Healthcare

ASCO Highlights: Spotlight on next-gen IO & ADCs

- **Innovent: ASCO data reinforce IBI363's potential as a potential next-generation IO**. We view IBI363 as a highly promising candidate in the IO-resistant sq-NSCLC space, supported by an impressive mPFS of 7.3 months in monotherapy, which is very competitive compared to other innovative agents. Innovent plans to initiate a Ph3 trial of IBI363 in IO-resistant sq-NSCLC in 2H25. In 3L+ CRC, IBI363 has shown superior early efficacy signals and a more favorable safety profile. IBI363 mono delivered an ORR of 12.7% and an mOS of 16.1 months—both significantly outperforming fruquintinib. IBI363 also appears even more competitive in combination with bevacizumab. Innovent plans to initiate a Ph3 study of IBI363 plus bevacizumab in 3L MSS CRC in 2H25, and is also running a Ph2 trial of IBI363 + SoC in the first-line setting. Moreover, IBI363 holds meaningful potential in melanoma, particularly in the immune-cold subtypes of acral and mucosal melanoma. In IO-treated acral and mucosal melanoma patients, the drug demonstrated an ORR of 28.4% and mPFS of 5.7 months—substantially better than currently available PD-1 mAbs. Innovent has initiated a pivotal Ph2 trial of IBI363 vs Keytruda in first-line acral or mucosal melanoma.
- **3SBio: BIC potential of SSGJ-707 in 1L PD-L1+ NSCLC.** SSGJ-707 (707) has demonstrated a 72% ORR in treatment-naïve PD-L1+ NSCLC patients, notably higher than AK112/Ivonescimab's 60% ORR in its Ph1b HARMONi-5 trial and BNT327's 47.1% ORR in its Ph1/2 trial (NCT05918445). 707 has also shown a comparable and manageable safety profile relative to its peers. The potential readout of mPFS for 707 in Ph2 1L PD-L1+ NSCLC in late 2025 will give us better visibility of its BIC potential. As globally the 2nd PD-(L)1/VEGF bsAb to initiate a Ph3 trial in 1L NSCLC, 707 has recently entered a H2H Ph3 trial vs Keytruda in 1L PD-L1+ NSCLC, with a similar study design to AK112's HARMONi-2. 3SBio recently out-licensed 707's ex-China rights to Pfizer, securing an upfront payment of US$1.25bn, up to US$4.8bn in potential milestones, and tiered royalties. We expect Pfizer to accelerate the global development of 707.
- **Henlius: Strong potential of HLX43 (PD-L1 ADC) in both IO-resistant sq- and nsq- NSCLC**. In early clinical data, HLX43 achieved an ORR of 40.0% (6/15) in IO-resistant sq-NSCLC and 33.3% (2/6) in IO-resistant nsq-NSCLC—competitive performance compared to other leading assets under development. In cross-trial comparisons, IBI363 (PD-1/IL2) and SKB264 (TROP2 ADC) reported ORRs of 43.3% and 30.0%, respectively, in IO-resistant sq-NSCLC, and 28.0% and 22.2% in IO-resistant nsq-NSCLC. HLX43 is currently being evaluated in a Ph2 trial for IO-resistant NSCLC, with additional Ph2 programs ongoing across broad tumor types, i.e. HNSCC, ESCC, HCC, NPC, etc. HLX43 is also being explored in combination with serplulimab (PD-1), which could bring its potential use in front-lines pending further validation. We think HLX43 presents a compelling opportunity for global partnerships.

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Content

Innovent (1801 HK)

IBI363 (PD-1/IL-2)

IBI363 in NSCLC (Oral, Clinical Science Symposium)

Data Summary:

Innovent reported results from a phase I, multicenter, first-in-human study (NCT05460767) of IBI363 in patients (pts) with advanced NSCLC (link). Eligible pts with advanced NSCLC who failed or were intolerant of standard therapy were enrolled and received IBI363 intravenously at dose levels of 2/10/300/600 ug/kg every week (QW), 0.3/0.6/1 mg/kg every two weeks (Q2W) or 1.5/2/3/4 mg/kg every three weeks (Q3W).

As of 6 Dec 2024, 136 NSCLC pts were enrolled (prior treatment lines ≥2: 72%). Most patients were treated with IBI363 at 0.6/1 mg/kg Q2W (n=56), 1.5 mg/kg Q3W (n=11) or 3 mg/kg Q3W (n=57).

TEAEs occurred in 135/136 pts (≥G3: 42.6%). TEAEs led to treatment discontinuation in 9 (6.6%) pts and TEAEs led to death in 4 (2.9%) pts with only 1 (0.7%) event considered as treatment-related (unexplained death). Most common TEAEs were arthralgia (51.5%; 3.7% ≥G3), anemia (43.4%; 3.7% ≥G3), and rash (38.2%; 4.4% ≥G3).

In pts with squamous cell carcinoma who had at least 1 post-baseline tumor assessment, 30 (including 1 pt who had not received PD-(L)1 before enrolled) and 27 pts had been treated with IBI363 3 mg/kg and 1/1.5 mg/kg, respectively; more encouraging efficacy signals were observed in the 3 mg/kg group: ORR 43.3% vs 25.9%, confirmed ORR 36.7% vs 25.9%, DCR 90.0% vs 66.7%, median PFS 7.3 (95% CI: 6.0-11.7) vs 5.5 (95% CI: 1.5-8.3) months, with a median follow up time of 7.3 vs 11.1 months.

In the PD-(L)1 treated adenocarcinoma pts with no actionable genomic alterations who had at least 1 post-baseline tumor assessment, 25 and 30 pts had been treated with IBI363 3 mg/kg and 0.6/1/1.5 mg/kg, respectively, similarly, 3 mg/kg group showed higher ORR (28.0% vs 16.7%), confirmed ORR (24.0% vs 13.3%), DCR (76.0% vs 63.3%) and median PFS (4.2 [95% CI: 3.0-not estimable] vs 2.8 [95% CI: 1.4-5.1] months, with a median follow up of 5.9 vs 16.5 months). A higher ORR of 29% versus 4% and a longer PFS of 5.3 months compared to 2.7 months were observed in smokers (N=31, 56.4%).

Notably, in patients at all dose levels with a tumor cell proportion score (TPS) under 1%, the ORR was 45.5% for squamous cell carcinoma (N=22) and 29.4% for adenocarcinoma (N=17).

IBI363 was well tolerated with encouraging and durable efficacy observed in pts with advanced NSCLC who progressed to PD-(L)1, especially in the squamous subtype.

CMBI's comments:

We view IBI363 as a highly promising candidate in the IO-resistant squamous NSCLC (sq-NSCLC) space, supported by an impressive mPFS of 7.3 months in monotherapy. In IO-pretreated sq-NSCLC patients, IBI363 demonstrated quite competitive efficacy compared to other innovative agents currently in development. The 7.3-month mPFS observed in the 3 mg/kg dose cohort of IBI363 notably outperformed SKB264 (TROP2 ADC, mPFS: 5.1 months) and YL201 (B7-H3 ADC, mPFS: 4.1 months) in similar patient populations. When benchmarked against next-generation immuno-oncology combinations, such as AK112 plus docetaxel (mPFS: 7.1 months in IO-treated NSCLC, including both squamous and non-squamous subtypes), IBI363 monotherapy remains highly competitive as a monotherapy. Akeso has recently initiated a Ph3 trial in China evaluating AK112 + docetaxel versus docetaxel alone in IO-treated NSCLC.

We maintain a positive stance on IBI363's outlook, particularly given its strong efficacy signal as a monotherapy in sq-NSCLC. We expect the Company to soon initiate a China Ph3 study of IBI363 monotherapy in IO-treated sq-NSCLC in 2H25.

While results in IO-treated non-squamous NSCLC (nsq-NSCLC) were more modest (mPFS: 4.2 months; cORR: 24.0%), they still compared favorably to docetaxel (mPFS: 3.6 months) as seen in the TROPION-Lung01 trial (link). We will keep an eye on the continuous follow-up of IBI363 in IO-treated nsq-NSCLC.

In parallel, Innovent is evaluating IBI363 in combination with chemotherapy in the first-line NSCLC setting through an ongoing Ph1b/2 trial.

Figure 1: Cross-trial comparison of innovative drugs in IO-resistant NSCLC

Drug	IBI363		AK112	SKB264		YL201		BL-B01D1	HLX43	
MoA	PD-1/IL-2 bsAb		PD-1/VEGF bsAb	TROP2 ADC		B7-H3 ADC		EGFR/HER3 ADC	PD-L1 ADC	
Company	Innovent		Akeso/Summit	Kelun-Biotech/MSD		MediLink		Biokin Pharma/BMS	Henlius	
Dose and regimen	IBI363 mono at 3mg/kg and lower dose levels		AK112 + docetaxel; AK112 10mg/kg or 20mg/kg Q3W	SKB264 mono; 5mg/kg Q2W		mono, 2.0/2.4 mg/kg		mono 2.5/3.0/3.5/5.0/6.0mg/kg	mono 2mg/kg	
Trial ID	NCT05460767		NCT04900363	NCT04152499		NCT05434234, NCT06057922		NCT05194982	NCT06115642	
Stage	Ph1a/1b		Ph1b/2	Ph2		Ph1		Ph1	Ph1	
Patient no.	136		20	21		68		62	21	
Baseline	later-line IO-treated sq- and nsq-NSCLC; 72% with ≥2 prior treatment		Progressed after platinum-doublet and PD-1	EGFR-wt; median prior 3 lines therapies including PD-(L)1		EGFR-wt, 96% with prior PD-(L)1		All had prior chemo, 90% (45/50) had prior anti-PD-1/L1 and chemo	NSCLC refractory to standard treatment	
Follow-up	5.9 vs 16.5 months	7.3 vs 11.1 months	16.8 months	17.2 months				as of Aug 2023	as of Jun 2023	
No. of pts	nsq-NSCLC (n=55) 25 pts in 3mg/kg vs 30 pts in 0.6/1/1.5mg/kg	sq-NSCLC (n=57) 30 pts in 3mg/kg vs 27 pts in 1/1.5mg/kg	nsq-NSCLC (n=13), sq-NSCLC (n=7)	nsq-NSCLC (n=9)	sq-NSCLC (n=12)	nsq-NSCLC (n=54, adeno 28, LELC 24)	sq-NSCLC (n=14)	NSCLC (n=62)	nsq-NSCLC (n=6)	sq-NSCLC (n=15)
ORR	ORR 28.0% vs 16.7% cORR 24.0% vs 13.3%	**ORR 43.3%** vs 25.9% cORR 36.7% vs 25.9%	40%	22.2%	30.0%	28.6% for adeno, 54.2% for LELC	8.3%	40.3% (cORR 30.6%)	33.3%	40.0%
mPFS	**4.2** vs 2.8 (3mg vs 0.6/1/1.5mg)	**7.3** vs 5.5 (3mg vs 1/1.5mg)	**7.1**	**5.8**	**5.1**	4.2 for adeno, 8.1 for LELC	4.1	5.4		
mOS			15.6	16.2	12.8					
12-month OS rate			65%	66.7%	50.0%					
Grade ≥3 TRAE	42.6%		41% for sq, 19% for nsq	69.8%		54.5%			33.3% (TEAE)	
TRAE leading to discontinuation	6.6%		11% for sq, 3% for nsq			5.4%				
TRAE leading to death	2.9% (1 TRAE-related death)		0 for sq, 4% for nsq			2.6%				
Source	Link		Link	Link		Link		Link	Link	

Source: Company data, Pubmed, CMBIGM

IBI363 in CRC (Oral, Clinical Science Symposium)

Data Summary:

The analysis of IBI363 in CRC were from 68 pts treated with IBI363 monotherapy and 73 pts treated with IBI363 plus bevacizumab (beva), respectively. Eligible pts were locally advanced unresectable or metastatic CRC who failed or were intolerant to the standard treatment. Data cutoff date was 6 Dec 2024.

A total of 68 pts and 73 pts (None were MSI-H/dMMR; MSS/pMMR: 86.8% and 90.4%; unknown microsatellite/MMR status: 13.2% and 9.6%; liver metastases: 61.8% and 54.8%; KRAS/NRAS mutations: 42.6% and 41.1%; previous treatment lines ≥ 3: 63.2% and 53.4%; previous immunotherapy: 27.9% and 16.4%) were treated with IBI363 monotherapy (0.1 mg/kg to 3 mg/kg QW, Q2W or Q3W) and IBI363 plus beva (0.6 or 1 mg/kg Q2W, 1.5, 2 or 3 mg/kg Q3W, plus beva 5 mg/kg Q2W or 7.5 mg/kg Q3W), respectively. Median follow-up time was 11.8 months (range: 0.4–22.5) for monotherapy and 5.1 months (range: 1.2–14.9) for combination.

In efficacy-evaluable pts (n = 63 for monotherapy and n = 68 for combination), the ORR was 12.7% and 23.5%. The median duration of response was 7.5 months for monotherapy and not mature for combination. The median OS was 16.1 months for monotherapy and not mature for combination.

Especially, in pts without liver metastasis who received the combination therapy (n = 31), the ORR was 38.7%, and median PFS was 9.6 months.

Grade ≥ 3 treatment-related adverse events were reported in 16 (23.5%) pts with monotherapy and 22 (30.1%) pts with combination. Arthralgia, rash, and thyroid disorders were commonly reported immune-related adverse events.

CMBI's comments:

We see IBI363 as a highly differentiated asset in colorectal cancer (CRC), showing superior early efficacy signals and a more favorable tolerability profile compared to existing third-line (3L+) treatment options. IBI363 monotherapy delivered an ORR of 12.7% and an mOS of 16.1 months—both significantly outperforming fruquintinib. In the China FRESCO trial, fruquintinib achieved an ORR of 4.7% and an mOS of 9.3 months. In the global FRESCO-2 trial, these figures were even lower, with a 1.5% ORR and 7.4-month mOS.

IBI363 also appears even more competitive in combination regimens with bevacizumab. The combination of TAS-102 and bevacizumab showed an ORR of only 6.1% and an mOS of 10.8 months in 3L CRC, despite enrolling patients with more favorable baseline characteristics (link). In contrast, IBI363 achieved ORRs of 12.7% (monotherapy) and 23.5% (combo with bevacizumab), along with an mOS of 16.1 months (monotherapy), with combination mOS data pending.

From a safety standpoint, IBI363 also compares favorably. Grade ≥3 TRAEs were reported in 23.5% of patients on monotherapy and 30.1% on combination therapy, lower than the 46.0% and 36.0% observed in the FRESCO and FRESCO-2 trials, respectively. Looking ahead, Innovent plans to initiate a Ph3 study of IBI363 plus bevacizumab in 3L MSS CRC in 2H25. Additionally, Innovent is running a Ph2 trial evaluating IBI363 in combination with standard-of-care therapy in the first-line MSS CRC setting, reflecting its ambition to position IBI363 in both refractory and frontline segments of this large market.

IBI363 in melanoma (Oral, Oral Abstract Session)

Data Summary:

Results of IBI363 from a phase 1 study (NCT05460767) and a phase 2 study (NCT06081920) of pts with IO-treated, advanced acral and mucosal melanoma were reported at ASCO (link). Eligible pts with IO-treated advanced acral and mucosal melanoma were enrolled. IBI363 was administered intravenously at 0.1 mg/kg every week, 0.3/0.6/1 mg/kg every 2 weeks (Q2W), or 1/1.5/2/3 mg/kg every 3 weeks (Q3W).

As of 6 Dec 2024, 91 pts were enrolled across the phase 1 (n = 76) and phase 2 (n = 15) studies (Asian: 100%; ECOG PS 1: 66%; stage IV: 89%); 47 pts had acral melanoma and 44 had mucosal melanoma. Median follow-up time was 8.2 months. Median treatment duration was 13.4 weeks (range: 2.0-72.4).

27 (29.7%) pts had grade ≥3 (≥G3) TEAEs. TEAEs led to treatment discontinuation in 3 (3.3%) pts, and 1 (1.1%) pt had a TEAE leading to death which was considered to be treatment-related (sepsis). Most common TEAEs were arthralgia (59.3%, with 4.4% ≥G3), rash (42.9%, with 3.3% ≥G3), and anemia (42.9%, with 2.2% ≥G3).

Among all pts with at least one post-baseline tumor assessment (n = 87), 1 pt had a complete response, 22 had partial responses. ORR was 26.4% with 16 responses confirmed and 2 pts still waiting for confirmation.

Among pts treated at 1mg/kg and above (n = 74), the ORR was 28.4%. Patients treated at 1 mg/kg Q2W (n = 30) had median DOR 14.0 months with a median follow-up of 9.1 months and 50.0% events; the median PFS was 5.7 (95% CI, 3.6-6.7) months with a median follow-up of 11.0 months and 73.3% events.

CMBI's comments:

We believe IBI363 holds meaningful potential in melanoma, particularly in the immune-cold subtypes of acral and mucosal melanoma, where treatment options remain limited and response to existing immunotherapies has been modest.

In IO-treated, advanced acral and mucosal melanoma patients receiving IBI363 at 1 mg/kg Q2W and above, the drug demonstrated an ORR of 28.4% and mPFS of 5.7 months—substantially more competitive than currently available immune checkpoint inhibitors. For reference, Keytruda received approval in China for second-line melanoma based on the KEYNOTE-151 trial, which reported ORRs of only 15.8% in acral melanoma and 13.3% in mucosal melanoma, with an overall mPFS of just 2.8 months (link). Even in the IO-responsive cutaneous melanoma population studied in the KEYNOTE-006 trial—which enrolled 66% first-line and 34% second-line patients—Keytruda achieved an mPFS of only 5.5 months (link).

To further validate IBI363's potential in melanoma, Innovent has initiated a pivotal Ph2 trial comparing IBI363 to Keytruda in first-line, IO-naïve acral or mucosal melanoma patients (NCT06797297). The study is designed without an interim analysis and aims to demonstrate superiority based on 118 PFS events out of 180 planned patients, with 90% statistical power (one-sided α=0.025).

IBI343 (CDLN18.2 ADC)

IBI343 in NSCLC (Oral, Rapid Oral Abstract Session)

Data Summary:

CLDN18.2 is highly expressed in nearly 60% of PDAC cases. Yet to date, there are no approved targeted therapies and prognoses for these patients (pts) remain poor. Results from a phase 1 study (NCT05458219) in pts with PDAC treated with IBI343 by CLDN18.2 expression status (≥60% vs < 60%) were reported at ASCO.

Eligible pts with advanced PDAC and moderate to high expression of CLDN18.2 (defined as IHC membrane staining intensity ≥2 in ≥40% of tumor cells) who failed or were intolerant to standard treatment were enrolled. IBI343 was administered every 3 weeks at multiple dose levels (1, 3, 4.5, 6, 8, and 10 mg/kg).

As of 27 December 2024, 83 pts from China and Australia were enrolled. 44 and 12 pts with CLDN18.2 expression ≥1 in ≥60% (+) and < 60% (-) of tumor cells, respectively, received IBI343 at 6mg/kg in the dose expansion phase (received prior treatments ≥2L, 61.4% and 83.3%).

Among all treated pts (n = 83), ≥Grade 3 (G3) TEAEs occurred in 42 (50.6%) pts. TEAEs led to treatment discontinuation in 6 (7.2%) pts. No TEAE led to death. Most common TEAEs were anemia (66.3%, 15.7% ≥G3), neutrophil count decreased (48.2%, 9.6% ≥G3), and WBC count decreased (47.0%, 9.6% ≥G3). The safety profile of IBI343 in PDAC was comparable to previous reports.

Among CLDN18.2+ pts (n = 44), confirmed ORR was 22.7%, median PFS was 5.4 months (mos), median OS was 8.5 mos. Among CLDN18.2+ pts who received 1 and 2 lines of prior treatment, median OS was 12.1 mos and 9.1 mos, respectively.

Among CLDN18.2- pts (n = 12), no pt had an objective response, median PFS was 1.4 (1.3–3.2) mos, which was shorter than what was seen in CLDN18.2+ pts and median OS was 6.2 mos.

CMBI's comments:

We see IBI343 as a potentially first-in-class targeted therapy for pancreatic ductal adenocarcinoma (PDAC), with promising early efficacy and clear differentiation in a high-unmet-need indication. In CLDN18.2-positive PDAC patients (≥60% CLDN18.2 expression of ≥1+ staining), where 61.4% had received ≥2 prior lines of therapy, IBI343 achieved an mPFS of 5.4 months—consistent with results previously reported at ESMO Asia in Dec 2024 (link).

PDAC represents a significantly larger market than gastric cancer (GC) in ex-China regions and remains a highly underserved indication, with no approved targeted therapies and poor

prognosis. Current standards of care for first-line and second-line PDAC consist of chemotherapy regimens, such as those evaluated in the NAPOLI-1 and GEMPAX trials, which yielded mPFS of only around 3.1 months. IBI343 is the first CLDN18.2-directed ADC to demonstrate encouraging activity in PDAC, and has been granted Fast Track designation by the FDA, reflecting its potential to address a critical treatment gap.

Innovent is also advancing a Ph1 trial of IBI343 in the US, with data expected in 2H25, which may support the initiation of global pivotal trials thereafter. Given the limited competition and high medical need in PDAC, we believe IBI343 carries meaningful global out-licensing potential, particularly as the first clinical-stage CLDN18.2 ADC candidate showing efficacy in this setting.

Henlius (2696 HK)

HLX43 (PD-L1 ADC)

HLX43 in NSCLC (Poster)

Data Summary:

Results of HLX43, a novel anti-PD-L1 ADC in patients with advanced/metastatic solid tumors was reported. This phase 1 study consisted of 2 parts. Parts 1 and 2 were dose escalation and dose expansion phases, respectively, to explore different doses of HLX43.

In Part 1, patients with histologically or cytologically confirmed advanced/metastatic malignant solid tumors refractory to or not amenable to standard therapies received intravenous HLX43 at 0.5 mg/kg, 1 mg/kg, 2 mg/kg, 3 mg/kg, or 4 mg/kg, Q3W. In Part 2, patients with advanced/metastatic NSCLC refractory to standard treatment received HLX43 at 2 mg/kg, 2.5 mg/kg, or 3 mg/kg, Q3W. As of 27 June 2023, 18 patients with NSCLC (n = 12, 66.7%), head and neck squamous carcinoma, cervical squamous carcinoma, thymic squamous cell carcinoma, nasopharyngeal cancer, uterine carcinosarcoma, or small cell lung cancer (n = 1, 5.6% for each) were enrolled in Part 1 and received HLX43 at 0.5 mg/kg (n = 3), 1 mg/kg (n = 3), 2 mg/kg (n = 3), 3 mg/kg (n = 3), or 4 mg/kg (n = 6). One patient in the 4 mg/kg dose group experienced DLTs of febrile neutropenia and decreased white blood cell count. Investigator-assessed ORR was 31.3% (95% CI 11.0-58.7).

In Part 2, only data from 21 patients enrolled to receive HLX43 at 2 mg/kg is available and presented here. Among these patients, 15 (71.4%) had squamous NSCLC and 6 (28.6%) had nonsquamous NSCLC. Investigator-assessed ORR were 38.1%; no complete response was achieved, and 8 patients (6 sqNSCLC and 2 nsqNSCLC) had partial response. Grade ≥3 TEAEs occurred in 7 (33.3%) patients.

CMBI's comments:

We view HLX43 as a highly promising PD-L1 ADC candidate in both squamous (sq-) and non-squamous (nsq-) NSCLC, demonstrating encouraging early efficacy in patients who have progressed on standard therapies. In early clinical data, HLX43 achieved an ORR of 40.0% (6/15) in IO-resistant sq-NSCLC and 33.3% (2/6) in IO-resistant nsq-NSCLC—competitive performance compared to other leading assets under development. In cross-trial comparisons (see Figure 1), IBI363 (a PD-1/IL-2 bispecific from Innovent) and SKB264 (a Trop2 ADC from Kelun-Biotech/MSD) reported ORRs of 43.3% and 30.0%, respectively, in IO-resistant sq-NSCLC, and 28.0% and 22.2% in IO-resistant nsq-NSCLC.

HLX43 is currently being evaluated in a Ph2 trial for IO-resistant NSCLC, with additional Ph2 trials ongoing across multiple tumor types, including head and neck squamous cell carcinoma (HNSCC), esophageal squamous cell carcinoma (ESCC), hepatocellular carcinoma (HCC), and nasopharyngeal carcinoma (NPC).

As one of the most advanced PD-L1 ADCs globally, HLX43 benefits from MediLink's proprietary tumor microenvironment-activatable linker-payload platform (TMALIN), which

enables selective payload release within the tumor microenvironment, enhancing both efficacy and safety. This advanced engineering may support HLX43's potential to become a best-in-class PD-L1 ADC, in our view. In addition, we see meaningful upside in combination strategies. HLX43 is being explored in combination with PD-1 monoclonal antibodies (e.g., serplulimab), which could expand its clinical utility to broader patient populations, including the potential use in front-line settings pending further clinical validation.

CSPC (1093 HK)

SYS6010 (EGFR ADC)

SYS6010 in NSCLC (Poster)

Data Summary:

SYS6010, an EGFR ADC, induces DNA damage leading to apoptosis, while resistance may occur through ATM-mediated DNA repair. SYH2051, an ATM inhibitor, disrupts DNA repair, enhancing SYS6010-induced apoptosis. This combination is hypothesized to exert synergistic anti-tumor effects.

The first-in-human trial of SYS6010 combined with SYH2051 in patients with advanced gastrointestinal tumors (link) was released at ASCO. Patients with advanced gastrointestinal tumors expressing EGFR who had progressed on at least one prior line of standard therapy were enrolled. SYS6010 was administered intravenously at a dose of 3.2 mg/kg on day 1 of each 14-day cycle, while SYH2051 was given orally at doses of 40 mg or 80 mg, once daily, for five consecutive days within the same cycle.

As of 31 Dec 2024, 25 patients were enrolled, including 18 with colorectal cancer and 7 with gastric cancer. Twelve patients had received ≥3 prior lines of therapy.

Among 6 evaluable gastric cancer patients, 3 achieved PR, resulting in an ORR of 50%. The median PFS was approximately 5.8 months (data not mature).

Among 18 colorectal cancer patients (9 with KRAS mutations and 9 wild-type), preliminary analysis showed a median PFS of approximately 4.2 months in wild-type KRAS patients (data not mature).

Common TRAEs included hematologic toxicity, gastrointestinal symptoms, and fatigue. Grade ≥3 TRAEs occurred in 12 patients (48%), including neutropenia (7 patients), anemia (6 patients), thrombocytopenia (3 patients), vomiting (3 patients), leukopenia (2 patients), interstitial lung disease (1 patient), infection (1 patient), and elevated bilirubin (1 patient). No treatment-related death was reported.

SYS6010 combined with SYH2051 was well tolerated and demonstrated preliminary antitumor activity in advanced gastrointestinal tumors, particularly in gastric cancer.

CMBI's comments:

We view the combination of SYS6010 (EGFR ADC) and SYH2051 (ATM inhibitor) as a promising regimen in gastric cancer (GC), particularly given its encouraging early efficacy in heavily pre-treated patients. In the reported study, among the 6 evaluated late-line GC patients, the combination achieved a 50% ORR and an mPFS of 5.8 months. Although the number of evaluated patients is small, these results compare favorably to the current second-line standard of care, ramucirumab plus chemotherapy, which demonstrated a 28% ORR and 4.4-month mPFS in the RAINBOW trial.

However, we see limited differentiation in colorectal cancer (CRC) of the combination of SYS6010 and SYH2051 based on current data. For third-line CRC, fruquintinib achieved an mPFS of 3.7 months in the FRESCO/-2 trials, while TAS-102 plus bevacizumab delivered a more competitive 5.6-month mPFS (link). In comparison, the 4.2-month mPFS observed for the SYS6010 + SYH2051 combination in CRC may fall short of the efficacy threshold needed for meaningful clinical or commercial impact.

Kelun-Biotech (6990 HK)

Sacituzumab tirumotecan (SKB264/sac-TMT/MK-2870, TROP2 ADC)

Sac-TMT + A167 in 1L NSCLC (Poster)

Data summary:

Updated results of sac-TMT plus tagitanlimab (anti-PD-L1, KL-A167) by PD-L1 expression with additional enrolled patients and extended follow-up from non-squamous cohort in the phase II OptiTROP-Lung01 study (NCT05351788) was reported at ASCO.

Advanced NSCLC pts with no prior systemic therapy and no actionable genomic alterations were enrolled to receive sac-TMT (5 mg/kg Q3W or Q2W) plus tagitanlimab (1200 mg Q3W or 900 mg Q2W) until disease progression or unacceptable toxicity.

As of 30 Dec 2024, 81 pts with non-squamous histology were enrolled. The majority (66.7%) had PD-L1 TPS< 50% (42.0% for < 1%, 24.7% for 1% - 49% and 33.3% for ≥ 50%). After median follow-up of 17.1 mo, the confirmed ORR was 59.3%; mPFS was 15.0 mo.

- For pts with PD-L1 TPS< 1%, the confirmed ORR was 47.1%; mPFS was 12.4 mo;
- For pts with PD-L1 TPS≥ 1%, the confirmed ORR was 68.1%; mPFS was 17.8 mo;
- For pts with PD-L1 TPS≥ 50%, the confirmed ORR was 77.8%; mPFS was 17.8 mo.

Most common (≥ 10%) Grade ≥ 3 TRAEs were neutrophil count decreased (45.7%), anemia (16.0%), white blood cell count decreased (14.8%) and stomatitis (11.1%). No TRAE led to treatment discontinuation or death.

CMBI's comments:

We see strong potential for sac-TMT in first-line non-squamous NSCLC across all PD-L1 expression levels, with particularly compelling differentiation in PD-L1-negative patients, where current PD-(L)1-based therapies offer limited benefit. The combination of sac-TMT with KL-A167 (PD-L1 mAb), across both high and low dose cohorts (sac-TMT Q2W and Q3W), demonstrated an mPFS of 15.0 months in 1L nsq-NSCLC—consistent with prior data and confirming the regimen's promising activity. At previous ASCO in 2024, Kelun-Biotech reported an mPFS of 15.4 months for sac-TMT + KL-A167 at the Q3W lower dose level in 1L NSCLC (combined nsq- and sq-). These results remain highly competitive when compared to current standard-of-care. In the KEYNOTE-189 trial for 1L nsq-NSCLC, pembrolizumab + chemotherapy achieved mPFS of 9.0 months in the intent-to-treat (ITT) population and 11.3 months in patients with PD-L1 TPS ≥50%, both of which fall short of the 15.0 and 17.8 months observed with sac-TMT + KL-A167 in corresponding subgroups. Notably, in patients with PD-L1 TPS <1%—a population with few effective options—sac-TMT + KL-A167 achieved an mPFS of 12.4 months, doubling the 6.2 months seen with pembrolizumab + chemo.

Kelun-Biotech is currently conducting a Ph3 trial in China (NCT06711900) comparing sac-TMT + pembrolizumab versus pembrolizumab + chemotherapy in 1L PD-L1-negative nsq-

NSCLC. In parallel, for PD-L1 positive patients, Kelun-Biotech is running a China Ph3 trial (NCT06448312) in 1L NSCLC with PD-L1 TPS >1%, and MSD is conducting a global Ph3 trial (NCT06170788) in PD-L1 TPS ≥50%, both comparing sac-TMT + pembrolizumab vs pembrolizumab alone.

Figure 2: Comparison of Sac-TMT results in 1L nsq-NSCLC to SoC (pembrolizumab + chemo)

Regimen	Pembrolizumab + chemo vs chemo		Sac-TMT + KL-A167		Sac-TMT + KL-A167			
Trial ID	KEYNOTE-189 Ph3		OptiTROP-Lung01 Ph2, 2025 ASCO		OptiTROP-Lung01 Ph2, 2024 ASCO			
Patients	**1L nsq**		**1L nsq**		**1L nsq & sq**			
Patient No.	410 vs 206		81		40		63 (34 nsq, 29 sq)	
Dose	-		sac-TMT (5 mg/kg Q3W or Q2W) plus KL-A167 (1200 mg Q3W or 900 mg Q2W)		Cohort 1A: sac-TMT (5 mg/kg Q3W) plus KL-A167 (1200 mg Q3W)		Cohort 1B: sac-TMT (5 mg/kg Q2W) plus KL-A167 (900 mg Q2W)	
PD-L1 expression	ORR (%)	PFS (months)	ORR (%)	PFS (months)	ORR (%)	PFS (months)	ORR (%)	PFS (months)
ITT	48.3 vs 19.9	**9.0** vs 4.9, HR 0.50	59.3	**15.0**	48.6	**15.4**	77.6	-
TPS ≥50%	62.1 vs 25.7	**11.3** vs 4.8, HR 0.35	68.1	**17.8**	-	-	63.2	-
TPS 1%-49%	50.0 vs 20.7	9.4 vs 4.9, HR 0.57	-	-	-	-	81.3	-
TPS <1%	33.1 vs 14.3	**6.2** vs 5.1, HR 0.67	47.1	**12.4**	-	-	87.0	-

Source: KEYNOTE-189 (link), Sac-TMT 2024 ASCO (link), Sac-TMT 2025 ASCO (link), CMBIGM

Sac-TMT in EGFRm NSCLC (Oral Abstract Session)

Data summary:

Results from a study comparing sac-TMT with docetaxel in previously treated EGFRm NSCLC pts (OptiTROP-Lung03, NCT05631262) was reported at ASCO, consistent to the updated drug label previously released online (link).

Pts with advanced EGFRm NSCLC who had progressed after EGFR TKI and platinum-based chemotherapy were randomized (2:1) to receive sac-TMT 5 mg/kg Q2W or docetaxel 75 mg/m2. Pts with verified progression on docetaxel could be crossed over to receive sac-TMT if eligible.

A total of 137 pts (93.4% prior 3rd EGFR TKI) were randomized to receive sac-TMT (n=91) or docetaxel (n=46). The study met its primary and key secondary endpoints. At a median follow-up of 12.2 mo (data cut-off: 31 Dec 2024), Sac-TMT achieved statistically significant clinical outcomes compared to docetaxel: confirmed ORR (BIRC: 45.1% vs 15.6%, 1-sided p=0.0004; investigator [INV]: 34.1% vs 8.7%), PFS (BIRC: median 6.9 vs 2.8 mo, HR 0.30 [95% CI: 0.20, 0.46], 1-sided p<0.0001; INV: median 7.9 vs 2.8 mo, HR 0.23 [95% CI: 0.15, 0.36]), and OS (median not reached [NR] for both groups, HR 0.49 [95% CI: 0.27, 0.88], 1-sided p=0.007), with 36.4% of pts in docetaxel group crossed over to receive sac-TMT. The RPSFT model adjusted median OS was 9.3 mo for docetaxel and NR for sac-TMT (HR for OS 0.36 [95% CI: 0.20, 0.66]).

Grade ≥ 3 TRAEs occurred in 56.0% of pts in sac-TMT group vs 71.7% in docetaxel group, and treatment-related SAEs were 16.5% vs 41.3%. Most common (≥10%) grade ≥3 TRAEs (sac-TMT vs docetaxel) were neutrophil count decreased (42.9% vs 58.7%), WBC count decreased (25.3% vs 52.2%), stomatitis (16.5% vs 2.2%), anemia (12.1% vs 4.3%) and febrile neutropenia (0% vs 19.6%). No cases of ILD were reported in sac-TMT group.

Sac-TMT demonstrated improved ORR, PFS and OS compared to docetaxel, with manageable safety profile in pts with previously treated advanced EGFRm NSCLC. These results highlight significant survival benefits and suggest that sac-TMT could emerge as a new standard of care for this population.

CMBI's comments:

We see sac-TMT as a highly competitive and differentiated asset in EGFR-mutant (EGFRm) NSCLC, particularly in the post-TKI setting, with the potential to secure meaningful global market share across multiple lines of therapy. In third-line (3L) EGFRm NSCLC patients who progressed after EGFR TKI and platinum-based chemotherapy, sac-TMT demonstrated an mPFS of 6.9 months (HR=0.30, vs docetaxel) in the OptiTROP-Lung03 trial—outperforming many other innovative therapies in this treatment-resistant segment. For comparison, Dato-DXd and HER3-DXd both reported 5.8 months of mPFS in the Ph2 TROPION-Lung05 and Ph3 HERTHENA-Lung02 trials, respectively. AK112 (PD-1/VEGF) + chemotherapy showed 7.1 months in the HARMONi-A trial (both 2L and 3L patients enrolled in the study), and amivantamab (EGFR/cMET) + chemotherapy demonstrated 6.3 months in the Ph3 MARIPOSA-2 trial, also in a mixed 2L/3L population. These benchmarks highlight sac-TMT's strong efficacy profile in a true 3L setting.

Importantly, sac-TMT is the only innovative agent to date that has shown a statistically significant overall survival (OS) benefit in EGFR-TKI–resistant EGFRm NSCLC. In the aforementioned trial, sac-TMT achieved an OS hazard ratio of 0.49 (95% CI: 0.27–0.88), despite allowing for cross-over—underscoring the robustness of the survival benefit.

Sac-TMT has already been approved in China for 3L EGFR-TKI–resistant non-squamous NSCLC and is currently under review by the CDE for the 2L EGFR-TKI–resistant indication, with full 2L data expected at ESMO this year. Additionally, MSD is running global Ph3 trials in both 2L and 3L EGFRm NSCLC, while Kelun-Biotech is advancing a China-based Ph3 trial of sac-TMT + osimertinib in 1L EGFRm NSCLC. Given the compelling efficacy, OS benefit, and broad development strategy across 1L–3L EGFRm NSCLC, we believe sac-TMT is well-positioned to capture meaningful global share in this high-value EGFRm NSCLC segment.

Sac-TMT in 1L TNBC (Oral, Rapid Oral Abstract Session)

Data summary:

The Phase II OptiTROP-Breast05 study (NCT05445908) evaluating sac-TMT as first-line treatment for pts with a/mTNBC was released at ASCO. Pts with a/mTNBC who had not received prior treatment for advanced disease were enrolled, regardless of PD-L1 or TROP2 status, to receive sac-TMT at **5 mg/kg Q2W** until disease progression or unacceptable toxicity.

As of 18 Nov 2024, a total of 41 pts (78.0% PD-L1 CPS < 10) were enrolled; 61.0% of pts had visceral metastases at baseline. The median follow-up was 18.6 mo. **The ORR was 70.7% (29/41, 3 unconfirmed PR) and median mPFS was 13.4 mo**, and the 12-mo PFS rate was 64.6%.

Among the 32 pts with PD-L1 CPS < 10, the ORR was 71.9% (23/32, 3 unconfirmed PR). The mPFS in this subgroup was 13.1 mo, with a 12-mo PFS rate 59.1%.

TRAEs of grade 3 or higher occurred in 63.4% of pts. The most common ≥ grade 3 TRAEs (occurred in ≥5% of pts) were neutrophil count decreased (46.3%), WBC count decreased (34.1%), anemia (12.2%), stomatitis (9.8%), lymphocyte count decreased (7.3%) and fatigue (7.3%). No treatment-related deaths occurred, and there were no reports of neuropathy or interstitial lung disease/pneumonitis.

CMBI's comments:

We see strong potential for sac-TMT in first-line TNBC, particularly among patients who are not candidates for PD-(L)1 inhibitors—a population that represents the majority of 1L TNBC cases and remains a significant unmet need. In updated clinical data, sac-TMT monotherapy demonstrated an mPFS of 13.4 months in 1L TNBC regardless of PD-L1

expression, and 13.1 months in patients with PD-L1 CPS <10. These results are highly competitive and broadly comparable to PD-(L)1–based combination regimens, in our view. For reference (refer to figure below for comparisons), Dato-DXd + Imfinzi (PD-L1) reported 13.8 months of mPFS, while Trodelvy + Tecentriq (PD-L1) showed 12.2 months in similar 1L TNBC populations. Both Dato-DXd and Trodelvy are currently in Ph3 trials for PD-(L)1–ineligible 1L TNBC and PD-L1 positive 1L TNBC, with Trodelvy's ASCENT-03/04 trials having met the primary endpoint, and Dato-DXd's trial to release data in 1H25.

Importantly, patients ineligible for PD-(L)1 inhibitors account for ~60% of the 1L TNBC population (per AstraZeneca disclosures), yet currently with limited treatment options. Recognizing this opportunity, Kelun-Biotech and MSD have initiated corresponding Ph3 trials in both China and globally to evaluate sac-TMT in this setting. Sac-TMT has already been approved in China for third-line TNBC, and ongoing Ph3 trials in the first-line setting have the potential to significantly expand its clinical utility and market coverage within the TNBC population, pending positive outcomes.

Figure 3: Cross-trial comparison of therapies for 1L TNBC

Drug	sac-TMT/ SKB264	Dato-DXd	Trodelvy	Keytruda
Company	Kelun-Biotech/ MSD	Daiichi Sankyo / AstraZeneca	Gilead	MSD
Trial ID	NCT05445908	BEGONIA	MORPHEUS-panBC (NCT03424005)	KEYNOTE-355
Trial stage	Ph1/2	Ph1b/2	Ph1/2	Ph3
Regimen	SKB264	Dato-DXd + Imfinzi (PD-L1)	Trodelvy + Tecentriq (PD-L1) vs chemo + Tecentriq	Pembro + chemo vs chemo
PD-L1 expression	**78% PD-L1 CPS < 10**	**87% PD-L1 CPS <10%**	**PD-L1+**	**62% PD-L1 CPS<10 19% PD-L1 CPS <1**
n (efficacy evaluable)	41	62	30 vs 9	847
median Follow up (month)	18.6	11.7	-	44.1
PFS (month)	**13.4 (13.1 for CPS<10, n=32)**	**13.8**	**12.2 vs 5.9 HR=0.27 (0.11-0.70)**	**7.5 vs 5.6 HR=0.82 (0.70-0.98)**
OS (month)	-	-	-	17.2 vs 15.5 HR=0.89 (0.76-1.05)
ORR	70.7% (71.9% for CPS<10, n=32)	79%	76.7% vs 66.7%	40.8% vs 37.0%
TRAEs Grade>=3	63.4%	36%	-	68.1% vs 66.9%
Key any grade TRAEs				
nausea		*55%*		*39% vs 41%*
stomatitis	*9.8%*	*51%*		*NA*
diarrhea		*13%*		*NA*
anemia	*12.2%*	*8.5%*		*41% vs 46%*
neutropenia	*46.3%*	*2.1%*		*41% vs 38%*
ILD	*0*	*5%*		pneumonitis 2.5% vs 0
Discontinuation due to AE		16%	3.3% vs 11.1%	
Source	Link	Link1; Link2	Link	Link

Source: CMBIGM

Figure 4: Ph3 trials of major TROP2 ADCs in 1L TNBC

Drug	Trial ID	Patient	Regimen	Status
Trodelvy	ASCENT-03	1L TNBC pts not suitable for PD-(L)1 inhibitors	Trodelvy mono vs chemo	positive results announced in May 2025 (link)
	ASCENT-04	1L PD-L1 positive pts	Trodelvy + Keytruda vs Keytruda + chemo	positive results announced in Apr 2025 (link); Met PFS endpoint; data to be released at ASCO 2025 (LBA)
Dato-DXd	TROPION-Breast02	1L TNBC pts not suitable for PD-(L)1 inhibitors (40% of TNBC)	Dato-DXd mono vs chemo	Started in 2022.05; Data expected in 1H25
	TROPION-Breast05	1L PD-L1 positive pts (60% of TNBC)	Dato-DXd+Imfinzi vs Imfinzi	Data expected in 2026
sac-TMT/ SKB264	NCT06279364 (China)	1L TNBC pts not suitable for PD-(L)1 inhibitors	SKB264 mono vs chemo	Started in 2024.02
	NCT06841354 (Global)	1L TNBC pts (PD-L1 CPS <10)	SKB264 mono vs SKB264 + Keytruda vs chemo	Started in 2025.03

Source: Clinicaltrials.gov, CMBIGM

3SBio (1530 HK)

707 (PD-1/VEGF bsAb)

707 in 1L PD-L1+ NSCLC (Poster)

Data summary:

SSGJ-707 is a recombinant humanized bispecific molecule built on IgG4 that targets the PD-1 and VEGF. The increase of 707 affinity for PD-1 was 10-fold more than that of Ivonescimab in the presence of VEGF. Ph2 results of 707 in 1L PD-L1+ NSCLC were reported (Link).

As of 10 Jan 2025, 83 pts were enrolled. 707 10mg/kg Q3W demonstrated promising efficacy results in treatment naive advanced NSCLC.

In 34 pts received 707 at dose of 10mg/kg Q3W and completed at least one efficacy evaluation, ORR was 61.8% (21/34) and DCR was 97.1% (33/34). The ORR were 54.5% (12/22) and 75% (9/12) in non-squamous and squamous pts, respectively. The ORR were 57% (12/21) and 69% (9/13) in PD-L1 TPS 1%-49% and ≥ 50% pts, respectively.

In 25 pts received 707 at dose of 10mg/kg Q3W and completed at least two efficacy evaluation, ORR was 72% (18/25) and DCR was 100% (25/25).

For the 83 pts, 78.3% were reported TRAEs, of which 20 pts (24.1%) experienced grade≥3 TRAEs. The most common TRAEs included hypercholesterolaemia (18.1%,15/83), hypertriglyceridaemia (18.1%,15/83), alanine aminotransferase increased (15.7%,13/83) and aspartate aminotransferase increased (15.7%,13/83). TRAE leading to discontinuation occurred in 6% of pts.

CMBI's comments:

We see BIC potential of SSGJ-707 (707) in 1L PD-L1+ NSCLC. In cross-trial comparison of the early trial results, for treatment-naïve PD-L1+ NSCLC patients, 707 has demonstrated a 72% ORR in treatment-naïve PD-L1+ NSCLC patients, notably higher than Ivonescimab's 60% ORR in its Ph1b HARMONi-5 trial and BNT327's 47.1% ORR in its Ph1/2 trial (NCT05918445). 707 has also shown a comparable and manageable safety profile relative to its peers. The readout of mPFS for 707 in Ph2 1L PD-L1+ NSCLC, expected in late 2025, will give us better visibility of its BIC potential in 1L NSCLC. In May, 707 entered a H2H Ph3 trial vs. Keytruda in 1L PD-L1+ NSCLC (CTR20251867), with a study design similar to Ivonescimab's HARMONi-2. Notably, 707 is globally the 2nd PD-(L)1/VEGF bsAb to initiate a Ph3 trial in 1L NSCLC.

Awaiting Pfizer's initiation of 707's global studies. On 20 May, 3SBio out-licensed 707's ex-China rights to Pfizer, securing an upfront payment of US$1.25bn, up to US$4.8bn in potential milestones, and tiered double-digits royalties on net sales. For reference, Summit and BioNTech launched the first global clinical trials of Ivonescimab and BNT327 within 5-7 months of acquiring ex-China rights, respectively. Therefore, we expect Pfizer to accelerate the global development of 707, particularly in 1L NSCLC. In addition, several assets in Pfizer's R&D pipeline have potential for combination with 707, including PD-L1 ADC, Nectin-4 ADC, IB6 ADC etc.

Figure 5: Cross-trial comparison of PD-(L)1/VEGF for 1L PD-L1+ NSCLC

Drug	707 (PD-1/VEGF)	Ivonescimab(PD-1/VEGF)		BNT327 (PD-L1/VEGF)
Company	3SBio	Akeso		Biotheus/ BioNTech
Trial ID	NCT06361927	NCT05499390 (HARMONi-2)	NCT04900363 (HARMONi-5)	NCT05918445
Trial stage	Ph2	Ph3	Ph1b	Ph1/2
Dosing group	Monotherapy	Monotherapy	Monotherapy	Monotherapy
N	83	398	108	61
Group: n	10mg/ kg Q3W: n=34	AK112(20 mg/kg Q3W): n=198	20mg/kg Q3W: n=15	Cohort 6 (1L PD-L1+ nsq-NSCLC): n=17
ORR	72% (n=25)* 61.8% (n=34)**	50.0%	60.0%	47.1%
DCR	100.0% (n=25)* 97.1% (n=34)**	89.9%	93.3%	100.0%
mPFS (month)	-	11.14 months, PFS HR=0.51 (P < 0.0001)	-	-
TRAE	78.3% (N=83)	89.8%	89.7% (n=29, including 1L TPS≥ 1%, 2L TPS≥ 1%, 1/2L TPS <1%)	85.2%***
TRAE (Gr3+)	24.1% (N=83)	29.4%	17.2% (n=29, including 1L TPS≥ 1%, 2L TPS≥ 1%, 1/2L TPS <1%)	18%***
Source	Link1	Link2	Link3	Link4

Source: ASCO, Akeso, CMBIGM
*10 mg/kg patients with ≥ 2 post-baseline tumor assessment scans (n=25)
**10 mg/kg patients with ≥ 1 post-baseline tumor assessment scans (n=34)
***Among 61 evaluable patients with advanced NSCLC, including 17 patients with previously untreated advanced non-squamous NSCLC (EGFR/ALK wild-type and PD-L1+), 36 patients with advanced non-squamous with EGFR mutations who had failed prior EGFR-TKI treatment, and 8 patients with EGFR/ALK wild-type who had failed anti-PD-1/L1 therapy and platinum-based chemotherapy regiments (NSCLC IO- and PBC-treated).

Figure 6: Global clinical trials of PD-(L)1/ VEGF bsAb

Target	Drug name	Company name	Trial ID	Regimen	Indication	Stage	Start date
PD-1/VEGF	Ivonescimab / AK112	Akeso/ Summit	NCT06396065 (HARMONi)	+ chemo	EGFR-TKI resistant nsq-NSCLC	Ph3	2023.05
			NCT05899608 (HARMONi-3)	+ chemo	1L NSCLC	Ph3	2023-06
			NCT06767514 (HARMONi-7)	mono	1L PD-L1 high NSCLC	Ph3	2025-01
PD-L1/VEGF	PM8002 / BNT327	Biotheus/ BioNTech	NCT06712355 (ROSETTA Lung-01)	+ chemo	1L SCLC	Ph3	2024-12
			NCT06712316 (ROSETTA Lung-02)	+ chemo	1L NSCLC	Ph2/3	2024-12
			NCT06449222	+ chemo	1L or ≥2L TNBC	Ph2	2024-06
			NCT06449209	+ chemo	1L or ≥2L SCLC	Ph2	2024-06
			NCT06841055	+ chemo	2L NSCLC	Ph2	2025-02
			NCT06827236	Mono / + BNT323	BC	Ph1/2	2025-02
			NCT06892548	+ BNT324	SCLC and NSCLC	Ph1/2	2025-03

Source: Pharmacube, CMBIGM

Figure 7: Global development of PD-(L)1/VEGF bsAb

Drug name	Target	Company name	Global phase	CN Phase	Target indications
Ivonescimab/ AK112	PD-1/VEGF	Akeso	Ph3	Approved	NSCLC, CRC, biliary tract, HNSCC, Pancreatic, TNBC, HCC, ovarian cancer, GC, HCC, SGC, GBM, RCC
707		**3SBio**	**-**	**Ph3**	**NSCLC, CRC, EC, ovarian cancer**
MHB039A		Minghui Pharma	-	Ph2	Solid tumor
RC148		RemeGen	-	Ph2	BC, NSCLC
JS207		Junshi Pharma	-	Ph2	NSCLC, CRC, HCC
SCTB14		SinoCellTech	-	Ph2	NSCLC
HC010		Hongcheng Pharma	-	Ph1	Solid tumor
LM-299		LaNova Medicines	-	Ph1	Solid tumor
PM8002/BNT327	PD-L1/VEGF	Biotheus/ BioNTech	Ph3	Ph3	SCLC, TNBC, NSCLC, malignant mesothelioma, HCC, BC
HB0025		Huaota	-	Ph2	RCC, EC, NSCLC
AP505/ B1962		APBio/ Tasly	-	Ph2	CRC
IMM2510		ImmuneOnco	-	Ph2	NSCLC, TNBC
SG1408		Sumgen Biotech	-	Ph1	Solid tumor

Source: Pharmacube, CMBIGM

Biotheus/BioNTech (BNTX US)

BNT327 (PD-L1/VEGF bsAb)

BNT327 in 1L unresectable malignant mesothelioma (Clinical Science Symposium)

Data summary:

BNT327 is an investigational bispecific antibody, targeting both PD-L1 and VEGF-A in the tumor and tumor microenvironment (TME). Ph2 results of BNT327 in 1L unresectable malignant mesothelioma were reported (Link).

As of 25 Oct 2023, 31 pts were enrolled, of which 23 had MPM and 8 MPeM. As of 20 Dec 2024, the median exposure duration was 16.0 mo (95% CI 8.1, 19.5) and median follow-up time 19.3 mo (95% CI 17.3, 20.9).

In 23 pts with MPM, cORR was 43.5% (10/23) and DCR was 87.0% (20/23). mPFS was 11.8 mo, and median DOR was 11.8 mo. The 12 mo OS rate was 82.6% (95% CI 60.1, 93.1), with median OS not yet reached. Among 13 pts with MPM of epithelioid histology, cORR was 30.8%, DCR was 84.6% and mPFS was 16.6 mo.

Among 8 pts with MPeM, cORR was 75.0% (6/8) and DCR was 100%. mPFS and OS were not yet reached, with an OS rate of 62.5% (95% CI 22.9, 86.1) at 12 mo. 6 pts with MPeM of epithelioid histology displayed a cORR of 83.3%, DCR of 100% and mPFS of 19.5 mo.

93.5% (29/31) reported Grade 3-4 TRAEs. 5 pts (16.1%) had Grade 3-4 treatment-related SAEs. 5 pts (16.1%) experienced an irAE, 1 (3.2%) of G 3-4. The most common TRAEs were decreased neutrophil count (27 pts, 87.1%), decreased white blood cell count (26 pts, 83.9%), proteinuria (24 pts, 77.4%), anemia (23 pts, 74.2%), decreased platelet count (19 pts, 61.3%), and nausea (16 pts, 51.6%). 6 pts discontinued treatment due to TRAEs; no treatment-related deaths occurred. 9 pts remain on treatment.

Huaota Biopharma

HB0025 (PD-L1/VEGF bsAb)

HB0025 + chemo in 1L EC (Poster)

Data summary:

HB0025, developed by Huaota, is a novel anti-PD-L1/VEGF bispecific antibody, with VEGFR1D2 linked at the N-terminal of anti- PD-L1 antibody. Ph2 results of HB0025 +chemo in 1L advanced or recurrent EC were reported (link).

As of 25 Dec 2024, 39 pts were enrolled, of which 31 pts had least one post-baseline tumor assessment.

The ORR and disease control rate (DCR) were 83.9% (26/31) and 100.0% (31/31), respectively. DoR and PFS were not reached.

18 pts (46.2%) were reported grade≥3 TRAEs. The most common grade ≥3 TRAEs (≥10%) included neutropenia (30.8%), leukopenia (15.4%), thrombocytopenia (10.3%). 2 pts(5.1%) experienced irAEs. 5.1% (2/39) were reported with SAEs. No TRAE led to treatment discontinuation or death. Any-grade hemorrhage events occurred in 7 (17.9%) patients which were all grade 1 in severity.

ImmuneOnco (1541 HK)

IMM2510/ AXN-2510 (PD-L1/VEGF bsAb)

IMM2510 in R/R STS (Poster)

Data summary:

IMM2510 is a novel bispecific antibody fusion protein targeting PD-L1 and VEGF. Ph1 results of IMM2510 in ⩾2L soft tissue sarcoma were reported (link).

As of 24 Dec 2024, 29 STS pts were enrolled, including 10 with ASPS, 5 with UPS, 8 with LMS, 5 with SS and 1 with other STS subtypes.

96.6% were reported with TRAEs. The most common TRAEs of any grade was infusion-related reaction (IRR) (37.9%), platelet decreased (31%) and AST increased (27.6%). 3 pts (10.3%) had ≥ Grade 3 TRAEs, including 1 platelet decreased, 1 transaminase increased and 1 hypoaesthesia. No TRAE leading to treatment discontinuation was observed.

Of 27 efficacy-evaluable STS patients, ORR was 7.4% (2/27) and DCR was 55.6%. 2 PR and 4 SD with tumor shrinkage were observed. PRs were noted in the UPS and LMS cohorts, with an ORR of 20% and 14.3%, and a DCR of 60% and 42.9%, respectively. The DOR was not reached in UPS and 3.68 months in LMS. The study is ongoing.

IMM2510 in Relapsed/Refractory NSCLC (Press release)

Data summary:

Ph1/2 results of IMM2510 in previously treated NSCLC were released. (Link).

As of 24 Dec 2024, 106 pts were enrolled. Among 13 efficacy evaluable NSCLC patients, ORR was 23.1% and DCR was 69.2%.

21.7% were reported ≥ Grade 3 TRAEs and 4.7% were reported TRAEs leading to discontinuation. 1 pts (0.9%) were reported TRAEs leading to death sue to hypersensitivity at 20mg/kg.

Disclosures & Disclaimers

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OUTPERFORM	: Industry expected to outperform the relevant broad market benchmark over next 12 months
MARKET-PERFORM	: Industry expected to perform in-line with the relevant broad market benchmark over next 12 months
UNDERPERFORM	: Industry expected to underperform the relevant broad market benchmark over next 12 months

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