Oscotec Inc.

October 2022

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Overview

“OUR VISION is to be the LEADING INNOVATION ENGINE that translates the science of LIFE into first-in-class medicine for unmet clinical needs”

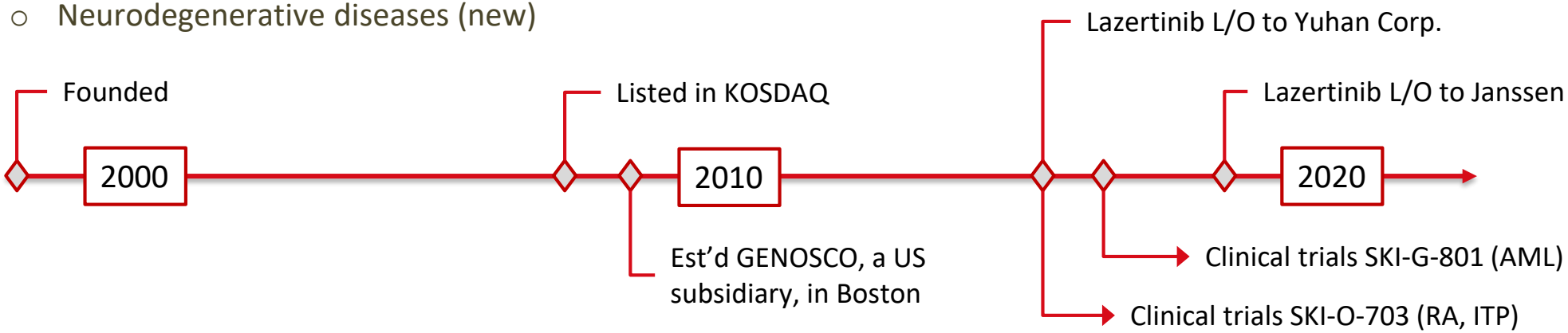
Profile

- Established in 1998, located at KoreaBioPark, Pangyo, South Korea
- Listed in KOSDAQ (2007); current market cap ~860M KRW (as of Aug 2022)
- Paid-in Capital : 15B KRW (Outstanding shares : 29,914,859)
- No. of Employees : 48 (R&D: 29)
- Subsidiaries : Genosco (Boston), Ectodor (Boston)

Area

- Oncology and immuno-oncology
- Inflammation and autoimmune diseases
- Neurodegenerative diseases (new)

History



Leadership

Oscotec Inc.

James Kim Ph.D., D.D.S CEO

- Ph.D. in biochemistry, Seoul National University
- Professor, Dankook Univ.
- Visiting Professor, Harvard Medical School

Taeyoung Yoon Ph.D. CEO

- Ph.D. in Organic Chemistry, Yale Univ.
- Postdoc, California Inst. of Technology
- Sr. Research Investigator, Novartis
- SVP and Head of Research, Dong-A ST

Yuntae Kim Ph.D. CTO

- Ph.D. in organic chemistry, Univ. of Pittsburgh
- Postdoc, California Inst. of Technology
- Sr. Research Fellow, Merck
- Director of Medicinal Chemistry, CKD

Scott Lee MBA CFO

- Director/Management
- MBA in Business Administration, Dankook Univ.

GENOSCO

John Koh Ph.D. CEO

- Ph.D. in Bio-organic Chemistry, California Institute of Technology
- President, KABIC
- R&D Head, LG Life Science

Steve Kim Ph.D., D.D.S CTO

- Ph.D. in Pharmacology, Seoul Nat. Univ.
- Professor, Dankook Univ.
- Visiting Professor, Harvard Medical School

Kevin Yang B.Sc CFO

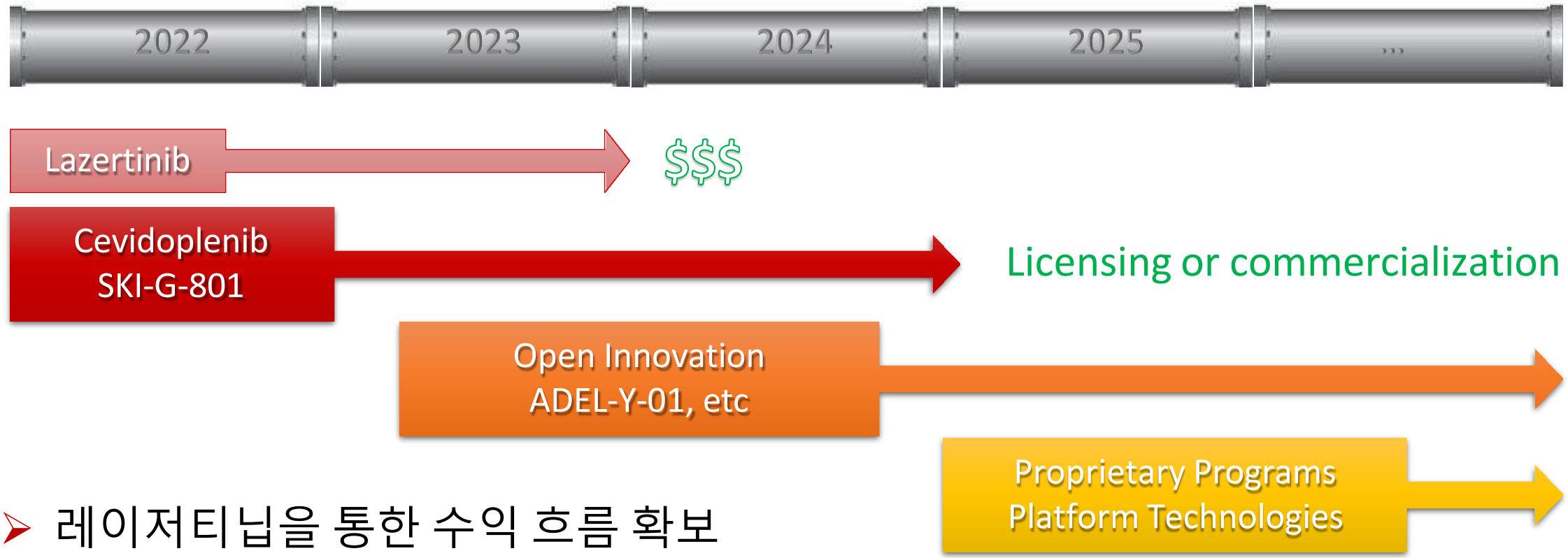
- Director/Management
- B. Sc in Communication from Seoul National Univ.

ectodor therapeutics

Katie Lee Ph.D. CEO

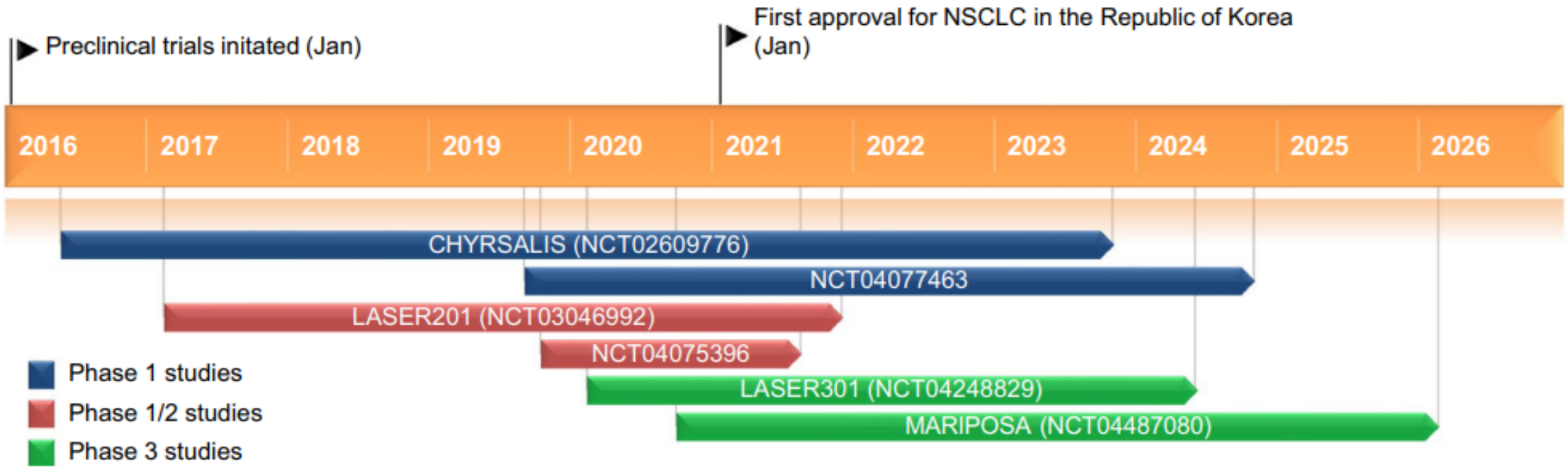
- Ph.D. in Organic Chemistry, Wesleyan University
- Postdoc, Yale Univ.
- Research Associate, Harvard Medical School and Broad Institute

오스코텍 성장 전략



- 레이저티닙을 통한 수익 흐름 확보
- 현 임상 파이프라인의 성공 기반 구축
- Open innovation을 통한 파이프라인 강화
- 오스코텍 고유의 discovery 과제와 플랫폼 기술의 구축을 통한 지속적인 성장

레이저티닙 주요 임상시험



- **CHRYSALIS;** 레이저티닙 병용투여군을 포함하는 아미반타맙의 EGFR 돌연변이를 가지는 표준치료에 실패한 비보세포성폐암 (NSCLC) 환자에서의 임상시험; 혁신치료제(BTD) 지정 및 가속승인(AA) 가능성.
- **Laser301;** 레이저티닙 단독투여 vs 1세대 EGFR TKI 비교 임상시험
- **MARIPOSA;** 1차치료제로 허가를 위한 레이저티닙/아미반타맙 병용투여군과 타그리소(오시머티닙) 비교 임상

Oscotec R&D Pipeline

	기전	적응증	Discovery	Lead Opt	Preclinical	Phase I	Phase II
Cevidoplenib (SKI-O-703)	SYK inhibitor	류마티스관절염 (RA)					
		면역혈소판감소증 (ITP)					
SKI-G-801	FLT3/AXL Dual Inhibitor	급성골수성백혈병 (AML)					
		고형암					
ADEL-Y01	Anti-TAU mAb	알츠하이머성 치매					
OCT-598	EP2/4	면역항암					
LSD	LSD1	고형암					
ONC1	(Undisclosed)	급성골수성백혈병(AML) /만성골수단핵구백혈병(CMML)					
ONC2	(Undisclosed)	고형암					
ONC3	(Undisclosed)	고형암					
…							

Cevidoplenib (SKI-O-703)

A Potential First-in-Class SYK Inhibitor

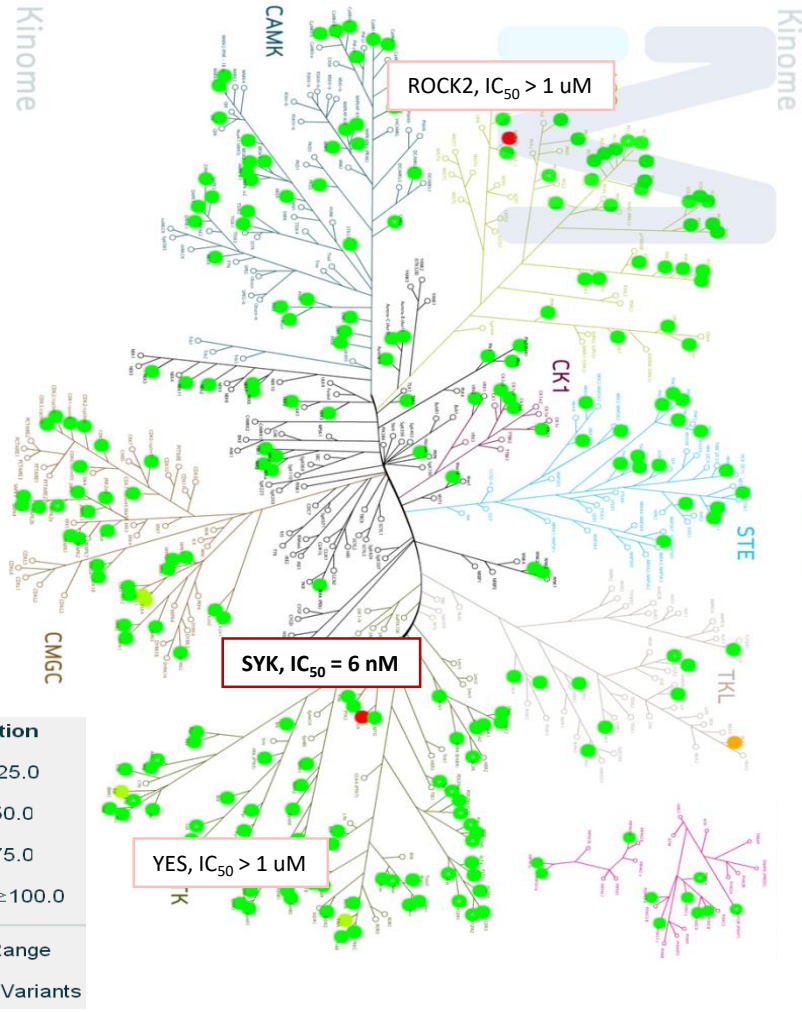
SYK Inhibitors; 경쟁사 현황

개발사	약물	적응증	개발단계	기타
Rigel	Tavalisse® (fostamatinib)	면역혈소판감소증 Immune thrombocytopenia (ITP)	승인	
		자가면역성용혈성빈혈 Autoimmune hemolytic anemia (wAIHA)	Phase III	
		COVID-19	Phase III	
Kronos Bio	Entospletinib	NPM1⁺ 급성골수성백혈병 NPM1⁺ acute myeloid leukemia (AML)	Phase III	From Gilead
Alexion	Cerdulatinib (**JAK/SYK dual**)	림프종 (Lymphoma)	Phase II (stopped)	From Portola
Dermavant		백반증 (Vitiligo)	Phase II	경피제제
Calithera	Mivavotinib	림프종 (Lymphoma)	Phase II	From Takeda
Hutchmed China	HMPL-523	면역혈소판감소증 Immune thrombocytopenia (ITP)	Phase III (China)	
		림프종 (Lymphoma)	Phase II	
Asana	Gusacitinib (**JAK/SYK dual**)	만성 손 습진 (Chronic hand eczema)	Phase II	FDA Fast Track

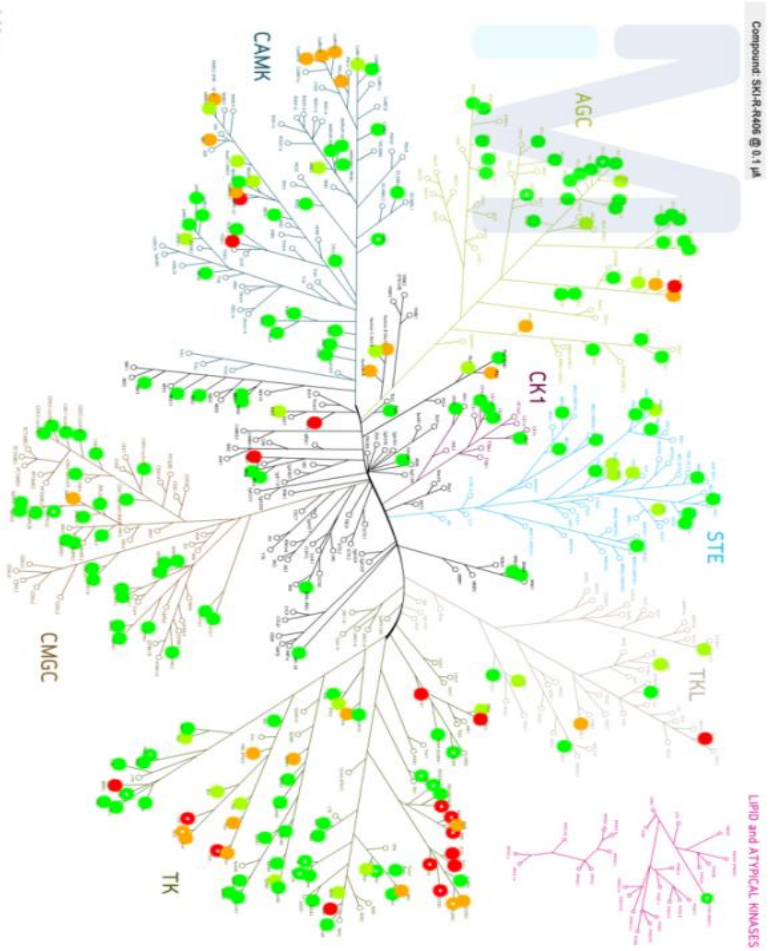
SYK 선택적 억제제로서 Cevidoplenib은 자가면역질환 분야에서 앞서가고 있음

Cevidoplenib vs Fostamatinib; kinase 선택성 비교

SKI-O-703 @100 nM

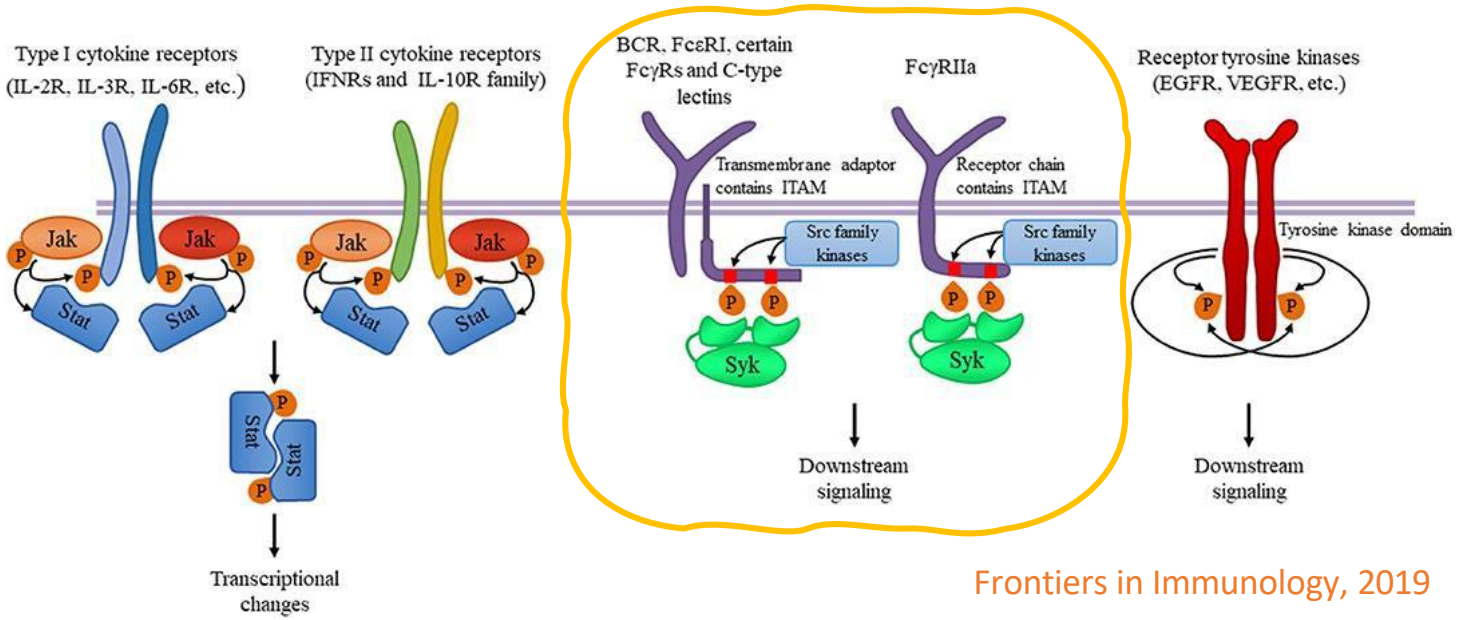


R406 (Rigel) @100 nM

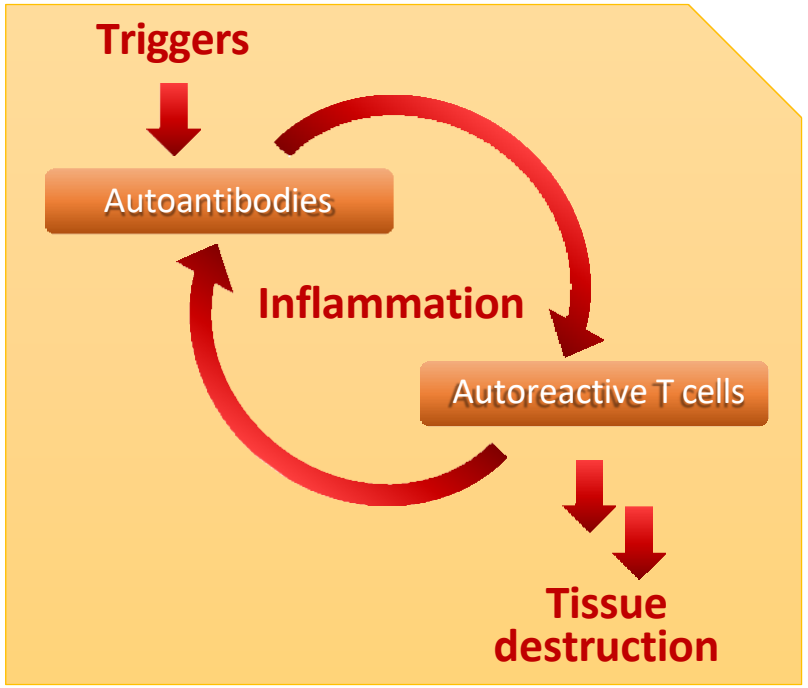


Kinase	SKI-O-703	R406
	IC_{50}, nM	IC_{50}, nM
SYK	**6.2**	**56.5**
JAK2	1859	1.3
JAK3	5807	16.3
RET	412	10.7
KDR	**687**	**18.8**
FLT3	1,783	0.5
FGFR1	16,960	88.9
FGFR2	>10,000	22.4
FGFR3	5,662	32.2
PYK2	709	24.3
AuroraB	>10,000	164.7

자가면역질환에서의 SYK 타겟



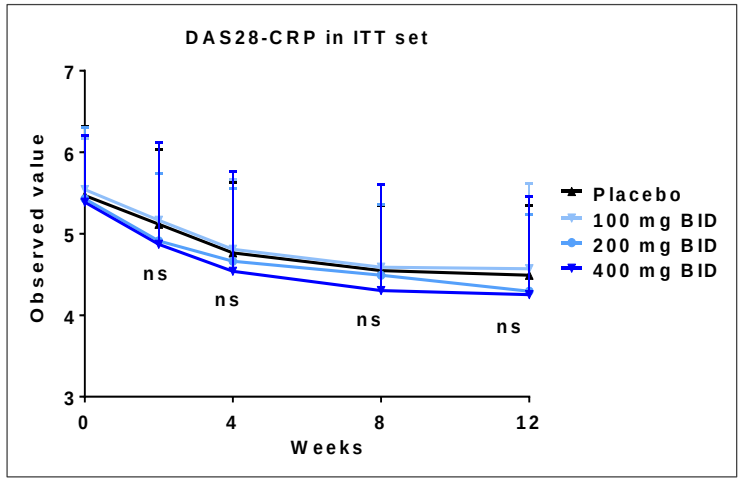
Frontiers in Immunology, 2019

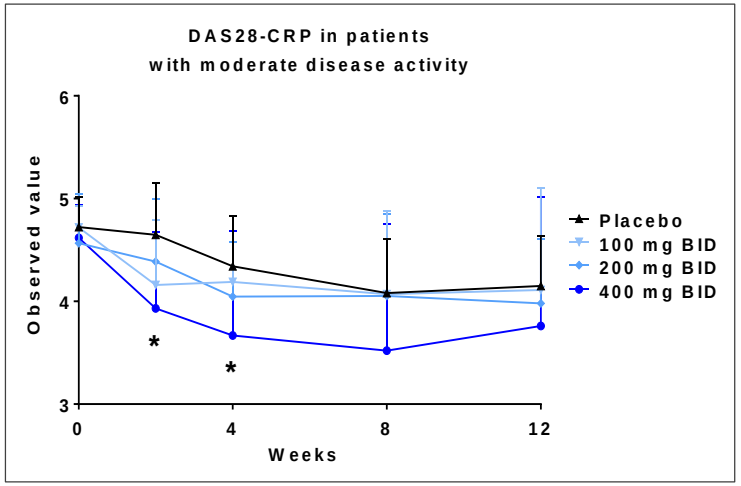


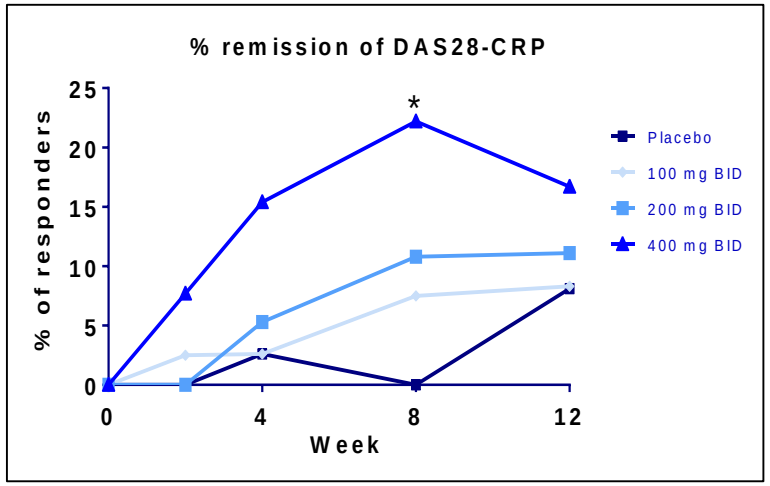
- 자가면역질환
  - 자가항원에 의해 유도 된 면역반응으로; 특정 기관부터 전신으로까지 영향
  - 자가항체 → 자가활성화 된 T 세포 → 사이토카인 분비 및 조직 손상 초래
- 기존 치료법은 대부분 **세포성 면역** (anti-TNFα, anti-IL-6, JAK, etc)에 집중하고 있음
- **SYK**는 B 세포 및 항체신호전달을 매개하여 **체액성 면역**에 중요한 역할을 함; 기존 치료법에 비해 **차별화 되고 보완적인 작용 기전**

류마티스관절염 환자를 대상으로 한 임상2a상 시험

- 기존 치료법 (csDMARDs, e.g., methotrexate, or bDMARDs, e.g., anti-TNFα drugs) 저항성 류마티스관절염 환자 모집 (163명, 12주 투약)
- 뛰어난 안전성 재확인 (투약순응도 99% 이상)
- 주요 1차효능지표의 통계적 유의성 확보 실패; 그러나 1차평가지표 중 하나인 DAS28-hsCRP의 감소
- 중요한 결과로, 증상이 낮거나 중등도인 환자군에서 고용량 투여시 (400mg bid) 빠른 기간에 유의미한 효과를 보임
- **SYK는 질병 발달 초기단계에 중요한 역할을 한다는 '생물학적 증명'**

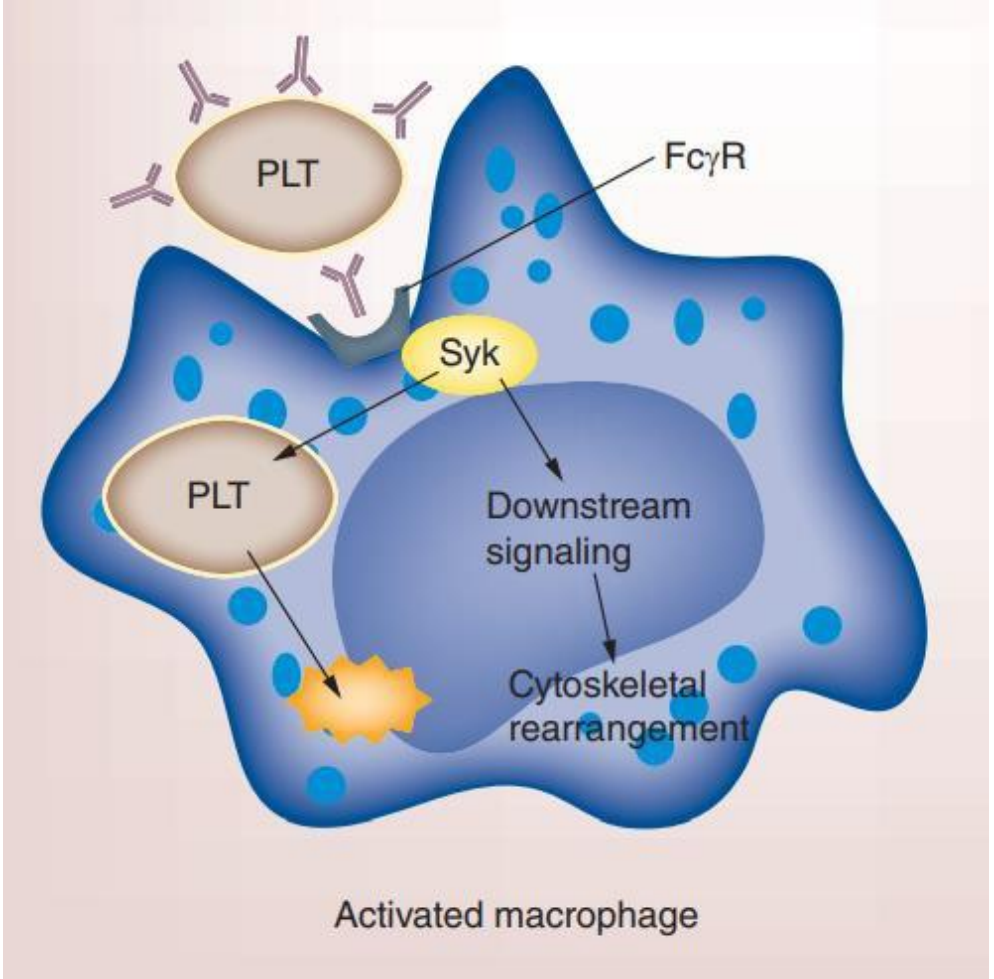






면역혈소판감소증 (ITP; Immune Thrombocytopenia)

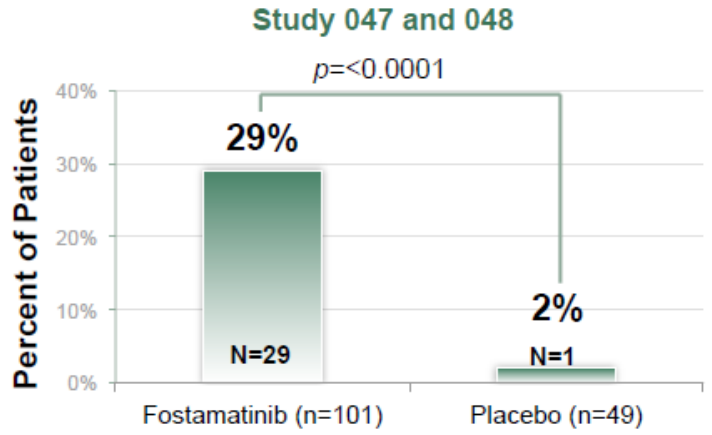
- 정의
  - 혈소판 수의 감소로 인해 과도한 멍이나 출혈, 피로감, 그리고 혈전증 위험 증가 등을 초래
  - 자가항체에 의한 혈소판의 파괴
  - 희귀질환 (성인 10만명 당 약 9.5명에서 발생)
- 치료법
  - 1차 치료제; 스테로이드 또는 면역글로불린
  - 2차 치료제; TPO(Thrombopoietin) receptor agonist (혈소판 증식인자 수용체 작용제), rituximab, 또는 비장절제술
  - **2018년 Fostamatinib US FDA 승인**
- Pipeline
  - BTK inhibitor (rilzabrutinib, Sanofi, 임상 3상 진행 중)
  - Anti-FcRn antibodies (UCB and Argenx 임상 3상 진행 중; Harbour/HanAll 임상 2상 진행 중)



Newland et al., Future Medicine Immunotherapy 2017

Fostamatinib in ITP

- Fostamatinib은 2018년 2차례의 임상3상시험을 근거로 FDA로 부터 승인을 받음.
  - 총 150명 환자 대상, active:placebo = 2:1
  - 100-150mg PO bid, 24주간 투여
  - 반응률 18% (혈소판 수치> 50K/uL for >4 of the last 6 visits); intermediate responder를 포함하면 29%
  - 고혈압 포함, 높은 부작용률을 보임.



Response	Fostamatinib	Placebo	
Stable	18/101	1/49	
Intermediate*	11/101	0/49	
Overall	**29/101**	**1/49**	
%;p	**29%**	**2%**	**P<0.0001**

Adverse Events - Combined Studies 047 + 048

Number (n) and % of Patients with ≥ one Adverse Event (AE)	Fostamatinib N=102 n (%)	Placebo N=48 n (%)
Any AE*	85 (83%)	36 (75%)
- Treatment-related AEs	60 (59%)	13 (27%)
Serious AEs (SAEs)	13 (13%)	10 (21%)
- Bleeding SAEs	4 (4%)	5 (10%)
- Treatment-related SAEs	4 (4%)	1 (2%)
Gastrointestinal complaints**	49 (48%)	15 (31%)
- Diarrhea	30 (29%)	7 (15%)
- Nausea	19 (19%)	4 (8%)
Infection	27 (27%)	10 (21%)
Hypertension	20 (20%)	4 (8%)
Transaminase elevation	14 (14%)	0 (0%)

Cevidoplenib for ITP

- 임상 2상시험
  - ITP 기존 치료에 실패하거나 재발한 ITP 환자 총 60명 대상
  - Cevidoplenib 400mg bid, 200mg bid, 그리고 위약군 무작위 배정 (2:2:1)
  - 환자모집 완료 (총 60명), 2023년 1Q topline 결과 발표 예정

- **중간결과**
  - **투여군에서 예상 반응률 >40%; 용량 의존적 반응이 나온다면 400 mg bid 투여군에서의 반응률은 >60% 예상**

- 류마티스관절염 임상2상 시험 안전성 결과 (총 163명)
  - 치료 관련 중대 이상반응(treatment-related serious adverse event) 없음

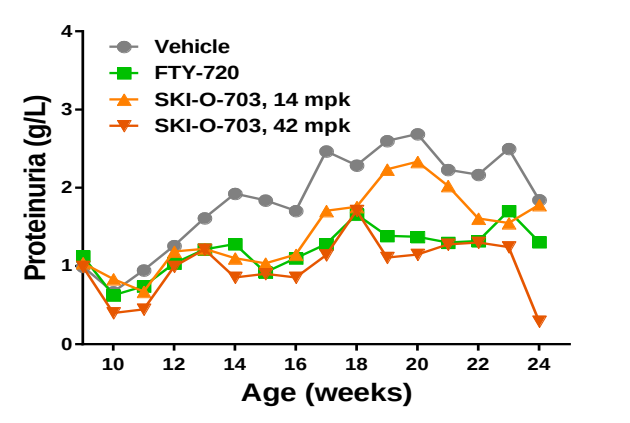
Event	Cevido 400 (n=41)	Cevido 200 (n=41)	Cevido 100 (n=41)	Placebo (n=41)
Any TEAEs	61%	58%	39%	46%
- Treatment-related AEs	34%	30%	10%	20%
Any SAEs	2%	0%	2%	2%
- Treatment-related SAEs	0	0	0	0
Hypertension	1	1	0	0

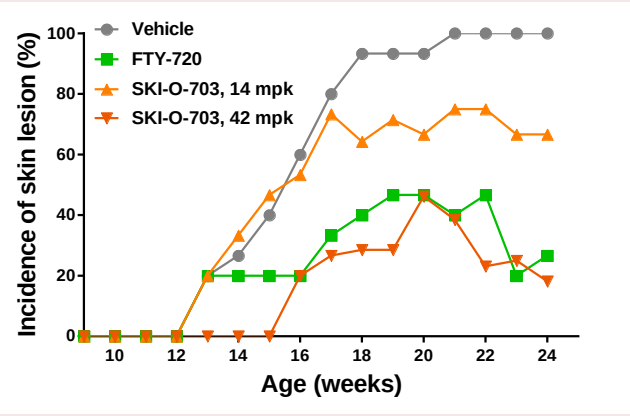
Screen ID	Screening	W1	W1	W2	W3	W5	W7	W9	W11	W12	W16	
300403	2	-	2	11	181	628	-	589	61	358	8	
100607	13	14	90	448	487	158	184	162	156	200	435	
400401	18	44	57	125	120	143	164	227	161	155	51	
200605	2	6	8	23	63	153	182	224	207	226	213	
300802	18	37	143	116	126	75	163	127	NT	NT	-	WD
301001	14	6	128	337	2	59	9	111	NT	NT	-	ET
300102	4	11	-	15	12	126	26	15	166	190	81	
100604	2	141	51	40	24	2	UTP	UTP	158	-	328	
100202	6	Aged	133	88	-	62	40	48	58	48	11	
100501	18	15	69	94	72	UTP	UTP	72	UTP	86	326	
200503	18	107	56	45	41	91	63	70	72	62	63	
400203	20	20	57	90	89	163	35	43	29	50	11	
100104	12	24	61	69	34	81	95	74	59	48	14	
100601	20	6	35	143	55	15	131	13	101	29	12	
300902	8	18	6	10	19	9	10	6	240	115	21	
200201	30	21	27	48	52	38	40	50	57	71	75	
100603	9	UTP	28	60	UTP	5	42	UTP	UTP	70	-	
100103	6	-	26	27	10	18	-	62	19	97	475	
300202	20	23	23	34	UTP	41	36	35	37	37	-	
200202	25	33	36	49	11	4	45	23	36	47	20	
400502	14	13	-	18	28	21	40	45	54	33	-	
200601	13	15	15	-	-	28	4	46	56	50	37	
200302	30	27	23	37	19	15	52	29	26	37	75	
100102	17	UTP	15	-	35	21	28	45	25	37	666	
100606	8	19	8	10	12	3	7	15	26	162	23	
300508	20	28	51	45	21	37	10	19	21	28	23	
400402	4	2	29	45	15	18	48	12	11	20	6	
100602	7	9	9	25	66	9	40	5	UTP	31	4	
400301	12	11	UTP	29	22	19	25	29	25	23	16	
400404	4	12	20	23	18	9	32	25	37	29	19	
200101	13	UTP	UTP	38	21	25	13	12	25	15	29	
500302	7	12	30	24	24	13	31	UTP	15	19	8	
300101	19	35	25	UTP	9	13	29	20	21	7	111	
200301	16	19	UTP	30	16	18	21	16	19	18	-	
200203	12	18	21	19	13	14	6	12	-	46	11	
300506	2	2	8	7	25	2	43	8	30	-	62	
100608	4	4	3	6	46	10	20	11	15	25	9	
100605	24	4	UTP	26	10	9	27	16	17	11	UTP	
100105	24	20	3	11	34	3	10	6	8	24	28	
300503	11	2	11	33	13	12	7	3	13	19	6	
200501	8	10	16	8	4	22	24	12	13	4	19	
300504	16	2	49	UTP	2	3	4	NT	NT	NT	-	ET
300502	5	13	9	18	8	8	2	21	6	21	2	
400501	7	6	21	5	9	18	12	4	UTP	17	22	
100609	25	10	4	20	21	2	12	8	9	11	44	
300701	3	16	8	10	7	8	2	5	12	25	UTP	
300801	4	4	-	-	7	10	13	5	-	5	3	
300501	17	5	-	UTP	11	4	16	3	3	4	3	
400102	7	5	4	4	5	4	NT	NT	NT	NT	-	ET (PD)
100205	3	3	2	4	3	NT	NT	NT	NT	NT	-	ET
400204	2	2	2	3	2	2	2	2	2	4	2	

적응증 확장

전신 홍반 루푸스 (Systemic lupus erythematosus)

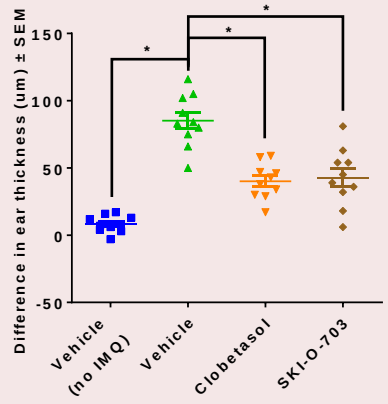
MRL-lpr/lpr mouse SLE model

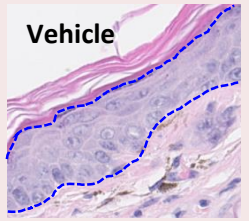


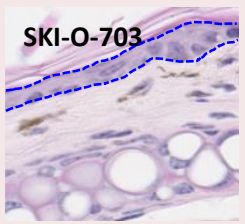


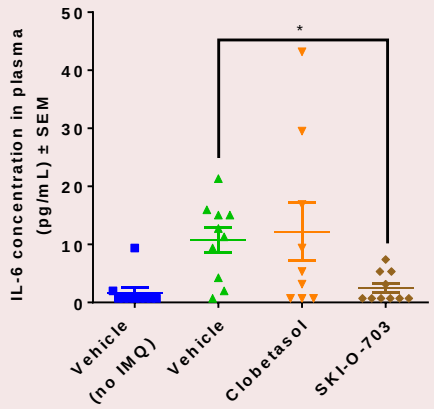
건선 (Psoriasis)

IMQ-induced mouse psoriasis model



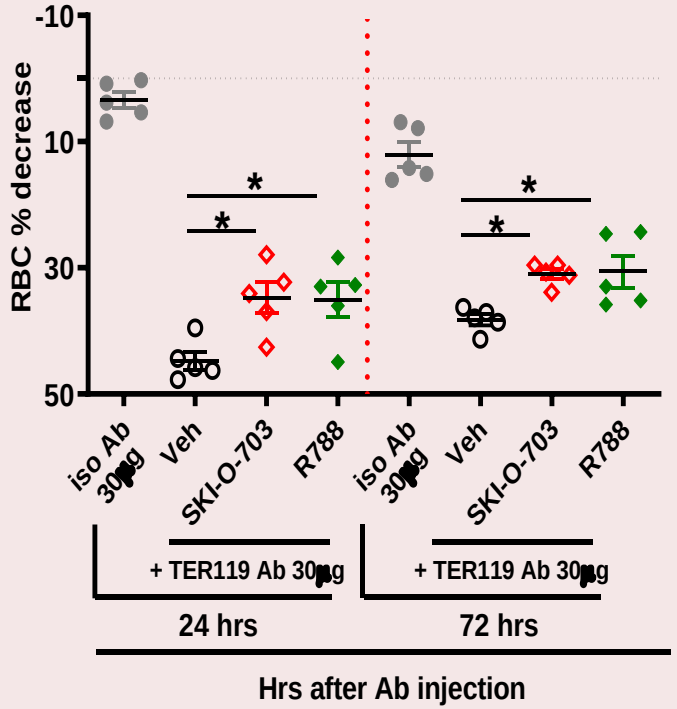




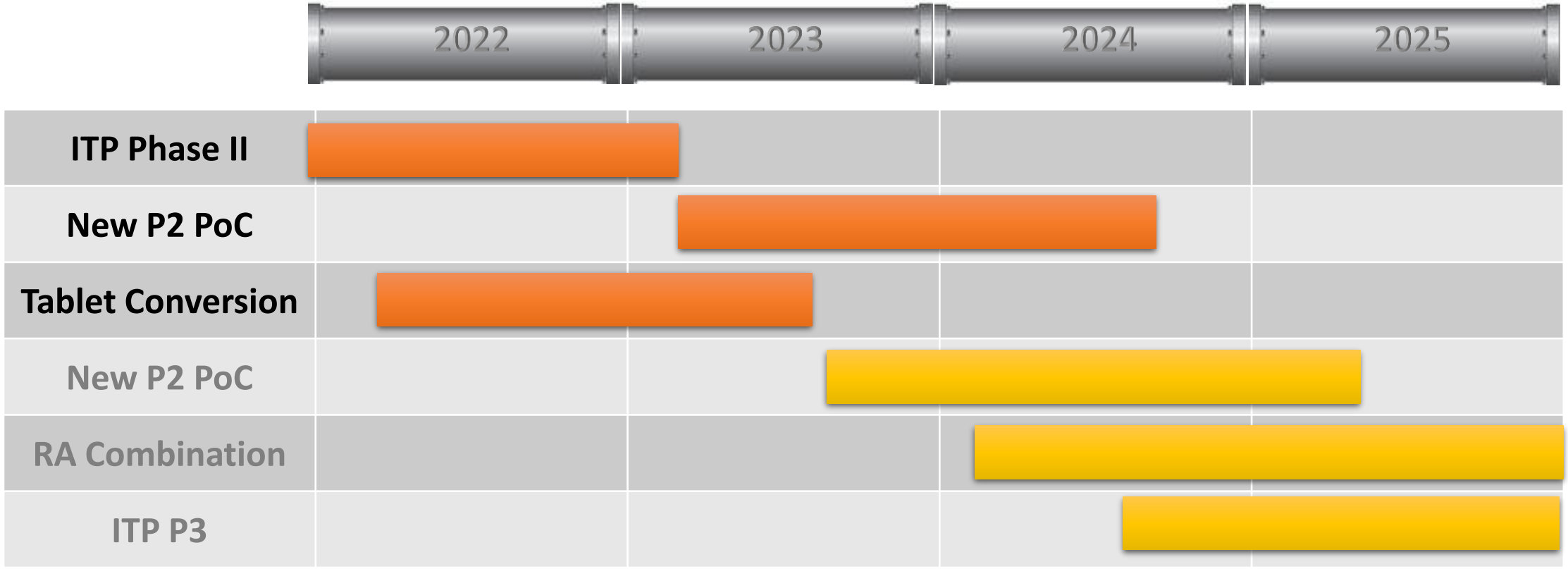


자가면역성 용혈성 빈혈 (Autoimmune hemolytic anemia)

α-TER119-induced mouse wAIHA model



Cevidoplenib, “Pipeline in a Product”



- ITP 임상2상 이후 글로벌 기술이전을 위한 활동 계획
- ITP pivotal 임상시험 준비

Planned
Tentative

SKI-G-801

The Best-in-class FLT3/AXL Dual Inhibitor

SKI-G-801 Executive Summary

Potent and selective, and differentiated FLT3/AXL dual inhibitor

FLT3 돌연변이를 가진 급성골수성백혈병 (AML)

- US FDA Orphan Drug designated (2018)
- **임상1상 용량증량시험 종료**
  - 정맥주사 (14일 투여, 14일 휴약)
  - 전반적으로 좋은 내약성
  - **1 환자에서 완전관해(Complete remission)**; 대부분의 FLT3 돌연변이를 가진 환자는 기대할 만한 반응을 보임
- 제형 개발을 통해 경구제제로 개발

고형암 적용 면역항암제

- 다양한 전임상 모델에서 면역반응에 의한 탁월한 항암효과 확인
  - 단독투여 및 anti PD-1과 병용투여에서 좋은 효과를 확인
  - Anti PD-1 으로 강화 된 고유한 항종양 면역반응
- **임상1상 용량증량시험 진행 중**
  - 경구용 정제, 100 to 500 mg qd
  - MTD 확인 후 코호트 확장 계획

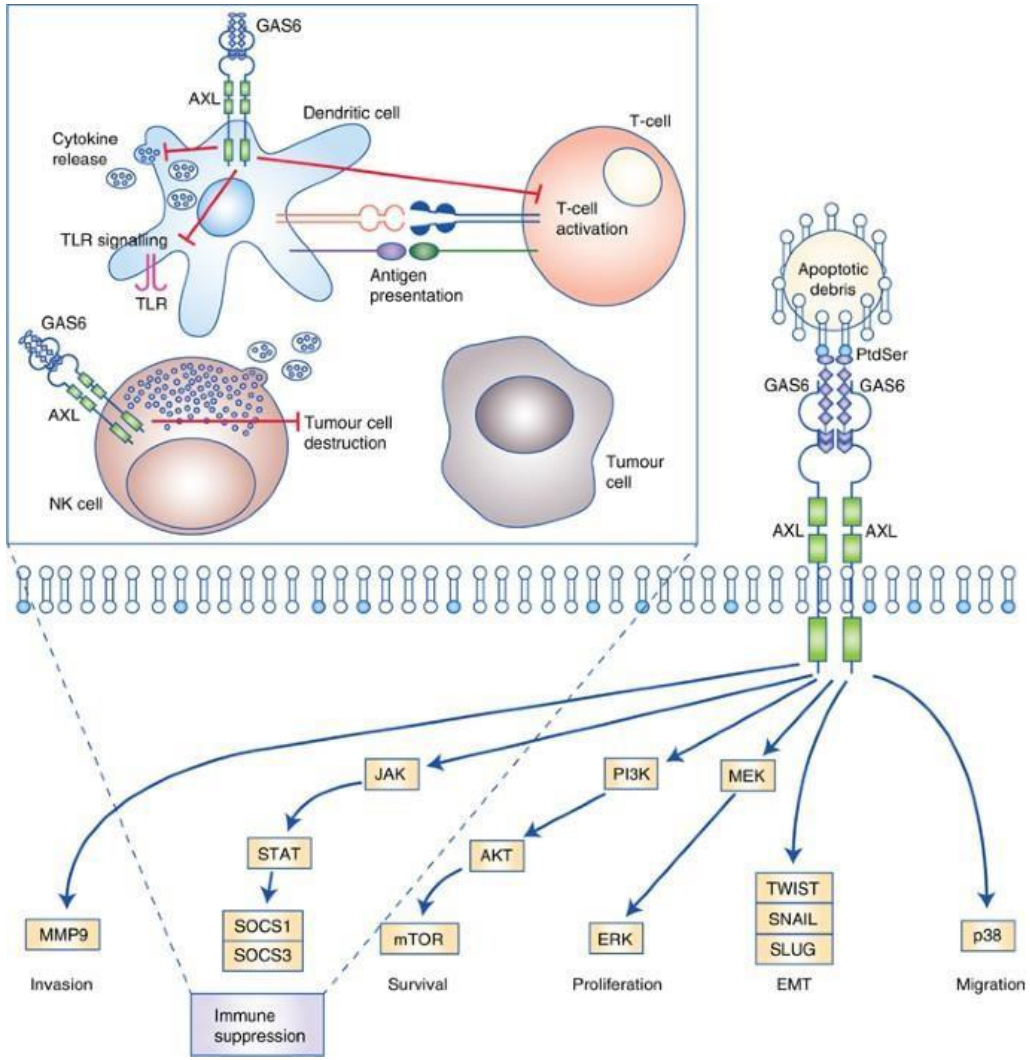
SKI-G-801 AML 용량증량시험 완료

Patient	FLT3 status	Dose (mg/kg)	Treatment-related SAE	Response (BM blast)
101	WT	0.45	None	PD
402	WT	0.68	None	PD
404	WT	1.04	None	PD
405	WT		None	PD
103	WT	1.58	None	PD
601	FLT3-ITD	2.41	None	SD in Cycle 1 (57% → 39%), then progressed in Cycle 2
602	FLT3-ITD	3.66	Gr 4 neutropenia	**CRi (72% → 0.5%)** after Cycle 1; DLT per protocol
603	WT		None	PD
604	FLT3-TKD		None	PR in Cycle 1 (73% → 12%), then progressed
605	WT	4.21	None	PD
607	WT		None	PD
801	WT		None	Not evaluable
608	FLT3-ITD	5.57	> Gr 3 pneumonia	(DLT)
802	FLT3-ITD		Gr 3 pneumonia, etc	(DLT)

경구제제로 전환 후 AML에 대항 임상개발을 계속 할 예정

SKI-G-801 고형암 적용; 치료의 근거

- AXL의 과발현은 **악성종양의 진행**과 관련이 있음
  - 여러 암종에서 좋지 않은 예후와 관련
  - Epithelial-mesenchymal transition (EMT)과 암의 전이를 촉진
  - 치료제 내성을 유도; esp. **TKI- 내성 EGFR-돌연변이 비소세포성폐암(NSCLC)**
- **선천 면역관문 (Innate immune checkpoint)**
  - AXL은 대식세포 (macrophage)와 수지상세포 (dendritic cell)에서 apoptotic cell 유래 면역억제를 강화하는 종양미세환경 (tumor microenvironment)을 조성
  - AXL은 **면역관문억제제 내성 종양에서 과발현** 돼 있음

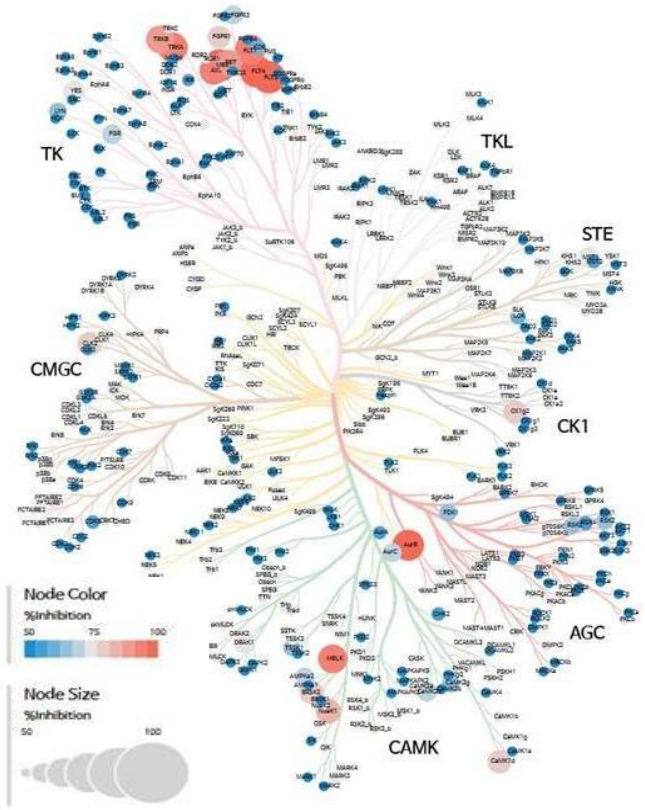


Gay et al., British J Cancer 2017

AXL Inhibitors; 경쟁사 현황

약물	개발사	AXL IC50	Others	적응증	임상단계	Remark
Bemcentinib (R428, BGB-324)	BerGenBio	14nM		급성골수성백혈병(AML), 골수이형성증후군(MDS)	II	Completed
				COVID-19	II	Completed
				비소세포성폐암 (NSCLC), 키트루다 병용	II	
ONO-7475	Ono Pharma	0.7 nM	Mer (1.0 nM), FLT3 (147 nM)	불응성/재발성 AML/MDS 단독 혹은 벤클렉스타 (venetoclax) 병용	I/II	
				진행성 혹은 전이성 고형암 단독 혹은 옵디보 (ONO-4538, nivolumab) 병용	I	
AB-329 DS-1205	Daiichi Sankyo	1.3 nM		EGFR-돌연변이 NSCLC 에서 이레사 (gefitinib) 병용 (n=21)	I	Completed
				EGFR-돌연변이 NSCLC 에서 타그리소 (osimertinib) 병용 (n=13)	I	Completed ORR = 0%
Dubermatinib (TP-0903)	Sumitomo Dainippon	27 nM		진행성 고형암 (n = 177)	I	
				만성 림프구성 백혈병 (CLL) 단독 혹은 임브루비카 (ibrutinib) 병용	I/II	Terminated
				FLT3-돌연변이 AML (n = 80)	Ib/II	
HH30134	Haihe Biopharma	AXL	FLT3, NTRK	진행성 고형암 (n =50)	I	
Q702	Qurient	0.7nM	Mer (0.8 nM) CSF1R (8.7nM)	진행성 고형암 (n = 78)	I	

SKI-G-801; a Potential Best-in-Class AXL inhibitor



Kinase	IC50 (nM)
FLT3	1
Mer	1
Aurora B	6
Ret	9
FLT1	18
Fms	19
Axl	20
Aurora C	24
FGFR1	25
FGFR3	30
KDR	39
c-Kit	142
IGF-1R	300
PDGFRa	300
PDGFRb	300
EGFR	300

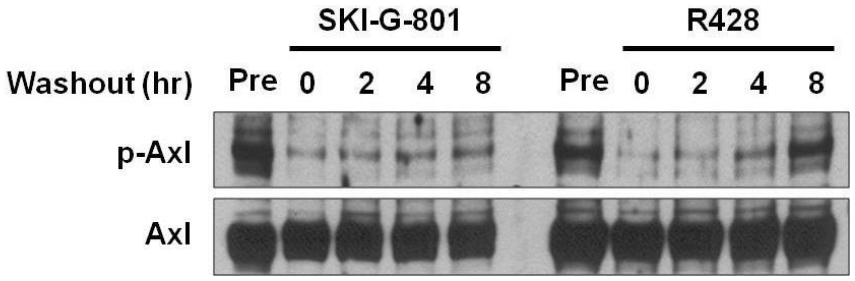
- 다수의 kinase들에 대해 뛰어난 선택성 확보
- 생리학적 ATP 농도에서도 좋은 potency를 유지
- 경쟁약물 대비 약물 처리 후 washout 이후에도 p-AXL 저해효과를 장시간 유지

Enzyme inhibition (Eurofins, UK)

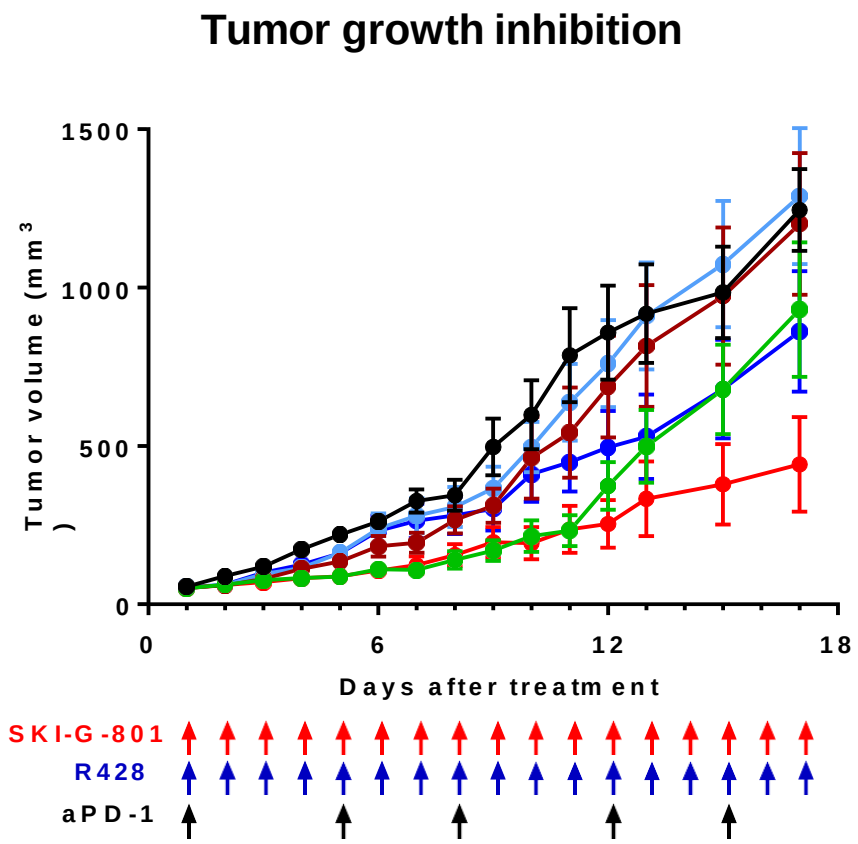
Kinase	IC_{50} (nM)	
	SKI-G-801	R428
Axl(h)	18	6
Mer(h)	2	9
Tyro(h)	>1,000	612

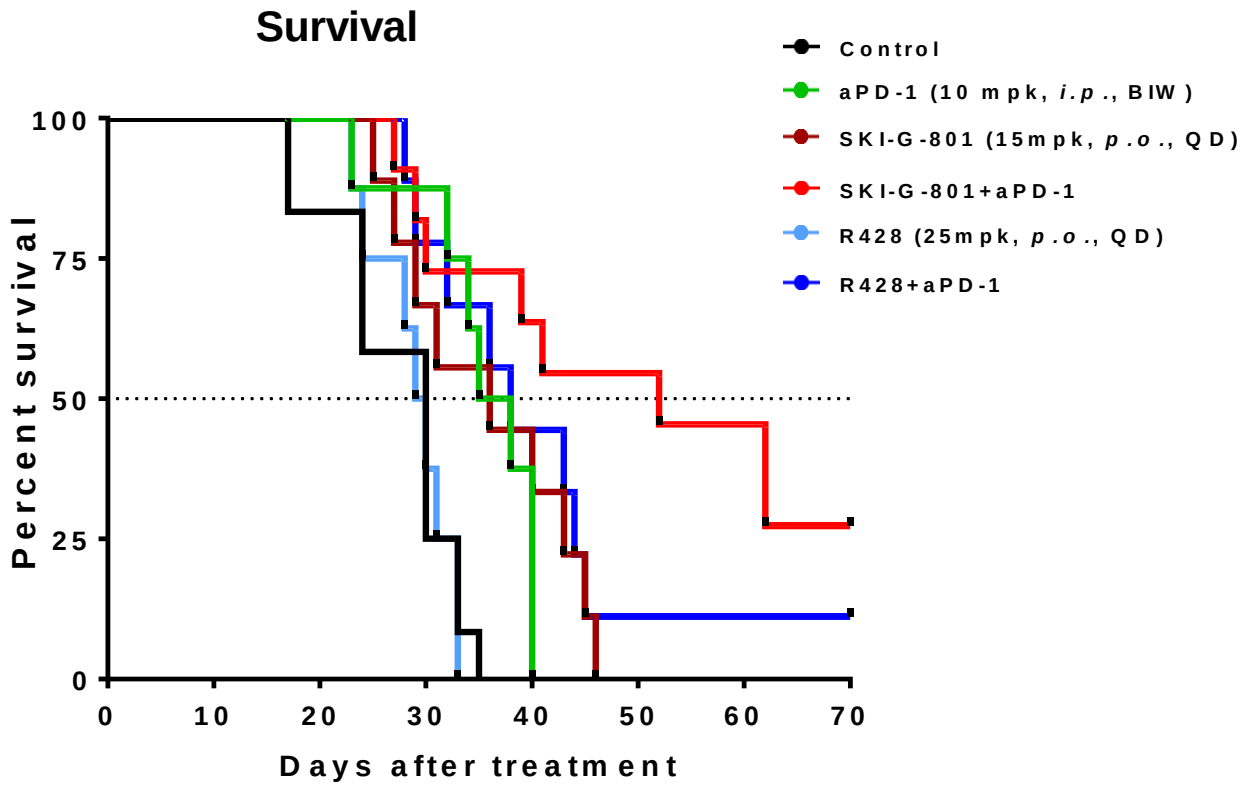
ATP dependency (in-house)

Compound	AXL (IC_{50}, nM)		
	ATP Km	1 mM ATP	Fold
SKI-G-801	12.5	113.9	9.1
R428	6.3	240.8	38.2



SKI-G-801; 전임상 효능시험 하이라이트 1

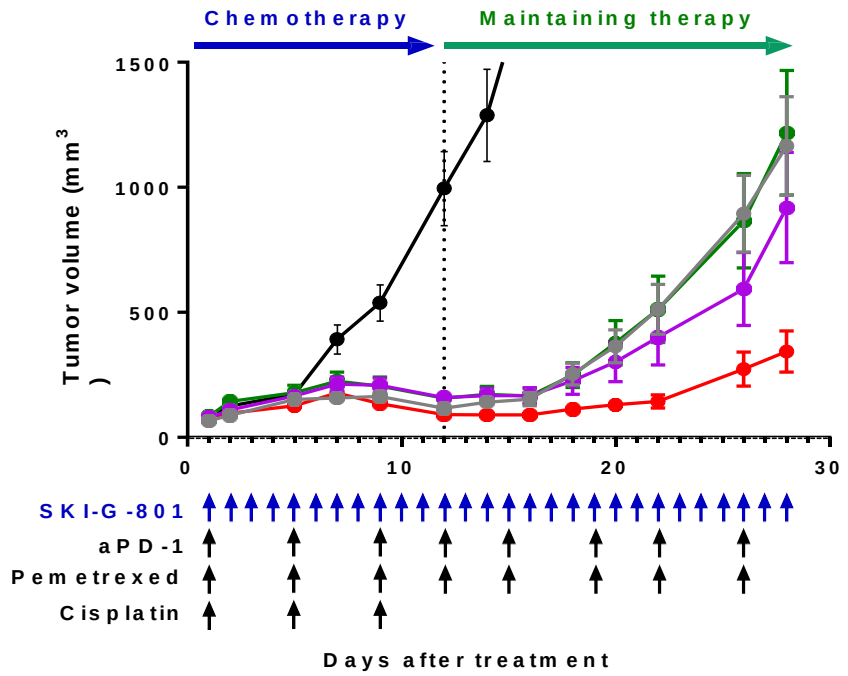


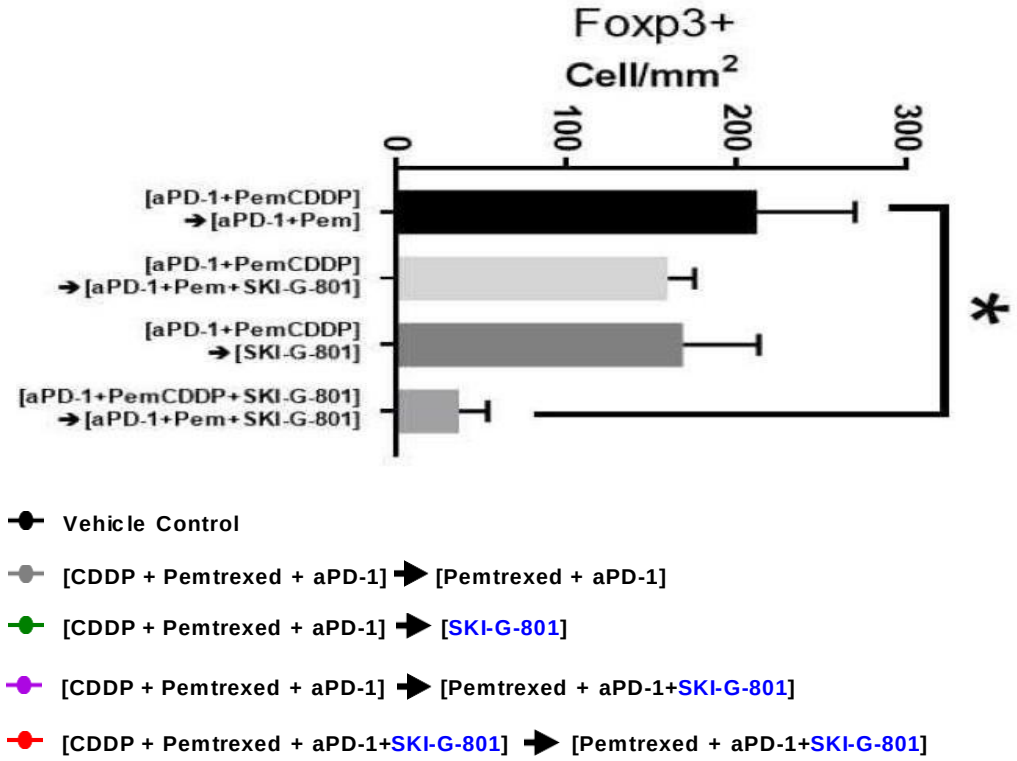


마우스 CT26 syngeneic 종양모델에서 단독요법 및 anti-PD-1과 병용투여 시 저용량에서도 경쟁 약물인 bemcentinib보다 우수한 효능을 확인

SKI-G-801; 전임상 효능시험 하이라이트 2

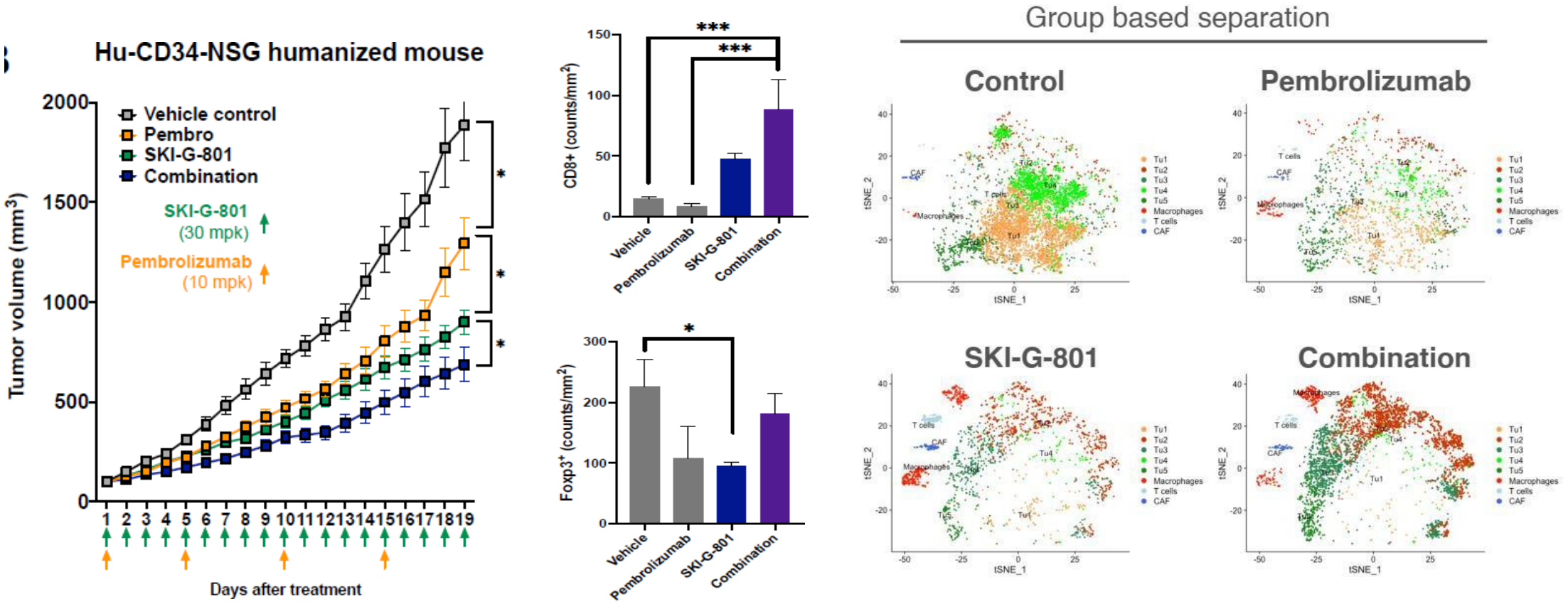
TC1 Lung adenocarcinoma model





SKI-G-801은 폐암 선암 (adenocarcinoma) 모델에서 표준요법 (standard of care)과 함께 투여 시 종양미세환경 (TME)의 FoxP3+ Treg 세포를 현격히 감소시켜 주고, 종양의 재성장 또한 크게 감소시켰으며, 마우스의 생존율을 증가시킴

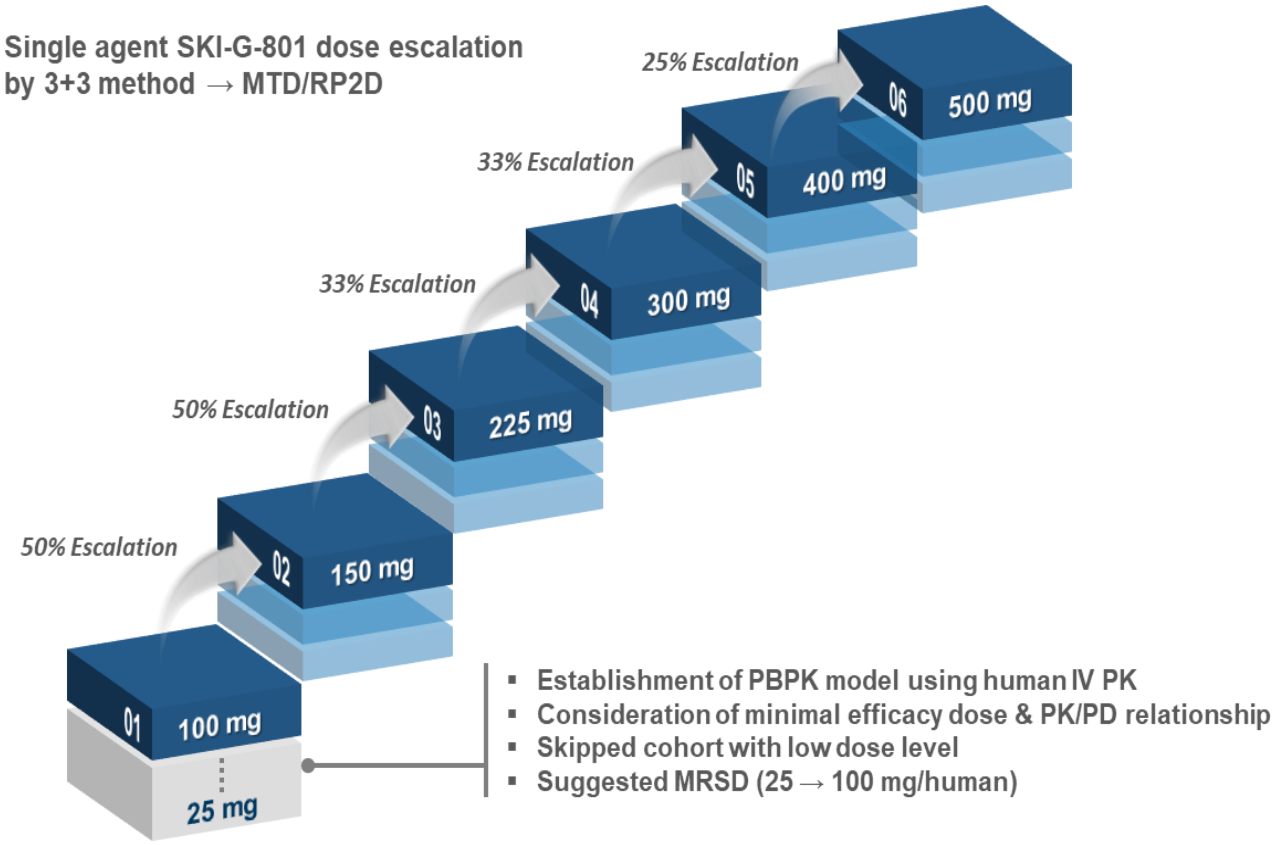
SKI-G-801; 전임상 효능시험 하이라이트 3



소세포성폐암 PDX model on humanized NSG 마우스에서 종양성장을 억제, 또한 anti-PD-1 병용투여군에서 시너지 효과 확인; CD8 T세포의 상당한 증가와 Treg 세포의 감소로 확인; 이는 anti PD-1 병용투여군에서 더 두드러짐을 single cell RNA sequencing으로도 추가 확인

SKI-G-801 고형암 적용; 임상개발

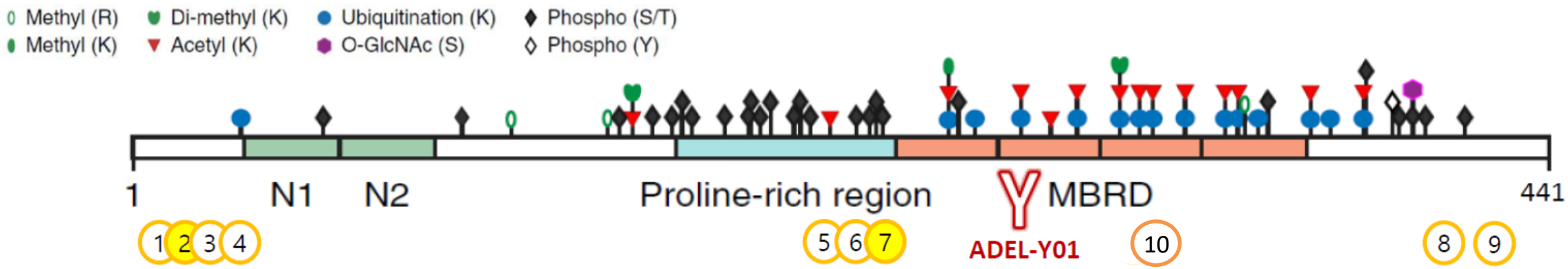
- Open-label, 다기관, 고형암 환자에서 안전성, 내약성, 그리고 약물동태 (pharmacokinetics) 평가, 단독 투여 용량탐색시험
- 경구용 정제 (100 to 500mg) 1 cycle 당 28일 투여
- 연구책임자 (Principal investigators)
  - 임선민 (연세암병원; lung cancer)
  - 이재련 (서울아산병원; GU cancer)
  - 박연희 (삼성서울병원; TNBC)
- **2번째 코호트 종료; 중대이상반응 (SAE) 없음**
- Extensive biomarker study
- 코호트 확장 예정, AML 포함



ADEL-Y01

Antibody Targeting Pathological Tau Protein

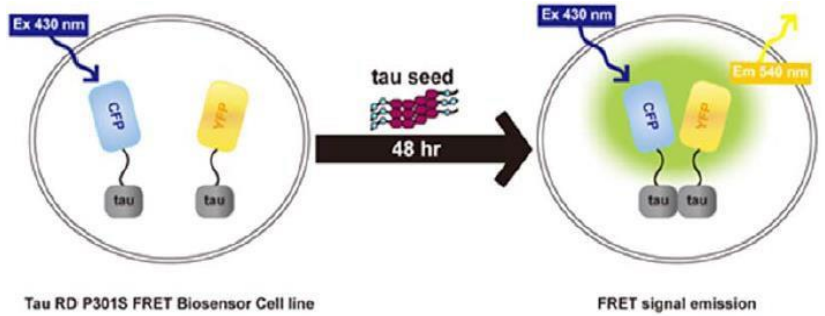
ADEL-Y01; 경쟁사 현황

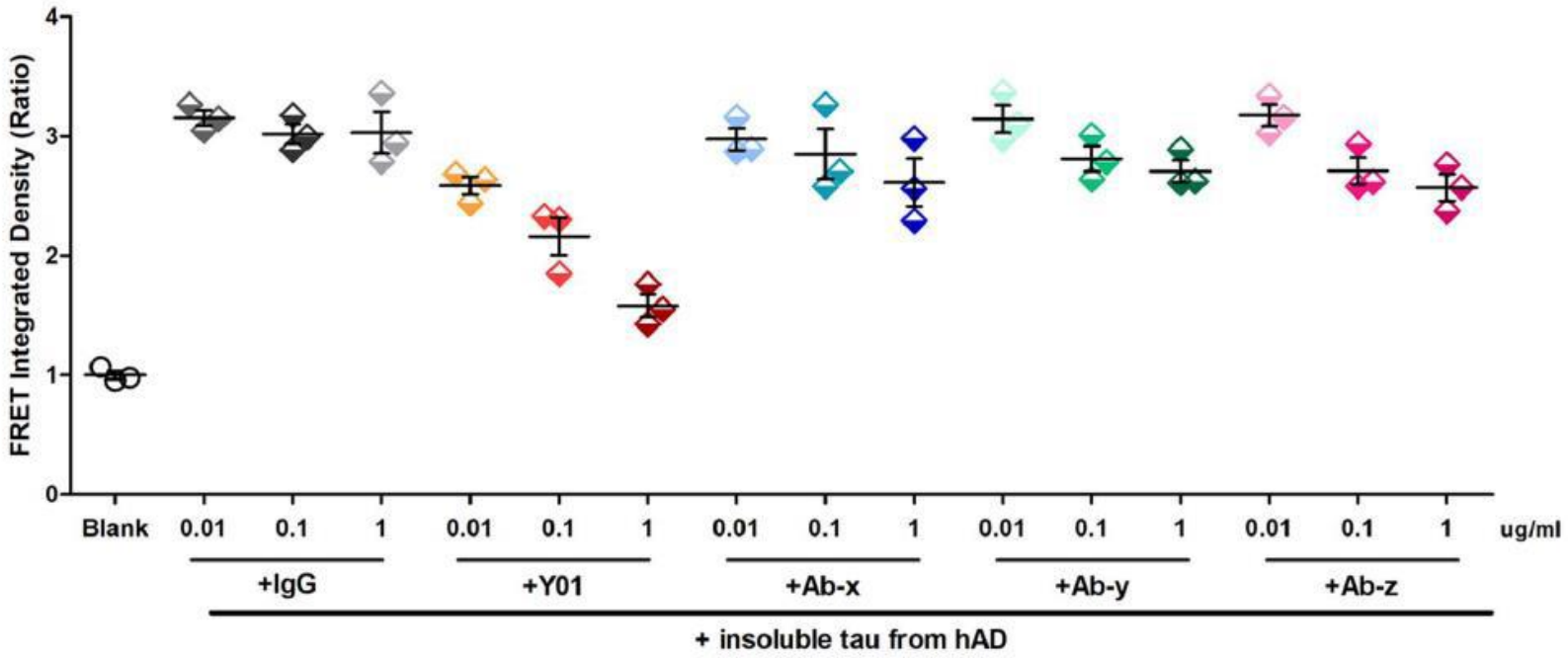


	약물	Synoyms	개발사	Epitope	임상시험 상황
1	Zagotenemab	LY3303560, MC1	Eli Lilly	Tau aggregate (7-9:313-322)	Failed in P2
2	Gosuranemab	BIIB092, BMS-986168, IPN007	Biogen, BMS, iPerian	Secreted N-term fragment (15-24)	Terminated at P2
3	C2N-8E12	HJ8.5 (m)	Abbvie, C2N	Extracellular tau (25-30)	Failed in P2
4	Semorinemab	RO7105705, RG6100	Roche, AC Immune	Tau N-term	Failed in P2; another ongoing
5	JNJ-63733657		Janssen	Phospho tau PRR (pT217)	P2 ongoing until 2025
6	PNT001		Pinteon	Phospho tau PRR (cis-pT231)	Stopped at P2 in TBI; AD pending
7	Bepranemab		UCB, Roche	Tau PRR (235-246)	P2 ongoing until 2025
8	Lu AF87908		Lundbeck	Phospho tau C-term (pS396)	P1 ongoing
9	RG7345	RO6926496	Roche	Phospho tau C-term (pS422)	Stopped at P1
10	E2814		Eisai	Mid domains (R2 and R4)	P1 onglong

ADEL-Y01; Inhibition of Tau Propagation

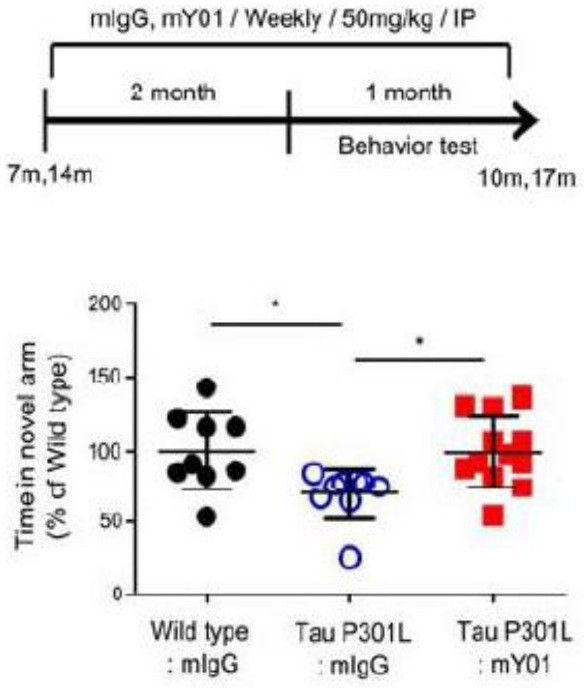
- Tau단백질의 spreading과 seeding을 측정하기 위한 biosensor assay
- ADEL-Y01은 경쟁 항체보다 우수한 활성을 보임
- 알츠하이머 환자의 뇌척수액 (CSF, cerebrospinal fluid)을 이용한 Ex vivo screening을 진행 중

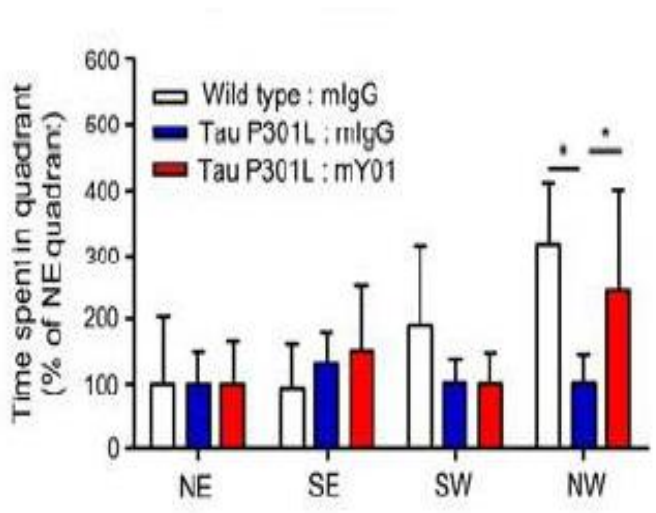


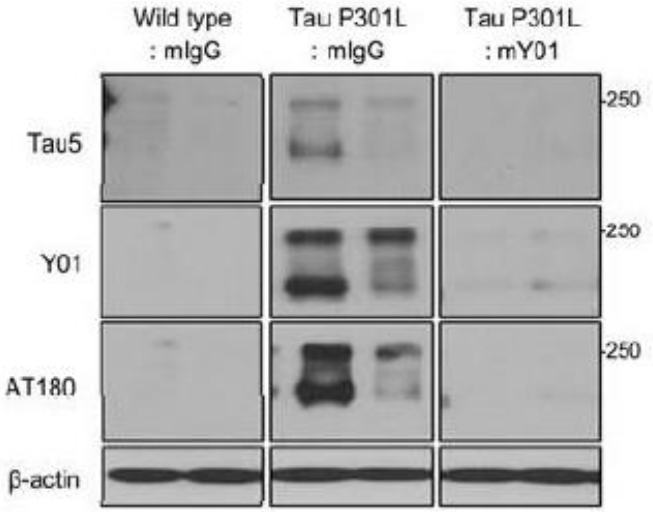


x = gosuranemab
y = bepranemab
z = E2814

ADEL-Y01; In Vivo 효능 시험 (P301L 마우스 모델)

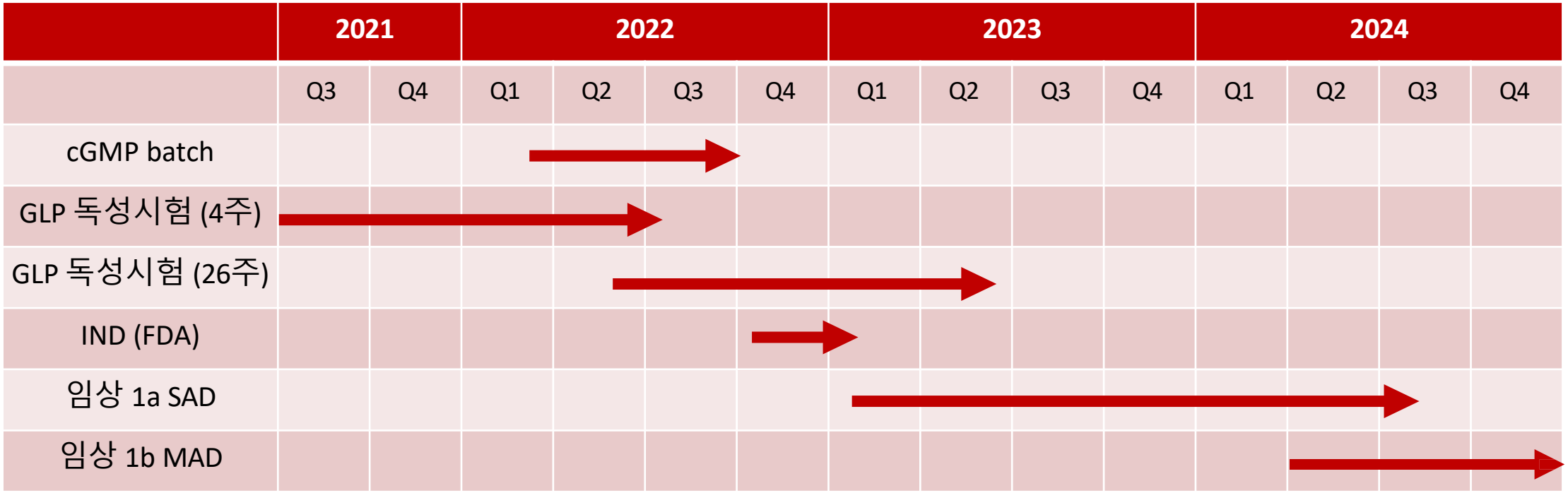






P301L Tau병증 마우스 모델에서 Y01 투여군은 대조군에 비해 뇌에서 타우 응집체의 축적을 방지하고 인지능력(Y-maze and water maze 시험)을 유의하게 개선함.

ADEL-Y01; Development Timeline



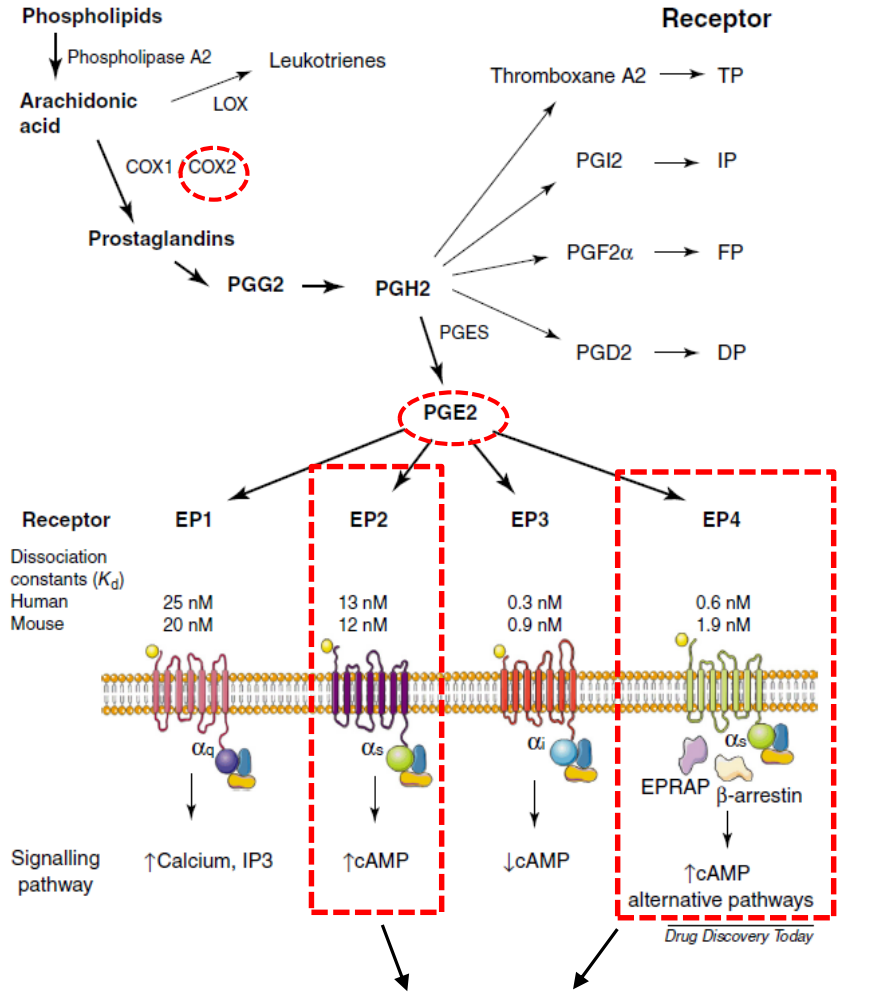
- GMP 생산 완료
- GLP 독성시험 (4 주; 설치류와 영장류) 완료
- **IND (US FDA) filing targeted in 2022 Q4; 임상1상 to start in 2023 Q1**
- Extensive pre/clinical biomarker studies ongoing/planned

OCT-598

EP2/4 Dual Antagonist

EP2/4 Dual Antagonist - Background

PGE2/EP2/EP4 signaling and cancer



Pro-tumorigenic (Tumor-promoting and immune-suppressive)

- **PGE2**와 PGE2 합성의 핵심적인 효소인 **COX2**는 결장암, 폐암, 유방암, 방광암, 피부암, 난소암 등 많은 암종에서 과발현 돼 있는데, 이는 종양의 개시, 증식, 전이 등에 기여함.
- **COX2 억제제**에 의한 PGE2 생성 저해는 동물종양모델에서 종양의 성장을 억제했으나 **심혈관계와 위장관계에 위험성**이 있어 추가 약물 개발이 이루어지지 않음
- PGE2는 **EP2와 EP4 수용체** 활성화를 통해 세포내 cAMP level을 증가시켜 종양 형성을 촉진
- **유전적으로나 약리적으로** EP2와 EP4를 억제시켰을 때 동물모델에서 종양 성장을 억제

Kalinski P (2011) J.Immunology; Nakanish M et al (2013) Semin Immuopathol; Markovic T et al (2017) Drug Discovery Today; Nagahisa A (2020) Frontiers in Immunology

경쟁사 현황

Drug development targeting EP2/4 is still in early stages

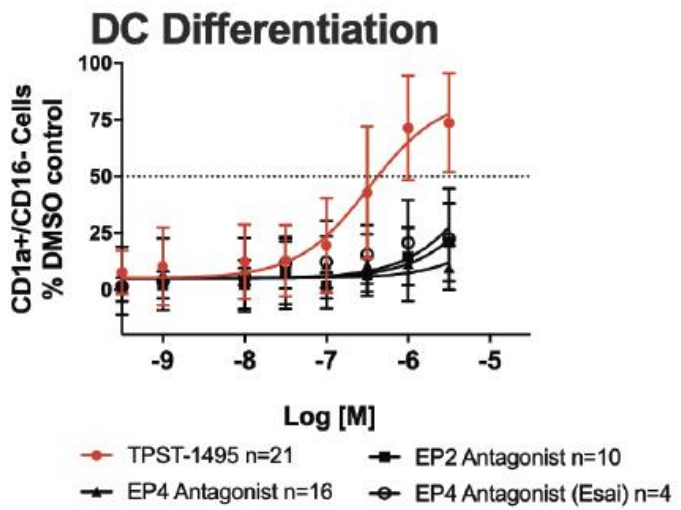
	EP2/EP4 dual antagonist	EP4 antagonist			
	TPST-1495	AN0025 (E7046)	ONO-4578 (BMS-986310)	IK-007 (Grapiprant)	INV-1120
구조	Not known	Known	Not known	Known	Known
개발사	Tempest	Adlai Nortye	BMS/Ono	Ikena Oncology	Shenzhen Ionova Life Sciences
목표 적응증	Solid Tumor, MSS CRC, Lung cancer, Head and Neck, Bladder Cancer, TNBC, Gastric Cancer	Neoadjuvant Therapy in Rectal Cancer, Solid tumors, Colorectal cancer	Solid tumors	NSCLC, colorectal cancer	Solid tumors
개발 상황	• NCT04344795 P1a/P2b (mono and with anti-PD-1) 5/7/2020: first patient dosed	• NCT03152370 P1, 2017 • NCT04432857 P1 (combo with anti-PD-1), 2020	• NCT03155061 P1 (mono and combo with anti-PD-1), 2017 • NCT03661632 P1 (mono), P2 (combo with anti-PD-1, 2018	• NCT03696212 P1/2 (combo with anti-PD-1), 2018 • NCT03658772 P1 (combo with anti-PD-1), 2018	• NCT04443088 P1 (mono), 2020
용량/용법	BID	QD		300mg BID, 450mg q12h, 600mg q12h	QD

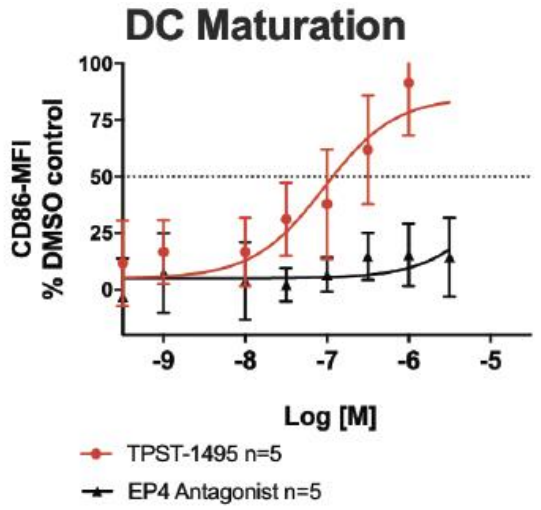
이중저해 효과의 근거

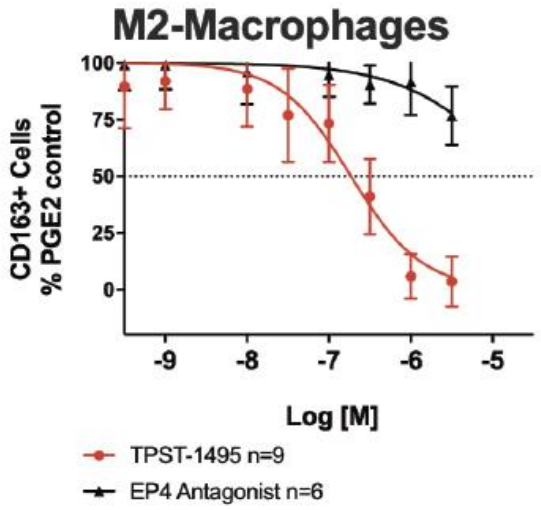
이중저해시만이 PGE2 유래 면역억제환경을 개선할 수 있음

- EP2의 경우 cAMP/PKA 신호자극을 통해 EP4의 여러 생리적 기능을 공유 함
- EP2와 EP4 모두 종양 형성 신호와 연관 됨
- **이중저해제 (TPST-1495)는** PGE2로 인한 수지상세포 (dendritic cell, DC)의 분화와 활성 억제 환경을 극복
- 이중저해제는 PGE2로 인한 단핵구(monocyte)의 M2 대식세포(M2 macrophage)로의 분화를 억제

DC differentiation from PGE2-treated human monocytes



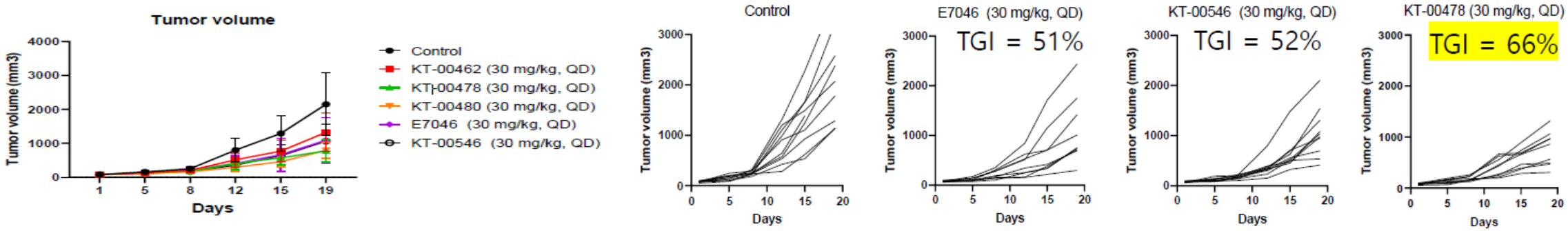




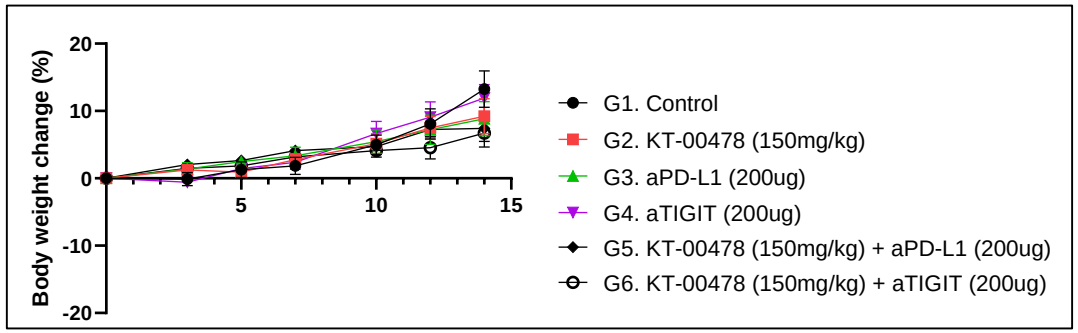
(2019-SITC-Poster—Tempest)

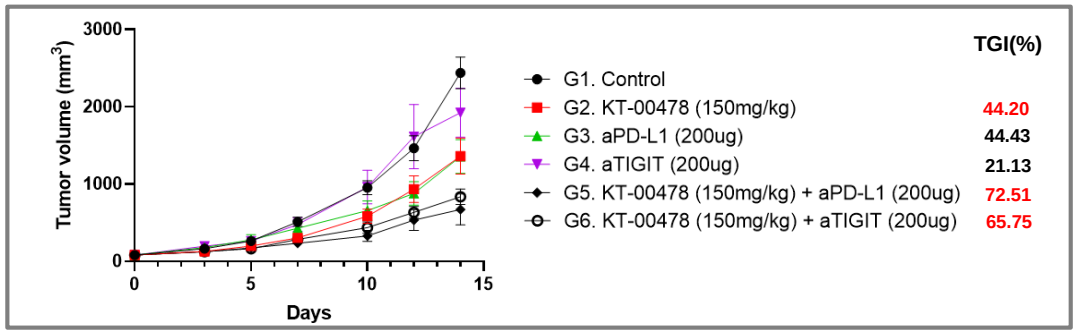
In Vivo 효능시험

OCT-598 (KT-00478)는 MC38 syngeneic 마우스 모델에서 단독투여시 항종양효과를 확인했고, 동일용량에서 경쟁사 화합물보다 우수한 종양성장억제 효과를 보임 (E7046 and KT-00546)



KT-00478는 MC38 마우스모델에서 anti-PD-1과 병용투여 시 더 좋은 종양성장억제 효과를 확인





The Best is Yet to Come

Q&A