CMB International Global Markets | Equity Research | Company Initiation

Akeso, Inc. (9926 HK)

A leading biopharma in bi-specific antibodies and other innovative biological therapies

- **A pioneer biopharma with rich innovative pipelines.** Akeso has developed a robust pipeline of over 30 drugs, covering oncology, autoimmune and metabolic diseases. These pipeline products consist of six bi-specific antibodies, including the two first-in-class BsAb drugs, AK104 (PD-1/CTLA-4) and AK112 (PD-1/VEGF), and other BsAb drug candidates at earlier stage of development, i.e. AK129 (PD-1/LAG3) and AK130 (TIGIT/TGF-β fusion protein). With 18 drug candidates having entered clinical trial stage, Akeso has launched 80+ trials in China, the US, Australia, New Zealand, etc. including more than a dozen pivotal/Ph3 trials.
- **AK104 (PD-1/CTLA-4) has the best-in-class potential for first-line treatment of various large indications.** AK104 was approved for 2/3L R/M CC in Jun 2022, becoming the globally first approved dual checkpoint inhibitor BsAb and filling the gap of immunotherapy treatment for R/M CC. With promising early clinical data released, AK104 has demonstrated its BIC potential in front-line CC, GC and HCC. As multiple registrational studies of AK104 are ongoing for these large indications, we see blockbuster potential in AK104. For commercialization, with a salesforce of 650+ employees (as of end-2022) achieving strong sales records, AK104 realized RMB546mn sales in 2H22, the first six months since launch. We are confident about Akeso's guidance to realize RMB1.2~1.3bn revenue from AK104 in 2023E.
- **AK112 (PD-1/VEGF) to become the first-in-class BsAb tapping the enormous lung cancer market across all treatment settings.** In China, AK112+chemo is in a Ph3 study for EGFR-m TKI-failed nsq-NSCLC, with the NDA filing expected this year. AK112 mono also entered a H2H Ph3 study vs pembrolizumab for PD-L1+ NSCLC. In addition, to beat the 1L SoC, AK112+chemo recently entered an H2H study vs tislelizumab +chemo for 1L sq-NSCLC. The all-spectrum coverage of NSCLC, plus the potential coverage of GC, BC, HCC, and CRC, supports the blockbuster potential of AK112. Akeso has out-licensed certain ex-China rights of AK112 to Summit through a blockbuster transaction, with the deal size up to US$5.0bn including the US$500mn upfront being paid. Based on the studies in China, Summit has started a Ph3 MRCT trial of AK112+chemo for EGFR-mutated TKI failed nsq-NSCLC in May 2023, and plans to start another Ph3 trial of AK112+chemo in 1L sq-NSCLC.
- **Initiate at BUY with TP of HK$52.65**. We estimate Akeso's total risk-adjusted sales from products and licenses of RMB4,927mn/ RMB3,536mn/ RMB5,077mn in FY23E/ 24E/ 25E. Considering the upfront payment from Summit, we expect Akeso to record attributable net income of RMB1,522mn in FY23E, while will incur net losses of RMB696mn/ RMB813mn in FY24E/ 25E. We derive our target price of HK$52.65 based on a DCF valuation (WACC: 10.60%, terminal growth rate: 3.0%).

Earnings Summary

(YE 31 Dec, RMB mn)	FY21A	FY22A	FY23E	FY24E	FY25E
Sales from products and licenses	340	1,108	4,927	3,536	5,077
Revenue	226	838	4,496	3,012	4,435
YoY growth (%)	na	271	437	(33)	47
Net profit	(1,075)	(1,168)	1,522	(696)	(813)
EPS (Reported) (RMB)	(1.32)	(1.42)	1.81	(0.83)	(0.97)
R&D expenses	(1,123)	(1,323)	(1,500)	(1,650)	(1,815)
Admin expenses	(244)	(199)	(334)	(483)	(763)

Source: Company data, Bloomberg, CMBIGM estimates

BUY (Initiation)

Target Price	**HK$52.65**
Up/Downside	**44.3%**
Current Price	**HK$36.50**

China Healthcare Sector

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Stock Data

Mkt Cap (HK$ mn)	30,699
Avg 3mths t/o (HK$ mn)	175
52w High/Low (HK$)	52.60/19.22
Total Issued Shares (mn)	841

Source: FactSet

Shareholding Structure

XIA Yu (夏瑜)	12.69%
Shenzhen Capital Group	7.99%

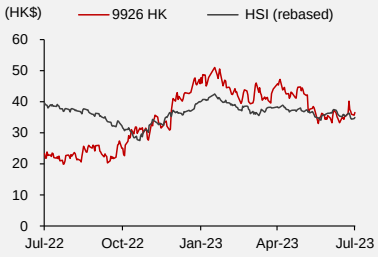
Source: Company data, as of Dec 2022

Share Performance

	Absolute	Relative
1-mth	0.3%	5.2%
3-mth	-19.1%	-11.0%
6-mth	-22.1%	-10.1%

Source: FactSet

12-mth Price Performance



Source: FactSet

Auditor: Ernst & Young
Web-site: https://www.akesobio.com

Contents

Investment thesis 3
Innovative pipelines with BIC/FIC potentials 3
Broad collaborations to pave the way of globalization 3
Sufficient and expanding manufacturing capacity 4
Robust talent pool to back up R&D and commercialization 4
Initiate at BUY with TP of HK$52.65 4
Investment risks 4
Domestic leading biopharma in bi-specific mAb 5
Innovative BsAb pipelines with BIC/FIC potentials 5
Proprietary R&D engine powered by comprehensive technology platform 9
Broad collaborations to pave the way of globalization 11
Abundant manufacturing capacity and rich talent pool to support business growth 13
Cadonilimab (AK104, PD-1/CTLA-4), globally first approved dual checkpoint inhibitor BsAb 15
First-in-class dual immene checkpoint inhibitor targeting the largest indications 15
2L/3L R/M CC: approved as the first dual checkpoint inhibitor BsAb globally 17
1L R/M CC: promising early efficacy data released for CC front-line treatment 19
Front-line HCC: encouraging early PFS results observed with favorable safety profile 22
1L G/GEJC: encouraging long-term PFS and OS efficacy results 23
Large potential in commercialization in China and potentially overseas 25
Ivonescimab (AK112, PD-1/VEGF), first-in-class BsAb to uncover the enormous lung cancer market 26
First-in-class BsAb for lung cancer across all treatment settings 26
AK112 monotherapy demonstrated promising preliminary efficacy for 1/2L NSCLC 28
AK112 combined with chemotherapy for NSCLC across all spectrum treatment settings 30
ES-SCLC: preliminary encouraging results for fist-line treatment 34
Pooled analysis continue to demonstrated AK112's favourable safety profile 35
To accelerate the globalization of AK112 through a landmark out-licencing deal 36
Ligufalimub (AK117, CD47), potential best-in-class CD47 mAb with favorable hematotoxicity 37
Pre-clinical evidence supports the favorable hematotoxicity of AK117 as a CD47 mAb 37
AK117 demonstrated favorable hematotoxicity and promising preliminary efficacy 38
Penpulimab (AK105, PD-1), backbone of Akeso's PD-1-based BsAbs 41
Near term commercialization of non-oncology pipelines 44
Ebdarokimab (AK101, IL-12/IL-23), potentially the first domestic IL-12/IL-23 mAb 44
Ebronucimab (AK102, PCSK9), approaching commercialization 48
Financial Analysis 52
Produce sales to ramp up fast 52
Valuation 55
Financial Statements 56
Investment Risks 58
Appendix: Company Profile 59

Investment thesis

Established in 2012, Akeso is a Chinese biopharma dedicated to the R&D, manufacturing and commercialization of innovative antibody drugs, especially in the bi-specific antibody area. The Company was listed on HKEx in Apr 2020.

Innovative pipelines with BIC/FIC potentials

The Company has a pipeline of over 30 drugs, covering the areas of oncology, autoimmune and metabolic diseases. These pipeline products consist of six bi-specific antibodies, including the two first-in-class BsAb drugs, AK104 (PD-1/CTLA-4) and AK112 (PD-1/VEGF), and other BsAb drug candidates at earlier stage of development, i.e. AK129 (PD-1/LAG3), AK130 (TIGIT/TGF-β fusion protein), AK131 (PD-1/CD73), and AK132 (Claudin18.2/CD47). With 18 drug candidates having entered clinical trial stage, Akeso has launched more than 80 clinical trials in China, the US, Australia, New Zealand, etc., including more than a dozen pivotal/Ph3 trials.

AK104 (PD-1/CTLA-4) has the best-in-class potential for first-line treatment of various types of cancer, including cervical, liver, stomach, and other cancers. AK104 was initially approved in China for 2/3L cervical cancer (R/M CC) in Jun 2022, becoming the globally first approved dual checkpoint inhibitor BsAb and filling the gap in immunotherapy treatment for R/M CC. With promising early clinical data released, AK104 has demonstrated its best-in-class potential in front-line treatment for large indications, including 1L CC, 1L HCC, and 1L GC. With multiple registrational studies of AK104 ongoing for these large indications, we expect AK104 to become a blockbuster medicine in the future. In terms of commercialization, with a strong salesforce of over 650 employees (as of end-2022) keeping achieving remarkable sales records, the sales of AK104 has reached RMB546mn in 2H22, during the first six months since commercial launch. We are confident about the Company's target to realize RMB1.2~1.3bn revenue from AK104 in 2023E. In addition, based on the smooth progress of the clinical development of AK104 in large indications, we anticipate AK104 could achieve a blockbuster out-licensing deal of its ex-China rights.

AK112 (PD-1/VEGF) is likely to become the first-in-class BsAb to uncover the enormous lung cancer market across all spectrum treatment settings. In China, AK112+chemo is in a Ph3 study for EGFR-m nsq-NSCLC patients who failed prior EGFR-TKI therapy, for which the current treatment options are very limited. The Company targets to file the NDA of this indication in China this year. Based on the promising Ph2 data of AK112 in PD-L1+ NSCLC patients, AK112 mono entered a head-to-head Ph3 study vs pembrolizumab for PD-L1+ NSCLC. In addition, to beat the current SoC treatment, AK112+chemo recently entered a head-to-head Ph3 study vs tislelizumab+chemo for 1L sq-NSCLC. The all-spectrum coverage of NSCLC, and potential coverage of gastrointestinal cancer, breast cancer, HCC, CRC (in Ph1b/2 trials), support the blockbuster potential of AK112. In the overseas markets, Akeso has out-licensed certain ex-China rights of AK112 to Summit Therapeutics through a blockbuster deal. Besides future sales royalties, the deal size was up to US$5.0bn and US$500mn upfront being paid, which was a landmark deal for Chinese biopharma companies. Based on Akeso's studies in China, Summit has started a Ph3 MRCT trial of AK112+chemo for EGFR-mutated nsq-NSCLC who failed in prior EGFR-TKI therapy (FPI in May 2023), and expects to start another Ph3 MRCT trial of AK112+chemo in 1L sq-NSCLC (FPI expected in 2H23).

Broad collaborations to pave the way of globalization

Akeso has been forging strategic partnerships globally to speed up the development and commercialization of its innovative products. The Company collaborates with leading MNC and domestic pharma companies, including Merck, Summit Therapeutics, Dawnrays Pharmaceutical, Sino Biopharm, etc. In 2015, Akeso out-licensed its self-developed CTLA-4 antibody (AK107) to Merck. In Dec 2022, Akeso out-licensed part of the ex-China rights of its breakthrough bispecific antibody, ivonescimab (AK112, PD-1/VEGF) to Summit Therapeutics through a landmark transaction. These out-licensing agreements

provide an expedited pathway for the global development of the Company's innovative drugs. The Company has also forged important partnerships with domestic pharma companies, including the partnership with Chia Tai Tianqing for PD-1 mAb penpulimab (AK105), and the partnership with Dawnrays Pharma for AK102 (PCSK9) and AK109 (VEGFR-2). These out-licensing and partnerships are not only endorsements of Akeso's R&D capabilities, but are also key drivers for the Company to accelerate the development and commercialization of its innovative product portfolio both in China and globally.

Sufficient and expanding manufacturing capacity

The Company has established an efficient GMP-compliant manufacturing system to meet its increasing product demand from internal research and commercialization. The GMP-compliant manufacturing facilities are designed and validated according to the FDA, EMA, and NMPA regulations. As of end-2022, Akeso has a total production capacity of 31,500L in operation. Akeso has a capacity expansion plan in Zhongshan and Guangzhou with a planned total capacity of more than 160,000L to meet the future clinical and commercialization needs.

Robust talent pool to back up R&D and commercialization

As of end-2022, the Company had a total of 2,300+ employees. 275 employees were in the pre-clinical R&D team, and 532 were in the clinical development team, with the research staff accounting for 34% of the total employee. As of end-2022, the Company has an internal commercial and marketing team of 652 employees (28% of the Company's total employees), which are currently mainly responsible for the commercial promotion of AK104. We expect Akeso to further expand its salesforce in 2023.

Initiate at BUY with TP of HK$52.65

We expect Akeso's product sales to ramp up quickly and AK104 and AK112 will be the major revenue drivers of the Company in a long run. We estimate Akeso's total risk-adjusted sales from products and licenses of RMB4,927mn/ RMB3,536mn/ RMB5,077mn in FY23E/ 24E/ 25E, respectively. Akeso recorded attributable net loss of RMB1,075mn/ RMB1,168mn in FY21A/ 22A. In 2023, considering the upfront payment of US$500mn from Summit related to the deal of AK112, we expect the Company to record net income of RMB1,522mn in FY23E. We expect the Company to incur net losses of RMB696mn/ RMB813mn in FY24E/ 25E, and to turn profitable in FY26E. We derive our target price of HK$52.65 based on a DCF valuation (WACC: 10.60%, terminal growth rate: 3.0%).

Investment risks

1) Failure of clinical development or regulatory approvals of drug candidates.

2) Competition of approved products both in China and overseas markets.

Domestic leading biopharma in bi-specific mAb

Akeso, Inc. (9926 HK), established in 2012, is a Chinese biopharma dedicated to the R&D, manufacturing and commercialization of innovative antibody drugs. Akeso has developed into a pioneer in bi-specific antibody in China, with the first-in-class PD-1/CTLA-4 bsAb (AK104) approved in China already, and PD-1/VEGF bsAb (AK112) achieved a landmark out-licensing deal. The Company currently has a pipeline of over 30 drugs, 18 of which have entered clinical stage, covering the areas of oncology, autoimmune and metabolic diseases.

Akeso was listed at HKEX in Apr 2020. The Company is also preparing its listing on the Shanghai STAR market. Akeso was able to keep amplifying its cash balance through various ways, i.e. secondary placement, asset out-licensing, government grants, etc. In Jul 2022, Akeso raised RMB0.51bn net cash from placement of new shares. In Nov 2022, Guangzhou Hi-tech Investment Group provided RMB0.5bn investment in the type of equity investment and long-term low-interest loan. Additionally, in 1Q23, Akeso received US$500mn upfront payment from Summit for out-licensing AK112. As of Mar 2023, the Company had a strong cash balance of RMB5.3bn.

Figure 1: Milestones of Akeso

Time	Milestones
Jan 2023	Penpulimab (AK105, PD-1) approved for 1L sq-NSCLC
Dec 2022	Out-licensed the rights of ivonescimab (AK112, PD-1/VEGF) in the US, Canada, Europe, and Japan, with up to US$5bn to Summit Therapeutics
Jun 2022	Cadonilimab (AK104, PD-1/CTLA-4) approved for the treatment of R/M cervical cancer (R/M CC) patients who has progressed on or after platinum-based chemotherapy
Aug 2021	Penpulimab (AK105, PD-1) approved for r/r cHL patients after at least second-line chemotherapy
Apr 2020	HKEX Listing (Stock Code: 9926)
Aug 2019	Established CTTQ-Akeso for the R&D and commercialization of penpulimab (AK105, PD-1)
Jun 2019	Obtained the IND approval for a trial of AK112 (PD-1/VEGF) in the US
Jun 2019	Formed Sino Biopharm (1177.HK) Collaboration to co-develop and co-commercialize penpulimab (AK105, PD-1)
Mar 2019	Obtained the IND approval for AK104 from the FDA to begin a Ph1b/2 trial in the US
May 2018	Initiated a Ph1 trial of ebronucimab (AK102, PCSK9) in China
Mar 2018	Obtained the IND approval for penpulimab (AK105, PD-1) with respect to cervical cancer and solid tumors from the FDA in the US
Jan 2018	Initiated a Ph1 trial for AK101 (IL-12/IL-23) in China
Dec 2017	Initiated a Ph1 trial for penpulimab (AK105, PD-1) in Australia
Oct 2017	Initiated a Ph1 trial for AK104 (with chemotherapy) for the treatment of solid tumors in Australia
Nov 2015	Out-licensed AK107 (CTLA-4) to Merck (code name in Merck is MK1308)
Apr 2012	Initiated the development of innovative ACE Platform and “TETRABODY” technology
Mar 2012	Company established in Zhongshan, China

Source: Company data, CMBIGM

Innovative BsAb pipelines with BIC/FIC potentials

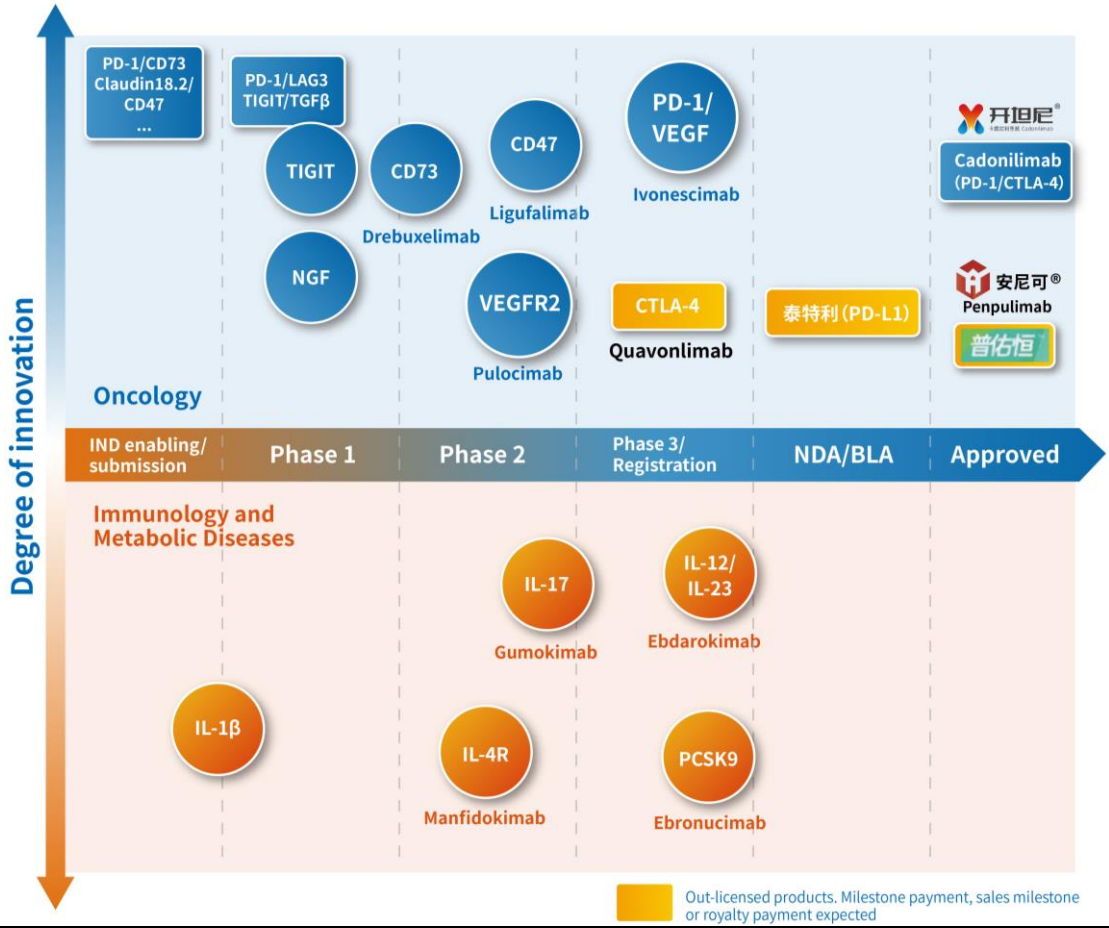
Since inception in 2012, Akeso has developed into a pioneer in innovative drugs, especially in bi-specific antibodies. The Company has established a comprehensive ACE Platform for antibody development, and a TETRABODY technology platform for bi-specific antibody drug development. The TETRABODY technology overcomes the CMC challenges of bsAb development.

Akeso currently has a diversified pipeline of over 30 innovative products, covering the areas of oncology, autoimmune and metabolic diseases. These pipeline products consist of six bi-specific antibodies, including the two first-in-class BsAb drugs, AK104 (PD-1/CTLA-4) and AK112 (PD-1/VEGF), and other BsAb drug candidates at earlier stage of development, i.e. AK129 (PD-1/LAG3), AK130 (TIGIT/TGF-β fusion protein), AK131 (PD-1/CD73), and AK132 (Claudin18.2/CD47). With 18 drug candidates having entered clinical trial stage, Akeso have launched more than 80 clinical trials in China, the US, Australia, New Zealand, etc., including more than a dozen pivotal/Ph3 trials.

Akeso has successfully promoted the commercialization of three innovative biological drugs in China, including cadonilimab (AK104, PD-1/CTLA-4), penpulimab (AK105, PD-1) and pucotenlimab (PD-1 mAb). In Jun 2022, cadonilimab (AK104) was approved by the NMPA and became the first tumor dual immune checkpoint inhibitor bi-specific antibody approved for marketing globally. Another internally developed oncology product, penpulimab (AK105) was granted marketing approval in China in Aug 2021, and has become the backbone of the Company's BsAb franchise. Pucotenlimab (PD-1 mAb, out-licensed to Lepu) was approved in Jul 2022 for marketing and Akeso is eligible to receive future milestone payments in addition to 7% of net sales.

Notably, in Dec 2022, Akeso out-licensed part of the ex-China rights of its self-developed breakthrough bispecific antibody, ivonescimab (AK112, PD-1/VEGF) to Summit Therapeutics (SMMT US) in a US$5bn deal, a landmark transaction in the Chinese biopharma sector in terms of out-licensing deal size.

Figure 2: Highlights of Akeso's pipelines



Source: Company data, CMBIGM

Figure 3: Overview of Akeso's pipelines

Oncology - Core Products				Current Status			
Product (Target)	Areas	Mono/Combo Therapy	Indication	Phase Ia	Phase Ib/II	Pivotal/Phase III	NDA Submitted/ Approved
Cadonilimab AK104 (PD-1/CTLA-4)	Cervical cancer	Mono	2L/3L cervical cancer				Approved on 2022.6.29
		+Chemo±Bevacizumab	1L cervical cancer			Enrollment completed	
	Gastric cancer	+XELOX	1L G/GEJ			Enrollment completed	
		+AK109 (VEGFR2) ±chemo	PD-1 r/r G/GEJ				
		+AK117 (CD47) ±chemo	1L G/GEJ, ESCC				
	Hepatocellular carcinoma	Mono	HCC Adjuvant therapy			Enrollment in process	
		+Lenvatinib	1L HCC				
		+Lenvatinib+TACE	HCC, intermediate stage				
		+AK109	PD-1 r/r HCC				
	Lung cancer	+Chiauranib	≥2L SCLC				
		+Docetaxel	PD-1 r/r NSCLC				
		+AK109±Docetaxel	PD-1 r/r NSCLC				
	Pancreatic cancer	+chemo	1L PDAC				
	Others	+AK117 (CD47)	Adv. solid tumors				
		+AK119 (CD73)	Adv. solid tumors				
		+AK127 (TIGIT)	Adv. solid tumors				
Ivonescimab AK112 (PD-1/VEGF)	Lung cancer	+Chemo	EGFR-TKI resistant NSCLC			Enrollment completed	
		Mono	1L PD-L1(+) NSCLC			Enrollment in process	
		+Chemo	1L sqNSCLC			Initiated	
		+Chemo	IO-r NSCLC				
		±Chemo	Neoadjuvant NSCLC				
		+AK119	EGFR-TKI resistant NSCLC				
	Gastrointestinal cancer	+AK117 +/- Chemo	Adv. solid tumors (GC, BTC, PDAC)				
	Breast cancer	+Chemo +/- AK117	1L TNBC				
	Head and neck cancer	+AK117 +/- Chemo	HNSCC				
	Hepatocellular carcinoma	Mono	Unresectable HCC				
	Colorectal cancer	+AK117 +/- Chemo	1L CRC				
	Ovarian cancer	Mono	Platinum resistant OC				
	Others	+AK112	Adv. solid tumors				
		Mono	Adv. solid tumors				
Ligufalimab AK117 (CD47)	Hematological tumor	+ azacitidine	1L MDS				
		+ azacitidine	1L AML				
	Solid tumor	+AK112 +/- Chemo	Adv. solid tumors (GC, BTC, PDAC)				
		+AK112 +/- Chemo	HNSCC				
		+AK112 +/- Chemo	1L CRC				
		+Chemo +/- AK112	1L TNBC				
		+AK104 +/- Chemo	1L GC/GEJ/ESCC				
		Mono	Adv solid tumors				
	Others	Mono	Adv solid tumors/lymphoma				

Global Large Indications NMPA approval Registrational Trials Breakthrough Therapy

Oncology - Other Products			Current Status			
Product (Target)	Mono/Combo Therapy	Indication	Phase Ia	Phase Ib/II	Pivotal/Phase III	NDA Submitted/ Approved
Penpulimab AK105 (PD-1)	Mono	3L R/R cHL				Approved on 2021.8
	+Chemo	1L sqNSCLC ▲				Approved on 2023.1
	Mono	3L NPC				Submitted in China
	+Anlotinib	1L HCC ▲				
	+Chemo	1L NPC 🌐				
	+Anlotinib	dMMR solid tumors				
	+Anlotinib	NSCLC, SCLC, HNC, thyroid cancer, mesothelioma and thymic cancer				
	+Anlotinib	ESCC, UC, GC/GEJ, cholangiocarcinoma, neuroendocrine tumor (NET)				
AK119 (CD73)	+AK112	Adv. solid tumors				
	+AK112	EGFR-TKI resistant EGFRm NSCLC				
	Mono	Adv. solid tumors				
	+AK104	Adv. solid tumors				
AK109 (VEGFR-2)	+AK104 ±chemo	PD-1 r/r G/GEJ				
	+AK104 ±Docetaxel	PD-1 r/r NSCLC ▲				
	+AK104	PD-1 r/r HCC				
	Mono	Adv. solid tumors				
AK127 (TIGIT)	+AK104	Adv. solid tumors 🌐				
	Mono	Adv. solid tumors				
AK115 (NGF)	Mono	Pain (including cancer pain)				
AK129 (PD-1/LAG-3)	Mono	Adv. solid tumors				
AK130 (TIGIT/TGF-ß)	Mono	Adv. solid tumors				

🌐 Global ▲ Large Indications ⚑ NMPA approval ⬚ Registrational Trials

Auto-immunity/Metabolism			Current Status			
Product (Target)	Mono/Combo Therapy	Indication	Phase Ia	Phase Ib/II	Pivotal/Phase III	NDA Submitted
Ebronucimab AK102 (PCSK9)	+ Statin/Ezetimibe	Primary hypercholesterolemia and mixed hyperlipidemia			Reached endpoint	
	+ Statin/Ezetimibe	HeFH			Reached endpoint	
Ebdarokimab AK101 (IL-12/IL-23)	Mono	Moderate-to-severe psoriasis			Reached endpoint	
	Mono	Moderate-to-severe ulcerative colitis				
AK111 (IL-17)	Mono	Moderate-to-severe psoriasis				
	Mono	Ankylosing spondylitis				
AK120 (IL-4R)	Mono	Moderate-to-severe atopic dermatitis				

🌐 Global ⬚ Registrational Trials

Source: Company data, CMBIGM. Notes: date as of 27 Apr 2023

A leading Chinese biopharma for oncology powered by strong R&D in innovative BsAb

Akeso's has 10+ assets in oncology assets in clinical trials including the core products cadonilimab (AK104, PD-1/CTLA-4), ivonescimab (AK112, PD-1/VEGF), and ligufalimub (AK117, CD47), which cover various indications in hematological and solid tumors. Some of these commercialized drugs and drug candidates have the potential to be the first-in-class or best-in-class therapies, as well as backbone drugs of combination therapies.

AK104 (PD-1/CTLA-4) has the best-in-class potential for first-line treatment of various large indications, including cervical, liver, stomach, lung, and other cancers. AK104 was initially approved in China for the treatment of 2/3L recurrent/metastatic cervical cancer (R/M CC) in Jun 2022, becoming the globally first approved dual checkpoint inhibitor BsAb and filling the gap of immunotherapy treatment for R/M CC. As promising early clinical data were already released with the efficacy profiles being enhanced as follow-up continues, AK104 has demonstrated its best-in-class potential in front-line treatment for large indications, including 1L CC, adjuvant HCC, 1L GC, etc. With multiple registrational studies of AK104 ongoing for these large indications, we expect AK104 to become a blockbuster medicine in the future. In terms of

commercialization, with a strong salesforce of over 650 employees (as of end-2022) keeping achieving outperformed sales records, the sales of AK104 has reached RMB546mn in 2H22, the first 6 months since launch. We are confident towards the Company's guidance to realize RMB1.2~1.3bn revenue from AK104 in 2023E. In addition, based on the smooth progresses of the clinical development of AK104 in large indications, we anticipate AK104 could achieve a blockbuster out-licensing deal of its ex-China rights, which would be one of the Company's major catalysts, in our view.

AK112 (PD-1/VEGF) is likely to become the first-in-class BsAb to uncover the enormous market of lung cancer across all spectrum treatment settings. In China, powered by BTD designations, AK112 monotherapy is under a head-to-head Ph3 study vs pembrolizumab for the treatment of PD-L1+ NSCLC. AK112 plus chemo is also under a Ph3 study for patients with EGFR-mutated NSCLC who failed in prior EGFR-TKI therapy, for which the current treatment options are very limited and AK112 has a BTD designation for this indication in China. In addition, in order to beat the current 1L NSCLC SoC treatment, AK112+chemo recently entered a head-to-head study vs tislelizumab+chemo for 1L sq-NSCLC. Moreover, as many NSCLC patients do not respond to the current standard PD-(L)1+chemo treatment, there is a huge unmet medical need for I/O-resistant NSCLC patents. With promising Ph2 early efficacy signals for I/O-resistant NSCLC patients, AK112+chemo has obtained BTD in PD-(L)1 resistant lung cancer treatment area in China, which is the only BTD in this treatment setting. The all-spectrum coverage of NSCLC, in addition to potential coverage of gastrointestinal cancer, breast cancer, HCC, CRC (in Ph1b/2 trials), support the blockbuster potential of AK112. To accelerate the global development and commercialization of AK112 in the oversea markets, Akeso has out-licensed the rights of AK112 in the US, Canada, Europe, and Japan to Summit Therapeutics in a blockbuster deal. Besides future sales royalties, the deal size was up to US$5.0bn, which was a landmark deal for Chinese biopharma companies. With US$500mn upfront payment been fully paid, we are confident about the global development of AK112 by leveraging the successful expertise of Summit's management team. Based on Akeso's studies in China, Summit has started a Ph3 MRCT trial of AK112+chemo for EGFR-mutated nsq-NSCLC who failed in prior EGFR-TKI therapy (FPI in May 2023) and expects to start another Ph3 MRCT trial of AK112+chemo in 1L sq-NSCLC (FPI expected in 2H23).

Near-term commercialization of products targeting autoimmune and metabolic diseases

Akeso's pipeline in autoimmune disease consists of valuable clinical assets including ebdarokimab (AK101, IL-12/IL-23), gumokimab (AK111, IL-17) and manfidokimab (AK120, IL-4R). Currently at the Ph3 development, AK101 (IL-12/IL-23) has the potential to become the first domestic IL-12/IL-23 mAb in China, and has delivered better efficacy signals over ustekinumab at early stage assessment in cross-trial comparisons. Johnson & Johnson's ustekinumab (Stelara), which has the same drug targets as AK101, has been widely used as one of the major treatments for psoriasis, psoriatic arthritis, Crohn's disease, and ulcerative colitis, and realized US$9.7bn revenue from global sales in FY22, highlighting the market potential of IL-12/IL-23 mAbs.

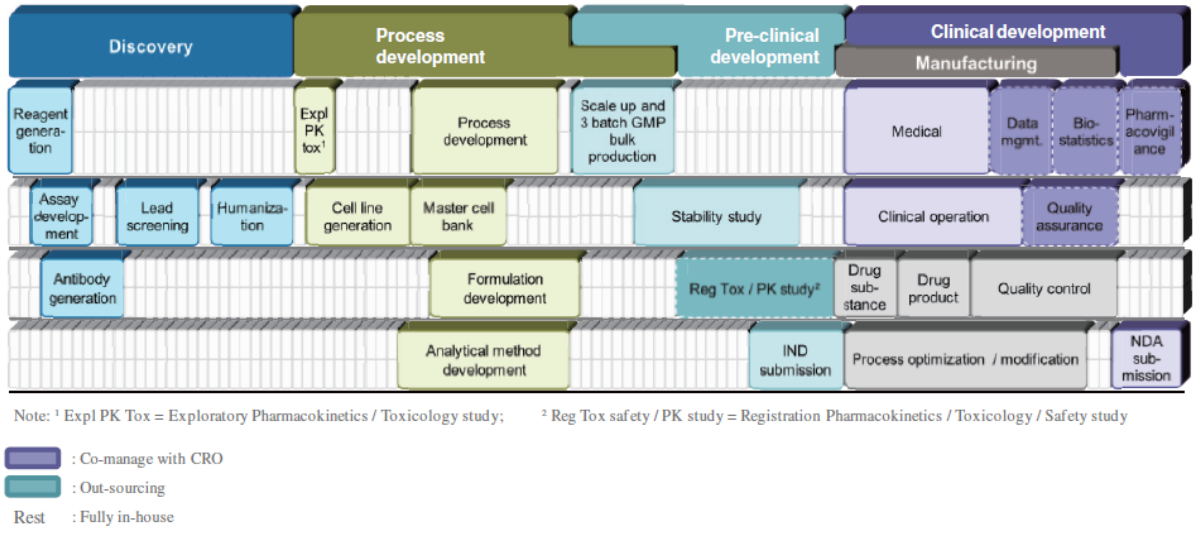
Akeso also has innovative drug candidates targeting metabolic diseases including ebronucimab (AK102, PCSK9), which is in collaboration under a joint venture agreement with Dawnrays Pharma (2348 HK). AK102 (PCSK9) is among the most advanced domestically developed PCSK9 mAbs in China, and is current under Ph3 studies for the treatment of primary hypercholesterolemia and mixed hyperlipidemia with positive results released. The Company has filed the BLA of AK102 in May 2023, to become the potential 3rd domestic PSCK9 antibody in China.

Proprietary R&D engine powered by comprehensive technology platform

Since establishment in 2012, Akeso has created a comprehensive ACE Platform for antibody development, and a TETRABODY technology platform for bi-specific antibody drug development, as the core of the Company's integrated R&D innovation system.

Akeso has developed an end-to-end platform, the Akeso Comprehensive Exploration platform (ACE Platform) for antibody development, encompassing comprehensive drug discovery and development functionalities, including (1) drug discovery, (2) process development, (3) pre-clinical development, (4) GMP-compliant manufacturing and (5) clinical development. Through the ACE Platform and the Tetrabody Technology, Akeso has consistently innovated and produced high quality drug candidates, with minimal dependence on external vendors. To date, Akeso has developed one of the richest and most diversified innovative antibody drug pipelines in China covering over 30 drug development programs, including 18 antibodies in clinical-stage development.

Figure 4: Functionalities of ACE Platform



Source: Company data, CMBIGM

Akeso has developed a proprietary Tetrabody technology platform incorporated in the ACE Platform. Tetrabody Technology helps overcome three recurrent CMC challenges in the development and manufacture of bi-specific antibodies, including (1) low expression levels due to a bi-specific antibody's high molecular weight, (2) process development hurdles as a result of bi-specific antibodies' structural heterogeneity, and (3) bad druggability due to a bi-specific antibody's lack of stability. Leveraging the Tetrabody technology, a couple of potential FIC/BIC BsAbs are being developed. The Company's PD-1-based BsAbs deliver therapeutic efficacy beyond blockade of PD-1 pathway alone. AK105, as the only IgG1 backbone PD-1 antibody (others are IgG4), demonstrates enhanced immunotherapeutic efficacy and reduced immune-related adverse reactions, and is the backbone of the Company's PD-1-based BsAbs franchise. With Tetrabody, Akeso is developing multiple PD-1 based bi-specific antibody drugs that cover diverse mechanisms of immune-suppression, including AK104 (PD-1/CTLA-4, approved), AK112 (PD-1/VEGF, Ph3), AK129 (PD-1/LAG3, Ph1), and AK131 (PD-1/CD73, IND filed). Additionally, based on discovery using the Tetrabody technology, AK130 (TIGIT/TGF-β fusion protein) has entered into Ph1 development and AK132 (Claudin18.2/CD47) is currently at the IND-enabling stage.

Figure 5: Tetrabody technology with example of AK104 (PD-1/CTLA-4)

Source: Company data, CMBIGM

Broad collaborations to pave the way of globalization

Akeso has been forging strategic partnerships globally to speed up the development and commercialization of its innovative products. The Company collaborates with leading MNC and domestic pharma companies since its inception, including Merck, Summit Therapeutics, Dawnrays Pharmaceutical, Sino Biopharm, etc.

In 2015 , Akeso out-licensed its self-developed CTLA-4 antibody (AK107) to Merck for a total consideration of up to US$200mn. In Dec 2022, Akeso out-licensed part of the ex-China rights of its breakthrough bispecific antibody, ivonescimab (AK112, PD-1/VEGF) to Summit Therapeutics through a landmark transaction with the deal size up to US$5bn. Those out-licensing agreements provide an expedited and winning pathway for the global development of the Company's innovative drugs. The Company has also forged important partnerships, including the partnership with Chia Tai Tianqing, the principal subsidiary of Sino Biopharm (1177 HK), for PD-1 mAb penpulimab (AK105), and the partnership with Dawnrays Pharma for AK102 (PCSK9) and AK109 (VEGFR-2). These out-licensing and partnerships are not only endorsements to Akeso's research and development, but also ways for the Company to accelerate the development and commercialization of the Company's innovative product portfolio both in China and globally.

With more potential FIC/BIC drug candidates entering into clinical development, including AK117 (CD47), AK129 (PD-1/LAG3), AK130 (TIGIT/TGFβ), AK131 (PD-1/CD73, to enter Ph1 in 2023), AK132 (Claudin18.2/CD47, to enter Ph1 in 2023), we expect the Company to continually integrate superior global resources and accelerate the global development of innovative drugs.

AK107 (CTLA-4)'s out-licensing to Merck

In Nov 2015, Akeso out-licensed the worldwide rights of its fully internally discovered CTLA-4 mAb AK107 to Merck in a total consideration of US$200mn, including upfront and milestone payments. Merck maintains the global rights of AK107 and bears all the development, manufacturing and commercialization costs. Akeso does not maintain any global rights to develop and commercialize AK107 and does not expect to receive any royalty, while it has the rights to develop bi-specific drugs with AK107. This ground-breaking collaboration was the first in-licensing transaction undertaken by Merck with a Chinese biopharma company in its core business sector. In 2017, Merck initiated a Ph1 trial of AK107 + pembrolizumab for the treatment of 1L NSCLC and 2L SCLC (NCT03179436). As of end-2019, Akeso

had received total upfront/milestone payment of US$20mn from Merck, and additionally, in 2021, Akeso received another milestone payment of RMB128.6mn. Merck is currently assessing AK107 in a Ph3 trial for clear cell renal cell carcinoma (ccRCC, EudraCT2020-002216-52) and Ph2 trials for NSCLC (NCT03516981), MSI-H/dMMR CRC (EudraCT2020-005114-18), and HCC (EudraCT2020-004490-52).

AK112 (PD-1/VEGF)'s out-licensing to Summit Therapeutics

In Dec 2022, Akeso granted an exclusive license to Summit Therapeutics to develop and commercialize AK112 in the US, Canada, Europe and Japan (the Summit territories) through a landmark out-licensing deal. Akeso retains the rights of AK112 except the Summit territories. In addition, Akeso will co-brand the product in the Summit territory. Akeso has received the US$500mn upfront payment, and will receive milestone payments of up to US$4.5bn. The Company will also receive low double-digit royalties on net product sales of AK112 in the Summit territories.

We view the cooperation itself a great step for Akeso in AK112's roadmap. The up to US$5.0bn deal size of the transaction is not only a landmark record for Chinese biopharma, but also a major step to realize the enormous global potential of AK112 for the treatment of lung cancer across all spectrum treatment settings. Akeso took an untraditional strategy to out-license its key asset AK112 - instead of cooperating with MNC. The Company values the experience of Bob Duggan (Summit CEO) and his team, who Akeso believes will focus on AK112 as Summit's most important pipeline product and can more smoothly accelerate the global development of AK112. Summit has started a Ph3 MRCT trial of AK112+chemo for EGFR-mutated nsq-NSCLC who failed in prior EGFR-TKI therapy (FPI in May 2023) and expects to start another Ph3 MRCT trial of AK112+chemo in 1L sq-NSCLC (FPI expected in 2H23). Mr. Duggan is a successful business administrator who brought over a dozen indications to market for the first-in-class blockbuster drug ibrutinib while serving as the CEO of Pharmacyclics. Mr. Duggan led both the multimillion-dollar collaboration and license deal for ibrutinib with Johnson & Johnson in 2011, and the subsequent sale of Pharmacyclics to AbbVie in 2015. Most of the management members of Summit previously had major roles at Pharmacyclics, whose experience we think will be a value add towards AK112's global development.

Joint venture with Sino Biopharm for AK105 (PD-1)

In Jun 2019, Akeso entered into a joint venture (JV) agreement with Chia Tai Tianqing (CTTQ), the principal subsidiary of Sino Biopharm for the development and commercialization of PD-1 antibody penpulimab (AK105). Leveraging the solid commercial capabilities of Sino Biopharm that has one of China's largest pharmaceutical sales forces, the sales of AK105 could witness a strong growth momentum. In 2022, AK105 recorded RMB558mn revenue, representing an unignorable market share in China's competitive PD-1 market. Under the JV agreement, Akeso agreed to provide all rights, title and interest in AK105 in exchange for 50% interest in the JV. CTTQ agreed to invest, and has fully paid approximately RMB344.7mn in cash in exchange for 50% interest in the JV. CTTQ obtained the exclusive sales rights for AK105 in China, selling AK105 on behalf of the JV, while the JV maintains the global rights to develop and commercialize AK105. CTTQ does not maintain any rights in AK105 outside China. The JV will bear all R&D and manufacturing costs related to AK105. The two parties are entitled to distributable profits of the JV in proportion to their respective paid-in capital contribution.

Joint venture with Dawnrays Pharma for AK102 (PCSK9) and AK109 (VEGFR-2)

In Dec 2016, Akeso entered into a JV agreement with Dawnrays Pharma to develop two drug candidates, ebronucimab (AK102, PCSK9) and AK109 (VEGFR-2). Akeso agreed to provide all rights, title and interest in AK102 and AK109 worldwide in exchange for 65% interest in the JV (AD Pharma/康融东方), and Dawnrays Pharma agreed to invest RMB150.0mn cash in exchange for 35% interest in the JV. Akeso takes the lead in the R&D of AK102 and AK109 through this partnership. The JV bears all R&D costs and owns the IP rights. The JV maintains the global rights to develop and commercialize AK102 or AK109

and it will generate income from sales upon the commercialization of such drug candidates. The two parties are entitled to distributable profits of the JV in proportion to the number of shares they hold.

Abundant manufacturing capacity and rich talent pool to support business growth

The Company has established an efficient GMP-compliant manufacturing system to meet its increasing product demand from internal research and commercialization. The Company has also developed its internal commercialization team to a relative large scale with an advanced operation mode.

Sufficient and expanding manufacturing capacity

As of end-2022, Akeso has a total production capacity of 31,500L in operation. Akeso has a steady capacity expansion plan in Zhongshan and Guangzhou with a planned total capacity of more than 160,000L to meet the future clinical and commercialization needs.

The GMP-compliant manufacturing facilities are designed and validated according to the FDA, EMA, and NMPA regulations. The FDA/NMPA-compliant GMP manufacturing facilities include (1) Zhongshan Torch Development District manufacturing site: with a capacity of 3,500L in operation; (2) Guangzhou commercialization and manufacturing site: the production capacity in operation is 28,000L, with additional 32,000L capacity under construction. Within the 28,000L capacity currently in operation, 20,000L was the first phase commenced in Mar 2021 mainly used for large-scale production of AK104. AD Pharma, a joint venture of the Company and Dawnrays Pharma, commenced operation with a new production capacity of 8,000L in May 2022, for the manufacturing of AK109 and AK102; (3) Zhongshan Cuiheng manufacturing site: the phase I and phase II projects under construction will provide up to 60,000L production capacity. Phase III is in planning, which will provide a production capacity of up to 40,000L once completed.

Figure 6: Manufacturing capacity of Akeso (as of Apr 2023)

Source: Company data, CMBIGM

Strong talent pool to back up R&D and commercialization

As of end-2022, the Company had a total of 2,300+ employees. 275 employees were in the pre-clinical R&D team, and 532 were in the clinical development team, with the research team accounting for 34% of the total employee. As of end-2022, the Company had an internal commercial and marketing team of 652 employees (28% of the Company's total employees), responsible for the commercial promotion of AK104. We expect Akeso to further expand its salesforce in 2023.

Cadonilimab (AK104, PD-1/CTLA-4), globally first approved dual checkpoint inhibitor BsAb

First-in-class dual immene checkpoint inhibitor targeting the largest indications

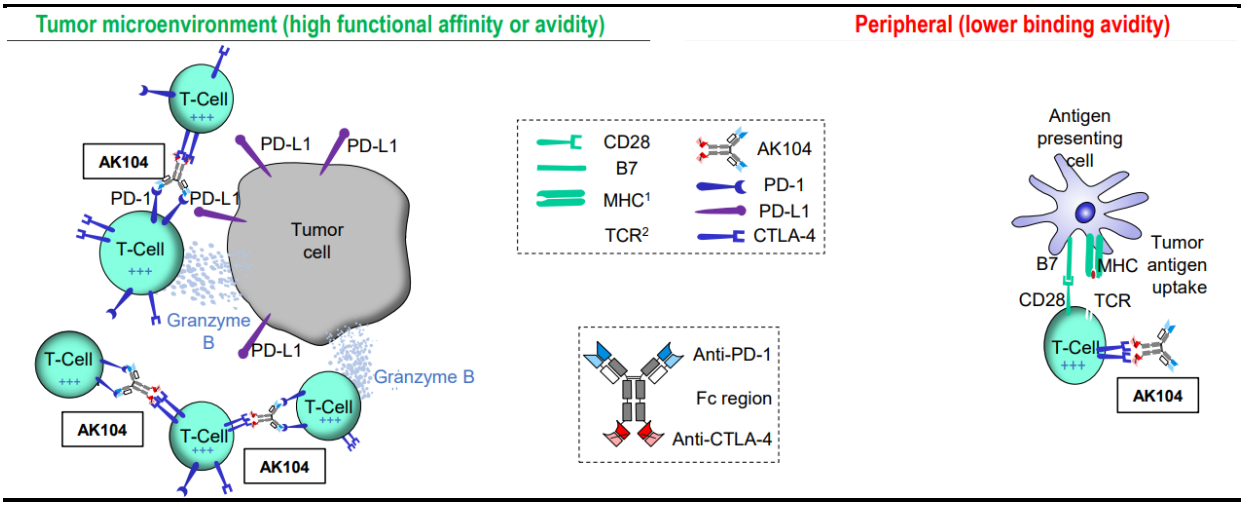
Cadonilimab (AK104/卡度尼利/开坦尼®), a PD-1/CTLA-4 bispecific antibody, is globally the first dual immune checkpoint inhibitor bi-specific antibody approved for marketing and China's first immunotherapy bi-specific antibody approved for marketing. In Jun 2022, AK104 was approved by the China NMPA for the treatment of 2/3L R/M CC patients who progressed on or after platinum-based chemotherapy. As a first-in-class bi-specific antibody, AK104 fully exploits the synergistic anti-tumor effect of two immune checkpoint inhibitors, PD-1 and CTLA-4, with significantly fewer side effects than the combined use of monoclonal antibodies with two targets.

AK104 targets the largest indications, and has multiple clinical trials in cervical, liver, stomach, lung, and other cancers ongoing with promising efficacy and manageable safety profile released. We see the potential of AK104 as a best-in-class/first-in-class dual immune checkpoint inhibitor BsAb.

Mechanism of action of AK104

Tumor infiltrating lymphocytes (TILs) co-express PD-1 and CTLA-4 at much higher levels compared to normal tissues and peripheral blood cells, thus anti-PD1/CTLA4 bi-specific antibody with a preferential tumor tissue enrichment over normal tissue would contribute to enhanced efficacy and safety.

Figure 7: MoA of AK104



Source: Company data, CMBIGM. Note: refer to link for more info on the MoA of AK104.

Current available anti-PD1 and anti-CTLA4 antibodies used in combination therapy are of residual bindings to FcγRs, which mediates antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), leading to compromise on efficacy and safety. The PD-1/CTLA-4 dual blockade has consistently demonstrated higher response rate compared to PD-1 monotherapy but higher toxicity. Moreover, activated macrophage in tumor microenvironment plays a key role in mediating immune suppression by secreting proinflammatory cytokines, such as IL-6.

Cadonilimab (AK104), a PD-1/CTLA-4 bispecific antibody, is an IgG1 scaffold Fc-engineered antibody, which binds to the antigens PD-1 and CTLA-4 simultaneously. AK104 cross-links cells expressing CTLA-4 with those expressing PD-1, and exhibited no binding to FcγRs or C1q, eliciting no apparent ADCC, ADCP or CDC. AK104 induced no remarkable IL-6 or IL-8 release by human macrophage compared with

combination of nivolumab (PD-1 mAb) and ipilimumab (CTLA-4 mAb). AK104 could preferentially binds to tumor-infiltrating lymphocytes (TILs) that co-express PD-1 and CTLA-4 with higher avidity in the tumor micro-environment than peripheral sites. Therefore, AK104 is designed to retain the efficacy benefit derived from the combination of anti-PD-1 and anti-CTLA-4, while conferring superior safety compared to the co-administration of these individual agents.

AK104 has broad application for large indications

Currently, multiple clinical trials of AK104 has been conducted in major cancer indications including cervical, liver, stomach, lung, and others, and has demonstrated promising early efficacy and safety profile of AK104 for the treatment of various largest cancer indications. Among them, multiple registrational studies are ongoing/completed, including:

1) 2/3L CC: A Ph2 trial (NCT03852251, cohort A) of AK104 in adult subjects with previously treated recurrent or metastatic cervical carcinoma (R/M CC). Based on this trial, AK104 received marketing approval from the China NMPA in Jun 2022, for the treatment of 2/3L R/M CC patients who progressed on or after platinum-based chemotherapy. In the US, AK-104 obtained orphan drug designation in Feb 2021 for treating cervical cancer (except very early stage IA1, link).
2) 1L CC: A Ph3 trial (NCT04982237) of AK104 combined with platinum-based chemotherapy +/- bevacizumab for the first-line treatment of R/M CC is ongoing. The trial has completed patient enrollment in Jun 2022.
3) 1L G/GEJC: A Ph3 trial (NCT05008783) of AK104 plus XELOX in 1L gastric or gastroesophageal junction (G/GEJ) cancer is also ongoing. The enrollment was completed in Mar 2023.
4) Early-stage adjuvant therapy for HCC: A Ph3 trial (NCT05489289) of AK104 as adjuvant therapy for early-stage HCC patients with high risk of recurrence after curative resection is ongoing. The IND of the trial was approved by CDE in Jun 2022.

Figure 8: Development pipeline of AK-104 (as of Apr 2023)

Oncology - Core Products				Current Status			
Product (Target)	Areas	Mono/Combo Therapy	Indication	Phase Ia	Phase Ib/II	Pivotal/Phase III	NDA Submitted/ Approved
Cadonilimab AK104 (PD-1/CTLA-4)	Cervical cancer	Mono	2L/3L cervical cancer				Approved on 2022.6.29
		+Chemo±Bevacizumab	1L cervical cancer			Enrollment completed	
	Gastric cancer	+XELOX	1L G/GEJ			Enrollment completed	
		+AK109 (VEGFR2) ±chemo	PD-1 r/r G/GEJ				
		+AK117 (CD47) ±chemo	1L G/GEJ, ESCC				
	Hepatocellular carcinoma	Mono	HCC Adjuvant therapy			Enrollment in process	
		+Lenvatinib	1L HCC				
		+Lenvatinib+TACE	HCC, intermediate stage				
		+AK109	PD-1 r/r HCC				
	Lung cancer	+Chiauranib	≥2L SCLC				
		+Docetaxel	PD-1 r/r NSCLC				
		+AK109±Docetaxel	PD-1 r/r NSCLC				
	Pancreatic cancer	+chemo	1L PDAC				
	Others	+AK117 (CD47)	Adv. solid tumors				
		+AK119 (CD73)	Adv. solid tumors				
		+AK127 (TIGIT)	Adv. solid tumors				

= Global Trial ▲ = Large Indications NMPA approval Registrational Trials

Source: CSCO, CMBIGM

2L/3L R/M CC: approved as the first dual checkpoint inhibitor BsAb globally

Therapeutic landscape of 2L/3L R/M CC

While the majority of early-stage cervical cancer patients are eligible for curative surgery, locally advanced cervical cancer patients will often recur. The prognosis is dramatically poor for recurrent and/or metastatic (R/M) cervical cancers, with a 5-year survival of less than 5% (link). China has the second largest population of cervical cancer patients in the world, with 110,000 new cases in 2020. There is no standard treatment for R/M CC patients who has progressed on or after platinum-based chemotherapy, and chemo monotherapy is a common clinical treatment option with limited efficacy and obvious toxicity.

Immunotherapy has emerged as a therapeutic possibility for cervical cancer that has recurred or spread to distant parts of the body. These treatments are now used in some cases to boost the immune system's ability to attack cancer cells. Immune checkpoint inhibitors (ICI) have been approved for the treatment of advanced CC patients progressing following chemotherapy. Pembrolizumab was approved in the US in 2018 for the treatment PD-L1+ advanced CC patients progressing following first-line chemotherapy, however with limited efficacy compared to AK104 in cross trial comparisons. Pembrolizumab has been recommended by NCCN and CSCO Guidelines (Class III) for the treatment of R/M CC patients with PD-L1 expression.

In Jun 2022, AK104 was approved by China NMPA for the treatment of R/M CC patients, regardless of PD-L1 expression, who progressed on or after platinum-based chemotherapy. There are limited treatment options for R/R CC in China and across the globe, except for widely used chemotherapy while with limited efficacy. The approval of AK104 addresses a huge unmet medical needs for advanced cervical cancer in China. AK104 has been included in the CSCO Guidelines as an immunotherapy for 2L R/R CC treatment (Class II recommendation, link).

Figure 9: CSCO Guideline for 2L R/R CC treatment in China

系统治疗	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
二线		白蛋白结合型紫杉醇[d] 多西他赛[d] 吉西他滨[d] 培美曲塞[d] 拓扑替康[d] 卡度尼利单抗[e, n]（含铂化疗治疗失败的复发或转移性宫颈癌） 斯鲁利单抗[f, n]（MSI-H 实体瘤） 替雷利珠单抗[g, n]（MSI-H 或 dMMR 实体瘤成人） 恩沃利单抗[h, n]（MSI-H 或 dMMR 实体瘤） 参加临床研究[i]	异环磷酰胺[d] 丝裂霉素[d] 氟尿嘧啶[d] 长春瑞滨[d] 伊立替康[d] 赛帕立单抗[j, n] 帕博利珠单抗（适用于 PD-L1 阳性或 MSI-H 或 dMMR 的肿瘤）[k, n][4, 5, 8, 18, 20] 纳武利尤单抗（适用于 PD-L1 阳性的肿瘤
其他		[20]	帕博利珠单抗（适用于 TMB-H 的肿瘤[l, n][20] Larotrectinib 或 entrectinib（适用于 *NTRK* 基因融合的肿瘤）[l, n]

Source: CSCO, CMBIGM

Clinical data of AK104 in 2L/3L R/R CC

The China approval of AK104 is based on the positive results from a pivotal Ph2 study (NCT03852251) of AK104 in R/M CC patients who progressed on or after platinum-based chemotherapy. The results were presented at the SGO Annual Meeting in Mar 2022 (link). There was no standard of care in the 2L+ setting for women with R/M cervical cancer. The study assessed AK104 as a 2L/3L treatment in immune checkpoint inhibitor (ICI) naïve patients with R/M CC, regardless of PD-L1 status.

The multi-center, open-label, single-arm, Ph2 study enrolled patients with advanced CC who had progressed on or after two or fewer previous doublet chemotherapy with or without bevacizumab. Patients received AK104 6mg/kg Q2W. The primary endpoint was ORR assessed by independent review committee (IRC), and the key secondary endpoint was the DoR.

The study demonstrated that AK104 monotherapy is efficacious and safe as 2L+ treatment of R/M cervical cancer in ICI naïve patients, regardless of PD-L1 status and whether or not with prior bevacizumab treatment. As of 5 Aug 2021, 111 pts had received at least one dose of AK104. The median age was 52.0 years. 36% of patients had received two prior lines of systemic therapy, 92.8% had squamous cell disease, 56.8% had an ECOG score of 1, 25.0% had received bevacizumab.

After median follow-up of 9.63 months, the IRC-assessed confirmed ORR in 100 patients evaluable for efficacy was 33.0%, with 12 (12.0%) CR and 21 (21.0%) PR. Median DoR was not reached; 6- and 12-mo DoR rates were 77.6% and 52.9%, respectively. Median PFS was 3.75 months; 6- and 12- mo PFS rates were 41.4% and 21.2%, respectively. Median OS was 17.51 months; 6- and 12- mo OS rates were 80.1% and 64.6%, respectively. Among 64 pts with PD-L1 positive tumors (CPS⩾1), the ORR was 43.8%, the median PFS was 6.34 months, and the median OS was not reached (95% CI 17.51 mo-NE). TRAEs occurred in 96.4% of 111 patients. Grade 3 to 4 TRAEs occurred in 28.8% of 111 patients; the most common were anemia (7.2%) and decreased appetite (2.7%).

Figure 10: Cross-trial comparison of drugs/drug candidates for 2L/3L R/M CC

	AK104		Pembrolizumab		HLX10	Tislelizumab	Zimberelimab	Tisotumab vedotin
Target	CTLA4/PD1		PD1		PD1	PD1	PD-1	tissue factor ADC
Company	Akeso		Merck		Henlius	BeiGene	Gloria Pharma	Seagen/Zai Lab
Trial	NCT03852251		KEYNOTE-158		NCT04150575		NCT03972722	innovaTV 204
Trial stage	Ph2		Ph2		Ph2	Ph2	Ph2	Ph2
Primary endpoint	ORR		ORR		Safety, ORR	ORR	ORR	ORR
Regimen	AK104 mono (all pts)	AK104 mono (PD-L1 positive, CPS>=1)	pembroli zumab mono (all pts)	pembroli zumab mono (PD-L1 positive, CPS>=1)	HLX10 + chemo (all PD-L1 positive pts)	tislelizumab + anlotinib	zimberelimab mono	tisotumab vedotin mono
Follow up period (mo)	9.63		36.9		14.6	as of Mar 2022	11.5	10.0
Patient number	111	64	98	82	21 (mean CPS of 39)	17	90	102
ORR	33.0%	43.8%	14.3%	17.1%	57.1%	35.30%	27.8%	24%
CR	*12.0%*		*5.1%*	*6.1%*	*14.3%*		*4.8%*	*7%*
PR	*21.0%*		*9.2%*	*11.0%*	*42.9%*		*23.3%*	*17%*
mPFS (mo)	3.75	6.34	2.1	2.1	5.7	-	3.7	-
mOS (mo)	17.51	not reached (17.51 - NE)	9.3	11	15.5	-	-	-
Grade ≥3 TRAEs	28.8%		12.2%		33.3%	-	22.9%	28%
Approval status in US and China for 2/3L R/M CC	Approved in China		Approved in the US, not yet in China		Not yet approved, included in China CSCO Guideline	Not yet approved, included in China CSCO Guideline	Approved in China in Jul 2023	Approved in the US, not yet in China
Data source	Link		Link1, Link2		Link	Link	Link	Link

Source: Pubmed, CMBIGM

AK104 demonstrated strong results for the treatment of 2/3L R/M CC patients. The efficacy of AK104 in the 2/3L treatment of R/M CC, especially PD-L1+ R/M CC, was much better than the results of pembrolizumab in cross-trial comparisons. Pembrolizumab has been approved in the US for the treatment PD-L1+ advanced CC patients progressing following chemotherapy, based on the KEYNOTE-158 trial. In the cervical cancer cohort of this KEYNOTE-158 trial (link), 98 R/M CC patients who had progressed

after at least one line of standard therapy were enrolled. 82 (83.7%) of the patients had PD-L1 positive tumors (CPS>=1). The ORR was 14.3%, all the 14 responses achieved in patients with PD-L1-positive tumors. In the PD-L1+ population, the ORR was 17.1% (follow up 36.9 months) and the median PFS and OS were 2.1 months and 11 months (follow up 10.2 months), respectively. It seems HLX10 (PD-1 from Henlius), in combo with chemotherapy, achieved better efficacy results for the treatment of R/M CC with an ORR of 57.1%. However, considering the probably high proportion of PD-L1-positive patients (mean CPS of 39) in the study, we think AK104 delivered satisfying efficacy as a monotherapy.

1L R/M CC: promising early efficacy data released for CC front-line treatment

Therapeutics landscape of 1L R/M CC

Platinum-based chemotherapy+/-bevacizumab has been widely used as standard first-line treatment for R/M CC, and is recommended by CSCO and NCCN Guidelines. The Ph3 GOG-240 study (link) showed the addition of bevacizumab to chemotherapy was associated with increased OS (17.0 vs 13.3 months; HR 0.71, P=0.004), PFS (8.2 vs 5.9 months; HR 0.67) and higher ORR (48% vs 36%, P=0.008).

Pembrolizumab plus chemotherapy+/-bevacizumab was approved in Oct 2021 by FDA to treat first-line R/M CC PD-L1 positive (CPS ≥1) patients, and has been included in the NCCN Guidelines. The approval was based on the results of Ph3 trial Keynote-826 (link1, link2). In the study, 617 patients were randomized to pembrolizumab + chemo ± bevacizumab (n=308) or chemo ± bevacizumab (n=309) with +/-bevacizumab per investigator discretion. With a median follow-up of 22 months, the ORR was of 65.9% vs 50.8%, mPFS was 10.4 vs 8.2 months (HR 0.65, 95%CI 0.53-0.79), and mOS was 24.4 vs 16.5 months (HR 0.67, 95%CI 0.54-0.84) in pembrolizumab+/-bevacizumab and chemo+/-bevacizumab group, respectively, regardless of PD-L1 expressions. Pembrolizumab plus chemotherapy+/-bevacizumab is a NCCN recommended preferred regimen and in China is also included as a Level II recommendation by CSCO Guideline for 1L treatment of R/M CC.

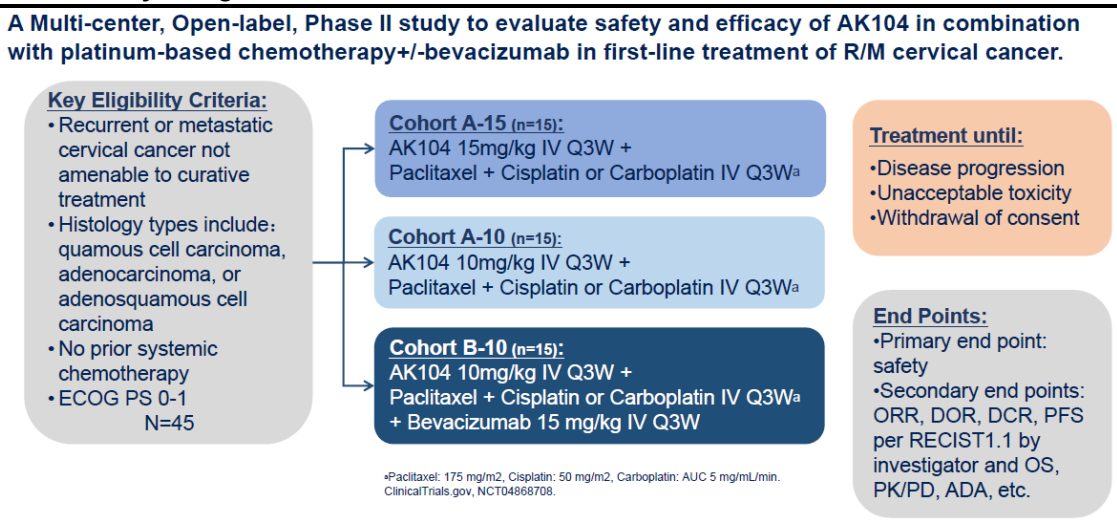
Figure 11: CSCO Guideline for 1L R/R CC treatment in China

系统治疗	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
一线	顺铂+紫杉醇+贝伐珠单抗 卡铂+紫杉醇+贝伐珠单抗 顺铂+紫杉醇 卡铂+紫杉醇（先前用过顺铂）	帕博利珠单抗＋顺铂+紫杉醇±贝伐珠单抗（适用于PD-L1阳性肿瘤） 帕博利珠单抗+卡铂+紫杉醇±贝伐珠单抗（适用于PD-L1阳性肿瘤） 拓扑替康+紫杉醇+贝伐珠单抗 拓扑替康+紫杉醇 顺铂+拓扑替康	顺铂 卡铂 紫杉醇

Source: CSCO, CMBIGM

AK104 monotherapy has shown promising efficacy and tolerable toxicity in pre-treated R/M CC. For front-line treatment, the Ph2 study (NCT04868708) of AK104 in combination with SOC (platinum-based chemotherapy +/- bevacizumab) in first-line treatment of R/M CC was presented at the 2022 ASCO annual meeting (link). The multicenter, open-label, Ph2 study enrolled R/M CC patients without previous systemic therapy. Patients were assigned to 3 cohorts (A-15/A-10: AK104 15/10mg/kg + chemo; B-10: AK104 10mg/kg + chemo + bevacizumab).

Figure 12: Study design of Ph2 trial of AK104 in 1L R/M CC



Source: Company data, CMBIGM

As of Apr 2022, 45 patients were enrolled, and the efficacy in patients with at least one tumor assessment result were assessed (link). ORR were 66.7% for A-15, 68.8% for A-10, 92.3% for B-10, respectively. The ORR for the A-10 and B-10 combined group was 79.3% (23/29) regardless of PD-1 expression (82.4% for patients with CPS≥1, and 75.0% for patients with CPS<1). The response to treatment group was favorable regardless of PD-L1 expression. PFS or OS were not mature.

Figure 13: Efficacy results of Ph2 trial AK104-210 regardless of PD-L1 expression

	A-15 (N=15)	A-10 (N=16)	B-10 (N=13)[a]	A-10+B-10 (N=29)
Objective Response Rate, n(%)	**10 (66.7)**	**11 (68.8)**	**12 (92.3)**	**23 (79.3)**
Disease Control Rate, n (%)	**15 (100.0)**	**15 (93.8)**	**13 (100.0)**	**28 (96.6)**
Best Overall Response, n(%)				
Complete Response	**2 (13.3)**	**0 (0.0)**	**1 (7.7)**	**1 (3.4)**
Partial Response	**8 (53.3)**	**11 (68.8)**	**11 (84.6)**	**22 (75.9)**
Stable Disease	5 (33.3)	4 (25.0)	1 (7.7)	5 (17.2)
Progressive Disease	0	1 (6.3)	0	1 (3.4)
Median DoR, [95%CI], months	NR (2.99, NE)	5.75 (2.86, NE)	NR (3.02, NE)	NR (4.27, NE)
Median TTR, (range), months	1.51(1.31,2.96)	1.35(1.22,4.24)	1.48(1.31,3.02)	1.48(1.22,4.24)

Source: Company data, CMBIGM. Notes: one patient died in the cohort B-10 before first tumor assessment and was judged as bevacizumab related.

Figure 14: Efficacy results of Ph2 trial AK104-210 by PD-L1 expression

	A-15		A-10		B-10		A-10+B-10	
	CPS≥1 (N=10)	CPS<1 (N=5)	CPS≥1 (N=8)	CPS<1 (N=8)	CPS≥1 (N=9)	CPS<1 (N=4)	CPS≥1 (N=17)	CPS<1 (N=12)
Objective Response Rate, n(%)	**7 (70.0)**	**3 (60.0)**	**6 (75.0)**	**5 (62.5)**	**8 (88.9)**	**4 (100.0)**	**14 (82.4)**	**9 (75.0)**
Disease Control Rate, n (%)	**10 (100.0)**	**5 (100.0)**	**8 (100.0)**	**7 (87.5)**	**9 (100.0)**	**4 (100.0)**	**17 (100.0)**	**11 (91.7)**
Best Overall Response, n(%)								
Complete Response	2 (20.0)	0	0 (0.0)	0	1 (11.1)	0	1 (5.9)	0
Partial Response	5 (50.0)	3 (60.0)	6 (75.0)	5 (62.5)	7 (77.8)	4 (100.0)	13 (76.5)	9 (75.0)
Stable Disease	3 (30.0)	2 (40.0)	2 (25.0)	2 (25.0)	1 (11.1)	0	3 (17.6)	2 (16.7)
Progressive Disease	0	0	0	1 (12.5)	0	0	0	1 (8.3)

Source: Company data, CMBIGM. Notes: one patient died in the cohort B-10 before first tumor assessment and was judged as bevacizumab related.

The safety profile of AK104 is generally better than that shown in the disclosed data of clinical studies on other tumor immunotherapies combined with chemotherapy +/- bevacizumab. In AK104's Ph2 trial above, Grade ≥3 TRAEs occurred in 60.0% pts. The most common Grade ≥3 TRAEs were anemia (20.0%), white blood cell count decreased (11.1%), neutrophil count decreased (13.3%), and platelet count decreased (11.1%). TRSAE occurred in 44.4% pts. Grade ≥3 irAE occurred in 15.6% pts. One death due to hemorrhagic shock occurred in cohort B-10 and was judged as bevacizumab-related.

Figure 15: Cross-trial comparison of approved drugs for 1L R/M CC

	AK104			Pembrolizumab		Bevacizumab	Tisotumab vedotin
Target	CTLA4/PD1			PD-1		VEGF-A	anti-tissue factor ADC
Trial	Ph2 AK104-210			Ph3 Keynote-826		Ph3 GOG-240	Ph1/2, NCT03786081
Primary endpoint	Safety			PFS, OS		OS	ORR
Regimen	AK104 + chemo +/- bev* (all pts)	AK104 + chemo +/- bev (CPS>=1)	AK104 + chemo +/- bev (CPS<1)	pembrolizumab + chemo +/- bev vs chemo +/- bev (all pts)	pembrolizumab + chemo +/- bev vs chemo +/- bev (CPS>=1)	bev + chemo vs chemo	tisotumab vedotin + pembrolizumab
Patient number	29	17	12	617 (307 vs 309)	548 (273 vs 275)	452 (227 vs 225)	33
ORR	**79.31%**	**82.35%**	75.00%	**65.9%** vs 50.8%	**68.1%** vs 50.2%	**48%** vs 36% P=0.008	41%
CR	3.45%	5.88%	0.00%	21.4% vs. 12.9%	22.7% vs. 13.1%	12.3% vs 6.2%	9%
PR	75.86%	76.47%	75.00%	44.5% vs 37.9%	45.4% vs 37.1%	35.7% vs 29.8%	31%
mPFS (mo)	not reached			10.4 vs 8.2 (HR 0.62, P<0.001)	10.4 vs 8.2 (HR 0.65, P<0.001)	8.2 vs 5.9 HR 0.67	5.3
mOS (mo)	not reached			24-month OS rate 53.0% vs 41.7% (HR 0.64, P<0.001) mOS 24.4 vs 16.3~16.5	24-month OS rate 50.4% vs 40.4% (HR 0.67, P<0.001) mOS not reached	17.0 vs 13.3 HR 0.71, P=0.004	not reached
Grade ≥3 TRAEs	60.0%			68.4% vs 64.1%		-	67% (TEAE)
Grade ≥3 irAEs	15.6%			11.4% vs 2.9%		-	-
TRAE related discontinuation	13.3%			37.5% vs 26.5%		25% vs 16%	-
Death	1 death (2.2%, bevacizumab related)			2 deaths (0.7%; related to pembrolizumab + SOC) vs 4 deaths (1.3%; related to SOC)		4 treatment-related death in each of the 2 group	-
Approval status in US and China	2/3L CC approved, 1L CC in Ph3			1L PD-L1 positive (CPS>=1) CC approved in the US, not in China yet		1L approved in China and the US	2L CC approved in the US, 1L in Ph2
Data source	Link			Link		Link	Link

Source: Pubmed, CMBIGM. Notes: *bev means bevacizumab. Efficacy data on AK104 refer to the combined cohort of A-10 (AK104 10mg/kg + chemo) and B-10 (AK104 10mg/kg + chemo + bev). Safety profile in the table above is based on the whole trial populations instead of the efficacy-evaluable patients.

In cross-trial comparisons, AK104 demonstrated better efficacy results and well-tolerated safety profile in the treatment of 1L CC patients, with an ORR of 79.31% vs 65.9% observed in pembrolizumab's study above, regardless of PD-L1 expression. Based on the promising results of the above-mentioned AK104 Ph2 study, a Ph3 trial is ongoing to evaluate the efficacy of AK104 plus standard therapy in first-line treatment for R/M CC (NCT04982237).

Cervical cancer is the 11th leading cancer in China in terms of number of new cases (~110,000 new cases in 2020 in China). However, the treatment options for cervical cancer are quite limited. Already approved for 2/3L CC treatment and with Ph3 trials ongoing for front-line treatment, we foresee the great potential of AK104 as a standard-of-care to cover across all treatment settings of the R/M CC patient population.

Front-line HCC: encouraging early PFS results observed with favorable safety profile

Hepatocellular carcinoma (HCC) is a leading cause of cancer death worldwide. The prognosis is especially poor for patients who have unresectable advanced HCC. In China, the first-line CSCO-recommended immunotherapy options mainly include sorafenib, lenvatinib, atezolizumab + bevacizumab, sintilimab + bevacizumab biosimilar, camrelizumab + rivoceranib, etc. Durvalumab + tremelimumab combination therapy, even if not yet approved in China, has been included in the CSCO Guidelines in China and is recommended for the treatment of 1L HCC.

The median OS in HCC patients with first-line sorafenib, which was the SoC for a decade after its approval in 2006, was 10 to 12 months in Ph3 studies. Lenvatinib was approved as a first-line treatment for advanced HCC based on its non-inferiority to sorafenib in REFLECT study, with a median OS of 13.6 months in the lenvatinib group vs 12.3 months in the sorafenib group. Notably, in the Imbrave150 trial, compared to sorafenib, atezolizumab + bevacizumab demonstrated a median OS of 19.2 months vs 13.4 months, and cut the risk of death by 34% (HR=0.66, p<0.001). Moreover, sintilimab + bevacizumab biosimilar IBI305 slashed the risk of death by 43% in the ORIENT-32 trial with the mOS not reached at the data cutoff (mOS not reached vs 10.4 months, HR=0.57). Camrelizumab + rivoceranib demonstrated much longer mOS of 22.1 months in its global registrational trial, as compared to 15.2 months in the sorafenib group (HR=0.62, 1-sided p<0.0001).

Figure 16: Cross-trial comparison of drugs/drug candidates for 1L HCC

	AK104	Atezolizumab	Sintilimab	Camrelizumab	Lenvatinib	Durvalumab	Pembrolizumab	Tislelizumab
Trial	NCT04444167	Imbrave150	ORIENT-32	NCT03764293	REFLECT	HIMALAYA	LEAP-002	RATIONALE 301
Phase	Ph2	Ph3	Ph3	Ph3	Ph3	Ph3	Ph3	Ph3
Regimen	AK104 + lenvatinib	atezolizumab + bevacizumab vs sorafenib	sintilimab + bevacizumab biosimilar vs sorafenib	camrelizumab + rivoceranib vs sorafenib	lenvatinib vs sorafenib	durvalumab + tremelimumab (CTLA-4) vs sorafenib	pembrolizumab + lenvatinib vs lenvatinib	tislelizumab vs sorafenib
Target	PD-1/CTLA-4, multi-kinase inhibitor	PD-L1, VEGFR	PD-1, VEGFR	PD-1, VEGFR2	multi-kinase inhibitor	PD-1, CTLA-4	PD-1, multi-kinase inhibitor	PD-1
Primary endpoint	ORR	OS, PFS	OS, PFS	OS, PFS	OS	OS	OS, PFS	OS (non-inferiority)
Patient number	30	501 (336 vs 165)	571 (380 vs 191)	543 (272 vs 271)	954 (478 vs 476)	782 (393 vs 389)	794 (395 vs 399)	674 (342 vs 332)
ORR	**44.4%**	29.8% vs 11.3%	20.5% vs 4.0%	25.4% vs 5.9%	24.1% vs 9.2%	20.1% vs 5.1%	26.1% vs 17.5%	14.3% vs 5.4%
CR	0	7.7% vs 0.6%	0 vs 0		1.3% vs 0.4%	3.1% vs 0		2.9% vs 0.3%
mPFS (mo)	**9.8** (as of 5 Dec 2022, 27 pts)	6.9 vs 4.3 HR=0.65	4.6 vs 2.8 HR=0.56	5.6 vs 3.7 HR=0.52	7.4 vs 3.7 HR=0.66	3.8 vs 4.1 (non-inferiority)	8.2 vs 8.1 HR=0.867 (non-inferiority)	2.1 vs 3.4, HR=1.11
mOS (mo)	not reached	19.2 vs 13.4, HR=0.66	not reached vs 10.4, HR=0.57	22.1 vs 15.2, HR=0.62	13.6 vs 12.3, HR=0.92, (non-inferiority)	16.4 vs 13.8, HR=0.78	21.2 vs 19.0 HR=0.84, (non-inferiority)	15.9 vs 14.1, HR=0.85, (non-inferiority)
Grade ≥3 TRAEs	**26.7%**	45% vs 47%	34% vs 36%	81% vs 52%	57% vs 49%	25.8% vs 36.9%	62.5% vs 57.5%	22.2% vs 53.4%
SAE		49% vs 33%	32% vs 19%					29.9% vs 28.1%
Approval status in US and China for 1L HCC	not approved yet	Approved in US and China	Approved in China	Approved in China; BLA filed in the US in May 2023	Approved in US and China	Approved in the US, not in China yet	missed primary endpoint	not approved yet
Data source	Link1, Link2	Link	Link	Link	Link	Link	Link	Link

Source: Pubmed, CMBIGM

Akeso is developing AK104 for the treatment of HCC in multiple trials with a target to preempt HCC market by covering earlier stage patients. Late-stage trials of AK104 for HCC include (1) a Ph3 registrational study (NCT05489289) of AK104 as adjuvant therapy in HCC with high risk of recurrence after curative resection, (2) a Ph2 study (NCT04444167) of AK104 plus lenvatinib as first-line treatment of unresectable

HCC, and (3) a Ph2 study (NCT05319431) of AK104 plus lenvatinib combined with on-demand TACE in participants with unresectable non-metastatic HCC.

The results of the Ph2 study (NCT04444167) of AK104 plus lenvatinib for 1L HCC were released at the 2021 ASCO meeting (link). As of Feb 2021, 30 patients in the study had received the combination therapy of (AK104 6mg/kg Q2W plus lenvatinib). Of 18 patients evaluable for antitumor activity, ORR was 44.4% (8/18), and DCR was 77.8% (8 PRs and 6 SDs). Median PFS was not reached. TRAEs occurred in 83.3% of patients (grade 3 TRAEs occurred in 26.7% [8/30], and no grade 4 TRAEs or TRAEs leading to death). Most common TRAEs were increased AST and ALT, decreased platelet count, decreased neutrophil count, and increased blood bilirubin, with the vast majority being grades 1 or 2.

As of Aug 2022, the mPFS of AK104+lenvatinib in the above-mentioned Ph2 study reached 9.8 months (link), which were the longest mPFS compared with other main immunotherapies (vs 6.9 months of atezolizumab + bevacizumab, 4.6 months of sintilimab + bevacizumab biosimilar, 7.4 months of lenvatinib). Additionally, in terms of safety, it indicated that AK104+lenvatinib has more acceptable safety profile - with 26.7% Grade ≥3 TRAEs observed in the study of AK104+lenvatinib, as compared to 45% Grade ≥3 TRAEs in the Imbrave150 study of atezolizumab + bevacizumab.

AK104 plus lenvatinib as first-line therapy for HCC has demonstrated promising early antitumor activity and a more acceptable safety profile. We look forward to the further follow-up of the Ph2 study of AK104+lenvatinib in first-line HCC, and the data readout of its ongoing Ph3 study of AK104 as a mono adjuvant therapy for early HCC after resection.

1L G/GEJC: encouraging long-term PFS and OS efficacy results

Therapeutics landscape of 1L G/GEJC

Gastric or gastroesophageal junction cancer (G/GEJC or GC) is the third most common cause of cancer-related death worldwide, posing a major clinical challenge due to limited treatment options. For first-line treatment of HER2-positive GC, targeted therapies trastuzumab in combination with chemotherapy has been widely used (Level I/II recommendation by CSCO). Pembrolizumab plus trastuzumab in combination with chemotherapy is also a CSCO-recommended (Level III) therapy to treat 1L HER2-positive GC patients.

For HER2-negative GC patients, chemotherapy plus nivolumab, chemotherapy plus sintilimab, and chemotherapy alone, are CSCO and/or NCCN Guidelines recommended first-line treatments, regardless of PD-(L)1 expression. Additionally, tislelizumab plus chemotherapy is also recommended by CSCO for PD-(L)1 positive patients.

Compared to chemotherapy alone, PD-1 mAbs plus chemotherapy as first-line therapy for advanced G/GEJ cancer yields OS and PFS benefits. As demonstrated in the Checkmate-649 trial, chemotherapy plus nivolumab extended the mOS by 2.2 months compared to chemotherapy (mOS 13.8 vs 11.6 months, HR=0.79) as a first-line treatment for HER2-negative GC patients regardless of PD-L1 expression. For patients with high PD-L1 expression (CPS≥5), the combination therapy further extended the mOS by 3.3 months (mOS 14.4 vs 11.1 months, HR=0.70). Chemotherapy plus nivolumab have been approved in the US, China and other regions for the treatment of 1L HER2-negative GC based on this trial.

In China, chemotherapy plus sintilimab was approved in Jun 2022 for 1L HER2-negative GC. As observed in the ORIENT-16 trial, chemotherapy plus sintilimab, compared to chemotherapy alone, extended the mOS for patients regardless of PD-L1 expression and patients with CPS≥5 by 2.9 months (mOS 15.2 vs 12.3 months, HR=0.77) and 6.3 months (mOS 19.2 vs 12.9 months, HR=0.66), respectively.

Tislelizumab plus chemotherapy was able to significantly improve mOS vs chemotherapy alone for patients whose tumors expressed PD-L1 (PD-L1 score≥5), meeting one of the primary endpoints of the Ph3 RATIONALE 305 trial (link). The trial enrolled 997 patients from 13 countries/regions, with 546 patients expressing PD-L1 at baseline. The interim results in the PD-L1+ population of the trial was recently released (link). Tislelizumab plus chemotherapy was able to extend the OS of GC patients by 4.6 months (HR=0.74), as compared to chemo alone, for PD-L1 positive patients. BeiGene/Norvatis will continue the study towards the OS final analysis in the ITT population with the results expected later 2023. Additionally, pembrolizumab plus chemotherapy recently demonstrated its superiority than pure chemotherapy for first-line HER2-negative GC treatment in a Ph3 trial KEYNOTE-859 (link) and the sBLA in the US has been accepted by FDA with PDUFA date of 16 Dec 2023.

Figure 17: Cross-trial comparison of drugs/drug candidates for 1L HER2-negative GC

	AK104	Nivolumab		Sintilimab		Tislelizumab		Pembrolizumab		
Trial	NCT03852251	Checkmate-649		ORIENT-16		Rationale 305		KEYNOTE-859		
Trial stage	Ph1/2 (China)	Ph3 (global)		Ph3 (China)		Ph3 (global)		Ph3 (global)		
Regimen	AK104+XELOX	nivolumab + chemo vs chemo		sintilimab + chemo vs chemo		Tislelizumab + chemo vs chemo		Pembrolizumab + chemo vs chemo		
Target	PD-1/CTLA-4	PD-1		PD-1		PD-1		PD-1		
Primary endpoint	ORR	PFS, OS		OS		OS		OS		
Patient number	94	1581 (789 vs 792)		650 (327 vs 323)		997		1,579 (785 vs 787)		
PD-L1 expression	**15% pts CPS≥5**	**60% pts CPS≥5**		**61% pts CPS≥5**				78% pts CPS≥1; 35% pts CPS≥10		
Sub-group	all pts	all pts	pts with CPS≥5 (473 vs 482)	all pts	pts with CPS≥5	all pts	pts with PD-L1 score≥5 (274 vs 272)	all pts	pts with CPS≥1	pts with CPS≥10
ORR	68.2%	50.6% vs 46.0%	59.8% vs 45.1%	58.2% vs 48.8%	-	-	50.4% vs 43.0%	51.3% vs 42.0%	52.1% vs 42.6%	60.6% vs 43.0%
CR	*5.7%*	*13% vs 7%*	*11% vs 6%*				*3.3% vs 1.8%*	*9.5% vs 6.2%*		
mPFS (mo)	**9.2**	**7.7** vs 6.9, HR=0.79	8.1 vs 6.1, HR=0.70	HR=0.638	HR=0.621	-	7.2 vs 5.9, HR=0.67	**6.9** vs 5.6, HR=0.76	6.9 vs 5.6, HR=0.72	8.1 vs 5.6, HR=0.62
mOS (mo)	**17.4** for all pts; 20.24 for pts with CPS≥5; 17.28 for pts with CPS<5	**13.8** vs 11.6, HR=0.79	14.4 vs 11.1, HR=0.70	**15.2** vs 12.3, HR=0.68	19.2 vs 12.9, HR=0.59	-	17.2 vs 12.6, HR=0.74	**12.9** vs 11.5, HR=0.78	13.0 vs 11.4, HR=0.74	15.7 vs 11.8, HR=0.65
Grade ≥3 TRAEs	70.2%	59.1% vs 44.5%		59.8% vs 52.5%		-	52.6% vs 48.5%	59.4% vs 51.1%		
Approval status in US and China for 1L GC (HER2-)	not approved yet	approved in the US and China		approved in China		primary endpoint met, to release data	approved in China for 1L PD-L1+ GC	US sBLA accepted (PDUFA date of 16 Dec 2023); pembrolizumab mono is CSCO-recommended (Level III) for CPS≥1 pts		
Data source	Link	Link		Link1, Link2		Link	Link	Link1, Link2		

Source: Pubmed, CMBIGM

Clinical data of AK104 in 1L GC

Akeso is developing AK104 for both 1L and 2L treatment of G/GEJ cancer in multiple trials. A Ph3 study (NCT05008783) of AK104 plus XELOX in 1L GC patients is ongoing with the enrollment completed in Mar 2023. A Ph2 study (NCT03852251) of AK104 plus XELOX or modified XELOX for 1L GC has data released at 2023 ASCO (link). AKeso is also exploring the combination of AK104 plus AK117 (CD47 mAb) for 1L G/GEJ cancer in a Ph1/2 study (NCT05235542), with the data released at 2023 ASCO as well (link). For 2L treatment, a Ph1/2 trial (NCT04982276) of AK104 + AK109 (VEGFR2 mAb) +/- chemotherapy as a second-line treatment for patients who progress after PD-1 treatment is currently ongoing.

At the 2023 ASCO meeting, the Company released the updated results of the Ph2 study (NCT03852251) of AK104 combined with XELOX (capecitabine combined with oxaliplatin) or modified XELOX (mXELOX) for 1L G/GEJ cancer (link). In this trial, patients with unresectable advanced G/GEJ adenocarcinoma and no prior systemic therapy, regardless of PD-L1 status, were enrolled, excluding known HER2-positive patients. Enrolled patients received AK104 (4 / 6 /10mg/kg Q2W or 10 /15mg/kg Q3W) + chemo (mXELOX

Q2W or XELOX Q3W). The primary endpoint was ORR. As of Oct 2022, 94 patients in the 10mg/kg Q3W were enrolled, and 45.7% of the patients had baseline liver metastasis. The median follow-up was 24.0 months. 88 patients (94%) had at least one post-baseline tumor evaluation. The ORR was 68.2% with 5.7% CR and 62.5% PR. The mPFS and mOS were 9.2 months and 17.4 months, respectively. In patients with PD-L1 CPS≥5 vs CPS<5, mOS was 20.24 months and 17.28 months, respectively. On the safety side, Grade ≥3 TRAEs occurred in 69.4% patients.

As cross-trial comparisons, we see the promising efficacy and manageable safety of AK104+chemo for 1L GC treatment. In the above studies, the 17.4 months of mOS in AK104's study, regardless of PD-L1 status, was much better than the mOS of 13.8 months, 15.2 months and 12.9 months showed in studies related to nivolumab, sintilimab and pembrolizumab, respectively. Worth mentioning, 15% of patients in AK104's study had PD-L1 CPS≥5, as compared to around 60% in the related studies of nivolumab and sintilimab. For patients with PD-L1 CPS≥5 specifically, AK104+chemo realized 20.3 months of mOS, better than the 14.4 months of nivolumab+chemo, 19.2 months of sintilimab+chemo, and 15.7 months of pembrolizumab+chemo. AK104+chemo is potentially a new treatment option for first-line GC patients. While on the safety side, the rate of Grade ≥3 TRAEs in AK104's trial was higher but at the same level than the approved PD-1+chemo SoC therapies. Akeso is conducting a Ph3 study of AK104 combined with chemo for 1L GC with patient enrollment completed in Mar 2023.

Large potential in commercialization in China and potentially overseas

The Company has established an efficient commercialization team of over 650 employees (as of end-2022) in China, covering 1,500+ hospitals. We expect Akeso to expand its salesforce in 2023. Akeso targets to reach RMB1bn sales from AK104 during the first 12 months since its approval in late Jun 2022. In FY22, with 6 months of commercialization, AK104 achieved RMB546mn sales. We are confident towards the Company's guideline to realize RMB1.2~1.3bn revenue from AK104 in 2023E.

The inclusion of AK104 in the CSCO Guidelines as the first immunotherapy for 2L R/R CC treatment facilitates the commercialization of the medicine. With registrational Ph3 trials ongoing for 1L CC, we expect AK104 to seize the market opportunity by covering the full spectrum of CC treatment. Additionally, with multiple late-stage trials ongoing for both first-line and later-line treatment of large indications, such as HCC and GC, we expect the additional approvals in these large indications to further boost the sales of AK104 in the future.

AK104 didn't pass the price negotiation of NRDL in Jan 2023. However, considering the favorable competitive landscape of R/M CC treatment and potential future approvals for large indications such as 1L CC, 1L GC and adjuvant HCC, AK104 could realize its best commercial value by maintaining a satisfying pricing level at the moment and to be added to the NDRL after the approvals of its other large indications, in our view. Meanwhile, Akeso proactively adjusted the PAP policy of AK104 since Feb 2023, with the annualized treatment cost of AK104 reduced.

Based on the first-in-class/best-in-class potential of AK104 in the treatment of multiple indications, we expect Akeso to reach a blockbuster deal to out-license the ex-China rights of AK104, which could be a major catalyst for the Company.

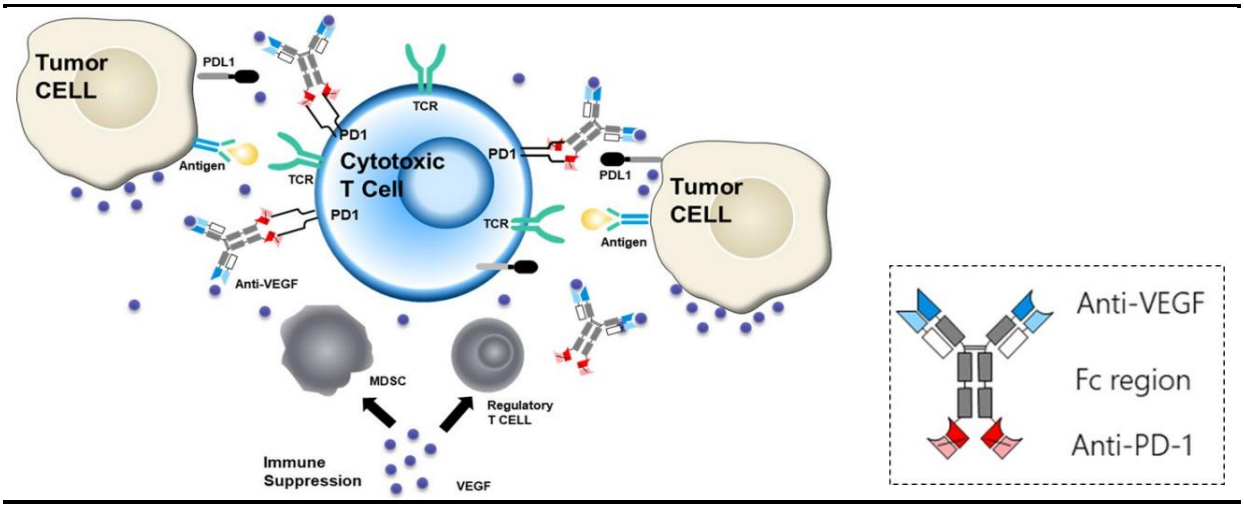
Ivonescimab (AK112, PD-1/VEGF), first-in-class BsAb to uncover the enormous lung cancer market

First-in-class BsAb for lung cancer across all treatment settings

Internally developed by Akeso, ivonescimab (AK112) is the first PD-1/VEGF bi-specific antibody to enter Ph3 clinical trial which has the first-in-class potentials. AK112 is a humanized IgG1 bispecific antibody targeting PD-1 and VEGF. Engineered with the Company's unique Tetrabody technology, AK112 blocks PD-1 binding to PD-L1 and PD-L2, and blocks VEGF binding to VEGF receptors.

PD-1 antibody combined with VEGF blocking agents have shown robust efficacy in various tumor types (including renal cell carcinoma, NSCLC and HCC). In view of the co-expression of VEGF and PD-1 in the tumor microenvironment, AK112, as a single agent to block these two targets, has the potential to block these two pathways more effectively to enhance the antitumor activity, as compared to combination therapy.

Figure 18: MoA of AK112



Source: Company data, CMBIGM

AK112 has been granted three breakthrough therapy designations (BTDs) by the China CDE, including: (1) AK112 monotherapy as a first-line treatment for PD-L1-positive NSCLC patients; (2) AK112 + chemotherapy for the treatment of EGFR-mutated nsq-NSCLC who have failed to EGFR-TKI treatment; (3) AK112 + docetaxel for the treatment of NSCLC patients who failed to prior PD-(L)1 inhibitor combined with platinum-based doublet chemotherapy. Worth mentioning, AK112 is currently the only innovative drug candidate that has obtained BTD in PD-(L)1 resistant lung cancer treatment area in China. Obtaining BTD designations will accelerate the registration progress of AK112.

AK112 is likely to become the first-in-class BsAb to uncover the enormous market of lung cancer across all treatment settings. Currently, the Company and its partner Summit are conducting multiple Ph3 studies for AK112, with several others in plan.

In China, AK112 is under late-stage trials covering all-spectrum treatment settings of NSCLC, as well as gastrointestinal cancer, breast cancer, HCC, CRC (in Ph1b/2 trials), which, in our view, supports the potential of AK112 to become a blockbuster medicine in the future. The ongoing/in planning Ph3 trials of AK112 in China include:

1) Obtained a BTD designation, AK112 monotherapy is under a head-to-head Ph3 study (NCT05499390) vs pembrolizumab for the treatment of PD-L1+ NSCLC who has no prior systemic therapy. Recall that pembrolizumab monotherapy has been approved in the US, China

and other regions as a first-line treatment for PD-L1 positive NSCLC patients based on the Ph3 KEYNOTE-042 study.

2) AK112 plus chemo is also under a Ph3 study (NCT05184712) for patients with EGFR-mutated nsq-NSCLC who failed in prior EGFR-TKI therapy, for which patients, the current treatment options are very limited and AK112 has a BTD designation for this indication in China as well. The patient enrollment of the study has been completed in Nov 2022. We expect the Company to file NDA for this indication by end 2023 mainly based on the PFS results of the trial. As the trial has been included into an MRCT trial, for which Summit is enrolling patients in overseas, we expect Akeso to release the results upon AK112's approval in China.
3) Additionally, in order to beat the current SOC of 1L NSCLC treatment, AK112+chemo recently entered a head-to-head study (NCT05840016) vs tislelizumab+chemo for 1L sq-NSCLC.
4) Moreover, many NSCLC patients do not respond to the current standard PD-(L)1+chemo treatment, and there is a huge unmet medical need for I/O-resistant NSCLC patents. With promising Ph2 efficacy signals for I/O-resistant NSCLC patients, AK112+chemo has obtained BTD for PD-(L)1 resistant lung cancer treatment in China, the only BTD in this treatment setting.

Figure 19: Development pipeline of AK112 in China (as of Apr 2023)

Oncology - Core Products				Current Status			
Product (Target)	Areas	Mono/Combo Therapy	Indication	Phase Ia	Phase Ib/II	Pivotal/Phase III	NDA Submitted/ Approved
Ivonescimab AK112 (PD-1/VEGF)	Lung cancer	+Chemo	EGFR-TKI resistant NSCLC ▲★			Enrollment completed	
		Mono	1L PD-L1(+) NSCLC ▲★			Enrollment in process	
		+Chemo	1L sqNSCLC ▲			Initiated	
		+Chemo	IO-r NSCLC ▲★				
		±Chemo	Neoadjuvant NSCLC ▲				
		+AK119	EGFR-TKI resistant NSCLC ▲				
	Gastrointestinal cancer	+AK117 +/- Chemo	Adv. solid tumors (GC, BTC, PDAC) ▲				
	Breast cancer	+Chemo +/- AK117	1L TNBC ▲				
	Head and neck cancer	+AK117 +/- Chemo	HNSCC				
	Hepatocellular carcinoma	Mono	Unresectable HCC ▲				
	Colorectal cancer	+AK117 +/- Chemo	1L CRC ▲				
	Ovarian cancer	Mono	Platinum resistant OC 🌐				
	Others	+AK112	Adv. solid tumors				
		Mono	Adv. solid tumors 🌐				

🌐 Global ▲ Large Indications ⚑ NMPA approval ⬚ Registrational Trials ★ Breakthrough Therapy

Source: Company data, CMBIGM. Notes: Global Ph3 trials not included.

In oversea markets, to accelerate the global development and commercialization of AK112, Akeso has out-licensed the rights of AK112 in the US, Canada, Europe, and Japan to Summit Therapeutics in a blockbuster deal. Besides future sales royalties, the deal size is up to US$5.0bn, which is a landmark deal for Chinese biopharma companies. With US$500mn upfront payment been fully paid, we are confident about the global development of AK112 by leveraging the successful expertise of Summit's management team. Based on Akeso's studies in China, Summit has started a Ph3 MRCT trial (HARMONi/ NCT05184712) of AK112+chemo for EGFR-mutated nsq-NSCLC who failed in prior EGFR-TKI therapy (FPI in May 2023). Summit also plans to start another Ph3 MRCT trial (HARMONi-3) of AK112+chemo vs pembrolizumab +chemo in 1L sq-NSCLC (FPI expected in 2H23).

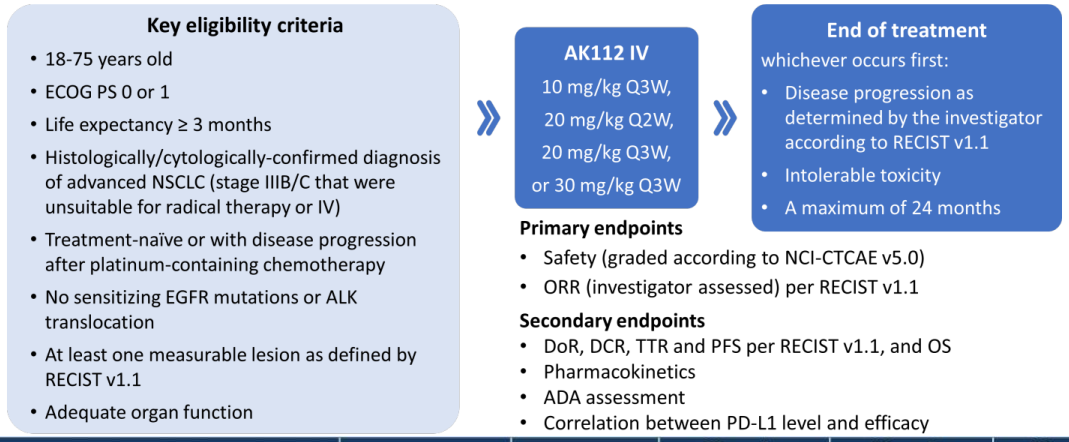
The HARMONi MRCT study is expanded based on the China Ph3 trial conducted by Akeso, and targets to enroll around 470 patients. The study will enroll patients from the US, Canada, Europe, and China. Akeso is responsible for enrollment in China, which has been completed in Nov 2022. Summit is responsible for enrollment in the US, Canada, and Europe. The study, designed with registration intent, has two primary endpoints: OS and PFS. The first patient of the study has been dosed in May 2023 in the

US (link). Leveraging the data from China, we expect Summit/Akeso will be able to accelerate the development process of AK112 in the global market.

AK112 monotherapy demonstrated promising preliminary efficacy for 1/2L NSCLC

The promising preliminary efficacy signals of AK112 monotherapy in early stage of clinical trials warrant further investigation of AK112 for the treatment of 1/2L PD-L1-positive NSCLC treatment in much larger studies. The results of early stage Ph1b/2 study (NCT04900363) of AK112 monotherapy as 1L or 2L therapy for advanced NSCLC was released at the 2022 ASCO meeting (link). In this trial, patients with stage IIIB/IIIC/IV NSCLC, ECOG PS 0-1 and negative oncogenic drivers received AK112 (10 mg/kg Q3W, 20 mg/kg Q2W, 20 mg/kg Q3W or 30 mg/kg Q3W) intravenously. As of 4 Mar 2022, 96 patients were enrolled, in which 66 (68.8%) were PD-L1 positive (TPS≥1%) and 81 (84.4%) were treatment-naïve.

Figure 20: Study design and patient characteristics of Ph1b/2 trial of AK112 mono in 1/2L NSCLC



Characteristics	Total (N=96)	10 mg/kg Q3W (N=30)	20 mg/kg Q2W (N=29)	20 mg/kg Q3W (N=29)	30 mg/kg Q3W (N=8)
Age, years					
Median (range)	65.5 (48-75)	64.0 (48-74)	68.0 (51-74)	65.0 (53-75)	63.5 (51-70)
Sex, n (%)					
Male	82 (85.4)	23 (76.7)	26 (89.7)	25 (86.2)	8 (100.0)
ECOG PS, %					
0/1	9.4/90.6	10.0/90.0	13.8/86.2	3.4/96.6	2.5/87.5
Histology, %					
Non-squamous/ Squamous	50.0/ 50.0	53.3/ 46.7	48.3/ 51.7	48.3/ 51.7	50.0/ 50.0
PD-L1 expression, n (%)					
TPS ≥1	66 (68.8)	21 (70.0)	22 (75.9)	19 (65.5)	4 (50.0)
Treatment condition, n (%)					
Treatment-naïve	81 (84.4)	26 (86.7)	25 (86.2)	22 (75.9)	8 (100.0)

Source: CSCO, CMBIGM

Dose-related efficacy was clearly observed in the study. As of the data cutoff date, 90 patients had at least one post-baseline tumor evaluation. ORR (unconfirmed) were 21.4%/ 37.9%/ 50.0% at dose of 10/ 20/ 30mg/kg Q3W, respectively. The ORR (unconfirmed) were 50.0% at dose of 20mg/kg Q2W, as compared to 37.9% at dose of 20mg/kg Q3W.

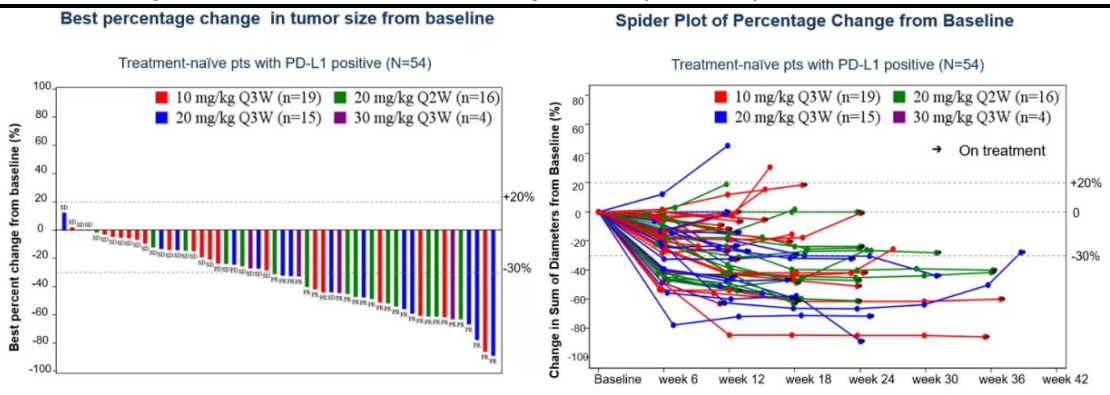
In the 54 treatment-naïve patients with PD-L1 positive (TPS≥1%), ORR was 50.0%. ORR was 31.6%/ 53.3%/ 75.0% at dose of 10/ 20/ 30mg/kg Q3W, respectively. The ORR were 62.5% at dose of 20mg/kg Q2W, as compared to 53.3% at dose of 20mg/kg Q3W (RP2D).

Figure 21: Response rate of Ph1b/2 trial of AK112 mono in 1/2L NSCLC

	Pts no.	Overall ORR	10 mg/kg Q3W	20 mg/kg Q2W	20 mg/kg Q3W	30 mg/kg Q3W
All evaluable pts	90		21.4%	50.0%	37.9%	50.0%
1L PD-L1 positive pts (TPS≥1%)	54	50.0%	31.6%	62.5%	53.3%	75.0%

Source: CSCO, CMBIGM. Note: 20 mg/kg Q3W was chosen as a RP2D.

Figure 22: Efficacy of AK112 mono in 1L PD-L1 positive (TPS≥1%) NSCLC



Source: CSCO, CMBIGM

In the 50 treatment-naïve patients receiving AK112 >10mg/kg Q3W, ORR was 46.0%. Patients with TPS 1-49% had an ORR of 50.0%, while patients with TPS ≥50% had a significantly higher ORR (76.9%).

Figure 23: Response rate of treatment-naïve patients receiving AK112>10mg/kg Q3W

PD-L1 TPS	≥ 1% (N=35)	1-49% (N=22)	≥ 50% (N=13)	< 1% (N=15)	Total (N=50)
ORR, %	60.0	50.0	76.9	13.3	46.0
DCR, %	97.1	95.5	100.0	66.7	88.0
CR, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
PR, n (%)	21 (60.0)	11 (50.0)	10 (76.9)	2 (13.3)	23 (46.0)
SD, n (%)	13 (37.1)	10 (45.5)	3 (23.1)	8 (53.3)	21 (42.0)
PD, n (%)	1 (2.9)	1 (4.5)	0 (0.0)	5 (33.3)	6 (12.0)
NE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: CSCO, CMBIGM

Grade≥3 TRAEs occurred in 13.5% (13/96) pts, in which the most common event was pneumonia (3.1%, 3/96). No TRAEs led to permanent treatment discontinuation. Most frequent any grade TRAEs were proteinuria (19.8%), hypertension (15.6%), blood urea increase (15.6%), etc. No significant difference in the incidences of TRAEs were observed between non-squamous and squamous patients. According to the management, 37 (77%) of the 48 patients with sq-NSCLC in the study had central-type lung cancer, which tended to lead to more safety issues. The 13.5% occurrence of Grade≥3 TRAEs demonstrated the favorable safety profile of AK112.

According to the updated data with a longer follow up period of 12.98 months, for the 67 PD-L1+ 1L NSCLC patients, the ORR reached 66.7% and the mPFS reached 10.0 months. The efficacy of AK112 mono was significantly better than that of pembrolizumab which delivered 27.3% ORR and 5.6 months mPFS in KEYNOTE-042 study. For patients with higher level of PD-L1 expression (TPS≥50%), AK112's efficacy was remarkable, with an ORR of 76.9% as compared to pembrolizumab's 39.1%. On the safety side, it seems AK112 was more tolerable than pembrolizumab - the rate of Grade≥3 TRAEs in AK112's trial was 13.5% as compared to 18.9% in pembrolizumab's trial.

Pembrolizumab monotherapy was approved for 1L treatment of PD-L1-positive NSCLC, and recommended by NCCN and CSCO for patients with PD-L1 TPS≥1% and without EGFR activating mutations/ALK fusions, based on the KEYNOTE-042 trial. In this trial, with 5 years of follow-up (data cutoff Apr 2021, link), OS outcomes favored the pembrolizumab group (vs chemotherapy alone) regardless of PD-L1 TPS (HR=0.68 for TPS ≥50%, HR=0.75 for TPS ≥20%, HR=0.79 for TPS ≥1%). Grade 3-5 TRAEs occurred in 18.9% patients in the pembrolizumab group and 41.8% in the chemotherapy group.

Figure 24: Key efficacy outcomes of KEYNOTE-042 study

ITT Population	PD-L1 TPS ≥50%		PD-L1 TPS ≥20%		PD-L1 TPS ≥1%	
	Pembrolizumab n = 299	Chemo n = 300	Pembrolizumab n = 413	Chemo n = 405	Pembrolizumab n = 637	Chemo n = 637
OS, median (95% CI), mo	20.0 (15.9–24.2)	12.2 (10.4–14.6)	18.0 (15.5–21.5)	13.0 (11.6–15.3)	16.4 (14.0–19.6)	12.1 (11.3–13.3)
OS, HR (95% CI)	0.68 (0.57–0.81)		0.75 (0.64–0.87)		0.79 (0.70–0.89)	
OS, 5 y rate (95% CI), %	21.9 (17.3–26.9)	9.8 (6.6–13.7)	19.4 (15.6–23.4)	10.1 (7.2–13.5)	16.6 (13.7–19.6)	8.5 (6.4–11.0)
PFS, median (95% CI), mo	6.5 (5.9–8.6)	6.5 (6.2–7.6)	6.2 (5.4–7.8)	6.9 (6.3–8.2)	5.6 (4.3–6.2)	6.8 (6.4–7.9)
PFS, HR (95% CI)	0.86 (0.72–1.02)		0.94 (0.81–1.09)		1.03 (0.91–1.16)	
PFS, 5 y rate (95% CI), %	9.2 (5.9–13.4)	2.1 (0.7–5.0)	7.8 (5.2–11.1)	1.6 (0.5–3.9)	6.9 (4.9–9.4)	1.2 (0.5–2.7)
PFS2[a], median (95% CI), mo	15.0 (11.6–19.2)	10.1 (8.9–11.2)	12.9 (10.9–15.5)	10.2 (9.1– 11.3)	11.3 (10.1–12.9)	9.4 (8.8–10.3)
PFS2[a], HR (95% CI)	0.64 (0.54–0.76)		0.67 (0.58–0.78)		0.74 (0.65–0.83)	
ORR (95% CI), %	39.1 (33.6–44.9)	32.3 (27.1–37.9)	33.2 (28.6–37.9)	29.1 (24.8–33.8)	27.3 (23.9–31.0)	26.7 (23.3–30.3)
DOR, median (range), mo	28.1 (2.1+ to 70.0+)	10.8 (1.8+ to 63.5+)	27.7 (2.1+ to 70.0+)	10.8 (1.8+ to 63.5+)	26.5 (2.1+ to 70.0+)	8.4 (1.8+ to 63.5+)

Chemo, chemotherapy; DOR, duration of response.
+, indicates no PD by the time of last assessment.
[a]PFS2: time from randomization to second/subsequent PD on next-line treatment or death.

Source: Pubmed, CMBIGM

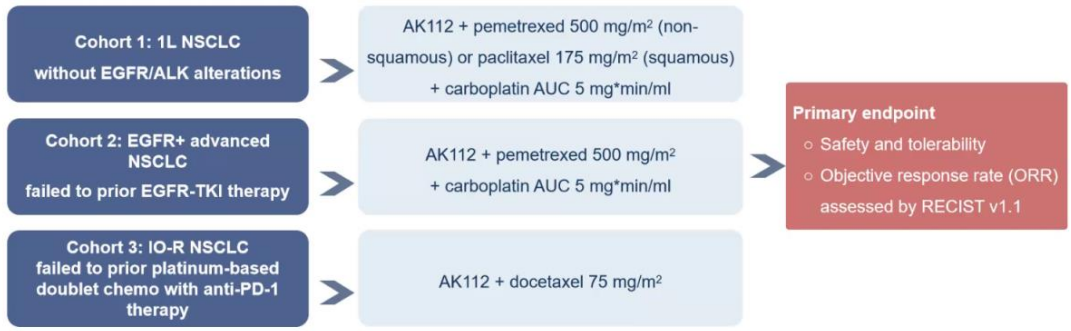
We believe the early clinical data indicates the promising efficacy profile of AK112 for NSCLC treatment, and look forward to the results of the ongoing head-to-head Ph3 trial (NCT05499390) comparing AK112 to pembrolizumab in 1L PD-L1-positive NSCLC patients.

AK112 combined with chemotherapy for NSCLC across all spectrum treatment settings

AK112 monotherapy has demonstrated tolerable safety and promising anti-tumor activity in patients with advanced NSCLC. AK112 plus chemotherapy may further improve anti-tumor efficacy with favorable safety in 1L NSCLC (compared to PD-1 plus chemotherapy), EGFR+ advanced NSCLC, and IO-R NSCLC.

A Ph2 study was conducted to assess the combo therapy of AK112 plus chemo in advanced NSCLC. The Ph2 study (NCT04736823) was an open-label, multi-center trial evaluating AK112 + chemotherapy in patients with advanced NSCLC (link). Enrolled patients were divided into three cohorts: (1) Cohort 1, previously untreated advanced NSCLC patients with wide-type EGFR/ALK; (2) Cohort 2, patients with EGFR mutations who had failed prior EGFR-TKI therapies without T790M mutation or failed osimertinib treatment; and (3) Cohort 3, patients who progressed after anti-PD-(L)1 and platinum-based chemotherapy. Patients were treated with 10mg/kg or 20mg/kg AK112 Q3W in combination with chemotherapy. Primary endpoint was ORR as assessed by investigator.

Figure 25: Study design and patient characteristics of the Ph2 trial of AK112 plus chemo in advanced NSCLC



Characteristics	Cohort 1 (N = 44)	Cohort 2 (N = 19)	Cohort 3 (N = 20)	Overall (N = 83)
Age, median (range), years	57.6 (44.3, 73.0)	60.2 (34.7 - 64.9)	60.0 (31.6 - 73.4)	58.03 (31.6 - 73.4)
Male, n(%)	28 (63.6)	6 (31.6)	16 (80.0)	50 (60.2)
ECOG performance status, n(%)				
1	42 (95.5)	14 (73.7)	19 (95.0)	75 (90.4)
Smoking status, n(%)				
Former or Current	24 (54.5)	4 (21.1)	15 (75.0)	43 (51.8)
Never	20 (45.5)	15 (78.9)	5 (25.0)	40 (48.2)
PD-L1 TPS, n(%)				
<1%	20 (45.5)	10 (52.6)	6 (30.0)	36 (43.4)
1-49%	16 (36.4)	6 (31.6)	8 (40.0)	30 (36.1)
≥50%	6 (13.6)	3 (15.8)	4 (20.0)	13 (15.7)
NE	2 (4.5)	0 (0.0)	2 (10.0)	4 (4.8)
Clinical Stage at Study Entry, n(%)				
IIIB/IIIC	4 (9.1)	0 (0.0)	3 (15.0)	7 (8.4)
IV	40 (90.9)	19 (100.0)	17 (85.0)	76 (91.6)
Histology, n(%)				
Squamous	18 (40.9)	0 (0.0)	7 (35.0)	25 (30.1)
Non-squamous	26 (59.1)	19 (100.0)	13 (65.0)	58 (69.9)
Brain metastasis, n(%)	8 (18.2)	7 (36.8)	1 (5.0)	16 (19.3)

Source: Company data, CMBIGM

As of 20 Mar 2022 (data cutoff), 83 patients were enrolled to cohorts 1-3 and received at least one dose of AK112 plus chemotherapy. Among the 83 patients, 25 were patients with sq-NSCLC, and 58 were patients with nsq-NSCLC. Of the 25 patients with sq-NSCLC, 52.0% were central type of squamous cell carcinoma and 28.0% had a history of hemoptysis.

AK112 demonstrated favorable safety profile. In this Ph2 trial, Grade ≥3 TRAEs occurred in 24.1% of patients, and TRAEs leading to permanent discontinuation of AK112 occurred in 3.6% of patients. There was no significant difference in the incidences of TRAEs between the sq- and nsq- group. Haemorrhage related AE of special interest included epistaxis (12.0%), hemoptysis (6.0%), haematuria, etc. Risk of haemorrhage correlated to anti-VEGF antibody declined significantly, even in patients with squamous NSCLC.

Figure 26: Safety overview of AK112 + Chemo for NSCLC

Categories, n(%)	Overall (N = 83)	Squamous (N = 25)	Non-squamous (N = 58)
Any TRAE	71 (85.5)	20 (80.0)	51 (87.9)
Grade[b] 3-5 TRAE	20 (24.1)	8 (32.0)	12 (20.7)
Treatment Related SAE	15 (18.1)	7 (28.0)	8 (13.8)
TRAE leading to AK112 discontinuation	3 (3.6)	0 (0.0)	3 (5.2)
TRAE leading to death	1 (1.2)	0 (0.0)	1 (1.7)
Most common TRAEs (≥10% of patients)			
Alanine aminotransferase increased	17 (20.5)	5 (20.0)	12 (20.7)
Aspartate aminotransferase increased	15 (18.1)	3 (12.0)	12 (20.7)
Anemia	13 (15.7)	2 (8.0)	11 (19.0)
Amylase increased	12 (14.5)	2 (8.0)	10 (17.2)
White blood cell count decreased	12 (14.5)	4 (16.0)	8 (13.8)
Neutrophil count decreased	10 (12.0)	4 (16.0)	6 (10.3)
Epistaxis	10 (12.0)	4 (16.0)	6 (10.3)
Platelet count decreased	9 (10.8)	3 (12.0)	6 (10.3)
Haemorrhage related AESI			
Epistaxis	10 (12.0)	4 (16.0)	6 (10.3)
Hemoptysis	5 (6.0)	4 (16.0)	1 (1.7)
Haematuria	1 (1.2)	1 (4.0)	0 (0.0)
Haematochezia	1 (1.2)	1 (4.0)	0 (0.0)
Gingival bleeding	1 (1.2)	0 (0.0)	1 (1.7)
Anal haemorrhage	1 (1.2)	0 (0.0)	1 (1.7)
Conjunctival haemorrhage	1 (1.2)	0 (0.0)	1 (1.7)

Source: Company data, CMBIGM

Figure 27: Results of Ph2 trial of AK112 plus chemo in advanced NSCLC and cross-trial comparisons

Patients	Cohort 1		Cohort 2 EGFR-TKI failed EGFR-mutated NSCLC (N=19)		Cohort 3 IO-R NSCLC failed to prior chemo plus PD-1 (N=20)
	1L sq-NSCLC	1L nsq-NSCLC			
% of PD-L1 TPS ≥1%	50.0%		47.4%		60.0%
ORR	79% (2022.03.20, N=18) 67% (2023.02.01, N=63)	52% (2022.03.20, N=25) 52% (2023.02.01, N=72)	68.4%		40.0%
DCR	100.0%	100.0%	94.7%		80.0%
mPFS (month)	not reached for sq- & nsq- as of 2022.03.20; 11.0 months for sq- as of 2023.02.01 12.3 months for nsq- as of 2023.02.01		8.5 *		7.1 *
Grade 3–5 TRAEs	24.1%				
Cross-trial comparisons					
Trial ID	**KEYNOTE-407** 1L sq-NSCLC (n=559)	**KEYNOTE-189** 1L nsq-NSCLC (n=616)	**ORIENT-31** (n=476)	**NCT03513666** (n=40)	**MRTX-500** (n=68)
% of PD-L1 TPS ≥1%	63.1%	63.0%	most pts (92%) not tested for PD-L1 expression	52.5%	-
Regimen	pembrolizumab + chemo vs chemo	pembrolizumab + chemo vs chemo	sintilimab + bevacizumab biosimilar + chemo vs sintilimab + chemo vs chemo	toripalimab + chemo	sitravatinib + nivolmab
ORR	62.2% vs 38.8%	48.3% vs 19.9%	43.9% vs 33.1% vs 25.2%**	50.0%	18%
mPFS (month)	8.0 vs 5.1 HR=0.62	9.0 vs 4.9 HR=0.50	7.2 vs 5.5 vs 4.3	7.0	5.7
mOS (month)	17.2 vs 11.6 HR=0.71	22.0 vs 10.6 HR=0.60	21.1 vs 20.5 vs 19.2	-	14.9
Grade 3–5 AEs	74.8% vs 70.0%	72.8% vs 67.3%	56% vs 41% vs 49%	65% (Gr≥3 TRAEs)	66% (Gr≥3 TRAEs)
Source	Link	Link	Link1, Link2	Link	Link

Source: Company data, Pubmed, CMBIGM. Notes: data on AK112 were as of the data cutoff of 20 Mar 2022, unless other specified. * data as of 1 Feb 2023. The efficacy of AK112 enhanced as follow-up continues. ** ORR of the ORIENT-31 trial is based on the first interim analysis.

In **Cohort 1 (1L NSCLC without EGFR/ALK alterations)**, as of 20 Mar 2022, with a follow-up of 9.2 months, in the 43 evaluable patients, ORR was 77.8% (including 3 unconfirmed PR) for sq-NSCLC, and 52.0% (including 1 unconfirmed PR) for nsq-NSCLC. The mPFS was not reached and 6-month PFS rate was 78.8% at the data cutoff date. With a longer follow-up (data cut-off Feb 2023, link), the mPFS for sq-NSCLC patients (N=63) reached 11.0 months, and the mPFS for nsq-NSCLC patients (N=72) reached 12.3 months.

The competitive landscape for 1L NSCLC is quite crowded with multiple PD-(L)1 being widely used. Guideline recommended I/O therapies for 1L sq-NSCLC mainly include pembrolizumab/ tislelizumab/ camrelizumab/ sintilimab/ sugemalimab plus chemotherapy for patients regardless of PD-L1 expression, or pembrolizumab/ atezolizumab monotherapy for PD-L1 positive patients. Similarly, for 1L nsq-NSCLC, the above-mentioned I/O therapies are all recommended by guidelines.

AK112 + chemo has the potential to provide a better therapeutic option for the treatment of 1L NSCLC as compared to the current standard of care PD-(L)1+chemo combination. Considering the 8.0 months of mPFS of pembrolizumab +chemo in 1L sq-NSCLC, the 11.0 months of mPFS of AK112 + chemo for 1L sq-NSCLC indicates promising efficacy of AK112. For 1L nsq-NSCLC, pembrolizumab +chemo reached a 9.0 months of mPFS, while AK112+chemo achieved a much longer mPFS of 12.3 months. Especially, 50% of patients in AK112's 1L NSCLC trial had baseline PD-L1 expression TPS≥1% (14% TPS≥50%), which was lower compared to 63% in pembrolizumab's trial (30% TPS≥50%).

The front-line NSCLC treatment space is crowded, while many patients do not respond to the current standard PD-(L)1 treatment. We believe AK112 in combo with chemo has the potential to become a more effective and tolerated I/O treatment option for NSCLC front-line treatment. Akeso has initiated a Ph3 head-to-head trial of AK112+chemo vs tislelizumab+chemo for 1L sq-NSCLC.

In **Cohort 2 (EGFR-mutated NSCLC failed to prior EGFR-TKI therapy)**, with a follow-up of 7.0 months at the data cutoff date, in 19 evaluable patients on AK112+chemo in the Cohort 2, the ORR was 68.4%. The mPFS has reached 8.5 months with a longer follow-up period of 16.8 months (link).

Multiple generations of EGFR inhibitors have been approved for the 1L treatment of EGFR-mutated NSCLC, including 3rd generation almonertinib/ osimertinib, 2nd generation dacomitinib/ afatinib, and 1st generation gefitinib/ erlotinib, etc. However, treatment option for EGFR mutated NSCLC upon progression after EGFR tyrosine kinase inhibitors (TKIs) is limited, especially for patients without T790M mutations. Besides the traditional chemotherapies with limited treatment outcomes, only sintilimab + bevacizumab biosimilar + chemo has been approved in China as a I/O therapy, based on the ORIENT-31 trial, for the EGFR-mutated NSCLC patients who have failed to prior EGFR-TKI therapy. Additionally, in the US, atezolizumab was approved for the 2L treatment of NSCLC patients who progressed on prior chemotherapy or EGFR/ALK-TKIs based on the Ph3 OAK study.

Sintilimab + bevacizumab biosimilar + chemo delivered 7.2 months of mPFS as compared to 4.3 months of mPFS in the chemo arm, as observed in the ORIENT-31 study. Based on the results, the combination therapy was approved in China in May 2023 and has been included in the CSCO Guideline for EGFR-m NSCLC patients who failed prior EGFR-TKI therapy. In addition, Junshi's toripalimab plus chemotherapy has demonstrated promising anti-tumor activity as a second-line treatment for EGFR-m NSCLC patients who failed from first-line EGFR-TKIs without T790M mutation (link). Forty patients were enrolled in its Ph2 study, and the ORR was 50.0% and DCR was 87.5%. The mPFS and mOS were 7.0 months and 23.5 months, respectively. Junshi has initiated a Ph3 trial (NCT03924050) based on this Ph2 study.

As cross-trial comparison, AK112 + chemo delivered better early efficacy in EGFR-TKI failed EGFR-m NSCLC patients (68.4% ORR and 8.5 month mPFS) compared to sintilimab+ bevacizumab + chemo (43.9% ORR, 7.2 months mPFS) and toripalimab + chemo (50.0% ORR, 7.0 months mPFS), together with favorable safety profile. Akeso is conducting a Ph3 trial (NCT05184712) of AK112 plus chemo in EGFR-mutated nsq-NSCLC patients who have failed prior EGFR-TKI treatment, with the enrollment completed in Nov 2022. We expect the Company to file NDA for this indication by end 2023 mainly based on the PFS results of the trial. As the trial has been included into an ongoing MRCT trial led by Summit, we expect Akeso to release the results upon AK112's approval in China.

In **Cohort 3 (IO-resistant NSCLC failed to prior platinum-based doublet chemo with PD-1)**, with a follow-up of 5.9 months, in 20 evaluable patients, the ORR was 40.0%. The mPFS reached 7.1 months with a longer follow-up period of 16.8 months (link).

For patients who progress after PD-(L)1 based therapies, the treatment options are limited and so far no I/O therapy is available for I/O resistant patients. Several clinical studies are ongoing to address the I/O-resistant NSCLC patents. For instance, nivolumab in combo with sitravatinib (a multi-kinase inhibitor under development by Mirati/ BeiGene) was assessed in a Ph2 study in nsq-NSCLC patients who have progressed on or after treatment with a PD-(L)1 and platinum doublet chemotherapy (link). With 68 patients enrolled and a follow-up of 33.6 months, the mPFS was 5.7 months and mOS was 14.9 months. The 6-month PFS rate was 45%, and the ORR was 18% (3% CR and 15% PR). However, the Ph3 SAPPHIRE study assessing sitravatinib + nivolumab in I/O resistant NSCLC patients failed to meet its primary endpoint of OS as of May 2023 (link).

As cross-trial comparison, AK112 plus chemo achieved 40.0% ORR, 7.1 months mPFS and 51% 6-month PFS rate, which was better than the 18% ORR, 5.7 months mPFS and 45% 6-month PFS rate of sitravatinib plus nivolumab, together with more favorable safety profile (rate of Gr≥3 TRAEs 24% vs 66%). While the failure of the Ph3 trial of sitravatinib plus nivolumab highlights the highly unmet needs in I/O resistant NSCLC, we see large potential of AK112 for the underserved NSCLC patients who progressed after checkpoint inhibitor. AK112 combined with docetaxel was granted BTD by the China CDE for the treatment of NSCLC patients who failed to prior PD-(L)1 + chemo treatment, becoming the only innovative drug candidate with BTD in this area in China. Akeso is planning a Ph3 study for AK 112 in I/O resistant NSCLC.

ES-SCLC: preliminary encouraging results for fist-line treatment

Apart from NSCLC, Akeso is also assessing AK112 for the first-line treatment of extensive-stage small-cell lung cancer (ES-SCLC), with promising preliminary results released. Lung cancer is one of the most common cancers globally and in China, with up to two-thirds of SCLC patients having ES-SCLC at first diagnosis. The first-line standard of care for ES-SCLC recommended by CSCO guideline includes PD-L1 antibody (i.e. atezolizumab or durvalumab) combined with etoposide and carboplatin. AK112, as a BsAb simultaneously binding to both PD-1 and VEGF, has demonstrated promising early clinical data in SCLC.

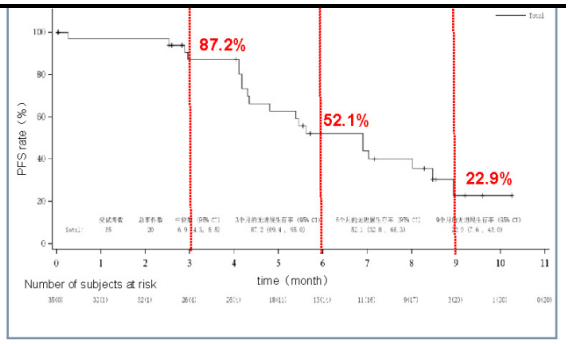
A Ph1b study (NCT05116007) of AK112 in combination with etoposide and carboplatin as first-line treatment of ES-SCLC is ongoing (link). This is an open-label Ph1b study, including dose escalation and dose expansion. In dose escalation part, safety of AK112 was assessed at 3 dose levels (3, 10, and 20mg/kg q3w) in a “3+3” design in combination with etoposide and carboplatin for up to 4 cycles treatment, followed by AK112 monotherapy maintenance. In dose expansion part, 2 doses of AK112 were selected to enroll no more than 30 patients in each cohort.

At date cut-off on 1 Jun 2022, 35 patients were enrolled, with a median follow up of 7.2 months. TRAE occurred in 32 (91.4%) patients, 19 (54.3%) patients experienced grade ≥3 TRAEs. The most common grade ≥3 TRAEs were neutropenia, leukopenia, anaemia, thrombocytopenia. 12 (34.3%) patients experienced irAE, and grade ≥3 irAE were reported in 3 (8.6%) patients. AK112 related SAE were reported in 7 (20.0%) patients. 2 (5.7%) patients discontinued the study medication due to TRAEs.

Analysis based on 32 patients’ confirmed tumor assessment result found that 29 patients achieved PR, 28 of which were confirmed, 3 patients achieved SD, with a confirmed ORR of 87.5% (28/32) and DCR of 96.9% (31/32). The mPFS was 6.9 months, and the 3-, 6- and 9-month PFS rates were 87.2%, 52.1% and 22.9%, respectively.

Figure 28: PFS outcomes of AK112 plus chemo for 1L ES-SCLC

	All Doses (n=35)
Median follow-up, months	**7.2(0.3-11.1)**
mPFS & 95% CI, months	**6.9 (4.3, 8.5)**
No. of Events, n (%)	20(57.1)
3-mo PFS rate,%(95% CI)	87.2(69.4<95)
6-mo PFS rate,%(95% CI)	52.1(32.8, 68.3)
9-mo PFS rate,%(95% CI)	22.9 (7.6, 43.0)
mDOR & 95% CI, months	**5.62(3.06, 7.69)**



Source: Company data, CMBIGM

AK112 in combination with etoposide and carboplatin showed favorable safety profile and promising anti-tumor efficacy as first-line treatment in patients with ES-SCLC. In cross-trial comparisons, AK112 plus chemo demonstrated superior efficacy signal and survival benefit, with ORR of 87.5% and mPFS of 6.9 months, vs ORR = 60.2% and mPFS = 5.2 months for atezolizumab + chemo and ORR = 67.9% and mPFS = 5.1 months for durvalumab+chemo. We expect the follow-up of the Ph1b study to continue.

Figure 29: Cross-trial comparison for drugs/drug candidates for 1L ES-SCLC

	AK112 (Akeso)	Atezolizumab (Roche)	Durvalumab (AZ)	Serplulimab (Henlius)	Adebrelimab (Hengrui)
Targets	PD-1/VEGF	PD-L1	PD-L1	PD-1	PD-L1
Trial ID	NCT05116007	IMpower133	CASPIAN	ASTRUM-005	CAPSTONE-1
Trial phase	Ph1b	Ph3	Ph3	Ph3	Ph3
Regimen	AK112 + chemo	atezolizumab + chemo vs chemo only	durvalumab + chemo vs chemo only	serplulimab + chemo vs chemo only	adebrelimab + chemo vs chemo only
Patients No.	35	201 vs 202	268 vs 269	389 vs 196	230 vs 232
ORR (confirmed)	87.5%	60.2% vs 64.4%	67.9% vs 57.6%	80.2% vs 70.4%	70.4% vs 65.9%
CR	0.0%	2.5% vs 1.0%	2.2% vs 0.7%	0.8% vs 0%	-
mPFS (month)	6.9	5.2 vs 4.3 HR=0.77	5.1 vs 5.4 HR=0.78 (95%CI 0.65–0.94, not tested for significance)	5.7 vs 4.3 HR=0.48	5.8 vs 5.6 HR=0.67
6-month PFS rate (%)	52.1%	30.9% vs 22.4%	45% vs 46%	-	49.4% vs 37.3%
mOS (month)	-	12.3 vs 10.3 HR=0.76	13.0 vs 10.3 HR=0.73	15.4 vs 10.9 HR=0.63	15.3 vs 12.8 HR=0.72
Gr≥3 TRAEs	54.3%	58.1% vs 57.6%	-	33.2% vs 27.6%	86% vs 85%
Gr≥3 Immune-mediated AEs	8.6%	-	4.5% vs 0.4%		5% vs 3%
Approval status in the US and China	-	approved in the US, China	approved in the US, China	approved in China	approved in China
Source	Link	Link	Link	Link	Link

Source: Company data, Pubmed, CMBIGM.

Pooled analysis continue to demonstrated AK112's favourable safety profile

As of Nov 2022, the pooled analysis of 504 subjects included various studies of AK112 in solid tumors, especially lung cancer, demonstrating favorable safety of AK112 as compared to bevacizumab for VEGF related toxicities. The rate of all grade TRAEs in hypertension (17.5%) and thrombosis/embolism (1.0%) was much lower than that of bevacizumab (31.0% and 15.3%, respectively). Additionally, the rate of Grade≥3 TRAEs in proteinuria was also lower in AK112's trials as compared to that in bevacizumab's trials (0.6% vs 8.1%). For sq-NSCLC patients (N=125) who usually have problems with bleeding, the rate of Grade≥3 TRAEs in hemoptysis/ pulmonary hemorrhage of AK112 was minimal compared to bevacizumab (0.8% vs 31.0%). Moreover, AK112's rate of irAE is comparable to that of PD-1 mAbs

according to the Company's pooled analysis. The favorable safety profile of AK112 supports AK112's potential as a best-in-class/first-in-class bispecific antibody targeting both VEGF and PD-1.

Figure 30: Pooled safety analysis of AK112 in solid tumors

Note:
1-数据来源：AK112-101, AK112-102, AK112-103 , AK112-201, AK112-202, AK112-203 (截至2022.5)
2-贝伐珠单抗, https://pharmacn.globaldata.com/ClinicalTrialsView

Source: Company slides, CMBIGM. Note: data as of 15 Nov 2022.

To accelerate the globalization of AK112 through a landmark out-licencing deal

In Dec 2022, Akeso granted Summit Therapeutics the exclusive rights to develop and commercialize AK112 in the US, Canada, Europe and Japan (the Summit territories) through a landmark out-licensing deal. Akeso has received an upfront payment of US$500mn and is eligible to receive potential regulatory and commercial milestones payments up to US$4.5bn. The Company will also receive low double-digit royalties on net product sales of AK112 in the Summit territories. Additionally, Dr. XIA Yu, CEO of Akeso, was appointed to the board of directors of Summit according to the agreement. In 1Q23, Akeso has received the US$500mn upfront payment from Summit, including US$474.9mn in cash and US$25.1mn in the form of 10,000,000 consideration shares allotted and issued by Summit at a price of US$2.51 per share. The out-licensing deal significantly increased the cash reserves of Akeso.

Based on Akeso's studies in China, Summit has started a Ph3 MRCT trial (HARMONi/ NCT05184712) of AK112+chemo for EGFR-mutated nsq-NSCLC who failed in prior EGFR-TKI therapy (FPI in May 2023) and plans to start another Ph3 MRCT trial (HARMONi-3) of AK112+chemo vs pembrolizumab +chemo in 1L sq-NSCLC.

Akeso took an untraditional strategy to out-license its key asset AK112. Instead of cooperating with MNC, the Company values the experiences of Bob Duggan (Summit CEO) and his team. We believe Summit will focus on AK112 as its most important pipeline product and will accelerate the global development of AK112. Mr. Duggan has successfully brought over a dozen indications to market for the first-in-class blockbuster drug ibrutinib while serving as the CEO of Pharmacyclics. Mr. Duggan led both the multimillion-dollar collaboration and the license deal for ibrutinib with Johnson & Johnson in 2011, and the subsequent sale of Pharmacyclics to AbbVie in 2015. Most of the management members of Summit previously had major roles at Pharmacyclics, whose experiences we think will be essential towards AK112's global development.

Ligufalimub (AK117, CD47), potential best-in-class CD47 mAb with favorable hematotoxicity

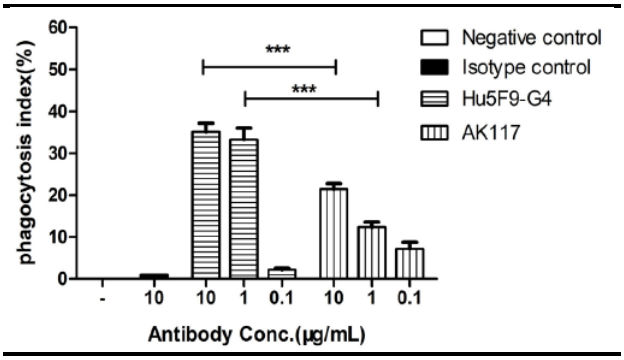
Pre-clinical evidence supports the favorable hematotoxicity of AK117 as a CD47 mAb

CD47 is a widely expressed transmembrane glycoprotein that delivers an antiphagocytic (抗吞噬) signal on macrophages through its interaction with SIRPα. CD47 is highly expressed in cancer cells and its overexpression is correlated with poor prognosis. CD47 blocking antibodies are actively being developed worldwide for cancer therapy in late stage of clinical trials, including Gilead's magrolimab (Hu5F9-G4), Akeso's AK117, I-Mab's lemzoparlimab, Innovent's IBI-188, etc. However, the most challenging concern of CD47 mAb is associated with hematotoxicity.

AK117 is a novel humanized IgG4 anti-CD47 antibody that binds to CD47 with high affinity and blocked the CD47-SIRPα interaction. Blockade of CD47-SIRPα pathway by AK117 leads to a promising therapeutic strategy for cancer treatment with unique safety features.

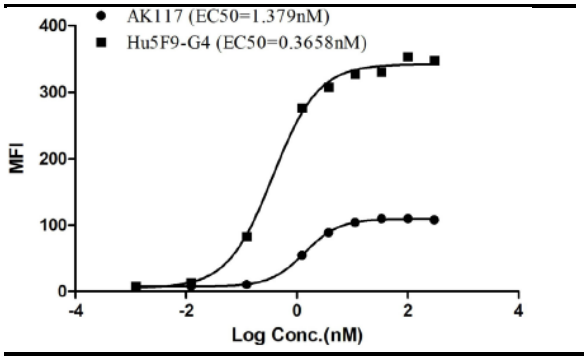
AK117 did not induce hemagglutination (血球凝集) and showed significantly lower degree of erythrophagocytosis (红细胞吞噬作用) compared with Hu5F9-G4. AK117 does not induce RBC agglutination in vitro. The hemagglutination test showed that AK117 did not induce RBC hemagglutination even at concentrations up to 3000nM, while Hu5F9-G4 induced RBC hemagglutination at concentrations as low as 4.1nM. AK117 induced a significantly lower degree of phagocytosis of erythrocytes compared with that of Hu5F9-G4 (left figure below). AK117 bind to human erythrocytes with an EC50 of 1.379 nM. The binding activity of AK117 to erythrocytes was significantly weaker than that of Hu5F9-G4 (right figure below). These results reveal that AK117 has superior safety features over Hu5F9-G4, particularly in terms of hematological toxicity.

Figure 31: AK117 induced lower phagocytosis of erythrocytes



Source: Company data, CMBIGM

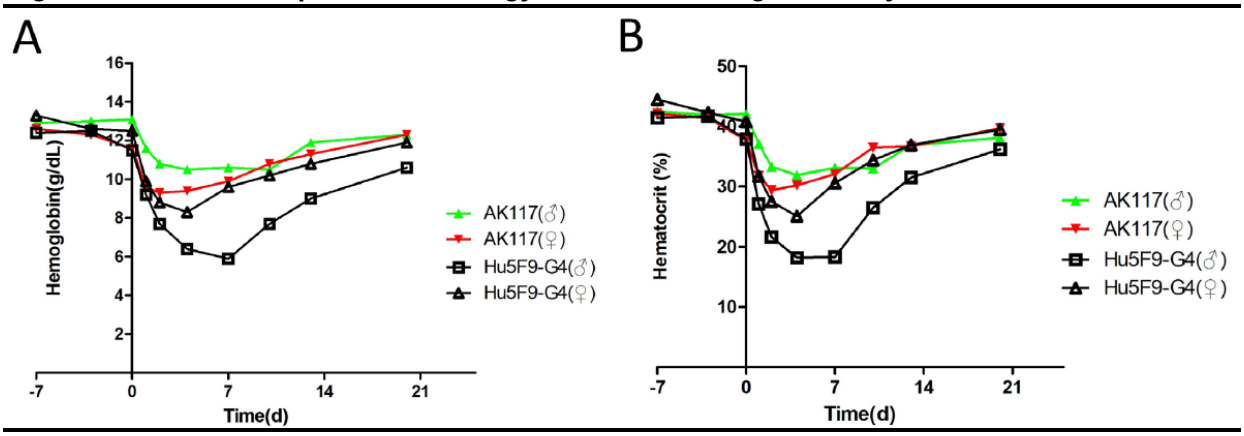
Figure 32: Weaker binding to human erythrocytes of AK117



Source: Company data, CMBIGM.

AK117 shows a favorable safety profile in non-human primates. AK117 was well tolerated and only caused transient anemia in cynomolgus monkeys.

Figure 33: Non-human primate toxicology studies showed good safety of AK117



Source: Company data, CMBIGM

The mechanism of resistance to hemagglutination of AK117 is correlated with the unique conformation of AK117/CD47 complex. AK117 and Hu5F9-G4 have different binding epitopes with several shared residues on CD47 through in silico analysis. AK117 is more likely to bind CD47 on one red blood cell (RBC), while Hu5F9-G4 is likely to bind CD47 on two separate RBCs, consequently leading to hemagglutination.

AK117 demonstrated favorable hematotoxicity and promising preliminary efficacy

In the cluster of drug candidates targeting CD47, Gilead's magrolimab (Hu5F9-G4), Akeso's AK117, I-Mab's lemzoparlimab, Innovent's IBI-188 are among the most advanced in clinical development. Due to much more favorable safety profile, we foresee AK117 as a potentially BIC/FIC CD47 mAb.

A series of clinical trials of AK117 as monotherapy or in combination with various agents such as AK112 are currently in progress, for the treatment of multiple hematologic malignancies and solid tumors. Akeso is planning a Ph3 MRCT trial of AK117 in the US and China for 1L MDS while waiting for more follow-up data of Ph2 studies.

Figure 34: Clinical trials of AK-117 (as of Apr 2023)

Oncology - Core Products				Current Status			
Product (Target)	Areas	Mono/Combo Therapy	Indication	Phase Ia	Phase Ib/II	Pivotal/Phase III	NDA Submitted/ Approved
Ligufalimab AK117 (CD47)	Hematological tumor	+ azacitidine	1L MDS				
		+ azacitidine	1L AML				
	Solid tumor	+AK112 +/- Chemo	Adv. solid tumors (GC, BTC, PDAC)				
		+AK112 +/- Chemo	HNSCC				
		+AK112 +/- Chemo	1L CRC ▲				
		+Chemo +/- AK112	1L TNBC ▲				
		+AK104 +/- Chemo	1L GC/GEJ/ESCC ▲				
		Mono	Adv solid tumors 🌐				
	Others	Mono	Adv solid tumors/lymphoma				

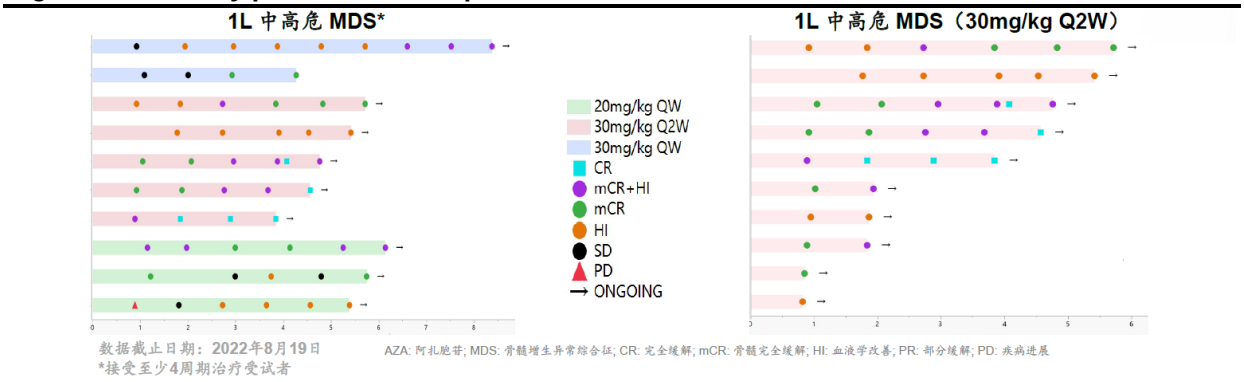
🌐 Global ▲ Large Indications NMPA approval Registrational Trials ★ Breakthrough Therapy

Source: Company data, CMBIGM

AK117 plus azacitidine (AZA) delivered promising early results in 1L MDS

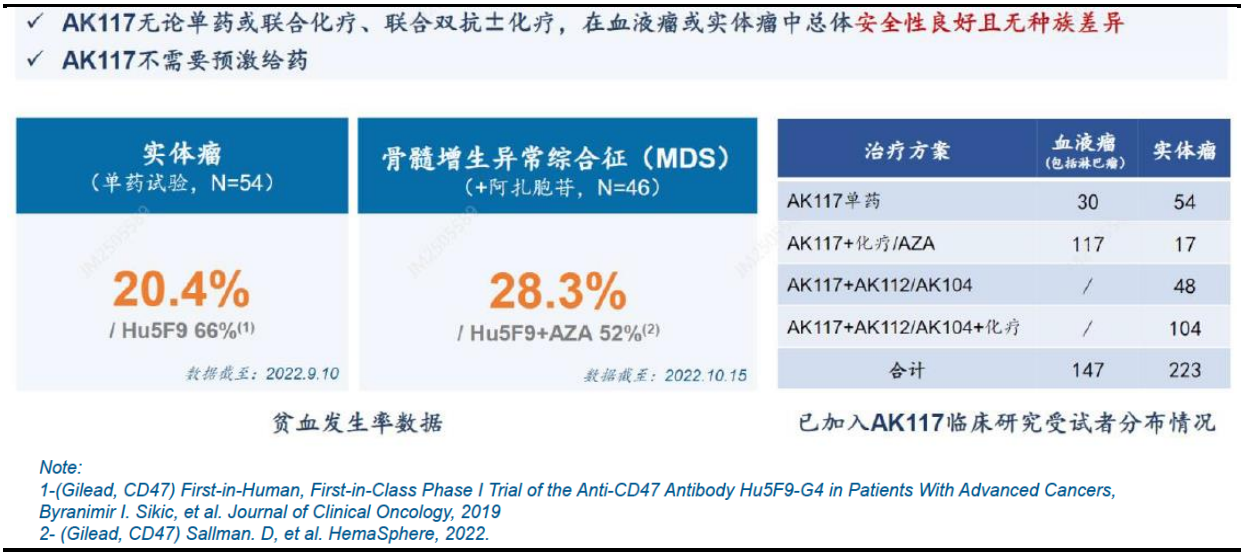
Several CD-47 mAbs are currently under late-stage development for 1L MDS, including Gilead's magrolimab (Hu5F9-G4), Akeso's AK117, I-Mab's lemzoparlimab, Innovent's IBI-188, while among which, AK117 delivered the best results in terms of both hematotoxicity and efficacy. In cross-trial comparisons, AK117 demonstrated the most favourable safety profile with the rate of anaemia (any grade) of 28.3% in the trial for 1L MDS combo with AZA. In comparison, 40% patients in lemzoparlimab's trial had grade 3/4 anaemia (TRAEs), 47% patients in magrolimab's trial had grade 3/4 anaemia (TEAEs), and 40% patients in IBI-188's trial had grade≥3 anaemia (TRAEs), all of which are less favourable than that of AK117. On the efficacy side, AK117 has demonstrated promising preliminary effectiveness, with 75% CR rate in its Ph1/2 trial, although the number of evaluable patients was limited with 8 patients having at least 6 cycles of treatment. Based on the preliminary trial data, we expect AK117 to deliver comparable efficacy profile for the treatment of 1L MDS, and importantly, favourable hematotoxicity compared to other investigational CD47 mAbs.

Figure 35: Efficacy profile of AK117 plus AZA in 1L MDS



Source: Company data, CMBIGM

Figure 36: AK117 demonstrated favourable hematotoxicity in rate of anaemia



Source: Company data, CMBIGM

Figure 37: Cross-trial comparisons for CD47 mAbs plus AZA in 1L MDS

	AK117 (Akeso)	Lemzoparlimab (I-Mab)	Magrolimab (Gilead)	IBI-188 (Innovent)
Trial ID & Stage	Phase 1/2, NCT04900350	Phase 2, NCT04202003	Phase 1b, NCT03248479	Phase 1b, NCT04485065
Data cutoff date	19 Aug 2022	31 Mar 2022	Jun 2022 (data release date)	20 Oct 2022
No. of patients	37	53	95	93
No. of evaluable patients	8 (at least 6 cycles of treatment)	15 (received initial treatment ≥ 6 months)	95 (median number of cycles was 6)	45 (pts with ≥ 6 months of follow-up)
ORR	100%	87%	75%	82%
CR	*75%*	*40%*	*33%*	*31%*
marrow CR + HI	*NA*	*13%*	*17%*	*20%*
marrow CR	*NA*	*20%*	*15%*	*16%*
HI only	*NA*	*13%*	*11%*	*16%*
Safety	as of 2022.10.15, N=46, rate of any grade of anemia was **28.3%**	Common Grade 3/4 TRAEs included decreased platelet count (60%), decreased neutrophil count (53%), decreased WBC count (53%) and anemia (40%). One patient had Grade 5 pneumonia TRAE.	Common Grade 3/4 TEAEs included anemia (47%), neutropenia (46%), thrombocytopenia (46%), and WBC count decreased (30%).	Common TRAEs were platelet count decreased (49.5%), anemia (44.1%), blood bilirubin increased (36.6%), neutrophil count decreased (36.6%), white blood cell count decreased (36.6%), and haemolysis (34.4%). Grade≥3 TRAE anemia was 39.8%. Nine pts (9.7%) discontinued treatment due to IBI188-related AE.
Data source	Link	Link	Link	Link

Source: Company data, Pubmed

Clinical studies of AK117 plus AK112 /AK104 in solid tumors ongoing

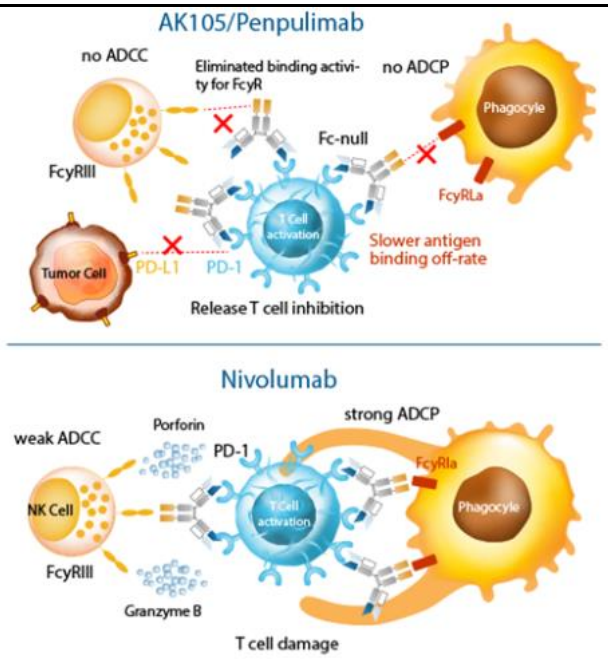
AK117 plus AK112 has demonstrated promising safety and efficacy signals in various solid tumors as well, such as head and neck squamous cell carcinoma (HNSCC), ovarian cancer (OC), SCLC, GC, sarcoma. Four investigational Ph1b trials of AK117 plus AK112 in solid tumors are currently ongoing. In a pooled analysis, in 18 patients who had progressed SoC (including I/O treatment) or ineligible for SoC, no DLT event or AK117 related anemia were observed, and the combo treatment demonstrated similar safety profile as AK112 monotherapy. On the efficacy side, the ORR was 27.8% (5/18) and the DCR was 66.7% (12/18). The preliminary encouraging data of AK117 + AK112 in solid tumors indicates the possibility of the application of AK117 for cancer treatment beyond hematological oncology. Akeso is conducting extension studies of AK117 +/- AK112 in 1L PD-L1 positive HNSCC and AK117+AK112+chemotherapy in 1L HNSCC.

Additionally, Akeso is also exploring the combo therapy of AK117 plus AK104. In Jun 2023, the results of AK117 plus AK104 in 1L GC was released at the ASCO meeting (link). 16 patients were treated with AK117 plus AK104 plus chemo, with a median follow-up time of 2.6 months, the grade≥3 TRAEs occurred in 25% patients. The most common TRAEs (incidence≥10%) were anemia, pyrexia and vomiting. The ORR was 75% (6/8) in the response-evaluable patients.

Penpulimab (AK105, PD-1), backbone of Akeso's PD-1-based BsAbs

Unlike most other marketed PD-1 antibodies which are IgG4 backboned, penpulimab is an IgG1 backbone anti-PD-1) antibody, designed to remove FcγR binding that mediates ADCC/ ADCP/ CDC, which can more effectively enhance immunotherapeutic efficacy and reduce immune-related adverse reactions. Penpulimab exhibited no apparent binding to FcγR, elicited no apparent ADCC and ADCP activities, and induced no remarkable IL-6 and IL-8 release by activated macrophages in vitro, which may contribute to its more favorable safety profile. Penpulimab demonstrated better stability and a lower level of host-cell protein residue, as well as potent binding to the antigen, compared with IgG4 backbone anti-PD-1 antibodies (link).

Figure 38: MoA of AK105



Source: CSCO, CMBIGM. Note: please refer to the video intro via link for more info on AK105's MoA.

Figure 39: Approved/BLA indications of penpulimab

Indication	Regimen	Status	Approval/BLA date	Trial ID	China NRDL	To participate China 2023 NRDL negotiation
China						
3L cHL	Mono	approved	2021-08	NCT03722147	N	Y
1L sq-NSCLC	+Chemo	approved	2023-01	NCT03866993	N	Y
3L NPC	Mono	NDA	2021-08	NCT03866967	not approved yet	N
The US						
3L NPC	Mono	NDA	2021-05	NCT03866967	-	-

Source: Company data, CMBIGM estimates

Figure 40: Clinical development of AK105

Oncology - Other Products			Current Status			
Product (Target)	Mono/Combo Therapy	Indication	Phase Ia	Phase Ib/II	Pivotal/Phase III	NDA Submitted/ Approved
Penpulimab AK105 (PD-1)	Mono	3L R/R cHL				Approved on 2021.8
	+Chemo	1L sqNSCLC ▲				Approved on 2023.1
	Mono	3L NPC				Submitted in China
	+Anlotinib	1L HCC ▲				
	+Chemo	1L NPC 🌐				
	+Anlotinib	dMMR solid tumors				
	+Anlotinib	NSCLC, SCLC, HNC, thyroid cancer, mesothelioma and thymic cancer				
	+Anlotinib	ESCC, UC, GC/GEJ, cholangiocarcinoma, neuroendocrine tumor (NET)				

🌐 Global ▲ Large Indications ⚑ NMPA approval ▭ Registrational Trials

Source: CSCO, CMBIGM.

Since more than a dozen of PD-(L)-1 products have been approved in China, penpulimab faces fierce competitions. Nevertheless, penpulimab delivered satisfying commercial performance in recent years. Akeso and CTTQ (正大天晴, a subsidiary of Sino Biopharm) formed a JV which is owned equally (50:50) by both parties, for the commercialization of penpulimab. CTTQ is fully responsible for the sales activities of penpulimab and the JV supplies the medicine to CTTQ. Penpulimab was initially approved in China for the treatment of 3L cHL in Aug 2021. Penpulimab realized RMB211.6mn sales in 2021 with approximately 4 months of commercial sales and reached RMB558mn sales in 2022. Penpulimab obtained approval from the NMPA for 1L sq-NSCLC in Jan 2023, which we expect will further drive the sales growth in 2023 and beyond. Moreover, Akeso is conducting registrational studies of penpulimab for 1L HCC and 1L NPC. To date, penpulimab is recommended by CSCO for the treatment of r/r cHL (Level I, 1A), 1L sq-NSCLC (Level II, 1A) and 2L or salvage treatment of r/m NPC (Level III, 2A). In addtion, penpulimab's BLA of 3L NPC is currently under US FDA review.

Additionally, Akeso out-licensed, pucotenlimab, a PD-1 mAb to Lepu Biopharma (2157 HK). The drug has been approved by the NMPA for 2L MSI-H/dMMR solid tumors in Jul 2022 and 2L melanoma in Sep 2022. Akeso will receive milestone payment and 7% sales royalty from the sales of pucotenlimab.

Figure 41: Approved PD-(L)1 drugs in China (as of Jul 2023)

Company	Drug	Target	Indication	Regimen	Approval date	NRDL coverage	NRDL valid period
BMS	Nivolumab	PD-1	2L NSCLC	Mono	2018/6/15	N	
			2L HNSCC	Mono	2019/9/30	N	
			3L GC	Mono	2020/3/13	N	
			1L Mesothelioma	+Ipilimumab	2021/6/10	N	
			1L GC	+Chemo	2021/8/30	N	
			1L ESCC	+Chemo	2022/6/23	N	
			Adj. ESCC	Mono	2022/6/23	N	
			Adj. UC	Mono	2023/1/18	N	
Merck	Pembrolizumab	PD-1	2L Melanoma	Mono	2018/7/26	N	
			1L nsq-NSCLC	+Chemo	2019/4/2	N	
			1L sq-NSCLC	+Chemo	2019/11/26	N	
			1L PD-L1+ NSCLC	Mono	2019/9/30	N	
			2L ESCC	Mono	2020/6/19	N	
			1L HNSCC	Mono	2020/12/11	N	
			1L CRC	Mono	2021/6/15	N	
			1L ESCC	+Chemo	2021/9/7	N	
			2L HCC	Mono	2022/10/10	N	
			Adj. TNBC	Mono	2022/11/8	N	
Astrazeneca	Durvalumab	PD-L1	Stage III unresectable NSCLC	Mono	2019/12/6	N	
			1L ES-SCLC	+Chemo	2021/7/19	N	
Roche	Atezolizumab	PD-L1	1L ES-SCLC	+Chemo	2020/2/13	N	
			1L HCC	+bevacizumab	2020/10/29	N	
			1L NSCLC	Mono	2021/4/29	N	
			1L NSCLC	+Chemo	2021/6/23	N	
			Adj. Stage II/IIIA NSCLC	Mono	2022/3/16	N	
Junshi	Toripalimab	PD-1	2L Melanoma	Mono	2018/12/21	Y	2022.01.01-2023.12.31
			2L NPC	Mono	2021/2/19	Y	
			2L UC	Mono	2021/4/12	Y	
			1L NPC	+Chemo	2021/11/29	N	

			1L ESCC	+Chemo	2022/5/12	N	
			1L nsq-NSCLC	+Chemo	2022/9/14	N	
Innovent	Sintilimab	PD-1	2L cHL	Mono	2018/12/24	Y	2023.03.01-
			1L nsq-NSCLC	+Chemo	2021/2/3	Y	2023.12.31
			1L sq-NSCLC	+Chemo	2021/6/3	Y	
			1L HCC	+bevacizumab	2021/6/27	Y	
			1L ESCC	+Chemo	2022/6/21	Y	
			1L GC	+Chemo	2022/6/24	Y	
			2L EGFRm nsq-NSCLC	+bevacizumab	2023/5/9	N	
Hengrui	Camrelizumab	PD-1	2L cHL	Mono	2019/6/3	Y	2023.03.01-
			2L HCC	Mono	2020/3/4	Y	2024.12.31
			1L nsq-NSCLC	+Chemo	2020/6/19	Y	
			2L ESCC	Mono	2020/6/19	Y	
			2L NPC	Mono	2021/4/29	Y	
			1L NPC	+Chemo	2021/6/10	Y	
			1L ESCC	+Chemo	2021/12/10	Y	
			1L sq-NSCLC	+Chemo	2021/12/10	Y	
			1L HCC	+apatinib	2023/1/31	N	
BeiGene	Tislelizumab	PD-1	2L cHL	Mono	2019/12/27	Y	2023.03.01-
			2L UC	Mono	2020/4/10	Y	2023.12.31
			1L sq-NSCLC	+Chemo	2021/1/13	Y	
			1L nsq-NSCLC	+Chemo	2021/6/23	Y	
			2L HCC	Mono	2021/6/23	Y	
			2L NSCLC	Mono	2021/12/31	Y	
			MSI-H/dMMR	Mono	2022/3/8	Y	
			2L ESCC	Mono	2022/4/8	Y	
			1L NPC	+Chemo	2022/6/7	Y	
			1L GC (PD-L1+)	+Chemo	2023/2/24	N	
			1L ESCC	+Chemo	2023/5/23	N	
Gloria/ Wuxi Bio	Zimberelimab	PD-1	2L cHL	Mono	2021/8/30	N	
			2L CC	Mono	2023/7/4	N	
Akeso/ CTTQ	Penpulimab	PD-1	3L cHL	Mono	2021/8/5	N	
			1L sq-NSCLC	+Chemo	2023/1/16	N	
Alphamab/ 3D Med	Envafolimab	PD-L1	2L MSI-H/dMMR CRC and other tumors	Mono	2021/11/25	N	
CStone	Sugemalimab	PD-L1	1L NSCLC	+Chemo	2021/12/21	N	
			Adj. Stage III NSCLC	Mono	2022/5/31	N	
Henlius	Serplulimab	PD-1	2L MSI-H solid tumors	Mono	2022/3/22	N	
			1L sq-NSCLC	+Chemo	2022/10/25	N	
			1L ES-SCLC	+Chemo	2023/1/17	N	
Lepu Biopharma	Pucotenlimab	PD-1	2L MSI-H/dMMR solid tumors	Mono	2022/7/22	N	
			2L melanoma	Mono	2022/9/29	N	
Hengrui	Adebrelimab	PD-L1	1L ES-SCLC	+Chemo	2023/3/3	N	

Source: Pharmcube, CMBIGM

Near term commercialization of non-oncology pipelines

Akeso has established a diversified non-oncology pipeline covering autoimmune and metabolic diseases. Akeso's pipelines in autoimmune diseases consist of ebdarokimab (AK101, IL-12/IL-23), gumokimab (AK111, IL-17) and manfidokimab (AK120, IL-4R). AK101 is potentially the first domestic IL-12/IL-23 mAb, which is currently at Ph3 development in China. In the area of metabolic diseases, the Company also has innovative drug candidates including ebronucimab (AK102, PCSK9), which is in collaboration under a joint venture agreement with Dawnrays Pharma. AK102 is one of the most advanced PCSK9 mAb currently at Ph3 development in China with BLA filing accepted by CDE in Jun 2023.

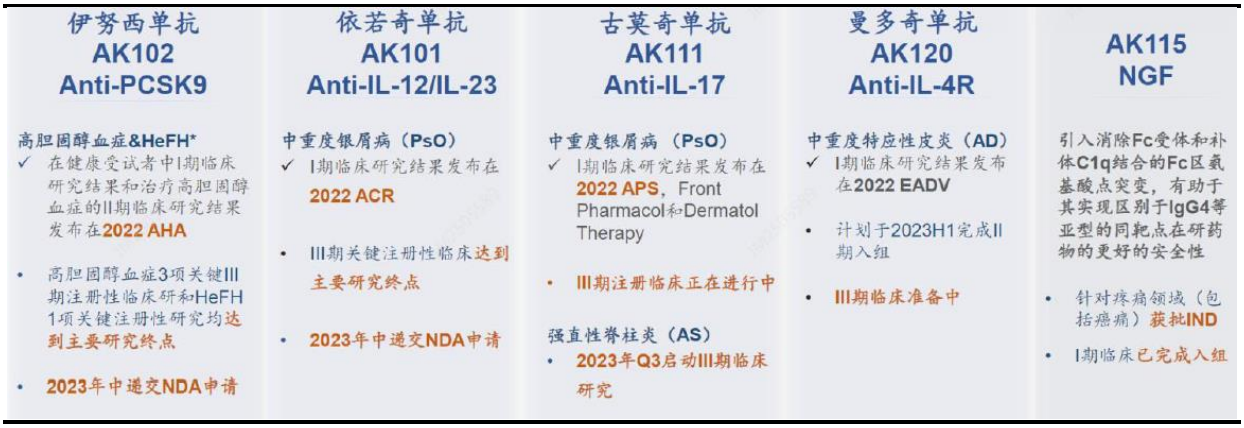
Figure 42: Akeso's non-oncology pipelines

Auto-immunity/Metabolism			Current Status			
Product (Target)	Mono/Combo Therapy	Indication	Phase Ia	Phase Ib/II	Pivotal/Phase III	NDA Submitted
Ebronucimab AK102 (PCSK9)	+ Statin/Ezetimibe	Primary hypercholesterolemia and mixed hyperlipidemia			Reached endpoint	
	+ Statin/Ezetimibe	HeFH			Reached endpoint	
Ebdarokimab AK101 (IL-12/IL-23)	Mono	Moderate-to-severe psoriasis			Reached endpoint	
	Mono	Moderate-to-severe ulcerative colitis				
AK111 (IL-17)	Mono	Moderate-to-severe psoriasis				
	Mono	Ankylosing spondylitis				
AK120 (IL-4R)	Mono	Moderate-to-severe atopic dermatitis				

Global Registrational Trials

Source: Company data, CMBIGM.

Figure 43: Progress of Akeso's non-oncology pipelines (as of Mar 2023)

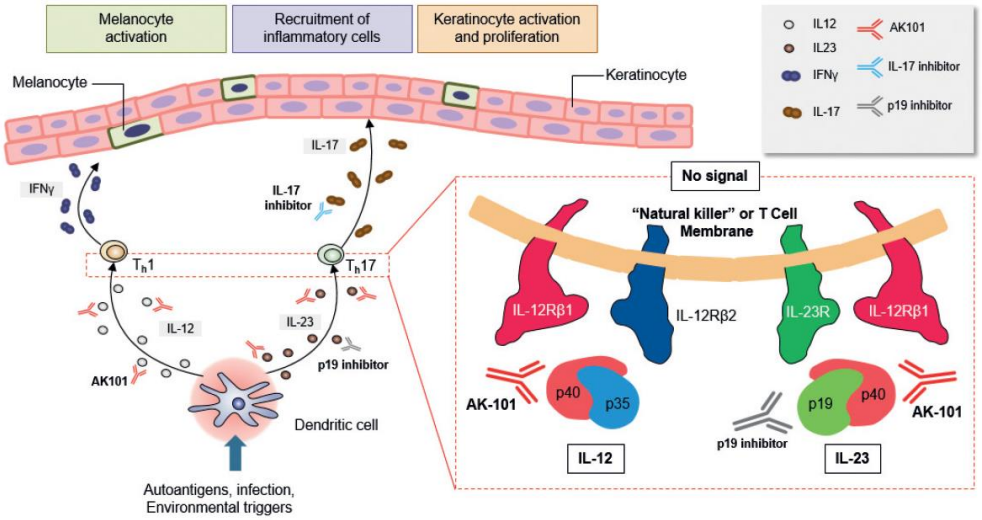


Source: Company data, annual report slides in Mar 2023, CMBIGM.

Ebdarokimab (AK101, IL-12/IL-23), potentially the first domestic IL-12/IL-23 mAb

Cytokines IL-12 and IL-23 have been implicated as important contributors to the chronic inflammation. IL-12 and IL-23 promote the differentiation of naïve Th0 cells into Th1 and Th17 cells responsible for initiating an inflammatory response. Internally developed by Akeso, ebdarokimab (AK101) is a human monoclonal antibody, which targeted against the common p40 subunit shared by IL-12 and IL-23 to block their biological activities. Johnson & Johnson's ustekinumab (Stelara), which is the global FIC IL12/23 antibody, has been widely used as one of the major treatments for psoriasis, psoriatic arthritis, Crohn's disease, and ulcerative colitis. In FY22, ustekinumab realized US$9.7bn revenue from global sales.

Figure 44: MoA of AK101 (IL12/23 antibody)



Source: Company data, CMBIGM

AK101, currently at Ph3 stage of development, has the potential to become the first local mAb targeting IL-12/IL-23 in China. The Company expects AK101 to deliver similar or potentially better efficacy over ustekinumab while offer a differentiated safety profile versus anti-TNF-a agents.

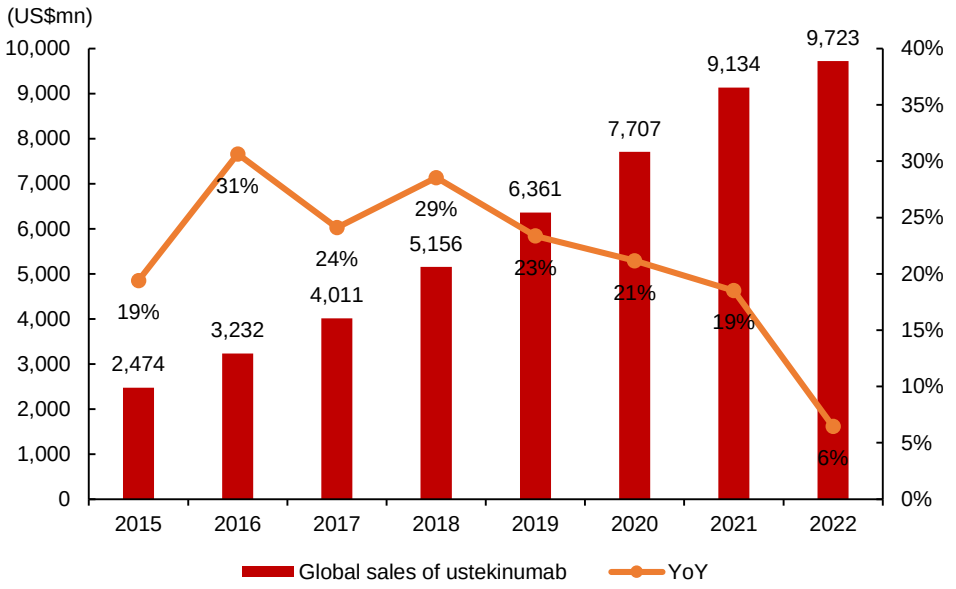
The major targeted indication of AK101 is psoriasis, of which plaque psoriasis is the most common subtype, accounting for 80-90% of all the psoriasis cases. Traditional biologic therapy for psoriasis includes TNF-a targeted mAbs, such as etanercept, infliximab, adalimumab, and certolizumab pegol. However, these therapies do not produce effective clinical responses in all patients and may be associated with serious infection. The next generation systematic therapies are commonly interleukin (IL) targeted, including IL-12/IL-23, IL-23, IL-17, IL-36 targeted medicines.

Figure 45: Next generation systematic therapies for psoriasis and other autoimmune diseases

Target	Drug name	China approved indications	Initial China approval time	US approved indications	Initial US approval time	2022 global sales	China NRDL	NRDL period	China annual cost (RMB)
Biologic therapies									
IL-12/IL-23	ustekinumab	PP, CD	2017	PP, PsA, DC, UC	2009	US$9,723mn	Y	2022.01.01-2023.12.31	21,590
IL-17	secukinumab	PP, AS	2019	PP, PsA, AS, etc	2015	US$4,788mn	Y	2023.03.01-2024.12.31	27,840
	ixekizumab	PP, AS	2019	PP, PsA, AS, etc	2016	US$2,482mn	Y	2022.01.01-2023.12.31	20,706
	brodalumab	PP	2020	PP	2017	-	N	-	-
IL-23	guselkumab	PP	2019	PP, PsA	2017	US$2,668mn	Y	2023.03.01-2024.12.31	31,997
	tildrakizumab	-	-	PP	2018	US$315mn	-	-	-
IL-36	spesolimab	GPP	2022	GPP	2022	-	-	-	-
Small molecule targeted drugs									
PDE4	apremilast	PP	2021	PP, PsA, etc	2014	US$2,288mn	Y	2023.03.01-2024.12.31	11,204
JAK1-3	tofacitinib	PsA, RA, AS	2017	PsA, AS, UC, RA, etc	2012	US$1,796mn	Y	2023.03.01-2024.12.31	11,952
	upadacitinib	PsA, RA, AD	2022	PsA, AS, UC, RA, etc	2019	US$2,522mn	Y	2023.03.01-2024.12.31	25,032
TYK2	deucravacitinib	-	-	PP	2022	US$8mn	-	-	-

Source: Company data, CMBIGM. Notes: TNF-a targeted mAbs, as traditional biologic therapy, are not included in the table. PP, plaque psoriasis; PsA, psoriatic arthritis; DC, Crohn's disease; UC, ulcerative colitis; AS, ankylosing spondylitis; RA, rheumatic arthritis; AD, atopic dermatitis; GPP, generalized pustular psoriasis.

Figure 46: Global sales of ustekinumab



Source: Company data, CMBIGM

Ustekinumab is currently the only approved IL-12/IL-23 mAb across the globe. It has been approved in China for the treatment of PP and CD, and approved in the US for PP, PsA, DC, and UC. Ustekinumab realized US$9.7bn global sales in 2022, showing the large market potential of IL-12/IL-23 mAb. In China, several ustekinumab biosimilars are under Ph3 development, including the relevant biosimilar candidates developed by CSPC, Huadong Medicine & Qyuns and Bio-Thera. With the same treatment target, AK101 has the potential to become the first domestic IL-12/IL-23 mAb in China. Akeso is currently evaluating AK101 in two Ph3 trials for the treatment of PP (NCT05120297, NCT05509361) which has met the primary endpoint with BLA filing targeted in 3Q23. AK101 is also under Ph1/2 trials for UC (link).

Figure 47: Global late-stage IL-12/IL-23 biologics

Drug Name	Target	Company	China Highest Phase	Global Highest Phase	Indication
ustekinumab	IL-12/IL-23	Mitsubishi, J&J, BMS	Approved	Approved	PP, PsA, DC, UC, etc
ustekinumab biosimilar	IL-12/IL-23	Alvotech, Fuji Pharma	IND filed	BLA filed	similar to the reference
ebdarokimab	IL-12/IL-23	Akeso	Phase III	Phase III	PP, UC, etc
ustekinumab biosimilar	IL-12/IL-23	Pharmapark, Hikma, Bio-Thera	Phase III	Phase III	similar to the reference
ustekinumab biosimilar	IL-12/IL-23	CSPC Pharmaceutical	Phase III	Phase III	similar to the reference
ustekinumab biosimilar	IL-12/IL-23	Huadong Medicine, Qyuns	Phase III	Phase III	similar to the reference
ustekinumab biosimilar	IL-12/IL-23	Formycon	No Application	Phase III	similar to the reference
ustekinumab biosimilar	IL-12/IL-23	Biocon	No Application	Phase III	similar to the reference
ustekinumab biosimilar	IL-12/IL-23	Amgen	No Application	Phase III	similar to the reference
ustekinumab biosimilar	IL-12/IL-23	Rani Therapeutics, Celltrion	No Application	Phase III	similar to the reference
ustekinumab biosimilar	IL-12/IL-23	Samsung BioLogics	No Application	Phase III	similar to the reference
ustekinumab biosimilar	IL-12/IL-23	Meiji Seika, Dong-A, Intas	No Application	Phase III	similar to the reference

Source: Pharmcube, CMBIGM. Notes: data retrieved from Pharmcube as of Jun 2023

Figure 48: Global late-stage IL-17 biologics

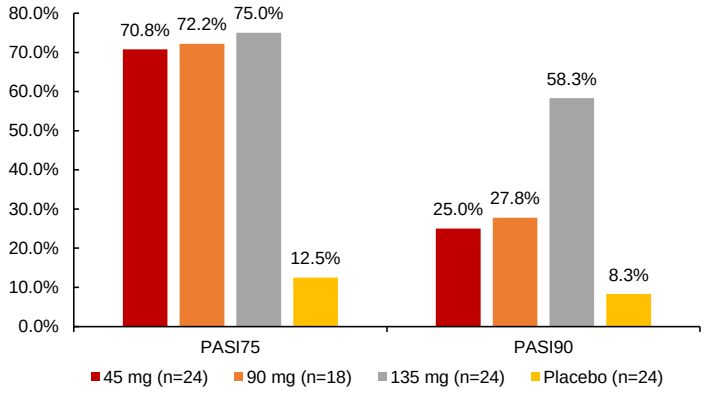
Drug Name	Target	Company	China Highest Phase	Global Highest Phase
ixekizumab	IL-17A	Eli Lilly	Approved	Approved
secukinumab	IL-17A	Novartis	Approved	Approved
netakimab	IL-17A	SPH-Project Biocad	Phase III	Approved
bimekizumab	IL-17A,IL-17F	UCB	BLA filed (in Apr 2023)	Approved
vunakizumab	IL-17A	Hengrui Medicine	BLA filed (in Apr 2023)	BLA filed
xeligekimab	IL-17A	Genrix Bio	BLA filed (in Mar 2023)	BLA filed
SSGJ-608	IL-17A	Guojian Pharmaceutical	Phase III	No Application
gumokimab	IL-17A	Akeso Biopharma	Phase III	Phase I
secukinumab biosimilar	IL-17A	Bio-Thera Solutions	Phase III	Phase III
izokibep	IL-17A	ACELYRIN, Affibody, Inmagene	Phase II	Phase II/III
tibulizumab	BAFF,IL-17	Zura Bio, Eli Lilly	No Application	Phase II/III
HB0017	IL-17A	Huabo Biopharm	Phase II	Phase II
JS005	IL-17A	Junshi Biosciences	Phase II	Phase II
QX002N	IL-17A	Palisade Bio, Qyuns Therapeutics	Phase II	Phase II
XKH004	IL-17A,IL-17F	Livzon Pharmaceutical, Kanova	Phase II	Phase II
CJM112	IL-17A	Novartis	IND filed	Phase II
CNTO6785	IL-17A	J&J, Fontacea, MorphoSys	IND filed	Phase II
MOR106	IL-17C	Galapagos, MorphoSys, Novartis	No Application	Phase II
S011806	IL-17A,IL-17F	DICE Therapeutics	No Application	Phase II
remtolumab	IL-17A,TNF-α	AbbVie	No Application	Phase II
sonelokinab	IL-17F,IL-17A,albumin	MoonLake, Sanofi, Merck, Avillion	No Application	Phase II

Source: Pharmcube, CMBIGM. Note: data retrieved from Pharmcube as of Jun 2023

AK101 delivered better efficacy signals over ustekinumab at early clinical assessment

In a Ph1/2 study of AK101 in moderate to severe psoriasis (link), 96 subjects with moderate to severe psoriasis were enrolled and received SC administration of either AK101 (n=72) or placebo (n=24). The average of baseline PASI score for AK101 groups was 25.9 versus 24.3 for the placebo group. Each subject had received AK101 or placebo SC injection at Week 0 and Week 4. More subjects in the AK101 groups achieved PASI75 at Week 12 than those in the placebo group (70.8%, 72.2% and 75.0% for AK101 at the dosage of 45 mg, 90 mg, and 135 mg vs 12.5% for placebo). The proportion of patients achieving PASI90 at Week 12 was significantly higher in the AK101 groups (25.0%, 27.8% and 58.3% for AK101 at the dosage of 45 mg, 90 mg, and 135 mg vs 8.3% for placebo group).

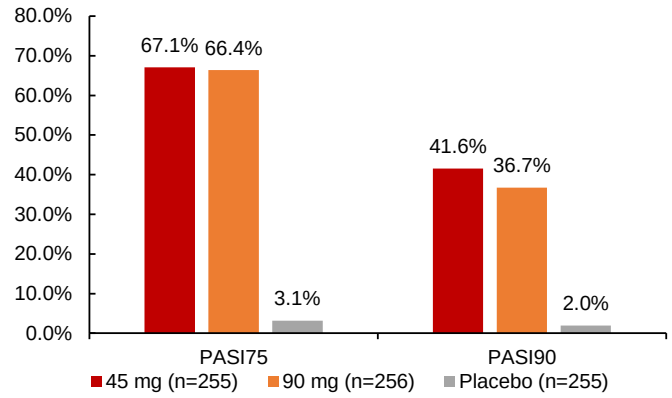
Figure 49: PASI75 and PASI90 response rates of AK101 at Week 12



Source: Company data, CMBIGM. Note: PASI75 / PASI90 mean at least 75% / 90% decrease in Psoriasis Area and Severity Index compared with the baseline.

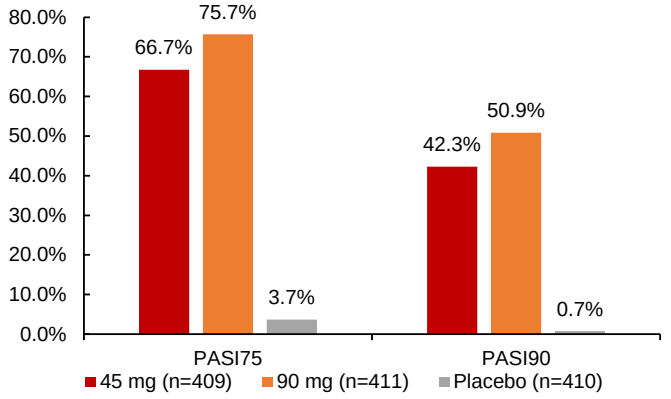
In the two Ph3 trials (PHOENIX 1 and PHOENIX 2), at week 12, ustekinumab demonstrated PASI75 response rates at the range of 66.4%-75.7%, and PASI90 response rates at the range of 41.6%-50.9%. As cross-trial comparisons, AK101 demonstrated a similar PASI75 results for moderate to severe psoriasis patients compared to ustekinumab.

Figure 50: PASI75 and PASI90 response rates of ustekinumab at Week 12 (PHOENIX 1 study)



Source: J&J (link), CMBIGM estimates

Figure 51: PASI75 and PASI90 response rates of ustekinumab at Week 12 (PHOENIX 2 study)



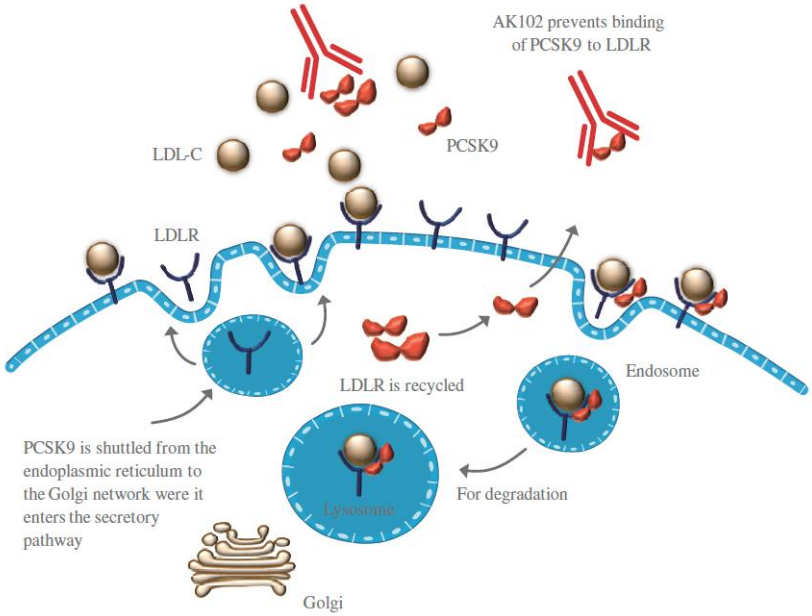
Source: J&J (link), CMBIGM estimates

AK101 was generally well-tolerated as observed in its Ph1/2 trial. The most common drug-related AE included respiratory tract infection (50.0%), triglycerides elevation (23.6%) diarrhea (20.8%), ALT elevation (13.9%), and itching (12.5%).

Ebronucimab (AK102, PCSK9), approaching commercialization

Elevated low-density lipoprotein cholesterol (LDL-C) is a well-recognized risk factor for cardiovascular disease. PCSK9 binds to LDL receptors (LDL-R), triggering receptor degradation. Inhibiting PCSK9 activity results in lowering LDL-C levels and further reducing the risk of cardiovascular events. Ebronucimab (AK102), a PCSK9 mAb jointly developed by the Akeso and Dawnrays Pharma is among the most advanced domestically developed PCSK9 mAbs in China. AK102 is currently under Ph3 stage of clinical development for the treatment of primary hypercholesterolemia and mixed hyperlipidemia, including HoFH, HeFH and hypercholesterolemia patients with atherosclerosis cardiovascular diseases.

Figure 52: MoA of AK102 (PCSK9 antibody)



Source: Company data, CMBIGM

In Nov 2022, Akeso announced that a Ph3 trial of AK102 for the treatment of primary hypercholesterolemia (including HeFH) and mixed hyperlipidemia met the primary endpoint. The results were released in May 2023 at the EAS Congress (link). In Jun 2023, NMPA has accepted the BLA of AK102 for two indications, including 1) primary hypercholesterolemia and mixed hyperlipidemia, and 2) heterozygous familial hypercholesterolemia (HeFH).

Oral-administrated statins (他汀类药物) medicines are first recommended therapies for the treatment of hypercholesterolemia, and are very cheap because of the volume-based procurement of generic drugs in China. Zetia (ezetimib, 依折麦布), an inhibitor of cholesterol absorption, is usually recommended in combination with stains to reduce cholesterol. Nevertheless, PCSK9 mAbs are usually adopted in combinations with stains, or after stains/zetia intolerance or dissatisfaction, especially for high-risk patients. In addition, new types of drugs are at late-stage of clinical development, i.e. siRNA therapies with long dosing interval and small molecular PCSK9 therapies administrated orally.

Figure 53: Approved PCSK9 therapies globally

Drug	Company	MoA	Initial US approval	Initial China approval	2021 sales (US$mn)	2022 sales (US$mn)	China NRDL	NRDL period	China annual price (RMB)	US annual price (US$)	Dosing cycle
evolocumab	Astellas Pharma, Amgen	PCSK9	2015/8	2018/7	1,117	1,296	Y	2022.01-2023.12	10,217	6,606	Q4W, SC*
alirocumab	Regeneron, Sanofi	PCSK9	2015/7	2019/12	421	467	Y	2022.01-2023.12	7,344	5,800	Q2W, SC
inclisiran	Novartis, Alnylam	ASGPR, siRNA	2021/12	Not approved yet	12	112	-	-	-	6,950	Q24W, SC

Source: Company data, CMBIGM. Notes: SC means subcutaneous injection. Inclisiran filed BLA in China in Nov 2022.

Competition of PCSK9 antibodies could be fierce in China. Evolocumab from Amgen and alirocumab from Regeneron/Sanofi, have already marketed in China for several years. In addition, tafolecimab from Innovent and inclisiran from Novartis have submitted NDAs in China in Jun 2022 and Nov 2022, respectively. Junshi and Hengrui recently also filed the NDA in China for their PCSK9 drug candidates. Several other PCSK9 antibodies are also at late-stage clinical development in China.

Figure 54: Late-stage PCSK9 drug candidates in China

Drug candidate	Company	Indications	Global stage	China stage	Best clinical data highlights
tafolecimab	Innovent Biologics, Adimab	primary hypercholesterolemia (including HeFH, non-FH)	-	BLA Filed in Jun 2022	met primary endpoint; BLA filed. non-FH: -65.0% LDL-C reduction at Week 48 (link); HeFH: -61.9% LDL-C reduction at Week 12 (link); hypercholesterolemia including non-FH and HeFH: -63.0% LDL-C reduction at Week 12 (link)
		mixed dyslipidemia	-	BLA Filed in Jun 2022	
		HoFH	-	Ph2/3	
AK102 (ebronucimab)	Kangrong Dongfang or (AD Pharmas) *	primary hypercholesterolemia	-	BLA Filed in Jun 2023	met primary endpoint; BLA filed hyperlipidemia: -60.4% LDL-C reduction at Week 12 (link)
		mixed dyslipidemia	-	BLA Filed in Jun 2023	
		HeFH	-	BLA Filed in Jun 2023	
		HoFH	-	Ph2	
ongericimab	Junshi Biosciences	hypercholesterolemia	-	BLA Filed in Apr 2023	met primary endpoint, data to be released (link1, link2)
		mixed dyslipidemia	-	BLA Filed in Apr 2023	
		HeFH	-	BLA Filed in Apr 2023	
		HoFH	-	BLA Filed in Apr 2023	
recaticimab	Hengrui Medicine	hypercholesterolemia	-	BLA Filed in Jun 2023	Hypercholesterolemia: -59.51% LDL-C reduction (link)
		mixed dyslipidemia	-	BLA Filed in Jun 2023	
		HeFH	-	BLA Filed in Jun 2023	
		HoFH	-	BLA Filed in Jun 2023	
lerodalcibep	Lib Therapeutics	hypercholesterolemia, cardiovascular disease, cerebrovascular disease (CVD)	Ph3	-	-71% LDL-C reduction (link)
		HoFH	Ph3	-	

Source: Company data, CMBIGM. Notes: Kangrong Dongfang or named AD Pharmaceuticals is a joint venture, owned 65% by Akeso and 35% by Dawnrays Biotechnology.

Figure 55: Clinical trials of AK102 (anti-PCSK9 antibody)

Trial ID	Trial stage	Indications	Patient number	Dose	Primary endpoint	Notes
NCT05255094	Ph3	primary hypercholesterolemia and mixed hyperlipidemia, excluding HoFH	450 pts	Q2W,Q4W	LDL-C change at week 12	Met primary end point; China BLA filed
NCT05255458	Ph3	primary hypercholesterolemia and mixed hyperlipidemia, excluding HoFH	122 pts	-	LDL-C change at week 52, long-term study	Trial close to be completed
NCT05260411	Ph3	primary hypercholesterolemia and mixed hyperlipidemia, excluding HoFH	240 pts	Q6W	LDL-C change at week 12	Trial close to be completed
NCT04173403	Ph2	hypercholesterolemia	200 pts	Q4W, Q2W	LDL-C change at week 52, long-term study	
NCT03933293	Ph2	HoFH	59 pts	Q4W	LDL-C change at week 12	
NCT04358432	Ph2	Hypercholesterolemia pts at very high or high risk of cardiovascular disease	260 pts	Q4W, Q2W	LDL-C change at week 12	
NCT04173793	Ph2	HeFH	168 pts	Q4W, Q2W	LDL-C change at week 12	

Source: Company data, CMBIGM

Strong clinical results to support the BLA of AK102

The results of a Ph2 study (NCT04358432) of AK102 in hypercholesterolemia patients at very high or high risk of cardiovascular disease were released in Oct 2022 (link). The study was a randomized, double-blind, placebo-controlled study. A total of 260 Chinese patients with hyperlipidemia were randomized to receive ebronucimab 450mg Q4W, 300mg Q4W, 150mg Q2W, 75mg Q2W or matching placebo via subcutaneous injection. The patients received treatment for up to 12 weeks (day 85).

In the Ph2 study, AK102 showed significant and dose-dependent LDL-C reductions from baseline. At week 12, the mean reductions in LDL-C were 65.48 %, 48.14%, 63.69% and 37.39% for 450mg Q4W,

300mg Q4W, 150mg Q2W and 75mg Q2W dose groups, respectively. Patients in the 450mg Q4W and 150mg Q2W groups achieved higher and more sustained LDL-C reduction compared with other dose groups. Similar trend was observed in serum levels of total cholesterol, apolipoprotein B, lipoprotien (a). On the safety side, a total of 49.6% (130/262) patients experienced at least 1 TEAE, 51.9% in AK102 groups and 40.4% in the placebo group. No adverse events were apparently dose dependent with AK102. The overall incidence of SAEs was 3.4 % (9/262). Overall, AK102 was generally safe and well-tolerated in Chinese patients with hyperlipidemia.

The Ph3 trials of AK102 for the treatment of primary hypercholesterolemia (including HeFH) and mixed hyperlipidemia met the primary endpoint, and the results were recently released at the EAS 2023 Congress (link). AK102 450mg Q4W and 150mg Q2W treatment groups achieved significant reduction in serum levels of LDL-C and other lipids. In the 450mg Q4W group, the level of LDL-C reduced by 64.9% from baseline or 59.1% compared to the placebo group, and in the 150mg Q2W group, the level of LDL-C reduced by 66.2% from baseline or 60.4% compared to the placebo group, comparable to other PCSK9 mAbs in the market.

Financial Analysis

Produce sales to ramp up fast

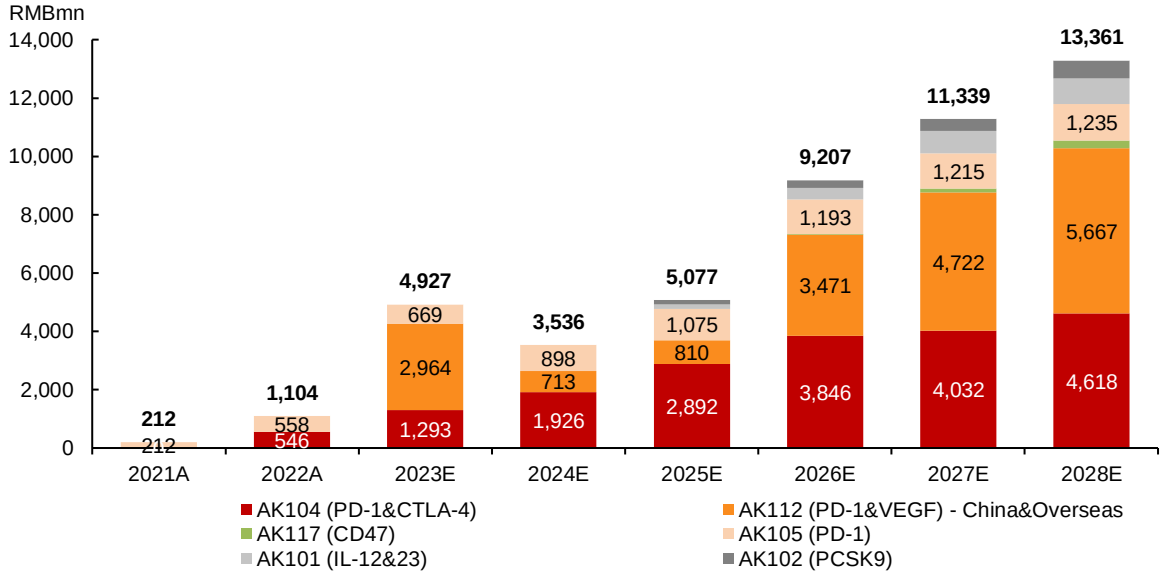
We expect Akeso's product sales to ramp up quickly and AK104 and AK112 will be the major revenue drivers of the Company in the long run. We estimate Akeso's total risk-adjusted sales from products and licenses of RMB4,927mn/ RMB3,536mn/ RMB5,077mn in FY23E/ 24E/ 25E, respectively.

Figure 56: Risk-adjusted sales and license income forecasts

YE Dec 31 (RMB mn)	2021A	2022A	2023E	2024E	2025E	2026E	2027E	2028E
Total product sales	**212**	**1,104**	**1,962**	**3,013**	**5,077**	**7,606**	**9,548**	**11,420**
AK104 (PD-1&CTLA-4)	0	546	1,293	1,926	2,892	3,846	4,032	4,618
AK112 (PD-1&VEGF) - China	0	0	0	190	810	1,870	2,931	3,726
AK117 (CD47)	0	0	0	0	0	20	141	264
AK105 (PD-1)	212	558	669	898	1,075	1,193	1,215	1,235
AK101 (IL-12&23)	0	0	0	0	145	382	757	893
AK102 (PCSK9)	0	0	0	0	156	265	412	607
Other products	0	0	0	0	0	30	60	78
License income (incl. sales royalty)	**0**	**0**	**2,964**	**523**	**0**	**1,601**	**1,791**	**1,941**
AK112 (PD-1&VEGF) - Overseas	0	0	2,964	523	0	1,601	1,791	1,941
Total sales from products and license	**212**	**1,104**	**4,927**	**3,536**	**5,077**	**9,207**	**11,339**	**13,361**
YoY growth		*422%*	*346%*	*-28%*	*44%*	*81%*	*23%*	*18%*

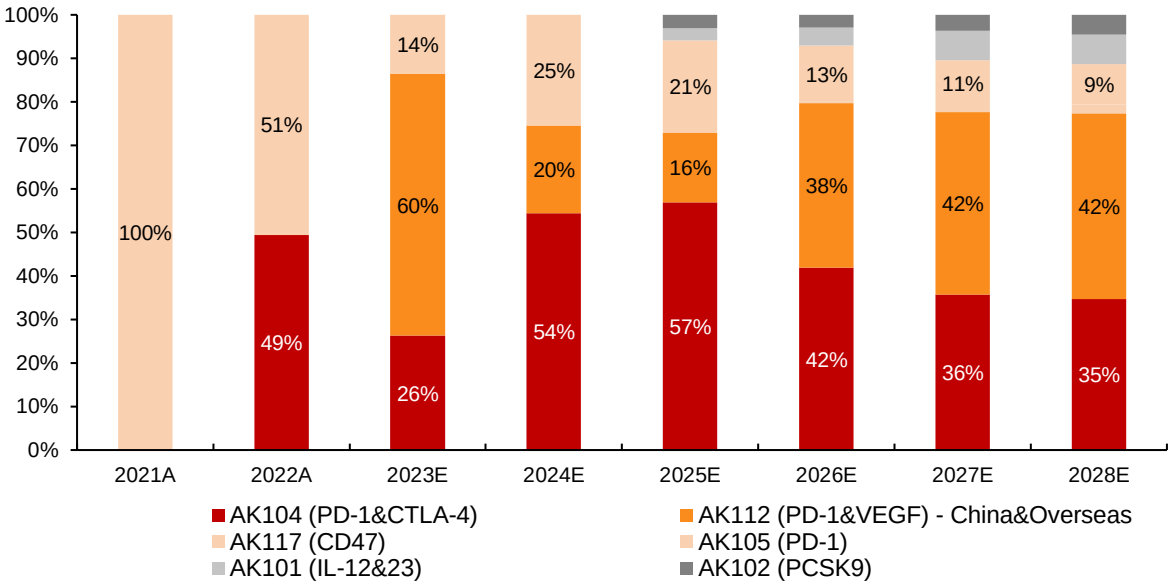
Source: Company data, CMBIGM estimates

Figure 57: Risk-adjusted sales and license income forecasts



Source: Company data, CMBIGM estimates

Figure 58: Risk-adjusted sales and license income breakdown



Source: Company data, CMBIGM estimates

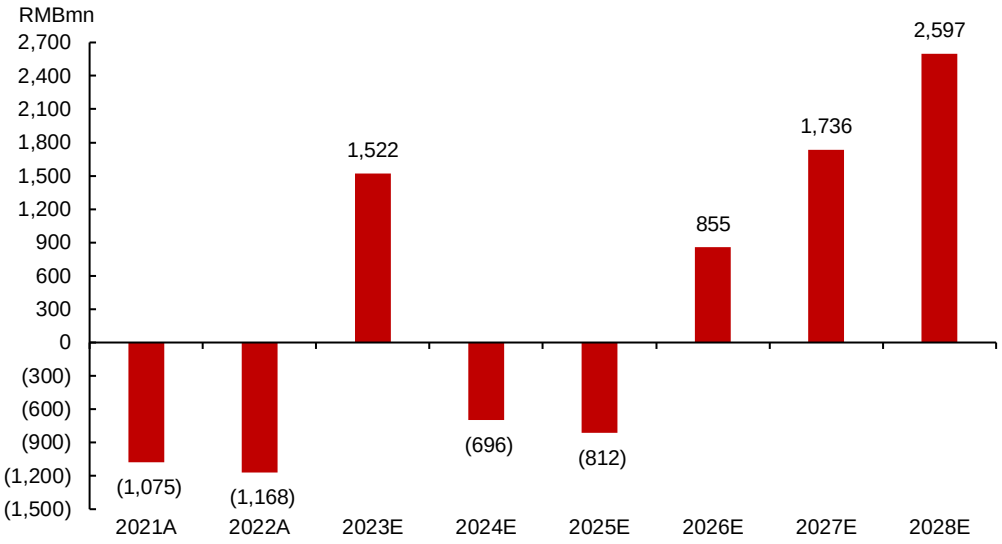
Akeso recorded attributable net loss of RMB1,075mn/ RMB1,168mn in FY21A/ 22A. In 2023, considering the upfront payment of US$500mn from Summit related to the deal of AK112, we expect the Company to record net income of RMB1,522mn in FY23E. We expect the Company to incur net losses of RMB696mn/ RMB812mn in FY24E/ 25E, and to turn profitable in FY26E.

Figure 59: P&L forecasts

YE Dec 31 (RMB mn)	2021A	2022A	2023E	2024E	2025E	2026E	2027E	2028E
Total sales from products and license	**212**	**1,104**	**4,927**	**3,536**	**5,077**	**9,207**	**11,339**	**13,361**
Less: Distribution cost	(115)	(271)	(431)	(524)	(642)	(678)	(685)	(706)
Revenue	**226**	**838**	**4,496**	**3,012**	**4,435**	**8,529**	**10,653**	**12,655**
YoY		*271%*	*437%*	*-33%*	*47%*	*92%*	*25%*	*19%*
Cost of sales	(31)	(94)	(294)	(512)	(762)	(1,445)	(1,766)	(2,056)
% of revenue	*14%*	*11%*	*7%*	*17%*	*17%*	*17%*	*17%*	*16%*
Gross profit	**194**	**744**	**4,201**	**2,500**	**3,673**	**7,084**	**8,887**	**10,600**
GPM	*86%*	*89%*	*93%*	*83%*	*83%*	*83%*	*83%*	*84%*
R&D expenses	(1,123)	(1,323)	(1,500)	(1,650)	(1,815)	(2,110)	(2,172)	(2,369)
% of revenue	*498%*	*158%*	*33%*	*55%*	*41%*	*25%*	*20%*	*19%*
Selling and marketing expenses	(179)	(553)	(832)	(1,236)	(2,007)	(2,857)	(3,337)	(3,671)
% of revenue	*79%*	*66%*	*19%*	*41%*	*45%*	*34%*	*31%*	*29%*
Administrative expenses	(244)	(199)	(334)	(483)	(763)	(1,066)	(1,243)	(1,373)
% of revenue	*108%*	*24%*	*7%*	*16%*	*17%*	*13%*	*12%*	*11%*
Profit/(loss) before tax	**(1,258)**	**(1,422)**	**1,614**	**(796)**	**(862)**	**1,095**	**2,198**	**3,270**
% of revenue	*-558%*	*-170%*	*36%*	*-26%*	*-19%*	*13%*	*21%*	*26%*
Income tax expense	0	0	(242)	0	0	(164)	(330)	(491)
Profit/(loss) for the year	**(1,258)**	**(1,422)**	**1,372**	**(796)**	**(862)**	**931**	**1,868**	**2,780**
Non-controlling interests	(183)	(254)	(150)	(100)	(50)	75	132	182
Attributable net profit/(loss)	**(1,075)**	**(1,168)**	**1,522**	**(696)**	**(812)**	**855**	**1,736**	**2,597**
NMP	*-476%*	*-139%*	*34%*	*-23%*	*-18%*	*10%*	*16%*	*21%*

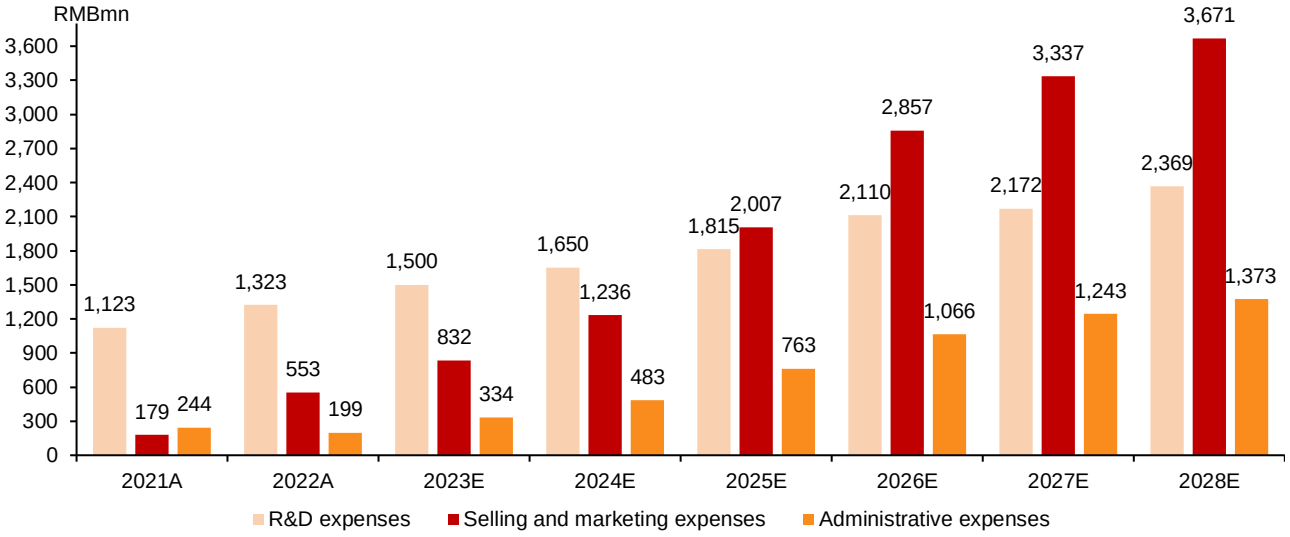
Source: Company data, CMBIGM estimates

Figure 60: P&L forecasts



Source: Company data, CMBIGM estimates

Figure 61: Expenses forecasts



Source: Company data, CMBIGM estimates

Valuation

Initiate at BUY with TP of HK$52.65

We derive our target price of HK$52.65 based on a DCF valuation (WACC: 10.60%, terminal growth rate: 3.0%).

Figure 62: Risk-adjusted DCF valuation

DCF Valuation (RMB mn)	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E
EBIT	**1,644**	**(759)**	**(802)**	**1,159**	**2,244**	**3,296**	**4,461**	**5,531**	**6,454**	**7,140**	**7,503**	**7,207**	**6,896**
Tax rate	*15%*	*0%*	*0%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*	*15%*
EBIT*(1-tax rate)	1,398	(759)	(802)	985	1,907	2,802	3,792	4,701	5,486	6,069	6,378	6,126	5,862
+ D&A	120	128	132	131	130	129	128	127	126	126	125	124	124
- Change in working capital	34	(132)	(357)	(335)	(319)	(301)	(233)	(72)	71	162	171	220	229
- Capex	(500)	(300)	(200)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)	(100)
FCFF	**1,052**	**(1,063)**	**(1,227)**	**681**	**1,618**	**2,530**	**3,587**	**4,656**	**5,583**	**6,256**	**6,574**	**6,371**	**6,114**
Terminal value													**82,890**
FCF + Terminal value	**1,052**	**(1,063)**	**(1,227)**	**681**	**1,618**	**2,530**	**3,587**	**4,656**	**5,583**	**6,256**	**6,574**	**6,371**	**89,004**

Present value of enterprise (RMB mn)	38,483
Net debt (RMB mn)	(1,130)
Non-controlling interests (RMB mn)	(238)
Equity value (RMB mn)	**39,851**
No. of shares (mn)	841
DCF per shares (RMB)	**47.38**
DCF per shares (HK$)	**52.65**
Terminal growth rate	**3.0%**
WACC	**10.60%**
Cost of Equity	13.5%
Cost of Debt	4.5%
Equity Beta	1.0
Risk Free Rate	3.5%
Market Risk Premium	10.0%
Target Debt to Asset ratio	30.0%
Effective Corporate Tax Rate	15.0%

Source: CMBIGM estimates

Figure 63: Sensitivity analysis (HK$)

	WACC				
Terminal growth rate	**9.60%**	**10.10%**	**10.60%**	**11.10%**	**11.60%**
4.0%	70.58	63.46	57.46	52.33	47.91
3.5%	66.64	60.30	54.88	50.21	46.15
3.0%	63.30	57.58	**52.65**	48.36	44.60
2.5%	60.43	55.22	50.69	46.72	43.21
2.0%	57.94	53.15	48.95	45.26	41.97

Source: CMBIGM estimates

Financial Statements

INCOME STATEMENT	2020A	2021A	2022A	2023E	2024E	2025E
YE 31 Dec (RMB mn)						
Revenue	**0**	**226**	**838**	**4,496**	**3,012**	**4,435**
Cost of goods sold	0	(31)	(94)	(294)	(512)	(762)
Gross profit	**0**	**194**	**744**	**4,201**	**2,500**	**3,673**
Operating expenses	**(1,313)**	**(1,442)**	**(2,122)**	**(2,528)**	**(3,229)**	**(4,453)**
Selling expense	0	(179)	(553)	(832)	(1,236)	(2,007)
Admin expense	(253)	(244)	(199)	(334)	(483)	(763)
R&D expense	(769)	(1,123)	(1,323)	(1,500)	(1,650)	(1,815)
Others	(291)	103	(48)	138	139	132
Operating profit	**(1,354)**	**(1,271)**	**(1,406)**	**1,644**	**(759)**	**(802)**
Net Interest income/(expense)	**(8)**	**(10)**	**(43)**	**(59)**	**(67)**	**(83)**
Pre-tax profit	**(1,321)**	**(1,258)**	**(1,422)**	**1,614**	**(796)**	**(862)**
Income tax	0	0	0	(242)	0	0
After tax profit	**(1,321)**	**(1,258)**	**(1,422)**	**1,372**	**(796)**	**(862)**
Minority interest	(144)	(183)	(254)	(150)	(100)	(50)
Net profit	**(1,177)**	**(1,075)**	**(1,168)**	**1,522**	**(696)**	**(812)**

BALANCE SHEET	2020A	2021A	2022A	2023E	2024E	2025E
YE 31 Dec (RMB mn)						
Current assets	**3,001**	**3,152**	**3,058**	**4,386**	**4,114**	**3,675**
Cash & equivalents	2,684	2,642	2,092	3,009	2,300	1,403
Account receivables	0	102	271	342	557	992
Inventories	61	197	342	681	904	927
Prepayment	144	212	157	157	157	157
Financial assets at FVTPL	110	0	196	196	196	196
Other current assets	2	0	0	0	0	0
Non-current assets	**855**	**1,654**	**2,437**	**2,818**	**2,990**	**3,058**
PP&E	608	1,353	2,000	2,390	2,572	2,650
Right-of-use assets	151	152	163	153	143	133
Intangibles	1	4	8	8	8	8
Financial assets at FVTPL	0	0	10	10	10	10
Other non-current assets	94	145	256	256	256	256
Total assets	**3,856**	**4,806**	**5,496**	**7,203**	**7,104**	**6,733**
Current liabilities	**170**	**656**	**1,361**	**1,697**	**1,893**	**1,885**
Short-term borrowings	14	46	446	446	446	446
Account payables	113	206	309	644	841	833
Other current liabilities	41	396	600	600	600	600
Lease liabilities	3	8	6	6	6	6
Non-current liabilities	**236**	**870**	**1,587**	**1,587**	**2,087**	**2,587**
Long-term borrowings	179	804	1,421	1,421	1,921	2,421
Deferred income	53	64	160	160	160	160
Other non-current liabilities	4	2	6	6	6	6
Total liabilities	**406**	**1,526**	**2,948**	**3,283**	**3,980**	**4,472**
Share capital	0	0	0	0	0	0
Other reserves	3,185	3,164	2,636	4,158	3,461	2,649
Total shareholders equity	**3,186**	**3,164**	**2,636**	**4,158**	**3,461**	**2,649**
Minority interest	265	116	(88)	(238)	(338)	(388)
Total equity and liabilities	**3,856**	**4,806**	**5,496**	**7,203**	**7,104**	**6,733**

CASH FLOW	2020A	2021A	2022A	2023E	2024E	2025E
YE 31 Dec (RMB mn)						
Operating						
Profit before taxation	**(1,321)**	**(1,258)**	**(1,422)**	**1,614**	**(796)**	**(862)**
Depreciation & amortization	22	58	106	120	128	132
Tax paid	0	0	0	(242)	0	0
Change in working capital	(1)	107	60	34	(132)	(357)
Others	682	92	16	(50)	(42)	(26)
Net cash from operations	**(618)**	**(1,001)**	**(1,240)**	**1,476**	**(842)**	**(1,114)**
Investing						
Capital expenditure	(444)	(712)	(776)	(500)	(300)	(200)
Net proceeds from disposal of short-term investments	(109)	120	(200)	0	0	0
Others	(3)	12	86	0	0	0
Net cash from investing	**(556)**	**(580)**	**(890)**	**(500)**	**(300)**	**(200)**
Financing						
Dividend paid	0	0	0	0	0	0
Net borrowings	37	645	1,005	0	500	500
Proceeds from share issues	2,636	978	495	0	0	0
Share repurchases	0	(52)	0	0	0	0
Others	206	15	(15)	(59)	(67)	(83)
Net cash from financing	**2,878**	**1,587**	**1,486**	**(59)**	**433**	**417**
Net change in cash						
Cash at the beginning of the year	1,186	2,684	2,642	2,092	3,009	2,300
Exchange difference	(206)	(49)	95	0	0	0
Cash at the end of the year	**2,684**	**2,642**	**2,092**	**3,009**	**2,300**	**1,403**

GROWTH	2020A	2021A	2022A	2023E	2024E	2025E
YE 31 Dec						
Revenue	na	na	271.3%	436.7%	(33.0%)	47.2%
Gross profit	na	na	282.5%	465.0%	(40.5%)	46.9%

PROFITABILITY	2020A	2021A	2022A	2023E	2024E	2025E
YE 31 Dec						
Gross profit margin	na	86.1%	88.8%	93.5%	83.0%	82.8%
Operating margin	na	(563.1%)	(167.9%)	36.6%	(25.2%)	(18.1%)
Return on equity (ROE)	(74.0%)	(33.9%)	(40.3%)	44.8%	(18.3%)	(26.6%)

GEARING/LIQUIDITY/ACTIVITIE	2020A	2021A	2022A	2023E	2024E	2025E
YE 31 Dec						
Current ratio (x)	17.7	4.8	2.2	2.6	2.2	1.9

VALUATION	2020A	2021A	2022A	2023E	2024E	2025E
YE 31 Dec						
P/E	na	na	na	18.2	na	na
P/B	4.6	10.2	6.6	7.1	8.9	12.3

Source: Company data, CMBIGM estimates. Note: The calculation of net cash includes financial assets.

Investment Risks

1) Failure of clinical development or regulatory approvals of drug candidates.

2) Intense competition of approved products both in China and overseas markets.

Appendix: Company Profile

Figure 64: Major shareholders

Shareholder	% of stake
XIA Yu (夏瑜)	12.69%
Shenzhen Capital Group	7.99%
LI Baiyong (李百勇)	6.50%
Green Court Capital	5.94%
Cantrust (Far East) Limited	5.87%
WANG Zhongmin Maxwell (王忠民)	5.62%

Source: Company financial report, CMBIGM. Note: as of Dec 2022.

Figure 65: Management profile

Name	Position
XIA Yu (夏瑜)	President and Chief Executive Officer
LI Baiyong (李百勇)	Executive Vice President and Chief Scientific Officer
WANG Zhongmin Maxwell (王忠民)	Senior Vice President, responsible for clinical operations, sourcing and legal affairs
XIA Yu (夏羽)	Senior Vice President, responsible for manufacturing, quality and regulatory affairs (brother of XIA Yu)
LEUNG Wai Yan (梁慧欣)	Company Secretary

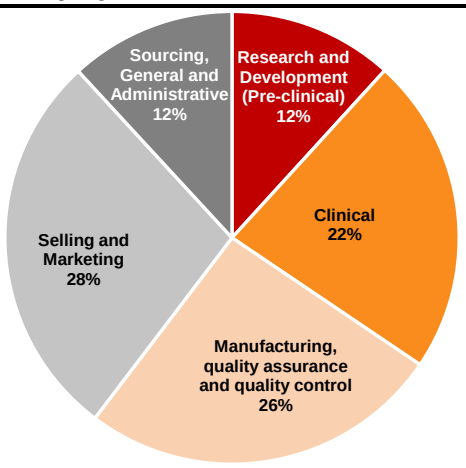
Source: Company data, CMBIGM

Figure 66: Employee structure

Function	# of staff	% of Total
Research and Development (Pre-clinical)	275	12%
Clinical	532	23%
Manufacturing, quality assurance and quality control	605	26%
Selling and Marketing	652	28%
Sourcing, General and Administrative	277	12%
Total	**2,341**	**100%**

Source: Company annual report (as of Dec 2022), CMBIGM

Figure 67: Employee number breakdown



Source: Company annual report (as of Dec 2022), CMBIGM

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