INITIATIVES IN IMMUNO-ONCOLOGY

TURNING INNOVATIVE SCIENCE INTO VALUE FOR PATIENTS

R&D Meeting - December 10, 2019

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CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING INFORMATION

In this material, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas Pharma. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas' intellectual property rights by third parties.

Information about pharmaceutical products (including products currently in development) which is included in this material is not intended to constitute an advertisement or medical advice.

AGENDA

I

Immuno-oncology (I/O): A Paradigm Shift in Cancer Treatment
Kenji Yasukawa, Ph.D., President and Chief Executive Officer

II

Our I/O Strategy: Unlocking the Full Potential of the Immunity Cycle
Peter Sandor, M.D., Primary Focus Lead, Immuno-oncology

III

Building the Clinical Evidence to Support Our I/O Portfolio
Steven Benner, M.D., M.H.S., President of Development

IV

Q&A

IMMUNO-ONCOLOGY (I/O)

A Paradigm Shift in Cancer Treatment

Kenji Yasukawa, Ph.D.
President and CEO

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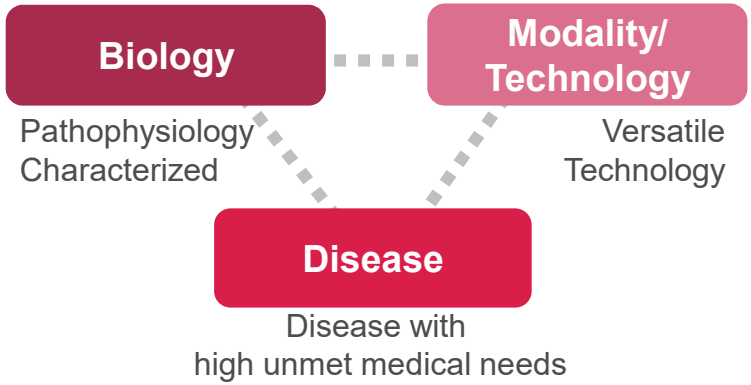
FOCUS AREA APPROACH

Focusing on the areas to turn innovative science to VALUE for patients

Focus Area approach

- Exploring multiple sets of combinations of Biology, Modality/Technology and Disease



Primary Focus

- Primary Focus is selected from Focus Areas based on;
  - Scientific evidence
  - Identified lead program
  - Potential follow-on programs

- Prioritize investment in 4 Primary Focus for now

Regeneration & blindness	**Immuno-oncology**
ASIM biology	**Mitochondria biology**

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ASIM: Antigen-specific immuno-modulation

OUR ACHIEVEMENTS IN ONCOLOGY TO DATE GIVE US CONFIDENCE IN PURSUING I/O

		Capability	Candidate	Product
Vertical start-up of oncology research	**2006** | Designated "Oncology" as a primary therapeutic area	Research for tyrosine kinase inhibitors		
	2007 | Acquired Agensys	Antibody foundation ADC technology	enfortumab vedotin ASP1235	
Expansion of foundation as a priority therapeutic area	**2009** | Entered into agreement with Medivation (acquired by Pfizer) to co-develop and co-commercialize enzalutamide			
	2010 | Acquired OSI	Expansion of R&D and marketing capabilities in oncology		**TARCEVA** (erlotinib)
	2015 | Started collaborative research program with Potenza	**I/O research started**		**XTANDI** (enzalutamide) **launched**
	2016 | Acquired Ganymed		zolbetuximab ASP1650	
Expansion of I/O pipeline	**2018** | Entered into exclusive licensing agreement with Tottori University for immunostimulating gene loading oncolytic virus	Oncolytic virus	ASP9801	
	2018 | Acquired Potenza		ASP8374 ASP1948 ASP1951	**XOSPATA** (gilteritinib) **launched**
	2019 | Entered exclusive licensing agreement with RIKEN for aAVC technology in oncology area	aAVC technology	ASP7517	

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Red: Related to immuno-oncology

ADC: Antibody-drug conjugate, aAVC: Artificial adjuvant vector cell, I/O: Immuno-oncology

OUR STRONG COMMITMENT TO, AND LEADERSHIP IN, ONCOLOGY SERVES AS THE FOUNDATION FOR OUR INITIATIVES IN I/O

- Prostate cancer
- Acute myeloid leukemia
- Urothelial cancer
- Gastric and gastroesophageal junction adenocarcinoma
- Pancreatic adenocarcinoma
- Testicular cancer

Phase 1	Phase 2	Phase 3	Filed	Approved/Launched
ASP1235/AGS62P1 (Acute myeloid leukemia)	**zolbetuximab** (Pancreatic adenocarcinoma)	**enzalutamide** (Non-metastatic hormone-sensitive prostate cancer)	**enzalutamide** (Metastatic hormone-sensitive prostate cancer: US, JP, EU)	**XTANDI (enzalutamide)** (Castration-resistant prostate cancer)
ASP8374/PTZ-201	**ASP1650** (Testicular cancer)	**gilteritinib** (Acute myeloid leukemia)	**enfortumab vedotin** (Metastatic urothelial cancer, platinum and PD1/L1 inhibitor pretreated: US)	**XOSPATA (gilteritinib)** (Relapsed or refractory acute myeloid leukemia)
ASP1948/PTZ-329		**enfortumab vedotin** (Urothelial cancer)		
ASP1951/PTZ-522		**zolbetuximab** (Gastric and gastroesophageal junction adenocarcinoma)		
ASP9801				
ASP7517				

I/O programs

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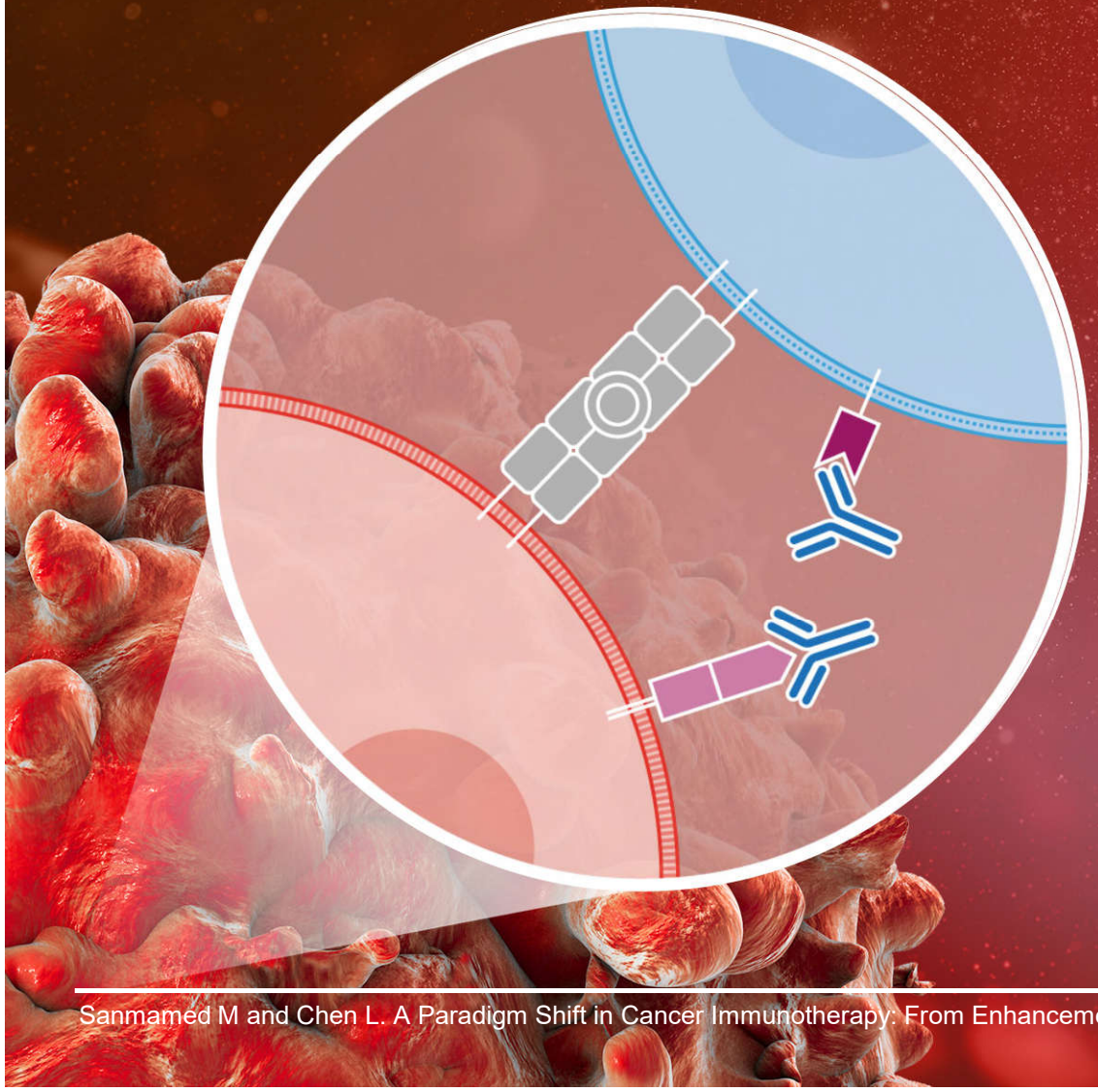
I/O: immuno-oncology

IMMUNO-ONCOLOGY – IN PARTICULAR, CHECKPOINT INHIBITORS – REPRESENTS A PARADIGM SHIFT IN CANCER TREATMENT



Unique features of checkpoint inhibitors (CPIs)

- Durable responses
- Efficacy demonstrated across multiple tumor types
- Good safety profiles in general
- Efficacy correlates with presence of tumor infiltrating lymphocytes

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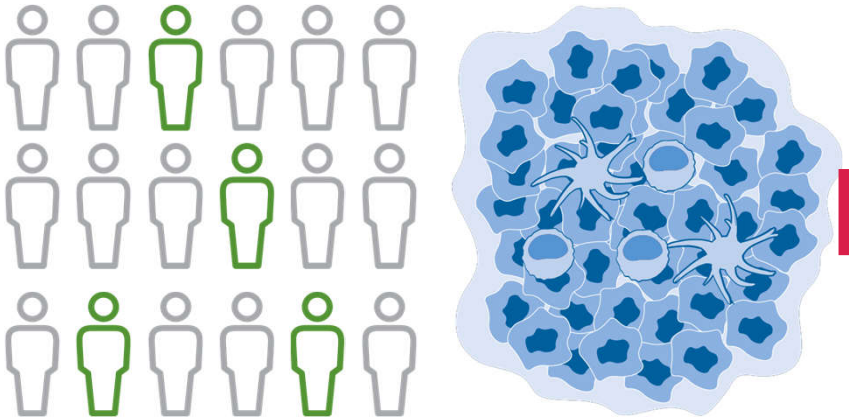
Sanmamed M and Chen L. A Paradigm Shift in Cancer Immunotherapy: From Enhancement to Normalization. Cell. 2018. 175(2);313–326.

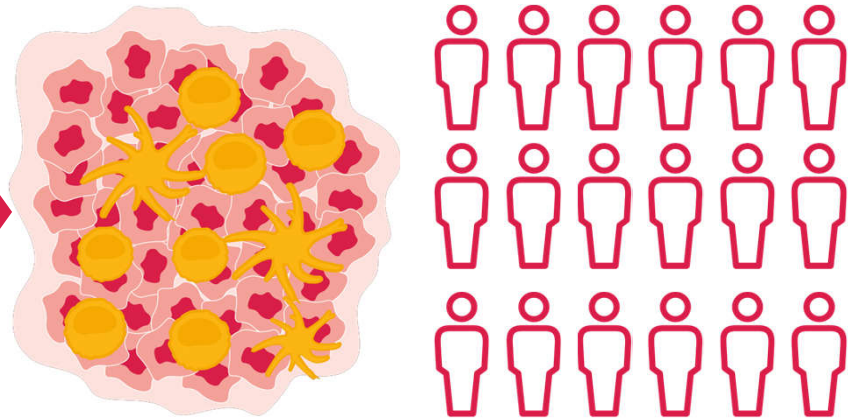
GOAL OF OUR I/O INITIATIVES

Developing therapies for the majority of patients who do not respond to current CPIs

Current



Our Goal



Only about **20%**
of patients with various types of cancer respond to approved CPIs as monotherapy[1]

We aim to:

- Create I/O drugs with different MoAs
- Improve efficacy when used alone or in combination with CPIs or other therapies

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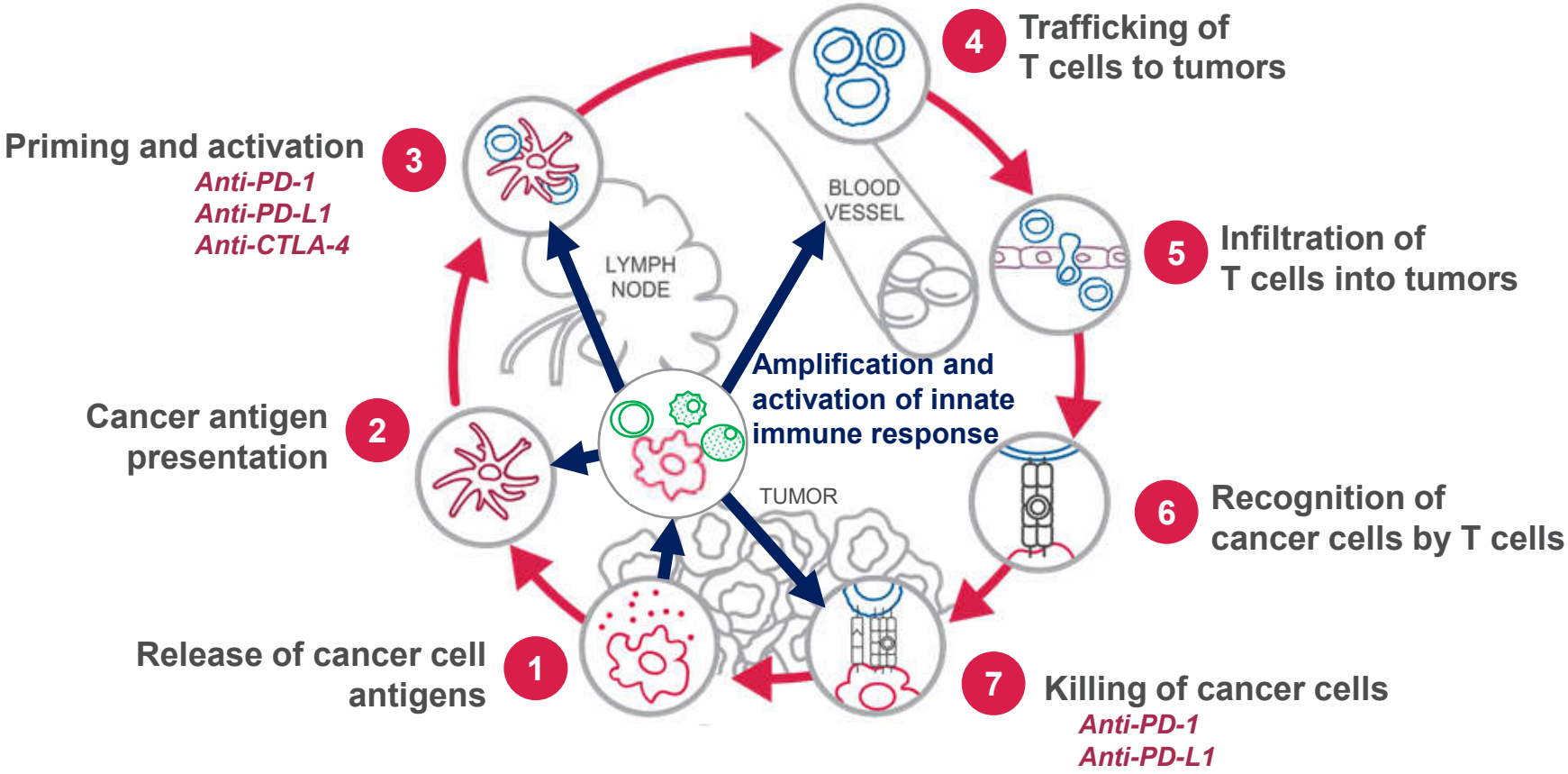
I/O: immuno-oncology, CPI: Checkpoint inhibitor, MoA: Mechanism of action

1: Kourie HR and Klastersky JA. Curr Opin Oncol. 2016. 28 (4): 306-13.

UNLOCKING THE POWER OF THE CANCER IMMUNITY CYCLE



→ Innate immune system → Acquired immune system

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Source: Chen DS & Mellman I. Immunity. 2013. 39(1);1-10. and Demalia O. et al Nature 2019. 574(7776), 45-56; "Innate immunity" concept added

OUR I/O STRATEGY

Unlocking the Full Potential of the Immunity Cycle

Peter Sandor, M.D.
Primary Focus Lead, Immuno-oncology

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OUR VISION IS TO DELIVER CURATIVE TREATMENT OPTIONS FOR PATIENTS WITH CANCER

- Cancer is a complex disease. Cancer cells have many ways to hide from the immune system and drive their extensive growth
- To find and kill cancer, we need to unlock multiple steps of the immune cycle
- Our goal is to establish a pipeline of multi-functional drugs which can re-program the immunity cycle and enable the immune system to eliminate the cancer
- We are focusing our efforts on multi-functional approaches either as monotherapy, or combinations with other I/O and non-I/O therapies, including our pipeline programs

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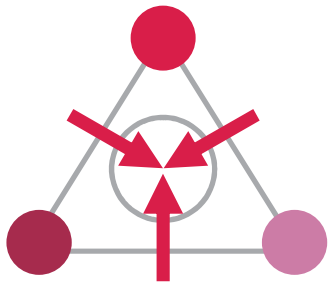
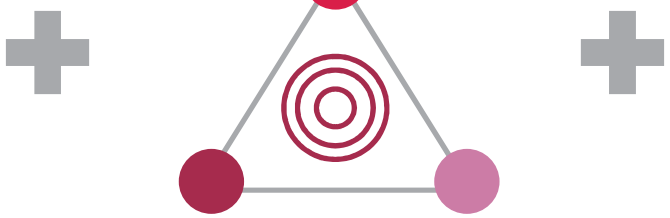
I/O: Immuno-oncology

HOW DO WE BUILD A DIFFERENTIATED I/O PIPELINE?

FOCUS



Establish core capabilities



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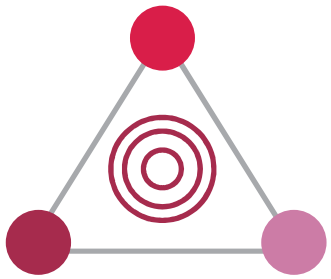
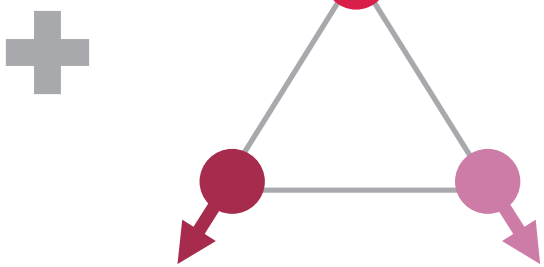


Build sustainable pipeline flow



EXPAND

Add synergistic, novel areas

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WE HAVE BUILT IN-HOUSE RESEARCH AND DEVELOPMENT CAPABILITIES

1

Tsukuba Research Center and Boston Innovation Hub
- Innovation acquisition (network in the US and Japan)
- Strong pharma capability with experienced experts in drug discovery

2

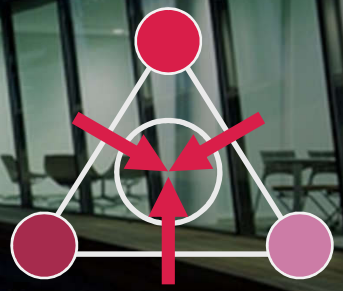
Translational Science Hub in Cambridge, Massachusetts
- Bridges discovery and clinical development
- Designs combinations and patient selection

3

Dedicated team to design and run first-in-human (FIH) studies and rational combination programs

4

Strong collaboration between the Therapeutic Area development teams and Primary Focus Lead to create an integrated and long-term strategy



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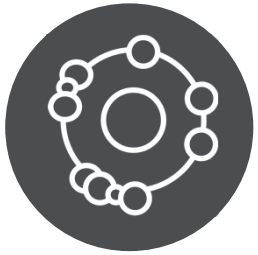
Background photo: Tsukuba Research Center

WE ARE BUILDING STRONG MULTI-FUNCTIONAL PLATFORMS TO LEVERAGE

Novel immune checkpoint

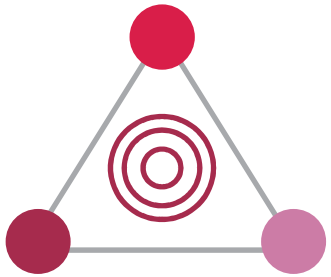
Oncolytic virus

Vaccination



Cell therapy

Combinations across our pipeline



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WE HAVE BUILT PARTNERSHIPS WITH THE BEST EXTERNAL INNOVATORS

Collaborations and partnerships with a broad range of academia and biotech since 2015 – *for example:*

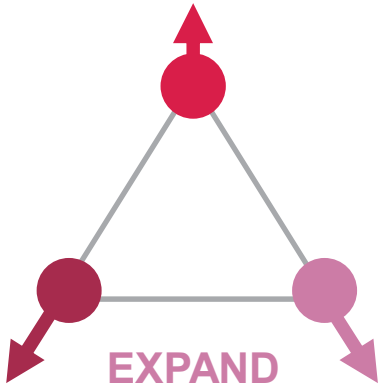
- Tottori University
- MD Anderson Cancer Center
- Riken
- Anaeropharma
- Xencor

Acquisitions – *for example:*

- Potenza Therapeutics (Dec 2018) further to exclusive R&D collaboration in 2015: three INDs (ASP8374, ASP1951 and ASP1948) now in Phase 1 development
- Universal Cells (Feb 2018): acquired world-leading capabilities in cell therapies

Driven by external innovation, venture and business development teams in Boston and Bay Area

- Established AIM Innovation Hub in Cambridge, Mass. (US)
- Sponsoring LabCentral's incubator in Cambridge, Mass. (US)
- Funding early innovation through AVM in Bay Area, Calif. (US)



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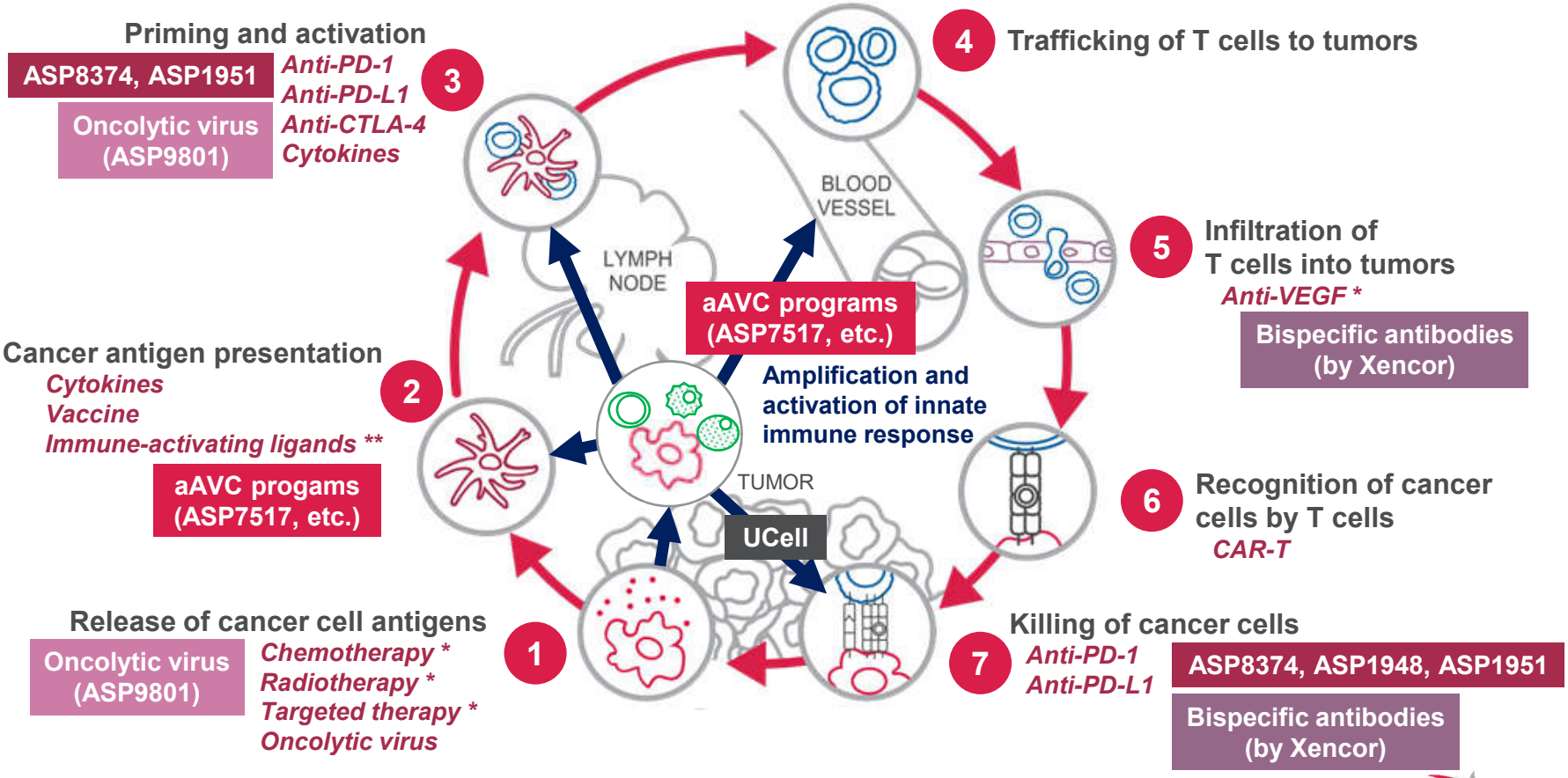
IND: Investigational New Drug, AIM : Astellas Innovation Management, AVM : Astellas Venture Management

UNLOCKING THE POWER OF THE CANCER IMMUNITY CYCLE WITH MULTI-FUNCTIONAL MODALITIES

*Astellas' pre-clinical and clinical research spans the **full cancer immunity cycle***



Source: Chen DS & Mellman I. Immunity. 2013. 39(1);1-10. and Demalia O. et al Nature 2019. 574(7776), 45-56. "Innate immunity" concept and Astellas immuno-oncology assets acting on each step added, ***Italic**: Existing agent/therapy acting each step (revised from the source reflecting the latest situations), * Not immuno-oncology agent/therapy, ** Not marketed yet*
Experimental assets. No claims regarding proof of concept or clinical efficacy are asserted or implied. aAVC: Artificial adjuvant vector cell, UCell: Universal Cell

BUILDING THE CLINICAL EVIDENCE

To Support Our I/O Portfolio

Steven Benner, M.D., M.H.S.
President of Development

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THROUGH STRATEGIC EXTERNAL COLLABORATIONS, WE HAVE ESTABLISHED A ROBUST AND COMPETITIVE DEVELOPMENT-STAGE I/O PORTFOLIO

Multiple assets in clinical stage including novel I/O programs

Compound	Modality/Mechanism	Origin/Partner	Target tumor	Current stage	
				Preclinical /Research	Clinical Phase 1
ASP8374	Anti-TIGIT antibody	POTENZA therapeutics *	(To be determined)		
ASP1948	Anti-NRP1 antibody	POTENZA therapeutics *	(To be determined)		
ASP1951	GITR agonistic antibody	POTENZA therapeutics *	(To be determined)		
ASP9801	Oncolytic virus	Tottori University **	(To be determined)		
ASP7517	WT1 loaded artificial adjuvant vector cell (aAVC)	RIKEN **	Acute myeloid leukemia, myelodysplastic syndrome (as the first targets)		
(Not disclosed)	Other tumor antigens loaded aAVCs	RIKEN **	(Not disclosed yet)		
(Not disclosed)	Bispecific antibodies	xencor **	(Not disclosed yet)		

* Acquired in 2018 (currently their programs classified into in-house ones), ** Programs developed under joint research

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I/O: Immuno-oncology

THREE CLINICAL PROJECTS TARGETING PATIENTS NON-RESPONSIVE TO EXISTING THERAPIES IN PHASE 1 DEVELOPMENT

Advancing immunomodulating therapies with novel mechanisms of action

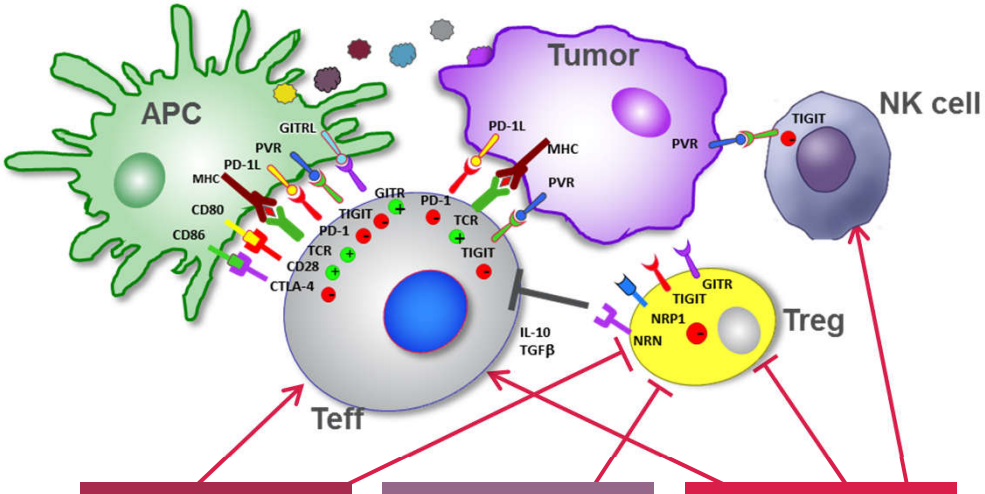
Strategy

- Harnessing the immune system to treat intractable cancers

Acquisition of Potenza Therapeutics

- In 2015, Astellas and Potenza Therapeutics entered an exclusive R&D collaboration to advance immunomodulating therapies in oncology with novel mechanisms of action, targeting immune checkpoint pathways, co-stimulatory signals and regulatory T-cells
- In Dec 2018, Astellas announced its acquisition of Potenza Therapeutics

Overview of programs



Enhance T cell response	Induce Treg instability	Release brake
GITR agonistic antibody (T cell priming & co-stimulation)	Anti-NRP1 antibody (Treg function inhibitor)	Anti-TIGIT antibody (Immune checkpoint inhibitor)
ASP1951	**ASP1948**	**ASP8374**

→ Enhance ⊣ Inhibit

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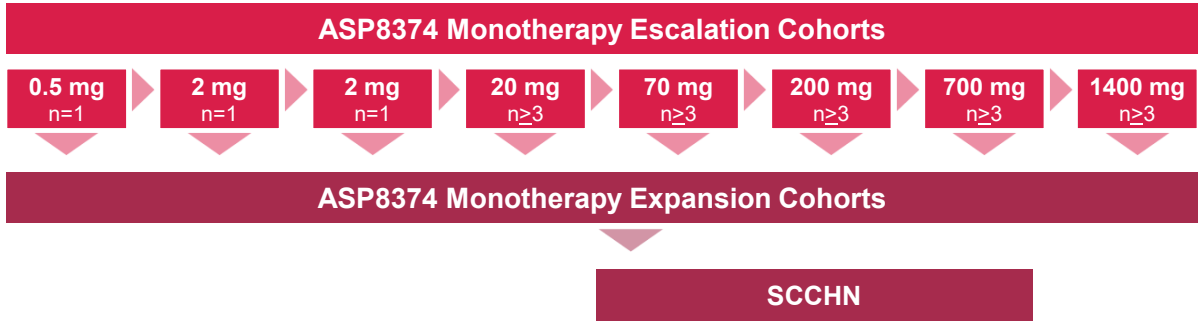
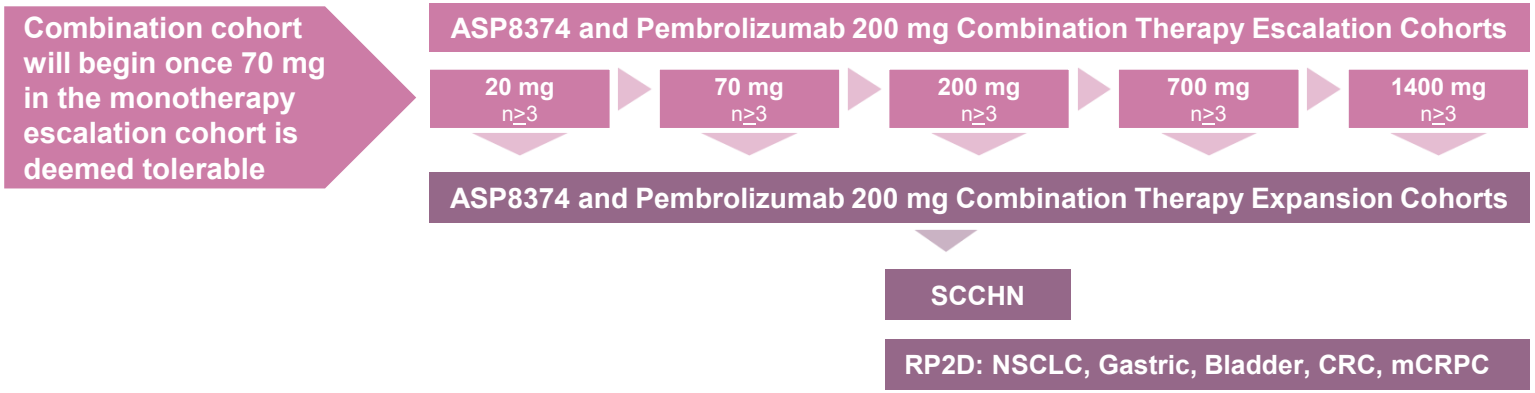
APC: Antigen-presenting cell, NK: Natural killer, Teff: Effector T cell, Treg: Regulatory T cell, GITR: Glucocorticoid-induced TNFR-related protein, NRP1: Neuropilin-1, TIGIT: T-cell immunoreceptor with Ig and ITIM domains

DEVELOPMENT STRATEGY: ASP8374, ASP1948 & ASP1951





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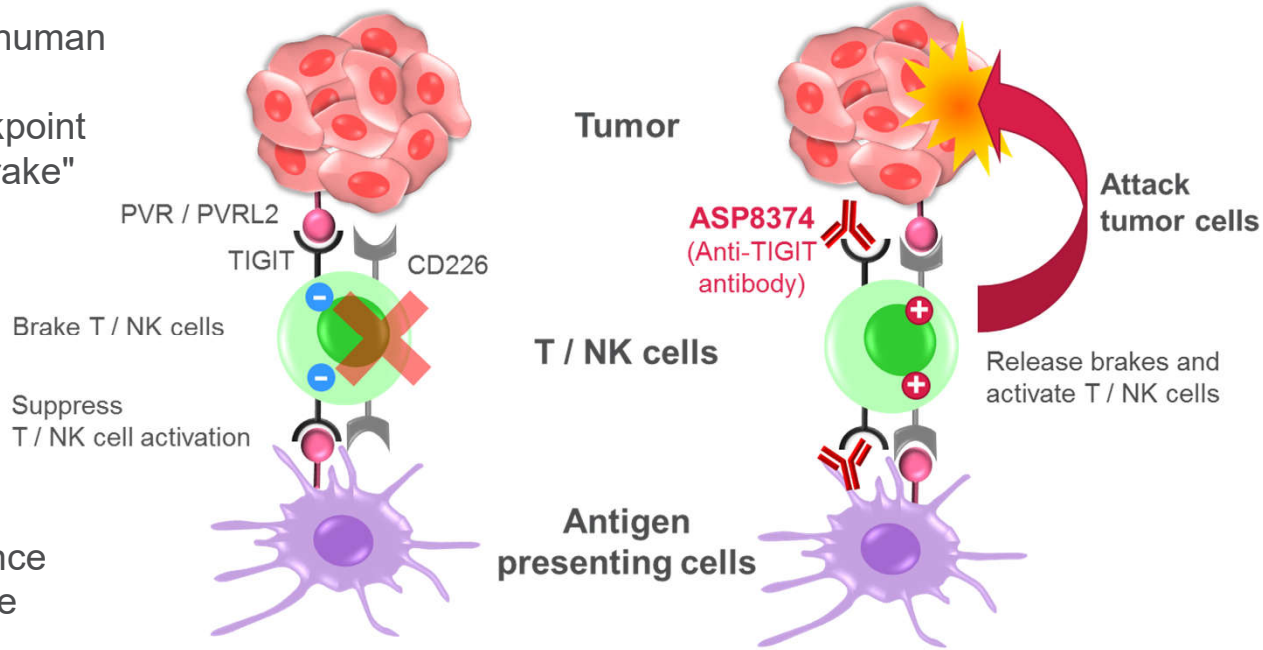
SCCHN: Head-and-neck squamous cell cancer, RP2D: Recommended Phase 2 dose, NSCLC: Non-small cell lung cancer, CRC: Colorectal cancer, mCRPC: Metastatic castration-resistant prostate cancer

ANTI-TIGIT ANTIBODY: ASP8374

Mechanism of action

- ASP8374 is a high affinity fully human anti-TIGIT IgG4 antibody, being developed as an immune checkpoint inhibitor (CPI) to release the "brake" mediated by the TIGIT pathway
- TIGIT is expressed solely on lymphocytes and limits T cell inflammation
- TIGIT represents a novel immune checkpoint target for therapeutic antagonistic monoclonal antibodies to enhance the anti-tumor immune response



Development status

- Currently in Phase 1 clinical trials in monotherapy and combination with anti-PD-1 antibody

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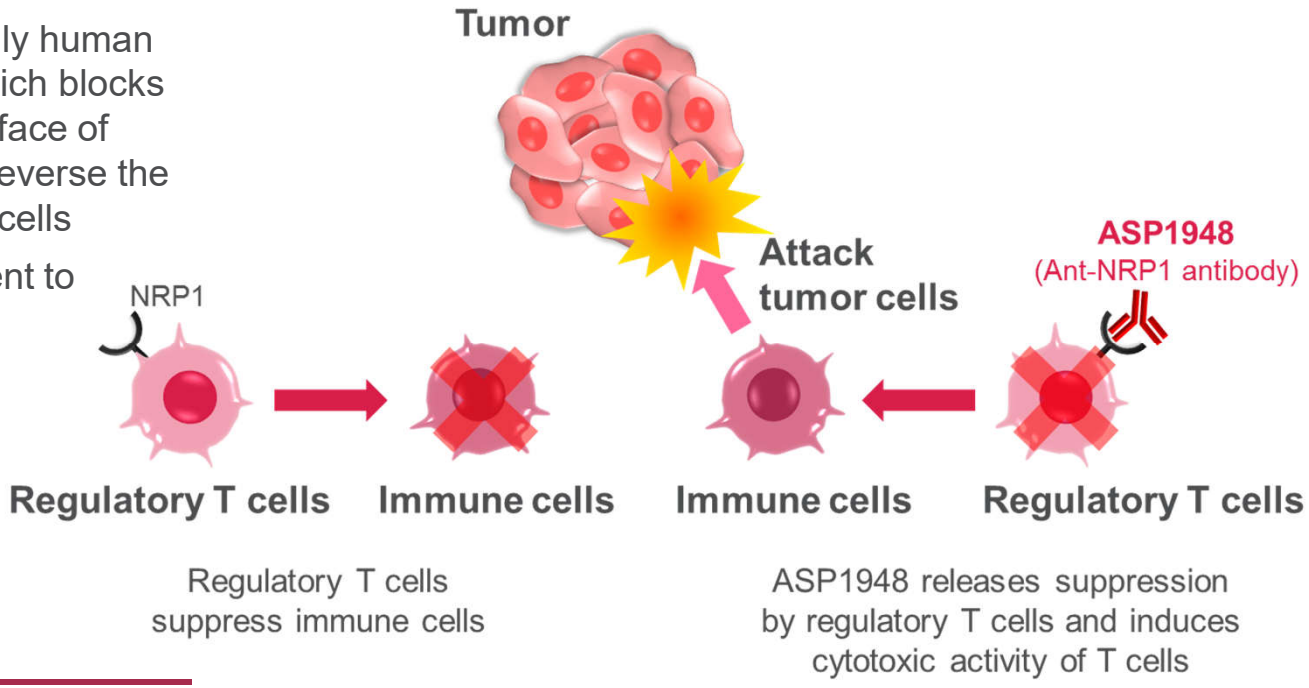
TIGIT: T-cell immunoreceptor with Ig and ITIM domains, IgG4: Immunoglobulin G4, NK: Natural killer

ANTI-NRP1 ANTIBODY: ASP1948

Mechanism of action

- ASP1948 is a high affinity, fully human anti-NRP1 IgG4 antibody, which blocks ligand interactions on the surface of regulatory T cells (Tregs) to reverse the suppressive activity of these cells
- NRP1 is required and sufficient to promote Treg survival and function *in vitro* and *in vivo*
- Antagonists to NRP1 can suppress Treg activity and demonstrate anti-tumor activity



Development status

- Currently in Phase 1 clinical trials in monotherapy and combination with anti-PD-1 antibody
- Potential as first agent in clinic to target NRP1 as an I/O treatment

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NRP1: Neuropilin-1, IgG4: Immunoglobulin G4, I/O: Immno-oncology

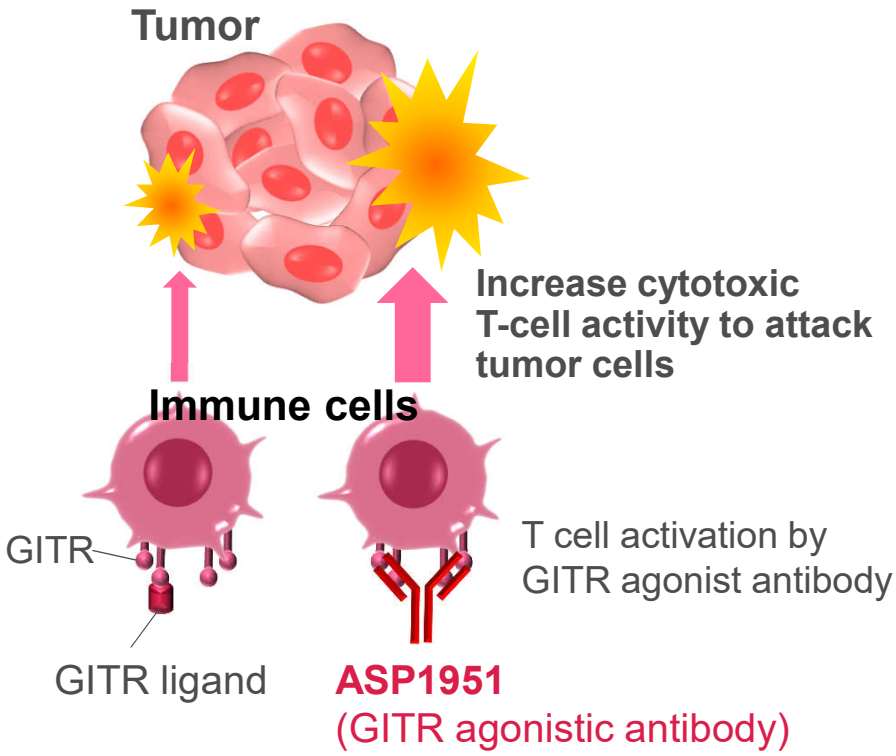
GITR AGONISTIC ANTIBODY: ASP1951

Mechanism of action

- ASP1951 is a high affinity, fully human IgG4 GITR agonistic antibody in a tetravalent monospecific (TM) format that activates GITR signalling
- GITR is a costimulatory molecule belonging to the tumor necrosis factor receptor superfamily
- The TM antibody format has the ability to effectively engage the receptor and produce an efficacious costimulation signal better than that of a traditional bivalent antibody

Development status

- Currently in Phase 1 clinical trials in monotherapy and combination with anti-PD-1 antibody



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IgG4: Immunoglobulin G4, GITR: Glucocorticoid-induced TNFR-related protein

NEXT STEPS: ASP8374, ASP1948, ASP1951

Complete ongoing Phase 1 trials, establish RP2D as monotherapy and in combination with anti-PD-1 antibodies supporting future studies

Further evaluation of best combination including internal assets is ongoing

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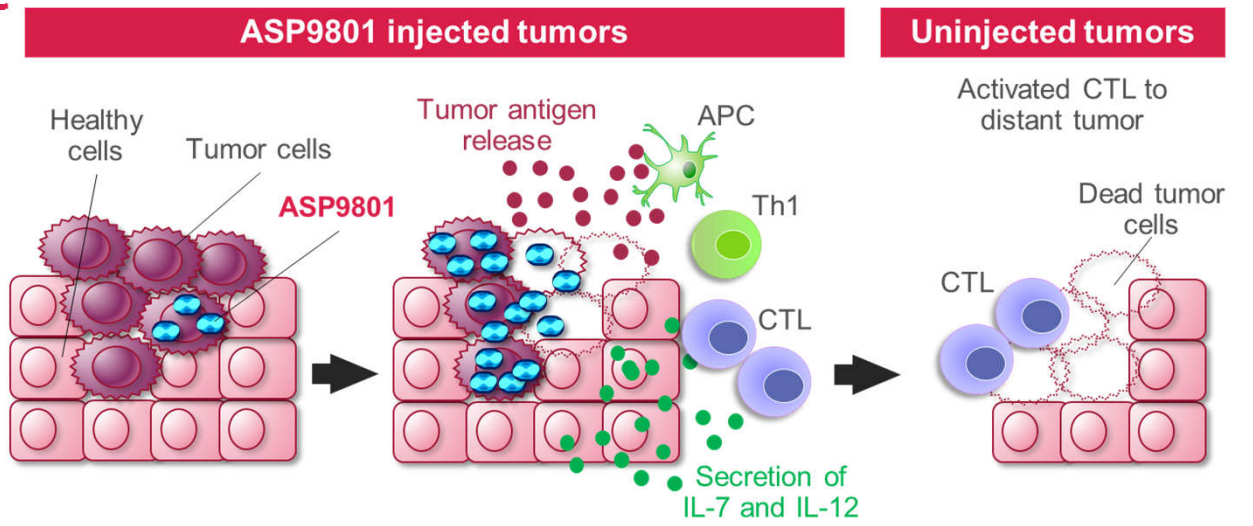
RP2D: Recommended Phase 2 dose

OUR ONCOLYTIC VIRUS PROGRAM ASP9801 HAS RECENTLY ENTERED PHASE 1 DEVELOPMENT

Mechanism of action

- Attenuated recombinant oncolytic vaccinia virus that expresses both IL-7 and IL-12 to induce an antitumor immune response
- Induction of systemic anti-tumor immune response through secretion of human IL-7 and human IL-12 in tumor, T-cell proliferation and CTLs activation
- Local tumor destruction through vaccinia virus resulting in enhancement of tumor antigen presentation



1) Local tumor destruction by tumor-selective virus replication
2) Tumor antigen release and secretion of IL-7 and IL-12 => Activation and proliferation of T cells

3) Induction of systemic anti-tumor immune responses

Target indication

- Advanced/metastatic solid tumors (cutaneous/sub-cutaneous and visceral)

Tottori University

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IL: Interleukin, APC: Antigen-presenting cell, Th1: Helper T cell, CTL: Cytotoxic T lymphocyte

ASP9801 DEVELOPMENT PROGRAM

Development status / Next steps

Concurrent development in US, Japan and China

US IND Open, enrollment underway for US Phase 1 study

Japan and China studies planned

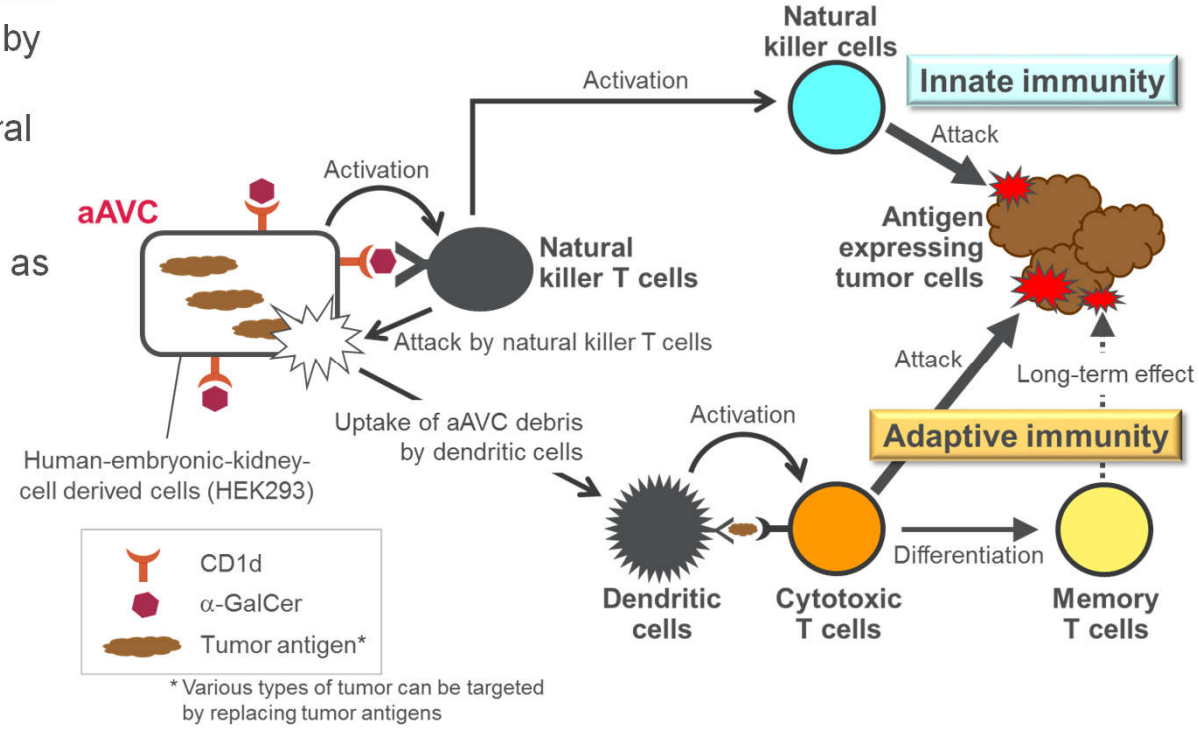
IND: Investigational New Drug application

THE aAVC PLATFORM ELICITS AN INNATE AND ADAPTIVE IMMUNE RESPONSE

Licensing agreement with RIKEN for aAVC technology as a novel and promising I/O platform

Mechanism of action

- Expects to show anti-tumor effects by activating both the:
  - ✓ "Innate immunity" - through natural killer cells
  - ✓ "Adaptive immunity" - through antigen-specific cytotoxic T Cells as well as long-term effects through long-lived memory T cells
- Unlike peptide vaccines, aAVC are loaded with full-length cancer antigens and are applicable for many patients regardless of their HLA types
- Has potential to target many tumor types by changing tumor antigen loaded into aAVC platform



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aAVC: Artificial adjuvant vector cell, I/O: Immuno-oncology, HLA: Human leukocyte antigen, α-GalCer: alpha-galactosylceramide, CD1d: Cluster of differentiation 1d

LEAD aAVC PROGRAM: ASP7517

ASP7517 profiles

- aAVC loading WT1, a tumor antigen highly expressed in acute myeloid leukemia
- FSFT in Phase 1/2 study in acute myeloid leukemia and myelodysplastic syndrome achieved in Oct 2019

Development status / Next steps

Dose escalation portion of Phase 1/2 study currently underway in Japan

US and China IND submissions planned for 2020

Dose expansion portion of Phase 1/2 study to be conducted globally (Japan, US, China and Canada)

Solid tumor studies are being planned

Potential for combination therapy with internal and external assets is being explored

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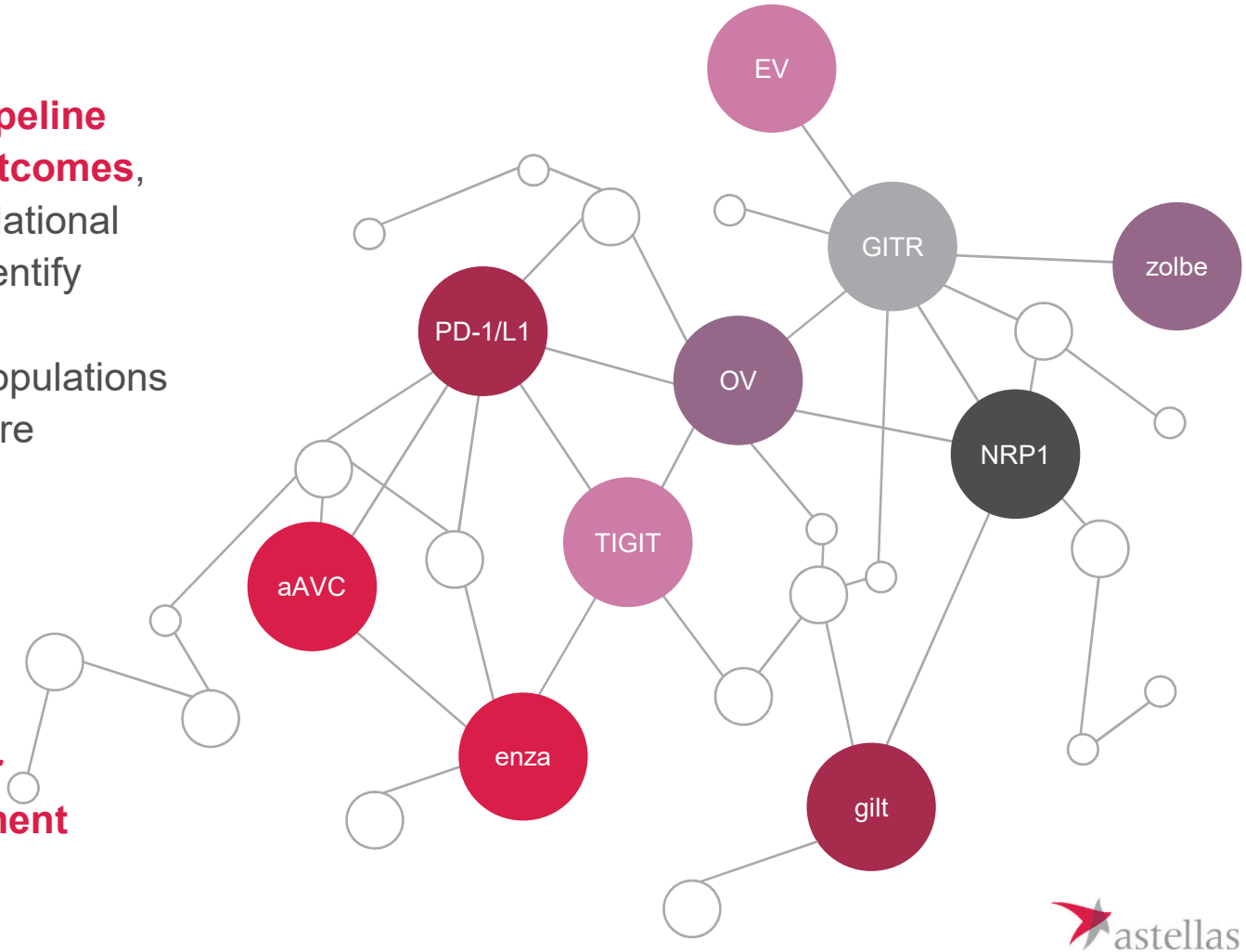
aAVC: Artificial adjuvant vector cells, FSFT: First subject first treatment, IND: Investigational New Drug application

OUR DIVERSE EARLY-STAGE I/O PIPELINE IS ENABLING US TO EXPLORE COMBINATION STRATEGIES

In order to **enrich our pipeline and improve patient outcomes**, we are building our translational science capabilities to identify biomarkers, select target indications and patient populations for treatments, and explore combination strategies

Our patient selection and combination strategy is based on connecting MoAs and **patient tumor immune microenvironment**



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I/O: Immuno-oncology, MoA: Mechanism of action

CONCLUSION

Astellas' strategy is strong in I/O, guided by a focused dedication to help address unmet patient needs

We remain committed to taking innovative approaches; through our in-depth understanding of cancer biology, we are building an I/O pipeline targeted to unlock multiple immune activation steps with multi-functional modalities

We have built a strong foundation through internal and external efforts, partnering and M&A

We continue to move forward our clinical and pre-clinical pipeline with our outstanding team members and partners to bring innovative medicines and value to patients worldwide

astellas

I/O: Immuno-oncology, M&A: Merger and acquisition

Turning innovative science
into value for patients,
by maximizing
the potential of
immuno-oncology
astellas

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