Oncology Pulse

New Oncology Agents – A Look Back and the Year Ahead

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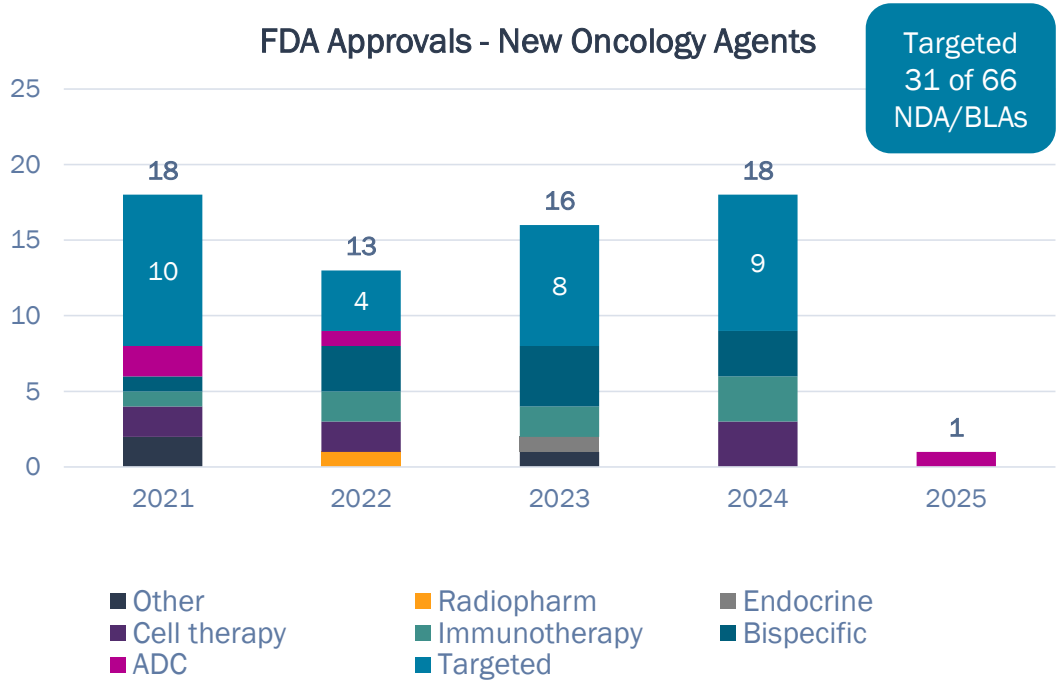
Bluestar BioAdvisors

Strategic Experts in the Business of Life Sciences

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, like DLL3 and claudin18.2
- The first cell therapies and T-cell engager for solid tumors approved in 2024
- Wave of ADC dealmaking not yet impacting practice – Datroway only new ADC in 3 years, with established TROP2 target

* FGFR, FLT3, IDH1, IDH2, MET, NTRK, PDGFR, PI3K, RET, KRAS G12C, ESR1, MAGEA-4, KMT2A

Source: FDA; Bluestar analysis

9 of 18 drugs approved in 2024 have novel MOAs, including the first cell therapies and T-cell engager for solid tumors

2024 New Oncology Agents

	Targeted	Cell/Gene Therapy	IO	Bispecific	ADC	Endocrine	Radiopharm/Other
Approved	**Ojemda (RAF)** **Rytelo (telomerase)** Voranigo (IDH1/2) Niktimvo (CSF1R) Lazcluze (EGFR) Itovebi (PI3K) **Revuforj (menin)** **Vyloy (claudin 18.2)** Ensacove (ALK)	**Amtagvi (TILs)** **Tecelra (MAGEA4)** Aucatzyl (CD19)	**Anktiva (IL-15)** Tevimbra (PD-1) Unloxcyt (PD-L1)	**Imdelltra (DLL3xCD3)** Ziihera (HER2xHER2) **Bizengri (HER2xHER3)**			
Rejected/ Deferred	Rivoceranib (VEGF)		Camrelizumab (PD-1)	Odronextamab (CD20xCD3) Linvoseltamab (BCMAxCD3)	**Patritumab-DXd (HER3)**		**Iopofosine Iomab-B (CD45)**

Select Novel MOAs

- **Imdelltra** (tarlatamab - DLL3xCD3; Amgen): T-cell engager for 2L+ SCLC brings back to life ~5 years after failure of StemCentrx's Rova-T ADC
- **Zolbetuximab** (claudin18.2; Astellas): approval in gastric cancer was held up by a CMC issue; carves out a new segment in this high unmet need tumor type; potential to expand into other GI tumors and many claudin 18.2 ADCs hot on its heels
- **Amtagvi and Tecelra:** First solid tumor cell therapies (TILs and TCR, respectively) will provide insight into market dynamics for autologous therapies

Source: TrialTrove; FDA; company press releases; Bluestar analysis

Bold = novel target

Fewer new MOAs are anticipated in 2025, while the oral SERD class in HR+/HER2- breast cancer is poised for significant competition, with 4 pivotal readouts/approvals on the horizon

2025 New Oncology Agents

	Targeted	Cell/Gene Therapy	IO	Bispecific	ADC	Endocrine	Radiopharm/Other
Approved					Datroway (TROP2)		
Filed	**Avutometinib (RAS) + Defactinib (FAK)** **Dordaviprone (ClpP/DRD2)** Sunvozertinib (EGFR ex20) Taletrectinib (ROS1) Zongertinib (HER2)		Penpulimab (PD-1) RP-1 (oncolytic virus)	Linvoseltamab (BCMAxCD3) Odronextamab (CD20xCD3)	Blenrep (BCMA) **Telisotuzumab vedotin (MET)**	Imlunestrant (oSERD)	Mitomycin gel (chemo)
Filing Expected	Ziftomenib (menin) **Rusfertide (hepcidin)**		Sasanlimab (PD-1)			Camizestrant (oSERD) Vepdegestrant (oSERD)	
Pivotal Readout Expected in 2025	**Ceralasterib (ATR)** Zongertinib (HER2) Zanzalintinib (multi-TKI) Bemarituzumab (FGFR) Iberdomide (CELMoD)		Fianlimab (LAG-3)		**Zilovertamab vedotin (ROR1)**	Giredestrant (oSERD)	

Fewer new MOAs poised for approval compared to last year

Select Novel MOAs

- **Ceralsertib (ATRi, AZ):** Looking to replicate the success of Ph2 Hudson trial in PD-1 pretreated NSCLC
- **Bemarituzumab (FGFR, Amgen):** Could bring a new biomarker to the gastric cancer landscape, though initial Ph3 does not include now SoC PD-1
- Two new potential ADC targets: **MET (teliso-v; AbbVie)** for NSCLC and ROR1 **(zilovertamab vedotin; Merck)** for DLBCL

Source: TrialTrove; FDA; company press releases; Bluestar analysis

Bold = novel target

Key Trends and Questions for 2025

Key Trends…	…Emerging Questions
Early-stage setting takes center stage with IO and targeted therapy approvals	*How will ODAC 'contribution of parts' recommendation impact trial designs? Are surrogates like pCR, ctDNA ready for prime time?*
Cracking KRAS: next-gen G12C, first G12D and pan-(K)RAS emerging	*Pros and cons of pan vs. specific inhibitors? How will order of entry impact opportunity and sequencing by tumor type?*
Beyond PD-(L)1: SC formulations as lifecycle plays; many players chasing VEGF bispecifics	*Can VEGF bispecific/bifunctional approach deliver improved outcomes as PD-(L)1 LOEs near?*
China licensing deals continue – picking up potentially "super me-too" assets in hot classes	*Are innovative molecules on the way? How long will the China licensing wave last given domestic funding environment?*
TROP2 disappointments and TOP1 sequencing data take ADC enthusiasm down a notch	*Have we reached saturation for TOP1 payloads in clinical development? What novel payloads could emerge?*

#ASCO25

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