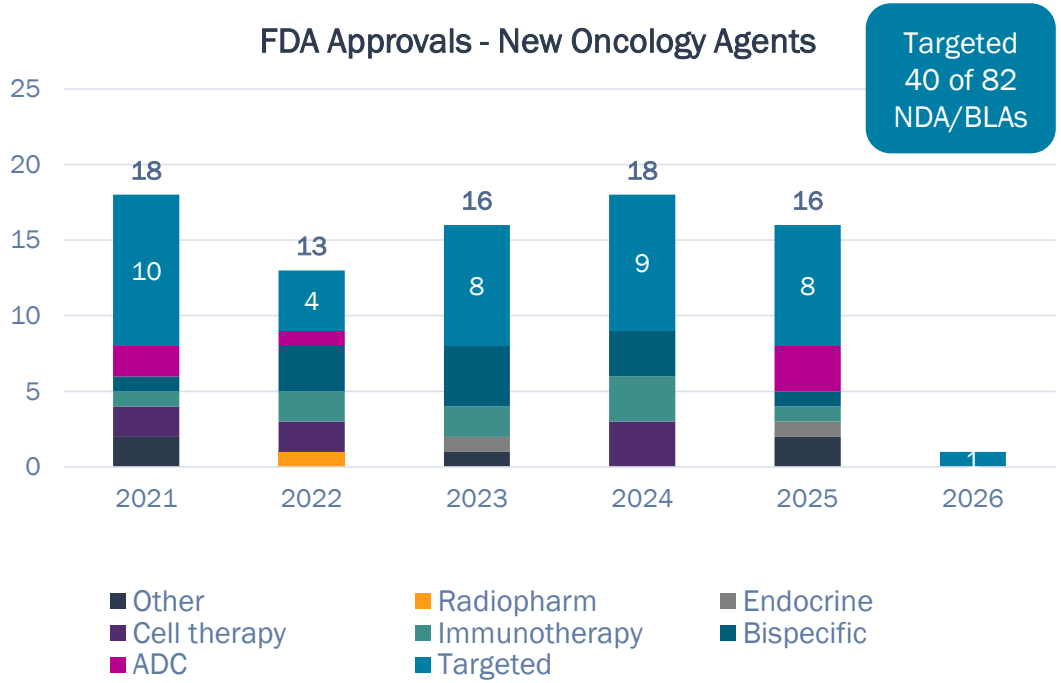
Disruptors and Trends for 2026

March 2026

Bluestar
BioAdvisors

Targeted therapy has been the driver of new oncology approvals in recent history, but a more diverse mix of MOAs have been approved in the past few years

New Oncology Agents – 2021 to Present



- Targeted therapies account for <50% of new approvals in past 5 years, down from >65% in the prior 5 years
- Half of drugs approved in 2024 had novel targets, while 2025 only had 3
- The first cell therapies and T-cell engager for solid tumors approved in 2024
- Wave of ADC dealmaking yet to crest in clinical practice - Datroway (TROP2) and Emrelis (MET) first new ADCs approved in 3 years

Source: FDA; Bluestar analysis

Of the 16 drugs first approved in 2025, there were few new MOAs, and all were approved for niche populations

2025 New Oncology Agents

	Targeted	Cell/Gene Therapy	IO	Bispecific	ADC	Endocrine	Radiopharm/Other
Approved	**Avmapki (RAS) + Fakzynja (FAK)** Ibtrozi (ROS1) Zegfrovy (EGFRex20) **Modeyso (ClpP/DRD2)** Hernexeos (HER2) Komzifti (menin) Hyrnuo (HER2)		Penpulimab (PD-1)	Lynozyfic (BCMAxCD3)	Datroway (TROP2) **Emrelis (MET)** Blenrep (BCMA)	Inluriyo (oSERD)	Inlexzo (chemo) Zusduri (chemo)
Filed	**Relacorilant (GR)**	**Tabelecleucel (EBV)** **Orca-T (T-cells)**	~~RP-1 (oncolytic virus)~~ Sasanlimab (PD-1)	Odronextamab (CD20xCD3)	~~**Patritumab-DXd**~~	Vepdegestrant (oSERD) Camizestrant (oSERD)	
Filing Expected	**Rusfertide (hepcidin)** Zanzalintinib (multi-TKI) ~~Bemarituzumab (FGFR)~~ Gedatolisib (PI3K) Iberdomide (CELMoD) Ozekibart (DR5)					Giredestrant (oSERD)	
Pivotal Readout Expected in 2025	**Ceralasterib (ATR)** Bezuclastinib (KIT)		Fianlimab (LAG-3) **Galinpepimut-S (WT1)**		**Zilovertamab vedotin (ROR1)**		

Novel MOA approvals: Avmapki+Fakzynja for KRASm low grade serous ovarian cancer (LGSOC), Modeyso for H327m diffuse midline glioma, and Emrelis for 2L+ cMET-high NSCLC

Source: TrialTrove; FDA; Company financial reports; Bluestar analysis

Bold = novel target; ~~Crossout~~ = Negative ODAC or filing withdrawn

Among the most exciting potential filings/approvals for 2026 are Roche's next gen G12Ci, divarasib, RevMed's pan-RAS, daraxonrasib, and Summit's PD-1xVEGF, ivonescimab

2026 New Oncology Agents

	Targeted	Cell/Gene Therapy	IO	Bispecific	ADC	Endocrine	Radiopharm/Other
Approved	**Lifyorli (GR)**						
Filed	Gedatolisib (PI3K) Sonrotoclax (bcl-2) Zidesamtinib (ROS1) Zipalertinib (EGFRex20) Zanzalintinib (multi-TKI) Bezaclustinib (KIT) **Rusfertide (hepcidin)**	~~**Tabelecleucel (EBV)**~~ **Orca-T (T-cells)** Anito-cel (BCMA)	RP-1 (oncolytic virus) Sasanlimab (PD-1) Cretostimogene grenadenorepvec (oncolytic virus)	Odronextamab (CD20xCD3) **Ivonescimab (PD-1xVEGF)**	Pivekimab sunirine (CD123)	Vepdegestrant (oSERD) Camizestrant (oSERD) Giredestrant (oSERD)	177Lu-DOTATOC Pegargiminase
Filing Expected	Iberdomide (CELMoD) Ozekibart (DR5) Mezigodomide (celMOD)						
Pivotal Readout Expected in 2026	Divarasib (G12C) **Daraxonrasib (panRAS)** Mevrometostat (EZH2)		Fianlimab (LAG-3) **Galinpepimut-S (WT1)** Gotistobart (CTLA4)	**SSGJ-707 (PD-1xVEGF)**	Sonesitatug vedotin (claudin18.2) **Sigvotatug vedotin (IB6)** Trastuzumab pamirtecan (ER2)		

Drugs to watch in 2026:

- Roche's **divarasib** (G12Ci) represents a potential 2nd generation, going head-to-head against approved sotorasib and adagrasib in 2L NSCLC
- RevMed's **daraxonrasib** (panRAS) could change 2L PDAC, cracking open the KRAS market beyond G12C inhibitors
- **Ivonescimab** (Summit, PD-1xVEGF) filed for 2L+ EGFRm NSCLC – will FDA approve despite lack of OS benefit at final analysis?

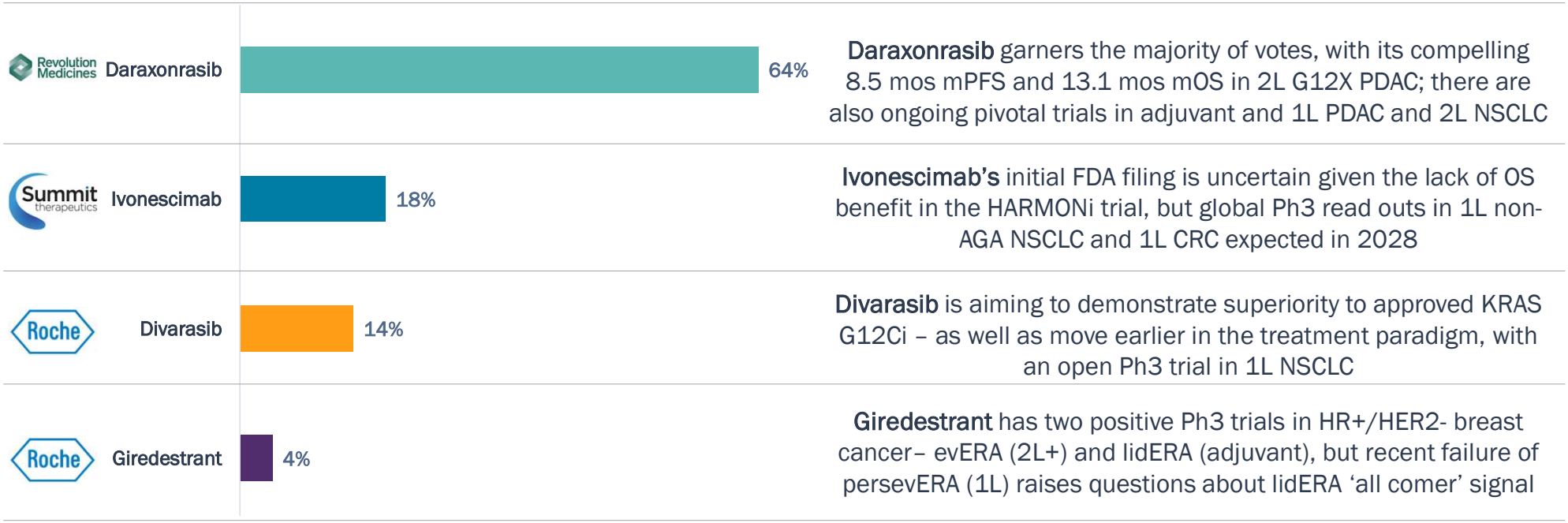
Source: TrialTrove; FDA; Company financial reports; Bluestar analysis

Bold = novel target; ~~Crossout~~ Negative trial or filing outcome

In a Bluestar poll, most selected daraxonrasib as the pivotal-stage drug with greatest potential disruption potential; there is more uncertainty around each of the other poll options

Bluestar Poll

Which Potential 2026 Approval or Pivotal Read Out Will Have the Most Impact on the Oncology Treatment Landscape?



Daraxonrasib garners the majority of votes, with its compelling 8.5 mos mPFS and 13.1 mos mOS in 2L G12X PDAC; there are also ongoing pivotal trials in adjuvant and 1L PDAC and 2L NSCLC

Ivonescimab's initial FDA filing is uncertain given the lack of OS benefit in the HARMONi trial, but global Ph3 read outs in 1L non-AGA NSCLC and 1L CRC expected in 2028

Divarasib is aiming to demonstrate superiority to approved KRAS G12Ci – as well as move earlier in the treatment paradigm, with an open Ph3 trial in 1L NSCLC

Giredestrant has two positive Ph3 trials in HR+/HER2- breast cancer– evERA (2L+) and lidERA (adjuvant), but recent failure of persevERA (1L) raises questions about lidERA 'all comer' signal

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Source: TrialTrove; FDA; Company financial reports; Bluestar analysis

Key Trends and Questions for 2026

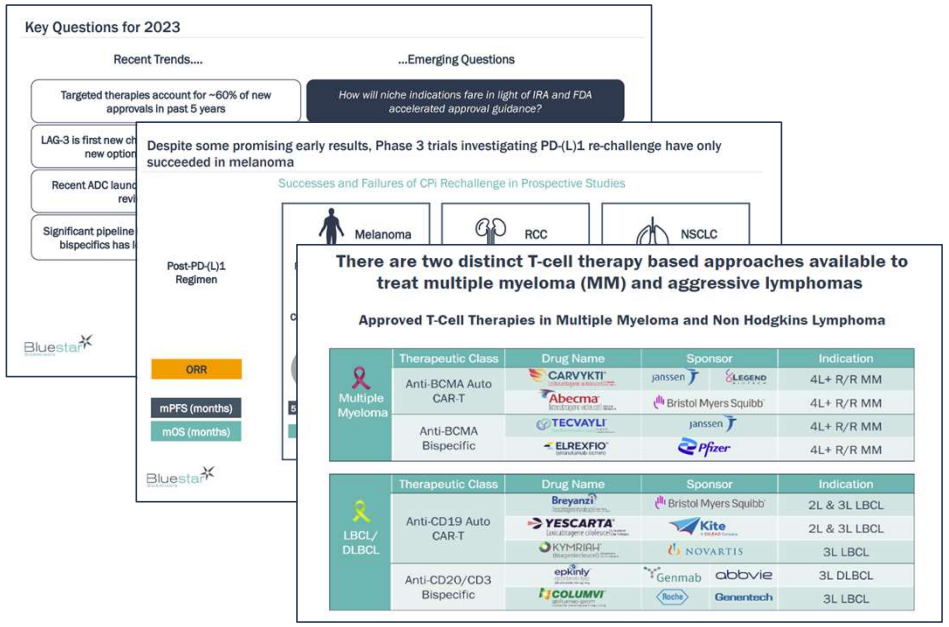
Key Trends…	…Emerging Questions
Novel treatment modalities (IO, targeted therapies, ADCs,) are securing approval in the early-stage setting	*How will these therapies impact the metastatic drug-treated population? Will recurrent patients be eligible for retreatment or need novel options (pushing up 2L)?*
Selecting the 'right' patient and right duration: using ctDNA/MRD to determine treatment	*Are surrogates like ctDNA and MRD ready for prime time in liquid and solid tumors? Should they be used to inform treatment escalation or de-escalation?*
Same target - different modality: defining the optimal positioning and sequencing for ADCs, T-cell engagers, radioligands, cell therapies	*Which approach is best – by tumor, setting, patient characteristics? What drives resistance - Can the same target be used across lines of therapy?*
The next wave of innovation: bispecifics (two targets, or three!, are better than one), in vivo CART, novel ADC payloads, and degraders	*Is the next wave of truly innovative molecules on the way? How can these new approaches address unmet need?*

Bluestar BioAdvisors

Our oncology team publishes regular thought pieces and podcasts on key emerging topics

Oncology Pulses and Biotech Matters Podcasts

- Pulse — Challengers to Auto CAR-T in Liquid Tumors
- Pulse — Flight to Safety or Breakthrough? Resurgence of ADCs and Radiopharmaceuticals
- Pod-cast — ADC Alchemy: A Post-ASCO Discussion
- Pulse — Oncology's Red and Blue Oceans: Survival Gains vs. Persistent Gaps



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