The Fiscal Year ending December 2017

Financial Results Presentation

February 9, 2018

Oncolys BioPharma Inc.

(TSE mothers: 4588)

Forward looking statements

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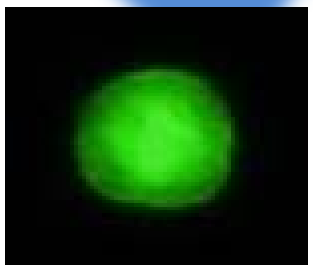
Oncolys BioPharma

Oncolytic virotherapy platform

TelomeScan®

Early detection

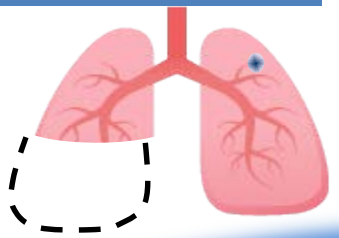


Telomelysin®

Regional treatment

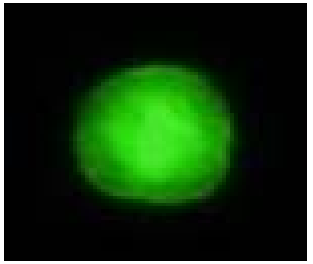
OBP-702

OBP-405



TelomeScan®

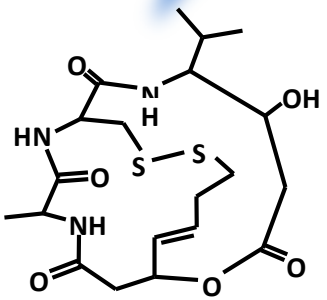
Prognosis follow-up



Telomelysin®

OBP-801

Systemic treatment



FY2017 full year earnings results

JPY in million

	Sales	OP	CP	NP
FY2017 Full Year	**229**	△1,078	△1,087	△1,090
FY2016 Full Year	178	△861	△864	△931
YOY	+51	△217	△223	△159

Sales

1. License fee for Telomelysin from Hengrui
2. Co-development fund from Medigen
3. Sales of TelomeScan to Deciphera

OP

1. Cost reduction efforts
2. Delay in R&D activities

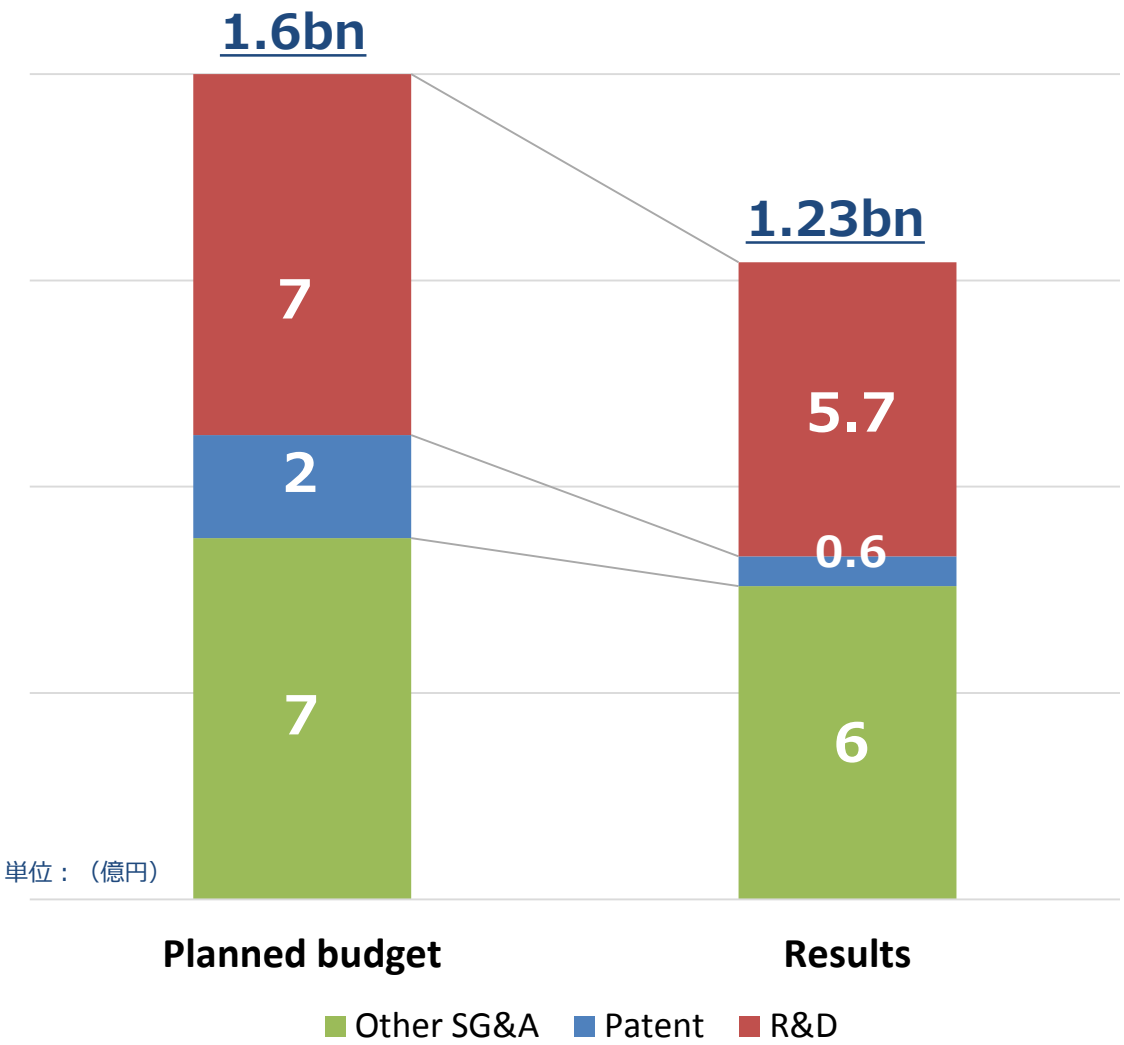
R&D costs JPY 570 million

Cash & equivalents JPY 2.8 bn

FY2017: achievements and status

Telomelysin® OBP-301 *"Telomelysin®"*	<R&D-related> 1. Melanoma P2 Started 2. Esophageal cancer P1 Started 3. HCC P1/2 Multiple administration (Cohort 5) in progress 4. Solid tumors, with PD-1 P1/2 Started 5. Esophageal caner (USA) Scientific Advisory Board（SAB) meeting 6. 9 conference presentations, 4 publications <Business-related> 1. Milestone fee from Hengrui 2. Co-Development fund from Medigen
TelomeScan® *Cancer Diagnosis*	1. PTC feasibility study for pancreatic cancer: IRB 2. Joint research agreement with Juntendo University 3. SAB for NSCLC 4. 9 conference presentations, 3 publications
OBP-801 *Epigenetic cancer treatment*	1. Solid tumor Phase 1 Cohort 3 in progress 2. Possibility of 2wks sustained delivery explored 3. Pre-clinical study with Kyoto Prefectural University of Medicine extending the application into ophthalmologic field
AI-004 *Novel HBV drug*	1. Compound screening at Kagoshima University in progress
Others	1. Completed 1.4 bn JPY financing by third-party allotment

Comparison: budget and actual expenses FY2017



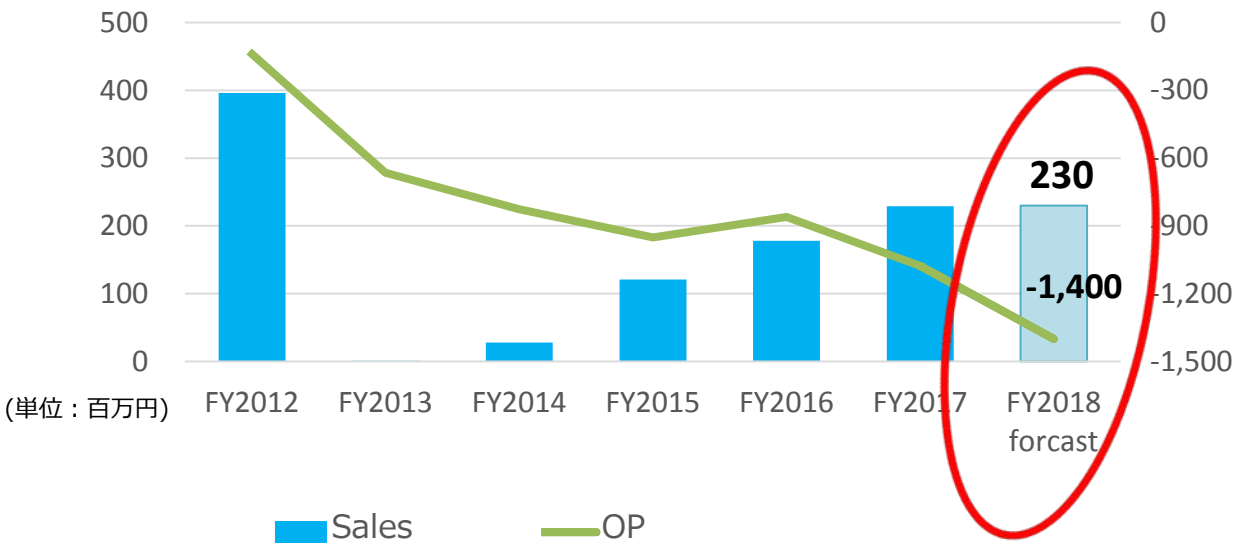
<Major factors>

1. Delay in Telomelysin-related clinical trials
2. Reduced Telomelysin-related patent costs
3. Reduced TelomeScan joint research costs

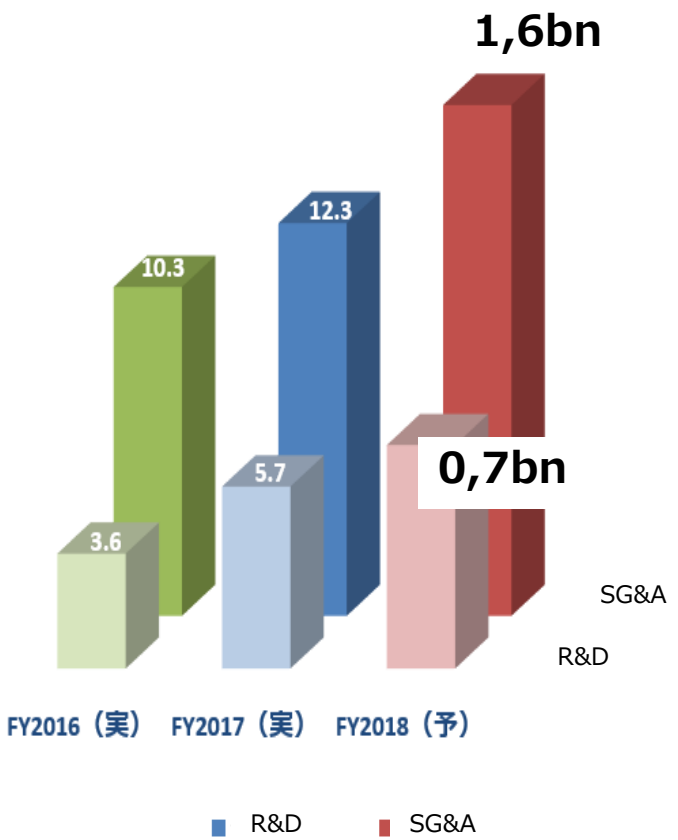
Financial year ending December 2018 full year forecast

(JPY: million)

	Sales	OP	CP	NP
Forecast FY2018	**230**	**△1,400**	**△1,400**	**△1,400**
Results FY2017	229	△1,078	△1,087	△1,090
yoy	+1	-322	-313	-310



R&D and SG&A



Our pipeline

Pharmaceutical Business

	Pipeline/Project	Indication	Exploratory	Pre-clinical	Phase Ⅰ	Phase Ⅱ	Phase Ⅲ
Oncolytic virus	Telomelysin®	Melanoma					
		Esophageal Cancer					
		HCC					
Small molecule	OBP-801	Solid tumors					
		Ophthalmic use					
Anti virus	OBP-601	HIV					
	OBP-AI-004	HBV					

Diagnostic Business

Category	Pipeline/Project		Indication	Basic Research	Clinical Study	Clinical Usefulness
Tumor diagnostics	Oncolytic virus	TelomeScan® OBP-401/1101	Solid tumors			

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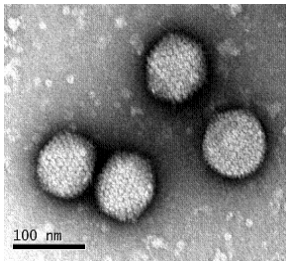
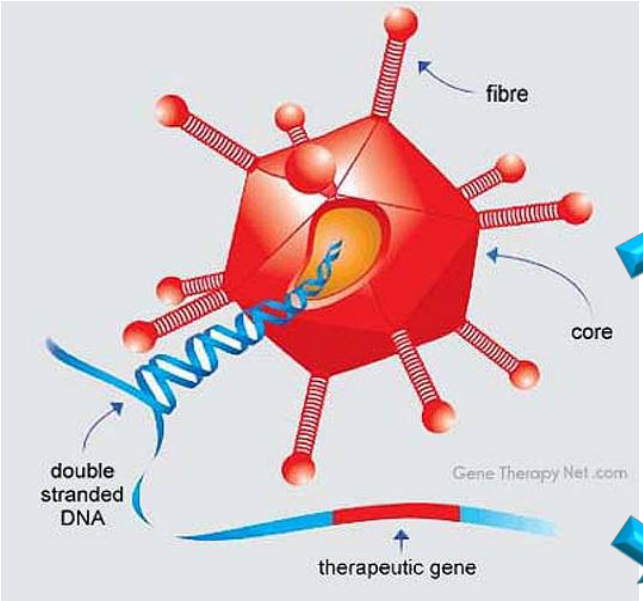
Oncolys BioPharma

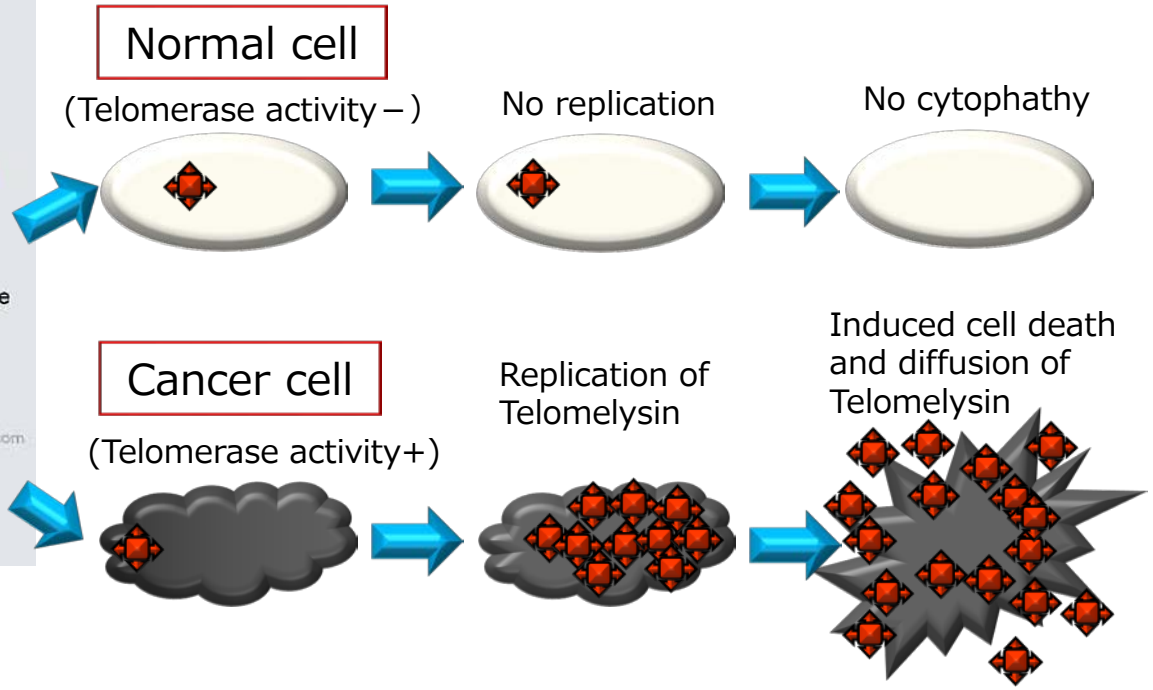
Telomelysin : oncolytic virotherapy

Telomelysin®





Ref.) *The Lancet Oncology Vol. 3* Jan. 2002



Colorectal cancer

(15 days after administration)

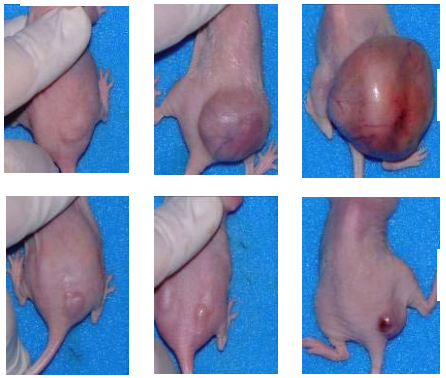
Control group

Telomelysin

Ref) *Curr. Cancer Drug Targets*, 7: 191-201, 2007

Lung cancer

Day 0 Day 14 Day 28



Control group

Telomelysin

Telomelysin project

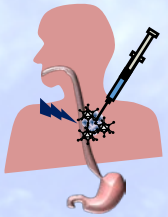
Telomelysin®

Tumor type	Treatment	Country	Pre-clinical	Phase Ⅰ	Phase Ⅱ	Phase Ⅲ
Esophageal Cancer	Radiation OBP sponsored clinical trial	JP	→			
	Radiation Investigator initiated clinical trial		→			
	Anti PD-1 Investigator initiated clinical research		→			
Melanoma	Monotherapy	US	→	→	→	
HCC	Monotherapy	Taiwan Korea	→	→		
HNSCC	Radiation	JP	→	Planning		
Sarcoma	Radiation	JP	→	Planning		

※Jiangsu Hengrui's project is not included in this table.

Telomelysin®

Esophageal Cancer



“Cure without operation”

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Investigator-initiated clinical research with radiation (1) Telomelysin®

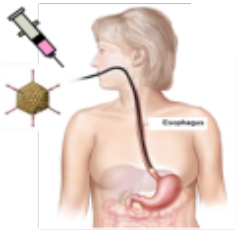
Some contents are For projection only

6 CR in 10 cases

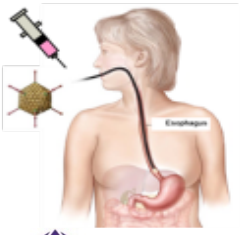
Radiation therapy

5 times/week (Mon- Fri) x 6 weeks

Day 1 Day 4 Day 18 Day 32



Telomelysin®



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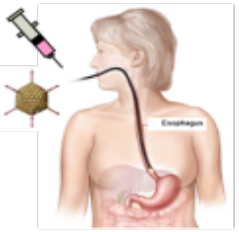

Telomelysin®

Toshiyoshi Fujiwara, M.D., Ph.D.
Professor & Chairman
Department of Gastroenterological Surgery, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences

出所：岡山大学プレスリリースほか

Investigator initiated clinical research with radiation (2)

Telomelysin®

Cases

Dose	Case	Age	Stage	Response
Level 1 $1x10^{10}$vp	001	82	cStage I	CR
	002	85	cStage I	CR
	003	92	cStage II	PR
	004	68	cStage Iva	SD
	005*	79	cStage III	PD
	006	88	cStage I	CR
	007	53	cStage II	CR
Level 2 $1x10^{11}$vp	001	89	cStage I	PR
	002	75	cStage II	CR
	003	85	cStage I	CR

(＊Level 1 005 dropped out as the enrollment was cancelled)

Some contents are For projection only

Cohort 3 completed

Data analysis

Ref.): presentation materials by Okayama University and the Company, etc.

Oncolys' Phase I clinical trial with radiation

Telomelysin®

1. Cohort 1 in progress
2. Cohort 2 to be completed within 2018
3. Start preparation for Phase II/III with radiation
   - Multicenter trial
   - Preliminary consultation with PMDA
   - Expected to start in 2019

Pembrolizumab combination therapy at NCCHE

Telomelysin®

Some contents are
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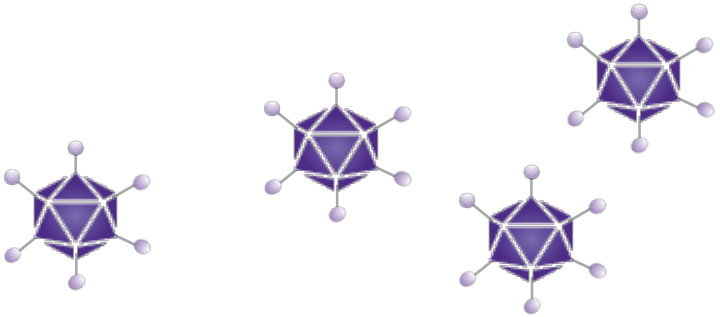
- Patients with advanced or metastatic tumors
- Main endpoint: Safety and tolerability



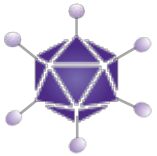
Esophageal Cancer : Scientific Advisory Board Meeting

Telomelysin®

Discussion on expanded indication of Telomelysin(20 Jan)

Some contents are For projection only

Name	Specialty	Institution
Manish Shah, MD	Medical Oncology	Weill Cornell Medicine/ NewYork-Presbyterian
David Ilson, MD, PhD	Medical Oncology	Memorial Sloan Kettering Cancer Center
Khaldoun Almhanna, MD	Medical Oncology	Moffitt Cancer Center
Toshiyoshi Fujiwara, MD, PhD	Surgical Oncology	Okayama University
Lawrence Kleinberg, MD	Radiation Oncology	Johns Hopkins
Tanguy Seiwert, MD	Immunologist	U. Chicago
Kenneth Wang, MD	Endoscope Specialist	Mayo Clinic
Field Willingham, MD	Endoscope Specialist	Emory University



<Stomach and gastroesophageal cancer>

Case	Stage		Combination
1	Stage IV	Metastatic	ICI
2	cStage II/III	Inoperable	CRT
3	cStage II/III	Operable	CRT

(ICI: Immune Checkpoint Inhibitor , CRT: Chemoradiotherapy)

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Tumor virotherapy: clinical trials

Telomelysin®

Indication	# of clinical trials	Sponsors
Melanoma	16	Amgen, Provectus, Takara Bio, Virttu, Viralytics , **Oncolys**
Solid tumor	11	VBL, Silla Jen, Targovax, Remplimune, VCM
Brain tumor（incl. GBM）	10	VBL, DNAtrix, Virttu, VCN
HCC（incl. metastatic to liver）	9	Amgen, Silla Jen, Virttu**, Oncolys**
Sarcoma & myeloma	7	Amgen, Oncolytics Biotech
SCCHN	6	Amgen, PsiOxus, Vyriad, Virttu
Bladder cancer	6	PsiOxus, Cold Genesys
Breast cancer	5	Amgen
NSCLC	5	Shanghai Sunway, Turnstone, Viralytics, Vyriad
Ovarian cancer	5	VBL, PsiOxus, Genelux
Pancreatic cancer	4	Amgen, Takara Bio, VCN, Lokon
Colorectral cancer	3	SillaJen, PsiOxus
Mesothelioma	2	Virttu, Targovax
Esophageal Cancer	**2**	**Oncolys only**
Others	11	—
Total	**102**	

Ref: data from ClinitalTrials.gov in Jan 2018

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Esophageal cancer treatment perspectives

Telomelysin®

- Number of patients: approx. 31,000 in 2014
- Estimated incidence: approx. 22,000 between 2015 - 2019
  (Incidence worldwide: approx. 456,000 in 2012)
  (Incidence USA: approx. 17,000 in 2017)

Stage Ⅳ
Metastasis/operation inapplicable patients

Telomelysin®
+
ICI: pembrolizumab

Stage Ⅰ・Ⅱ・Ⅲ
Operation applicable

Telomelysin®
+
Pre-operative chemotherapy/radiation

Stage Ⅰ・Ⅱ
Operation/chemotherapy inapplicable patients

Telomelysin® **+ Radiation**

Ref.) PMDA 2014 Patient Report (2014), NCC Center for Cancer Control and Information Services, Cancer today IARC website.

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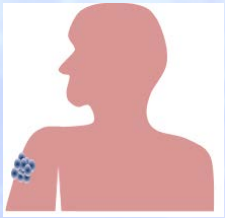
Melanoma



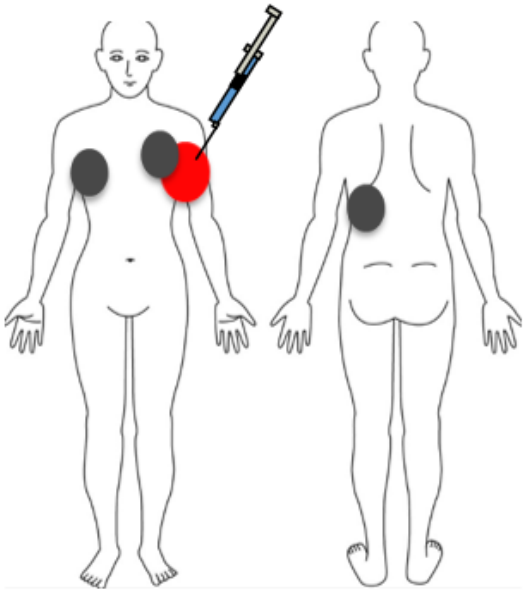
“Challenge to remote cancer”

Oncolys BioPharma

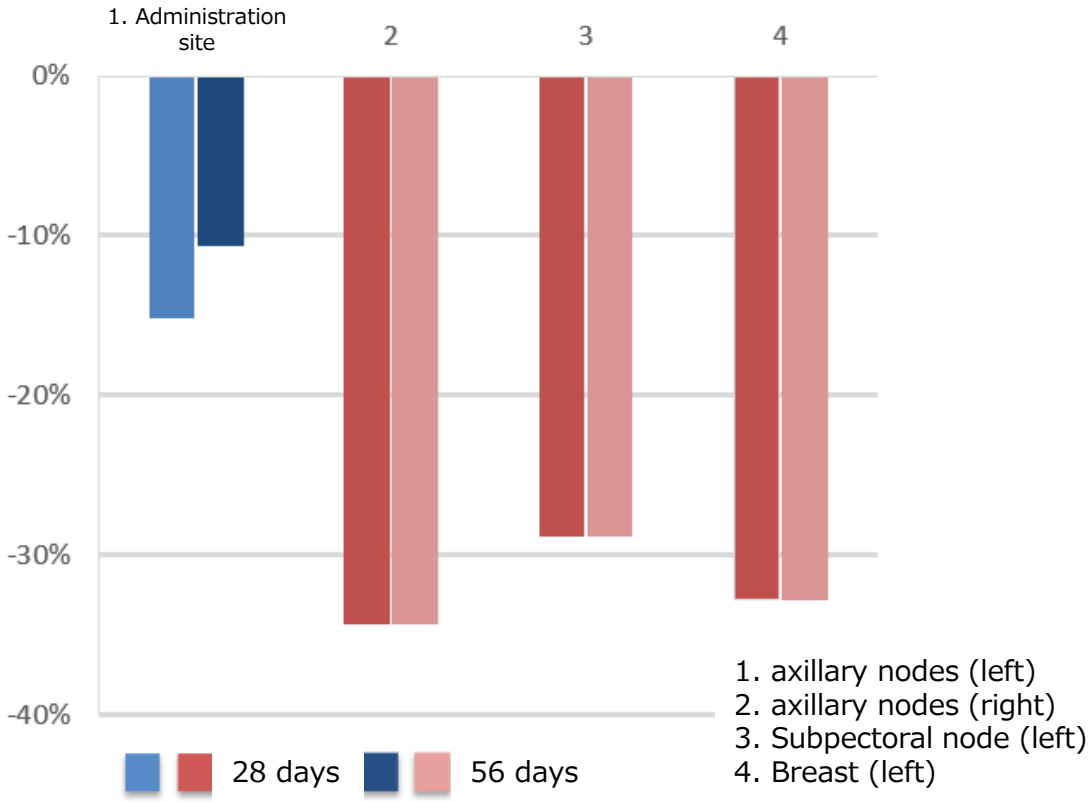
Abscopal Effect observed in melanoma patients

Telomelysin®

Age: 54
Sex: Male
Race: Caucasian
Stage: IV
Cohort 1: $1x10^{10}$VP
Metastases: 5



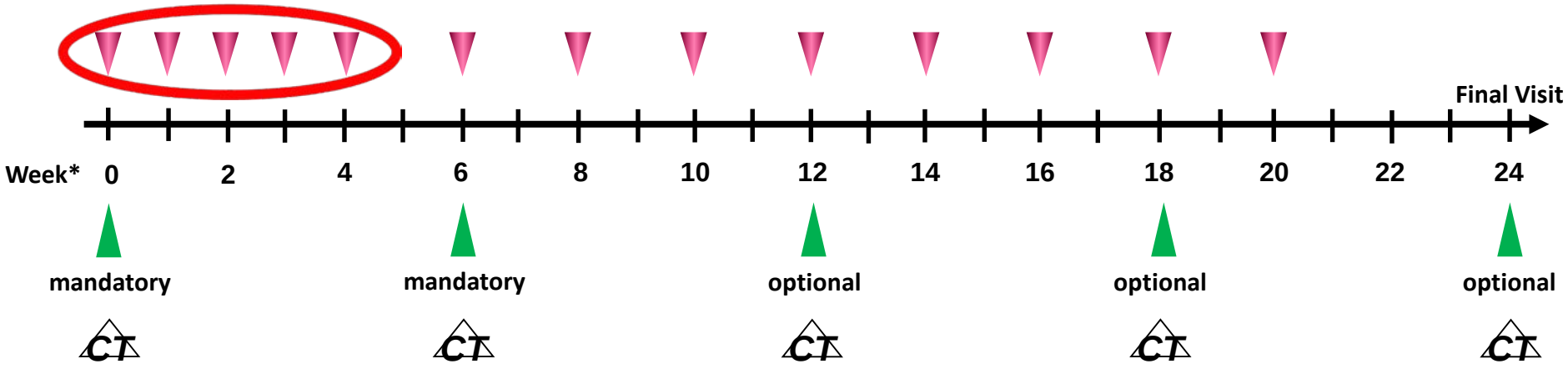
Cytoreductive effect on administration/non-administration sites



Melanoma : 2 patients enrolled

Telomelysin®

- **Total 4 clinical trial sites are open in the US so far**
- **Accelerating patient recruiting to realize an interim analysis**



- Unresectable or metastatic melanoma
- 4 x 10^{12}vp /multiple location
- Efficacy, safety and immunological response

Trial sites
Atlantic Health Systems (NJ)
Huntsman Cancer Institute (UT)
University of Iowa (IA)
St. Luke's University Health Network Inc. (PA)
Stanford University (CA)

Telomelysin®

HCC

“Challenge to refractory cancer”

Oncolys BioPharma

HCC: Phase I/II in Taiwan and Korea

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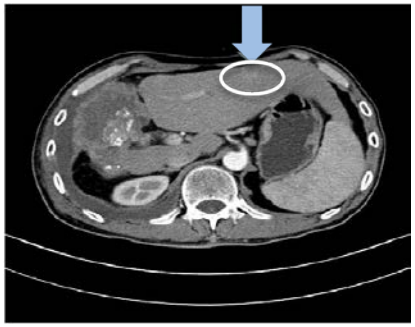
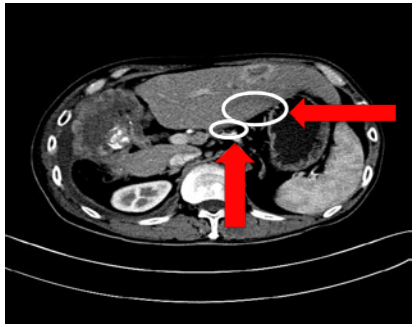
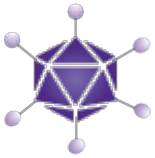
基亞生物科技股份有限公司
MEDIGEN BIOTECHNOLOGY CORP.



Before administration



After 4 weeks



3 more cases

Moving on to PII after P I
→ monotherapy or combination with ICI?

Telomelysin®

Next Generation Telomelysin

Oncolys BioPharma

Next Generation Telomelysin①

Telomelysin®

Telomelysin®

Local therapy
└virotherapy

Next Generation
Telomelysin®

Systemic therapy
└Virotherapy
└T lymphocyte therapy
└CP Inhibitors

Changing tumor microenvironment

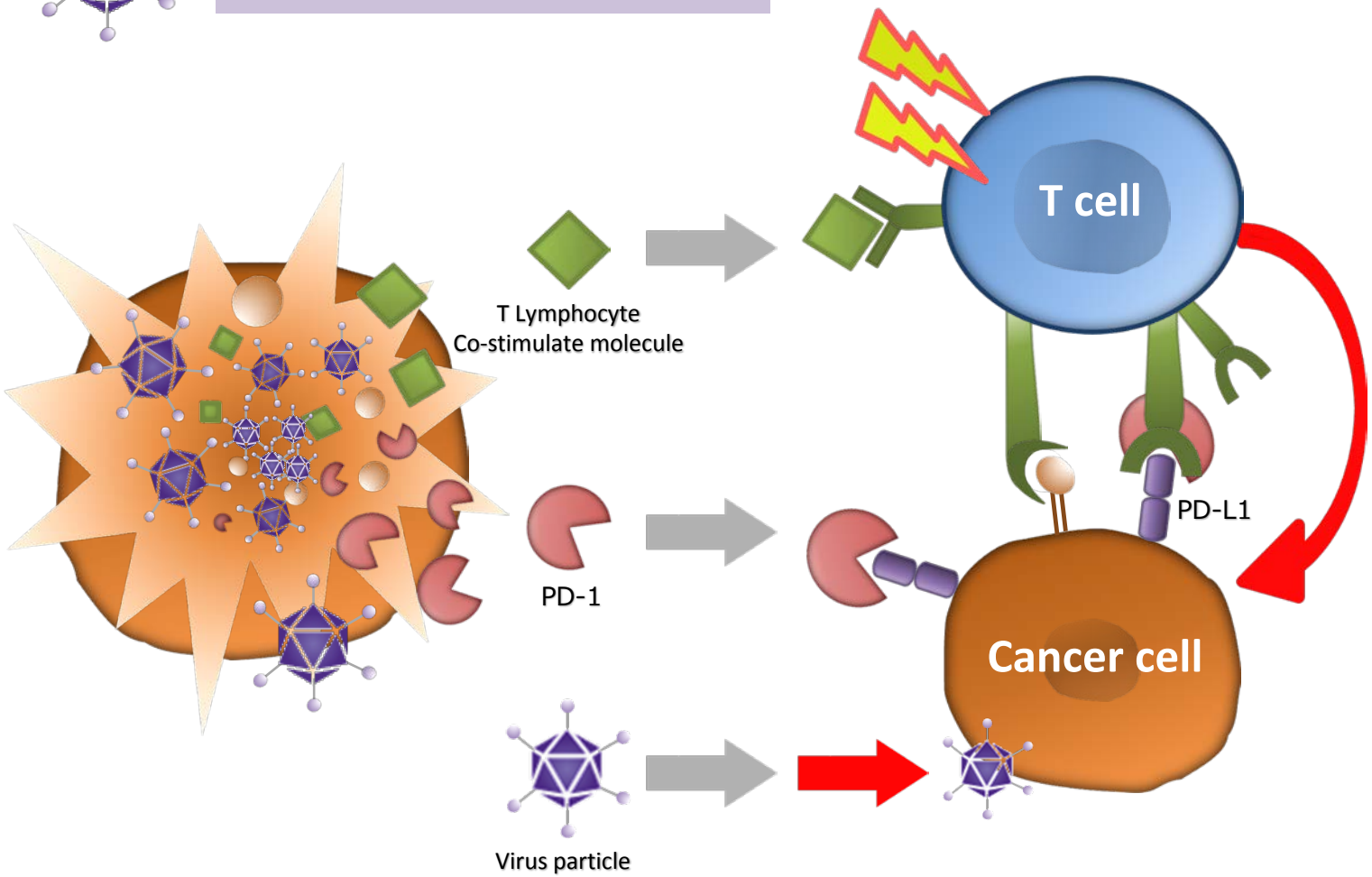
OBP	Telomelysin	h4-1BBL	hPD-1	
A社	E1A-E3	h4-1BBL		
B社	E1A-E3	hOX-40		+ anti-PD-1 Ab

Virus + **Lymphocyte stimulation** + **CPI**

Next Generation Telomelysin ②

Telomelysin®

NG Telomelysin



Immunotherapy

＋

CPI

＋

Oncolytic virus

Telomelysin project picture after 2020

Telomelysin®

Tumor type	Treatment	Country	Pre-clinical	Phase Ⅰ	Phase Ⅱ	Phase Ⅲ
Esophageal Cancer	Radiation	JP				
	Anti PD-1 Investigator initiated clinical trial				Complete	
	Radiation Investigator initiated clinical research				Complete	
	ICI	US				
	CRT					
HCC	Monotherapy	Taiwan Korea				
	ICI					
Melanoma	Monotherapy	US				
	ICI併用					
HNSCC	Radiation	JP				
Sarcoma	Radiation	JP				
NG Telomelysin Lung・Colorectal cancer	—	US				

（ICI: Immune Checkpoint Inhibitor）

Oncolys BioPharma JPX

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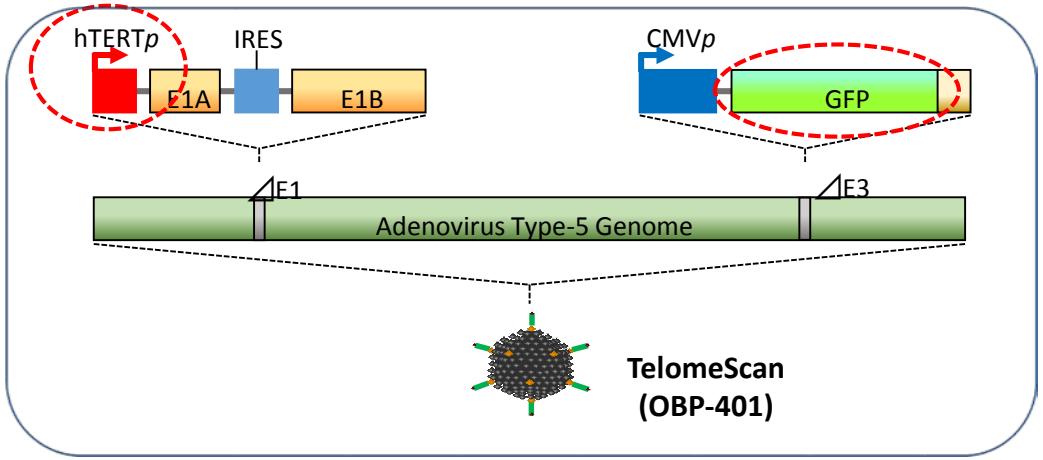
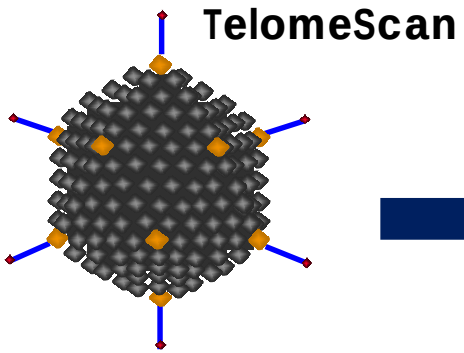
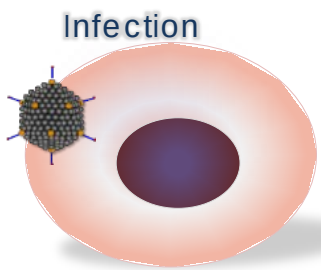
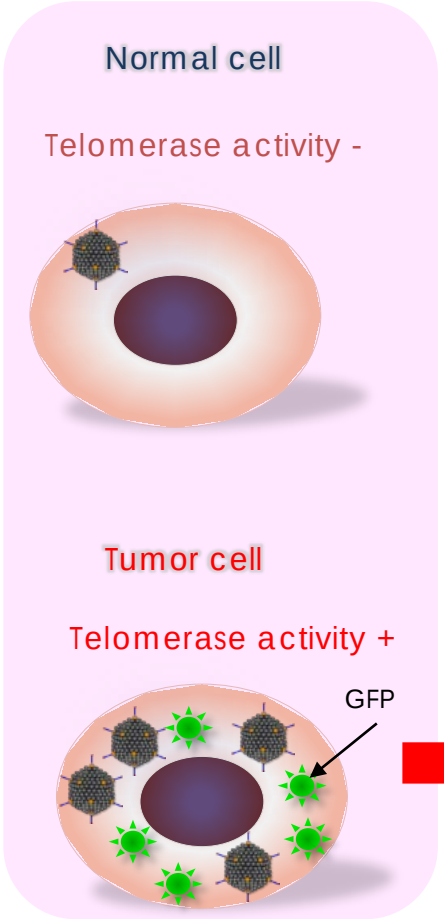
TelomeScan overview

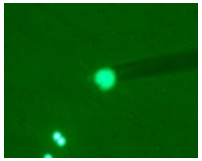
TelomeScan is a gene-modified adenovirus which replicates and express GFP when infected to telomerase activity-positive tumor cells.



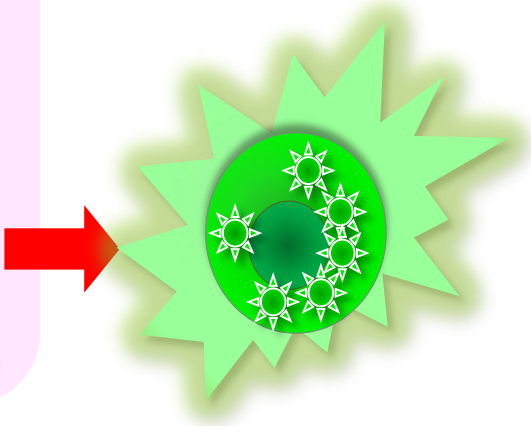








Fluorescent emission by GFP

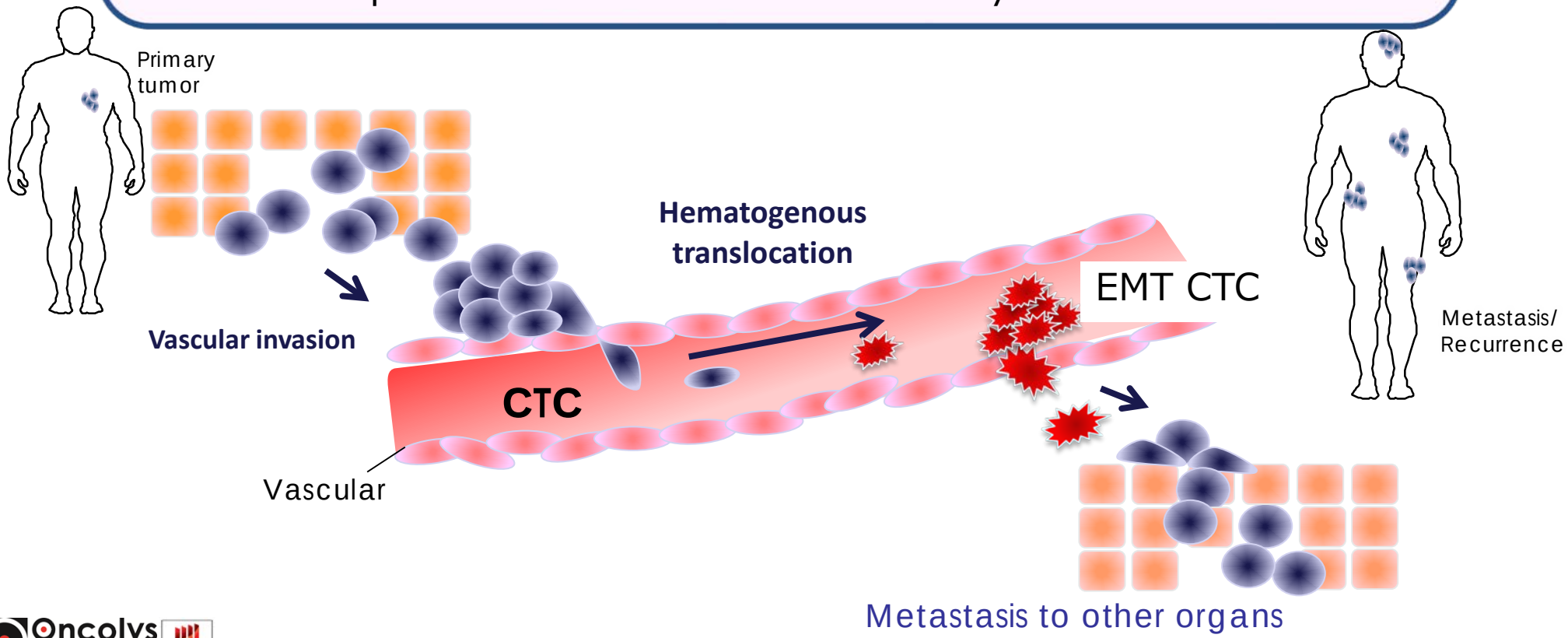


Tumor Metastasis and CTC Phenotype

1. Detection rate using tumor diagnostic markers currently available is around 30-40%.

2. PET and MRI only detect tumor cells bigger than 1cm

3. CTCs seep from tumor cells undetectable by PET and MRI



Joint research towards the practical use

- Joint research with Division of Respiratory Medicine, Juntendo University started in Nov. 2017 and promoted as a cross-sectional research project joined by medical doctors in wide range of oncology-related fields.

Juntendo University

Oncolys Biopharma

Long term targets

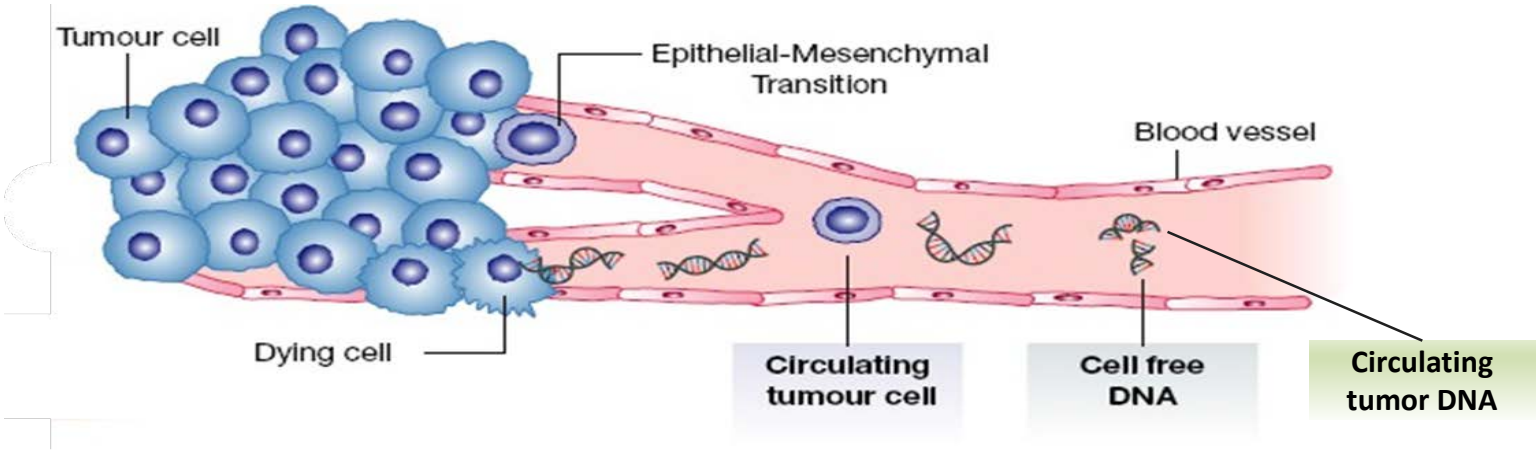
1. **Practical use in clinical settings across Japan for detection of early and recurrent tumors**
2. **Automation of tumor detection system**

Future development

1. Differentiation from ctDNA/cfDNA
2. Precision Medicine
3. New CTC application

   → HPV detection

Comparison of Liquid Biopsy



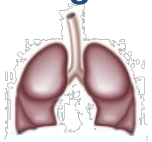
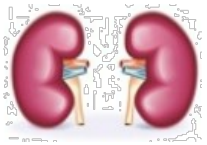
		CTC	cfDNA	ctDNA
Phenotyping	Protein	+	-	-
Genotyping	RNA	+	-	-
	DNA	+/-	+	+
Clinical Benefit	Early Detection	+/-	+	+/-
	Longitudinal Monitoring	+	+	+
	Treatment Response	+	+	+

Figure was modified from Wyatt AW and Gleave ME, EMBO Mol Med (2015)

Our Target Cancers

TelomeScan

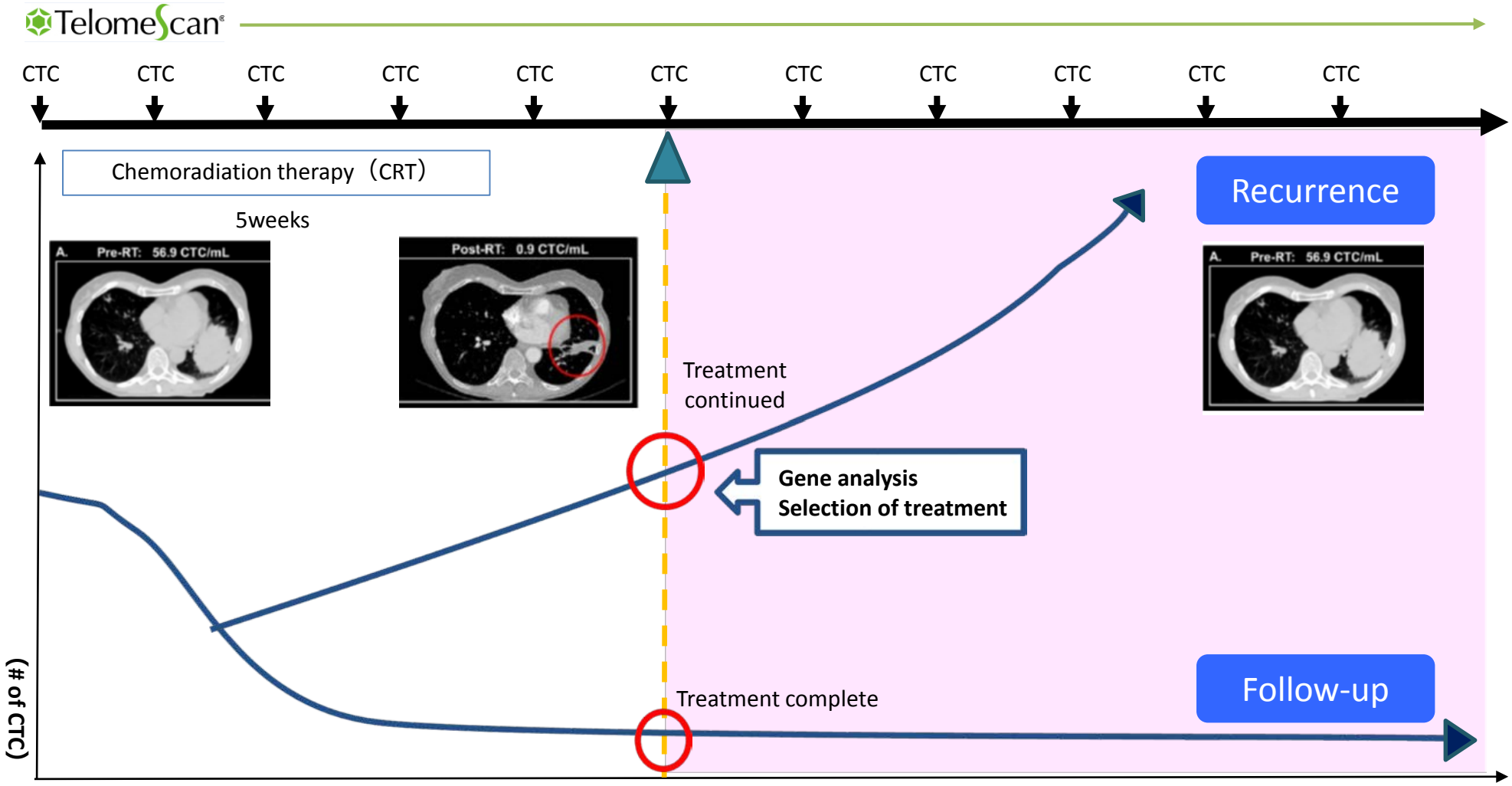
Challenge to Impossible for cf/ctDNA

Phenotyping **“PD-L1”**	Lung Ca. 	Urothelial Ca. 	RCC 	Melanoma 
Genotyping **“HPV/KRAS/BRAF/T790M”**	Cervical Ca. 	SCCHN 	Vaginal Ca. 	Anal Ca. 
RNA **“AR-V7”**	Prostate Ca. 	Breast cancer 		
Non-CTC **“PTC”**	Pancreatic Ca. 	Gastric Ca. 		

PTC : Peritoneal Tumor Cell

Application to precision medicine

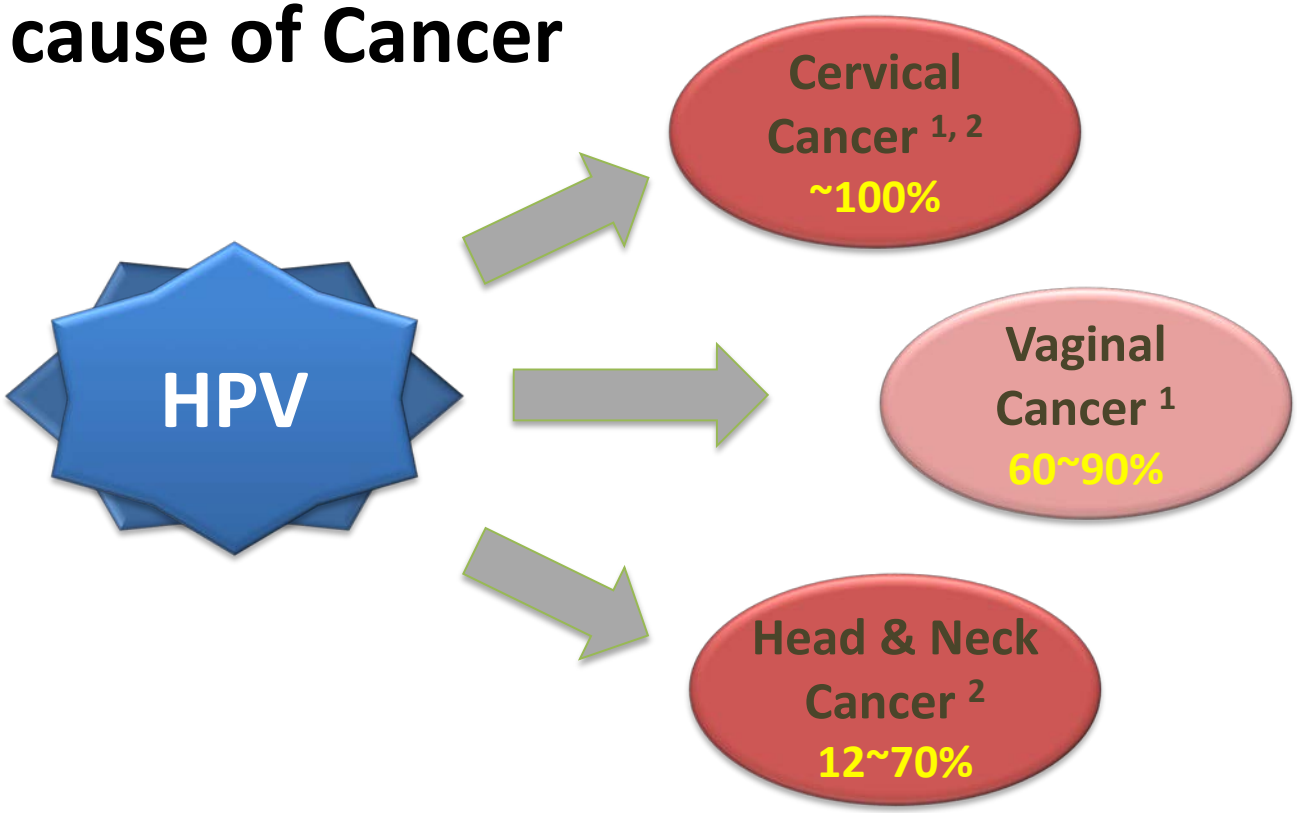
<NSCLC> Project led by University of Pennsylvania



HPV Detected in Cancer Cell

TelomeScan

HPV is the cause of Cancer



HPV is **NOT** detected in Blood Stream, but in **ONLY** CTC

1; Braaten KP et al. Rev Obstet Gynecol. (2008)
2; IARC. IARC monographs on the evaluation of carcinogenic risks to humans. Human papillomaviruses. Vol 90. Lyon, France:IARC (2007)

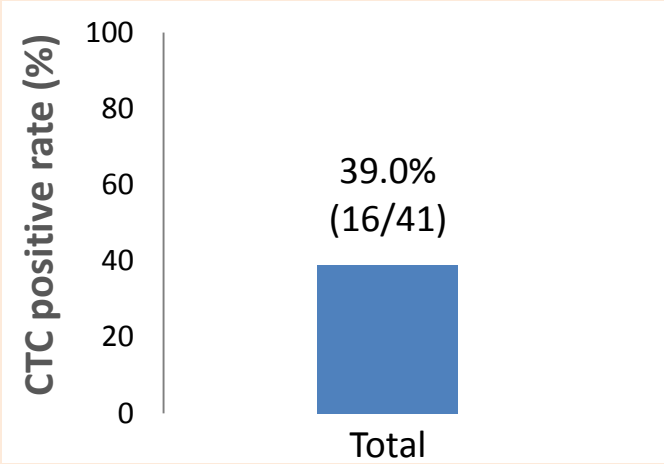
HPV Typing in CTCs

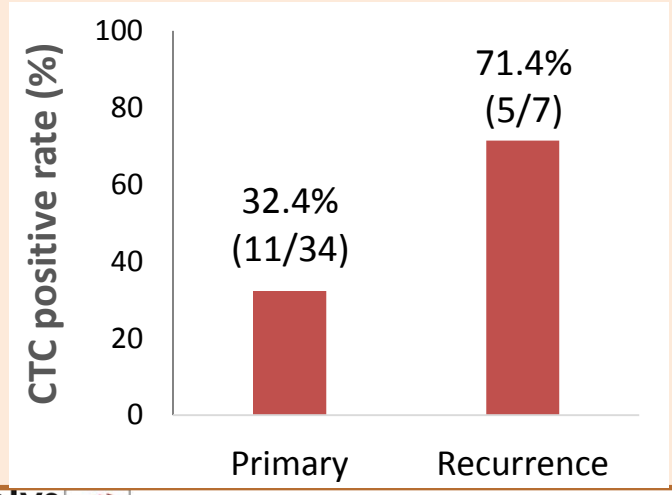
TelomeScan

Cervical Cancer

< Sensitivity >

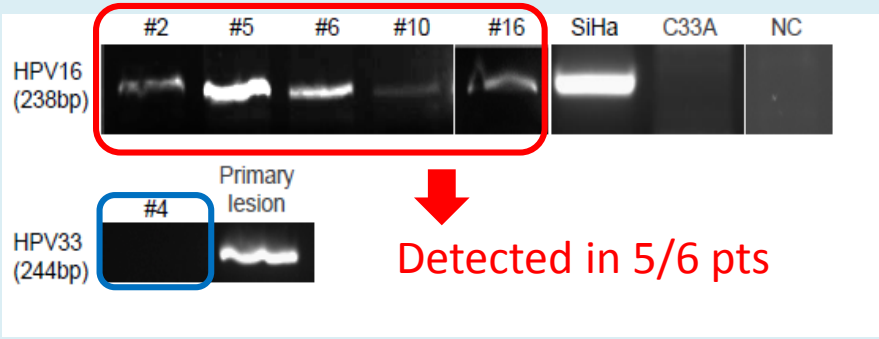
(≥1 cell/7.5ml of peripheral blood tested positive)





< HPV Typing in CTCs >

#	Stage	HPV type	
		CTC	Primary
2	IIA	16	16
4	recurrence	undetected	33
5	IB1	16	16
6	IB1	16	16
10	recurrence	16	16
16	IB1	16	16



Takakura et al., Cancer science (2017)

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Oncolys BioPharma

Oncolys' financial grounds in mid-long term

Further Growth & Business Expansion

Stronger financial grounds

New pipeline: explore and develop

Current pipieline: accelerate development

More license agreements

- New pipeline
- Next generation Telomelysin

OBP-XXXX | OBP-YYYY

New license agreements

Telomelysin® TelomeScan®

Milestone fees & virus sales based on current license agreements

Jiangsu Hengrui, Wonik Cube, Deciphera, etc.

Steady income

Co-development fund from Medigen

Oncolys BioPharma

Thank you!