

Next Wave Antibodies and Biologics: Is IO Poised for a Sea of Change?

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Head of Oncology Practice, Defined Health

Panelists:

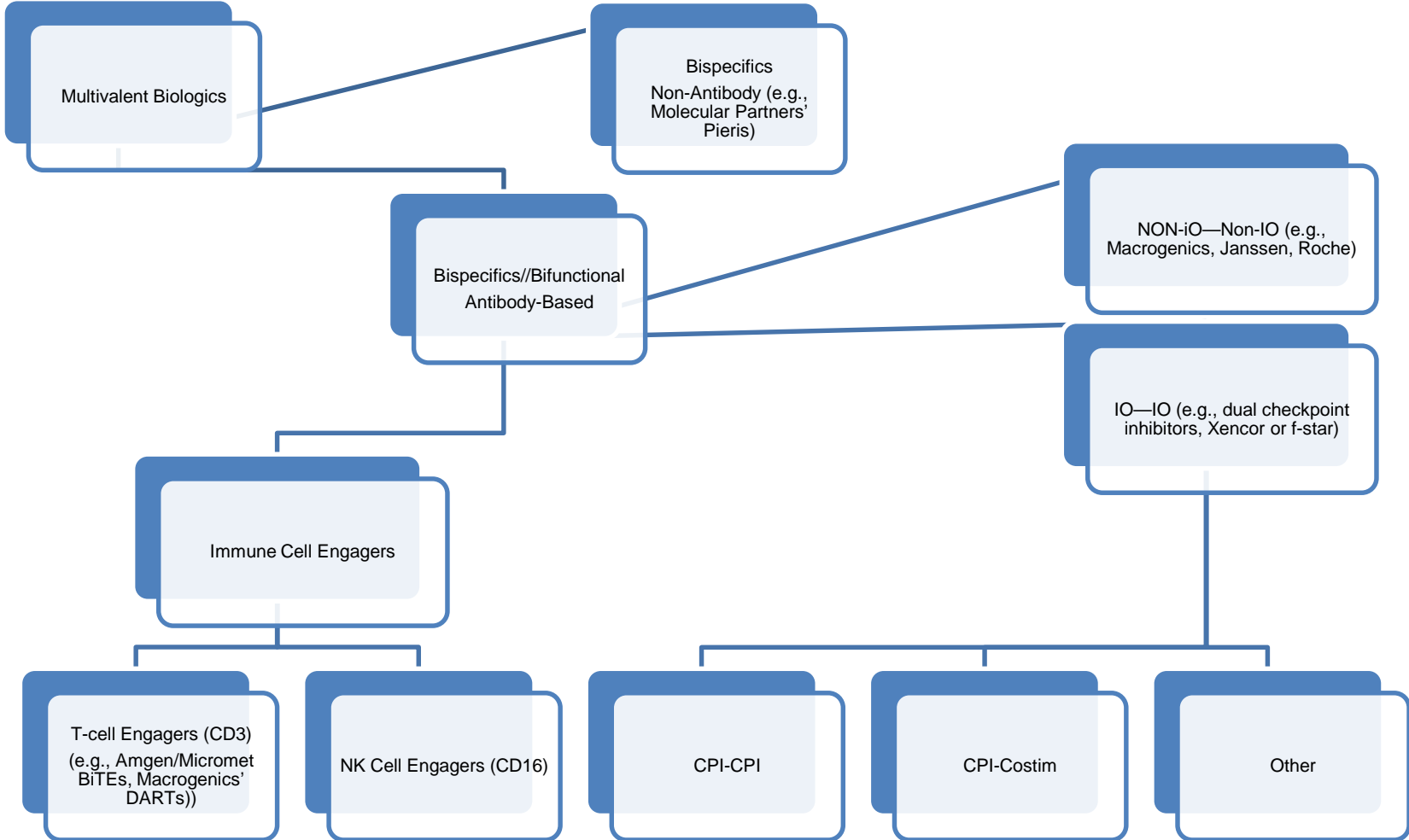
- Mike Curran, PhD, Assistant Professor, The University of Texas, MD Anderson Cancer Center
- John Haurum, MD, DPhil, Chief Executive Officer, F-Star
- Louis Matis, MD, Chief Development Officer, Pieris Pharmaceuticals
- Carsten Reinhardt, MD, PhD, Chief Medical Officer, Immatics
- Taylor Schreiber, MD, PhD, Chief Scientific Officer, Shattuck Labs, Inc.



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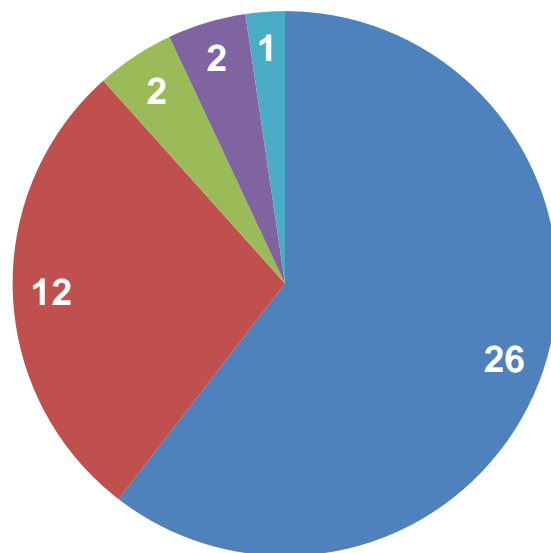


Multivalent Biologics Have Various Mechanisms of Action, & Can Be Bucketed by Whether They Are Immune Cell-Redirecting, Direct Immune Receptor or Ligand Targeting, Or Non-Immune Receptor/Ligand Targeting



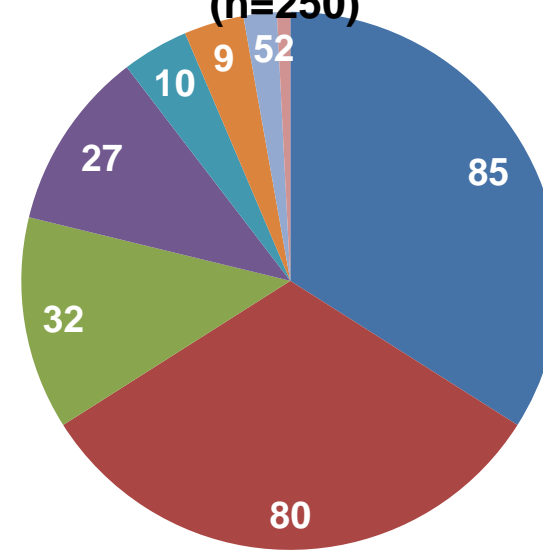
These Biologics Are Dominated by Cell Redirecting Programs (>50%), With Activity for Redirectors & Dual IO, and Dual Non-IO Bispecifics

Clinical Stage Bispecific Pipeline by Target Type (n=43)



- CIT Cell Redirecting: T Cell (CD3)
- Dual Non CIT
- CIT Cell Redirecting: Other Cell Types
- Other
- Dual CIT

Preclinical/Research Stage Bispecific Pipeline by Target Type (n=250)



- Undisclosed
- CIT Redirecting: T Cell
- Dual Non-CIT
- Dual CIT
- CIT/Non-CIT Combo
- CIT Redirecting: Other
- CIT Trispecific

Source: Defined Health

Competitive Activity

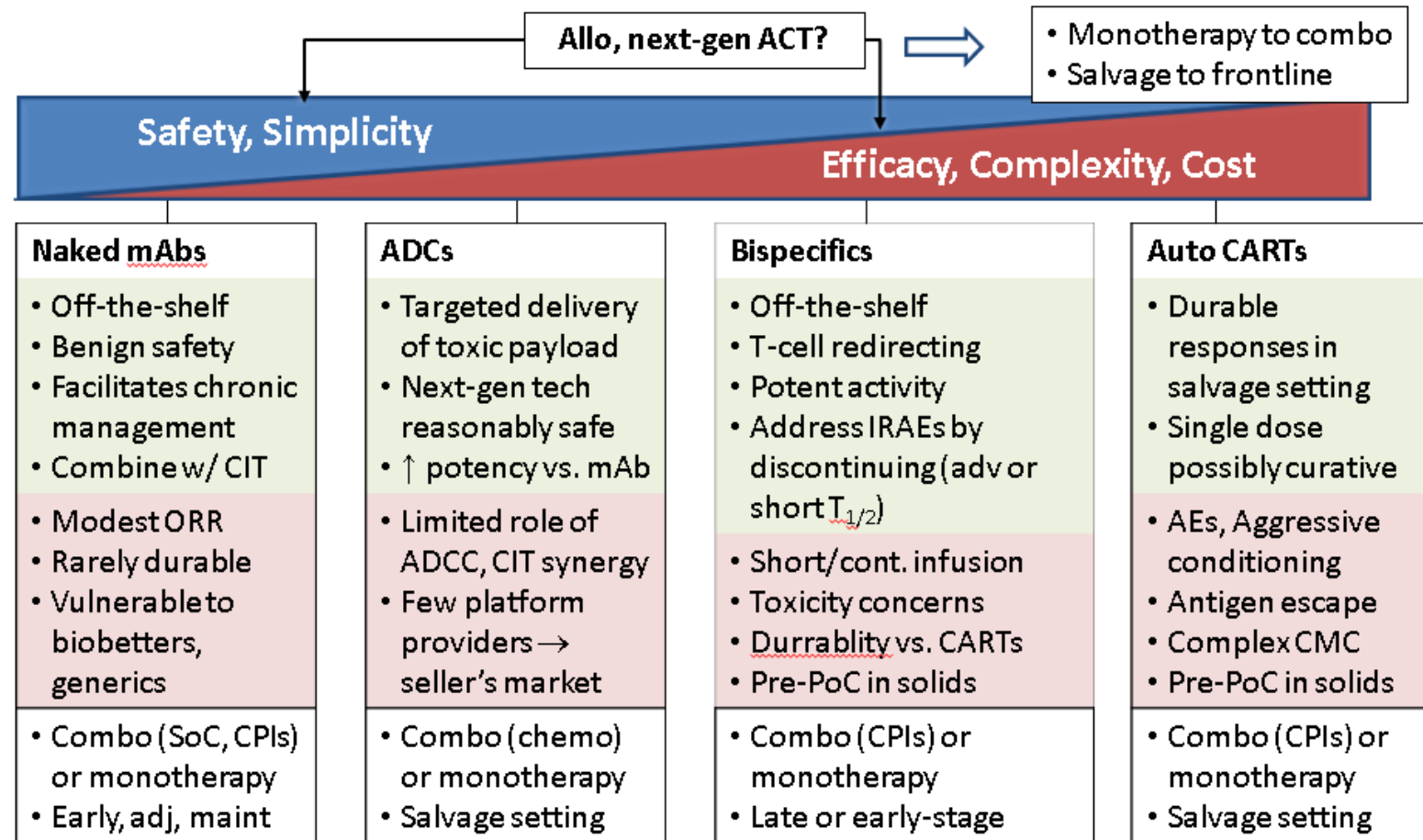
	Heme Malignancies								Solid tumor																
	ALL	AML	Multiple myeloma	NHL	Hodgkin's lymphoma	DLBCL	Hematological malignancies	Cancer	Solid tumor	Thyroid cancer	Breast cancer	Ovarian cancer	Peritoneal cancer	Fallopian tube cancer	Prostate cancer	Colorectal cancer	NSCLC	Small cell lung cancer	Lung cancer	Melanoma	Ocular melanoma	Pancreatic cancer	HCC/Liver cancer	Gastrointestinal cancer	Gastric cancer
Overall	M	P1	P1/2	P2/3	P2	P2	P2/3	P1	P1/2	P1/2	P1/2	P2	P2	P2	P1	P2	P1/2	P1/2	P1	P1/2	P2	P2	P1	P1	P2
CIT Cell Redirecting: T Cell (CD3)	M	P1	P1	P2/3		P2	P2/3		P1			P2	P2	P2	P1	P1				P1/2	P2			P1	P2
Dual Non CIT			P1/2				P1/2	P1	P1/2		P1	P1	P1	P1		P2	P1		P1			P2	P1		
Dual CIT									P1																
CIT Cell Redirecting: Other Cell Types					P2				P1																
Other										P1/2	P1/2					P2	P1/2	P1/2							

Key					
P1	P1/2	P2	P2/3	P3	M

- The majority of bispecific agents are in early-stage development, with the exception of marketed agents Blynicyto (blinatumomab) in ALL Removab (catumaxomab) is also marketed for malignant ascites ex-US (not pictured here as an indication)

Source: Defined Health

The Competitive Landscape Is More Than Ever Before Not Just About In-Class Competition But Inter-Modality Competition



Competing with Bispecifics by Target: A Range of Therapeutic Modalities Are Going After Many of the Same Key Bispecific/Bifunctional Targets

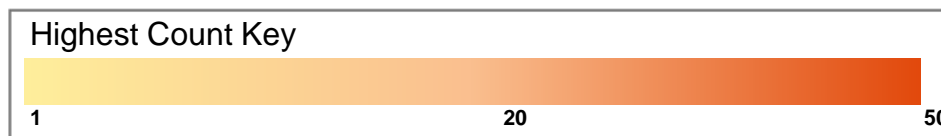
Number of Agents in Development per Target, by Modality PC → MRKT	Key Targets					CEA/CEACAM5	CD33	CD123	EpCAM	ROR1	GPC3	5T4	B7H3	P-cadherin	A33	CEACAM6	CEACAM1	CLEC12A
	HER2	CD19	CD20	PSMA	BCMA													
CAR-T cells	6	55	6	5	12	2	6	7	1	3	6	1				2		1
Antibody-drug conjugate	45	10	7	12	2	2	9	4	8	2	1	2	4	3	2			
Bispecific/trispecific antibody	20	15	12	7	13	5	5	6	7	4	3	1	1	1	1			1
Naked monoclonal antibody	23	9	18			3	1	2		3	3		1		1	1	3	
Small molecule	33			8			1			3								
Cancer vaccine	32					4				1	1			1				
Fusion protein	12	4	6			3	1	2	1			1						
Other cell therapy	3	6	1	1	4	1					1							
Peptide	4																	
Oncolytic virus						3						1						
Undefined		1	1	1														
Recombinant product	1																	
Other						1												

Key (# of agents)				
1-5	6-10	11-15	16-20	>20

Source: Defined Health

Competing with Bispecifics by Indication: A Range of Therapeutic Modalities Are Going After Many of the Same Settings and Sometimes Also the Same Target

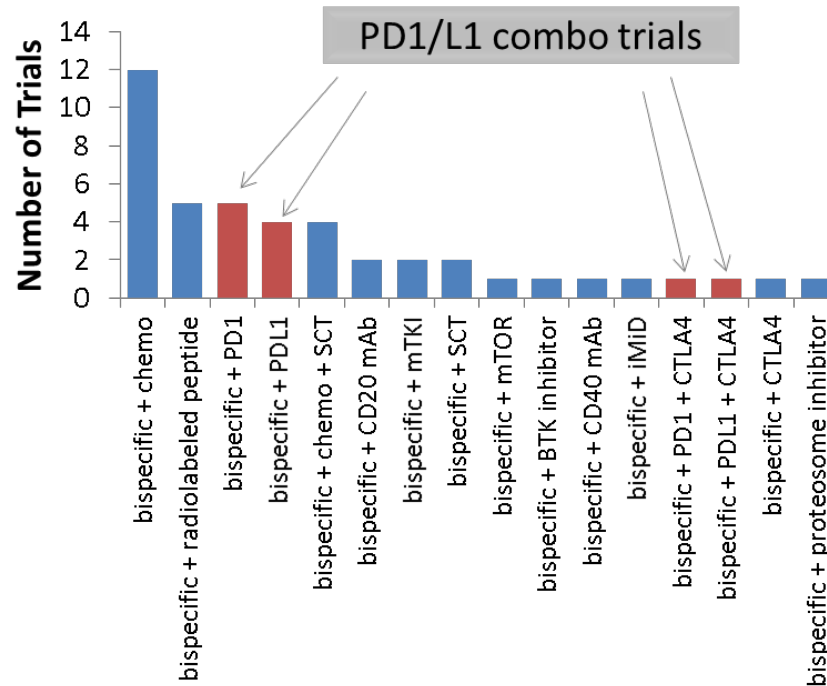
Count of Agents in Development per Modality by Indication P1->MRKT	Cancer	Solid tumor	GBM/Glioma	Head and neck cancer	Thyroid cancer	Breast cancer	Ovarian cancer	Prostate cancer	RCC/Renal cancer	Bladder cancer	Colorectal cancer	NSCLC	Small cell lung cancer	Lung cancer	Melanoma	Pancreatic cancer	HCC/Liver cancer	Esophageal cancer	Gastric cancer	Gastrointestinal cancer	Sarcoma	Carcinoma	Cancer metastases
Cancer vaccine	24	19	22	7	1	42	24	29	8	6	12	18	3	7	34	8	4	4	3		3		2
CAR-T cells	9	3	9			1	3	2						1		3					3		1
Cell therapy	4	9	4	8		1	2	2		1	2	1			8	2	2			1	1		3
Checkpoint	9	37	7	9	3	6	7	6	9	4	8	10	8	2	9	6	7	6	8	1	2		4
Costim	4	16	2	3		1		2	2		1	1			4	1	1						1
Cytokine	8	12	2	2		7	2	5	3	4	4	3			14	5	1						1
Innate Immunity	3	6	1	3		3	2			1	5	2	1		5	2							1
Oncolytic virus	7	14	10	10	1	6	11	9	2	3	10	5	1	3	10	6	6	2		3	2		2
Other cell therapy		1																					
Other IO	6	20	3	2		2	5	3		1	2	3	1	1	3	2	1		1	1		1	



Source: Defined Health

Bispecifics, like Everything Else, Is Much About Combinations

Bispecific Clinical Trials: by Combo Type
Direct Combo or Sequential Combo, N=39*

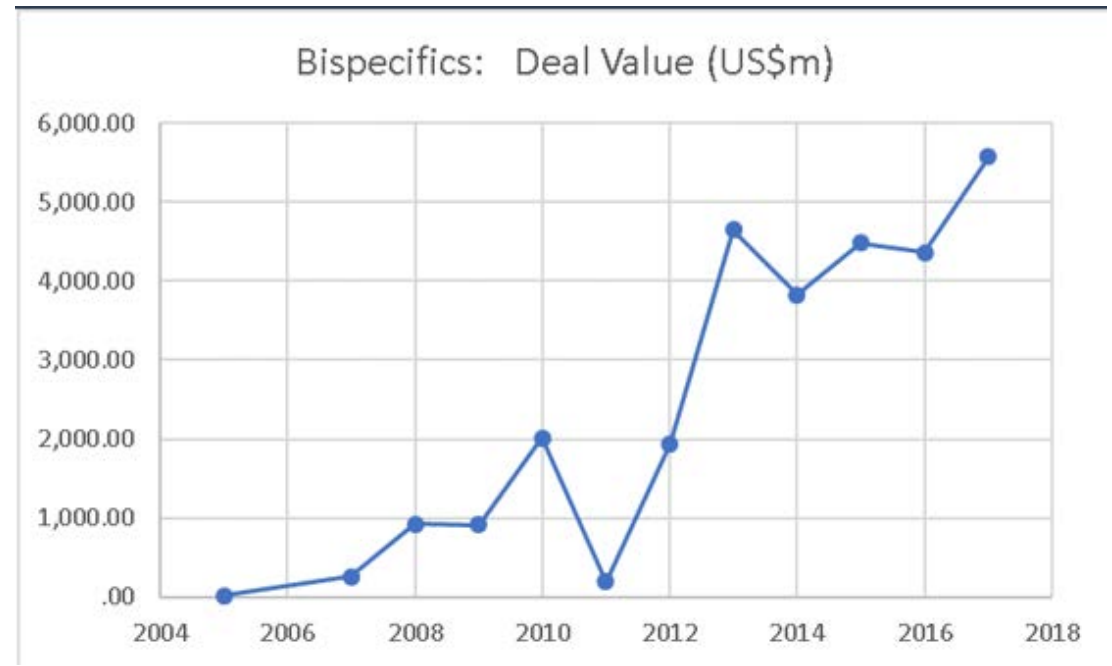
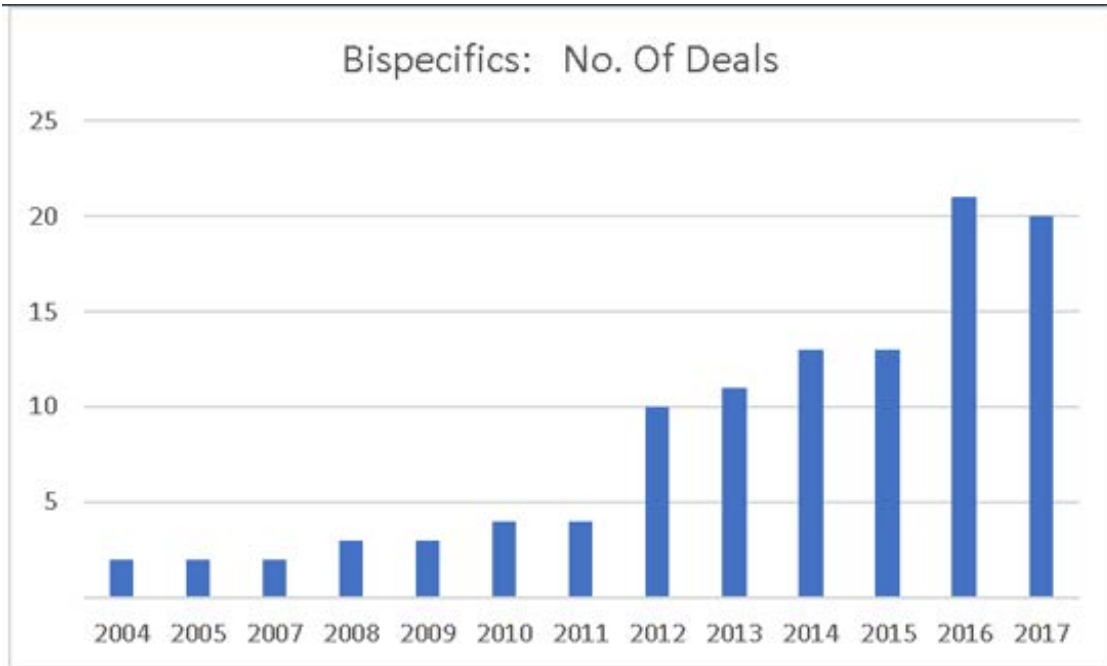


Combo Type	Bispecifics in Combo
bispecific + chemo	ABT-165, blinatumomab, catumaxomab, istiratutumab, navicixizumab, vanucizumab
bispecific + radiolabeled peptide	TF 2-targeted cancer therapy peptide
bispecific + PD1	ABBV 428, AFM 13, blinatumomab, REGN 1979
bispecific + PDL1	RO 6958688, vanucizumab, IMC gp100
bispecific + chemo + SCT	blinatumomab
bispecific + CD20 mAb	RG 7828, RO 7082859
bispecific + mTKI	blinatumomab
bispecific + SCT	blinatumomab
bispecific + mTOR	istiratutumab
bispecific + BTK inhibitor	blinatumomab
bispecific + CD40 mAb	vanucizumab
bispecific + iMiD	blinatumomab
bispecific + PD1 + CTLA4	blinatumomab
bispecific + PDL1 + CTLA4	IMC gp100
bispecific + CTLA4	IMC gp100
bispecific + proteasome inhibitor	MP 0250

**Trials are double counted if there is >1 arm with different bispecific combination*

Source: Defined Health

Deal-Making Continues to Be Active



Source: Linda Pullan (Pullan's Pieces #133, Jan 2018)