



STOCK CODE  
2096.HK

# CHINA AND BEYOND

SIMCERE Innovation Strategy  
and R&D Update

Jan 9, 2024

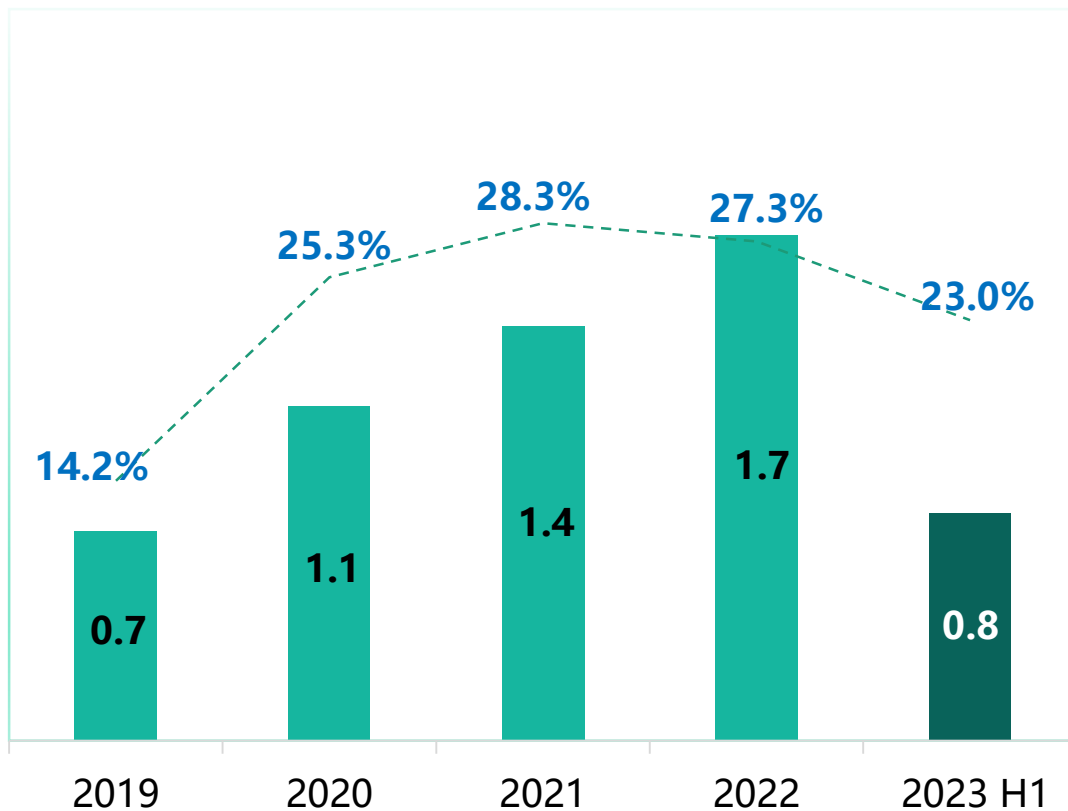


STOCK CODE  
2096.HK

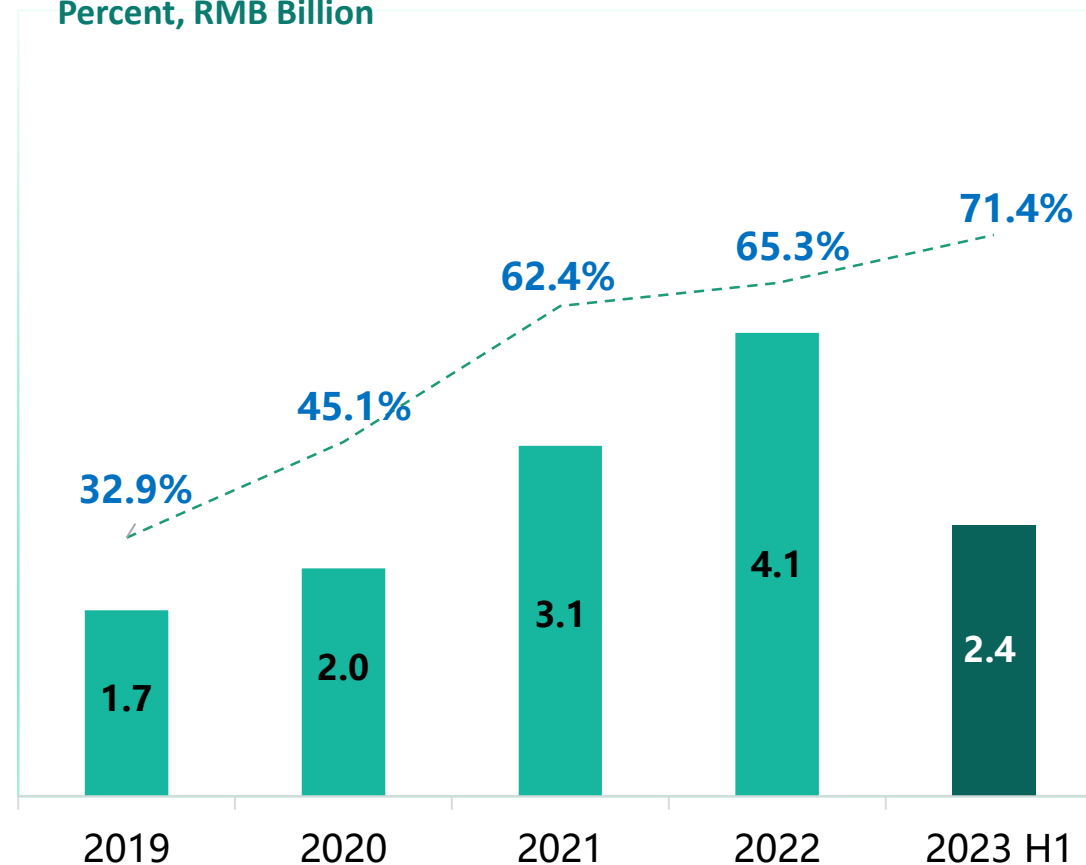
# Simcere Strategy Highlights

# In recent years, increasing R&D investment has propelled Simcere's innovation transformation to new heights

R&D investment amount and percent of revenue  
Percent, RMB Billion

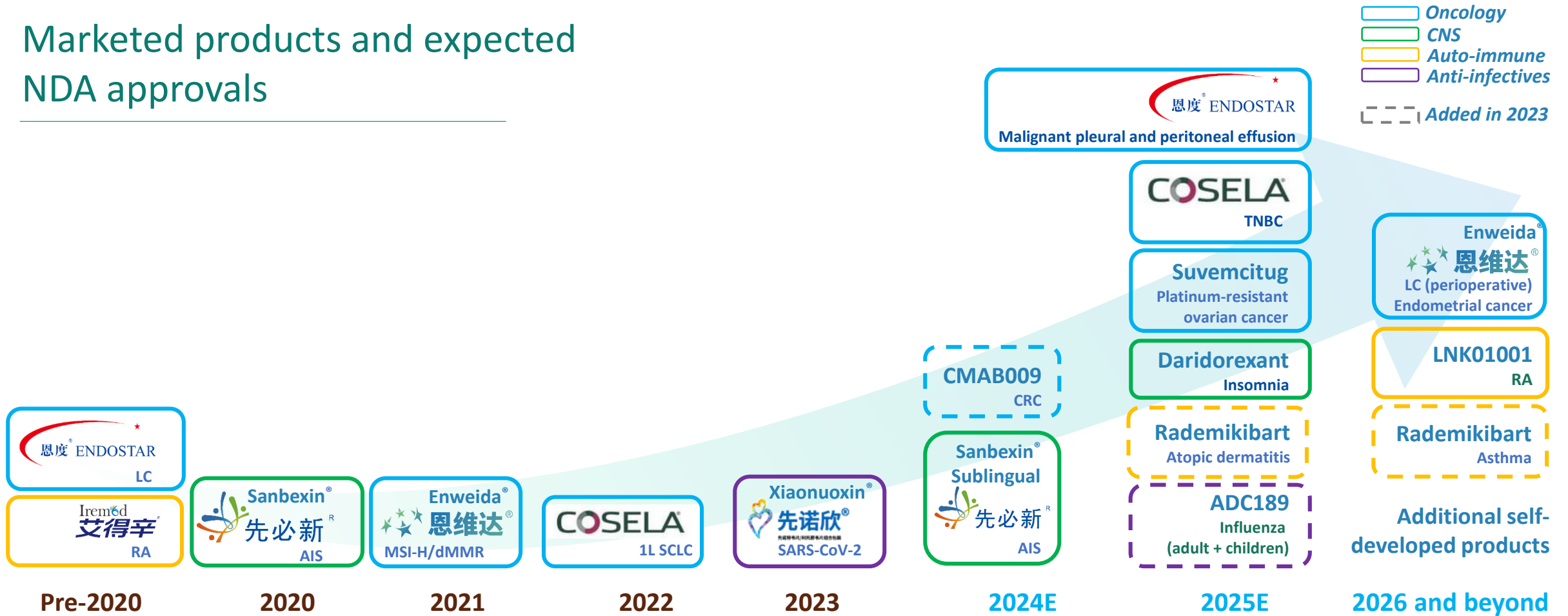


Innovative drug revenue and percent of total revenue  
Percent, RMB Billion



# Going forward, internal R&D and BD efforts combined will double the number of Simcere's commercialized innovative products

Marketed products and expected NDA approvals



# Proven clinical and regulatory capabilities underlie our transformation

From PCC to  
NDA Approval

**14 months**



**Xiannuoxin®**

43 sites, enrolled 1208 subjects in 5 months, 6 days from NDA submission to approval and started commercial manufacturing within 12 days after approval.

Industry Record from  
signing to NDA  
approval

**23 months**



**COSELA®**

Utilized Lecheng Real-world Study, a breakthrough from 0 to 1 was achieved in China, which greatly accelerated the listing process

Direct Phase III with Phase  
II exemption;  
Enrollment completed  
ahead of schedule

**11 months**



**Sanbexin® Sublingual Tablet**

Adaptive clinical design; an avg. 91 cases per month were enrolled, 10 months earlier than scheduled



Fully accelerating the commercial development of Daridorexant (dual orexin receptor antagonist - DORA) and other products

Parallel Approval for NDA  
and New Manufacturing  
Site

After NDA submission, tech transfer to the new manufacturing facility was completed without delay and were approved simultaneously.



**Sanbexin®**

# Portfolio strategy and synergistic commercial capabilities maximize value of innovation

## Oncology

Lung cancer



恩度 ENDOSTAR

COSELA

Enweida®  
恩维达®

GI cancer



Enweida®  
恩维达®

CMAB009

Gynecologic Cancer



Enweida®  
恩维达®

## CNS

Stroke



先必新®

Sanbexin® IV

Sanbexin®  
Sublingual  
tablets

Insomnia



Daridorexant

## Autoimmune

RA



Irem6d  
艾得辛®

LNK01001

Derm



Rademikibart

## Anti-infectives

Respiratory  
viral infections



Xiaonuoxin®  
先诺欣®  
先诺特韦片/利托那韦片组合包装

ADC189

Commercial team of 5000+ FTEs covering hospital and retail channels in large cities and broad market

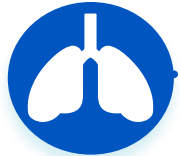


STOCK CODE  
2096.HK

# Oncology R&D Progress

# Zaiming R&D Strategy

## CORE INDICATIONS



Lung Cancer



Gastrointestinal  
Cancer



Gynecological Cancer

## MECHANISMS OF INTEREST

### Immuno-oncology

- Engineered cytokines and fusion proteins
- Targeting inhibitory immune cells
- Novel immune checkpoints and their combination

### Tumor driver gene Tumor TAA

- Targeting tumor driver genes and targeted protein degradation
- Target tumor antigen
- T cell engager, ADC

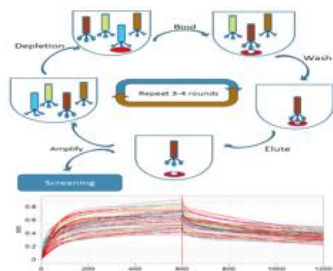
### DDR Synergistic lethal mechanism

- Multiple types of synergistic lethality: DNA damage repair, tumor metabolism, gene transcription

# Zaiming Technology Platform

*Deploy technology application potential, Differentiation-by-Design*

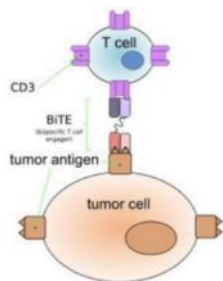
## Protein Engineering Platform



**SIM0237**

Mutational attenuation, potentially IO resistance solution

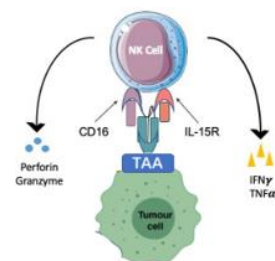
## TCE platform



**SIM0500**

Optimized CD3 binding with better efficacy and lower risk of CRS adverse reactions

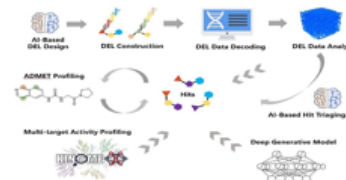
## NKCE Platform



**SIM0602**

First-in-class cytokine-NKCE fusion, plasma IgG level insensitive

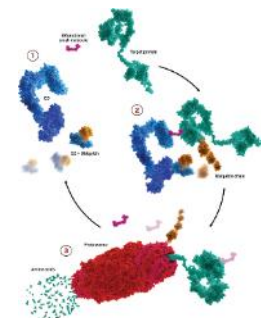
## AI-assisted Molecule Generation Platform



**SIM0520**

First-in-Class Target Hit Compound Discovery

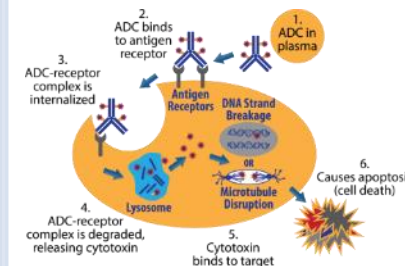
## Protein Degradation Platform



**SIM0510**

Own E3 binder ligase and linker






## ADC Platform



**SIM0505**

Own Payload, Stable Linkers and Coupling Technology

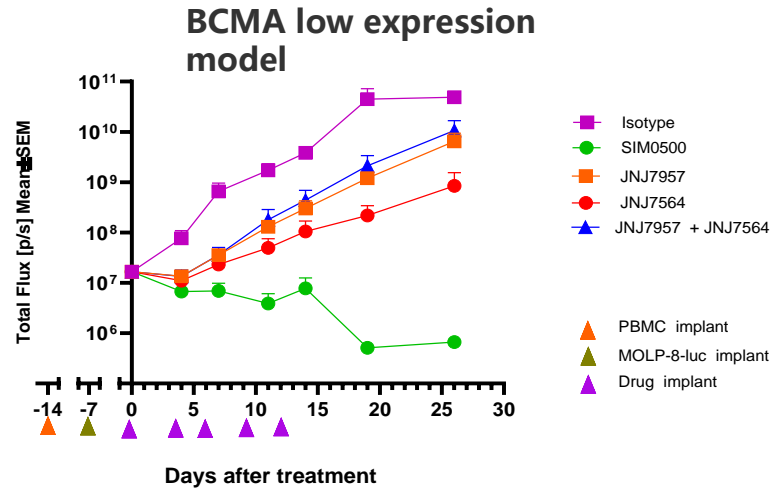
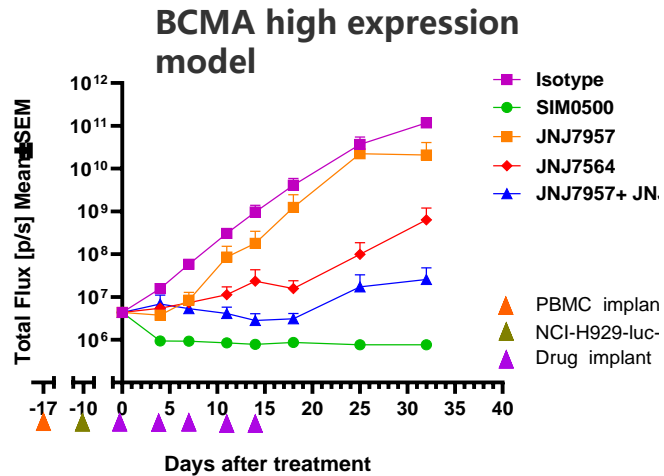
# Innovative Drug Pipeline

Pre-Clinical		IND Enabling	Phase 1a	Phase 1b/2	Pivotal/Phase III	NDA and post marketing
SIM 0512	SIM 0510	SIM 0502 Solid tumor	PD-L1/IL15v Solid tumor 	Enweida® + Jielien® Endometrial cancer <input checked="" type="checkbox"/>	COSELA® Triple negative breast cancer 	COSELA® 1L ES-SCLC Formal Approval
SIM 0526	SIM 0520	SIM 0505 CDH6-ADC OC, RCC	PD-L1/IL15v NMIBC	SERD BTC: HR+ BC	Suvemcitug Platinum-resistant ovarian cancer	COSELA® Manufacturing application in China
SIM 0552	SIM 0528	SIM 0686 Fgfr2b-ADC GC, LC	TIGIT/PVRIG Solid tumor	TNFR2 Solid tumor 	Endostar® Malignant pleural and peritoneal effusion	COSELA® 2/3L ES-SCLC
SIM 0562	SIM 0558	SIM 0508 polQ OC, BC, CRPC	CD80/IL2 Solid tumor  <input checked="" type="checkbox"/>		Paxalisib Glioblastoma  <input checked="" type="checkbox"/>	CMAB009 mCRC <input checked="" type="checkbox"/>
SIM 0612	SIM0606	SIM 0618 EGFR cMET ADC LC	SIM 0500 CD3-BCMA-GPCR5D MM			
SIM 0620	SIM 0622		SIM 0501 USP1 OC, BC			
SIM 0680						
SIM 0682						

- Innovative monoclonal antibody
- Bi/multi specific
- ADC drug
- Small molecule drug
-  Global Development
- Advancing by partner

# High-potential innovative product: SIM0500 GPRC5D-BCMA-CD3

Potentially best-in-class multiple myeloma drugs



China IND submitted

S.C administration route

*Johnson & Johnson*

Teclistamab (BCMA-CD3)

63% ORR

Talquetamab (GPRC5D-CD3)

74% ORR

Tec + Tal

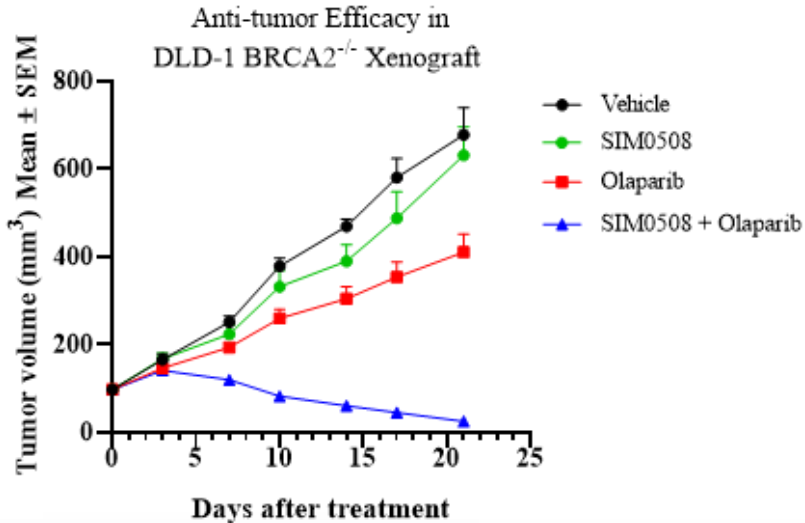
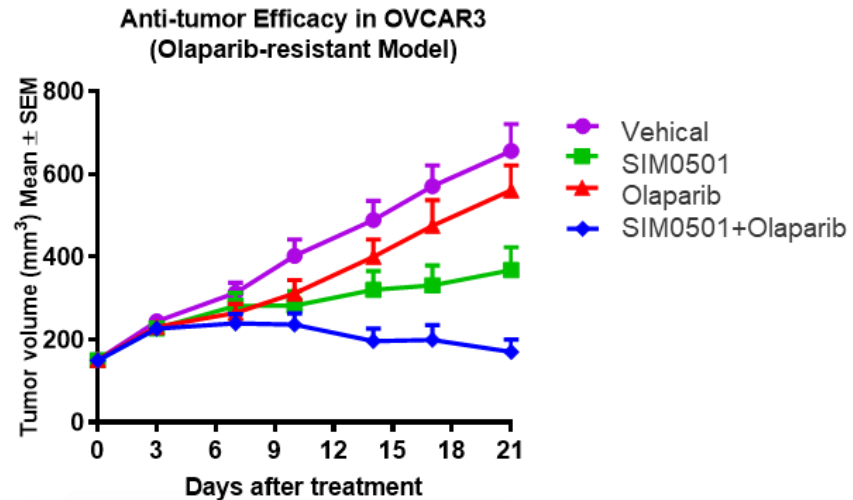
**94% ORR**

## Unmet Clinical Need

- Tri-specific T cell Engager, capable of covering multi-line (CD38, BCMA) drug resistance in multiple myeloma, with lower side effects
- Prolongs progression-free survival and reduces the risk of relapse in patients with MM
- The multiple myeloma market in China has compound annual growth of 30% in the past 5 years; the total overseas market has exceeded 20 billion US dollars in 2022

# Innovative Products with High Potential: SIM0501 USP1 & SIM0508 PoI $\theta$

*Novel targets related to DNA damage repair*



**2023 Q3**

**SIM 0501, US IND, initiated clinical development**

**2024 Q2**

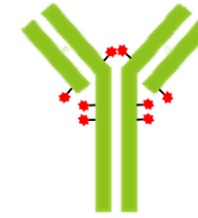
**SIM 0508, US IND submission, initiated clinical development**

## Unmet Clinical Need

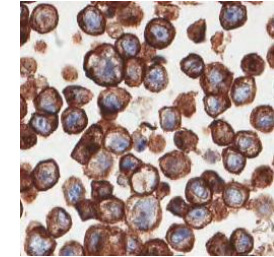
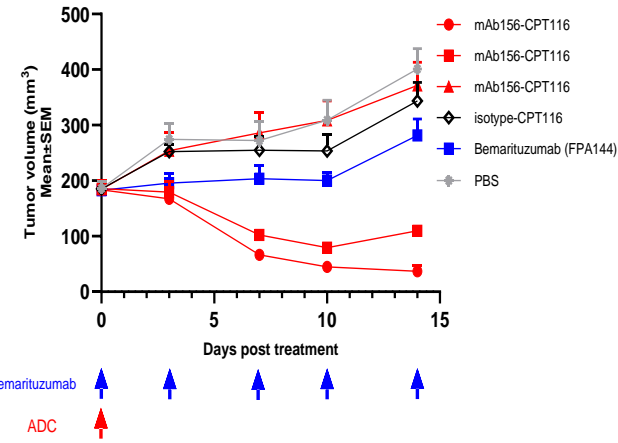
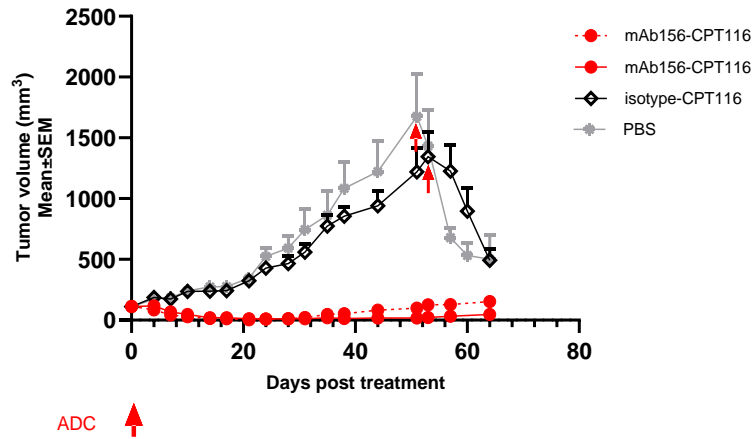
- Capable of overcoming PARPi resistance and synergize with PARPi or chemoradiation
- Monotherapy in multiple solid tumors with HRD or BRCA mutations
- Poor efficacy of posterior line monotherapy, poor expansion of other indications except ovarian cancer, breast cancer, prostate cancer and pancreatic cancer, and huge population and clinical needs

# High-potential innovative products of conjugation platform: FGFR2b-ADC

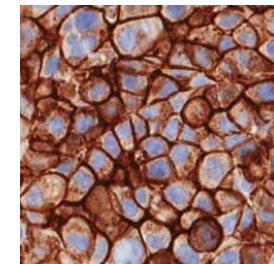
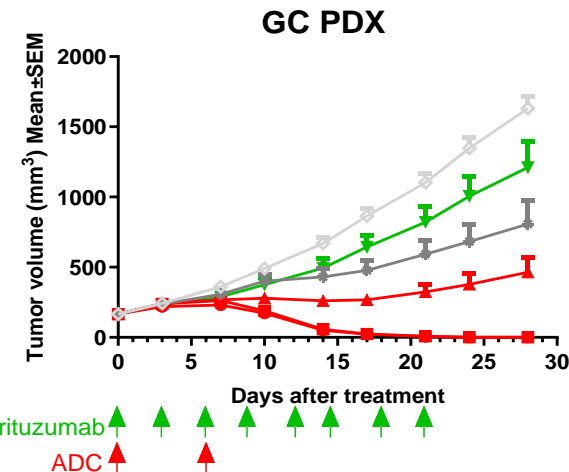
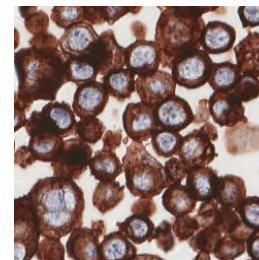
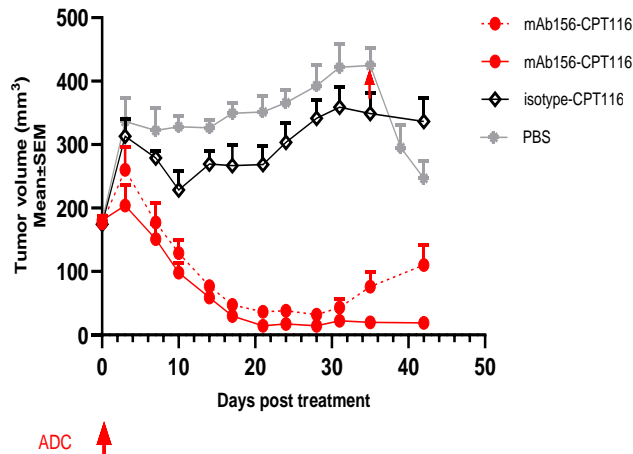
*In vivo efficacy*



**SNU16**



**KATOIII**





STOCK CODE  
2096.HK

# Non-Oncology R&D Progress

# Non-oncology R&D disease focus

Strengthen the core advantages in stroke treatment and execute Alzheimer's disease and insomnia programs

## Neurology



Breakthrough the limitations of existing treatments and focus on indications that lack effective treatments

## Autoimmune



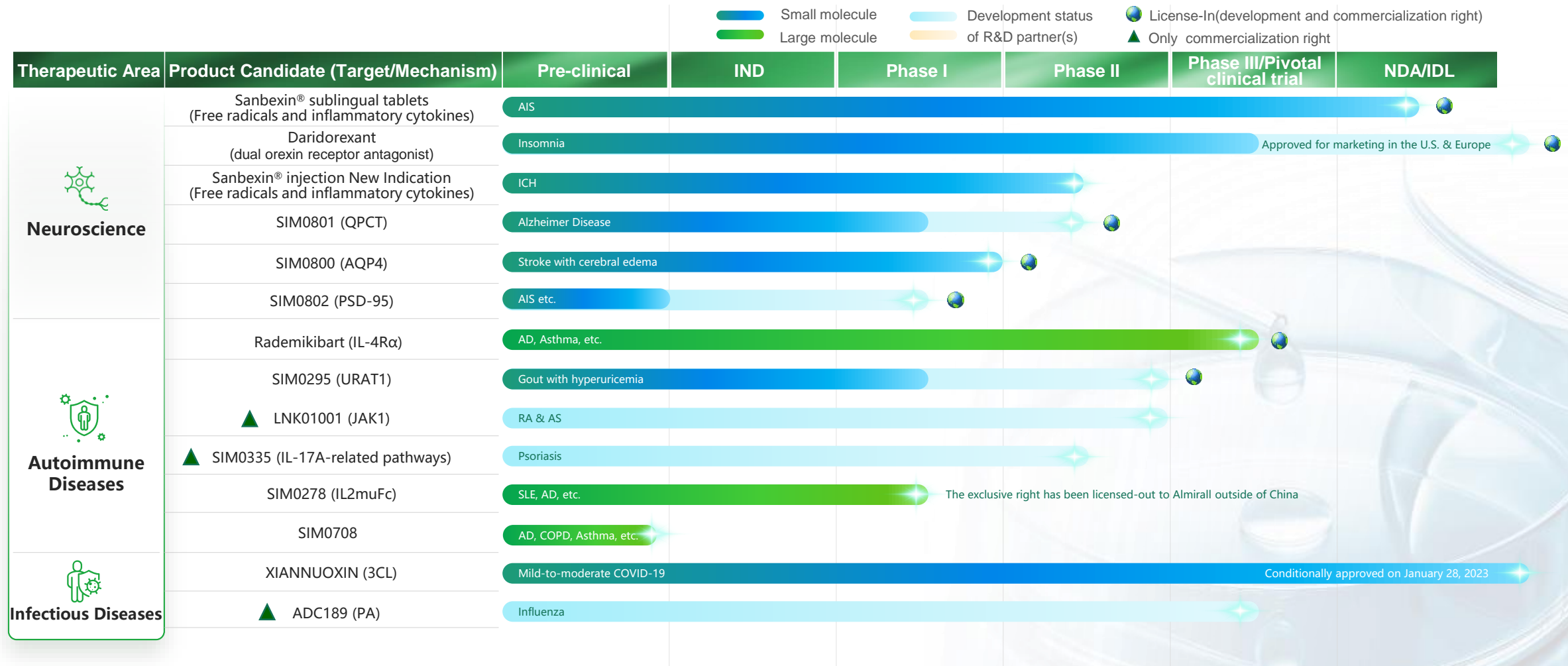
Focus on infectious diseases with significant clinical unmet needs and provide better treatment options for patients

## Infection



Focus on Greater Efficacy  
Adhere to Differentiation

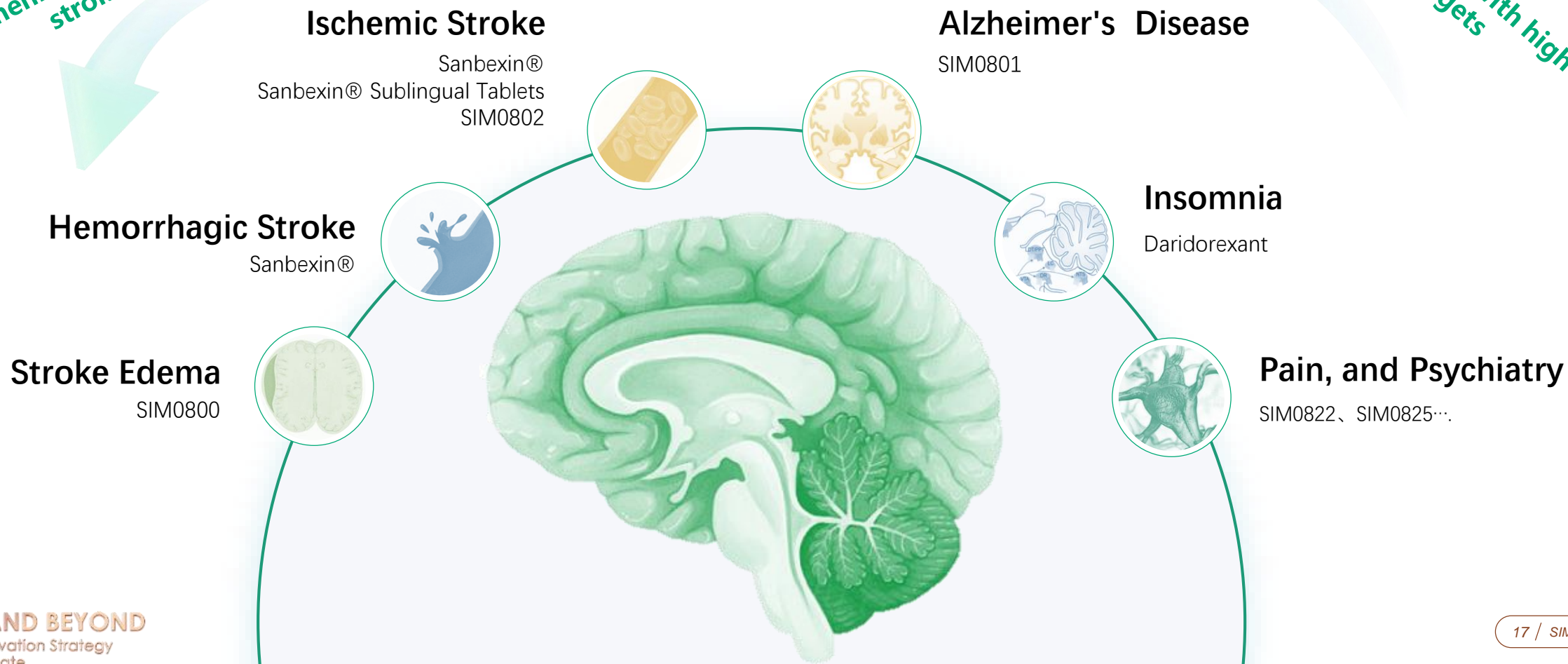
# Non-oncology development pipeline



# Neurology development strategy

Strengthening and advance to improve stroke treatment

Execute and expand with high potential targets



# Neurology: Sanbexin sublingual tablets

Easy to administer. *Improve stroke treatment outcome from onset to recovery*

Unmet Medical Needs

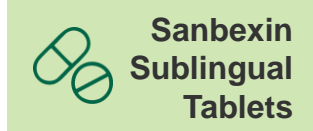
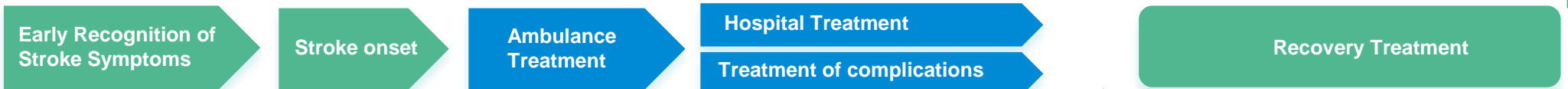
Pre-hospital care – no treatment

Cerebral ischemia (AIS) - treatment need beyond reperfusion therapy.

Cerebral hemorrhage (ICH) - no drug.

Stroke complications - no effective treatment for cerebral edema, etc.

Stroke recovery - effective treatment for limb disability, prevention of secondary dementia, depression, etc.  
Stroke recurrence - effective prevention



Home medicine for emergency use during new onset or recurrence of stroke.

Sequential treatment to completion of the treatment cycle of 14 days

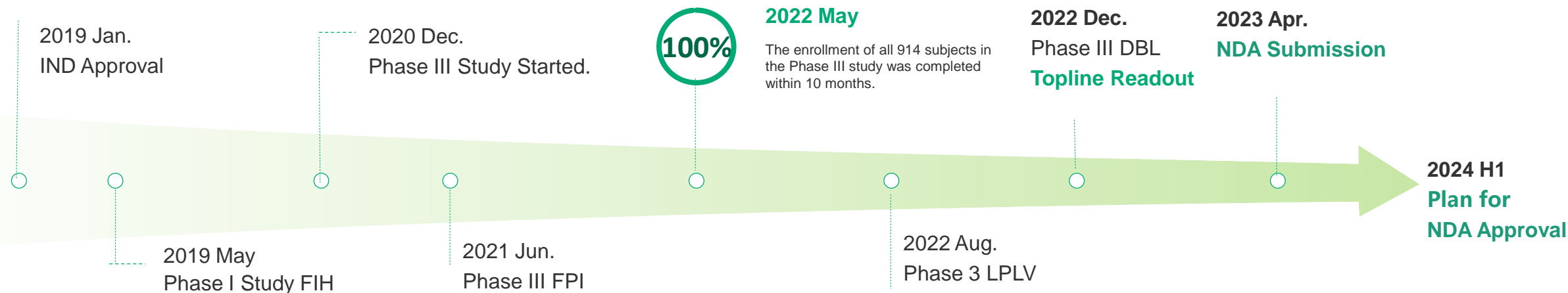
Stroke Recovery Treatment

Drug R&D

# Successful completion of Sanbexin sublingual tablets (SST) phase III clinical trial in AIS: ahead of target date



SST can significantly improve the convenience and flexibility of stroke treatment, have great potential to cover the full course of Stroke therapy. The two active ingredients, Edaravone and Dexborneol, are highly brain penetrable and exert potent anti-inflammatory and antioxidant effects.

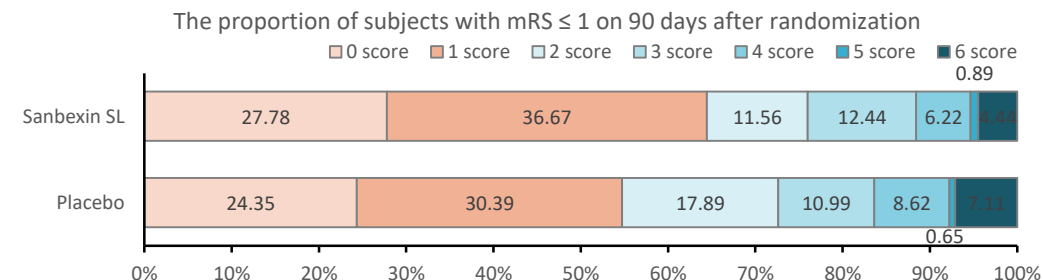


## Primary Endpoint of Sanbexin sublingual (TASTE SL) Study

- A favorable outcome of mRS score  $\leq 1$  on day 90 occurred in 290 of 450 patients (64.4%) in the Sanbexin SL group and in 254 of 464 patients (54.7%) in the placebo group (P=0.003)

mRS score  $\leq 1$   
on day 90

**64.4%**  
**Sanbexin SL** vs **54.7%**  
**Placebo**



## Daridorexant

### Novel MOA- Dual Orexin Receptor Antagonists (DORA)

- Improving for falling asleep and maintaining asleep
- Only hypnotic drug approved by EMA for the indication of impacting on daytime functioning
- Better tolerated, much less dependence, long-term use

- Fast-onset
- Sleep maintenance
- Improve daytime function
- Safe for long-term use
- No rebound insomnia

#### Benzodiazepines

GABAA receptor agonist

##### Triazolam

- Lack of effect on sleep maintenance
- Obvious residual effect
- Noticeable hangover
- Risk of addiction, short time use
- Rebound insomnia
- Not well-tolerated

#### Non-benzodiazepines

##### Zolpidem

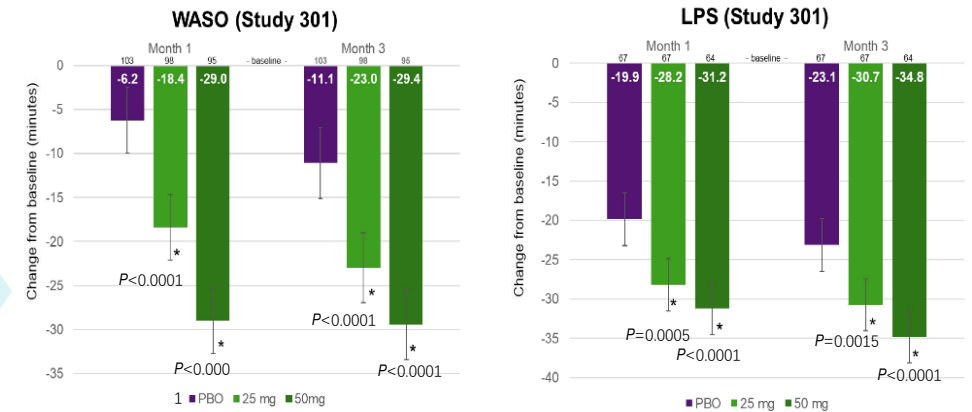
- Short time use
- Lack of effect on sleep maintenance
- Risk of safety: fall; complex sleep behaviors (Be seriously injured or injure other person) ; impair daytime function
- Addiction

#### Antidepressants

##### Agomelatine

- Only acts on melatonin
- For patients with depression and anxiety accompanied by insomnia symptoms. Limited evidence
- No studies on long-term treatment
- More AEs, not well-tolerated
- Routine monitor liver function: may increase, and even induce liver damage

### Sustained efficacy and Well tolerated

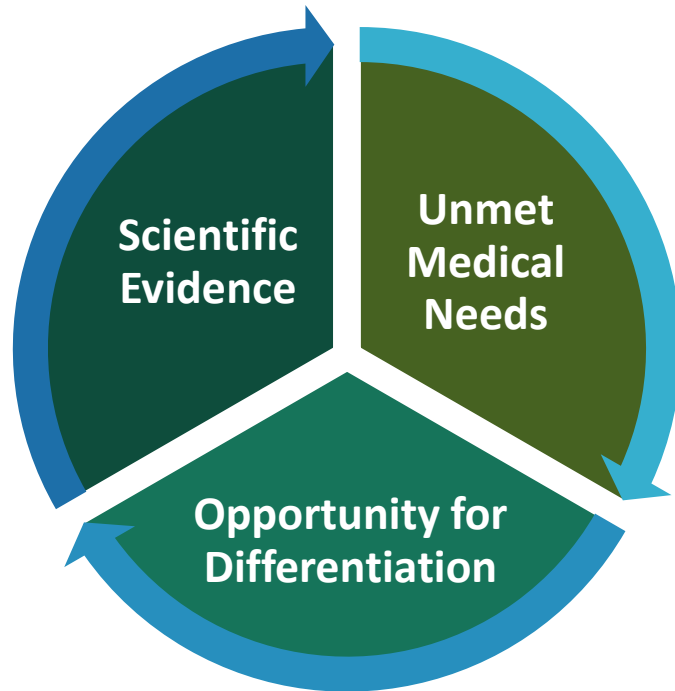


Daridorexant 50 mg and 25 mg significantly improved both sleep onset (LPS) and sleep maintenance (WASO)

One tablet daily, one extra night of sleep per week

# Autoimmune : Strategic considerations for new products, disease areas and targeted pathways

## Strategic Decision



## Disease Areas

### RHEUMATOLOGY

- Disease Modifying
- Maintain Remission
- RA, AS, PsA, SLE

### DERMATOLOGY

- Durable Skin Health
- AD, Pso, Alopecia

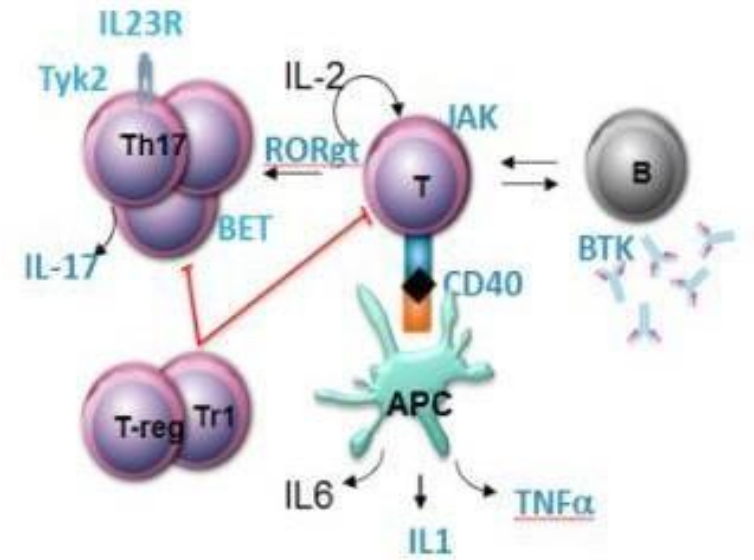
### RESPIRATORY

- Disease Modifying
- Exacerbation Prevention
- Asthma, COPD

### GASTROENTEROLOGY

- Durable Remission
- UC, CD

## Targeted Pathways



Immunomodulation  
of Adaptive and  
Innate Cells

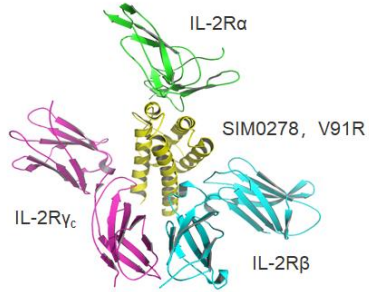
Eg: JAK, TYK2, IL-2, IL-4, IL-6, IL-23

# SIM0278: IL-2mu-Fc;

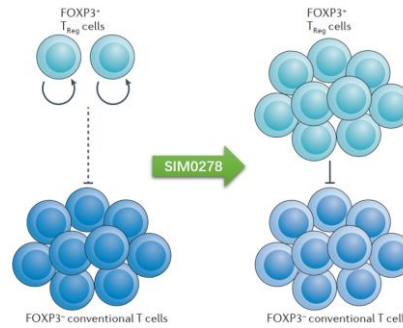
Simcere's innovative biologic, out-licensed to Almirall 2023



Selectively activate Treg, immune re-balance, target multiple immune diseases



- Lower IL-2Rβγ affinity
- Keep high IL-2Rαβγ affinity
- Prolonged T half

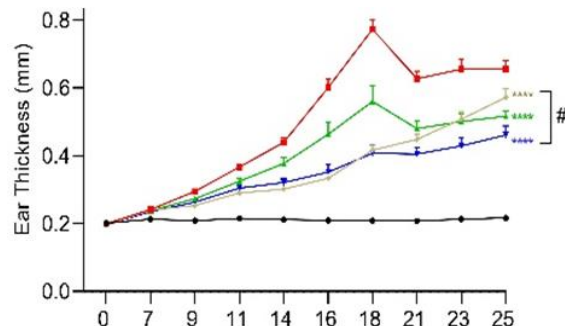


- Selectively activate Treg
- Better efficacy in animal models

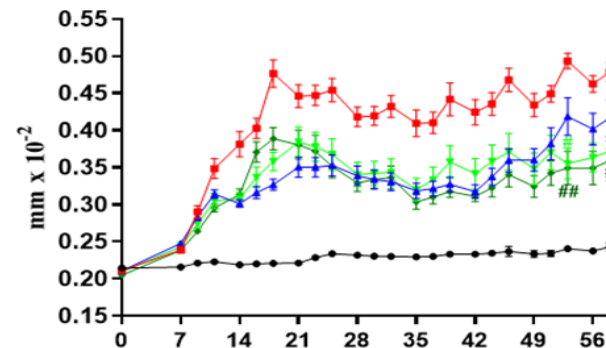


- Licensed to Almirall (outside CN)
- Target diseases: SLE, cGvHD, Atopic dermatitis(AD), vitiligo and alopecia areata

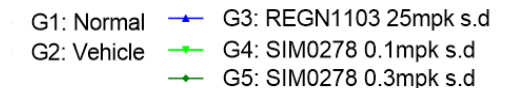
## Long-lasting effect in Atopic Dermatitis (AD) animal model



Significantly alleviated ear swelling in AD model; Better efficacy vs AMG592 at 0.1mg/kg

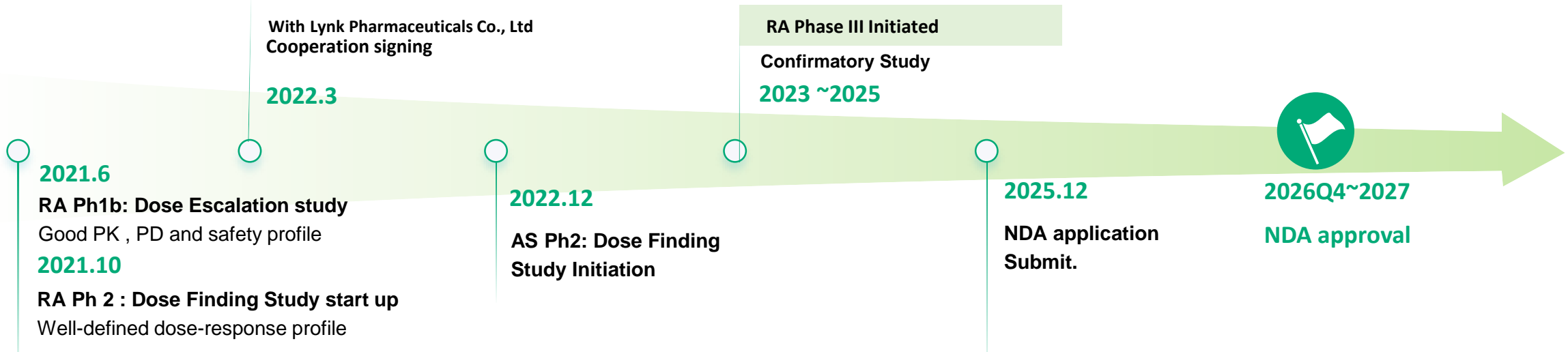


Better long-lasting effect vs dupilumab surrogate after single dose.

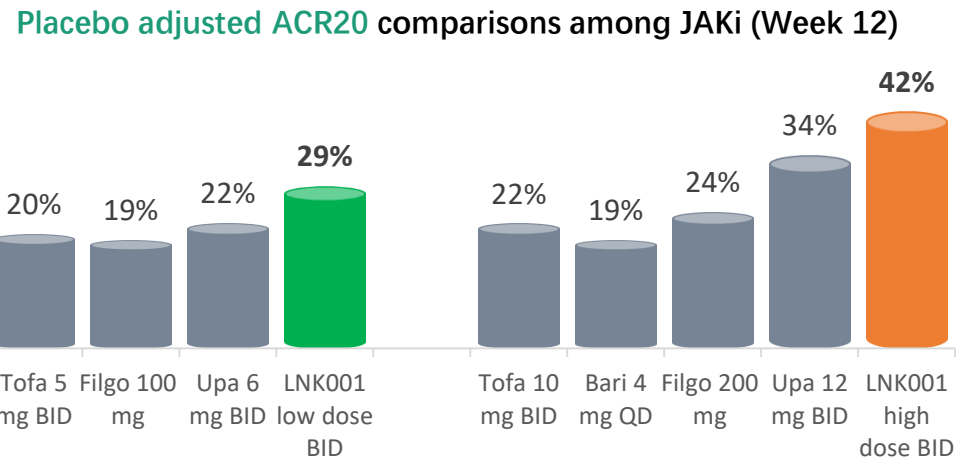
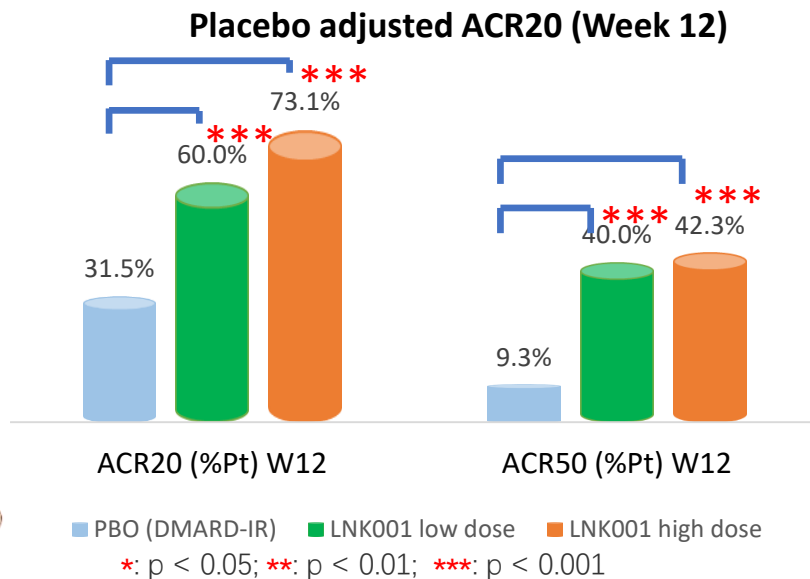


# LNK01001 : A Highly Selective JAK1 Inhibitor

in collaboration with Lynk Pharmaceuticals Co., Ltd



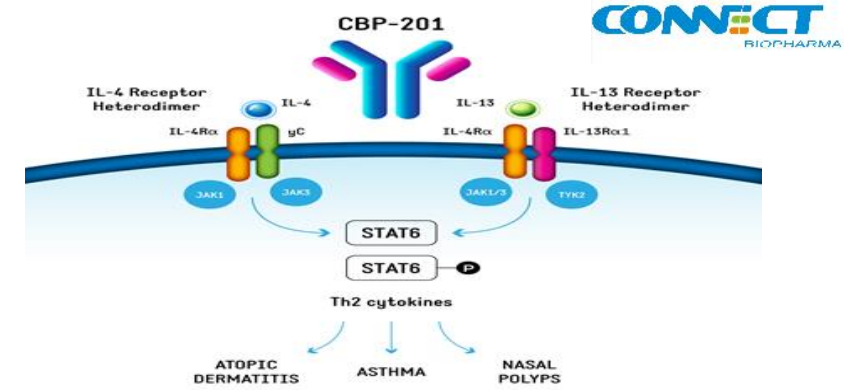
## LNK01001 clinical phase II Rheumatoid Arthritis study results showed excellent efficacy profile



# Rademikibart (CBP-201) an IL-4R $\alpha$ antibody, targeting Th2- mediated diseases.

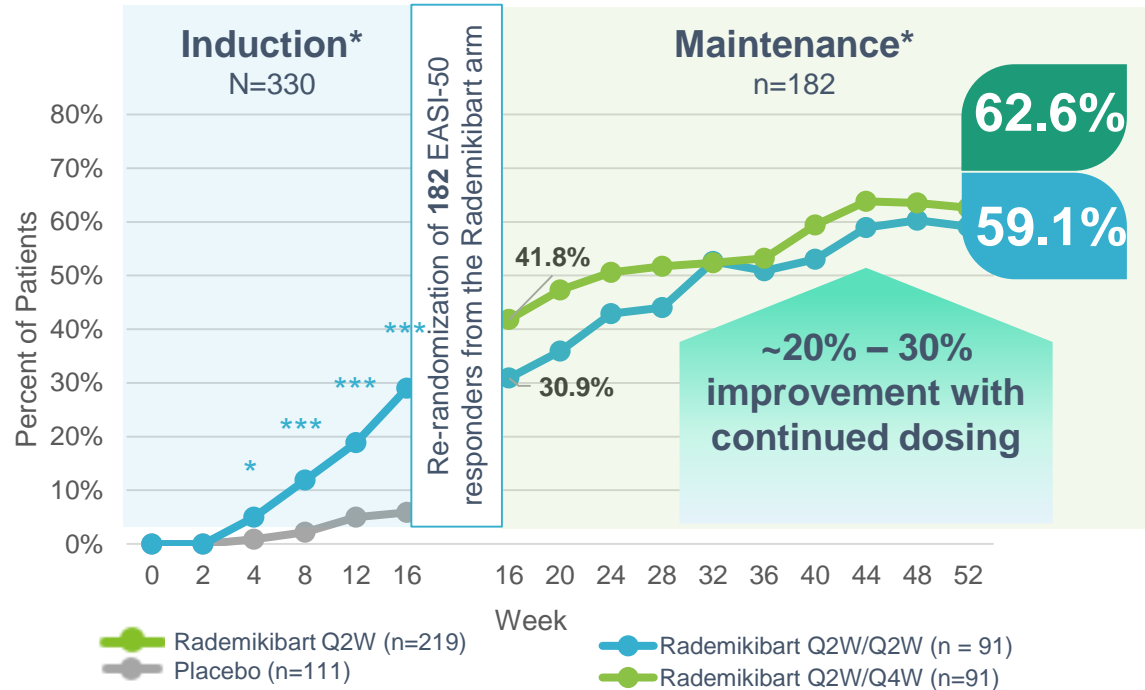
## Maintaining efficacy for 52 weeks

- Rademikibart is a fully human IgG4 mab inhibits both IL-4 and IL-13- mediated signaling pathways.
- The potential differentiation from other IL-4 (eg; dupilumab) are based on:
  - different amino acid sequences
  - Binds to different epitope on IL-4R $\alpha$
  - Has higher affinity and inhibitory activity towards IL-4R $\alpha$

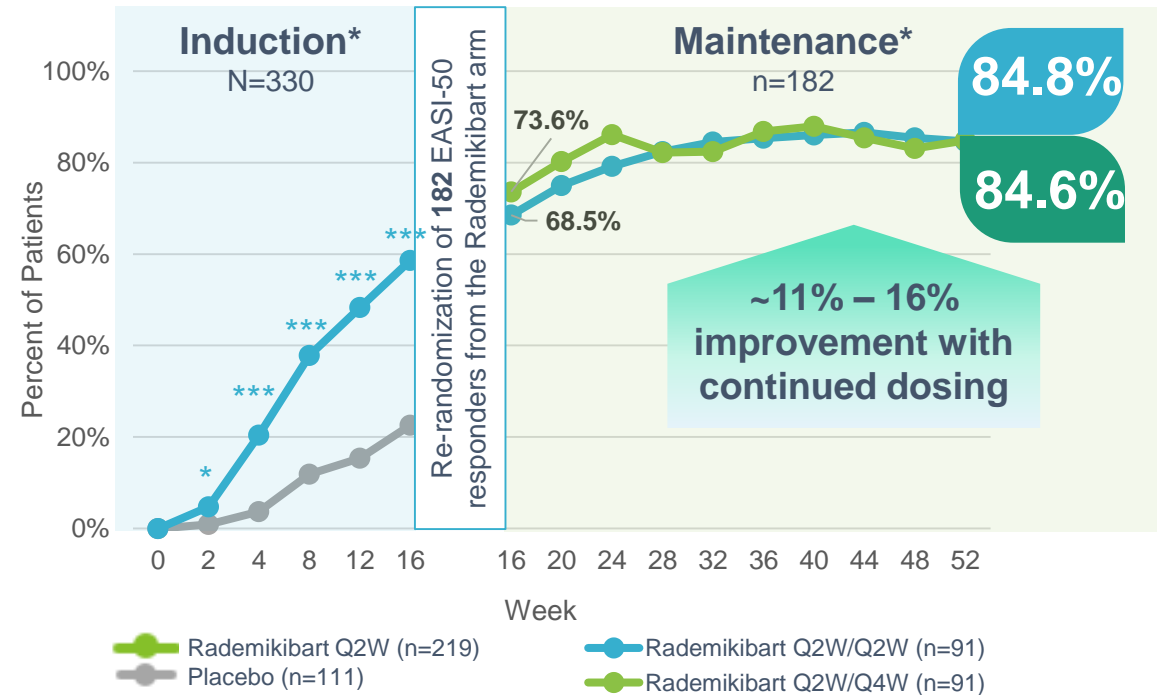


## Results from the Atopic Dermatitis pivotal study

### IGA 0/1 over 52 weeks of treatment (NRI-MI)



### EASI-75 over 52 weeks of treatment (NRI-MI)





STOCK CODE  
2096.HK

# Thank you!

*Providing Today's Patients with Medicines of the Future*

