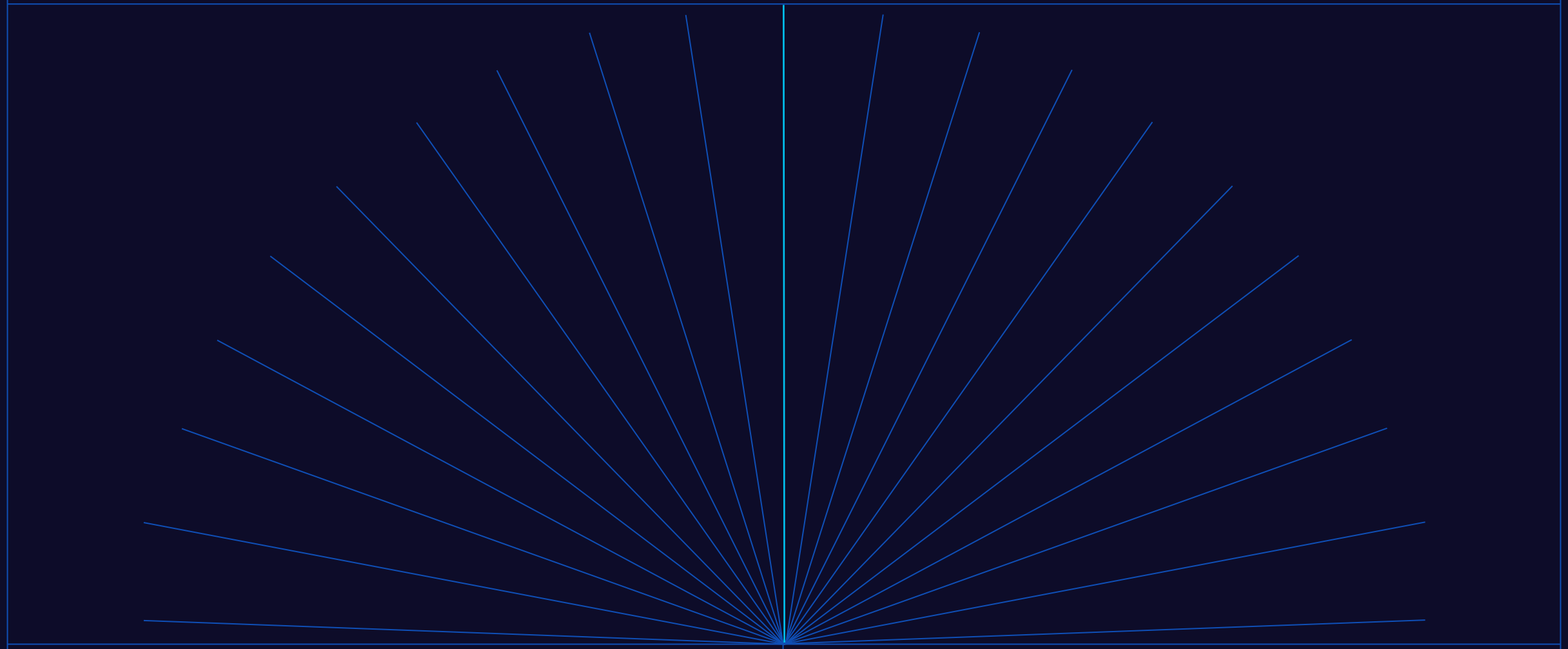

Sleuth

Sleuth Intel Hub
ADC Intelligence Report, Q3 2026

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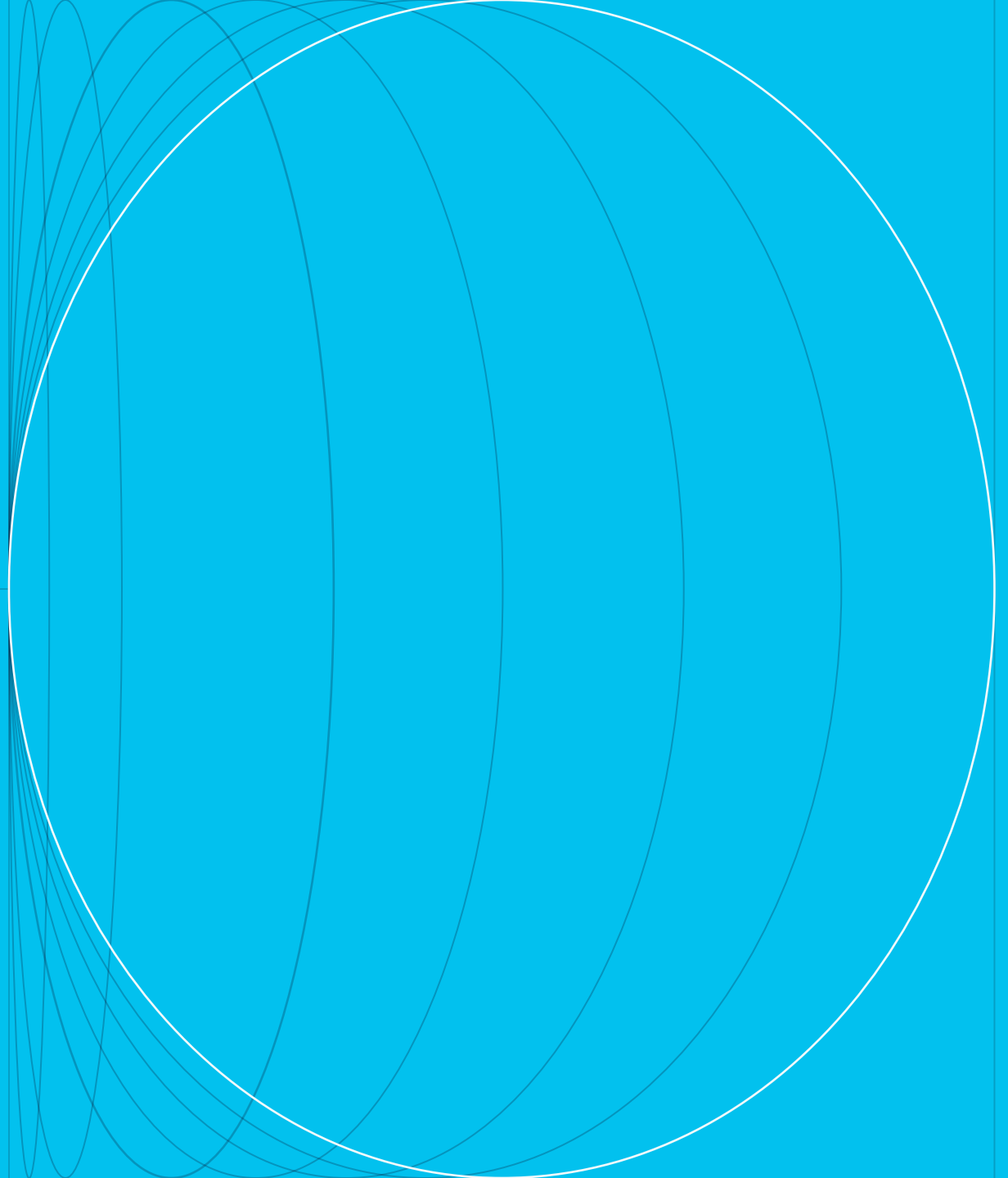
Section 1: The Data

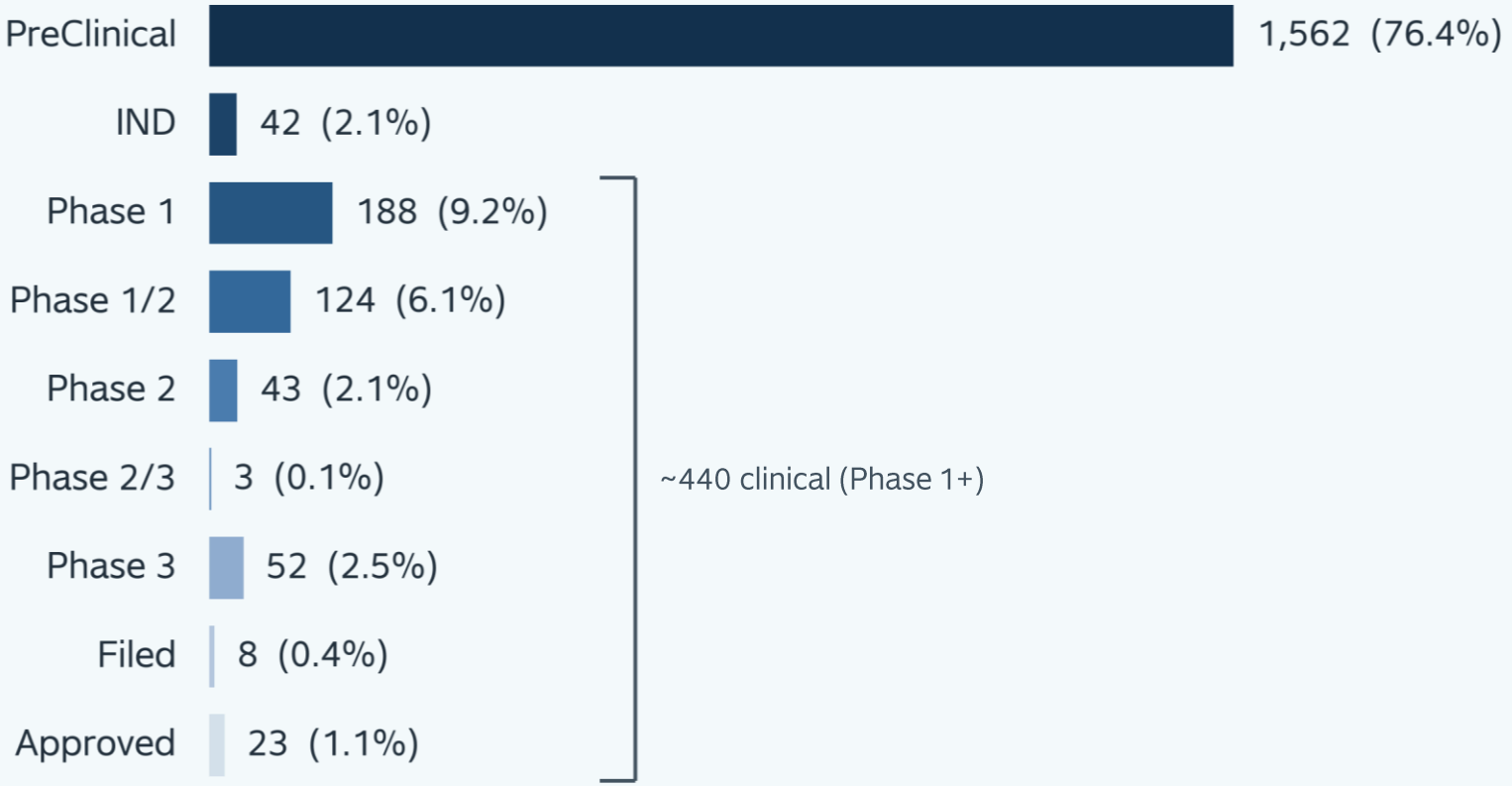


ADC is a mature modality with a crowded clinical core

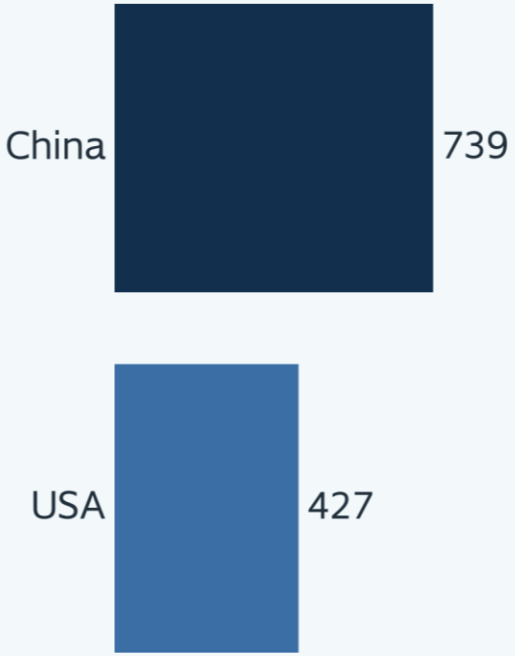
Despite strong preclinical activity, ADCs are well established with 23 approvals and ~50 Phase 3 programs

ADC Program Universe by Development Phase

n = 2,045 ADC programs (incl. discontinued and inactive)



China vs U.S. Preclinical Volume

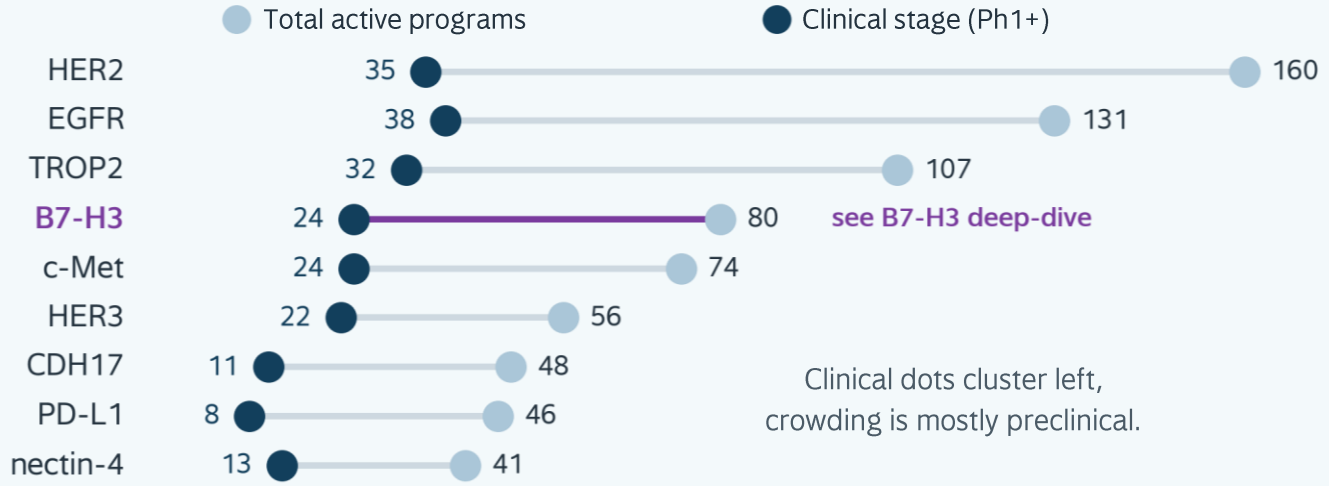


Competitive intelligence analysis of about 2,045 ADC programs, the full universe across all statuses (including discontinued and inactive). Phase and geography are program counts.

Crowding marks validated targets, while differentiation shifts to payload / linker

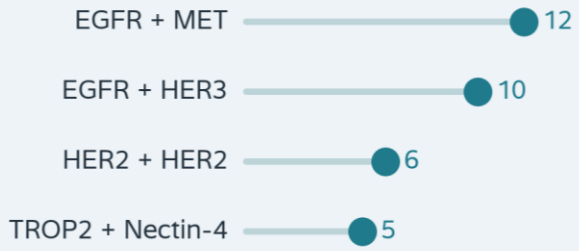
HER2, EGFR, TROP2, B7-H3, c-Met, and HER3 lead the clinic with 20+ clinical programs each

Active ADC Programs by Target and Stage



9 of 313 active targets. Multi-target drugs count in every bucket, target counts overlap above the 1,838 active program[1] base.

Bispecific fold clusters (Top 4 receptor-escape pairs)



Sleuth uncovered 75 unique bispecific pairs, of which 40 are in the clinic and 4 are in Phase 3. 46 of 75 use a non-DXd topo-1 payload

- Despite 313 targets in active development, the top targets cluster within a narrow band of clinical-stage counts
- Past a minimum level of validation the clinical count stops scaling, with HER2's 160 active programs falling to 35 clinical, nearer to B7-H3, c-Met and HER3 which have half or fewer total active programs
- There's less pressure to pursue new biology when the chemistry offers so many variables (payload, linker, conjugation) to build a differentiated asset

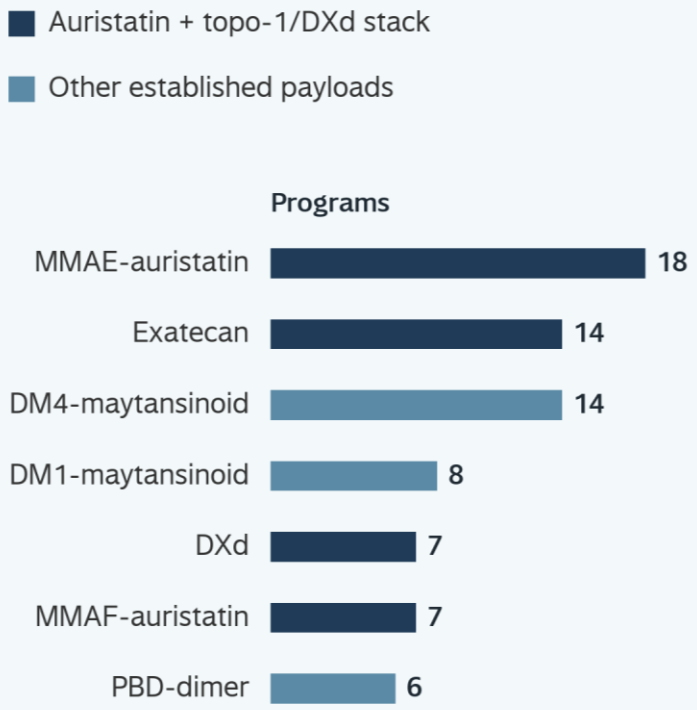
Competitive intelligence analysis of 1,838 active ADC programs across 313 distinct targets, with the 9 highest-count targets shown. [1] The 1,838 is the active universe, a subset of the 2,045 all-status count on the prior slide (which includes discontinued and inactive programs). Target counts sum above 1,838, with each multi-target drug landing in every one of its target buckets. The clinical-stage cut counts programs at Phase 1 and later.

Two payload families carry most of the clinical field

About 44% of clinical programs sit on two payload families, and the core chemistry is commoditizing

- Beyond the top six programs listed, there are 15 more payload classes with 1 to 4 programs each, totaling 36 additional programs
- Two payload families carry ~44% of the clinical field, and topoisomerase-1 has overtaken MMAE as the most contested warhead to license
- About 75% of clinical programs do not disclose their payload (i.e., only ~110 of ~440 programs disclosed)
- Protein-degrader payloads remain early, with only 1 to 2 clinical programs today

Payload classes by program count (highest first)



Auristatin and topo-1/DXd are the validated stack

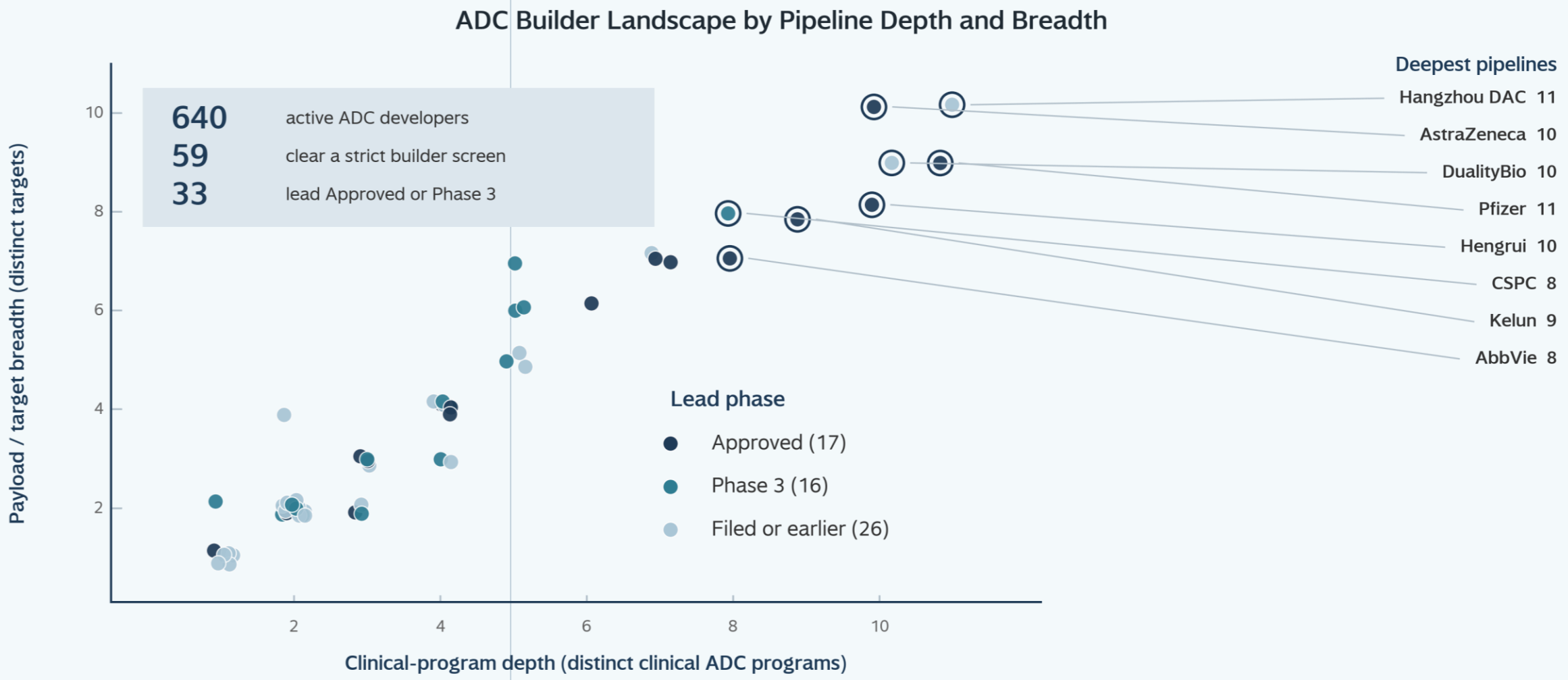
Linker chemistry and conjugation

- Protease-cleavable Val-Cit/PABC
  Cys, stochastic
- Hydrophilic protease/glucuronide-cleavable
  Cys or site-specific
- Cleavable disulfide (sulfo-SPDB)
  Lys, stochastic
- Non-cleavable thioether (MCC)
  Lys, stochastic
- Tetrapeptide GGFG, cleavable
  Cys, stochastic
- Non-cleavable maleimidocaproyl
  Lys or Cys
- Cleavable Val-Ala/PABC or glucuronide
  Cys, stochastic

Competitive intelligence analysis of at least 110 clinical-stage ADC programs across 22 payload classes, one primary payload class per drug. Payload-undisclosed programs were excluded rather than counted as zero. Auristatin and topo-1 or DXd together carry about 44% of the 110. This 110 counts payload-disclosed clinical-stage programs only, a narrower base than the 1,838 active universe. Each payload class shows its typical linker and conjugation.

Only 59 of the 640 active ADC developers would be considered 'multi-program'

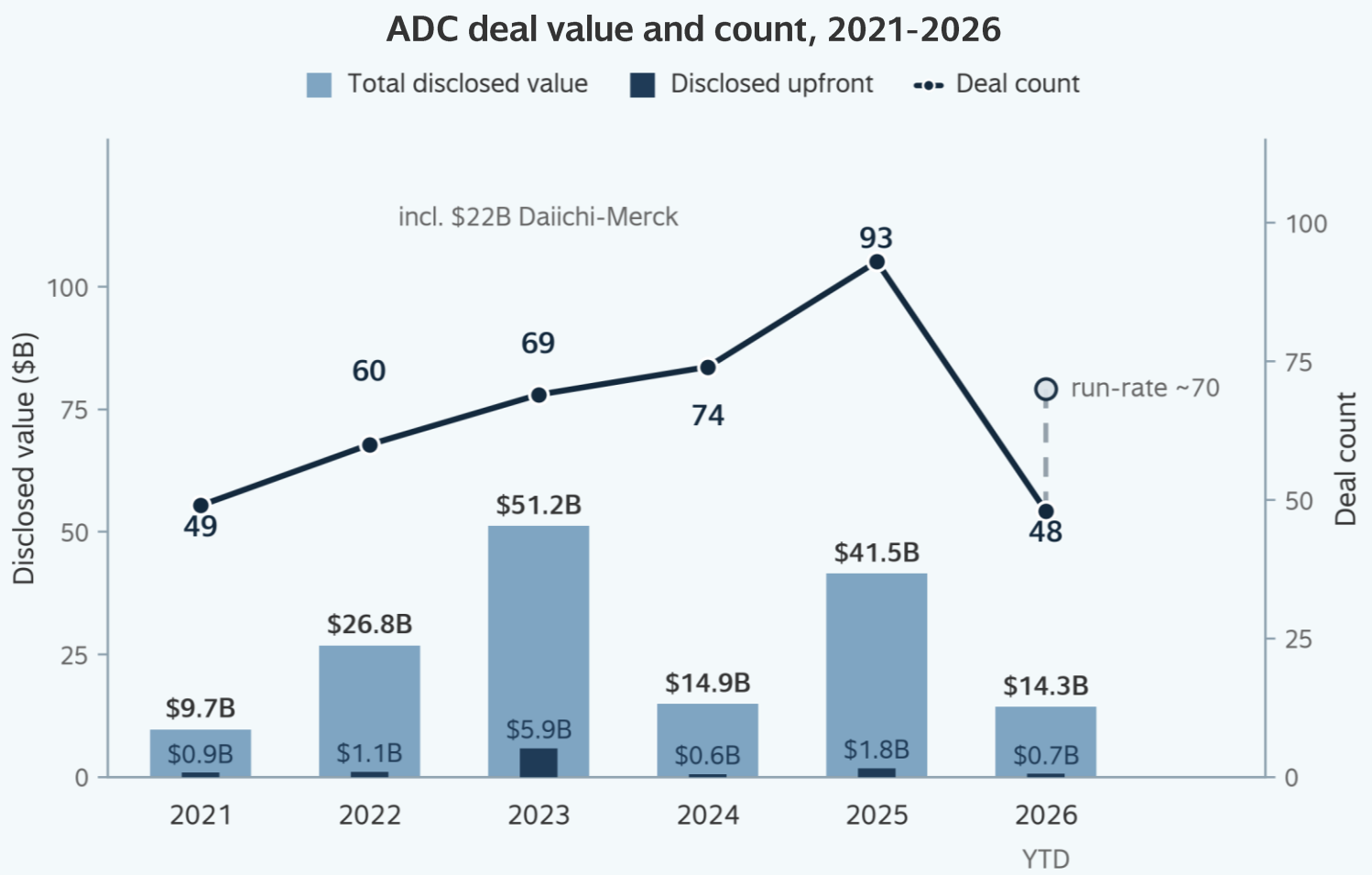
Multi-program[1] developers run several clinical programs or license ADCs repeatedly



Competitive intelligence analysis of the active ADC developer landscape. [1] 'Multi-program' was defined as qualifying on at least one of three tests: two or more clinical programs across two or more payload classes, a multi-target clinical portfolio, or repeat ADC out-licensing. On that screen, 59 of about 640 active developers qualify, counted separately from that base.

ADC dealmaking is at record activity as buyers pay for pre-proof bets

Deal count hit 93 in 2025, with disclosed upfronts a thin slice of headline value

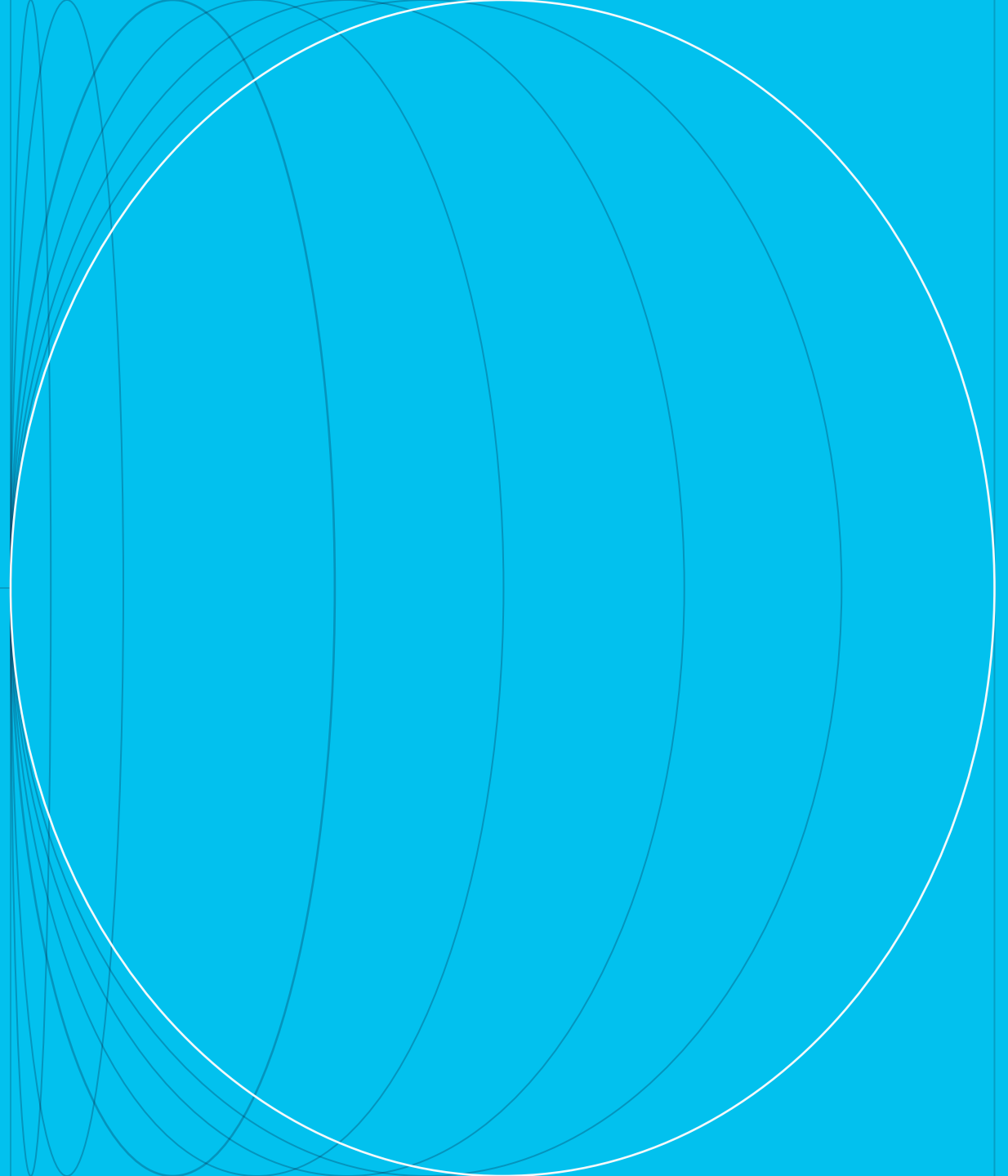


Disclosed value only. Disclosure varies year to year.

- Deal count climbed from 49 in 2021 to 93 in 2025 and 2026 is on a run-rate near 70
- About 72% of deals (219 of 303), were struck at preclinical stages, with buyers underwriting platforms before clinical proof
- With ~70+ deals a year and thin upfronts, a wait-and-see BD approach could end up being more expensive

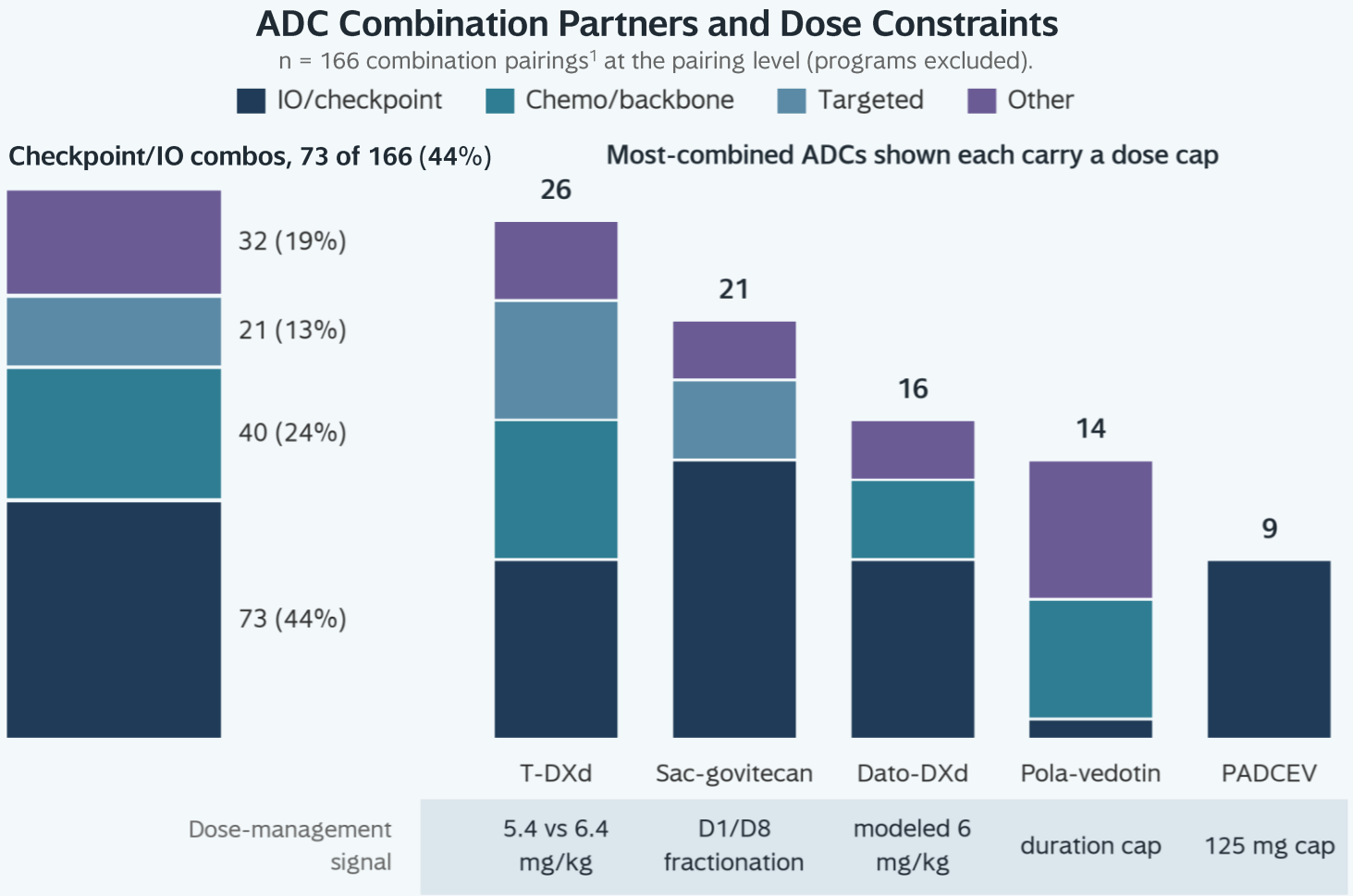
Competitive intelligence analysis of 393 ADC deals announced 2021 through August 2026 (2026 is a partial year). Dollar figures are disclosed value only and disclosure varies year to year, and annual totals are lumpy and megadeal-driven (2023 includes the $22B Daiichi Sankyo and Merck deal). Deal count is the cleaner momentum signal. Deal counts are kept separate from pipeline program totals.

Section 2: Sleuth Perspectives



The therapeutic window decides how far an ADC can combine

Clean-dose ADCs stack at full dose, dose-capped assets combine at reduced intensity



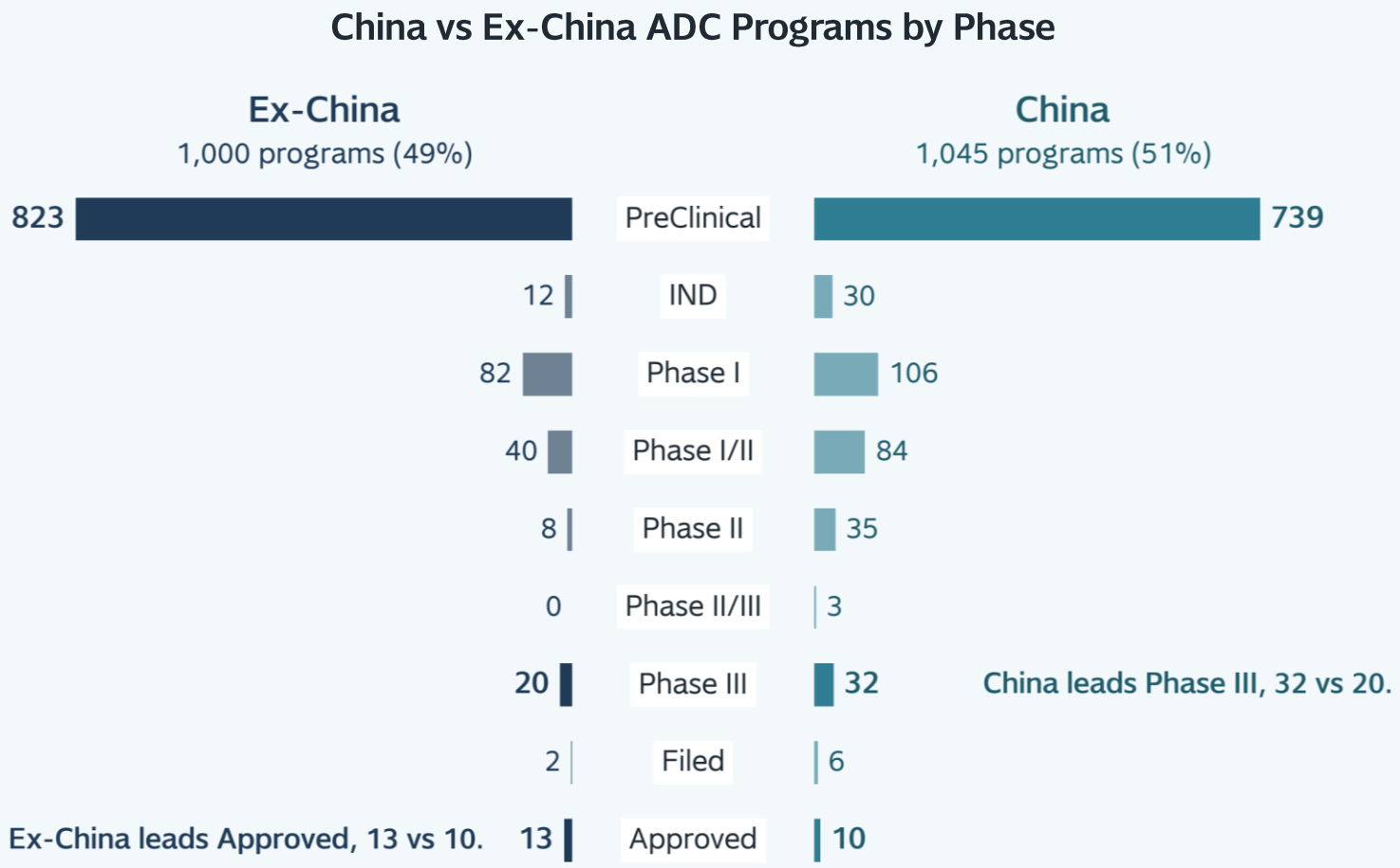
- Checkpoint pairing is the crowded default combination and adds little real differentiation
- T-DXd, Sac-govitecan and Dato-DXd all carry explicit dose caps, forcing their combinations to reduced intensity and bleeding efficacy
- **Sleuth Insight:** Combination breadth is an output of the therapeutic window. Clean-dose assets stack at full dose while dose-capped assets bleed efficacy. Watch wider-window designs like Sutro's STRO-004

[1] Competitive intelligence analysis of 166 ADC combination pairings, counted as pairings rather than programs, with checkpoint pairings normalized across sub-labels. Dose signals draw on 24 Project Optimus dose-optimization instances. Both are kept separate from the 1,838 active and 2,045 full pipeline counts.

China is now responsible for half the global ADC pipeline

China originates ~1,045 of ~2,045 programs and leads Phase 3 development

- China leads Phase 3 development vs the combined rest of the world (32 programs to 20); however, ex-China still leads in ADC approvals (13 to 10)
- China's Phase 3 mix could open a massive late-stage partnering wave or signal a new era of domestic global launches
- **Sleuth Insight:** China's structural advantage concentrates where medicinal chemistry and development execution dominate. ADCs are the clearest example, and as a result China now originates more than half the global pipeline



Full-pipeline ADC programs across all statuses. Ex-China = global minus China.

Dual-payload collapses combination therapies into a single therapeutic window

Aims to address the limitations of single-agent ADCs by combining two cytotoxic payloads with distinct MoAs

Dual ADC Landscape by Phase and Origin

n = 106 dual ADC programs · 86% preclinical

Engineering approach
overlapping flags (not additive)

Dual-target	42
ADC + inhibitor	13
Dual-payload	11

Dual-payload warhead pairs
11 programs · 8 warhead pairs

TOP1i + RNA Pol II	**KH815, KHN922**
TOP1i + MMAE	JSKN021, Otsuka
DX-8951 + MMAE	STRO-227
MMAF + exatecan	YB-811
DX-8951 + gemcitabine	MC003
DX-8951 + triptolide	Kanghong
DXd + immune payload	Tras-DXd
Tubulin + TOP1i	YB-800

a TOP1 warhead anchors every named pair

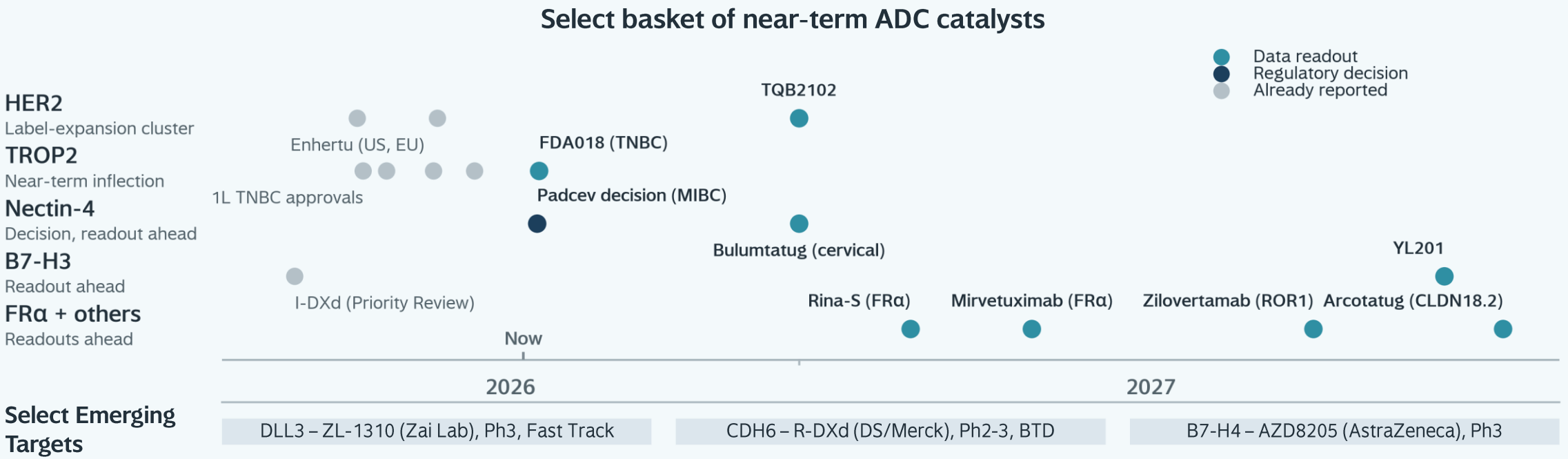
Big Pharma: 4 of 106 programs
Pfizer, Lilly, AstraZeneca, Novartis

- Leading pairs are coupled rather than additive, matching a TOP1 warhead with a 2nd payload that blocks the damage response (ATRi, RNA Pol II). Preclinical models show regression even where each payload alone has failed
- Some buyers (i.e., Lilly / Crossbridge) are paying platform prices early, but upcoming Ph1 safety readouts are the adjudicating events for the field
- **Sleuth Insight:** Combination efficacy is capped by the dose window. Dual-payload moves the combination inside the molecule, so one window covers both mechanisms

Competitive intelligence analysis of a 106-program dual and next-generation ADC landscape. Three engineering approaches are shown: dual-target or bispecific ADCs at 42, ADC plus inhibitor combinations at 13, and dual-payload ADCs at 11.

Incumbents own the near-term catalyst calendar

Of 51 pivotal programs, HER2's near-term events are label expansions while TROP2 brings new approvals



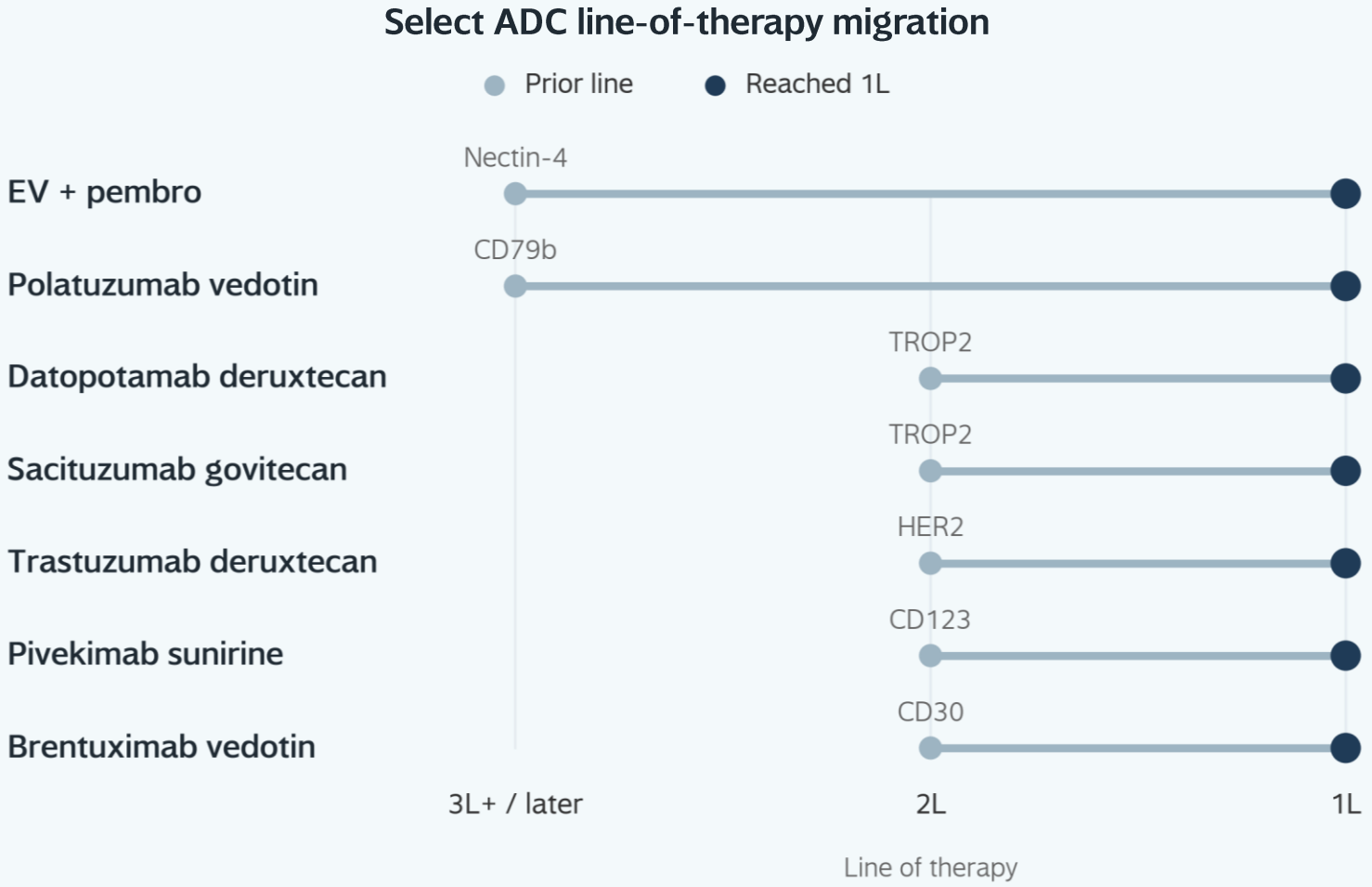
- HER2 anchors the late-stage calendar, but its catalysts are mostly label expansions on approved franchises like Enhertu
- TROP2, by contrast, is the near-term inflection, mixing label expansions with new approvals including triple-negative breast cancer
- **Sleuth Insight:** The coming year of catalysts reflects incumbents compounding their leadership position with label expansions (particularly HER2). The live opening is TROP2, where a run of first-approval decisions can reset the competitive order

Competitive intelligence analysis of 51 active Phase 3 or pivotal ADC programs, each updated to its current status. Catalysts are classified as data readouts or regulatory events. Comparisons across programs are cross-trial rather than head-to-head.

Owning a first-line indication is the real value trigger

A select set of ADCs that have crossed into first-line, where frontline economics drive disproportionate use

- First-line entry stays rare and hard-won, and most assets in 1L had approvals in later lines before moving into 1L – underwrite the migration path, not the entry point.
- Flagship 1L moves include EV+P in urothelial (EV-302, PFS 12.5 vs 6.3 months) and Trodelvy in TNBC (ASCENT-03 and ASCENT-04)
- **Sleuth Insight:** Clean-dose assets are the only credible frontline challengers – every ADC that reached 1L got there in combo with SOC, so conversion requires stacking at full dose

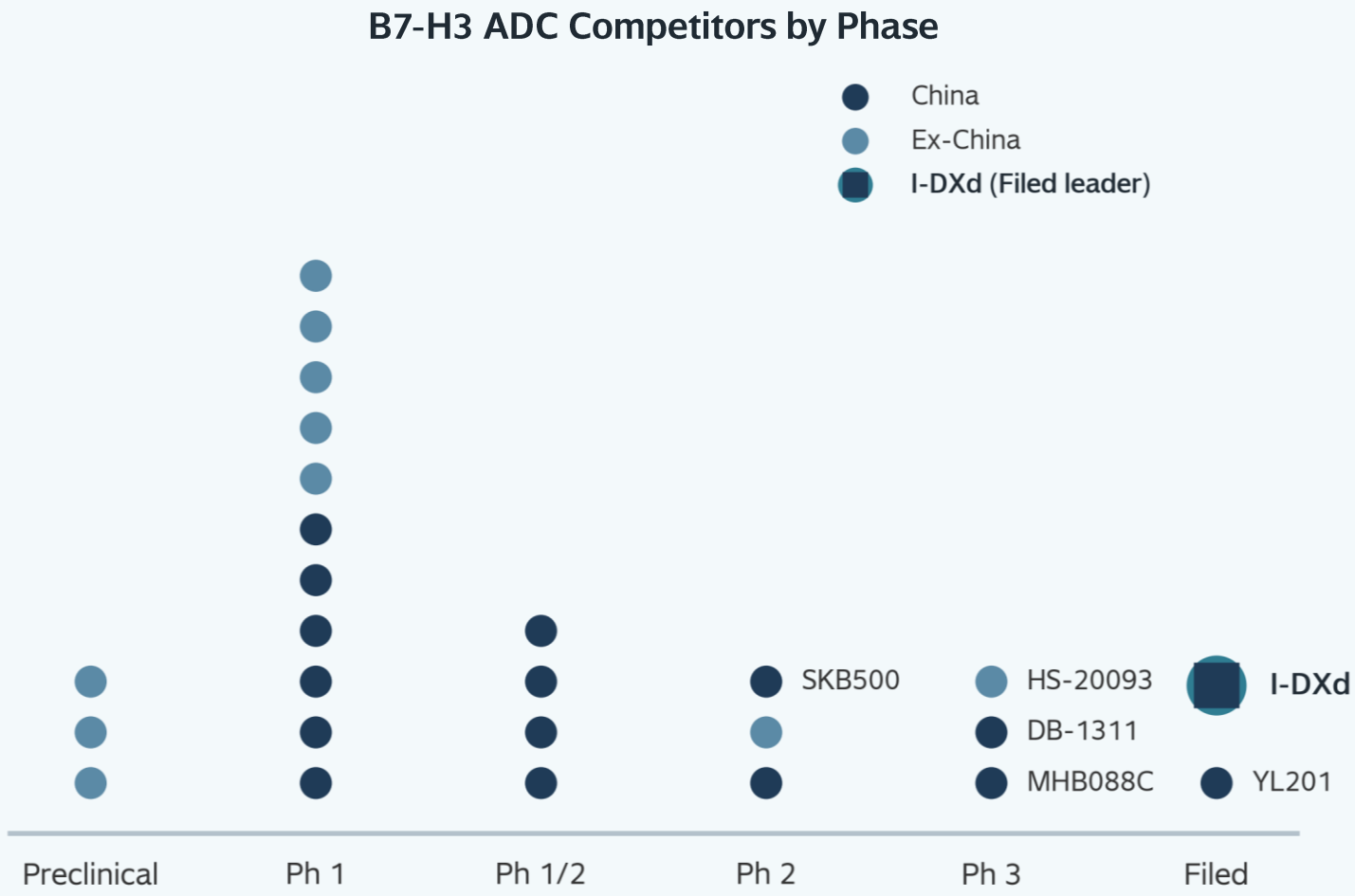


Competitive intelligence analysis of ADC line-of-therapy milestones from 2021 to 2026, counted as data events like approvals, pivotal readouts and filings, across the US FDA, China NMPA and global pivotal trials. This is a curated view of the assets that have reached first-line rather than an exhaustive census

In B7-H3, only a differentiated construct still has room

The entry window is closing behind I-DXd, whose lead is regulatory speed rather than exclusive biology

- I-DXd leads on regulatory speed, with a BLA filed with Breakthrough and 48.2% ORR in pretreated ES-SCLC
- The field runs deep, with 15 of 26 disclosed assets being China-based
- **Sleuth Insight:** A straight DXd copy fights a leader that already owns the timeline. The defensible entry is a bispecific or non-DXd payload the incumbent cannot out-file, like IDEAYA's B7-H3 x PTK7 bispecific (IDE034)

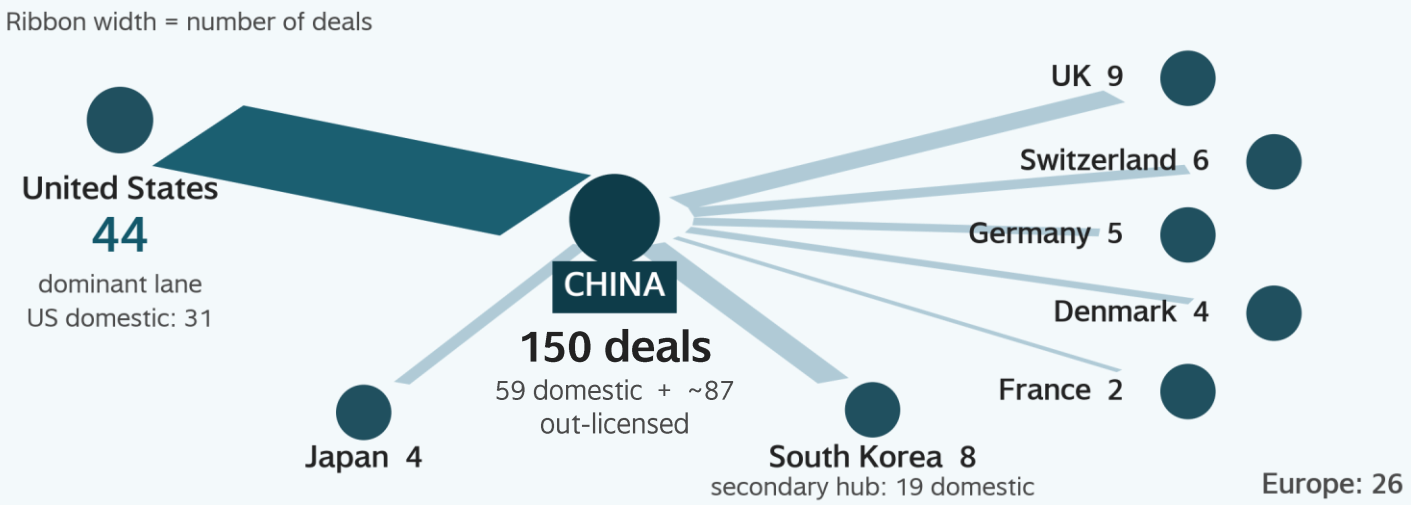


Competitive intelligence analysis of the B7-H3 ADC field, at least 80 active programs, with a clinically disclosed subset of 26 named competitors plotted by phase and sponsor geography. I-DXd (ifinatamab deruxtecan) carries a Filed status with FDA Breakthrough and Priority Review in ES-SCLC, which is a designation and filing status and not an approval.

China is now a standing ADC sourcing channel

Of 150 mapped China-origin deals, about 87 are out-licensed and roughly 60% are WuXi-enabled

China ADC Out-Licensing Geography and Developer Depth



Clinical depth over scale

Platform-scale but clinically thin

- Biocytogen 30 programs, 1 clinical
- Synaffix 21 deals, linker-tech only

Clinically deep developers

- MediLink 14 of 14 clinical, Filed
- CSPC 10 of 10 clinical, Ph3
- Biokin 10 clinical, iza-bren approved
- Kelun NDA-stage TROP2 ADC
- DualityBio Ph3, 5 out-licensing deals

Top out-licensing lanes shown, from deals with known origin and destination geography, a subset of the 393-deal set

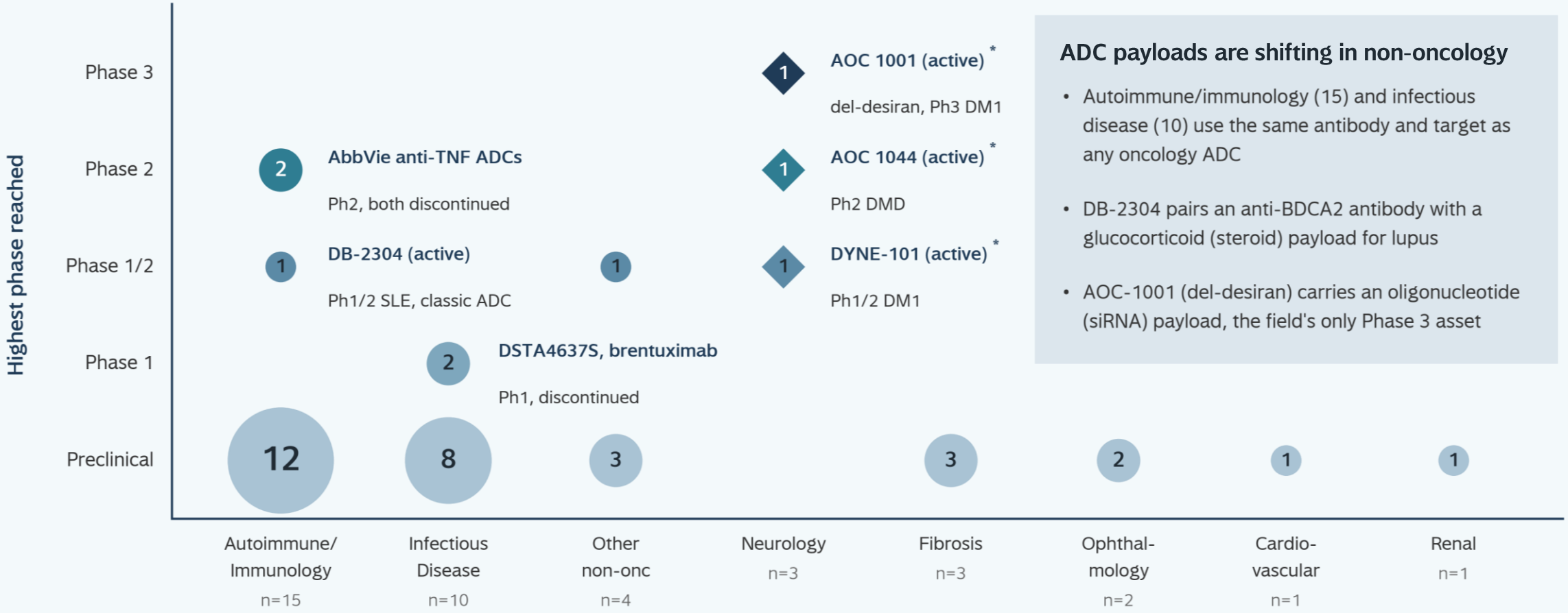
- China is now a repeatable, leading source of advanced ADC assets. Track its deep developers continuously rather than one deal at a time, as it can serve as a sourcing channel for pharma and a partner map for biotechs
- Platform-scale owners run clinically thin, while MediLink, CSPC, Biokin, Kelun and DualityBio combine depth and repeat validation
- **Sleuth Insight:** About 60% of China-to-global deals are WuXi-enabled, signaling a significant supply-chain concentration

Competitive intelligence analysis mapping China-origin ADC deal flow, a mapped subset of the five-year deal set with known origin and destination and likely an undercount, alongside a depth cut of leading China-based developers. Deal-flow counts are kept separate from pipeline counts.

Beyond oncology, ADC becomes a payload-innovation story

The payload turns non-cytotoxic, from glucocorticoids to oligonucleotides

Non-Oncology ADC Programs by Area and Phase



ADC payloads are shifting in non-oncology

- Autoimmune/immunology (15) and infectious disease (10) use the same antibody and target as any oncology ADC
- DB-2304 pairs an anti-BDCA2 antibody with a glucocorticoid (steroid) payload for lupus
- AOC-1001 (del-desiran) carries an oligonucleotide (siRNA) payload, the field's only Phase 3 asset

Competitive intelligence analysis of 39 countable non-oncology ADC programs, 43 audited less 4 with insufficient evidence, classified by therapeutic area and highest phase. Autoimmune and immunology is the largest area, ahead of infectious disease at 10. The only Phase 3, del-desiran, is an antibody-oligonucleotide conjugate carried for context. Diamond markers (*) flag these adjacent AOC and oligonucleotide conjugates, never summed into the oncology counts. Sponsors are North-America-led, unlike oncology.

Sleuth predictions

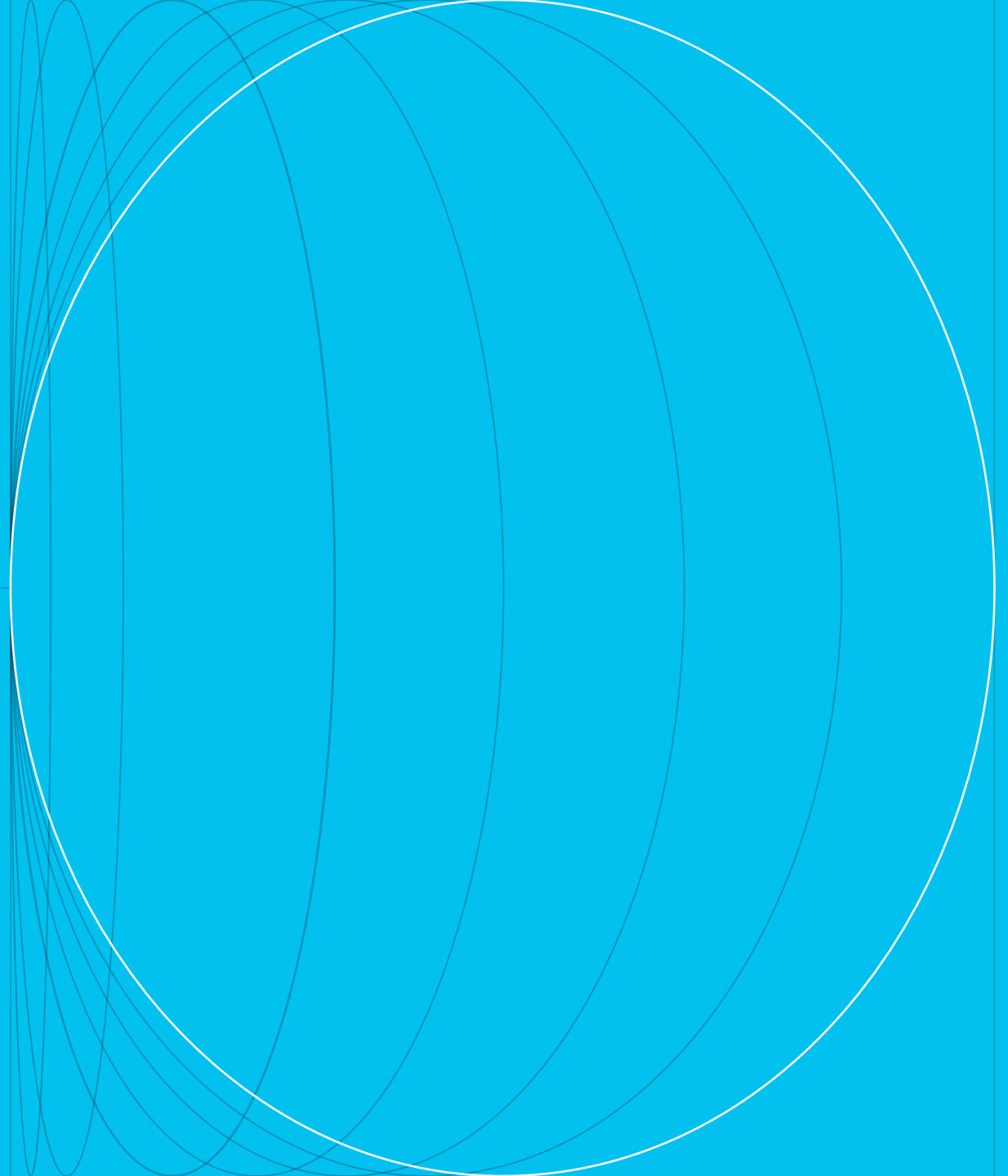
Our read when we look beyond the data

1. **A dual-payload platform trades for more than $1B in headline value:** Lilly paid up to $300M for CrossBridge before the clinic. Phase 1 safety readouts are a gating proof-of-concept milestone for the space, but once that clears, the next platform will reset multiples.

2. **Non-oncology becomes the next pre-proof platform bet:** Just like dual-payloads showed platform chemistry can attract buyouts before clinical readouts, we expect the same pattern in non-oncology.

3. **The biggest buyouts will reward therapeutic index, not novel targets:** The most successful next-gen ADCs will be those delivering the therapeutic index that first generation ADCs failed to achieve, against the same targets. Tubulis is a good reference point for this model, with the success with NaiPi2b.

How Sleuth can help



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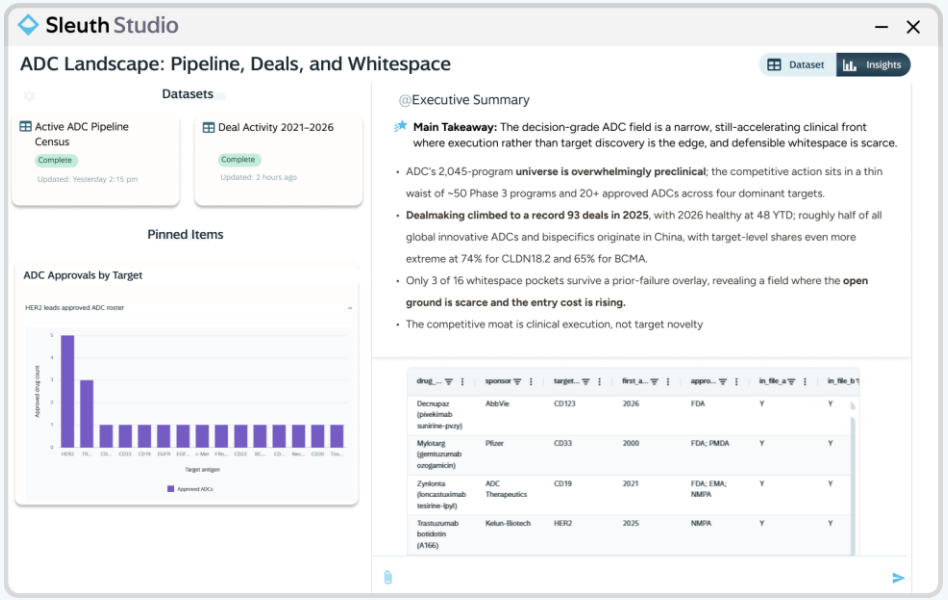
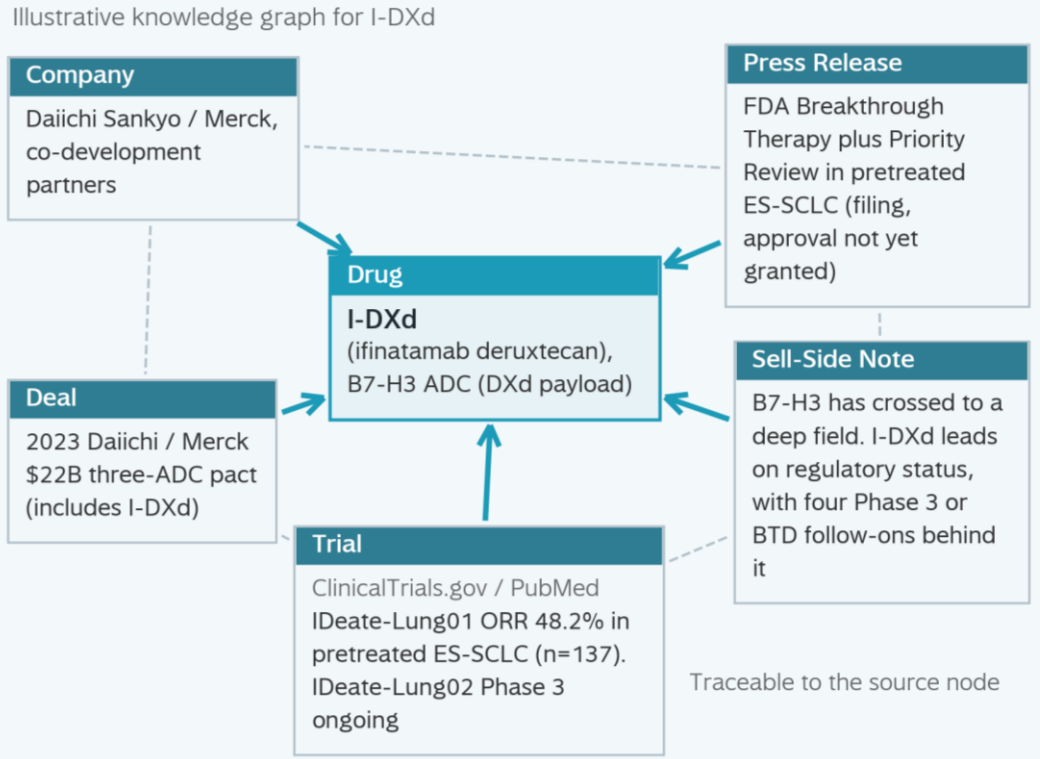
Main Takeaway: The ADC field is a narrow, still-accelerating clinical front where execution rather than target discovery is the edge. Defensible whitespace is scarce.



Intelligence you can stand behind

Bring Sleuth your questions, and pre-connected intelligence surfaces automatically. Our knowledge graph connects data across the landscape, with full traceability.



Case study: Epana Bio indication prioritization

What happens when you evaluate 167 indications with the same effort as six? Read the full case here.

Stakes: Epana Bio needed to make a high-stakes decision on which indications to pursue first for their targeted cell depletion therapeutics.

Challenge: Standard evaluation is often limited by bandwidth, forcing teams to choose from just a few familiar diseases.

Approach: Epana ran a comprehensive evaluation of 167 indications, using an iterative framework to challenge scores and pressure-test every assumption.

Outcome: Leadership built the conviction needed to select lead indications and raise capital with an investor-ready narrative.

167	Indications evaluated
25	Evaluated with a tailored Epana focus that most processes never reach
4	Shortlisted for deep commercial diligence
1	Optimized basket

"All the strategy that used to be proprietary to pharma — the 'game within the game' that actually drives strategic decisions — Sleuth made that accessible to a nine-person biotech. **I think it's the most disruptive, amazing thing for small organizations like ours.** A massive, massive unlock."

Danny Wells, PhD
CEO, Epana Bio