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Next-Generation Antibodies: A New Era in Immuno-Oncology
The opportunity is real – but only for those who move fast and outpace the competition
August 2025

The immune checkpoint inhibitor (ICI) patent cliff sets the stage for transformative innovation and growth in solid tumors

Early movers with sharp clinical strategies or winning combinations will lead

A $50B opening in immuno-oncology (IO)

To expand the market, new IO therapies for solid tumors must go beyond the limits of legacy ICIs by:

- Improving overall survival
- Expanding coverage across tumor types and lines of therapy
- Overcoming resistance

Bispecifics and beyond: the next wave of innovation

Recent setbacks in novel ICI targets are shifting focus toward next-gen antibody platforms where momentum is accelerating:

- Anti-PD(L)1/VEGF bispecifics are gaining traction, with a wave of deals in 2024 and Pfizer entry in 2025
- Emerging modalities including ADC-IO combinations, trispecifics, and anti-TGFβ are drawing investment

The race is on, and the clock is ticking

The next 24-36 months are critical, and success will depend on:

- Targeting high-value niches
- Designing fast, adaptive trials
- Building clearly differentiated products

The upcoming ~$50B patent cliff in IO represents one of the decade's most significant opportunities for R&D-driven growth

ICI drugs facing loss of exclusivity over the next 6 years

Company	Brand (drug)	Mechanism of action	2023 Revenue	Projected LOE (US)
MERCK	Keytruda (pembrolizumab)	anti-PD1	$25.0B	2028
Bristol Myers Squibb	Opdivo (nivolumab)	anti-PD1	$10.0B	2028
AstraZeneca	Imfinzi (durvalumab)	anti-PDL1	$4.72B	2031
Genentech A Member of the Roche Group	Tecentriq (atezolizumab)	anti-PDL1	$4.19B	2028
Bristol Myers Squibb	Yervoy (ipilimumab)	anti-CTLA4	$2.24B	2025
EMD SERONO	Bavencio (avelumab)	anti-PDL1	$771M	2030
			~$50B total	

The race is on: Which emerging IO therapies could challenge Keytruda's dominance in solid tumors?

Source: GlobalData; non-exhaustive; Note: Logos shown are for illustrative purposes only. All trademarks and brand logos are the property of their respective owners

To expand the market, new IO therapies must go beyond the limits of legacy ICIs

3 key paths to drive IO growth in solid tumors

1

Improve survival

Improve poor survival outcomes in advanced solid tumors—especially metastatic cases treated with ICIs[1]

2

Expand tumor coverage

Gain approvals beyond the 13 current indications by targeting new tumors, additional lines of therapy, and peri-surgical (adjuvant/neoadjuvant) use[2]

3

Overcome resistance

Address the 60% of patients who don't respond to first-line ICIs and ~80% who fail in later-line settings[3]

Sources: [1]Siegel et al. Cancer Statistics (2025); [2]Sun et al. STTT (Aug 2023); [3]Carretero-Gonzalez et al. Oncotarget (2018)

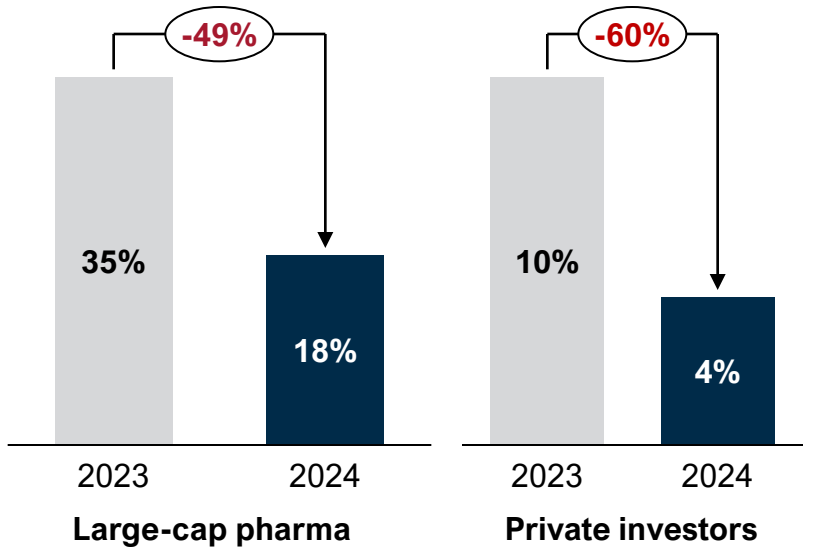
Recent Phase 3 failures cooled enthusiasm in new IO targets, prompting a pivot toward alternate strategies

The failure of several high-profile IO therapies to meet overall survival (OS) endpoints, reinforces the persistent challenge of outperforming standard of care

Company	Pipeline drug (+ combo)	Target	Phase 3 trial (indication)	Key results (termination date)
NOVARTIS	Sabatolimab (+ azacitidine)	TIM-3	STIMULUS-MDS2 (high-risk MDS)	No OS benefit (Jan 2025)
MERCK	Favezelimab (+ Keytruda)	LAG-3	KEYFORM-008 (r/r cHL)	OS futility (Dec 2024)
MERCK	Vibostolimab (+ Keytruda)	TIGIT	KEYVIBE-003/007 (1L & 2L NSCLC)	OS futility (Dec 2024)
Genentech A Member of the Roche Group	Tiragolumab (+ Tecentriq)	TIGIT	SKYSCRAPER-01 (1L PDL1-high NSCLC)	No OS benefit (Nov 2024)

As a result, pharma and investor interest in IO dropped sharply in 2024 compared to 2023[1]

% of respondents who ranked IO among their top 3 technology priorities for the next 12 months

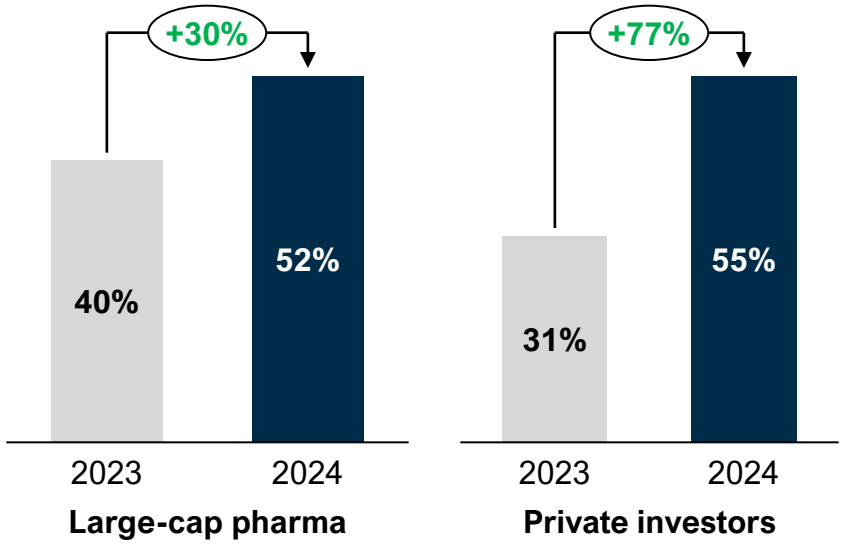


Sources: [1]Lazard Global Biopharmaceutical Leaders Study (Sep 2024, Sep 2023); company press releases; r/r = relapsed or refractory; cHL = classical Hodgkin lymphoma; 1L = first-line; 2L = second line; NSCLC = non small cell lung cancer; OS = overall survival

Focus has shifted to next-generation antibodies, which may hold the greatest promise for powering the future of IO therapies

Pharma and investor interest in next-gen antibodies rose substantially in 2024 compared to 2023[1]

% of respondents who ranked next-gen antibodies among their top 3 technology priorities for the next 12 months



Next-gen antibodies are gaining traction for their strong efficacy, high commercial potential, and lower development risk

✓ **Clinical potential:**
- Next-gen antibodies (bispecifics, multispecifics, nanobodies) have shown superior efficacy in solid tumors over prior standard of care
- For example, J&J's Rybrevant (EGFR/MET bsAb) + Lazcluze cut risk of progression or death by 30% (HR = 0.70) vs. Tagrisso in first-line EGFR-mutant NSCLC patients[2]

✓ **Commercial upside:**
- 13 FDA-approved bsAbs span major indications (e.g., melanoma, NSCLC, ALL, DLBCL)
- Global bsAb market hit $8.65B in 2023 and is projected to reach $485B by 2034 (44% CAGR)[4]

✓ **De-risked pathway:**
- bsAbs in Phase 3 trials have a 52% success rate, outperforming the broader oncology average (44% PTRS)[5]

Sources: *[1]Lazard Global Biopharmaceutical Leaders Study (Sep 2024, Sep 2023); [2]PR Newswire (Oct 2023); [3]Roots Analysis (Sep 2023); [4]Precedence Research (Jul 2024); [5]Pharma Phorum (Aug 2023); bsAb = bispecific antibody; ALL = acute lymphoblastic leukemia; DLBCL = diffuse large B-cell lymphoma*

Anti-PD(L)1/VEGF bispecific antibodies are gaining special attention for their synergistic potential in treating solid tumors

Bispecific anti-PD(L)1/VEGF antibodies are emerging as a potential replacement for conventional ICIs due to their synergistic effects

Leading the charge

- Summit Therapeutics' **ivonescimab**, licensed from Akeso, was the first **tetravalent bsAb** of its kind demonstrating clinical proof of concept, sparking a wave of similar dual-target therapies

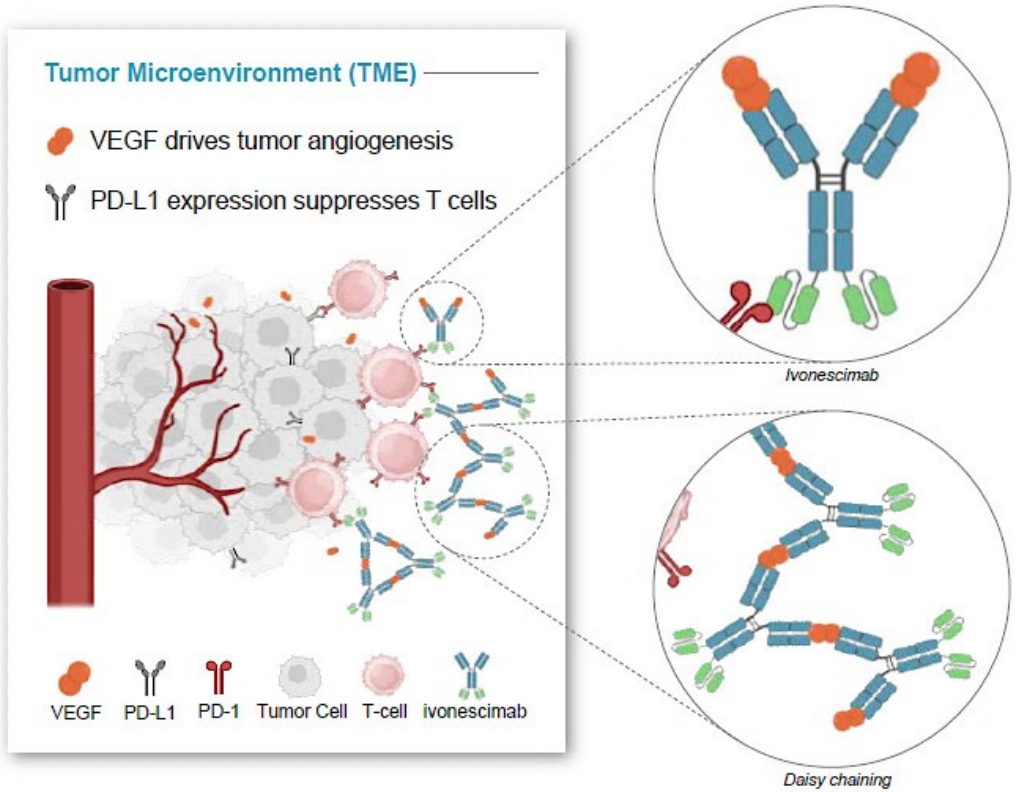
Why is it expected to be superior?

- ✓ **Enhanced immunotherapy:** VEGF inhibition enhances immune cell infiltration while PD1 blockade boosts T-cell activation
- ✓ **Cooperative binding:** Ivonescimab's unique binding mechanism makes it more effective than standard anti-PD(L)1 + anti-VEGF combinations
  - VEGF increases PD1 binding affinity by **18-fold**
  - PD1 increases VEGF binding affinity by **4-fold**

Other theorized benefits

- **Reduced toxicity:** anti-PD1 arm selectively directs VEGF inhibition to the TME, potentially sparing healthy tissue
- **Increased binding:** VEGF dimers leads to "daisy chaining" effect, which may lead to more effective T cell binding

Ivonescimab's tetravalent mechanism of action (anti-PD1/VEGF)



Sources: Left: Summit Therapeutics website (Mar 2025); Right: Crescent Biopharma Corporate Deck (Mar 2025)

Summit's HARMONi-2 trial drew strong interest, but ivonescimab's blockbuster future hinges on OS results from HARMONi-7

Positive results in HARMONi-2 boosted enthusiasm for the class…

Topline PFS (Sept 2024)

- ✓ PFS HR of 0.51 indicates a 49% reduction in risk of progression or death vs. Keytruda in PD-L1+ first-line NSCLC
- ✓ Safety profile manageable and consistent with PD1 and VEGF inhibitors
- ✓ Modeling suggests 1.4x-2x improvement in survival
- ✓ Supported accelerated approval in China

Interim OS (Apr 2025)

- Interim OS HR of 0.777 indicates a 22.3% reduction in risk of death vs. Keytruda

Study limitations and concerns

- No comparison to standard of care (Keytruda + chemo)
- China-only trial (398 patients)
- Underpowered for OS; insufficient for global approval

…but achieving significant OS benefit in HARMONi-7 trial is critical

Trial design (topline results expected 2025)

- Global Phase 3 ivonescimab vs. Keytruda in first-line PDL1-high NSCLC
- 780 patients, powered for OS significance
- Positive OS results could support global approval and shift standard of care

Strategic takeaways

- ➢ Ivonescimab is a bellwether for anti-PD(L)1/VEGF bsAbs
- ➢ Broader success hinges on demonstrating clear OS benefit
- ➢ With no clear coverage or resistance advantage, its value as a monotherapy appears limited

Sources: [1]Press Release (May 2024); Fierce Pharma (Apr 2025); Biopharma Dive (Apr 2025)

A flurry of anti-PD(L)1/VEGF bispecific deals closed in 2024—Pfizer's 2025 move signals continued momentum

Recent deals involving anti-PD(L)1/VEGF bispecific antibodies

Buyer	Seller	Asset	Deal terms	Development status
Pfizer	三生制药 3SBIO INC.	SSGJ-707 (PD1/VEGF)	• **May 19, 2025:** Pfizer acquired exclusive ex-China rights to SSJ-707 from Chinese biotech 3SBio for $1.25B upfront and up to $4.8B in milestones[1]	• Ph 3-ready in China
BIONTECH	BIOTHEUS 普米斯生物技术	BNT327 (PDL1/VEGF)	• **Nov 15, 2024:** BioNTech acquired Chinese biotech Biotheus for $800M, including exclusive rights to BNT327, with up to $150M in milestones[2]	• Ph 3 trial in 1L SCLC • Ph 3 trial in 1L TNBC
MERCK	礼新医药 LaNova Medicines	LM-299 (PD1/VEGF)	• **Nov 14, 2024:** Merck acquired exclusive rights to LM-299 from Chinese biotech LaNova Medicines for $588M upfront, with a total deal value up to $3.3B[3]	• Ph 1 in solid tumors in China • US IND expected in 1H 2025
InstilBio	宜明昂科 ImmuneOnco	SYN-2510 (PDL1/VEGF)	• **Aug 1, 2024:** InstilBio acquired exclusive ex-China rights to SYN-2510 from Chinese biotech ImmuneOnco for $50M upfront, plus potential milestones >$2B[4]	• Ph 1b/2 in 1L NSCLC in China • Ph 1b/2 in 1L TNBC in China • US IND in 2L NSCLC
Summit therapeutics	Akesobio	Ivonescimab (PD1/VEGF)	• **Dec 6, 2022:** Summit acquired exclusive ex-China rights to Ivonescimab from Chinese biotech Akeso for $500M upfront, with a total deal value up to $5B[5]	• Global Ph 3 trials in 1L NSCLC • Approved for 1L PDL1+ NSCLC in China

Note: Development has thus far focused on lung and breast cancers

Sources: [1]Pfizer (May 2025); [2]Reuters (Nov 2024); [3]Reuters (Nov 2024); [4]InstilBio (Aug 2024); [5]FirstWord Pharma (Sep 2024)

Several early-stage US biotechs have entered the market with differentiated therapies under development

Early-stage US biotechs developing anti-PD(L)1/VEGF bispecific antibodies

Company	Asset	Company financing	Development status
OTTIMO PHARMA	Jankistomig (PD1/VEGFR2)	• **Dec 2024:** Raised $140M Series A with David Epstein, former Seagen CEO, as its CEO	• IND for Jankistomig expected in late 2025[1]
OncoC4	AI-081 (PD1/VEGF)	• **Sep 2024**: Merged with AcroImmune to acquire AI-081 • Founded in 2020 with $50M in seed funding; secured $200M from a 2023 licensing deal	• Phase 1/2 BIPAVE-001 trial expected to start in Q1 2025[2]
CRESCENT BIOPHARMA	CR-001 (PD1/VEGF)	• **Oct 2024:** Went public via reverse merger with GlycoMimetics (GLYC), securing $200M in financing	• Phase 1 trial for CR-001 expected to start in Q4 2025[3]
COMPASS THERAPEUTICS	CTX-10726 (PD1/VEGF-A)	• **Nov 2021:** Went public via IPO (CMPX), securing $125M in financing	• IND expected YE 2025[4]

Note: At least 6 additional PD1/VEGF and 4 PDL1/VEGF bispecific antibodies are in development in China

With many PD(L)1/VEGF bispecifics in development, the challenge is clear: how can companies stand out in an increasingly crowded field?

Sources: [1]Biopharma Dive (Dec 2024); [2]Press Release (Dec 2024); [3]Fierce Biotech (Oct 2024); [4]Press Release (Jan 2025)

New ADC combinations and emerging trispecific antibodies in China may drive further dealmaking

On Feb 24, 2025, Summit announced a collaboration with Pfizer to evaluate ivonescimab in combination with Pfizer ADCs[1]

Summit therapeutics × Pfizer

- Pfizer will provide multiple vedotin-based ADCs for evaluation with ivonescimab in distinct solid tumor settings
- Clinical trials expected to start mid-2025

Which other companies will follow in testing new combinations?

GILEAD AstraZeneca astellas Roche Daiichi-Sankyo

Several unlicensed trispecific antibodies are being developed in China, presenting additional BD opportunities

PD-(L)1/VEGF trispecific antibodies[2]

Company	Asset	Target	Status
基石药业 CSTONE PHARMACEUTICALS	CS2009	PD1/VEGF/CTLA-4	Phase 1 solid tumors
道尔生物 DOER BIOLOGICS	DR30206	PD-L1/VEGF/TGFβ	Phase 1 solid tumors
GENOR BIOPHARMA	GB268	PD1/VEGF/CTLA-4	Preclinical
HC BIOPHARMA	HC010	PD1/VEGF/CTLA-4	Phase 1 solid tumors

US companies may be waiting for clinical proof of concept to de-risk this approach before pursuing BD

Are bispecific therapies a bridge toward ADC-bispecific combinations, multi-specific antibodies, or new IO modalities?

Sources: [1]Press Release (Feb 2025); [2]Non-exhaustive; GlobalData, Synapse; ADC = antibody-drug conjugate; BD = business development

Anti-TGFβ therapies show strong potential to overcome ICI resistance as future partners for anti-PD(L)1/VEGF therapies

TGFβ-targeting cancer therapies in development for use with anti-PD(L)1

Company	Asset	Target(s)	Description	Status
BICARA THERAPEUTICS™	Ficerafusp alfa (BCA101)	EGFR/TGFβ ("TGFβ ligand trap")	• Bifunctional fusion protein combines an anti-EGFR mAb with the extracellular domain of TGFβRII	• Phase 2/3 in 1L PD-L1+ HNSCC
ScholarRock	Linavonkibart (SRK-181)	TGFβ1 proprotein	• mAb selectively targets all latent forms of TGFβ1, blocking their activation	• Phase 2-ready
abbvie	Livmoniplimab (ABBV-151)	GARP:TGFβ1 proprotein	• mAb selectively targets GARP-TGFβ1, preventing T_{regs} from releasing active TGFβ1	• Phase 2 in UC; Phase 2/3 in HCC and NSCLC
Roche	RG6440 (SOF10)	TGFβ1 proprotein	• mAb preferentially inhibits protease-induced activation of latent TGFβ1	• Phase 1 ongoing in Japan and US

- On Sep 16, 2024, **Bicara Therapeutics** closed a $362M IPO following the success of BCA101 + pembrolizumab in a Phase 1/1b 1L r/m HNSCC trial. The oversubscribed IPO, **among 2024's largest biotech offerings**, highlights strong interest in this approach

Sources: GlobalData; company press releases; SEC filings

A&M projects that anti-PD(L)1/VEGF therapies could reach $25B, but most value will accrue to early movers and those with smart combos

Value will concentrate in the hands of a few

- Anti-PD(L)1/VEGF therapies could reach **$25B in peak sales**,[1] mostly by replacing legacy ICIs in regimens
- Based on first-generation IO therapies, 2-3 market leaders are likely to capture over **70% of the market value**
- Assuming robust OS benefit, expected to see strong early uptake and become the new backbone of IO, while legacy ICIs remain relevant in select markets

On their own, growth potential is limited

- Current clinical data support survival gains in advanced/metastatic disease, **only one of 3 IO growth levers**
- No evidence yet of overcoming ICI resistance or enabling new biomarker-driven segmentation
- Likely to follow a **similar label expansion path** to earlier ICIs, starting with **lung and breast cancers**

Combinations are key to expanding the market

- Greatest potential lies in novel combinations with ADCs, anti-TGFβ, or other orthogonal MoAs
- Strategic focus must **shift toward combo regimens** to address resistance and expand indications
- Expect strong deal activity over the next 12 months as players seek winning combination strategies

Sources: [1]A&M modeling

The next 24 to 36 months will be critical for defining IO leadership—and smart clinical strategies will separate the winners

Clinical strategies to stand out in a crowded field

Target high-value niches

- Use multi-omics to **identify high responders** and segment accordingly
- Prioritize biomarker-defined, high-unmet-need populations to **secure Tier-1 guideline inclusion**
- Target **underserved indications** to gain early share and reduce competitive pressure

Design smarter trials

- Design **adaptive trials** that allow early stopping or rapid pivots
- Embed **experimental combinations** early to accelerate differentiation, boost OS outcomes, and avoid outdated comparators
- **Streamline paths to pivotal readouts** in defined patient groups

Build a differentiated product profile

- Avoid capital trapped in me-too programs
- Emphasize **secondary differentiators** like lower discontinuation rates, fewer severe AEs, and brain metastasis activity
- Highlight real world benefits such as **dosing convenience and administration advantages**

Immuno-oncology is entering a new era – those who move fast will define it.

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