ASKAT

A Novel Immuno-Oncology Therapy

EP4 Antagonists
AAT-007/grapiprant and AAT-008

February 2026

Non-confidential Information

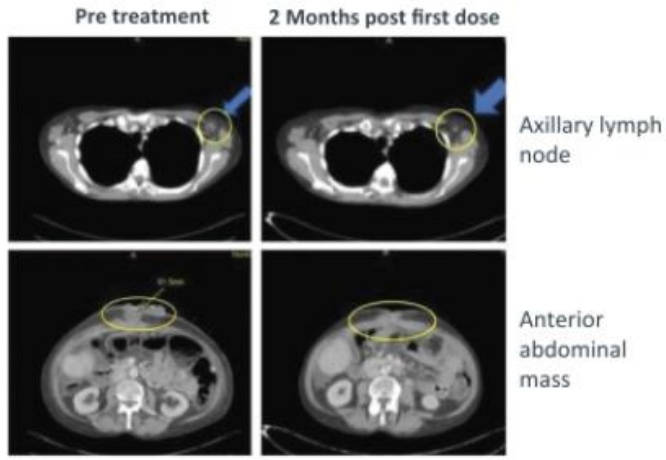
Contents

1. Executive Summary - General -

- AskAt owns two proprietary antagonists of prostaglandin E_2 (PGE_2) receptor 4 (EP4), AAT-007 (clinical stage) and AAT-008 (non-clinical stage) with mutually different chemical core-structures.
- AAT-007 and AAT-008 are potent and selective antagonists of EP4 with pA_2 values for human of 8.32 and 8.97, respectively.
- One each of CR and PR was demonstrated for patients with microsatellite-stable colorectal cancer (MSS-CRC) in combination with anti-PD-1 antibody in Phase 1 study.
- Oral AAT-007 and AAT-008 demonstrated both analgesic and antitumor effects in animal models. Combination of AAT-007 or AAT-008 with anti-PD-1 antibody potentiated antitumor effects in animal models.
- Safety of AAT-007 and AAT-008 was confirmed by safety pharmacology and toxicology studies in rats and dogs.
- Key Intellectual Properties
  - AAT-007 crystal forms: effective until March 1, 2026
  - AAT-007 and AAT-008 cancer use: effective until April 22, 2030
  - AAT-007 combination use: effective until April 16, 2039
  - AAT-007 synthesis, and crystal form: effective until July 11, 2039

1. Executive Summary - AAT-007/grapiprant -

- AAT-007/grapiprant in clinical Studies
  - Safe and well-tolerated in pain and oncology clinical studies with >1,000 human subjects
  - Proof of concept for osteoarthritis (OA) pain was achieved in Phase 2 studies
  - In the oncology clinical study, one case each of CR* and PR** was demonstrated for MSS-CRC when combined with pembrolizumab (see Figures below and Page 9)
  - Marketed worldwide for the treatment of pain and inflammation of OA in dogs



*: Complete response
**: Partial response

Figures are representative abdominal CT scan images of the patient showing CR.

- The patient who reached a CR had received five prior lines of therapy. This highly refractory patient's tumor also exhibited low tumor mutational burden, or TMB.
- Tumor response was observed soon after commencement of dosing with AAT-007. A significant shrinkage of 48% of the tumor size was observed by CT scan after approximately two months of combined therapy.
- With additional cycles of treatment, evidence of tumor in this patient disappeared and the patient was classified as a complete responder.

ESMO Immuno-Oncology Annual Congress 2022
https://cslide.ctimeetingtech.com/immuno22hybrid/attendee/confcal/session/calendar?q=161P

1. Executive Summary - AAT-008 -

- AAT-008 is a selective EP4 antagonist with a different chemical core structure from AAT-007.
- AAT-008 monotherapy demonstrated significant antitumor effects in mouse models of various tumor types.
- Combined dosing with anti-PD-1 antibody demonstrated significant antitumor effects and restored the antitumor immune environment (pages 14-17).
- Radiotherapy combined with AAT-008 significantly delayed the progression of murine colon tumor compared to the radiation monotherapy (page 19).
- One-month repeated-dosing GLP toxicity and PK studies in rats and dogs were completed, enabling the start of the first in human study.
- GMP grade drug substance is available.
- An estimated efficacious dose for cancer therapy in human is 20 mg QD.

2. Unmet Medical Need and Market Opportunity

- Unmet Medical Need
  - A high rate of refractory to immune checkpoint inhibitors (ICI) still exists.
    - » Refractory rate of the ICI therapy across all tumor types is 76%[1].
    - » Combination of ICI and AAT-007/AAT-008 can restore the therapeutic efficacy of ICI for cancer refractory to the ICI.
- Market of Immuno-Oncology Drugs
  - The global cancer immunotherapy market size was $101.5 billion in 2024 and is projected to reach over $ 228 billion in 2033[2]
  - The immune checkpoint inhibitor market accounted for $52.3 billion in 2024 and is expected to reach over $289 billion by 2035[3]
  - Sales of Keytruda reached $29.5 billion in 2024

1. Oncology 2023, 37(5):210-219. DOI: 10.46883/2023.25920995
2. https://www.globalgrowthinsights.com/market-reports/cancer-immunotherapy-market-110074?utm_source=chatgpt.com
3. https://www.metatechinsights.com/industry-insights/immune-checkpoint-inhibitors-market-1146?utm_source=chatgpt.com

3. EP4 in Cancer Immunity

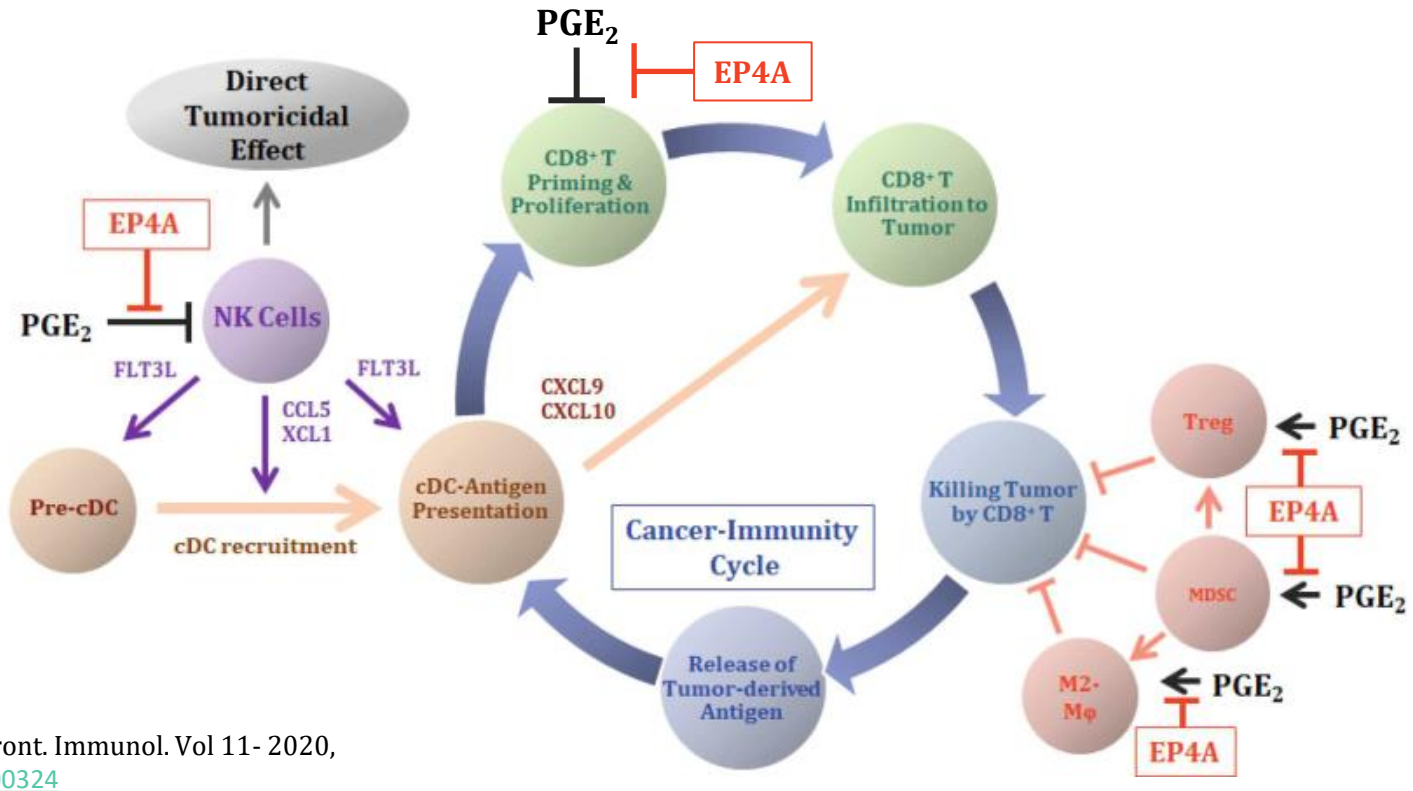
- PGE_2-EP4 Signaling Promotes Immune Suppression [1]
  - PGE_2 through EP4 inhibits cancer-immunity cycle (C-IC), an immune system that recognizes and eliminates tumor cells, and accelerates tumor growth.
  - EP4 is highly expressed in tumors and EP4 activation suppresses host's antitumor immunity.
  - EP4 is expressed in tumor cells and immune cells such as NK, DC, macrophages, T cells, and MDSCs.
- EP4 Antagonist Accelerates C-IC [1] by;
  - Restoring antitumor NK cell functions suppressed by tumor-derived PGE_2.
  - Inhibiting the immune-suppressive functions of tumor-associated M2 macrophages, MDSCs, and Treg cells in tumors (page 8).
- PGE_2-EP4 Signaling Suppresses $CD8^+$ T Cells Expansion and Differentiation [2]
  - PGE_2 acts locally within the TME to limit $CD8^+$ TIL expansion and differentiation.
  - Inhibition of PGE_2-EP4 signaling in $CD8^+$ T cells induces TIL-mediated antitumor immunity.
- EP4 Antagonists Inhibit *in vitro* and *in vivo* Cancer Stem-like Cell Proliferation [3]

TIL: Tumor infiltrating lymphocytes, TME: tumor microenvironment

1. Take, Y., Koizumi, S., Nagahisa, A. Front. Immunol. Vol 11- 2020 https://doi.org/10.3389/fimmu.2020.00324
2. Lacher et al. Nature 629, 417-425, 2024 https://www.nature.com/articles/s41586-024-07254-x
3. Majumder et al., Cancer Science https://doi.org/10.1111/cas.12475 ; Kundu et al., Breast Cancer Res Treat https://link.springer.com/article/10.1007/s10549-013-2779-4

3. EP4 Antagonist in Cancer Immunity

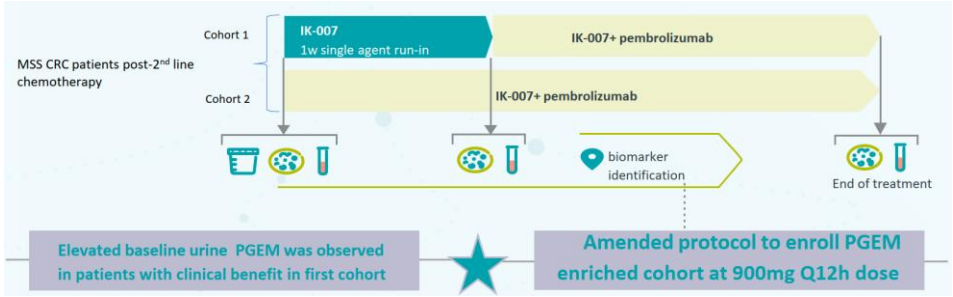
- EP4 antagonist (EP4A) acts on $CD8^+$ T, NK, Treg, MDSC, and M2-Macrophage cells and accelerates cancer-immunity cycle to exert antitumor effects.



1. Take, Y., Koizumi, S., Nagahisa, A. Front. Immunol. Vol 11- 2020, https://doi.org/10.3389/fimmu.2020.00324
2.Lacher et al. Nature 629, 417-425, 2024 https://www.nature.com/articles/s41586-024-07254-x

4. Phase 1 Clinical Study of AAT-007 in Oncology: MSS-Colorectal Cancer

- Advanced or metastatic MSS-CRC patients who received at least 2 lines of prior therapy were enrolled.
- AAT-007 in combination with pembrolizumab was tested for safety, tolerability, and pharmacodynamic endpoints.
- One CR and one PR were observed in 40 subjects of the Response-evaluable Population.
- DCRs[1)] were 41.7%(AAT-007 200 mg) and 66.7 % (AAT-007 600 mg) in Cohort 1 and was 33.3% (AAT-007 300 mg) in Cohort 2.
- PGE_2 metabolite, PGEM[2)] was high in baseline in CR and PR patients.



	Cohort 1				Cohort 2	
Treatment drugs	**AAT-007 + Pembrolizumab 200 mg Q3W**					
AAT-007, Dose	**300 mg BID**	**450 mg Q12h**	**600 mg Q12h**	**900 mg Q12h**	**300 mg BID**	**900 mg Q12h**
N	12	2	3	3	9	11
Complete Response (CR)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Partial Response (PR)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)
Stable Disease (SD)	4 (33.3)	0 (0.0)	2 (66.7)	0 (0.0)	3 (33.3)	0 (0.0)
DCR (CR+PR+SD)	5 (41.7)	0 (0.0)	2 (66.7)	0 (0.0)	4 (33.3)	1 (9.1)
Progressive Disease (PD)	7 (58.4)	2 (100.0)	1 (33.3)	3 (100.0)	6 (66.7)	9 (81.8)
Not Evaluable	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)
Not Available	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

1) DCR: disease control rate (CR+PR+SD); 2) PGEM: a PGE2 metabolite

4. Phase 1 Clinical Study of AAT-007: Advanced Solid Tumors

- Patients with histologically or cytologically confirmed advanced solid tumors, CRC, esophageal, H&N, breast, cervical, etc.
- The study included three phases: Ia (dose-escalation of AAT-007 monotherapy), Ib (dose-escalation in combination with toripalimab, an anti-PD-1antibody), and Ic (dose-expansion with toripalimab). A total of 45 patients were enrolled (17 in phase Ia, 12 in phase Ib, and 16 in phase Ic)
- Safety, pharmacokinetics, pharmacodynamics, and efficacy were assessed. The best response was stable disease, reported in 64.7%, 28.6%, and 18.8% of patients in phase Ia, Ib, and Ic, respectively
- AAT-007 was safe and well tolerated in the late-stage cancer patients.

https://doi.org/10.1007/s10637-025-01512-z

Efficacy of AAT-007 as monotherapy or in combination with anti-PD-1 Ab, toripalimab

	Number of subjects (%)									
Cohort	**Ia**						**Ib**			**Ic**
	Monotherapy						**Toripalimab combination**			
AAT-007 Dose group	**200 mg BID (n=1)**	**300 mg BID (n=3)**	**400 mg BID (n=4)**	**500 mg BID (n=3)**	**650 mg BID (n=6)**	**Total (n=17)**	**500 mg BID (n=7)**	**650 mg BID (n=5)**	**Total (n=12)**	**500 mg BID (n=16)**
Complete response	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	**0 (0)**	0 (0)	0 (0)	**0 (0)**	**0 (0)**
Partial response	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	**0 (0)**	0 (0)	0 (0)	**0 (0)**	**0 (0)**
Stable disease	1 (100)	2 (66.7)	2 (50.0)	2 (66.7)	4 (66.7)	**11 (64.7)**	2 (28.6)	0 (0)	**2 (16.7)**	**3 (18.8)**
Progressive disease	0 (0)	1 (33.3)	1 (25.0)	1 (33.3)	2 (33.3)	**5 (29.4)**	5 (71.4)	5 (100)	**10 (83.3)**	**7 (43.8)**
Not evaluate	0 (0)	0 (0)	1 (25.0)	0 (0)	0 (0)	**1 (5.9)**	0 (0)	0 (0)	**0 (0)**	**6 (37.5)**
Objective response rate	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	**0 (0)**	0 (0)	0 (0)	**0 (0)**	**0 (0)**
Disease control rate	1 (100)	2 (66.7)	2 (50.0)	2 (66.7)	4 (66.7)	**11 (64.7)**	2 (28.6)	0 (0)	**2 (16.7)**	**3 (18.8)**

5. Non-clinical Pharmacology Studies of AAT-007/AAT-008 in Oncology

5.1 *In vitro* Pharmacology Summary

1 *In vitro* Properties of AAT-007 and AAT-008

2 VEGF Production in RAW264 cells

5.2 *In vivo* Pharmacology Studies

1 Mouse Colon Cancer (CT-26): Combination of AAT-008 with PD-1 Antibody

2 Mouse Breast Cancer (4T1): Combination of AAT-008 with PD-1 Antibody

3 Mouse Colon Cancer (CT-26): Combination of AT-008 with radiation

5.1.1 *In vitro* Properties of AAT-007 and AAT-008

AAT-007 and AAT-008 are potent and selective EP4 antagonists.

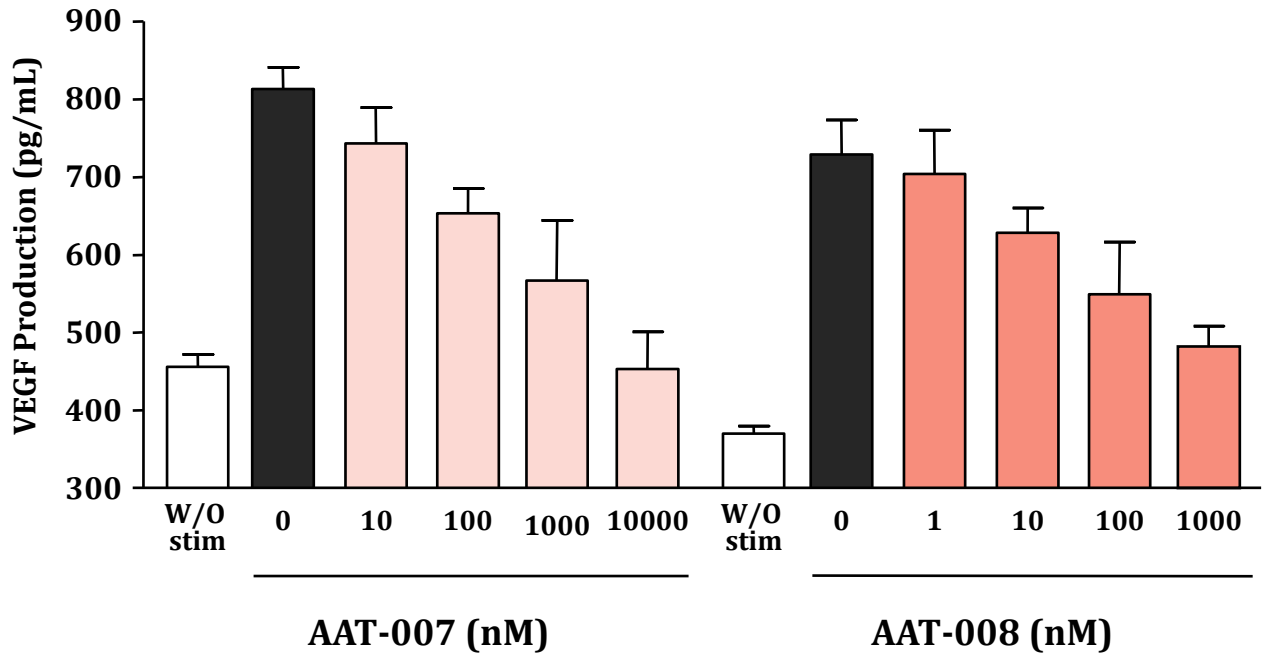
***In vitro* Assays**	**Compound**	
	AAT-007	**AAT-008**
Human EP4 binding (*K*i)	13 nM	<10 nM
Human EP4 function (pA_2*)	8.32	8.97
Selectivity panel	>200-fold**	>1000-fold**

* Inhibition of PGE_2-induced cAMP elevation
** Selectivity against over 100 enzymes and receptors

5.1.2 VEGF Production in RAW264 Cells

Vascular endothelial growth factor (VEGF) is known as an immune-suppressive factor.

AAT-007 and AAT-008 dose-dependently reduced PGE_2-induced VEGF production with IC_{50} values of 150 and 120 nM, respectively.



RAW264 (mouse macrophage) cells were incubated with 100 nM PGE_2 for 72 hrs in the presence of AAT-007 or AAT-008. The supernatant was subjected to VEGF ELISA. Data represent mean + SD (N = 3).

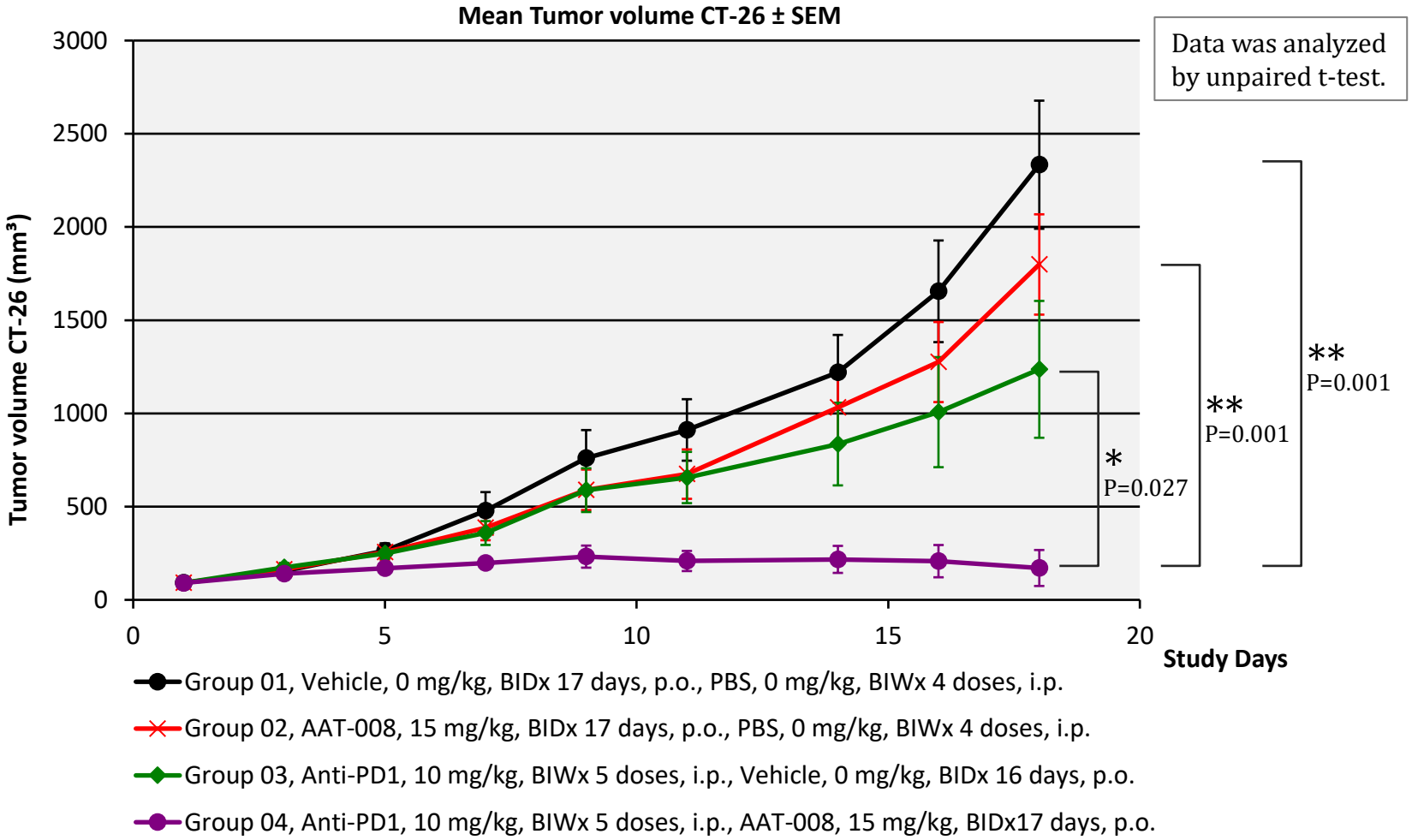
5.2.1 Mouse Colon Cancer (CT-26): Combination of AAT-008 with PD-1 Antibody

- Antitumor effect of AAT-008 was tested in mice SC inoculated with CT-26 mouse colon cancer.
- AAT-008 was orally dosed as monotherapy or in combination with anti-PD-1 antibody.

Model	CT-26 colon cancer in BALB/c mice
Dose	AAT-008: 15 mg/kg PO, BID for 3 weeks Anti-PD-1 antibody: 10 mg/kg IP, BIW for 3 weeks Control: PBS or vehicle
N/Group	7
Endpoint	Tumor size, body weight

5.2.1 Mouse Colon Cancer (CT-26): Combination of AAT-008 with PD-1 Antibody

- Combination of AAT-008 and anti-PD-1 antibody showed synergistic efficacy over respective monotherapy.
- Tumors completely disappeared in 4 of 7 mice of the combination group.



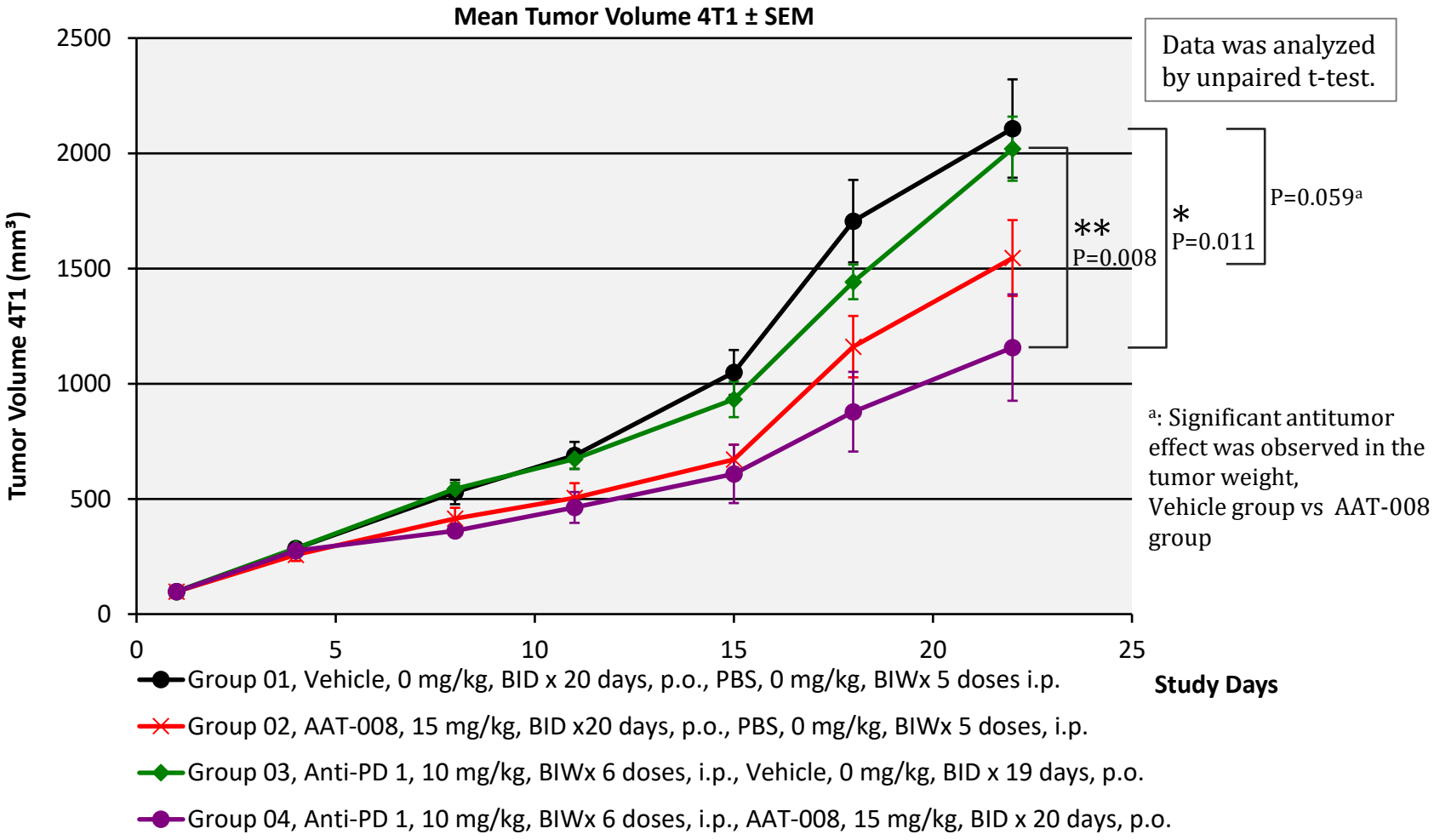
5.2.2 Mouse Breast Cancer (4T-1): Combination of AAT-008 with PD-1 Antibody

- Antitumor effect of AAT-008 was tested in mice SC inoculated with 4T-1 mouse breast cancer.
- AAT-008 was orally dosed as monotherapy or in combination with anti-PD-1 antibody.

Model	4T1 triple-negative breast cancer in BALB/c mice
Dose	AAT-008: 15 mg/kg PO, BID for 3 weeks Anti-PD-1 antibody: 10 mg/kg IP, BIW for 3 weeks Control: PBS or vehicle
N/group	7
Endpoint	Tumor size, body weight

5.2.2 Mouse Breast Cancer (4T-1): Combination of AAT-008 with PD-1 Antibody

- Combination of AAT-008 with anti-PD-1 antibody significantly potentiated the antitumor effect of anti-PD-1 antibody.



5.2.3 Mouse Colon Cancer (CT-26WT): Combination of AAT-008 with Antitumor Radiation Therapy

- Antitumor effect of AAT-008 was tested in mice SC inoculated with CT-26WT mouse colon cancer.
- AAT-008 was orally dosed as monotherapy or in combination with radiation.
- Effector and regulatory T cells in the tumor tissue were quantitated by FACS.

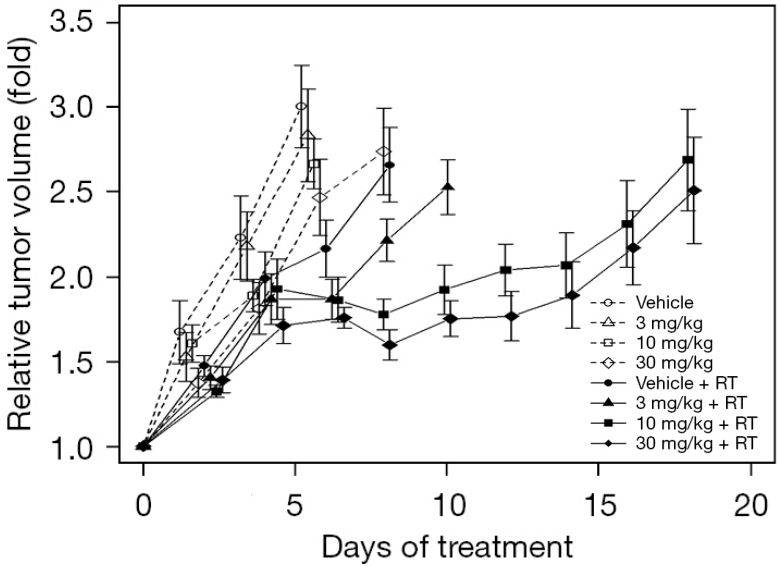
Model	CT26WT colon cancer in BALB/c mice
Dosing	AAT-008: 3, 10 and 30 mg/kg, PO, BID (19 Day), N = 12 Control: vehicle Radiation: 9 Gy on day 3
Endpoint	Tumor volume (Day 0 - 18) Body weight (Day 0 - 18) Ratio of effector T cells and regulatory T cells

Translational Cancer Res., https://dx.doi.org/10.21037/tcr-22-1857

5.2.3 Mouse Colon Cancer (CT26WT): Combination of AAT-008 with Antitumor Radiation Therapy

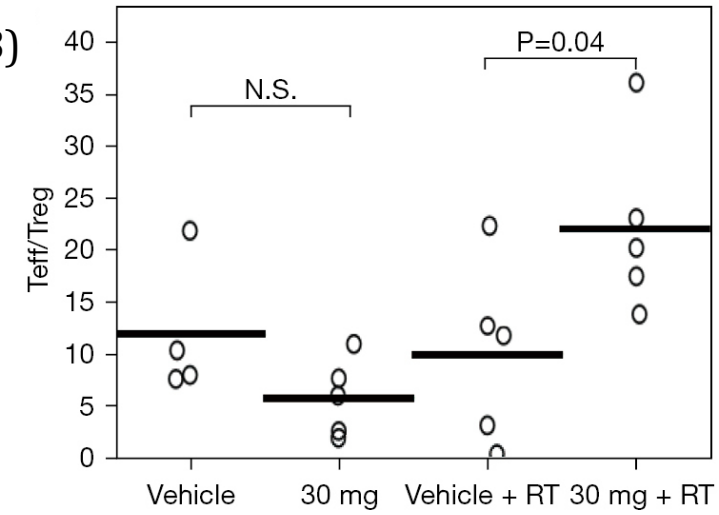
- AAT-008 (10, 30 mg/kg, PO, BID) combined with radiation significantly delayed the tumor growth (A).
- Teff/Treg ratio by combination was significantly increased compared to radiation monotherapy (B).

(A)



Growth curves for CT26WT tumors after oral administration of vehicle, AAT-008 (3, 10, or 30 mg/kg/day, twice daily until termination of tumor size measurement: from day 0 to up to day 18, open symbols), and vehicle or AAT-008 plus radiation with 9 Gy on day 3 (closed symbols). Bars represent standard errors of 12 mice.

(B)



Ratio of Teff to Treg in the tumors after administration of vehicle, AAT-008 (30 mg/kg/day, twice daily from day 0 to day 12), vehicle plus RT (9 Gy), and AAT-008 plus RT. Teff, effector T cells; Treg, regulatory T cells; N.S., not significant; RT, radiation.

Translational Cancer Res., https://dx.doi.org/10.21037/tcr-22-1857

6. Non-clinical Safety and Pharmacokinetic Studies of AAT-007
- Study List -

Study Type and Duration		Route of Administration	Species / Cell Line
Absorption	Single Dose	IV and PO	Rat, Dog, Monkey
	Multiple Dose (10-Day)	PO	Rat, Dog
Distribution	Tissue Distribution	PO	Rat
	Serum Protein Binding	-	Mouse, Rat, Rabbit, Dog, Monkey, Human
	RBC Partitioning (Blood / Plasma Ratio)	-	Rat, Dog, Human
	Brain Penetration	PO	Mouse, Rat
Metabolism	*In vivo* Metabolism	PO	Rat, Dog
	In vitro Metabolism	-	Rat / Human Liver Microsome, Rat / Human Hepatocyte
	Inhibition of Drug Metabolizing Enzymes (DDI)	-	Human
Excretion	Excretion into Urine	IV	Rat, Dog, Monkey
	Biliary Secretion	IV	Rat
Others	Cell Permeability Assay	-	Caco-2
	Transporter Assay	-	MDCK / MDR1

6. Non-clinical Safety and Pharmacokinetic Studies of AAT-007
- Study List -

Study Type			Route of Administration	Species
Core Battery	CNS		PO	Rat
	CVS		PO	Dog
	Respiratory System		PO	Rat
	CVS	hERG Assay	-	Human
Follow-Up	CVS	Purkinje Fiber	-	Dog
Supplemental	Renal and Urinary System	Renal and PK	PO	Rat
		Renal Blood Flow	IV Bolus and Infusion	Rat
		Plasma Renin Activity	PO	Rat
	Broad Ligand Assay		-	Human

6. Non-clinical Safety and Pharmacokinetic Studies of AAT-007
- Study List -

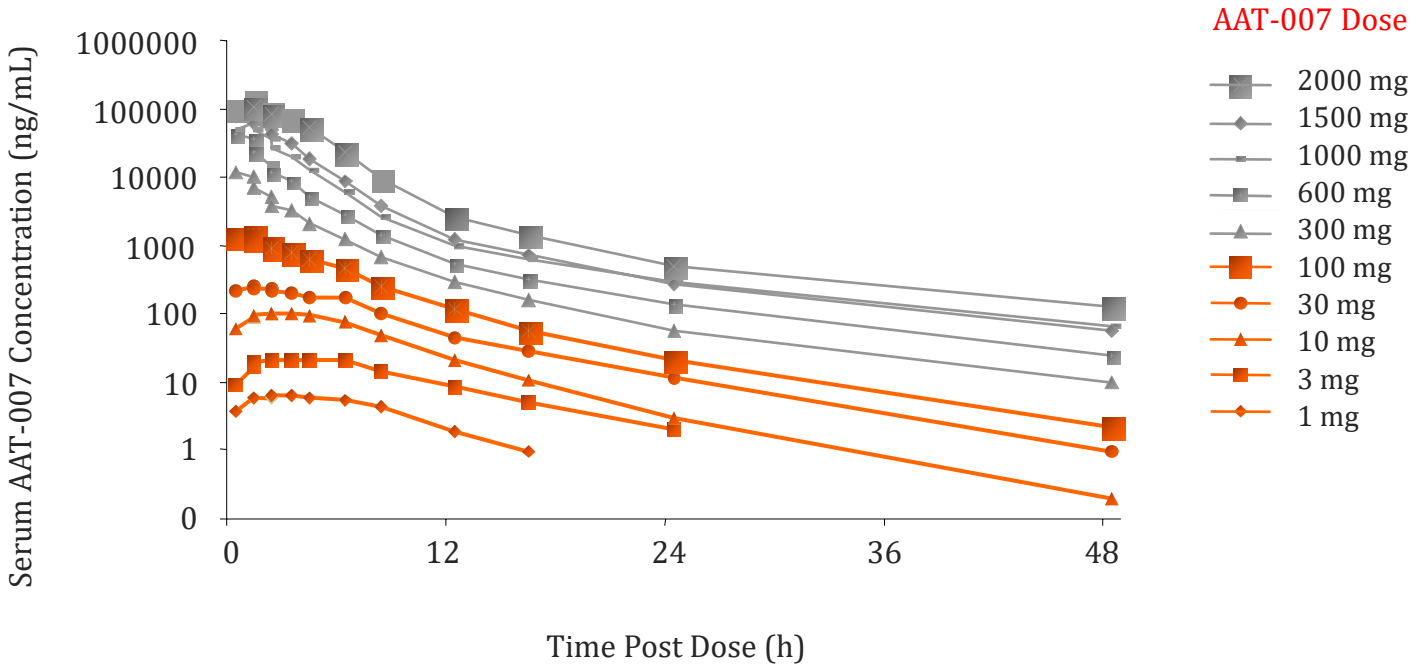
Study Type and Duration		Route of Administration	Species
Single-Dose Toxicity		PO	Rat, Dog
Repeated-Dose Toxicity	10-Day Range-Finding	PO	Rat, Dog
	1-Month	PO	Rat, Dog
	3-Month	PO	Rat
	9-Month	PO	Dog
Genotoxicity	Mutagenicity Assay (Ames)	-	Bacteria
	Clastogenicity Assay (Human Lymphocyte)	-	Human
	In vivo Micronucleus Assay	PO	Rat
	Other Genetic Toxicology Assay	*In vivo* and *In vitro*	Rat
Carcinogenicity	2-Week	PO	Mouse
	2- to 4-Week Range-Finding	PO	Mouse
	1-Month Range-Finding	PO	Mouse

7. Clinical Studies of AAT-007 in Pain Therapy
- Study List -

Stage	Study	Subjects (N)
Phase 1	Single Dose Tolerability and PK	Healthy Volunteers (78)
	Food Effect	Healthy Volunteers (12)
	Multiple Dose Tolerability and PK	Healthy Volunteers (36) Elderly Volunteers (21)
	Gastroduodenal Endoscopy	Healthy Volunteers (193) Elderly Volunteers (165)
Phase 2	OA Pain (2-week)	Subjects with OA Pain (201)
	OA Pain (4-week)	Subjects with OA Pain (739)

7. Clinical Studies of AAT-007 in Pain

- Single-dose study in healthy subjects
  - Well tolerated up to 1,000 mg.
  - Exposure increased with dose in an approximately dose proportional manner between 1~100 mg, and between 600~2,000 mg.
  - The average terminal elimination half-life was ~9 hrs, with a fast distribution phase.
  - Systemic exposure parameters decreased slightly with food.



7. Clinical Studies of AAT-007 in Pain

- 14-day multiple-dose study
  - Well tolerated at 300 mg BID in healthy subjects.
  - Well tolerated at 250 mg BID in elderly subjects with mild renal impairment.
- Endoscopic GI safety study
  - No significant difference in incidence of GI ulcer compared to placebo after 7 days treatment at 75 mg BID.
  - Significantly lower incidence of GI ulcer compared to Naproxen at 500 mg BID in elderly subjects after 7 days treatment.

Treatment Group (Elderly)	Number of Ulcer* Subject (Incidence %)
AAT-007 (N = 63)	3 (5%)
Naproxen (N = 63)	11 (18%)
Placebo (N = 39)	1 (3%)

Comparison	P-value
AAT-007 vs Naproxen	0.018
AAT-007 vs Placebo	0.619
Naproxen vs Placebo	0.020

*: Any break in the mucosa >3 mm in diameter with unequivocal depth

7. Clinical Studies of AAT-007 in Pain

- Phase 2 Studies
  - Two Phase 2 studies were conducted for OA pain in the US.
  - AAT-007 was efficacious in relief of signs and symptoms of OA pain following once- or twice-a-day dosing for 4 weeks.
  - The analysis using E_{max} model demonstrated;
    - Total daily dose of 96 mg was estimated to show the same efficacy achieved by Naproxen at 1,000 mg per day.
    - Minimum efficacious dose range was between 19.5 and 32.0 mg/day.
  - Efficacious dose without safety issues was identified.

8. Non-clinical Safety and Pharmacokinetic Studies of AAT-008
- Study List -

Study Type and Duration		Route of Administration	Species / Cell Line
Absorption	Single Dose	IV and PO	Rat, Dog, Monkey
	Multiple Dose (10-Day)	PO	Rat, Dog
Distribution	Plasma Protein Binding	-	Rat, Dog, Monkey, Human
	RBC Partitioning (Blood / Plasma Ratio)	-	Rat, Dog, Human
	Brain Penetration	PO	Rat
Metabolism	*In vivo* Metabolism	IV	Rat
	In vitro Metabolism	-	Rat / Human Liver Microsome, Rat / Human Hepatocyte
	Inhibition of Drug Metabolizing Enzymes (DDI)	-	Human
Excretion	Excretion into Urine	IV	Rat, Dog, Monkey
	Biliary Secretion	IV	Rat
Others	Cell Permeability Assay	-	Caco-2
	Transporter Assay	-	MDCK / MDR1

8. Non-clinical Safety and Pharmacokinetic Studies of AAT-008
- Study List -

Study Type			Route of Administration	Species
Core Battery	CNS		PO	Rat
	CVS		PO	Dog
	Respiratory System		PO	Rat
	CVS	hERG Assay	-	Human
Supplemental	Broad Ligand Assay		-	Human

8. Non-clinical Safety and Pharmacokinetic Studies of AAT-008
- Study List -

Study Type and Duration		Route of Administration	Species
Repeated-Dose Toxicity	4-Day Tolerance	PO	Rat, Dog
	10-Day Range-Finding	PO	Rat, Dog
	1-Month	PO	Rat, Dog
Genotoxicity Carcinogenicity	Mutagenicity Assay (Ames)	-	Bacteria
	Clastogenicity Assay (Human Lymphocyte)	-	Human
	In vivo Micronucleus Assay	PO	Rat

8. Non-clinical Safety and Pharmacokinetic Studies of AAT-008
- Human Efficacious Dose Estimation -

Estimated Human Efficacious Dose for Oncology Therapy

- Efficacious Dose : 20 mg QD
- Efficacious C_{ave}: 160 ng/mL

Method of Calculation

- Efficacy dose of AAT-008 is calculated using pA_2, protein binding in the mouse and human, and average plasma concentration of AAT-008 dosed at 3 mg/kg QD in the mouse.
  - Minimum efficacious dose of AAT-008 is not available in animal efficacy pharmacology studies in oncology.
  - The Lowest efficacious dose (3 mg/kg QD) was obtained from mouse gastric cancer and used as a starting dose for human dose calculation.
  - PK profiles in human are not available.

9. Patents of AAT-007 and AAT-008

Patent	Int'l Publication Number (Int'l Application Number)	Int'l Filing Date	Status as of January 28, 2026
AAT-007 Crystal Forms	WO 2006/095268 (PCT/IB2006/000754)	March 1, 2006*	Granted: BR, CA, CN, EP (FR, DE, GB, IE, IT, ES, TR, GR, PL, NL, BE), IN, JP, KR, MX, RU, US
AAT-007 & AAT-008 Use for Cancer	WO 2010/123049 (PCT/JP2010/057114)	April 22, 2010	Granted: BR, CA, CN, HK, CN-Div., HK-Div., EP (FR, DE, GB, IE, IT, ES), HK, EP-Div. (FR, DE, GB, IE, IT, ES, AT, CH), EP-Div2. (FR, DE, GB, IT, ES), HK-Div., HK-Div2., JP, KR, MX, MX-Div., RU, US, US-Con., US-Con2., US-Con3, US-Con4.
AAT-007 & AAT-008 Use for NASH-Associated Liver Cancer	WO 2018/084230 (PCT/JP2017/039680)	November 2, 2017	Granted: CA, CN, HK, EP (FR, DE, GB, IE, IT, ES, AT, CH), HK, IN, JP, MX, US Under examination: BR
AAT-007 Use for Cancer Treatment with Combination	WO 2019/204257 (PCT/US2019/027603)	April 16, 2019	Granted: US
AAT-007 Synthesis Thereof	WO 2020/014445 (PCT/US2019/041351)	July 11, 2019	Granted: - Under examination: US
AAT-007 Crystal Forms	WO 2017/258534 (PCT/US2019/041378)	July 11, 2019	Granted: US

* Five-year patent term extension for Galliprant: GB, FR, DE, IE, IT, ES, GR, PL, NL, BE, JP, US

10. Competitors of EP4 Antagonist in Oncology Therapy

Compound	Target	Indication (Combination)	Phase	Company	Reference
ONO-4578	EP4	Advanced solid tumors (+ nivolumab)	1/2	Ono Pharmaceuticals	NCT03155061
		Gastric cancer (+ nivolumab)	**2**	Ono Pharmaceuticals	NCT06256328
		Advanced colorectal cancer (+ nivolumab)	**2**	Ono Pharmaceuticals	NCT06948448
CR-6086	EP4	pMMR-MSS Metastatic colorectal cancer (+ balstilimab)	1b/2a	Rottapharm Biotech	NCT05205330
HTL0039732	EP4	Advanced solid tumors (atezolizumab or other anti-cancer therapy)	1/2a	Heptares Therapeutics Sosei	NCT05944237
INV-1120	EP4	Advanced solid tumors (+ pembrolizumab)	1a/1b	Shenzhen Ionova Life Science Co Ltd	NCT04443088
Palupiprant (AN-0025/E7046)	EP4	Advanced solid tumors, metastasis (+ pembrolizumab)	1	Adlai Nortye Pharmaceutical Co Ltd	NCT04432857
		Esophageal Cancer Chemoradiotherapy (paclitaxel, carboplatin, radiotherapy)	1	Adlai Nortye Pharmaceutical Co Ltd	NCT05191667
		Advanced Solid Tumors Double/Triple combination (atezolizumab, AN2025)	1	Adlai Nortye Pharmaceutical Co Ltd	NCT04975958
		Rectum cancer in combination with radiotherapy or chemoradiotherapy in preoperative treatment	1	Adlai Nortye Pharmaceutical Co Ltd	NCT03152370
DT-9081	EP4	Advanced, recurrent or metastatic solid tumors	1	Domain Therapeutics SA	NCT05582850
KF-0210	EP4	Advanced solid tumors (+ atezolizumab)	1a/1b	Keythera Pharmaceuticals Co Ltd	NCT04713891
TPST-1495	EP2+EP4	Familial Adenomatous Polyposis	2	Tempest Therapeutics Inc	NCT06557733

Created based on Schlicher L. et al., Frontiers Immunology, https://doi.org/10.3389/fimmu.2023.1297175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