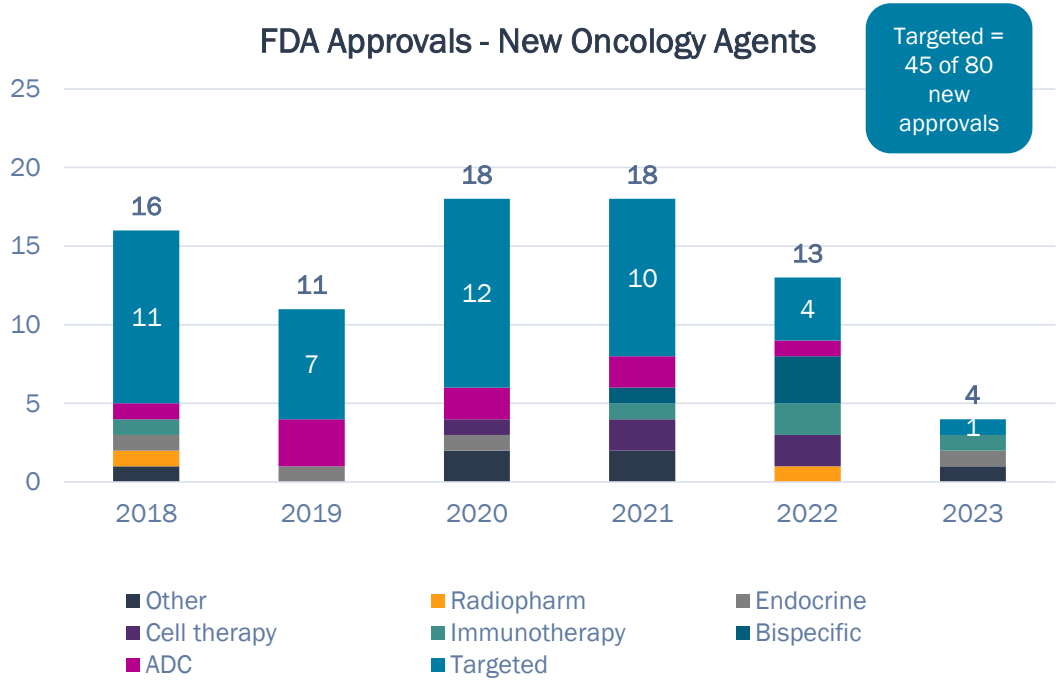
Oncology Update

May 2023

Targeted therapy has been the driver of new oncology approvals, accounting for 60% of new oncology drugs in the past five years

Targeted therapy has dominated approvals – but 2022 new entrants were a more diverse mix



- Targeted therapies account for ~60% of new approvals in past 5 years
- 10 new biomarkers have been added to the list busy oncologists need to track*
- Recent approval of LAG-3 is first new checkpoint since PD-1 – creating a new option for melanoma patients
- Recent ADC launches and partnering have revived the category
- Significant pipeline investment in cell therapies and bispecifics has led to eight approvals… so far

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* FGFR, FLT3, IDH1, IDH2, MET, NTRK, PDGFR, PI3K, RET, KRAS G12C, ESR1

Source: FDA; Bluestar analysis

2022 saw fewer oncology approvals than in recent years, in large part due to weak AA filings from follow-on PI3K and PD-1 inhibitors

2022 New Oncology Agents

	Targeted	Cell/Gene Therapy	IO	Bispecific	ADC	Radiopharm
Approved 13 (6 AA)	Vonjo (JAK)[AA] Lytgobi (FGFR)[AA] Rezlidhia (IDH1) Krazati (KRAS G12C)[AA]	Carvykti (BCMA) Adstiladrin (IFNα2b)	**Opdualag (LAG-3)** Imjudo (CTLA-4)	**Kimmtrak (gp100xCD3)** Tecvayli (BCMAxCD3)[AA] Lunsumio[AA] (CD20 x CD3)	**Elahere (FRα)**[AA]	Pluvicto (PSMA)
Withdrawn/ Rejected (11) (6 AA)	Parsaclisib (PI3K)[AA] Ubilituximab (CD20)[AA] Dovitinib (VEGF) Zandelisib (PI3K)[AA] Surufatinib (VEGF) Poziotinib (pan-HER)[AA]		Tislelizumab (PD-1)(delayed) Torapalimab (PD-1) (delayed) Sintilimab (PD-1)		**Blenrep (BCMA)**[AA]	**Omburtamab**[AA] **(B7H3)**

FDA signaled a tougher stance toward accelerated approval (AA) as well as use of ex-U.S. data to support filing

- Incyte withdrew parsaclisib filing, and MEI Pharm discontinued zandelisib because AA pathway was no longer an option (indications for three additional PI3Ki were withdrawn)
- Blenrep (belantamab mafodotin) AA was withdrawn in Nov 2022, within one month of GSK announcing a failed confirmatory
- FDA rejected filings based predominantly on Asian data for sintilimab and surufatinib; inability to complete inspections in China delayed decisions on two PD-1 inhibitors

2023 could see the approval of agents with new targets such as panRAF, claudin18.2, and GPRC5D, as well as cell therapies for solid tumors – Iovance TILs and AdaptImmune's MAGE A4 TCR

2023 New Oncology Agents

	Targeted	Cell/Gene Therapy	IO	Bispecific	ADC	Other	Radiopharm
Approved	Jaypirca (BTK)[AA]	**Omisurge (enhanced CD34+ stem cells)**	Zynyz (PD-1)			Orserdu (SERD)	
Filed	Momelotinib (JAK) **Nirogacestat (γ secretase)** Fruquitinib (VEGF) Quizartinib (FLT3)	**Lifileucel (TILs)[2]** **Afimi-cel (MAGEA4)[2]**	Penpulimab (PD-1) **ALT-803 (IL-15)** Cosibelimab (PD-L1)	Glofitamab (CD20xCD3)[AA] Epcoritamab (CD20xCD3)[AA] **Talquetamab (GPRC5DxCD3)[AA]** Elrantamab (BCMAxCD3) [AA]	Trastuzumab duocarmazine (HER2)		
On Deck	**DAY101 (panRAF)** **Zolbetuximab (claudin18)**	**Tabelecleucel (T cells) *(filed in EU)***	Tislelizumab (PD-1) (delayed) Torapalimab (PD-1) (delayed)				**Iomab-B (CD45)**
Rejected	Hypericin (PDT[1])						

- **Claudin18.2** provides some OS benefit in gastric – KOLs hopeful it could translate into other GI tumors
- **PanRAF** starting in pediatric glioma (niche), MOA may have potential to expand beyond BRAF V600
- **Cell therapy for solid tumors** – initial indications likely to see limited uptake: AdaptImmune MAGEA4 in rare synovial sarcoma, and melanoma TILs carries IL-2 requirement

[1] PDT = photodynamic therapy [2]Rolling BLA initiated [AA] accelerated approval

Source: TrialTrove; FDA; Bluestar analysis

Key Questions for 2023

Recent Trends....	...Emerging Questions
Targeted therapies account for ~60% of new approvals in past 5 years	*How will niche indications fare in light of IRA and FDA accelerated approval guidance?*
LAG-3 is first new checkpoint since PD-1 – creating a new option for melanoma patients	*Will Roche's SKYSCRAPER 1 in NSCLC validate TIGIT? (Est final OS Q3) What is the next wave of promising IO targets?*
Recent ADC launches and M&A/partnering have revived the category	*Can the vision of replacing chemo be achieved? Where do ADCs demonstrate incremental vs. substantial benefit?*
Significant pipeline investment in cell therapies and bispecifics has led to eight approvals... so far	*Will auto CAR-T logistics and durability improve in the near term? How will physicians position bispecific T cell engagers relative to CAR-T?*

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ASCO 2023 – abstracts we're watching

Topic	Tumor	Regimen	Abstract #
Can LAG-3 reach the $4B+ potential for Opdualag laid out by BMS?	NSCLC	Neoadjvuant **relatlimab + nivo** [randomized Ph2]	8500
	Melanoma	2-yr follow up for 1L **relatlimab + nivo** [Ph3]	9502
	Melanoma	**Fianlimab + PD-1** in adjuvant PD-1 progressors	9501
Lessons learned in PD-1 retreatment?	RCC	**Atezo + cabo** in 2L PD-1 pretx [Ph3]	LBA4500
A win for PD-L1 or efficacy driven by PARP?	Ovarian	**Durva + olaparib** in 1L BRCA WT [Ph3]	LBA5506
What outcomes drive change in indications with high 1L efficacy?	cHL	**Nivo +AVD vs. brentuximab vedotin +AVD** in 1L advanced [Ph3]	LBA4
Can ADCs improve the IO tail?	UC	**Enfortumab vedotin + pembro** in 1L cis-ineligible – long-term follow up [Ph2]	4505
How will EGFR MT tx paradigm evolve?	NSCLC	**Amivantamab + lazertinib** in 1L – long term follow up [Ph1]	9134
	NSCLC	**BLU945 (4th gen TKI) +/- osimertinib** in 2L+ [Ph1/2]	9011
A 'new' liquid tumor for CAR-T?	CLL	**Liso cel** in 3L+ CLL [Ph2]	7501

IO | ADC | Targeted | Cell

#ASCO23

Bluestar BioAdvisors

PAUL ZHANG, MBA
Partner
pzhang@bluestarbio.com

ERIN OLSEN, MBA
Managing Director
eolsen@bluestarbio.com

MICHELLE WHANG
Senior Engagement Manager
mwhang@bluestarbio.com

ELIA FARAH, PhD
Senior Consultant
efarah@bluestarbio.com

About Bluestar

Bluestar
BioAdvisors

Our therapeutic area experience is broad-based, with oncology our number one area of focus

Our Areas of Focus

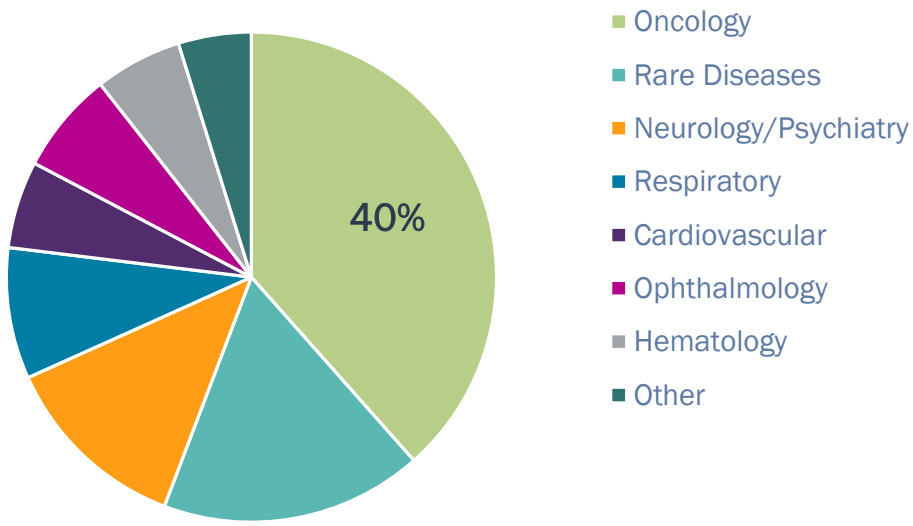
We work in all therapeutic areas in which our clients have assets in development

Oncology is an area of excellence for our team

- Our expertise is based on the senior leadership team's 20+ years of experience in both consulting and biopharma roles
- We support clients in evidence-based indication prioritization strategy, asset forecasting and valuation, and business development decisions

Rare diseases and **neuroscience** are also areas of focus and expertise based on a broad spectrum of experiences in both academia and industry

Recent Engagements by Therapeutic Area



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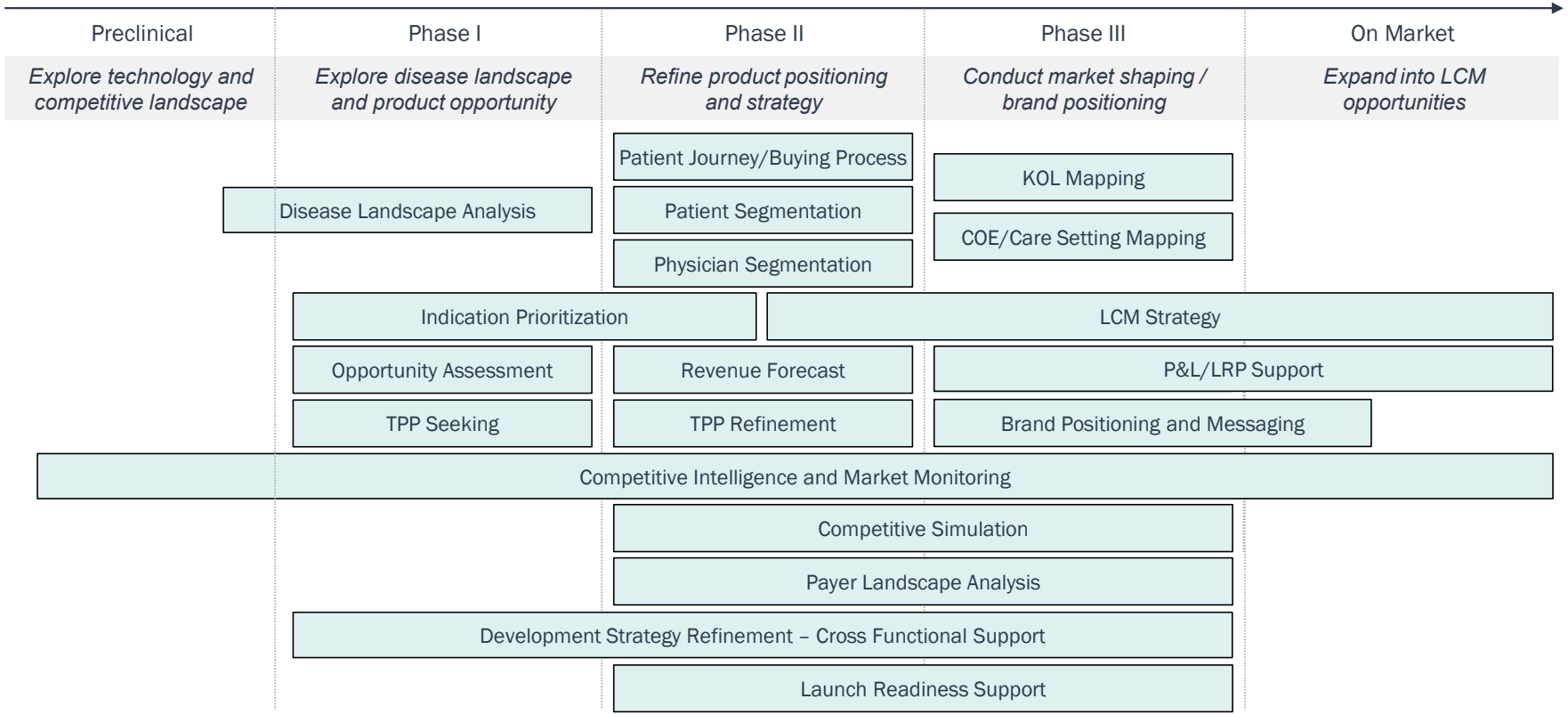
Our services cover a range of topics from early stage market landscape analysis to post launch LCM strategy

Illustrative Project Types



Bluestar BioAdvisors

We commit to deliver insights that make an impact to client business and an enjoyable client experience throughout the collaboration

Why We Stand Out

Bluestar BioAdvisors

521 Fifth Ave.
25th Floor
New York, NY 10175
www.bluestarbioadvisors.com

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