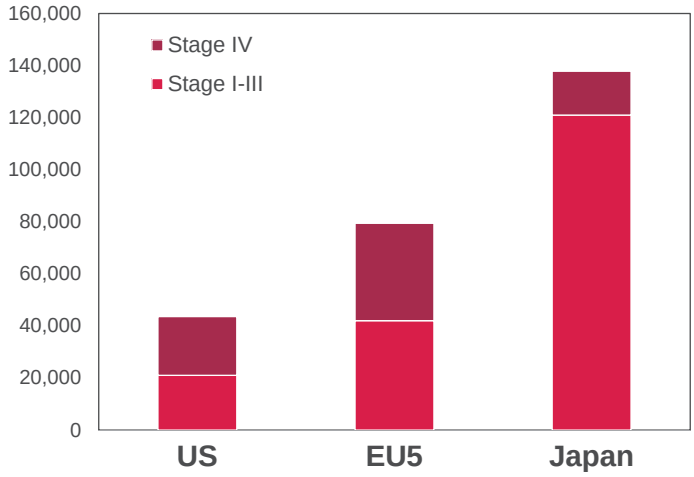
- Low-grade disease (Ta, Tis, T1) is localized to the urothelium and has not invaded the surrounding muscle
- Intermediate-grade disease (T2, T3a) has invaded the muscle layer of the bladder
- High-grade disease (T3b, T4) has invaded beyond the muscular wall

- Urothelial cancer consists primarily bladder cancer, but also ureter and renal pelvis carcinoma[1]
- Approximately 222.000 new patients are diagnosed annually (US, EU5, JP)[2]
- Patients with early stage disease treated with curative intent, however the recurrence rate is <50%[2]
- Median survival in treated metastatic patients is ~15 months[1]
- Frontline standard of care for metastatic disease is chemotherapy
- PDL-1 and PD-1 inhibitors are emerging as therapeutic options in urothelial cancer, but many patient fail to respond and are in need of improved therapies
- Prescriber group is highly synergistic with our current sales force coverage

Source: 1. SEER; UpToDate; National Cancer Institute; , 2. Kantar Cancer Impact 2016

IMAB362: GASTRO ESOPHAGEAL ADENOCARCINOMA REPRESENTS LARGE UNMET NEED WORLDWIDE

Patient Number[1]



Rank among cancers[1]	16th	12th	1st

- One of the leading causes of cancer death[1]
- Higher incidence in Asia[1]
- First line treatment is combination chemotherapy, or Herceptin (~20% HER2 positive)[2,3]
- 10-14 months median OS for Stage IV gastric cancer[2,3]
- Large unmet need remains
- ~50% of the patients is CLDN18.2 positive[4]

Sources: 1. Incidence, Kantar Cancer Impact 2016, 2. Cunningham at al, NEJM, 2008; 3. Van Cutsem et al, Lancet, 2010, 4. Al-Batran et al, ASCO 2016
CLDN: Claudin

OUR JOURNEY

Turn innovative science into value for patients by

delivering paradigm changing treatment options.

STRATEGY FOR CREATING INNOVATION
R&D MEETING 2016

Kenji Yasukawa Ph.D.
Senior Corporate Executive
Senior Vice President & Chief Strategy Officer
Astellas Pharma Inc.
December 8, 2016

PURPOSE OF DRUG DISCOVERY RESEARCH

Turn innovative science into value for patients by

addressing unmet needs.

OPPORTUNITIES TO PURSUE & NEW STRATEGIES FOR DRUG DISCOVERY RESEARCH

Opportunities to pursue

- Innovative drug discovery in TAs with high UMNs
- New modalities such as cell therapies, gene therapies, etc.
- Increasing number of technologies with applicability in various fields

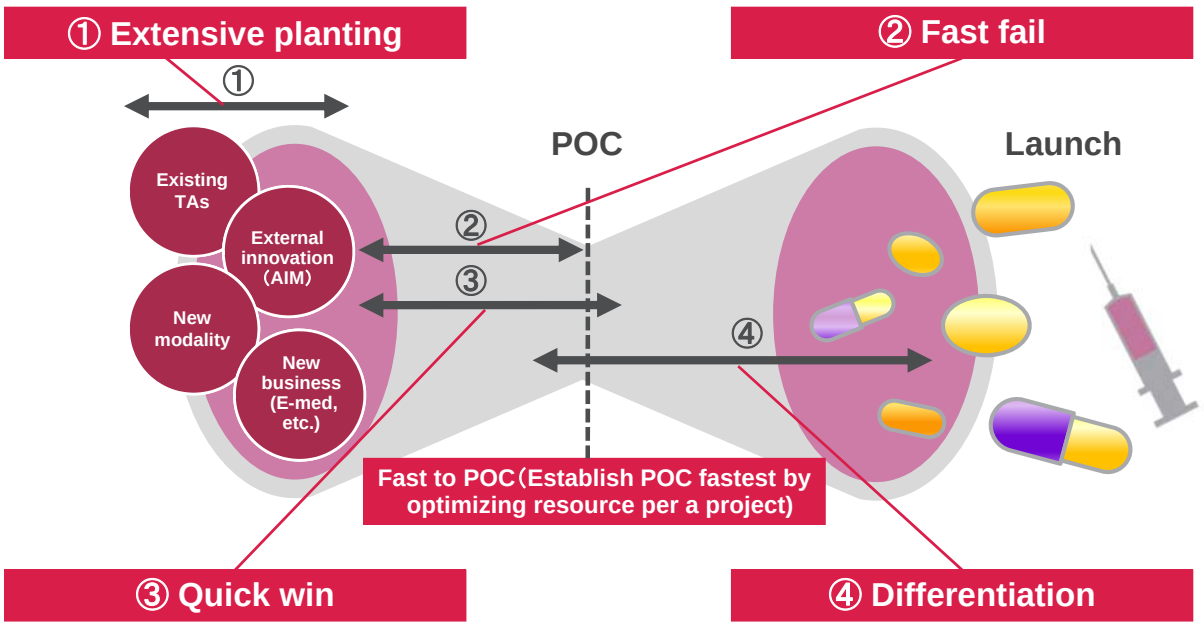
  ⇒ Opportunities to create innovative value for patients still exist

New strategies for drug discovery research

- Research with using strengthens in existing TAs + Advancing into new TAs
- Challenges in Rx business + α (new business): to provide medical solutions
- Utilization of external R&D resources through Network Research System: Best Science / Best Place / Best Talent
- Extensive input
- FASTEN (Multi-tracking of R&D process)

TAs: Therapeutic areas, UMNs: Unmet medical needs

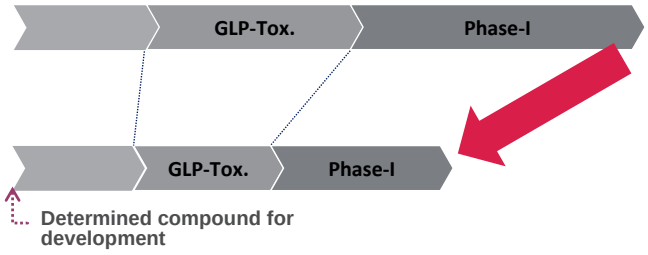
FOUR PILLARS FOR ENHANCING CAPABILITIES TO DELIVER INNOVATIVE MEDICINES



POC: Proof of concept, E-med: Evolving medical solutions

OUTCOME OF R&D RESHAPING

- Sharply increased number of theme inputs
- Shortened timeframe of exploratory R&D stage by 30% after FASTEN implementation

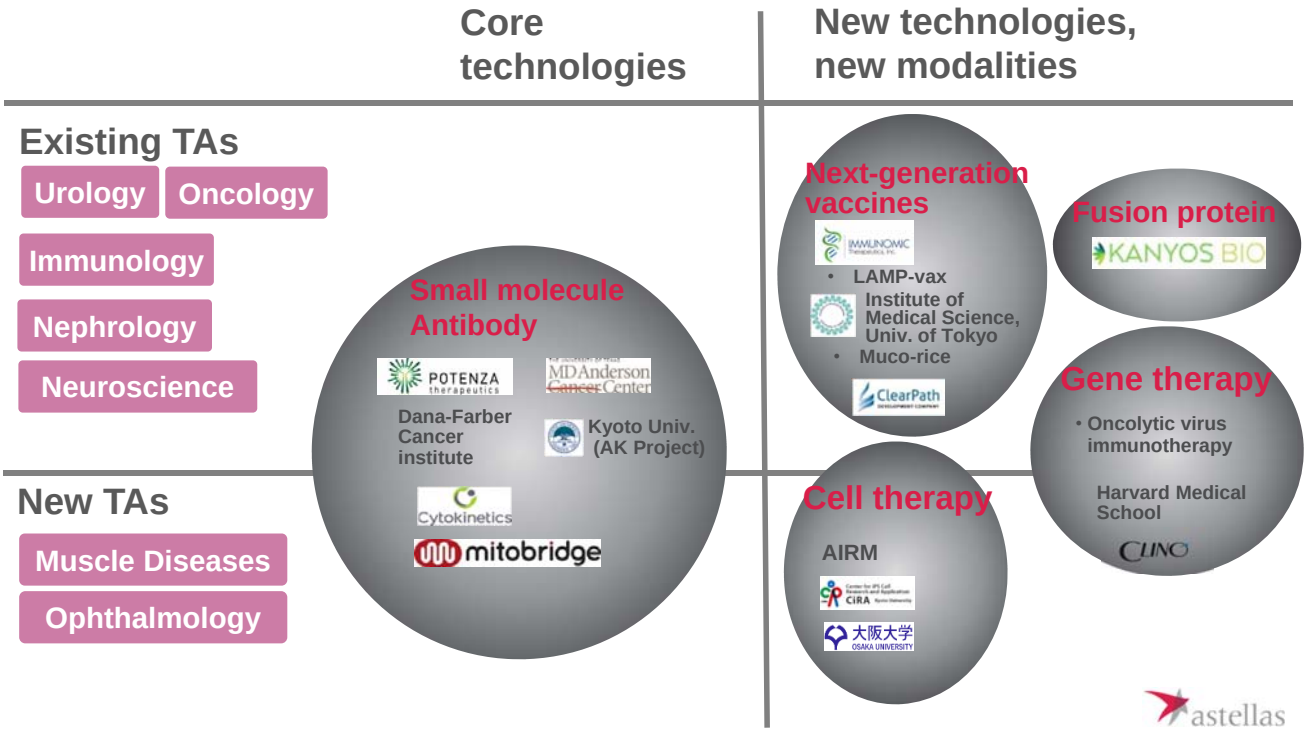


*For illustrative purposes only

- Confirmed a trend of cost reduction during exploratory R&D stage, also

GLP: Good Laboratory Practice

FOCUSED RESEARCH PROGRAMS



DRUG DISCOVERY RESEARCH

R&D MEETING 2016

Wataru Uchida Ph.D.
Senior Vice President,
President, Drug Discovery Research
Astellas Pharma Inc.
December 8, 2016

AGENDA

I **Creating innovation**

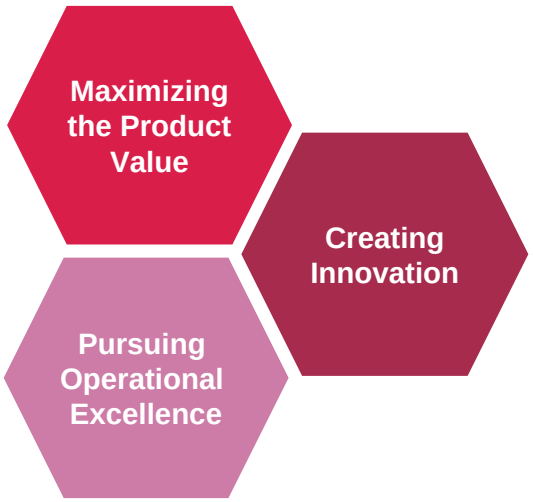
II Therapeutic area: Oncology

III Therapeutic area: Muscle Disease

IV Therapeutic area: Immunology

CREATING INNOVATION

On the forefront of healthcare change to turn innovative science into value for patients



- Enhancing capabilities to deliver innovative medicines
- Advancing into new opportunities

✓ Network-type research system
3B (Best Science, Best Talent, Best Place)

✓ Multitrack R&D project management
FASTEN

✓ Renovate HR system to create innovation
aiPaths, DISC

CREATING INNOVATION

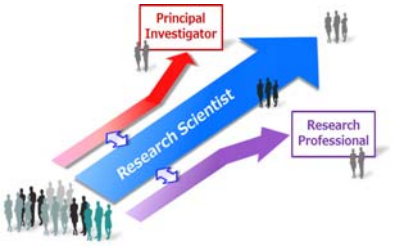
Renovate HR system to create innovation

New HR program to encourage the creation of innovation from a personnel perspective
aiPaths（Astellas Research Multi-Career Paths）

Career paths for researchers

Principal Investigator (PI)
The goal is to encourage researchers to ambitiously develop innovative ideas that were difficult to take on under existing systems and produce concrete R&D results in a timely manner. PIs will be given a certain degree of discretionary authority for personnel and budgets to initiate drug development for incorporating cutting-edge science.

Research Professional
The goal is strengthening research base by acquiring cutting-edge science and technologies through a range of specialties based on abundant knowledge and experience.



Recruitment for diverse researcher to create innovation
DISC (Drug Discovery Innovator Selection Camp)

Astellas has incorporated a unique program called DISC into the process of recruiting drug discovery researchers who are able to constantly create new forms of value with sharing of multifaceted values and solve issues by drawing upon all resources including specialized expertise, experience, knowledge, information and human networks.

AGENDA

I Creating innovation

II **Therapeutic area: Oncology**

III Therapeutic area: Muscle Disease

IV Therapeutic area: Immunology

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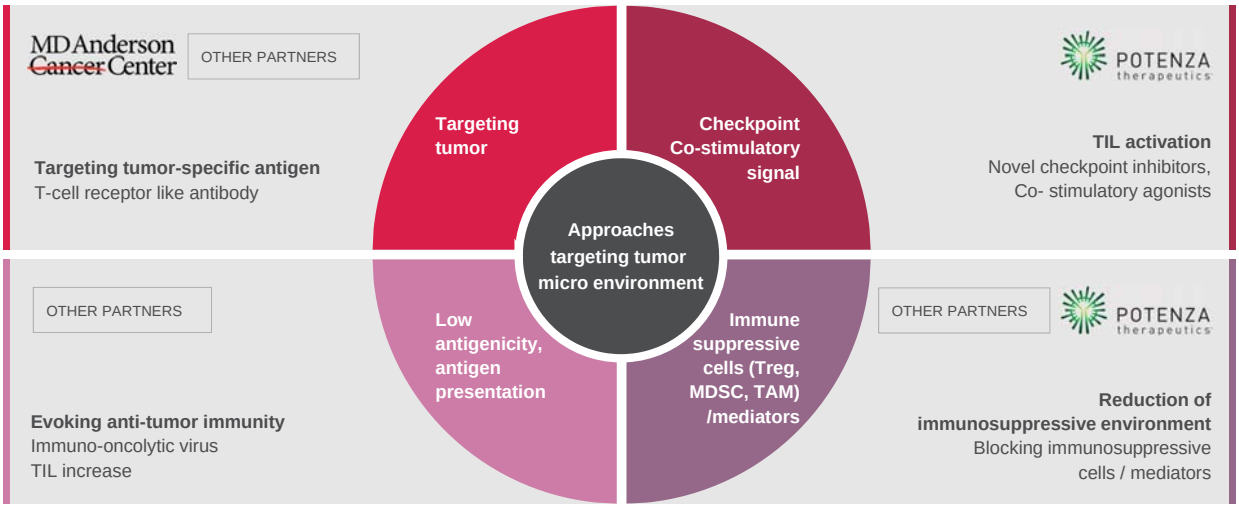
ONCOLOGY

Building a portfolio of novel immuno-oncology therapeutics targeting tumor microenvironments to address tumor types unresponsive to anti-PD-1/PD-L1



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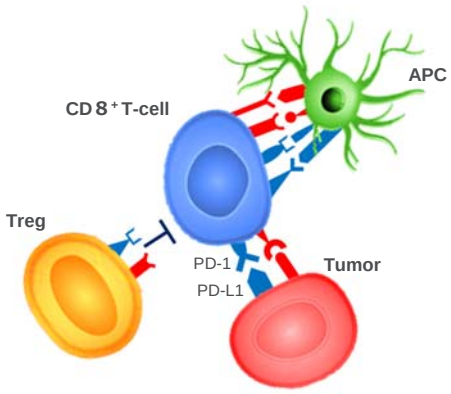
PD-1: Programmed cell Death-1, PD-L1: Programmed cell-Death Ligand 1, TIL: Tumor Infiltrating Lymphocyte,
Treg: regulatory T cell, MDSC: Myeloid-Derived Suppressor Cell, TAM: Tumor-Associated Macrophage

ONCOLOGY: Potenza Therapeutics COLLABORATION

A pipeline of novel checkpoint inhibitor, co-stimulatory agonist and modulator of immunosuppressive cells etc. for patients and tumor types unresponsive to PD-1/L1 blockers

Immunomodulatory mechanisms



Potenza program portfolio

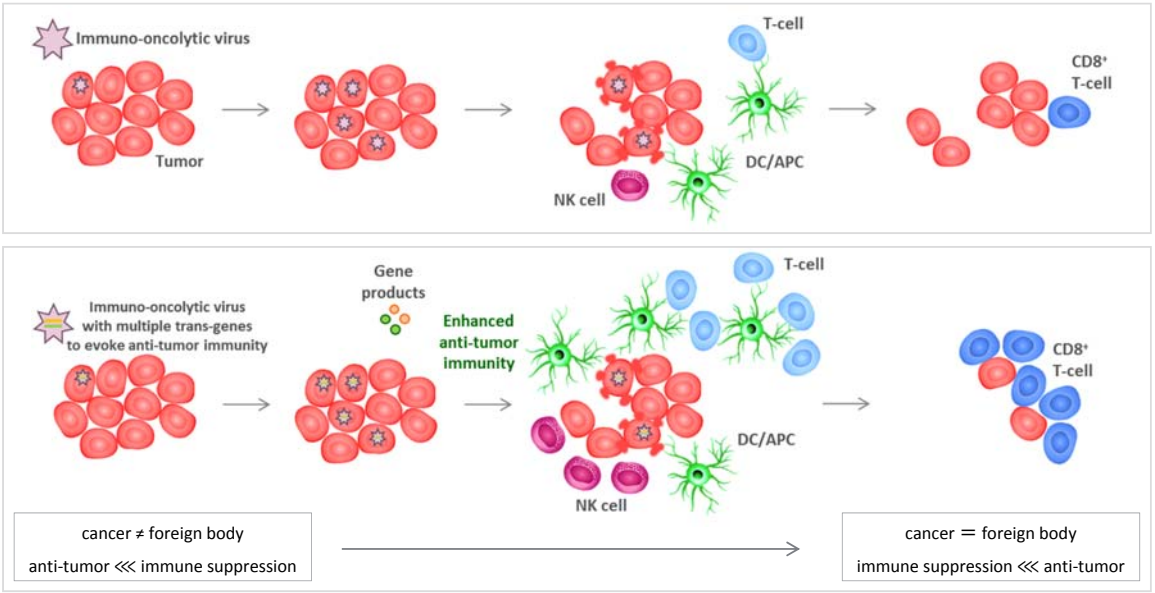
Program	Development Progress	
	Pre-clinical	Clinical
Checkpoint inhibitor		2017 IND scheduled
Treg modulator		2017 IND scheduled
Co-stimulatory agonist		

POTENZA therapeutics astellas

PD-1: Programmed cell Death-1, PD-L1: Programmed cell-Death Ligand 1,
Treg: regulatory T cell, APC: Antigen Presenting Cell

ONCOLOGY: IMMUNO-ONCOLYTIC VIRUS APPROACH

Immuno-oncolytic virus with multiple trans-genes to evoke anti-tumor immunity (Collaboration)



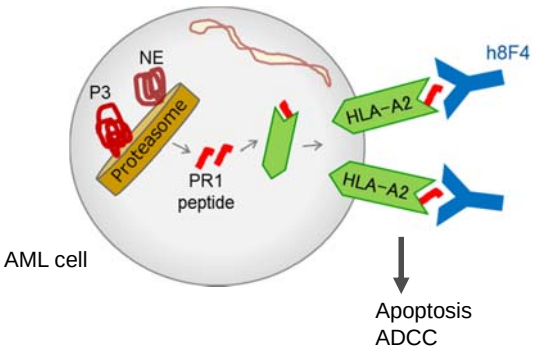
astellas

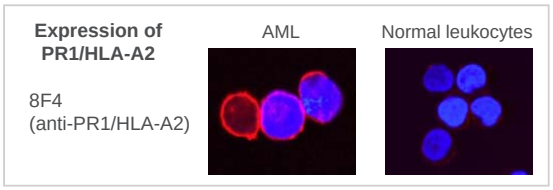
NK cell: Natural Killer cell, DC: Dendritic Cell, APC: Antigen Presenting Cell

ONCOLOGY: MD Anderson COLLABORATION

T-cell receptor like antibody, h8F4 against PR1/HLA-A2 which eliminates the target positive human AML cells

Anti-tumor mechanism of h8F4





Development progress

Program	Development Progress	
	Pre-clinical	Clinical
h8F4	→	2017 IND scheduled

MD Anderson Cancer Center astellas

AML: Acute Myeloid Leukemia, P3: Proteinase 3, NE: Neutrophil Elastase,
ADCC: Antibody-Dependent Cell-Mediated Cytotoxicity

AGENDA

I Creating innovation

II Therapeutic area: Oncology

III **Therapeutic area: Muscle Disease**

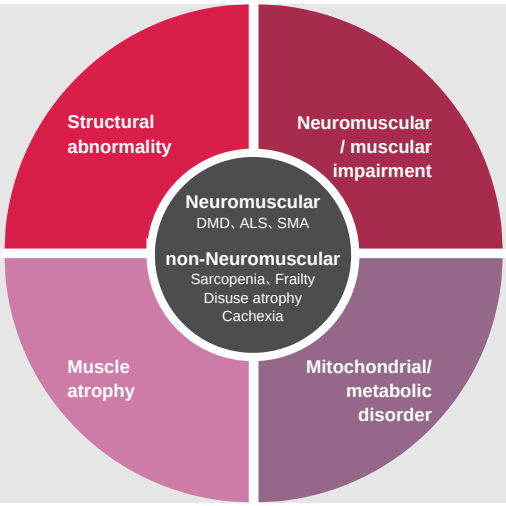
IV Therapeutic area: Immunology

astellas

MUSCLE DISEASE

Create novel NMEs by innovation from research collaborations and in-house R&D capability based on the approach to improve muscle functions

Reinforce structure
Gene therapy
Cell therapy
New modality



Cytokinetics

Increase power
Troponin act.
Neuromuscular junction act.
with amplify neuromuscular junction

Maintain muscle mass
Increase growth
Increase regeneration
Decrease degeneration

mitobridge

Mitochondria
Increase energy
Increase mitochondrial number
Improve mitochondrial quality

astellas

DMD: Duchenne Muscular Dystrophy, ALS: Amyotrophic Lateral Sclerosis,
SMA: Spinal Muscular Atrophy

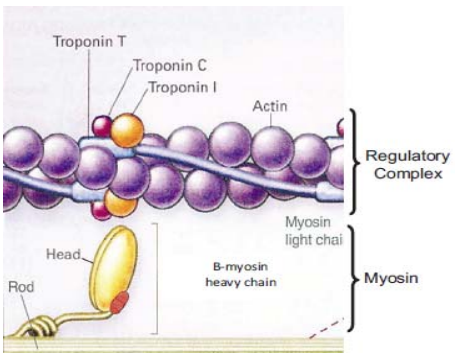
MUSCLE: Cytokinetics COLLABORATION

Combat against muscle impairment/weakness with innovative approaches

Skeletal muscle biology-driven treatments for diseases

Advantages of Cytokinetics, Inc.

- Great expertise in muscle biology
- Broad technical platform to assess muscle functions in non-clinical/clinical studies
- Extensive human network in the muscle research field
- Experience in clinical development including ALS



Progress in the fast skeletal muscle activators

CK-2127107

- Fast skeletal troponin activator

CK-3672889

- Next-generation activator

Program ・Disease	Development Progress	
	Pre-clinical	Clinical
CK-2127107 ・SMA, ・COPD		Ph2
CK-2127107 ・ALS		Ph2 ready
CK-3672889		

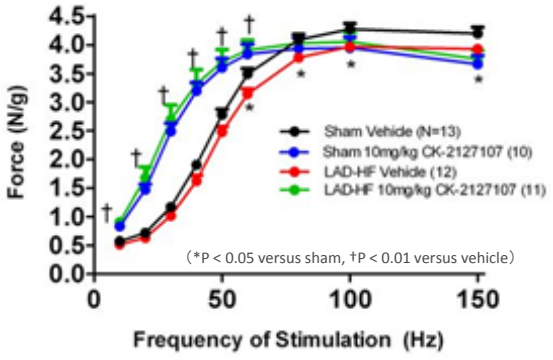
Cytokinetics astellas

ALS: Amyotrophic Lateral Sclerosis
SMA: Spinal Muscular Atrophy, COPD: Chronic Obstructive Pulmonary Disease

MUSCLE: Cytokinetics COLLABORATION

CK-2127107 improves muscle contractility and exercise tolerance in a rat model of heart failure

Isometric force-frequency



CK-2127107 significantly increased isometric tension in LAD-HF plantarflexor.

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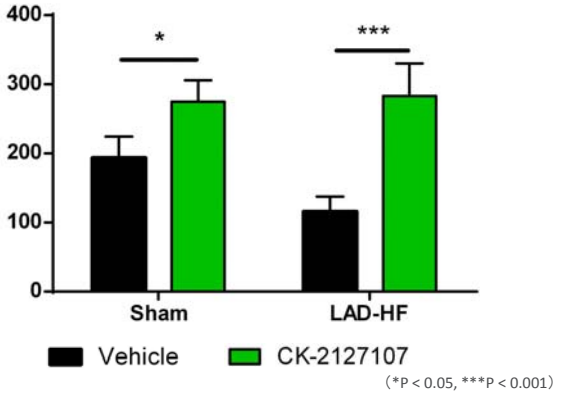
Time on rotarod (sec)



CK-2127107 significantly increases running performance in LAD-HF rats with exercise intolerance.

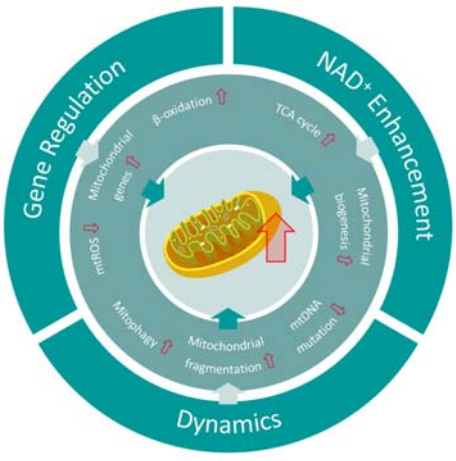
Cytokinetics astellas

J Pharmacol Exp Ther 353:159 (2015)
LAD-HF: Left Anterior Descending coronary artery Heart Failure

MUSCLE: Mitobridge COLLABORATION

Create novel NMEs for broad indications by Mitobridge's proprietary strength of mitochondrial biology and biotech-style research

Activation of mito. function by multiple biological approach



Identify gene regulator "MTB-1" for clinical trial

Strength of Mitobridge

Biology-based approach

- Research platform based on mitochondrial biology
- Plural research pipeline by multiple approach

Biotech-style research

- Agile research using enriched network
- Hybrid R&D with Astellas' developmental capability

Scientific Advisory Board and talented researchers

- Research expertise based on mitochondrial biology
- Intake of newest science by prompt cooperation among researchers

mitobridge astellas

TCA: TriCarboxylic Acid, NAD: Nicotinamide Adenine Dinucleotide

MUSCLE: Mitobridge COLLABORATION

Candidate（MTB-1）for clinical development is now on preparation toward IND for Duchenne muscular dystrophy therapy

Consultation with TREAT-NMD

Mitobridge had a meeting with TREAT-NMD advisory committee to discuss potential of MTB-1 for the treatment of DMD.

http://www.treat-nmd.eu/resources/tact/reviews/past/mtb-1/

- Action of MTB-1 to activate mitochondrial function could be reasonable for the possible use in DMD treatment because mitochondrial dysfunction in muscle has been reported in DMD patients.
- Additional experimental data to increase clinical benefits of MTB-1 and proactive investigation of regulatory guidance from the FDA and EMEA could accelerate early entry to clinical trials.

Development progress

Program ・Disease	Development Progress	
	Pre-clinical	Clinical
MTB-1 ・DMD		2017 IND scheduled
Other programs		

mitobridge astellas

TREAT-NMD: Translational Research in Europe-Assessment and Treatment of NeuroMuscular Diseases,
DMD: Duchenne Muscular Dystrophy

AGENDA

I Creating innovation

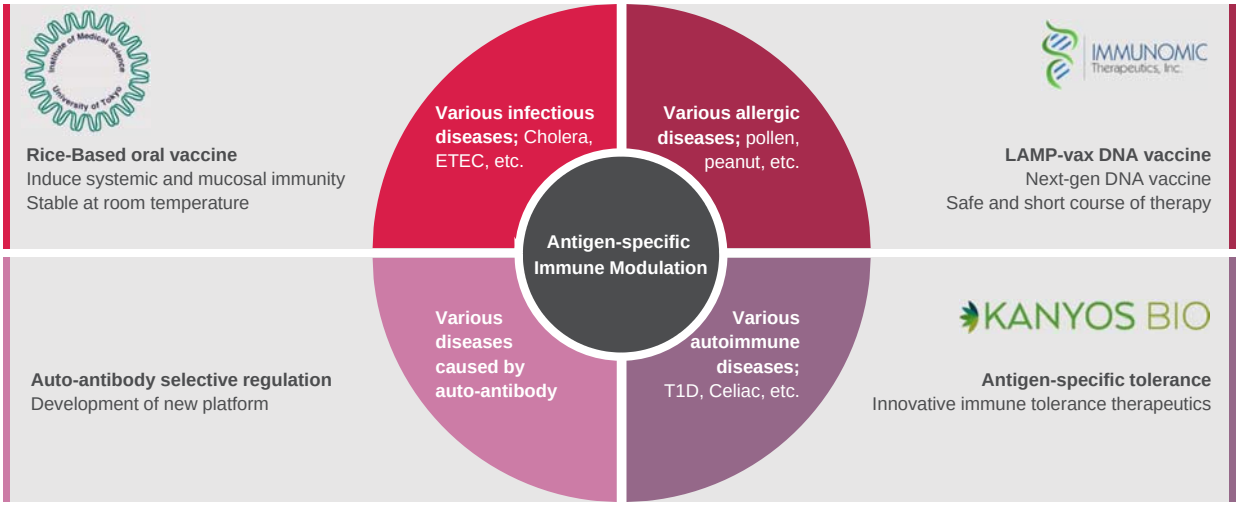
II Therapeutic area: Oncology

III Therapeutic area: Muscle Disease

IV **Therapeutic area: Immunology**

IMMUNOLOGY

Develop an innovative platform which can achieve antigen-specific immune modulation, and create curative and safe therapeutics against allergy, autoimmune diseases and infectious diseases



astellas

ETEC; EnteroToxigenic *E coli*, LAMP: Lysosomal Associated Membrane Protein,
T1D: Type 1 Diabetes

IMMUNOLOGY: Immunomic Therapeutics COLLABORATION

LAMP-vax DNA vaccine platform

Revolutionary Technology

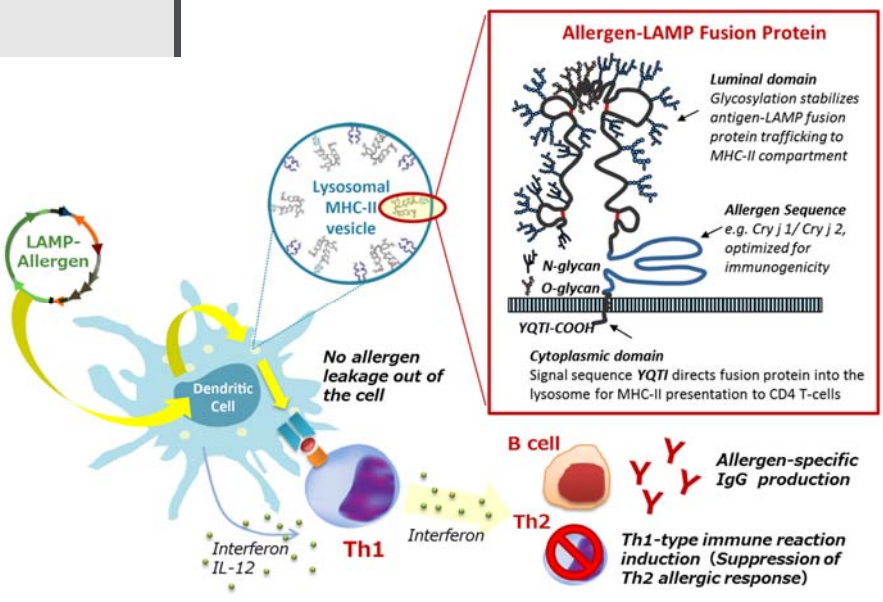
- LAMP-vax induce a robust Th1 immune response

High Safety and Convenience

- Short course curative therapy without systemic allergen exposure

Versatile platform

- Applicable to a wide variety of allergic diseases



IMMUNOMIC Therapeutics, Inc.

astellas

IMMUNOLOGY: Immunomic Therapeutics COLLABORATION

Versatile platform which can be applied to a wide variety of allergic diseases by changing inserted allergen DNA sequence

Food allergy
e.g. peanut, milk, wheat, egg, etc.

Seasonal pollen allergy
e.g. cedar, cypress, ragweed, grass, etc.

Perennial allergy
e.g. house dust mite, pet, mold, etc.

Program	Development Progress	
	Pre-clinical	Clinical
ASP0892 [peanut]		Ph1
Other food allergies		
ASP4070 [Japanese red cedar]		Ph1
Other seasonal allergies		
Perennial allergies		

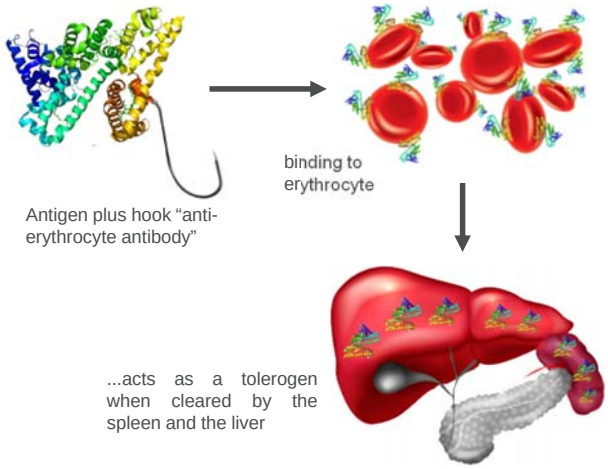
IMMUNOMIC Therapeutics, Inc. astellas

IMMUNOLOGY: Kanyos Bio COLLABORATION

New platform for the induction of antigen-specific immune tolerance

- "Endogenous tolerogenic pathway" in liver and spleen is exploited to prevent autoimmunity
- The technology targets antigens to the surfaces of red blood cells in vivo; the associated antigens are processed to induce antigen-specific T cell deletion and Treg
- Applicable to a wide variety of autoimmune diseases whose pathogenic antigens are identified, including Type 1 Diabetes and Celiac Disease
- Additional tolerance induction platforms are being explored with Kanyos Bio
- Pre-clinical stage

Mechanism of action



KANYOS BIO astellas

Turn innovative science into value for patients by

embodying outcome of Network Research System.

REGENERATIVE MEDICINE
R&D MEETING 2016

Robert Lanza, M.D.
Head of Astellas Global Regenerative Medicine
and Chief Scientific Officer Astellas Institute for Regenerative Medicine (AIRM)
December 8, 2016

AGENDA

I **Introduction**

II Ophthalmology program
(Retinal pigment epithelium, Photoreceptor progenitors, Retinal ganglion progenitors and Corneal endothelium)

III Application in other fields
(Hemangioblast-derived MSCs and Vascular progenitors)

IV Joint research with academia in Japan

MSCs: mesenchymal stem cells

ADVANTAGE OF CELL THERAPY

Cell Therapy has a huge potential in clinical usage

Information : Cell >>> Biotherapeutics > chemical compound

- **Safe** : Cell is an ultimate “natural product” of human origin
- **Efficacious** : Efficacy is not limited to depressing progression, but complete recovery of function is expected theoretically
- **Responsive** : Only cells recognize its environment and respond
  ex. sugar sensor →insulin secretion by β-cells

Advantages of PSC-derived Tissues in Regenerative Medicine

- Virtually unlimited supply of cells
- Can be derived under GMP conditions pathogen-free
- Can be produced with minimal batch-to-batch variation
- Can be thoroughly characterized to ensure optimal performance

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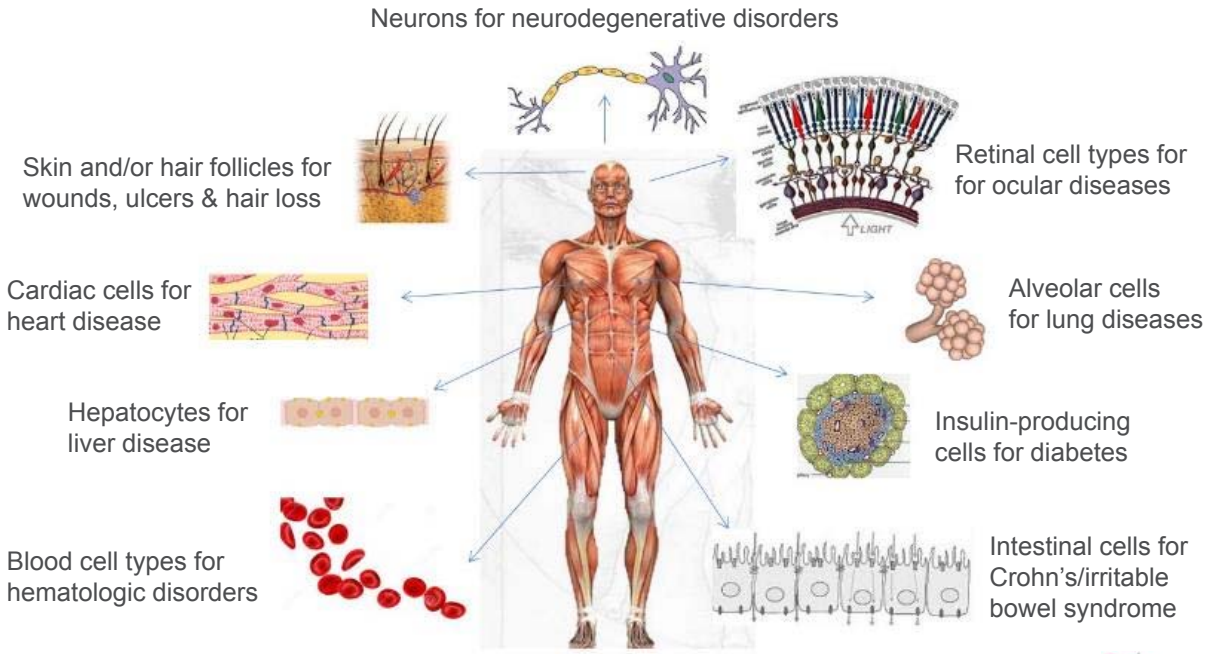
PSC: pluripotent stem cell

PLURIPOTENT STEM CELLS (PSCs) – THE BODY’S MASTER CELLS



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Modified from Kimbrel & Lanza, NATURE REVIEWS / Drug Discovery 2015 Oct,14(10):681-92

ADVANTAGE OF ASTELLAS INSTITUTE FOR REGENERATIVE MEDICINE (AIRM)

Advanced technology that can establish fully-differentiated cells from pluripotent stem cells (PSCs) and strengths in clinical studies and manufacturing for cell therapy

Research

- Technology to establish differentiated target cells from PSCs that could provide functional replacement or trophic support to worn-out or dysfunctional cells and tissues
- Strong IP positions
- Cutting-edge science accepted by top journals

Development

- Expertise in cell-based therapy for high and unmet needs in ophthalmology
- 38 patients treated safely to date
- Active programs currently for macular degeneration (dry AMD and SMD)

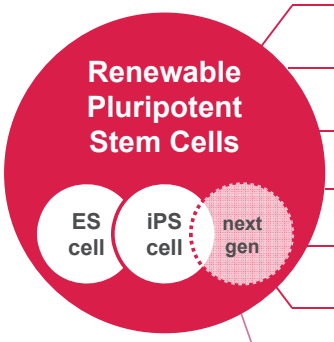
Manufacturing

- Capabilities and track records to manufacture clinical grade cell product that was supplied to US and UK
- Strong process and analytical development capabilities (e.g. hyper sensitive impurity cell detection method, novel cell formulation)

AMD: age-related macular degeneration, SMD: Stargardt's macular dystrophy

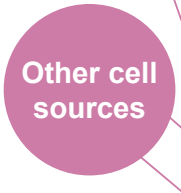
CURRENT R&D PROGRAMS

AIRM (US)



Program	Potential Disease	Development Progress: Pre-clinical	Development Progress: Clinical
Retinal pigment epithelium (RPE)	• Dry AMD • SMD	■	
Photo-receptor progenitors (PhRPs)	• Retinitis pigmentosa • Macular degeneration	■	
Retinal ganglion progenitors (RGPs)	• Glaucoma • Optic neuropathies	■	
Hemangioblast-derived MSCs (HMCs)	• Autoimmune diseases • CNS/vascular indications	■	
Vascular progenitors	• Critical limb ischemia • Pulmonary hypertension	■	
Corneal endothelium	• Corneal diseases • Corneal injuries	■	

DDR RML (JP)



Joint research with Kyoto Univ. CiRA	• Kidney diseases	■
Joint research with Osaka Univ.	(non-disclosure)	■
Other programs	(non-disclosure)	■

ES cell: embryonic stem cell, iPS cell: induced pluripotent stem cell, CiRA: Center for iPS Cell Research and Application

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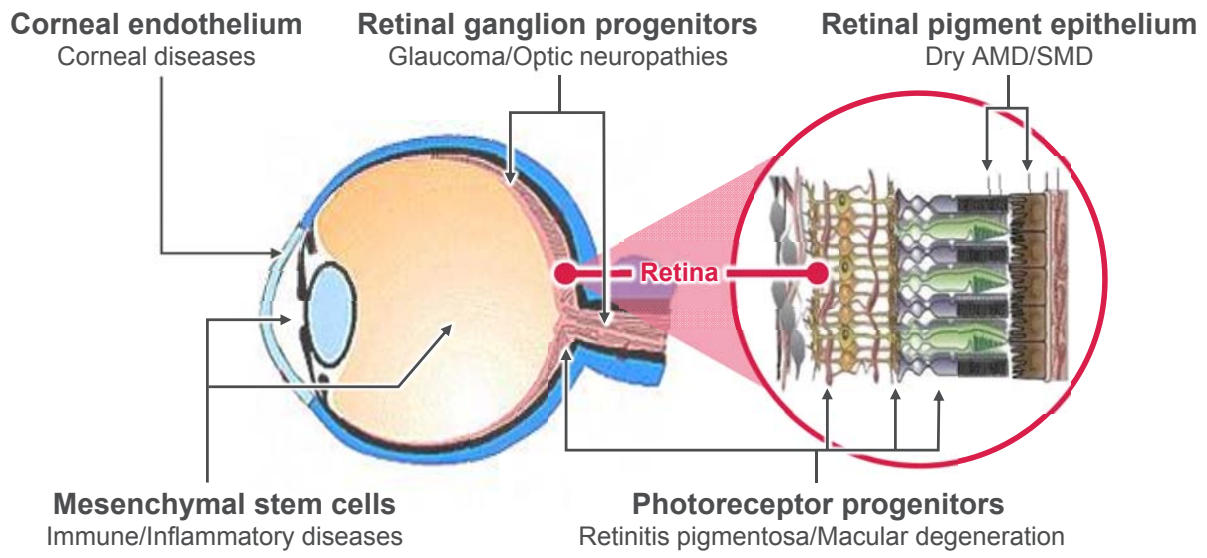
OPHTHALMOLOGY PROGRAMS



Vision loss costs $3 Trillion worldwide

Modified from Kimbrel & Lanza, NATURE REVIEWS / Drug Discovery 2015 Oct,14(10):681-92
http://www.amdalliance.org/

RPE

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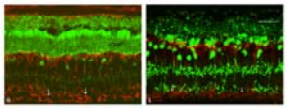
RPE PROGRAM - TRACK RECORD

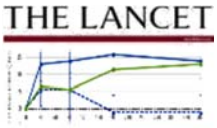
Start of human RPE program



Published first-ever paper showing hESC-RPE can prevent visual loss in animals

MHRA

UK approval for Stargardts trial **NCT01469832**



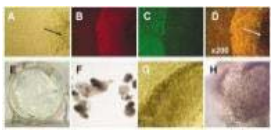
Paper on long-term safety and possible efficacy signal of hESC-RPE

astellas AIRM

Acquired Ocata Therapeutics Changed the name to AIRM

2003 2004 2006 2010 2011 2012 2014 2015 2016

Published first-ever paper describing the derivation and characterization of RPE from human pluripotent stem cells



FDA approval for Stargardts trial **NCT01345006**

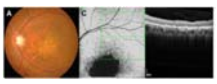
FDA approval for dry-AMD trial **NCT01344993**

KFDA approval for Stargardts & dry AMD trials in South Korea

Published first-ever report of the safety of pluripotent stem cells (hESC-RPE) in humans with any disease

THE LANCET

Study published showing hESC-RPE safe in Asian patients



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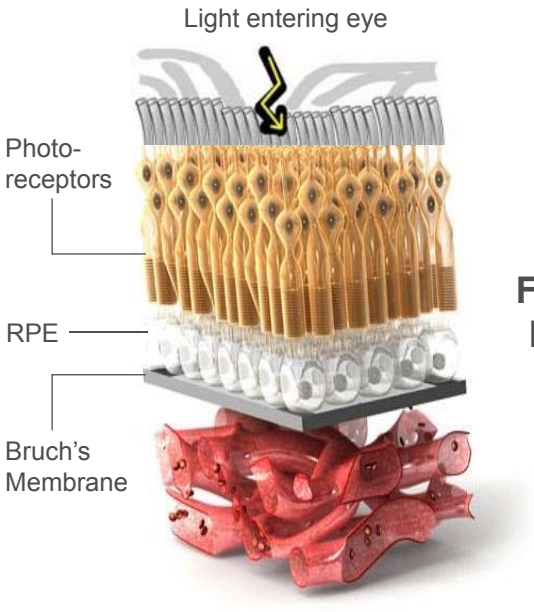
RPE – LIFE SUPPORT TO PHOTORECEPTORS



Function of RPE Layer

- Provides critical nutrients, growth factors, ions and water
- Recycles photopigments & vitamin A
- Phagocytosis of photoreceptor fragments
- Detoxifies photoreceptor layer
- Prevents abnormal blood vessel growth
- Maintains Bruch's Membrane
- Absorbs stray light and protects from UV

Modified from scienceofamd.org

RETINAL DEGENERATIVE DISEASES

AMD & SMD are the leading causes of adult & juvenile blindness in the developed world

- Number of people with AMD is projected to increase to 288 million worldwide by 2040
- SMD & dry AMD (which accounts for 80-90% of all AMD cases) are currently untreatable
- In US alone, the economic burden of vision loss/blindness is expected to reach $717B by 2050

http://www.preventblindness.org/cost-vision-problems-reach-717-billion-2050

AIRM RPE PROGRAM

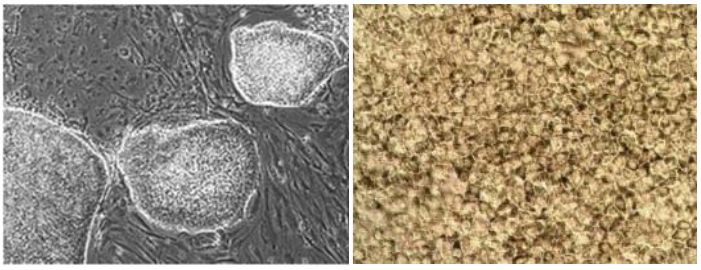
AIRM successfully completed two Phase I/II clinical trials in the U.S. using RPE derived from hESCs to treat macular degeneration:

- Dry AMD
- SMD

Completed the only clinical trial in Europe using pluripotent stem cells hESC-RPE to treat SMD

RPE can be reliably generated from embryonic stem cells

- We have studied dozens of hESC lines – all reproducibly generate RPE lines that can be passaged, characterized, and expanded
- We have secured an extensive patent protection



hESC RPE

NEXT STEPS FOR AIRM RPE PROGRAM

Take a new step toward product launch:
Phase-Ib/II dose-ranging and proof-of-concept trial for dry AMD is planned to start with a new ES cell line and formulation in 1H/2017

Advantages of new cell line and formulation

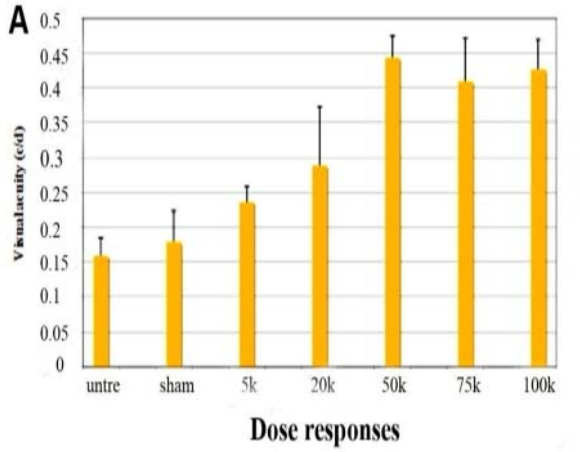
- Comparable preclinical data to RPE cells derived from the previous ES cell line
- Fully comport with the FDA tissue donor compliance regulations revised in 2005
- Non-xenogeneic product which allows to eliminate patient blood sampling
- Larger cell bank which ensures a stable supply
- Longer shelf-life which enables centralized DP preparation
- Protective effect on cells which reduces cell loss during extrusion and debris at injection site
- More clinical trial feasibility

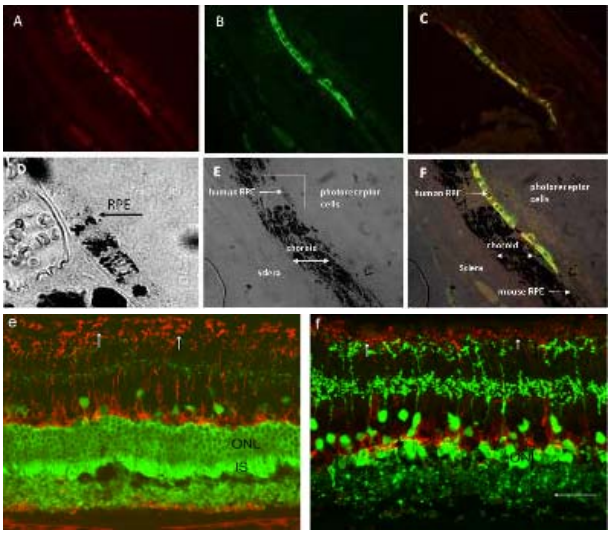
Phase-II PORTRAY study for dry AMD with the conventional cell line has been suspended due to cell line change

DP: drug product

RPE IMPROVE VISUAL ACUITY & RESCUE PHOTORECEPTORS IN ANIMALS

RCS Rats (d90)





RCS: Royal College of Surgeons
Lanza and colleagues, Cloning and Stem Cells 8(3):189-199, 2006

hESC-RPE CLINICAL TRIALS

Treated 38 patients and confirmed safety

US Clinical Trial

Dry AMD
Thirteen patients treated
(50K – 200K cells)

SMD
Thirteen patients treated
(50K – 200K cells)

European Clinical Trial

SMD
Twelve patients treated
(50K – 200K cells)

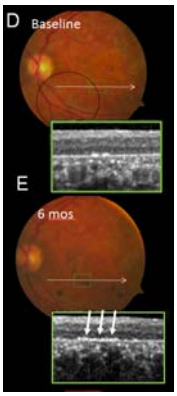
ClinicalTrials.gov
NCT01345006 and NCT01344993

FOLLOW-UP OF PHASE I/II STUDIES

THE LANCET

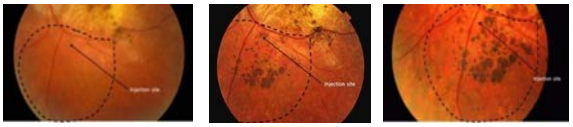
Human embryonic stem cell-derived retinal pigment epithelium in patients with age-related macular degeneration and Stargardt's macular dystrophy: follow-up of two open-label phase 1/2 studies

Steven D Schwartz, Carl D Regillo, Byron L Lam, Dean Eliott, Philip J Rosenfeld, Nimd Z Gregori, Jean-Pierre Hubschman, Janet L Davis, Gad Heilwell, Marc Spirn, Joseph Maguire, Roger Gay, Jane Bateman, Rosaleen M Ostrick, Debra Morris, Matthew Vincent, Eddy Anglade, Lucian V Del Priore, Robert Lanza



Overall Results

- No safety issues related to the transplanted cells
- Clear signs of long-term engraftment & survival



DAY 1 | 2 MONTHS | 6 MONTHS

During the 1-year follow-up period, patients in both the SMD and dry AMD clinical trials have shown significant improvement in visual acuity in the RPE-treated eyes

- 8/18 (44%) patients improved >3 lines
- 3/18 (17%) patients improved 1-3 lines
- 6/18 (33%) patients remained stable
- 1/18 (6%) patients decreased >1 line

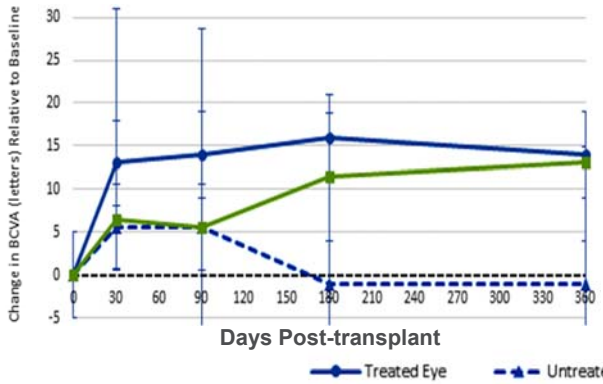
Untreated eyes did not show similar improvements in visual acuity during the same time period

Lanza and colleagues, Lancet 2015; 385: 509-16

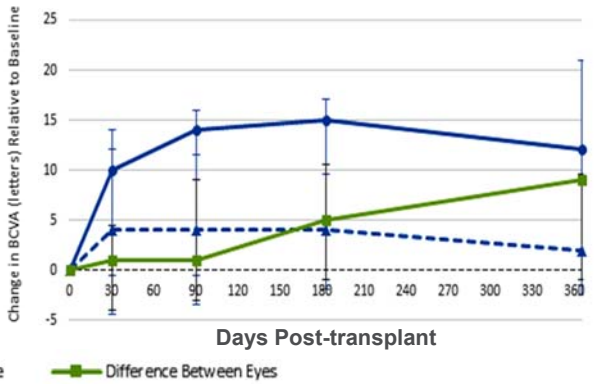
PHASE I/II STUDY RESULTS

Confirmed positive change in BCVA in AMD & SMD patients relative to baseline

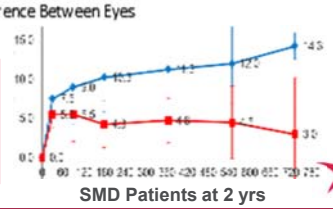
AMD Patients



SMD Patients



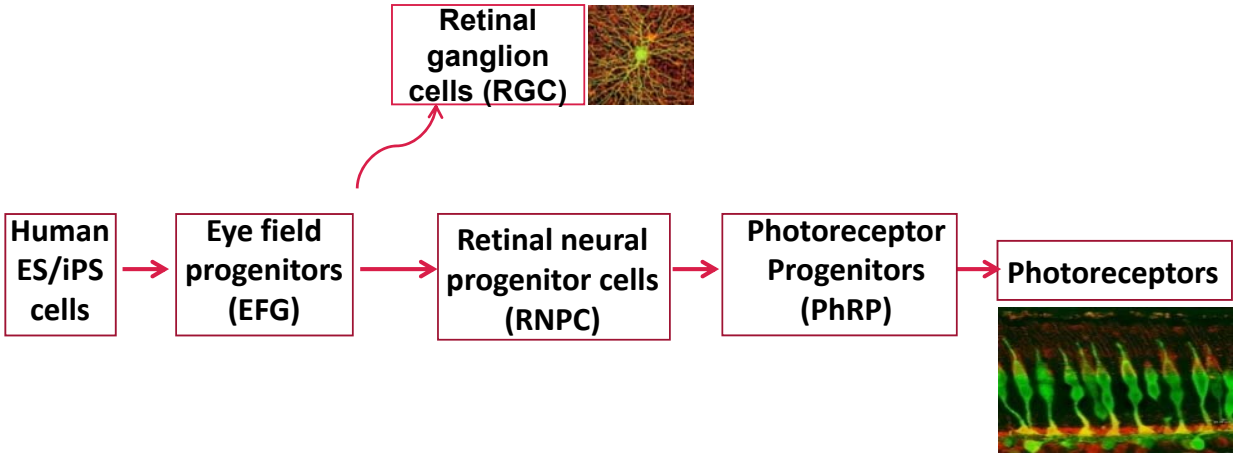
UPDATE:
BCVA improvement continues to be sustained 2–3 years after transplantation in both AMD & SMD patients



SMD Patients at 2 yrs

BCVA: best-corrected visual acuity
Lanza and colleagues, Lancet 2015; 385:509-16

GENERATION OF NON-RPE RETINAL CELL TYPES FROM PSCs



- 3-4 month differentiation process from PSCs resulting in high purity (~95%) PhRPs
- 2 month differentiation process from PSCs resulting in high purity (~99%) RGPs

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PHOTORECEPTOR PROGENITORS

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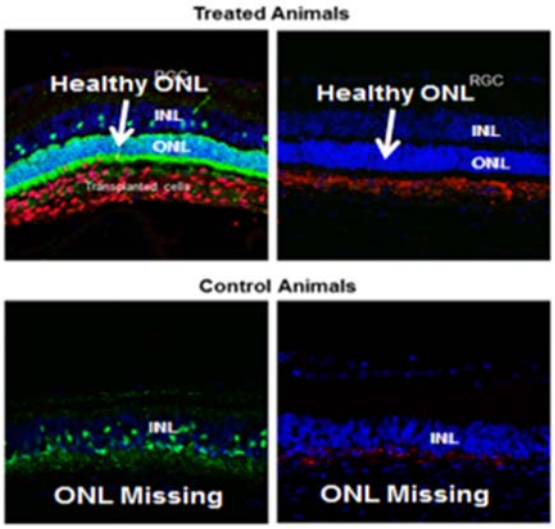
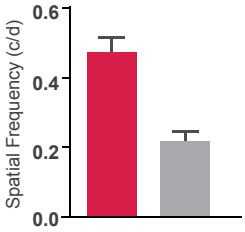
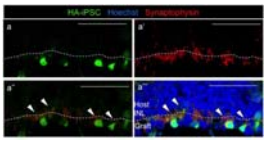
PHOTORECEPTOR PROGENITORS IN RCS RATS & Rd1 MICE

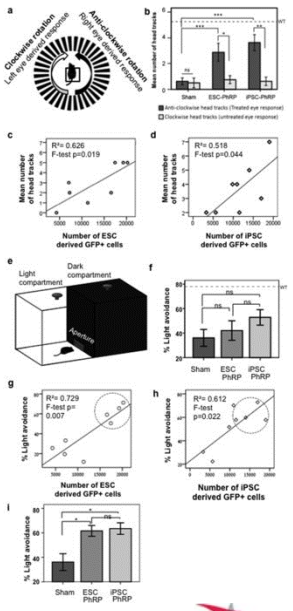
Photoreceptor progenitors restore vision in completely blind animals







Graft-Host Connectivity
Synaptophysin is localized between the host and graft indicating synaptic transmission between the grafted cells & host retina (dashed line delineates the boundary between them).



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Lanza and colleagues, Nature Scientific Reports 2016 Jul13;6:29784. doi: 10.1038/srep29784

RETINAL GANGLION PROGENITORS

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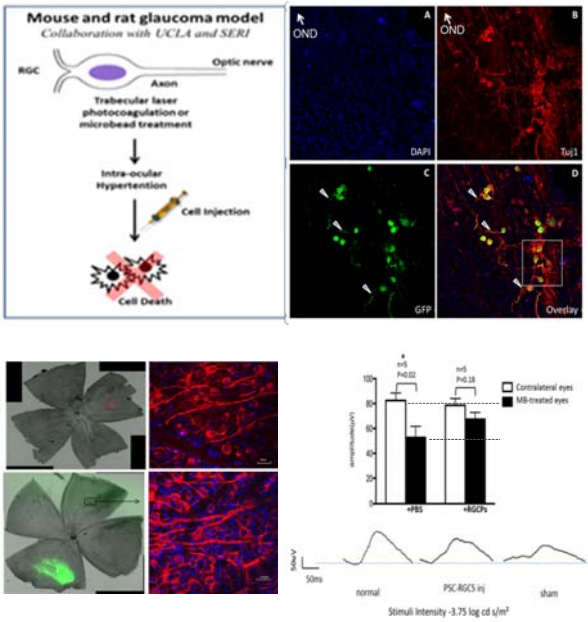
RGP TRANSPLANTATION IMPROVES HOST RGC SURVIVAL IN MICROBEAD/MOUSE GLAUCOMA MODEL



RGPs enhance pSTR amplitude in glaucoma mice

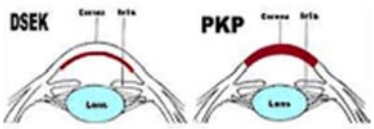
pSTR is the most sensitive indicator of RGC function in the mouse

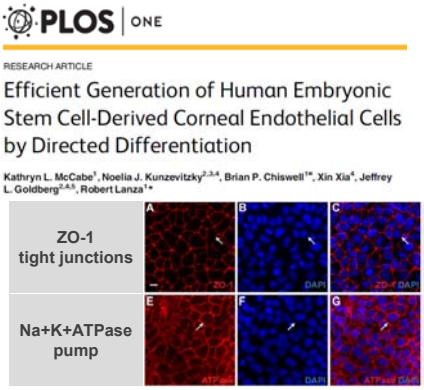
CORNEAL ENDOTHELIUM

CORNEAL REPAIR: CORNEAL ENDOTHELIUM DERIVED FROM hESCs

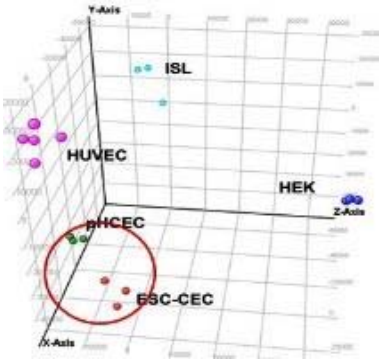
Corneal endothelial cells (CECs) can be generated from hESCs that closely resemble normal adult CECs

- 10 million people with corneal blindness
- Cornea the most transplanted organ (1/3 due to endothelial failure)
- Solutions: Tx of whole cornea “Penetrating Keratoplasty”
  More popular: Tx corneal endothelium & Descemet’s membrane (DSEK)





hESC-CEC resemble normal CEC



Global gene analysis: hESC-CEC & adult-CECs almost identical

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Lanza and colleagues, PLoS One 2015 Dec 21;10(12):e0145266. doi: 10.1371/journal.pone.0145266. eCollection 2015.
Washingtoneye.com

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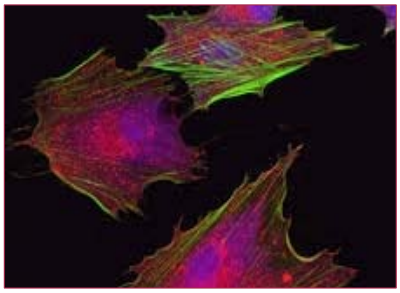
HMCs

HEMANGIOBLAST-DERIVED MESENCHYMAL STEM CELLS (HMCs)

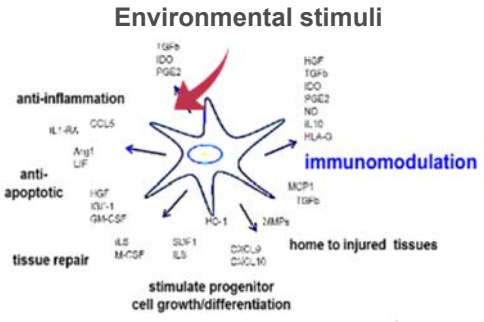
HMCs more youthful (30,000X greater expansion than BM-MSCs) and potent than tissue-derived MSCs. Proof-of-concept demonstrated in six pre-clinical models

- Developed an efficient method of HMC generation
- HMCs are immunomodulatory/no need for immunosuppression
- Cells persist transiently/minimal risk of tumorigenicity
- Platform technology (therapeutic potential shown in 6 different indications



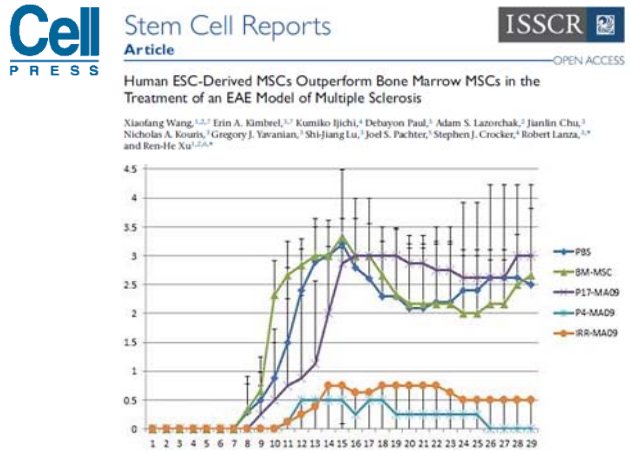
HMCs superior to other clinically used MSCs

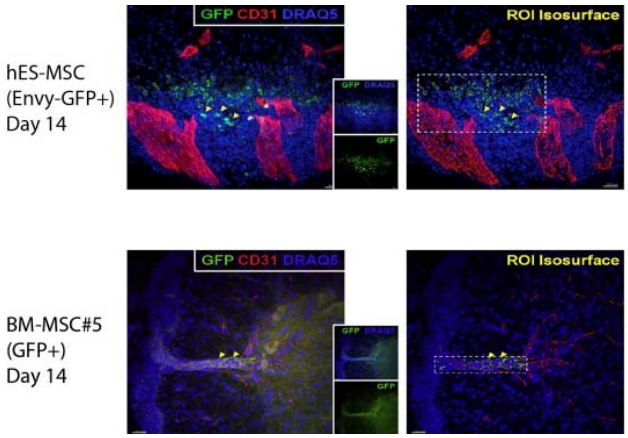
- Greater therapeutic potency vs. BM & CB MSCs
- Better migratory properties vs. BM & CB MSCs
- Reduced IL6 levels vs BM & CB MSCs
- Unlimited (and non-variable) cell source



MS: multiple sclerosis, BM: bone marrow, CB: cord blood

HMCs (BUT NOT BM-MSCs) DRAMATICALLY REDUCE CLINICAL SYMPTOMS IN EAE MODEL OF MS





- **HMCs dramatically reduce clinical symptoms of EAE**
  - **both prophylactic and therapeutic inhibition**
- ***In vitro* inhibition of T-cell function**
- **Differential cytokine expression (HMCs vs BM-MSCs)**
- **Differential ability to migrate into damaged tissues (hESC-MSCs vs BM-MSCs)**

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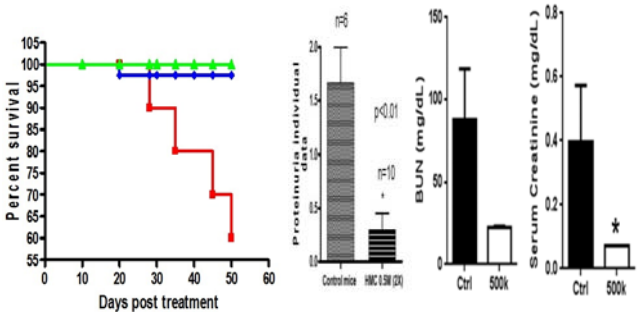
EAE: experimental autoimmune encephalomyelitis
Lanza and colleagues, Stem Cell Reports 2014 Jun 6;3(1):115-30. doi: 10.1016/j.stemcr.2014.04.020. eCollection 2014.

HMCs HAVE POTENT THERAPEUTIC EFFECT IN ANIMALS WITH LUPUS AND CROHN'S DISEASE

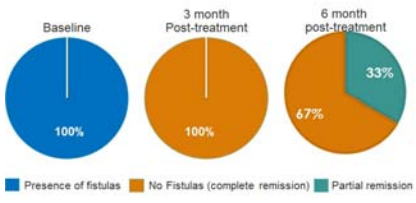
SCIENTIFIC REPORTS
nature

Human embryonic stem cell-derived mesenchymal cells preserve kidney function and extend lifespan in NZB/W F1 mouse model of lupus nephritis
Austin Thiel, Gregory Yavanian, Maria-Dorothea Nastke, Peter Morales, Nicholas A. Kouris, Erin A. Kimbrel & Robert Lanza



Tufts UNIVERSITY
Research Article
For reprint orders, please contact: reprints@futuremedicine.com
Regenerative Medicine

Treatment of perianal fistulas with human embryonic stem cell-derived MSCs: a canine model of human fistulizing Crohn's disease



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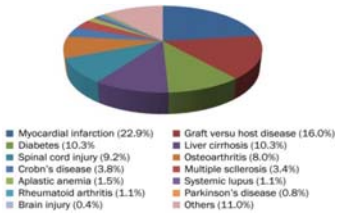
Lanza and colleagues, Nature Scientific Reports 2015 Dec 2;5:17685. doi: 10.1038/srep17685.
Lanza and colleagues, Regenerative Medicine 2016 Jan;11(1):33-43. doi: 10.2217/rme.15.69.

POTENTIAL THERAPEUTIC APPLICATIONS FOR MSCs

- >100 autoimmune diseases
- Multiple Sclerosis
- Osteoarthritis
- Lupus
- Aplastic Anemia
- Crohn's Disease/IBS
- Chronic Pain
- Limb Ischemia
- Heart Failure/MI
- Stroke
- Graft-versus-host Disease
- Spinal Cord Injury
- Liver Disease
- Kidney Disease
- Emphysema/Pulmonary Diseases
- Wound healing (ulcers/decubitus/burns)
- HSC engraftment/irradiated cancer patients
- Eye diseases (uveitis, retinal degeneration, glaucoma)

Percentages of diseases now treated with MSCs



hES/hiPS-MSCs are ideal for clinical translation

- No need for immunosuppression
- Persist transiently
- Can be irradiated

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Xin Wei et al. Acta Pharmacol Sin 2013; 34:747-754.

VASCULAR PROGENITORS

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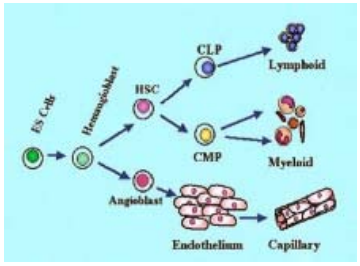
VASCULAR REPAIR

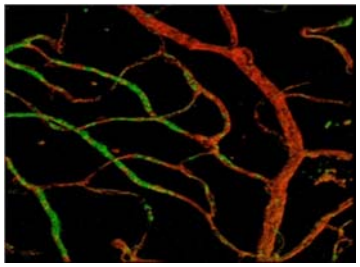
Vascular progenitor cells generated from PSCs repair vascular injury

nature methods

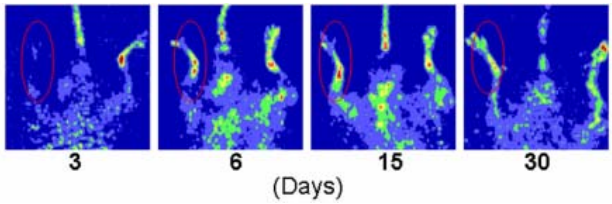
Generation of functional hemangioblasts from human embryonic stem cells

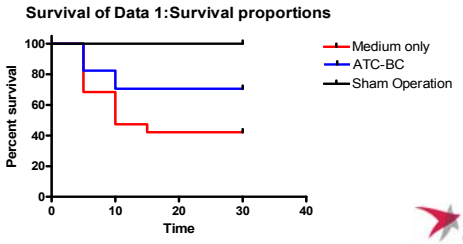
Shi-Jiang Lu[1], Qiang Feng[1], Sergio Caballero[2], Yu Chen[3], Malcolm A S Moore[3], Maria B Grant[2] & Robert Lanza[1]





Hemangioblasts restore blood flow to ischemic limbs and cut mortality rate after severe MI in half





Lanza and colleagues, Nature Methods 2007 Jun;4(6):501-9.

AGENDA

I Introduction

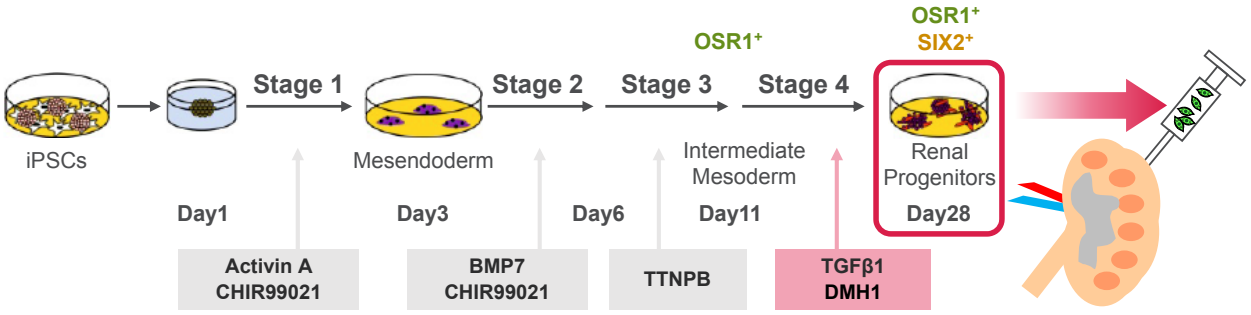
II Ophthalmology program
(Retinal pigment epithelium, Photoreceptor progenitors, Retinal ganglion progenitors and Corneal endothelium)

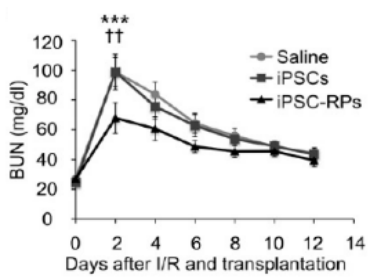
III Application in other fields
(Hemangioblast-derived MSCs and Vascular progenitors)

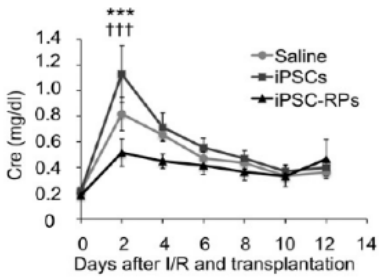
IV **Joint research with academia in Japan**

COLLABORATION WITH PROF. OSAFUNE, CiRA, KYOTO UNIVERSITY ON CELL THERAPY FOR KIDNEY DISEASES

Explore the possibility to develop new cell-based therapies for renal diseases







Transplantation of human iPSC-derived renal progenitors ameliorated acute kidney injury (AKI) in mouse model

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T. Toyohara et al, Stem Cells Trans Med 2015; 4:980-992

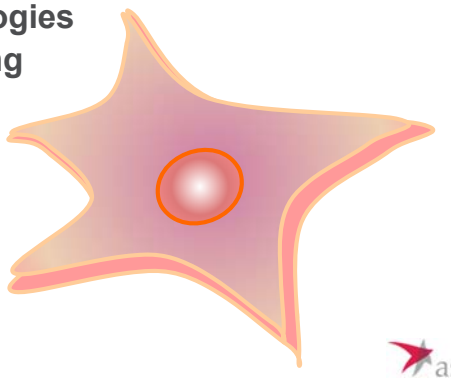
JOINT RESEARCH CHAIR WITH OSAKA UNIV.

Osaka University and Astellas establish joint research chair for R&D on next-generation cell therapy

Osaka University × astellas

With a view developing fundamental technologies for next-generation cell therapies and bringing those technologies into practical use

- Develop cell sources
- Develop cell processing technologies
- Make cells highly functional
- Enhance therapeutic effects



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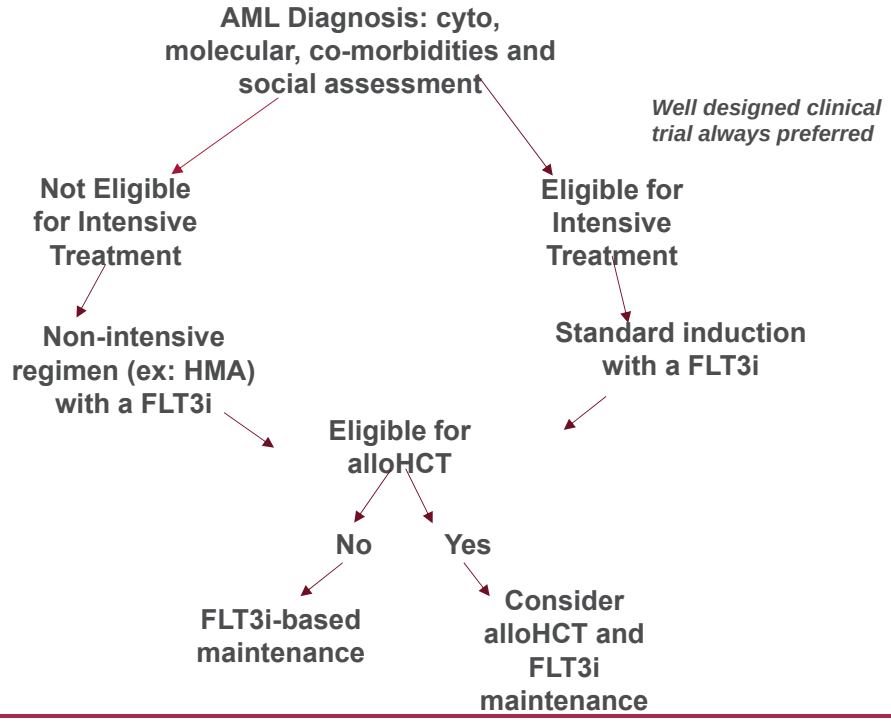
Turn innovative science into value for patients by

maximizing the potential of regenerative medicine.

MY EXPECTATION FOR TREATING AML IN YOUNGER ADULTS IN THE FLT3 INHIBITOR ERA (IN THE NEAR FUTURE)

- Induction: dauno x 3d (or ida) + ara-C x 7d c.i + FLT3i;
- Post remission therapy:
  - HiDAC + FLT3i
  - Allogeneic HCT
- Maintenance post transplant or consolidation with FLT3i
- Relapse: FLT3i alone or re-induction chemo with FLT3i

NOT TOO DISTANT HORIZON: OLDER ADULT WITH FLT3 MUTATED AML



In part adapted from: Ossenkoppele and Löwenberg *Blood* 2015 125:767-774

FUTURE OF GILTERITINIB AND REMAINING QUESTIONS

- Eagerly awaiting approval for patients with recurrent FLT3 mutated disease
  - single agent activity
  - tolerance
- Await data from combination studies in newly diagnosed patients with standard chemotherapy
  - midostaurin + 7+3 data
  - data needed to understand comparison
  - will specificity of inhibitor matter in upfront setting?
- Await results from combination studies with HMA
  - set apart than other available agents
- Post transplant maintenance
- All settings where clinicians will want to utilize gilteritinib if activity confirmed

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CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING INFORMATION

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