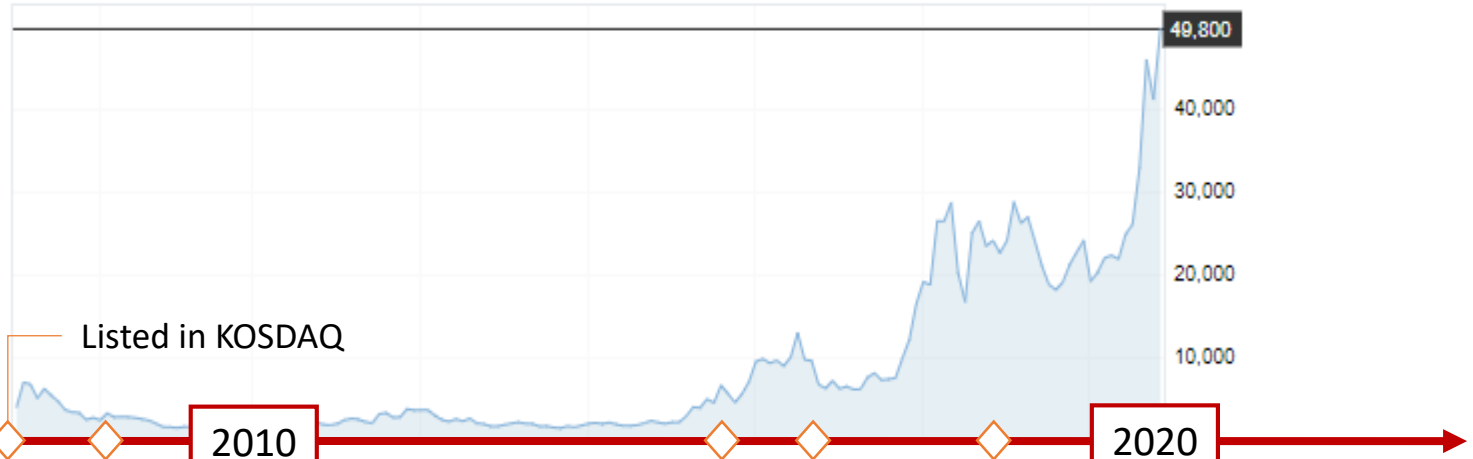
Oscotec 3.1

Agenda

- Oscotec R&D
  - Vision
  - Strategy
    - Platform technologies
    - In-house discovery programs
    - Pipeline via open innovation
      - LSD1; Beactica partnership
      - Y-01; ADEL partnership
- Clinical pipeline update
  - SKI-G-801
  - Cevidoplenib
- Business update
- Q&A

Oscotec 3.0; the New Beginning

Oscotec Inc.



Founded

2000

Listed in KOSDAQ

2010

Established a US subsidiary, GENOSCO, in Boston

2020

Lazertinib L/O to Janssen

Lazertinib L/O to Yuhan Corp.

Clinical trials SKI-G-801 (AML)

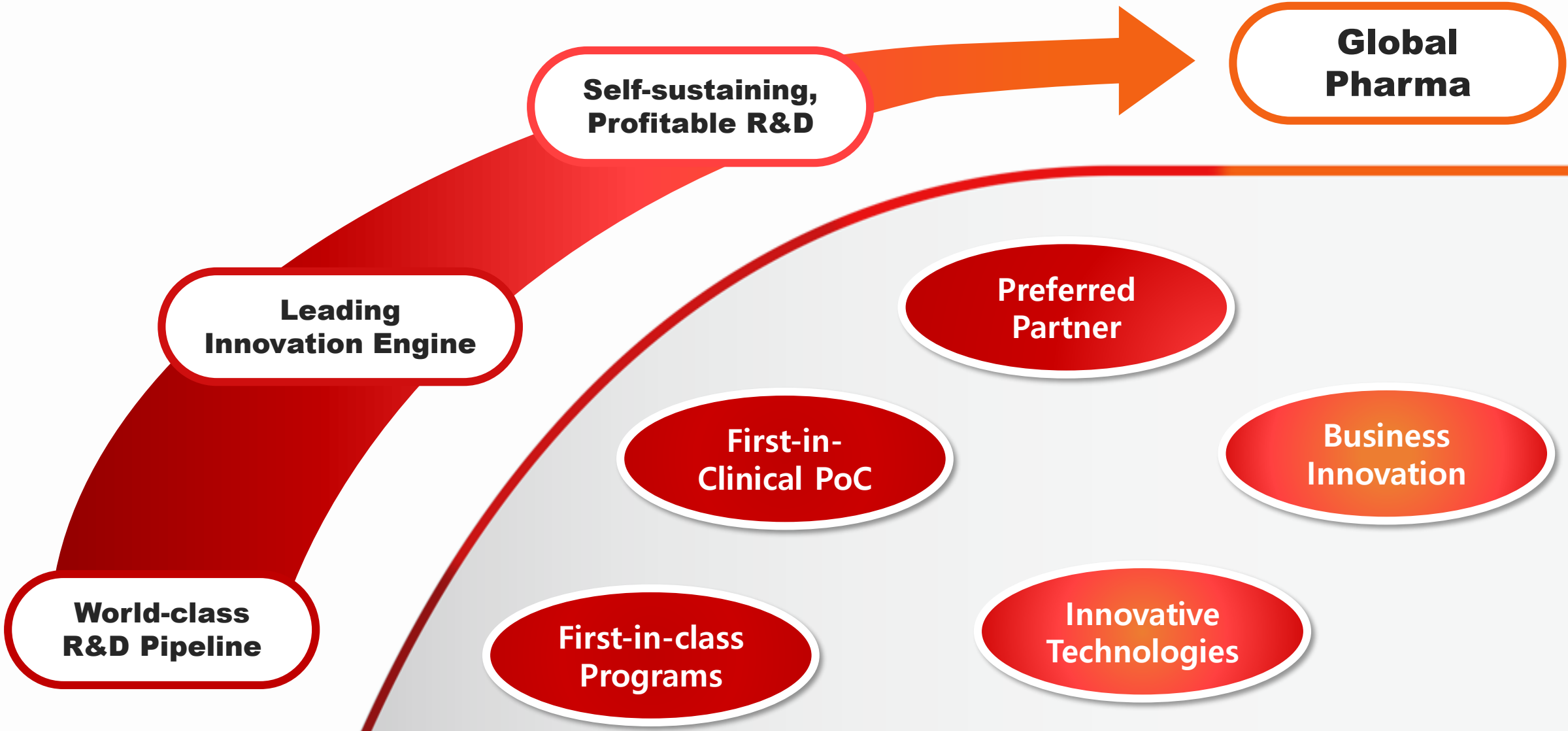
Clinical trials SKI-O-703 (RA, ITP)

Stage 1. Start Up

Stage 2. Grow Up

Stage 3. Scale Up

On the Horizon and Beyond



The Best is Yet to Come

Clinical Pipeline

- ≥1 L/O Every Year
- ≥1 NME IND Every Year

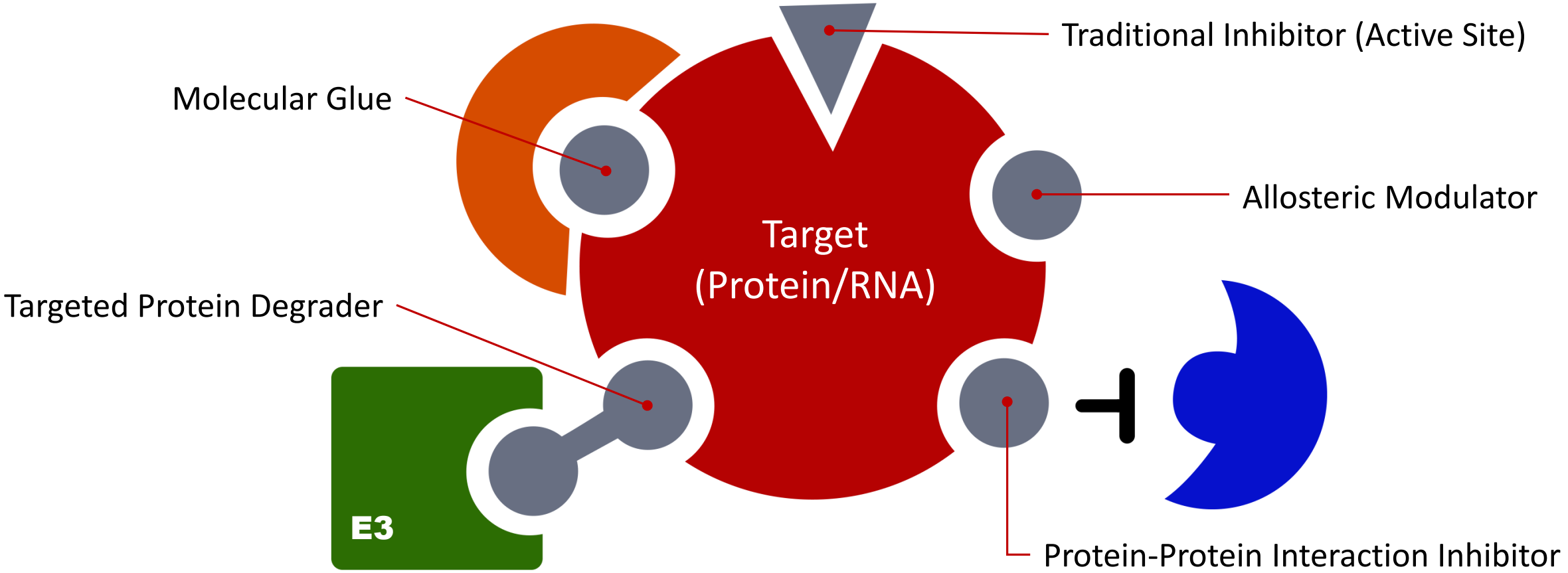
Discovery Pipeline

- Open Innovation
- In-house Programs

Platform Technologies

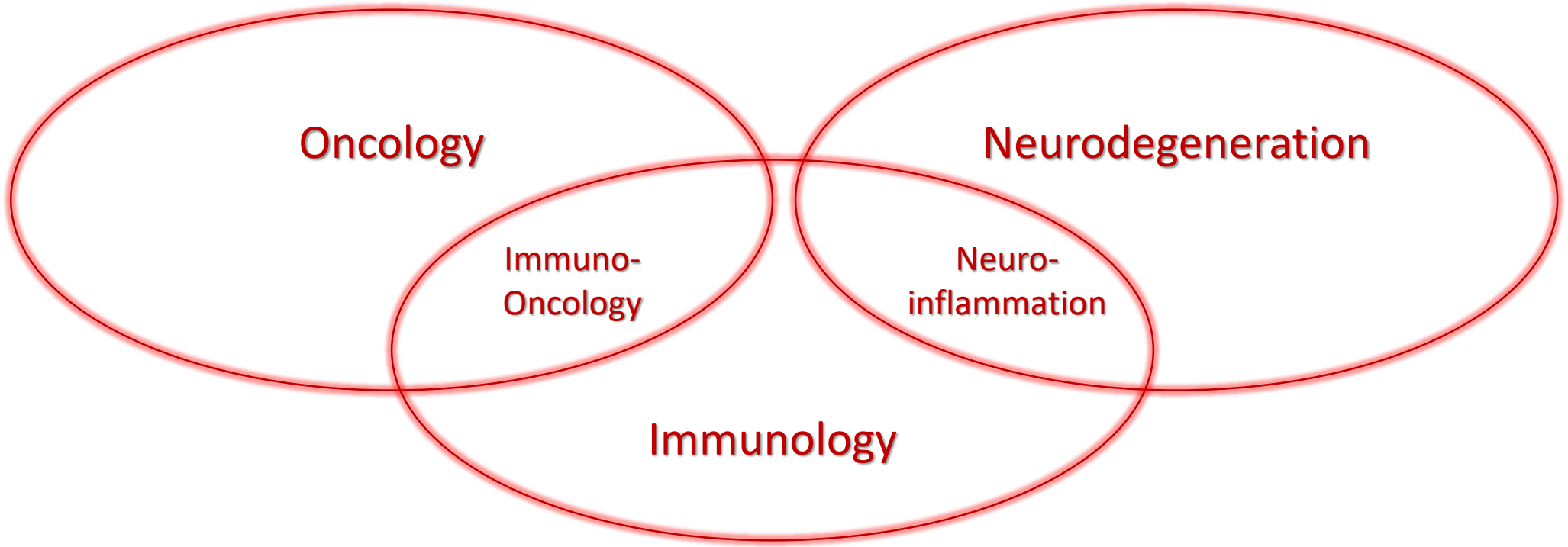
- Transformative Hit-finding Tech
- “Undrugged” Target Classes

New Grammar of LMW Drug Discovery



"Undrugged" Target Class <<< Oscotec Inc. >>> Ultrafast Hit/Lead Finding

Discovery Pipeline Strategy

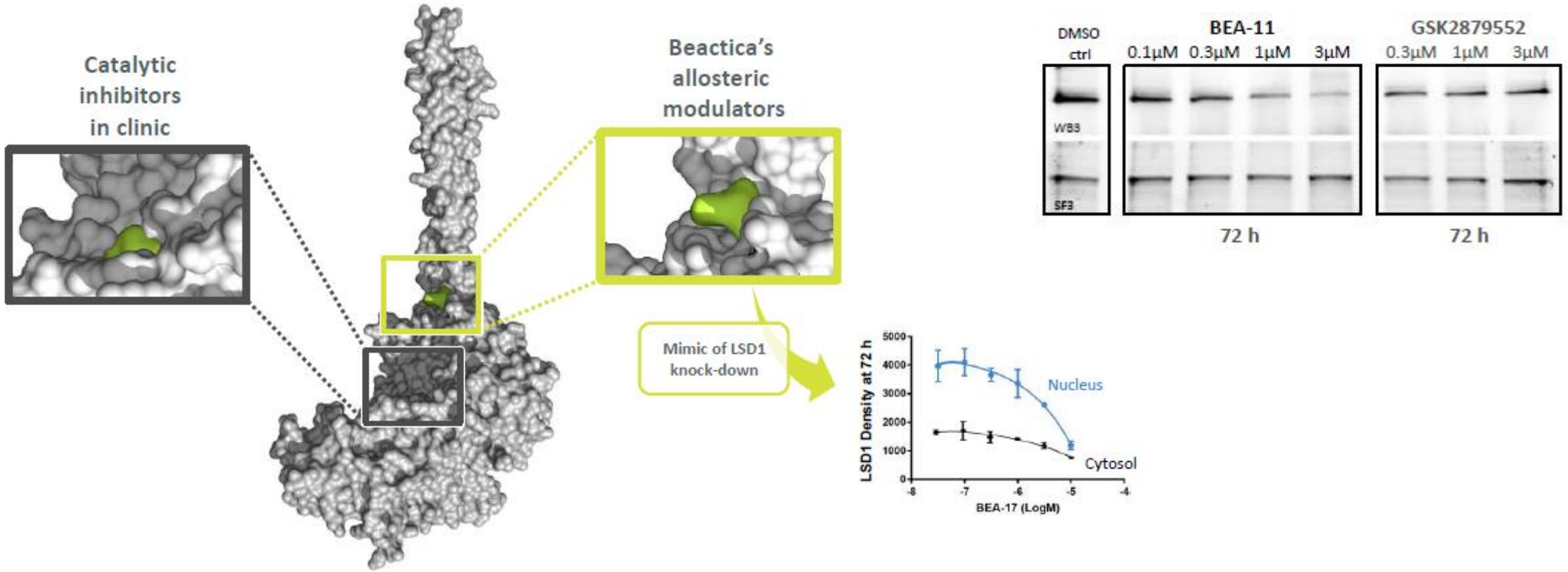


Internal Programs **External Programs**

Oscotec R&D Pipeline

Program	Target	Hit ID	Hit2Lead	Lead Op	Preclinical	Phase I	Phase II
Cevidoplenib	SYK						
SKI-G-801	FLT3						
	AXL						
ADEL-Y01	TAU				2022		
LSD	LSD1			2022	2023		
(New)				2022	2023		
(New)				2023			
ONC1	(Undisclosed)		2022	2023			
ONC2	(Undisclosed)		2022	2023			
ONC3	(Undisclosed)	2022	2023				
…							

Beactica LSD1 Allosteric Modulator

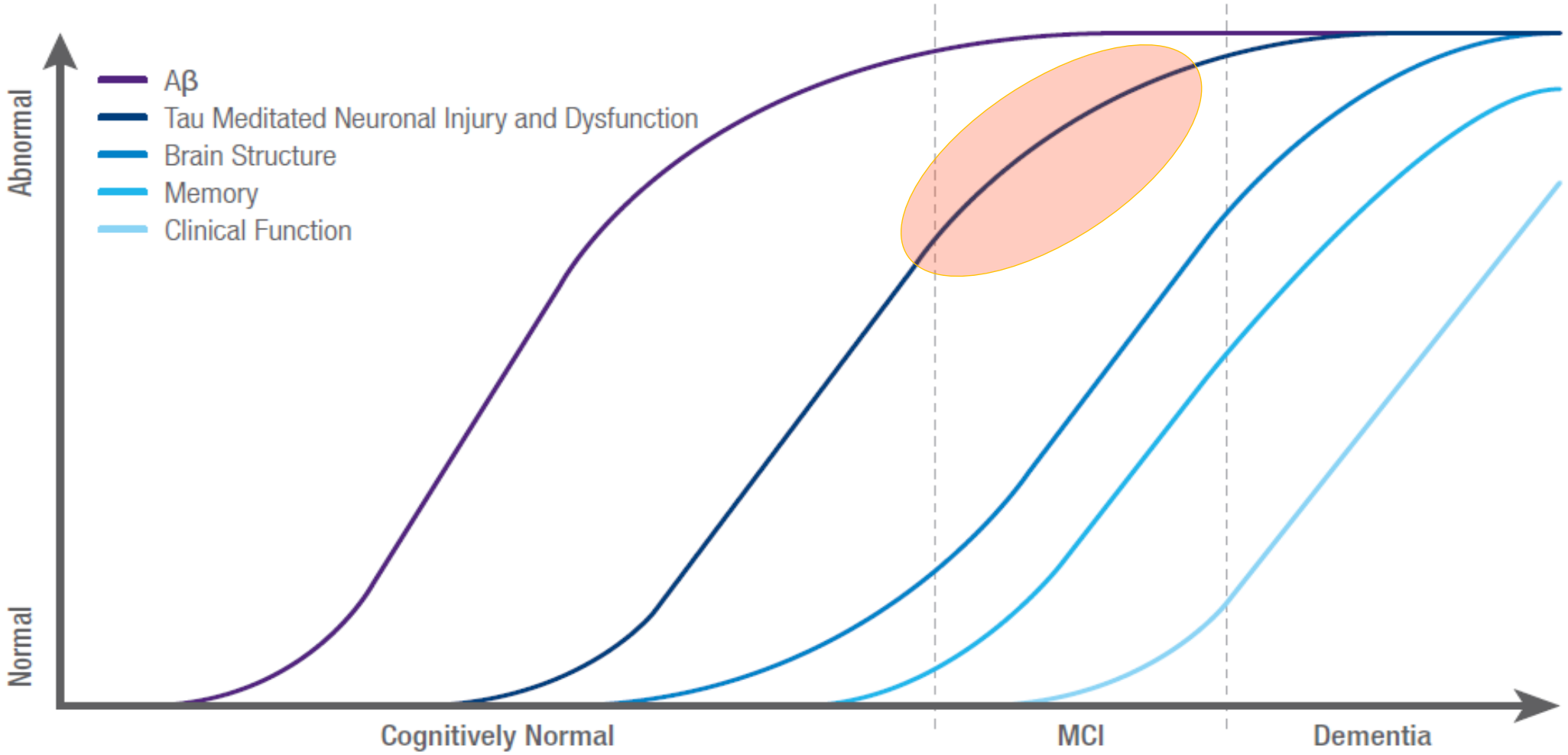


- LSD1 catalytic inhibitors in clinical trials (Incyte, Celgene, Imago, Oryzon, Salarius, etc)
- Beactica lead compound binds to an allosteric site; no inhibition of the enzyme activity
- Effects LSD1 degradation in selected cells; tumor growth inhibition in vivo in anti-PD1 combination
- Oscotec-Beactica research collaboration with an exclusive option for in-licensing

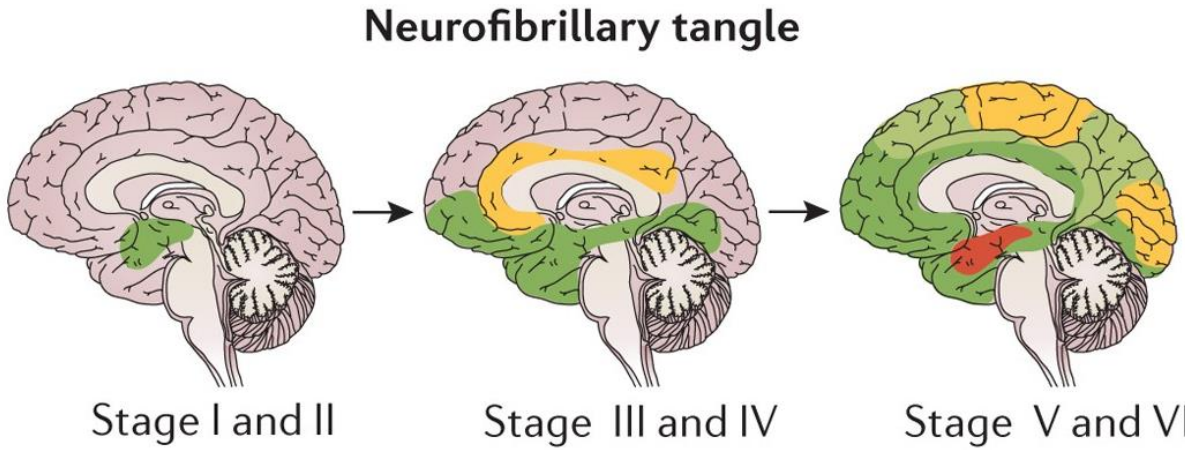
ADEL-Y01

Antibody Targeting Pathological Tau Protein

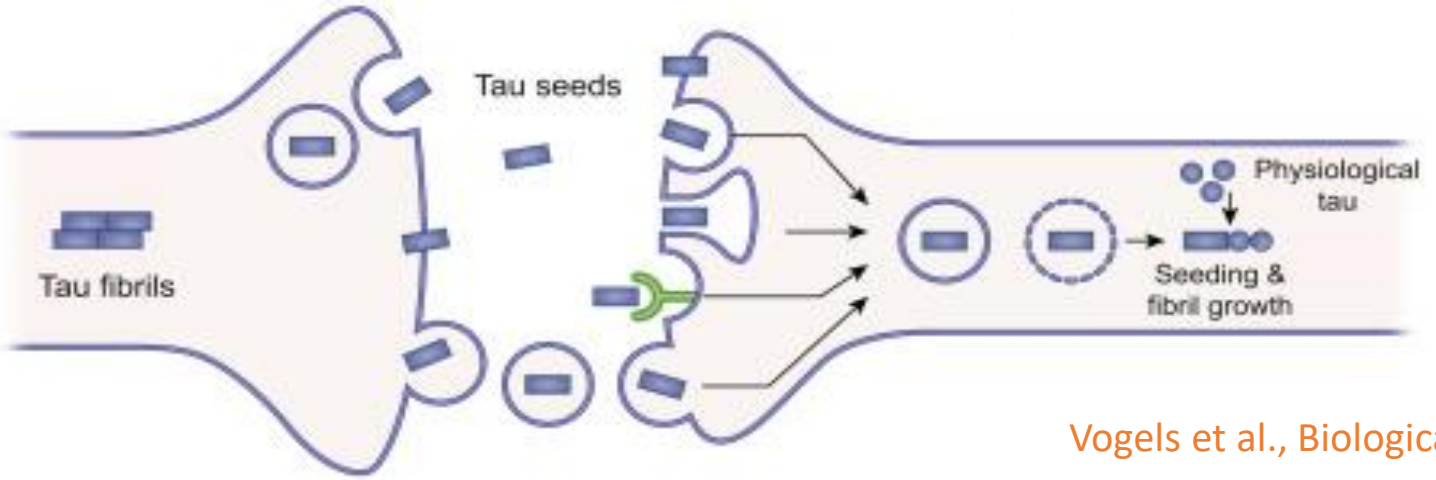
ADEL-Y01; Tau in Alzheimer's Disease



ADEL-Y01; Tau Propagation in AD

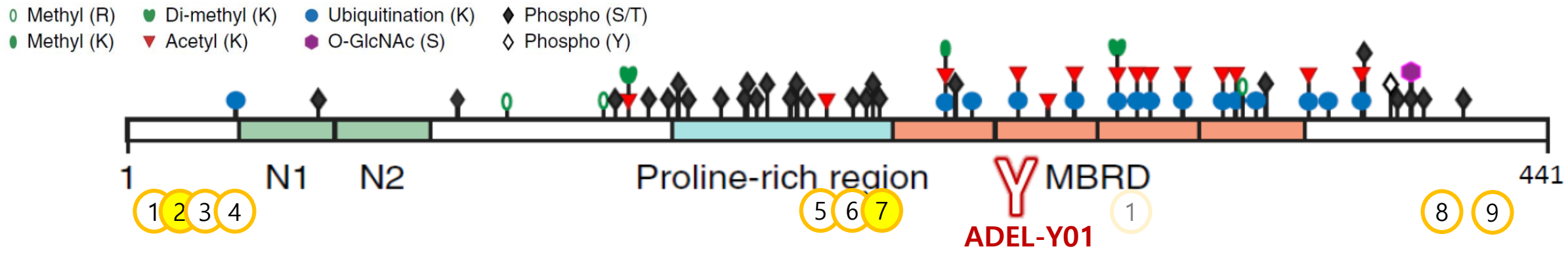


Masters et al., Nat Rev Disease Primers 2015



Vogels et al., Biological Psychiatry 2020

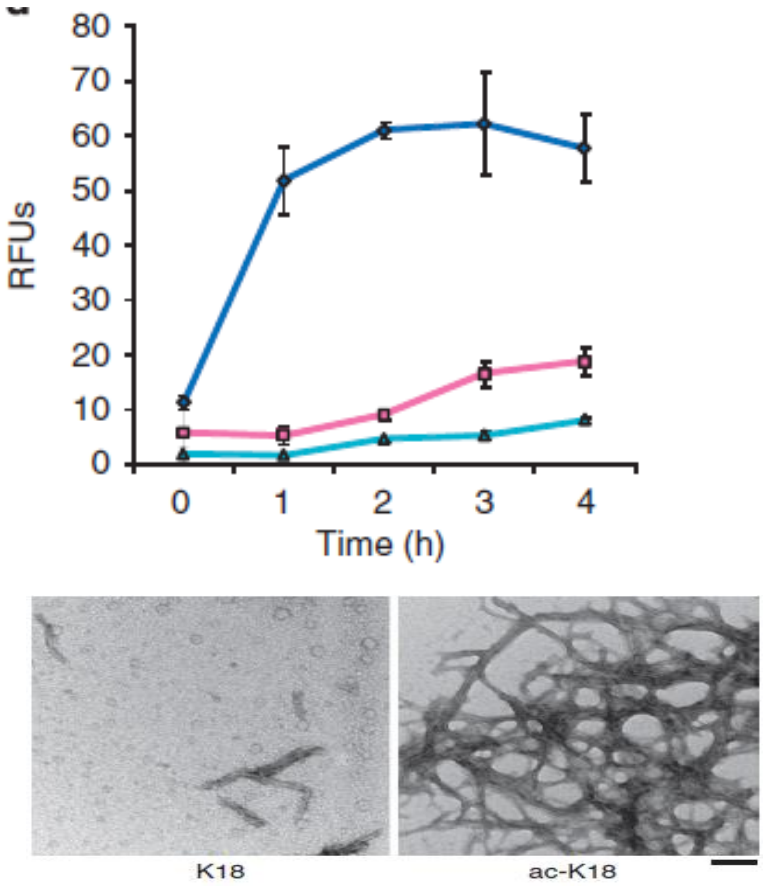
ADEL-Y01; Competitive Landscape



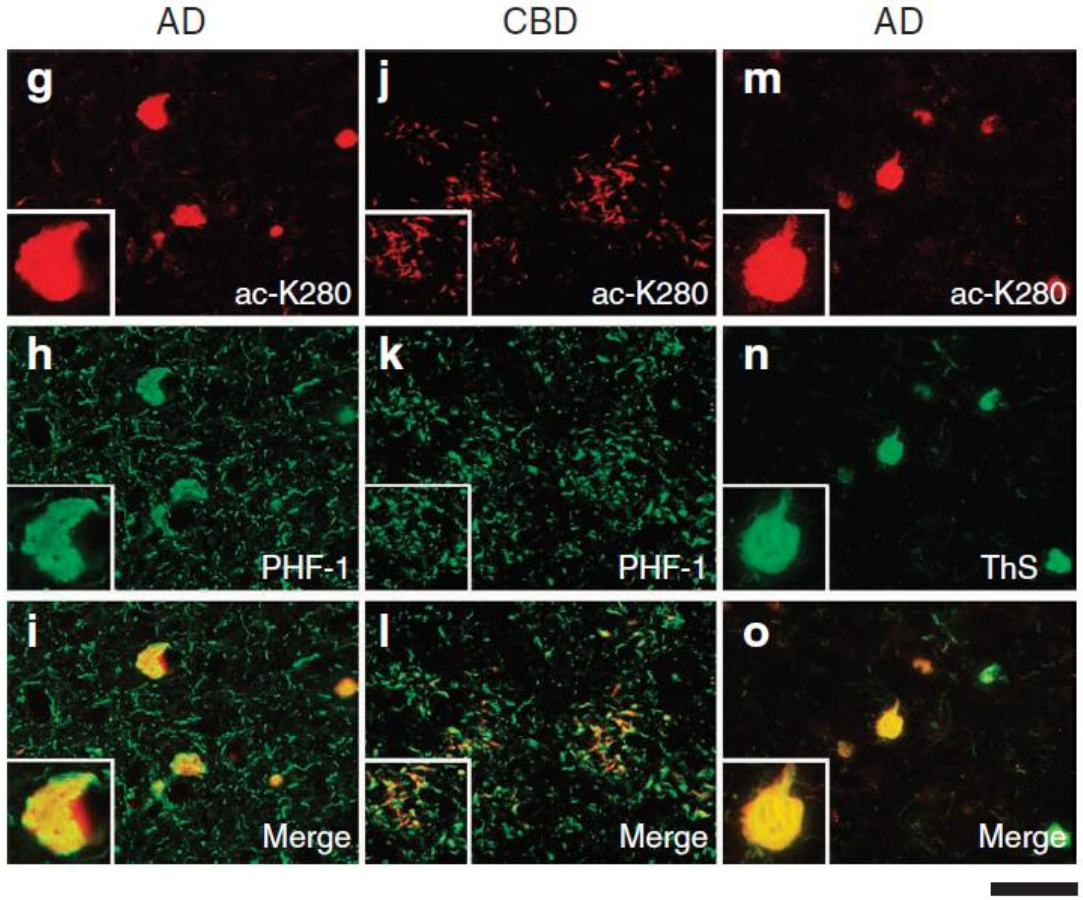
	Drug	Synoyms	Companies	Epitope	Clinical Trial Status
1	Zagotenemab	LY3303560, MC1	Eli Lilly	Tau aggregate (7-9:313-322)	P2 (early AD)
2	Gosuranemab	BIIB092, BMS-986168, IPN007	Biogen, BMS, iPerian	Secreted N-term fragment (15-24)	P2 (early AD), Stopped
3	C2N-8E12	HJ8.5 (m)	Abbvie, C2N	Extracellular tau (25-30)	P2 (early AD), Stopped (PSP)
4	Semorinemab	RO7105705, RG6100	Roche, AC Immune	Tau N-term	P2 (AD)
5	JNJ-63733657		Janssen	Phospho tau PRR (pT217)	P1
6	PNT001		Pinteon	Phospho tau PRR (cis-pT231)	P1
7	UCB0107		UCB	Tau PRR (235-246)	P2 (PSP)
8	Lu AF87908		Lundbeck	Phospho tau C-term (pS396)	P1 (AD)
9	RG7345	RO6926496	Roche	Phospho tau C-term (pS422)	Stopped (HV)
-	BIIB076		Biogen	Monomeric and fibrillar tau	P1

ADEL-Y01; AcK280 is a Pathological Tau Form

- Tau acetylation dramatically accelerates fibrilization



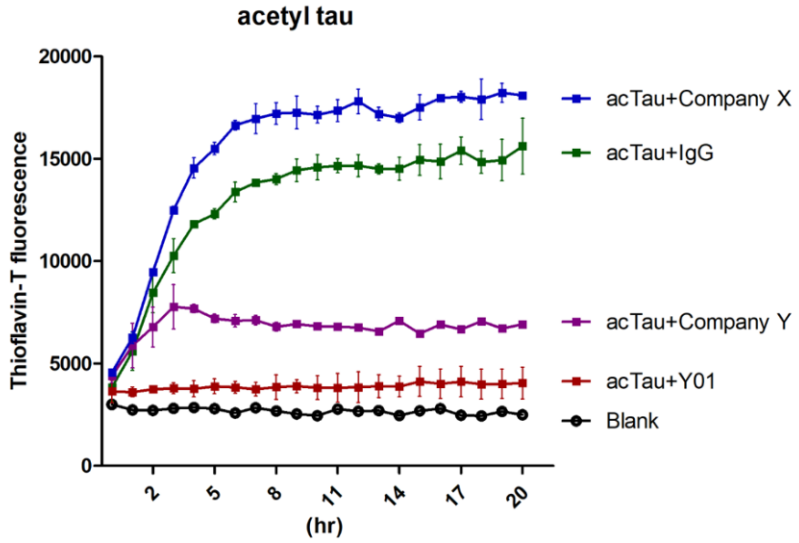
- Tau(AcK280) is associated with tau aggregates in human tauopathies

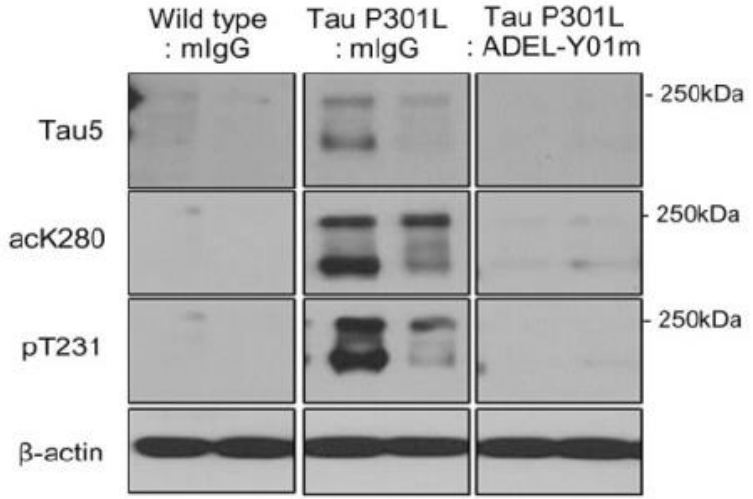


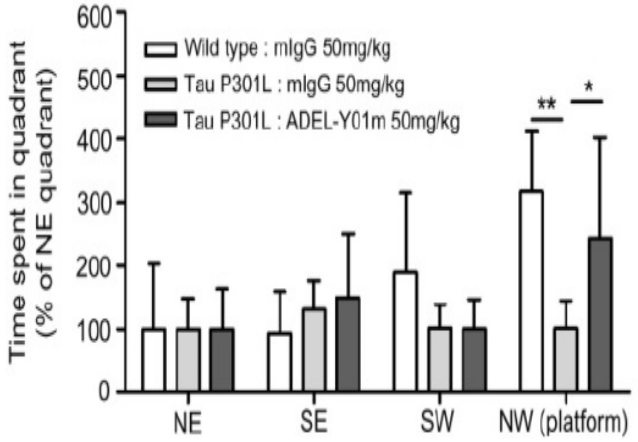
Cohen et al., Nat Commun 2011

ADEL-Y01; Inhibition of Tau Aggregation

- Dramatic inhibition of Tau aggregation in vitro
- Suppressed p-Tau aggregate accumulation and improved cognitive behaviors in mouse tauopathy models

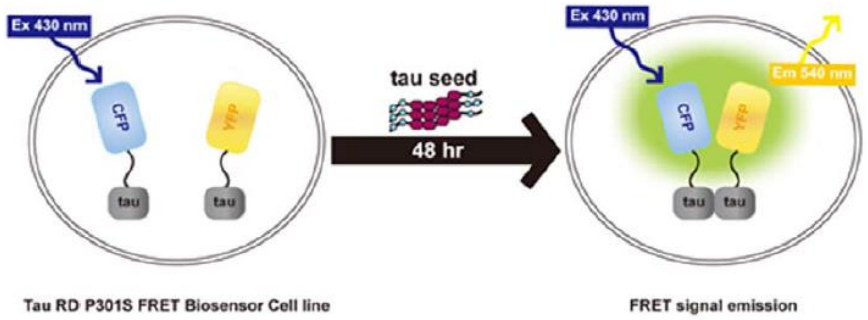


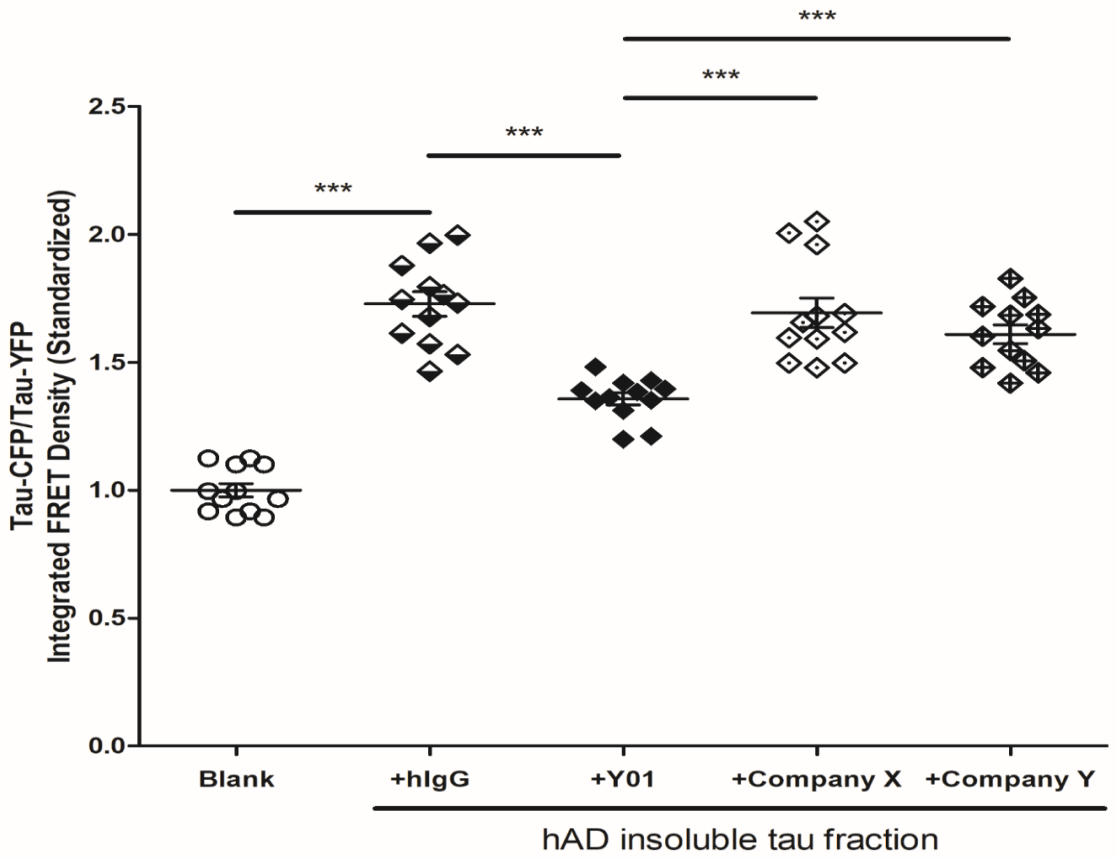




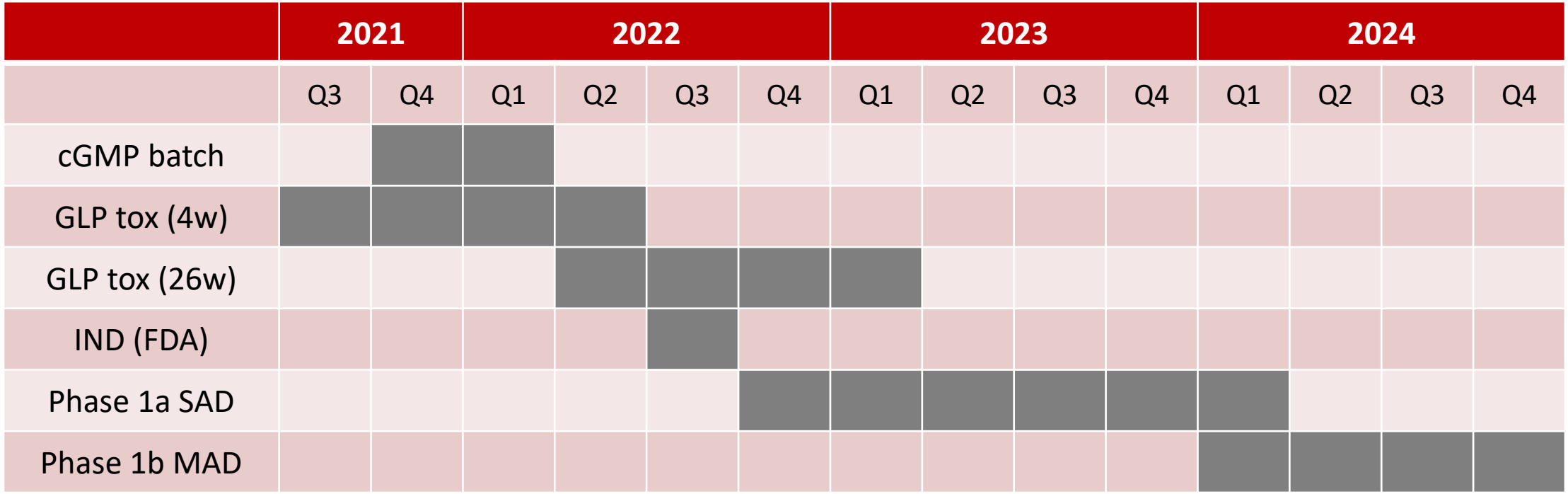
ADEL-Y01; Inhibition of Tau Propagation

- Biosensor assay to measure Tau spreading and seeding
- ADEL-Y01 displays superior inhibition to competitor antibodies





ADEL-Y01; Development Timeline



- GLP tox studies (rodents and primates) underway
- IND (US FDA) and Phase 1 to start in 2022
- Extensive pre/clinical biomarker studies to be incorporated

Clinical Pipeline Update

SKI-G-801

The Best-in-class FLT3/AXL Dual Inhibitor

SKI-G-801 Clinical Development Status for AML

Clinical Rationale

- FLT3 driver mutation in 1/3 of AML patients
- SKI-G-801, a potent FLT3 inhibitor (IC_{50} = 2.2 nM)
- Highly efficacious in tumor xenograft models
- Anti-leukemic activities superior to existing FLT3 inhibitors (quizartinib and gilteritinib)

Phase Ia Clinical Trial

- IV infusion (1 cycle = 14d on/14d off)
- FDA Orphan drug designated (Nov 2018)
- CRM-based dose escalation design
- 14 patients >1 cycle
- No severe toxicity up to 5.57 mg/kg
- MTD to be determined

Next Steps

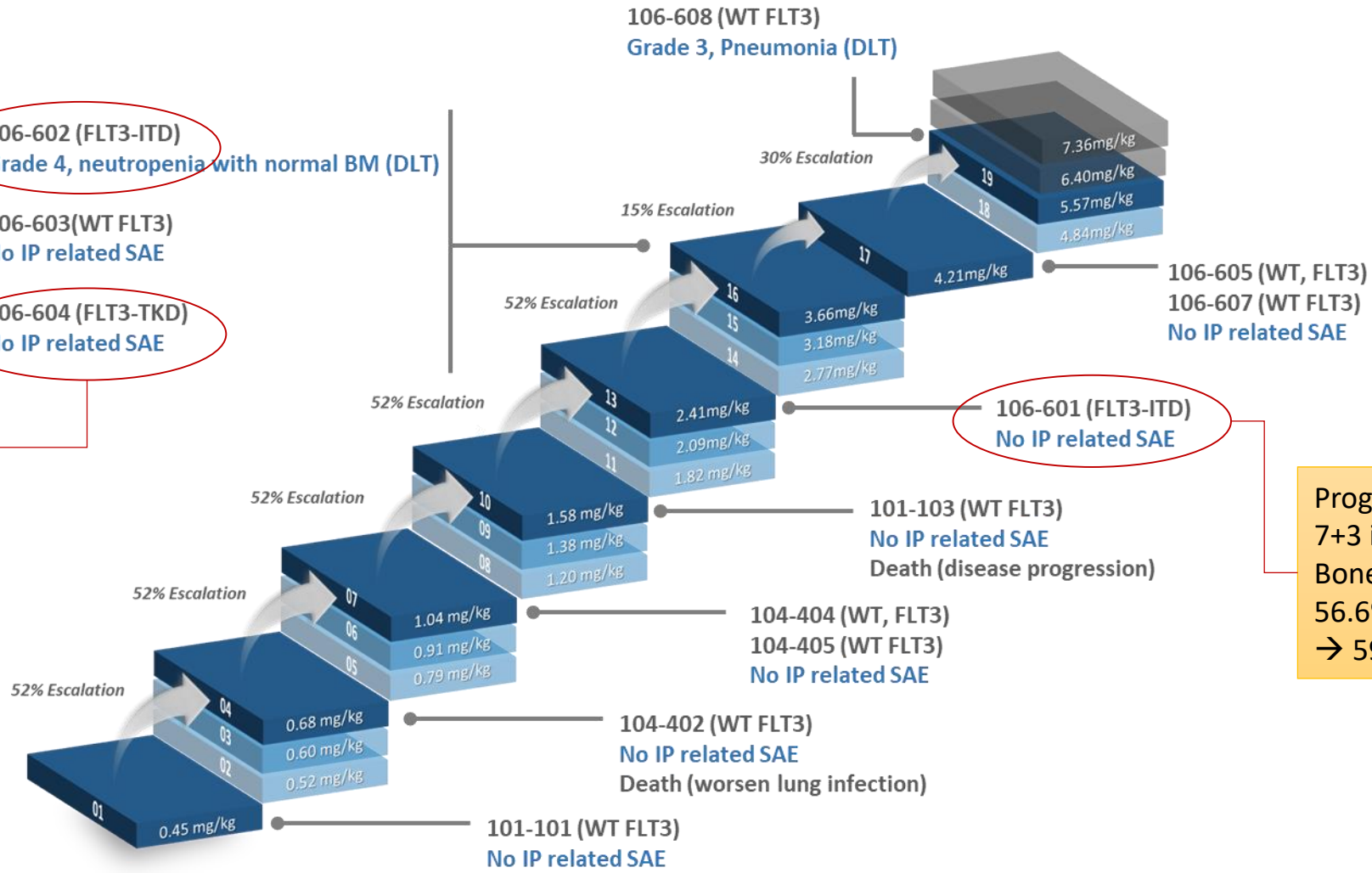
- Cohort expansion to FLT3(+) patients to resume after oral tablet conversion

blood

Prepublished online February 14, 2014;
doi:10.1182/blood-2013-04-493916

G-749, a novel FLT3 kinase inhibitor can overcome drug resistance for the treatment of Acute Myeloid Leukemia

SKI-G-801 AML Dose Escalation Study; Sneak Peek



106-602 (FLT3-ITD)
Grade 4, neutropenia with normal BM (DLT)

106-603(WT FLT3)
No IP related SAE

106-604 (FLT3-TKD)
No IP related SAE

106-605 (WT, FLT3)
106-607 (WT FLT3)
No IP related SAE

106-601 (FLT3-ITD)
No IP related SAE

101-103 (WT FLT3)
No IP related SAE
Death (disease progression)

104-404 (WT, FLT3)
104-405 (WT FLT3)
No IP related SAE

104-402 (WT FLT3)
No IP related SAE
Death (worsen lung infection)

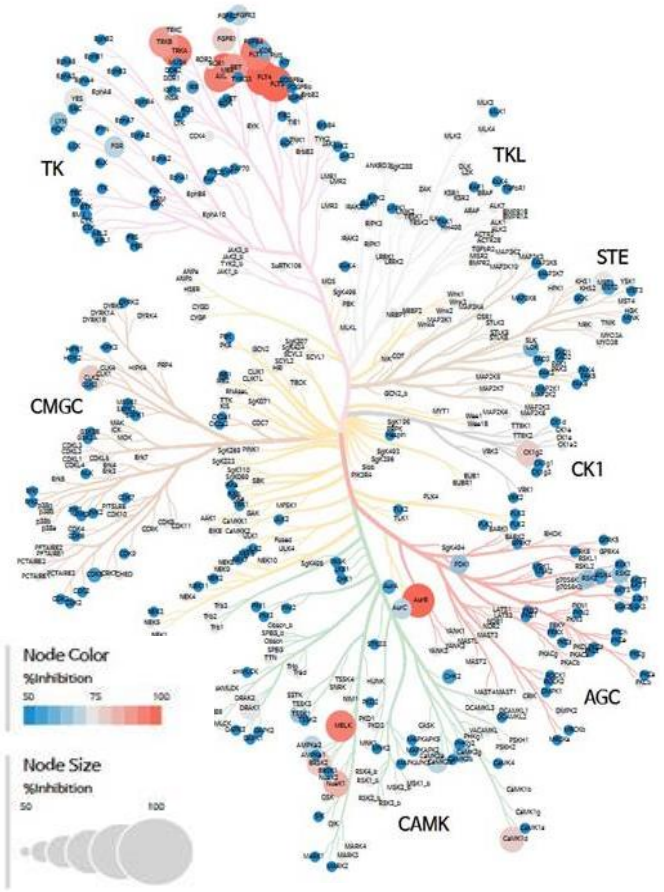
101-101 (WT FLT3)
No IP related SAE

Progressed upon
Chemo/Nivolumab;
Bone marrow blast
72.0% → 0.5% (Cycle 1)

Progressed upon
Midostaurin/Gilteritinib;
Bone marrow blast
73.0% → 12.2% (Cycle 1)

Progressed upon
7+3 induction;
Bone marrow blast
56.6% → 38.8% (Cycle 1)
→ 59.0% (Cycle 2)

SKI-G-801; the 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

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)

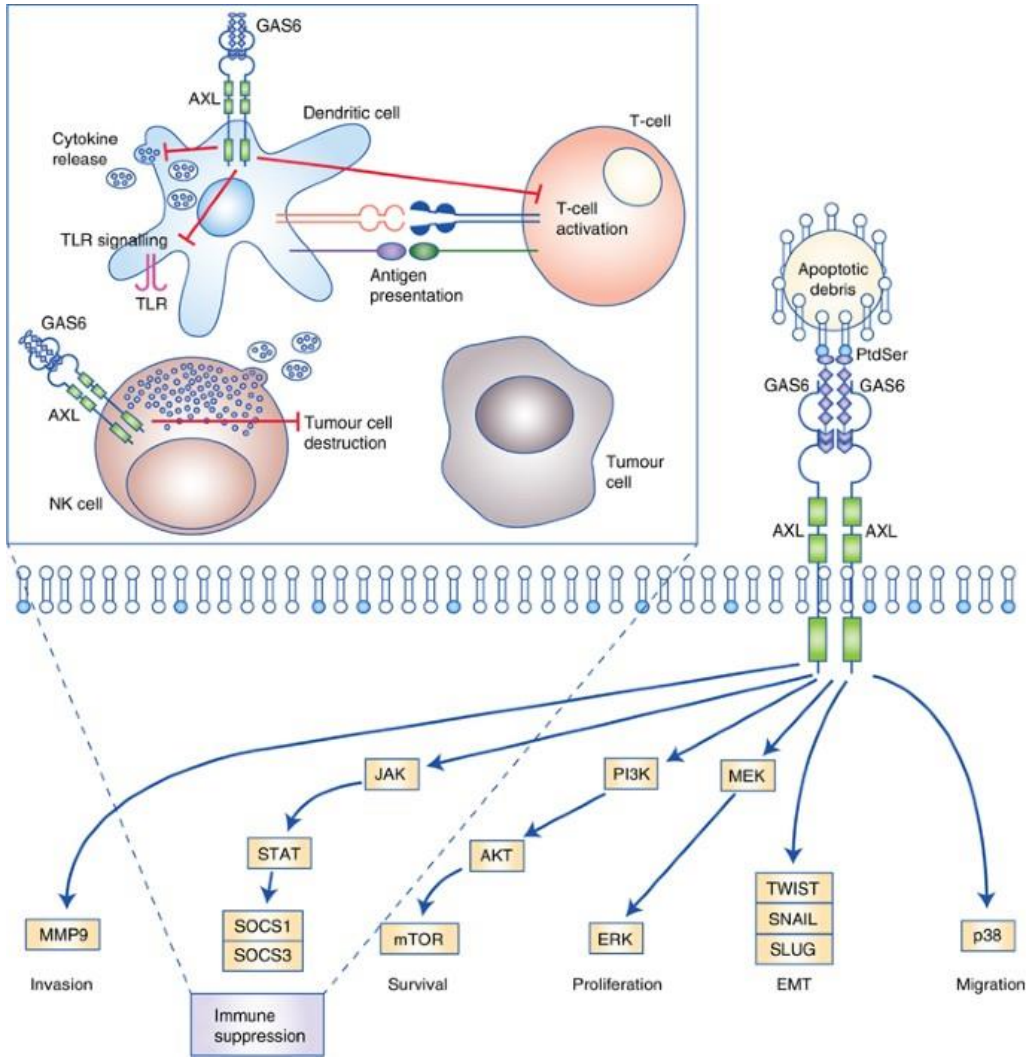
Compound	AXL (IC_{50}, nM)		
	ATP Km	1 mM ATP	Fold
SKI-G-801	12.5	113.9	9.1
R428	6.3	240.8	38.2

Compound	MerTK (IC_{50}, nM)		
	ATP Km	1 mM ATP	Fold
SKI-G-801	4.0	872.0	218.0
R428	8.2	1174.0	143.1

- Narrow spectrum kinome selectivity
- Potent inhibition of AXL even at high ATP concentrations

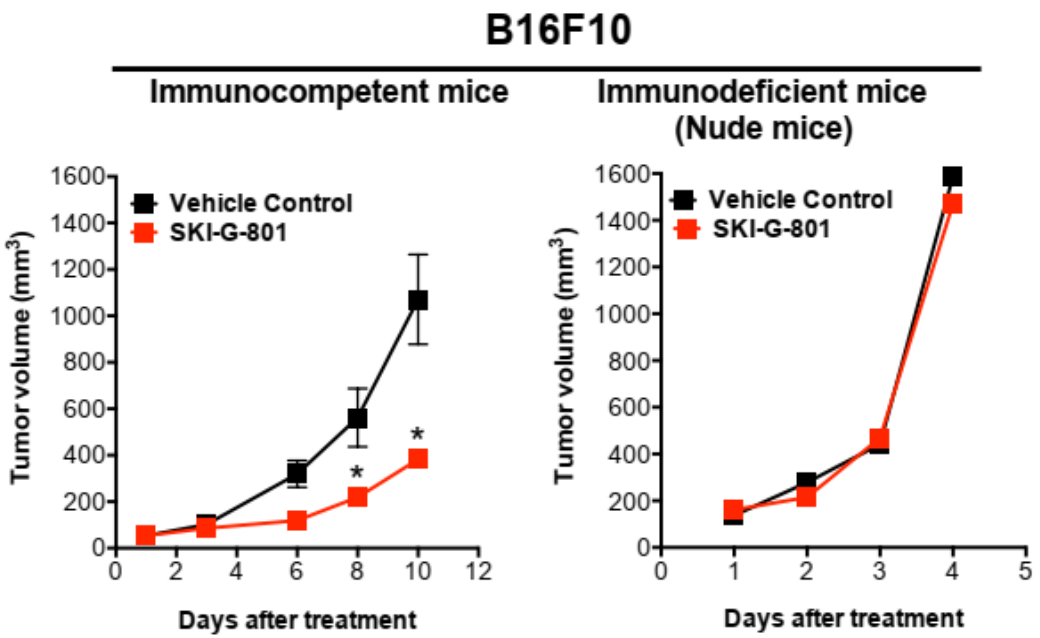
SKI-G-801 for Solid Tumors; Therapeutic Rationale

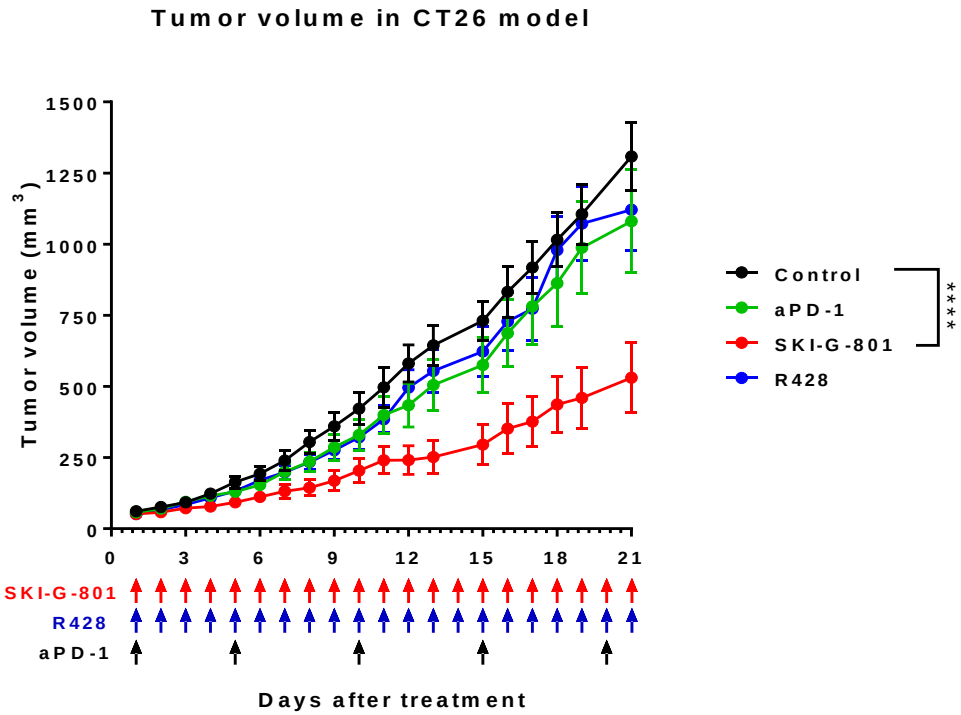
- AXL overexpression is correlated with malignant tumor progression
  - Associated with poor prognosis in multitudes of cancers
  - Promotes epithelial-mesenchymal transition (EMT) and metastasis
  - Drives drug resistance and immune evasion
- Innate immune checkpoint
  - AXL in macrophages and DCs reinforces apoptotic cell-mediated immune suppression in the tumor microenvironment
  - AXL is upregulated in checkpoint inhibitor-resistant tumors
- Bemcentinib (BGB324, R428) in multiple P2 clinical trials
  - Fast track designated for AXL-positive NSCLC in anti-PD-1/L1 combination



Gay et al., British J Cancer 2017

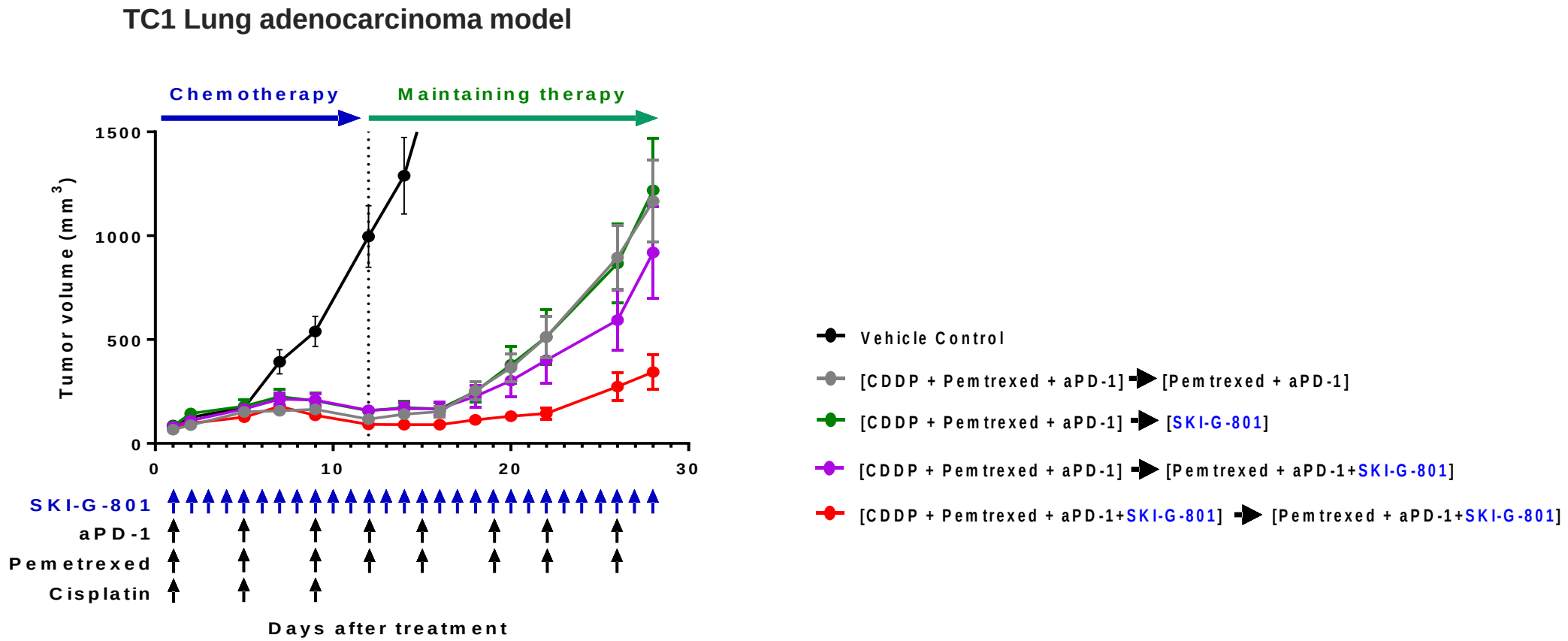
SKI-G-801; Preclinical Efficacy Highlight (1)





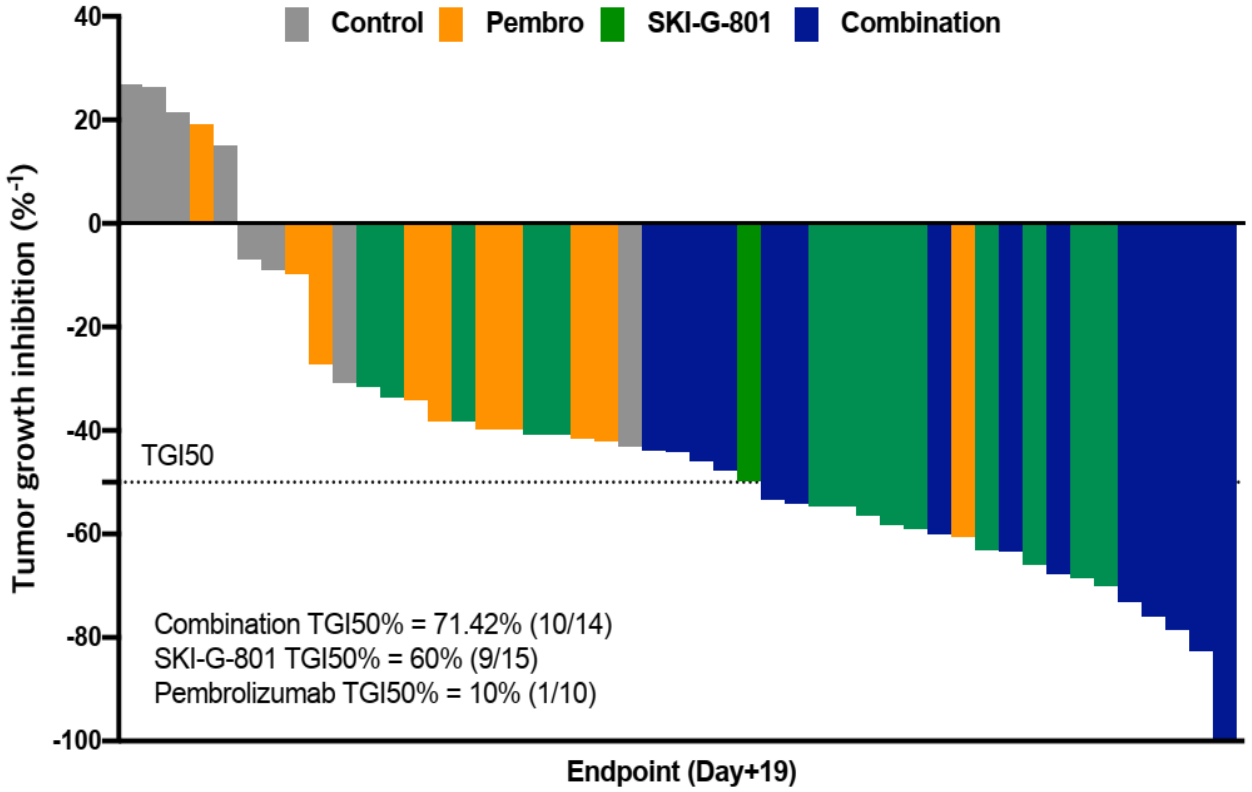
- Significant, immune-mediated, single-agent antitumor activities in numerous syngeneic ‘cold-tumor’ models (B16F10, 4T1, LLC, etc)
- SKI-G-801 (30 mg/kg) superior to R428 (bemcentinib; 50 mg/kg)

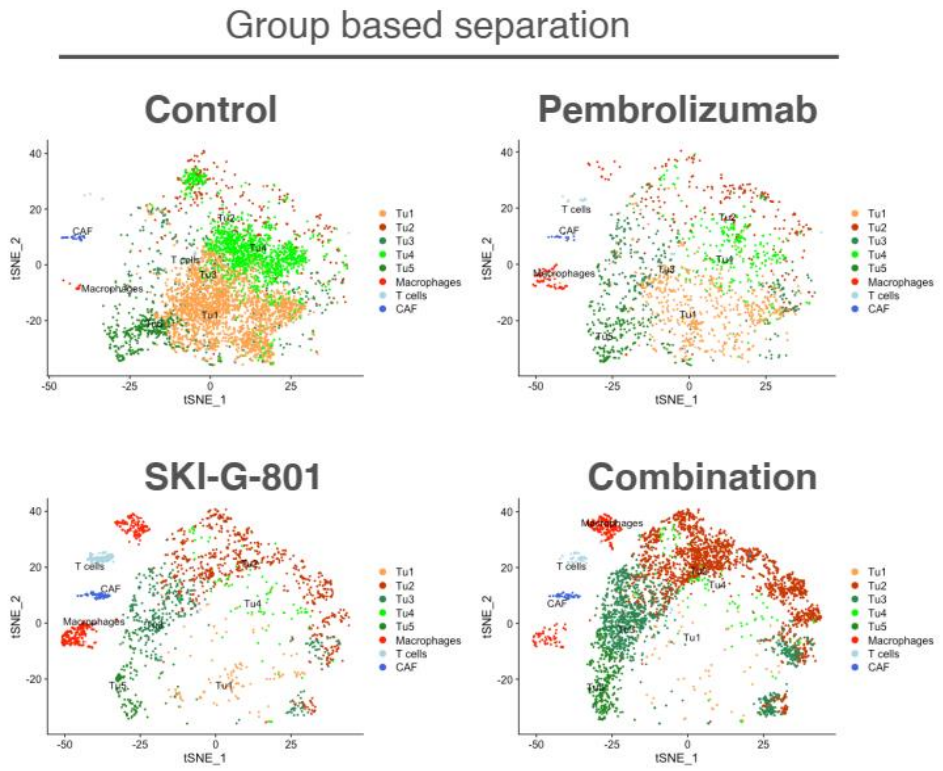
SKI-G-801; Preclinical Efficacy Highlight (2)



- Significantly delayed relapse when SKI-G-801 is present in the induction phase of lung adenocarcinoma standard-of-care regimen

SKI-G-801; Preclinical Efficacy Highlight (3)

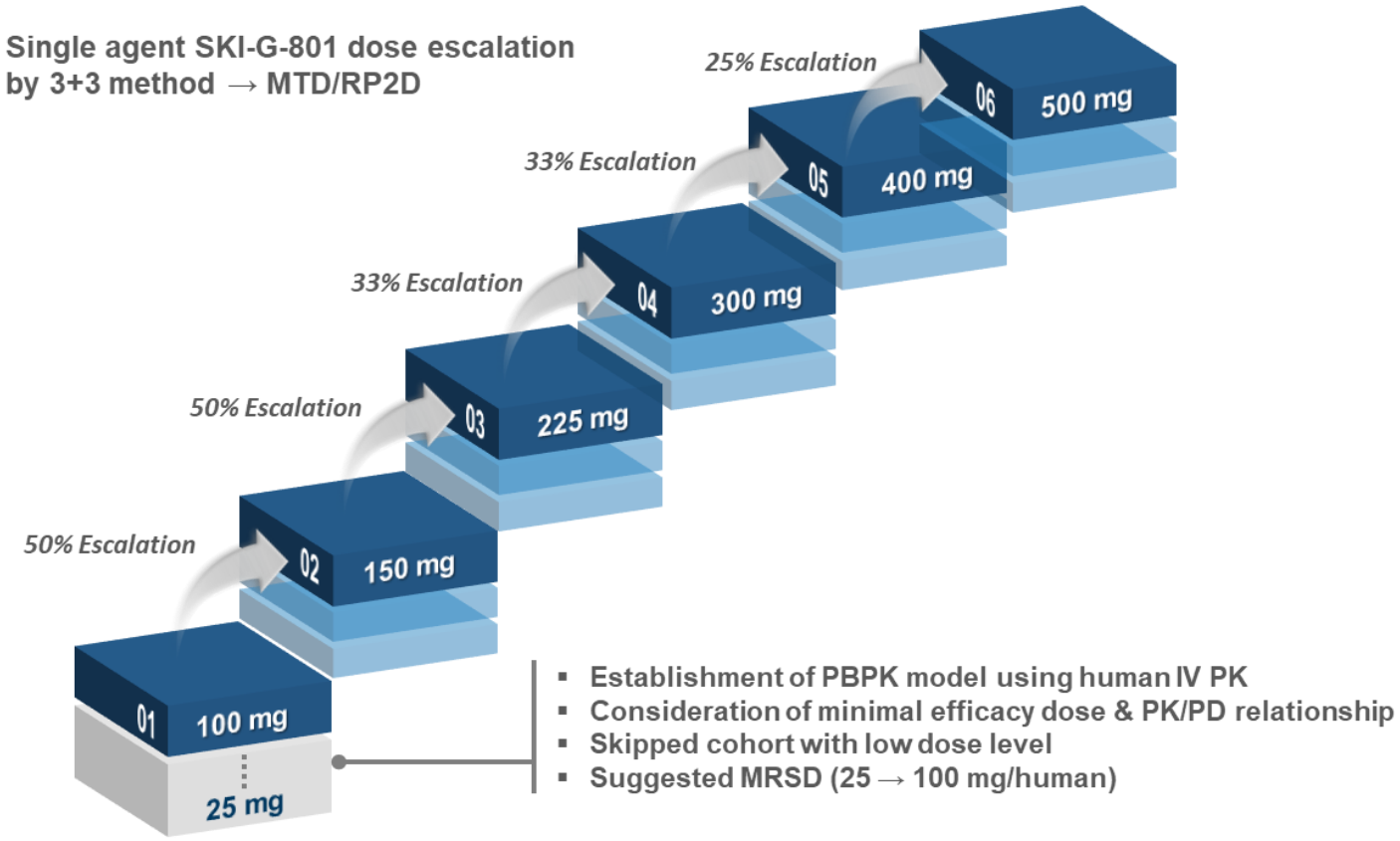




- Pronounced tumor growth inhibition in SCLC PDX model engrafted on humanized mice; further enhanced by pembrolizumab as supported by single cell RNA sequencing

SKI-G-801 for Solid Tumors; Clinical Development Plan

- Open-label, multi-center dose-finding study as monotherapy in patients with solid tumors to assess safety, tolerability, and PKs
- Oral tablet (100 to 500mg) administered for 28 days
- Principal investigators
  - Cho, Byuong Chul (YUHS)
  - Lee, Jae Lyun (AMC)
  - Park, Yeon Hee (SMC)
- MFDS IND submitted; FIH FPV expected in Oct 2021
- Extensive biomarker study
- Cohort expansion to follow



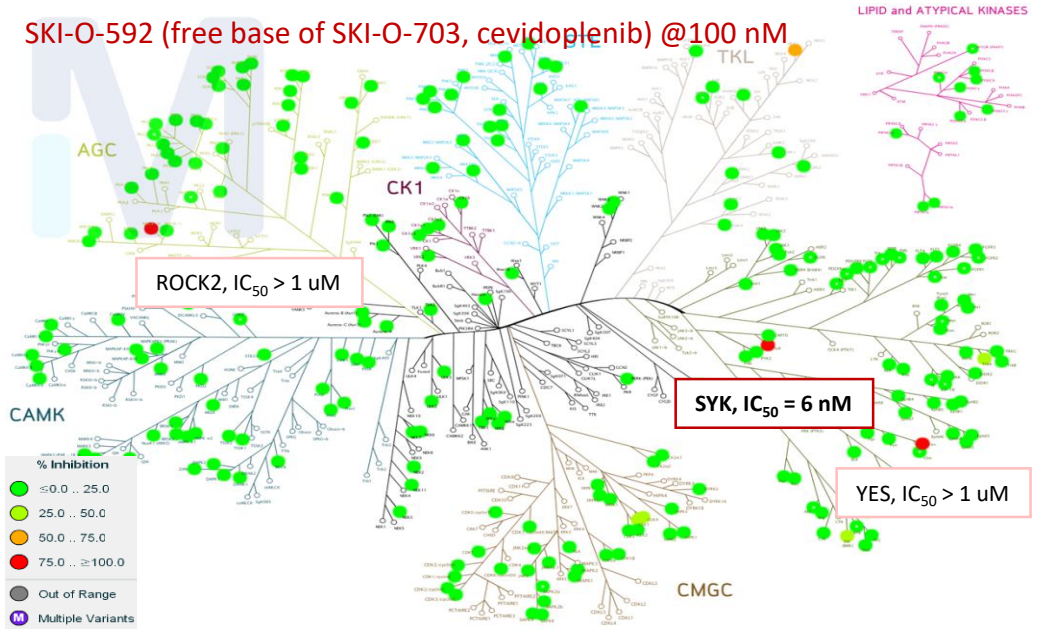
Cevidoplenib (SKI-O-703)

The ‘True’ First-in-Class SYK Inhibitor

Cevidoplenib, the 'True' First-in-Class SYK Inhibitor

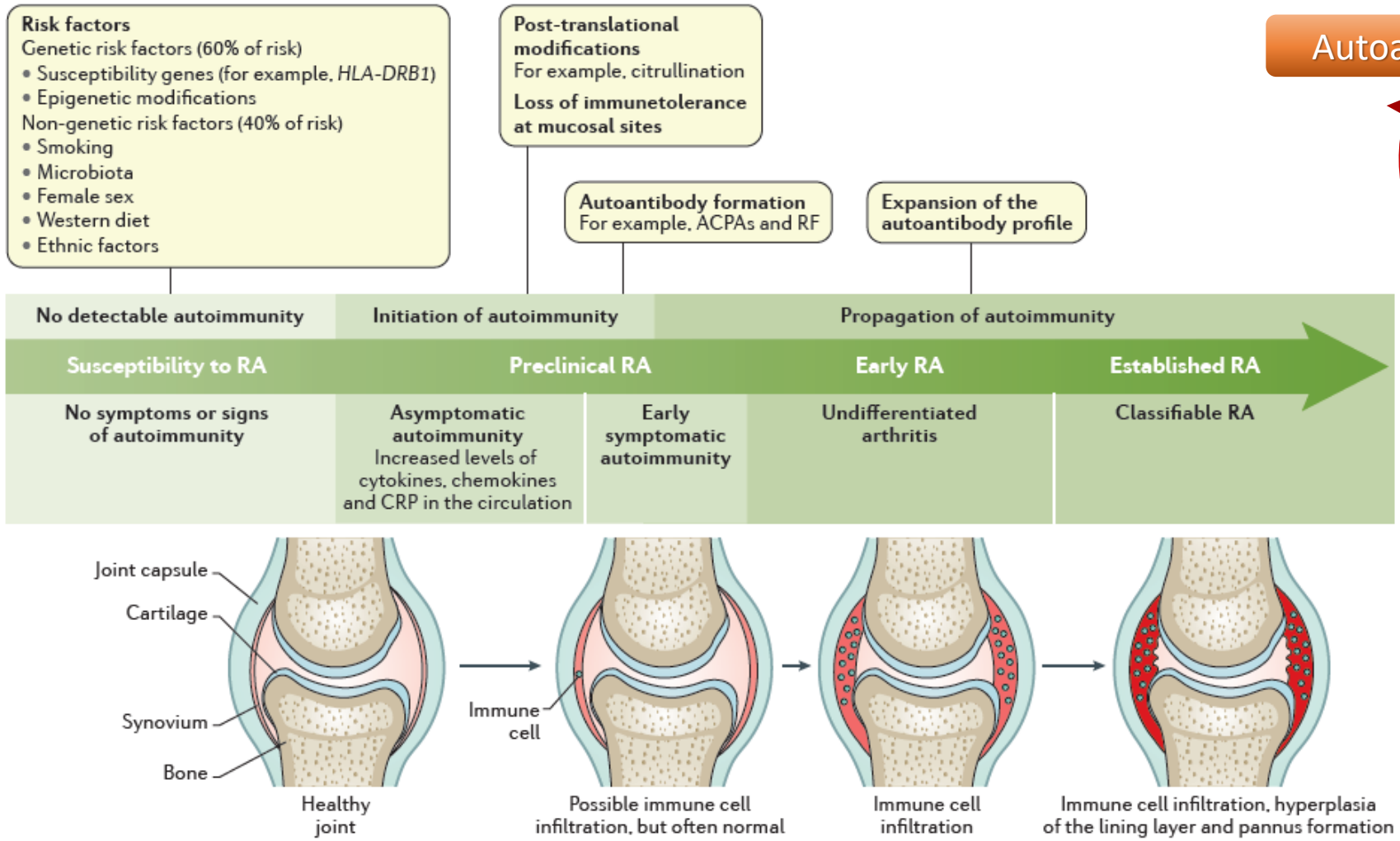
- Unparalleled kinome selectivity
  - Outstanding safety margin
  - Specific inhibition of B cell- and antibody-driven immunological responses

- Proven safety in Phase I
  - Few treatment-emergent adverse events (TEAEs) observed at up to 600mg (SAD) and 400mg bid (MAD)
  - All TEAEs were mild to moderate and reversible; no dose-related trends

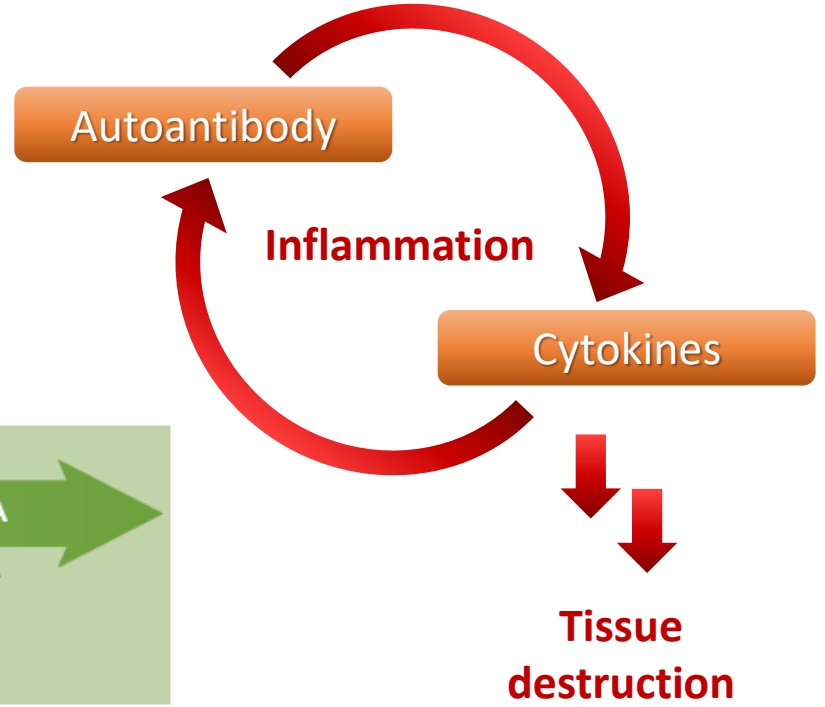


Assay (IC50)	Cevidoplenib	Fostamatinib
IgG-induced TNFa production (SYK-dependent)	52 nM	217 nM
CD3/CD28-induced IL-2 production (SYK-independent)	2892 nM	100 nM

Rheumatoid Arthritis; Therapeutic Rationale

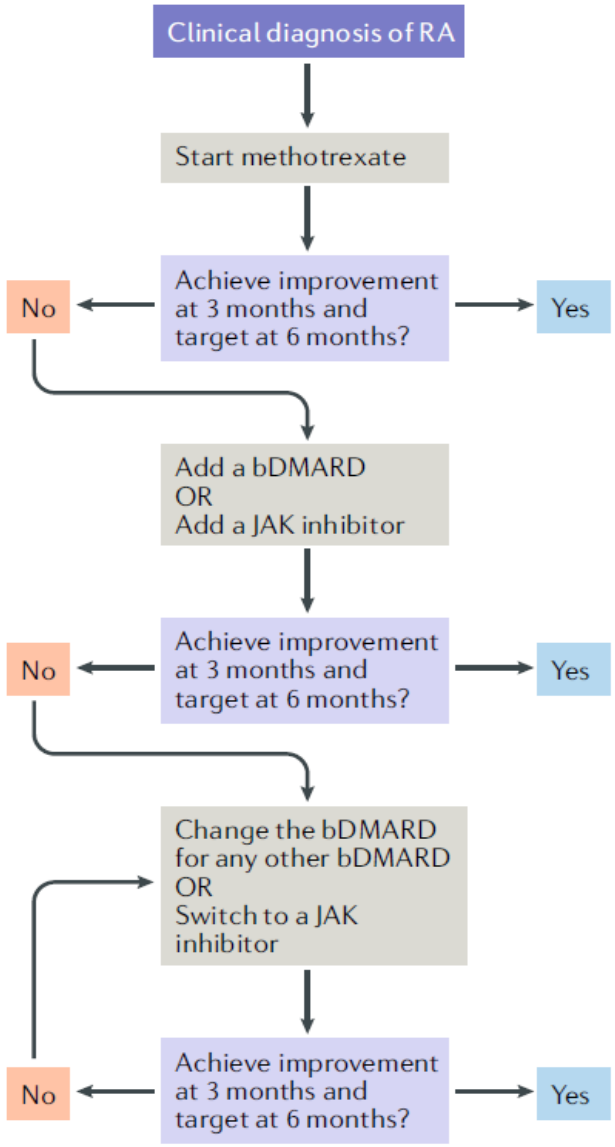


NATURE REVIEWS | DISEASE PRIMERS



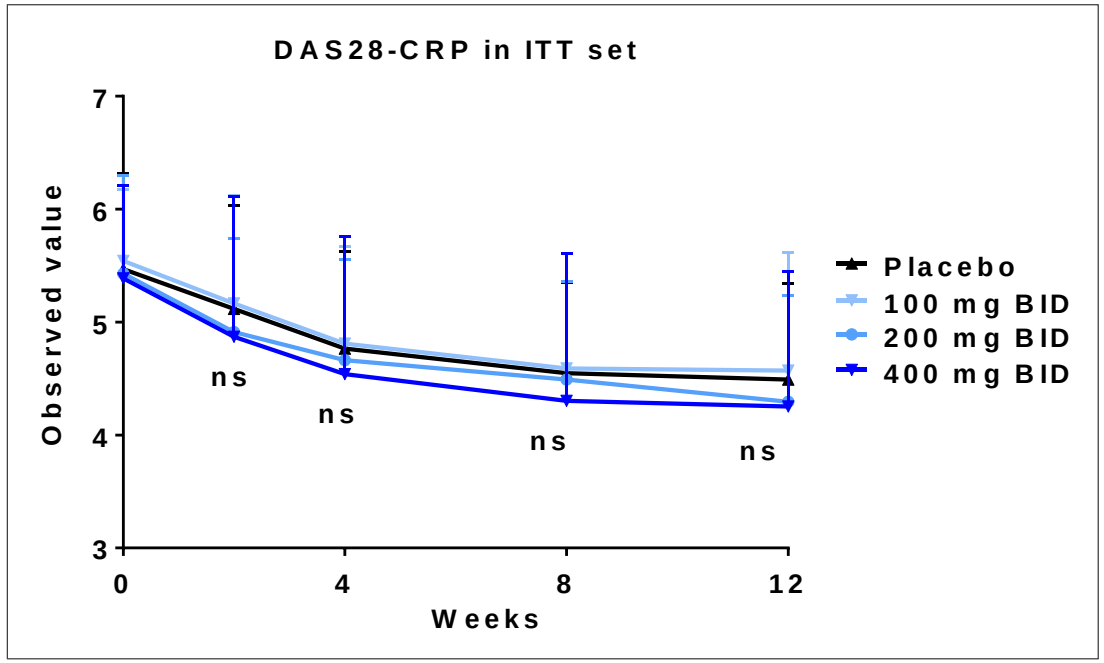
Cevidoplenib; RA P2a Summary

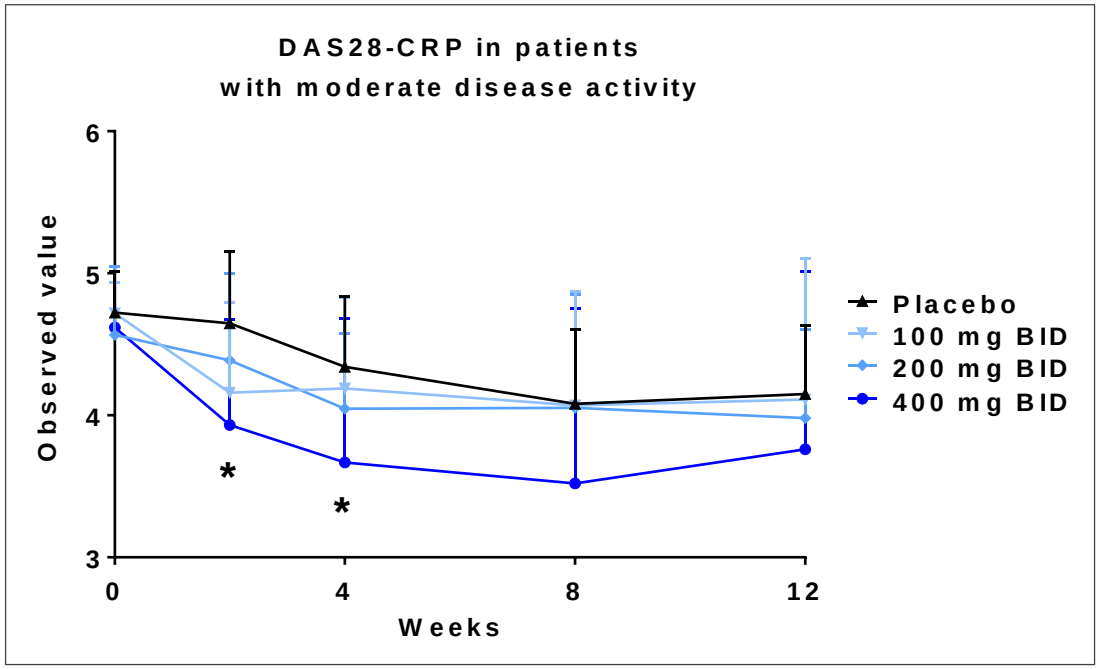
- Enrolled active RA patients with inadequate response to csDMARDs or anti-TNFα drugs (n = 163, 12 weeks); the highest unmet needs in RA
- Excellent safety reconfirmed (median treatment compliance >99%)
  - Headache, nausea, constipation, mild ALT/AST elevation
  - Grade 3/4 TEAEs; drug hypersensitivity (2.4%) and angioedema (2.4%)
- No statistically significant decrease of DAS28-hsCRP (primary endpoint)
- Significant, early-onset response in patients with moderate disease activity at the baseline in the high dose group (400mg bid)



Vellenhoven, Nat Rev Rheumatology 2019

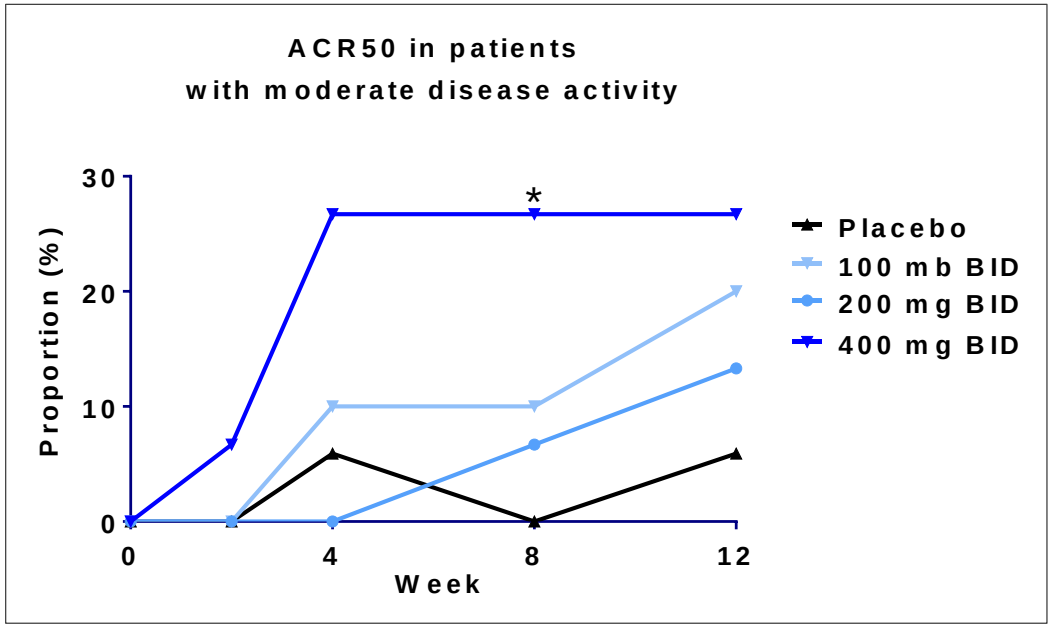
Cevidoplenib in RA P2a Study Snapshot (1)

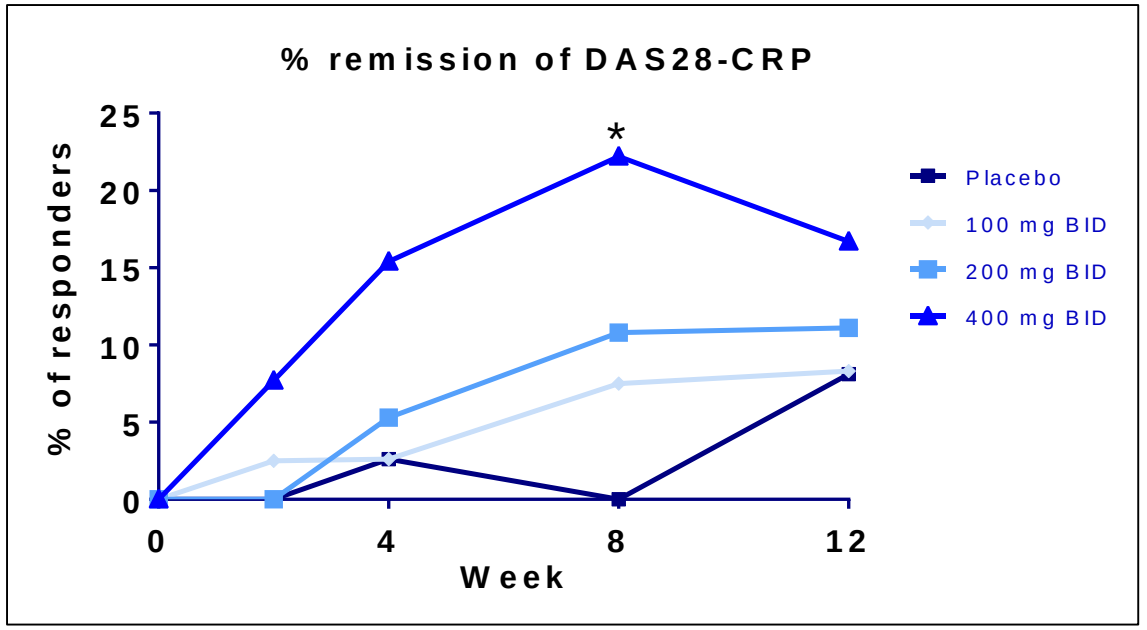




- While there were little differences overall between the treatment groups, significant early efficacy was observed at high dose in patients of moderate disease activity at enrollment (DAS28-CRP < 5.1; 37%)
- This is in line with the biological action of SYK in the RA pathology

Cevidoplenib in RA P2a Study Snapshot (2)

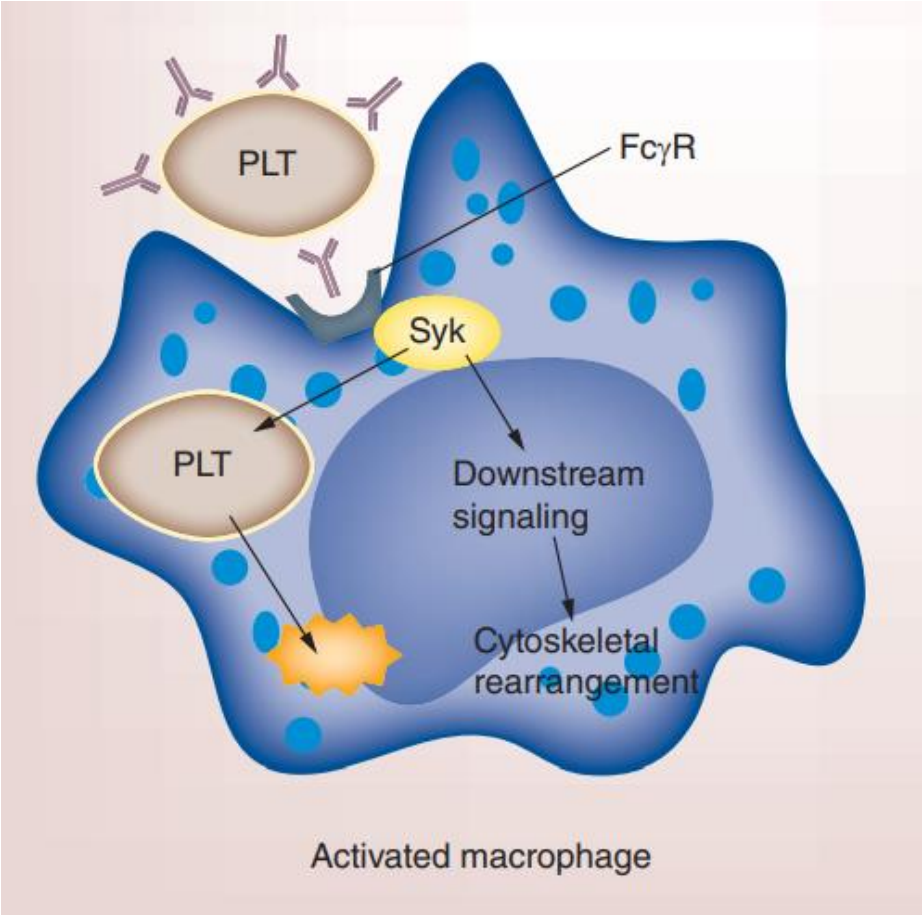




- Fast-onset efficacy in the 'early RA' patients is reiterated in the secondary endpoints (ACR20/50/70)
- Effectiveness in early RA patients led to significant increase in the number of patients achieving remission (DAS28-CRP < 3.2)

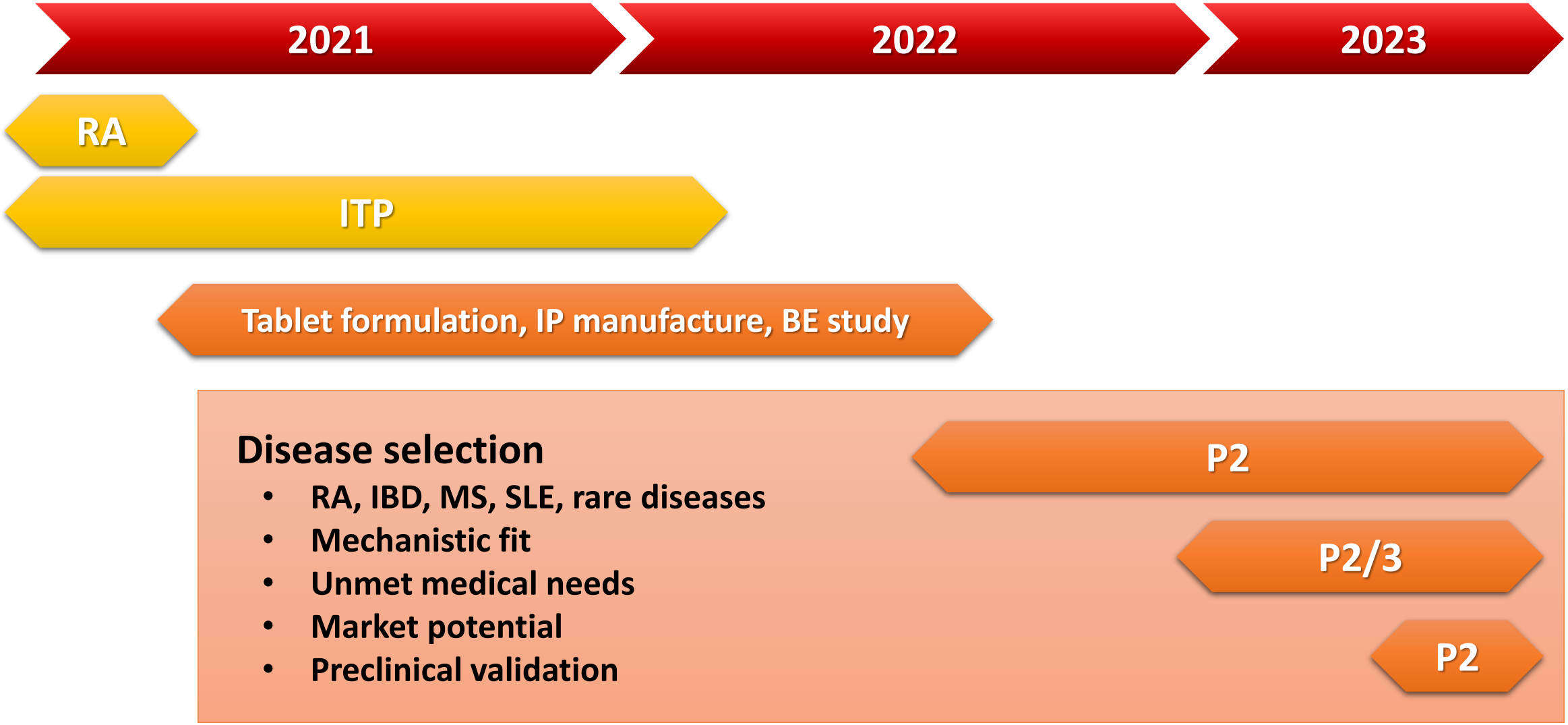
Cevidoplenib; P2 in Immune Thrombocytopenia (ITP)

- Immune thrombocytopenia
  - Auto-antibody-mediated destruction of platelets; increased risk of severe bleeding
  - Orphan disease (~9.5 per 100,000 adults)
- Fostamatinib (R788, R406; Rigel)
  - Approved by FDA in 2017 based on 2 P3 studies (n = 150) ; overall responder rate 29% vs 1% placebo
  - TEAE 59% vs 27% placebo, including hypertension (20% vs 8%)
- Cevidoplenib (SKI-O-703)
  - Current enrollment 39/60 in 3 cohorts (placebo/200mg/400mg); LPLV expected in Q4
  - <u>Highly favorable platelet count responses in the blinded data</u>



Newland et al., Future Medicine Immunotherapy 2017

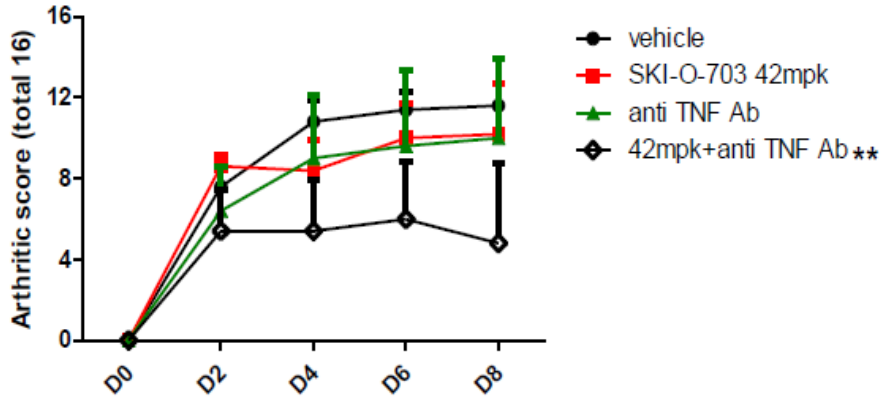
Cevidoplenib; the Next Chapter

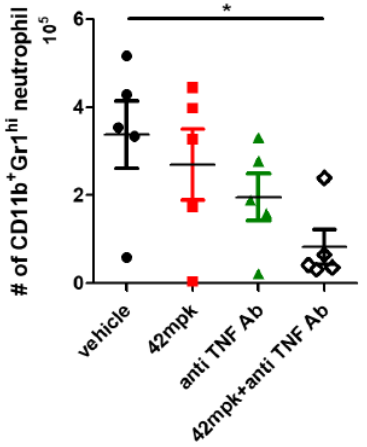


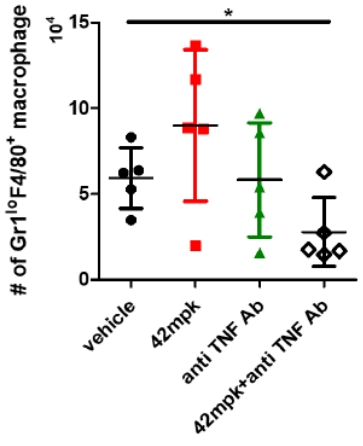
Cevidoplenib; Pipeline in a Drug (1)

➢ RA in combination

- K/BxN serum transfer arthritis model

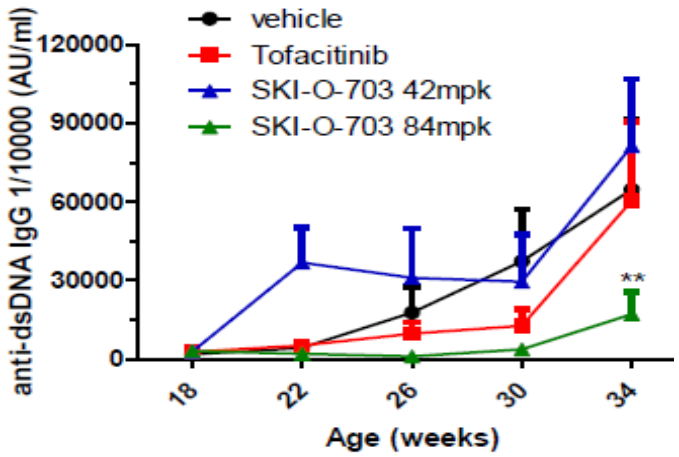


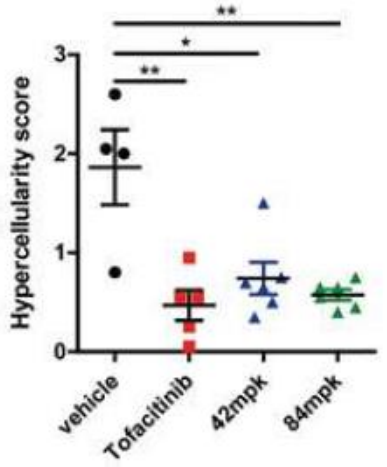


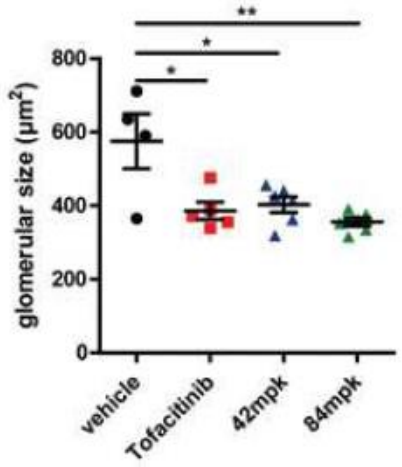


➢ Systemic lupus erythematosus (SLE)

- NZB/W model



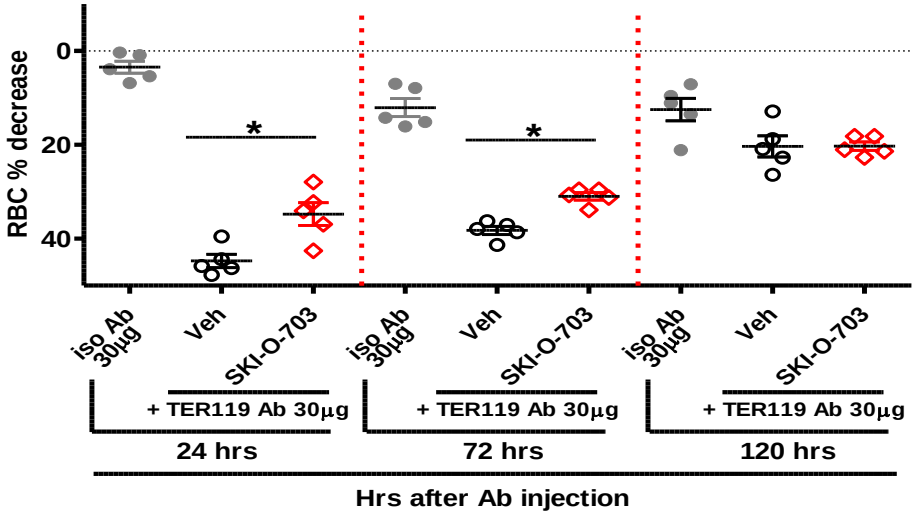




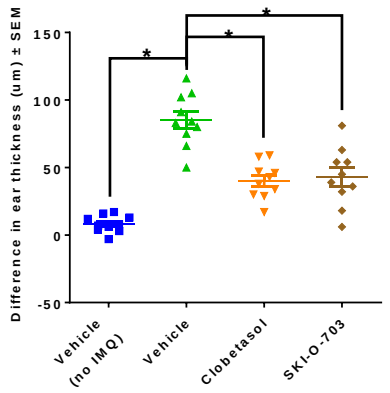
Cevidoplenib; Pipeline in a Drug (2)

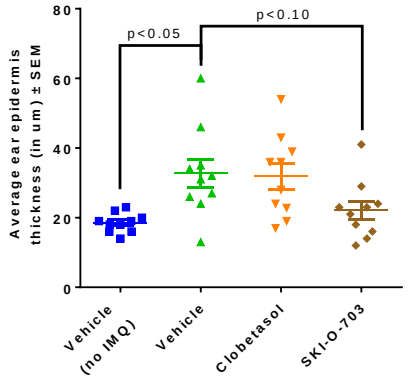
- Warm type autoimmune hemolytic anemia (wAIHA)
  - Fostamatinib in P3
  - Cevidoplenib prevented autoantibody-induced RBC reduction in vivo
- Psoriasis
  - Primarily driven by Th17 cells (IL-17, IL-12/23), but γδT cells (SYK) are also involved
  - Cevidoplenib effective in IMQ mouse model
- ANCA-associated vasculitis (AAV)
  - Autoantibody-mediated vasculitis
  - A rat model established; studies underway
- Others
  - Pemphigoid disease
  - Systemic sclerosis
  - IgA nephropathy …

- Anti-TER119-induced mouse anemia model



- IMQ-induced mouse psoriasis model





The Best is Yet to Come

Clinical Pipeline

- ≥1 L/O Every Year
- ≥1 NME IND Every Year

Discovery Pipeline

- Open Innovation
- In-house Programs

Platform Technologies

- Transformative Hit-finding Tech
- “Undrugged” Target Classes

Business Update