

# IO Session I: Combination Failures & Futures— Much Ado About What?

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**Mai-Britt Zocca**, PhD, Chief Executive Officer, IO Biotech

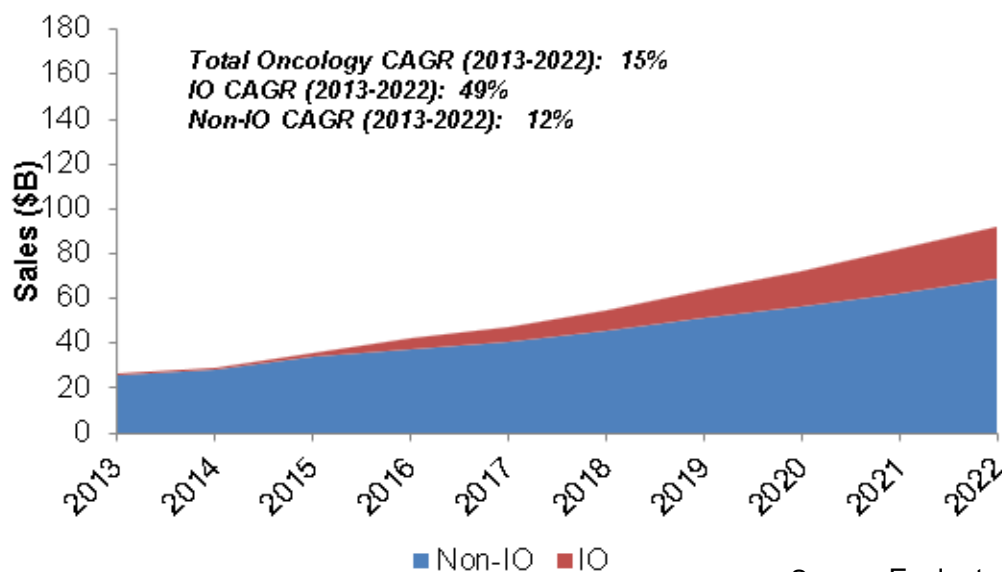


Cancer Progress  
New York, NY | May 7 - 8, 2019

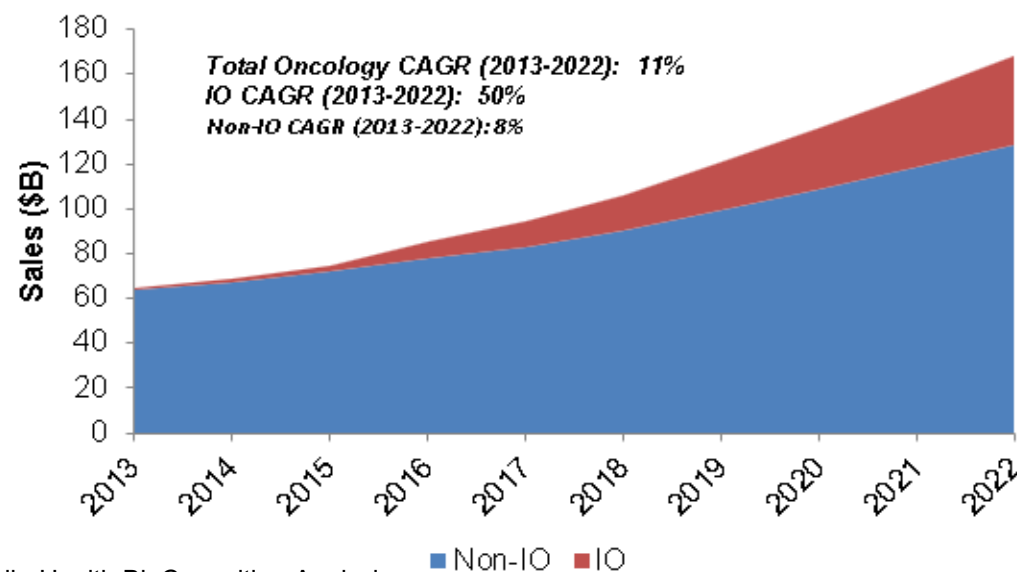


# Immuno-Oncology Dominates Growth, But Does Not Dominate Sales – At Least Not Yet

**US Oncology Products Sales:  
IO vs. Non-IO**



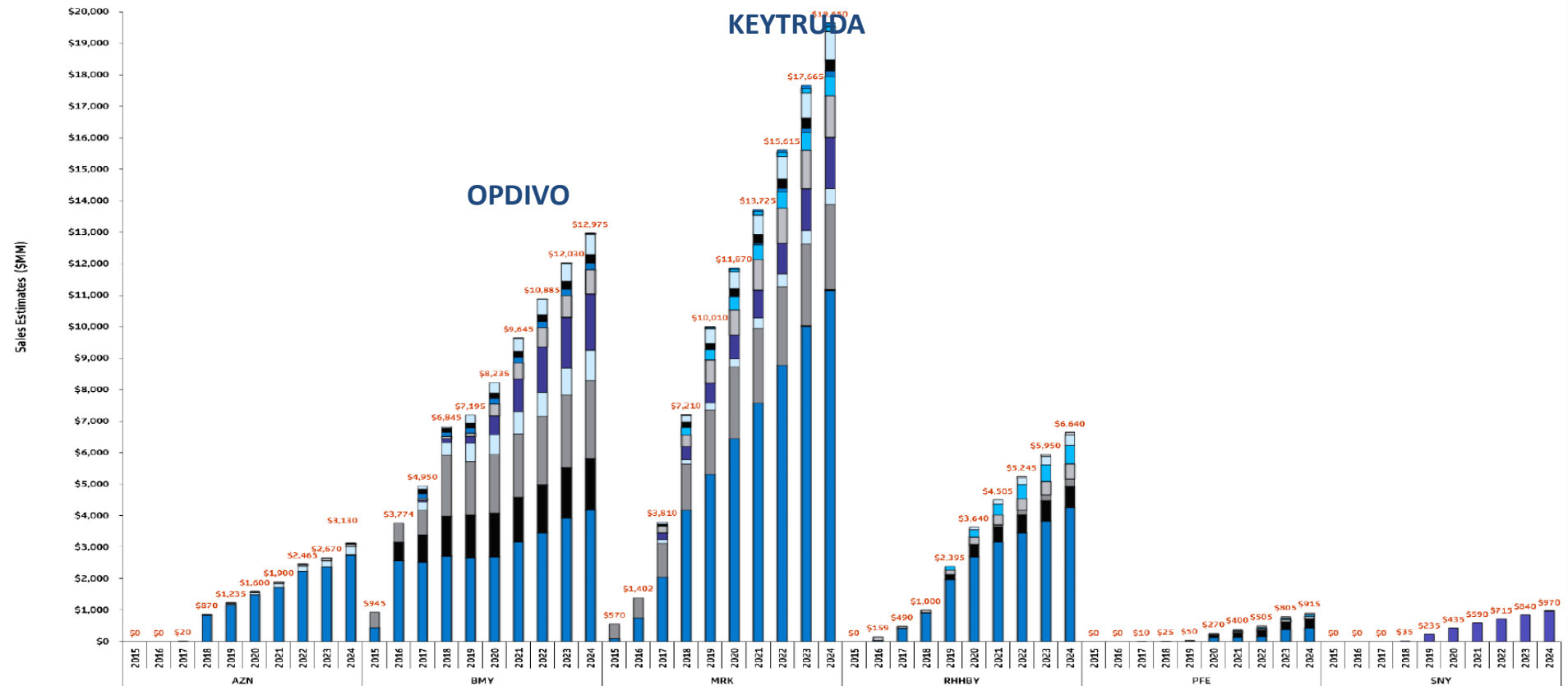
**WW Oncology Products Sales:  
IO vs. Non-IO**



Source: Evaluate Pharma, Cello Health BioConsulting Analysis

# Checkpoint Inhibitor Sales (Anti-PD-1/PD-L1): The Taxanes of the IO World - Foundational

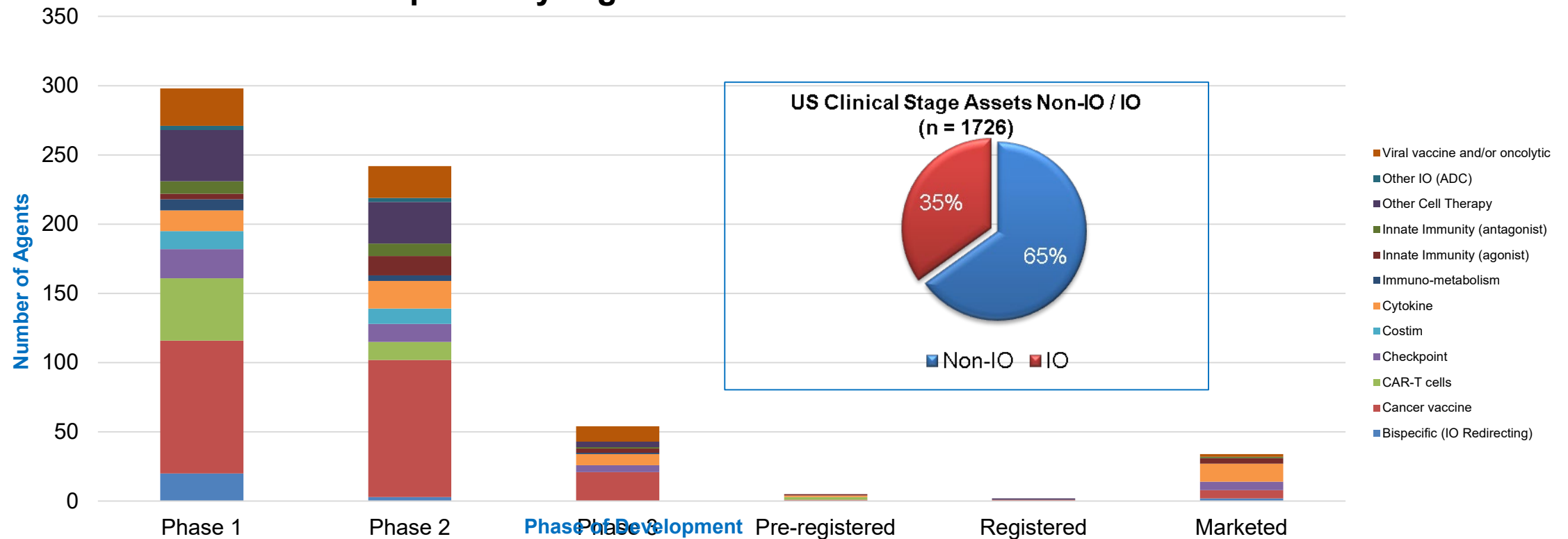
PD-1/PD-L1 Sales Estimates By Company And Tumor Type (Total annual sales reported in red)



Cowen, Sept 4 2018: Investors' Guide To Immuno-Oncology

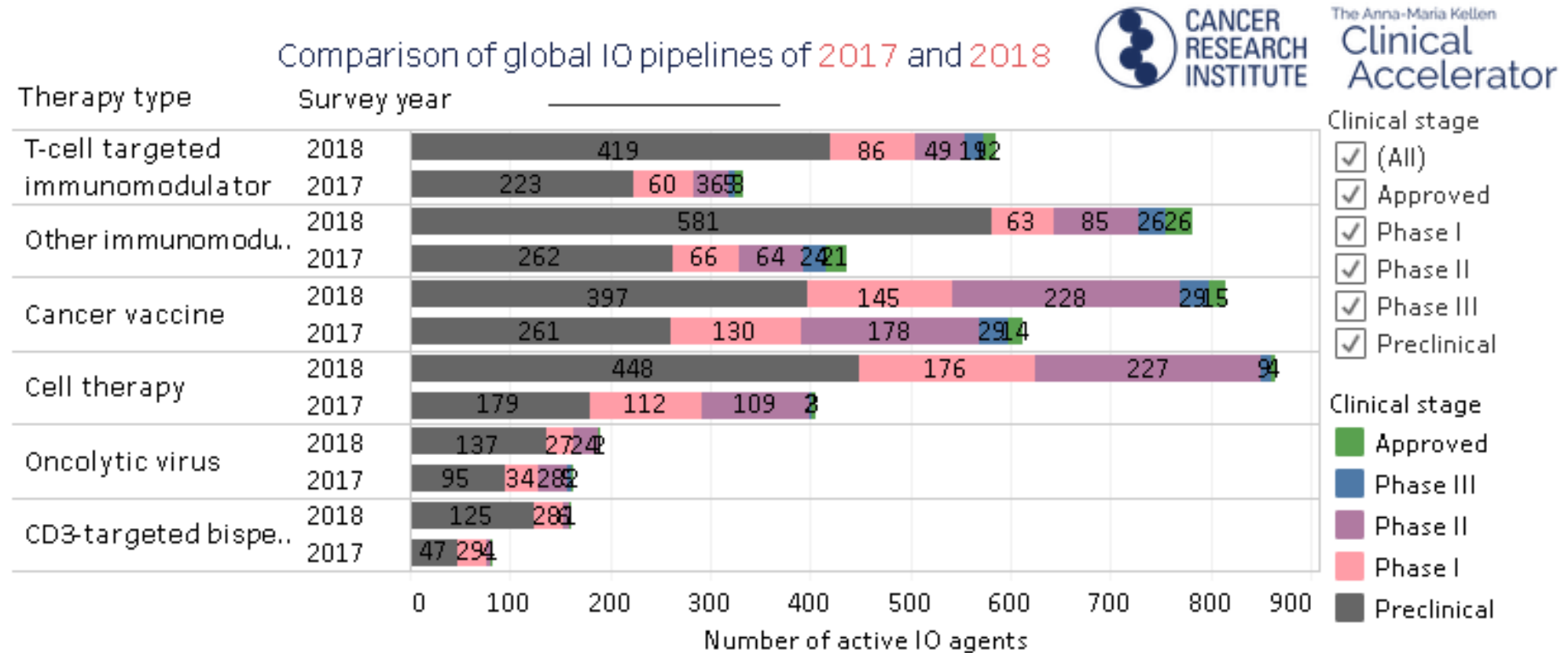
# The Clinical Pipeline Reflects a Diverse Set of MOAs & Therapeutic Modalities: Reflecting a Richness of Targets But Perhaps Insufficient Translational Insights

## US IO Pipeline by Highest WW Phase and Mechanism



Source: Adis R&D Insight; Clarivate Analytics Cortellis; company websites; clinicaltrials.gov; Cello Health BioConsulting Analysis

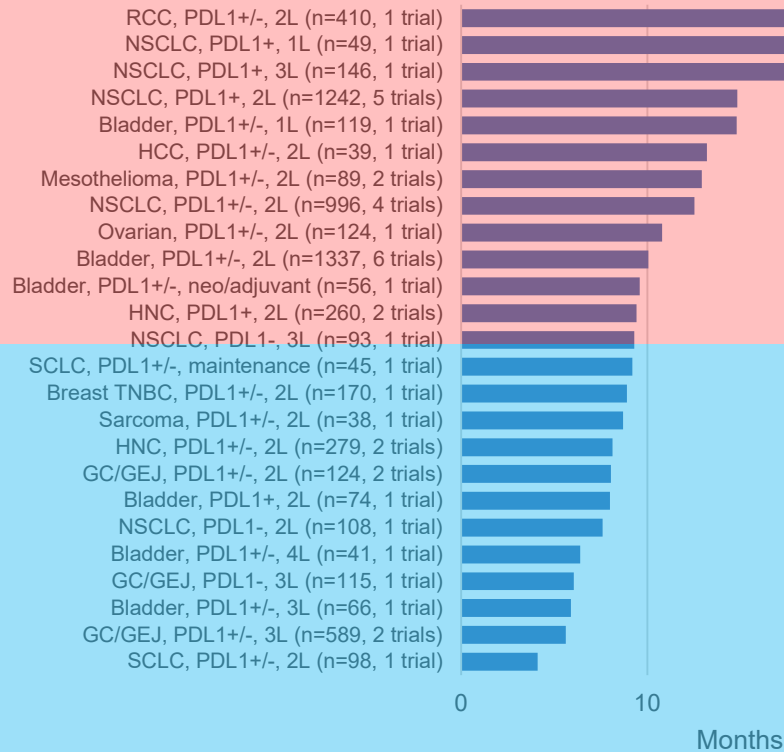
# CRI's Analysis Shows the IO Pipeline Growth: Mostly Spaces That Are Well-Trodden



Source: CRI

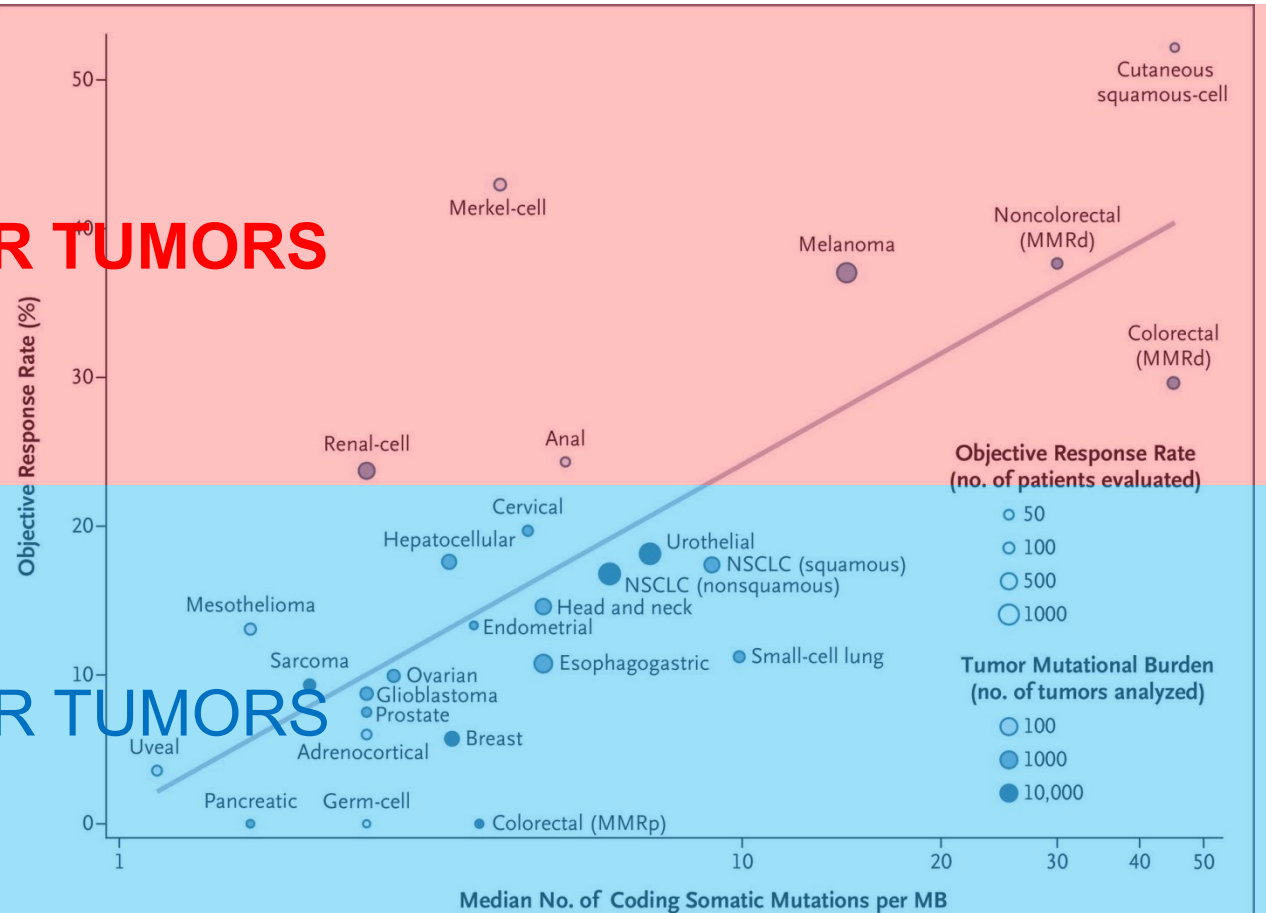
# Advances with CPIs, While Dramatic in Selected Settings, Remain Incremental and/or Limited in Many Others

Aggregated PD1/L1 Efficacy per Tumor Type and Setting: mOS



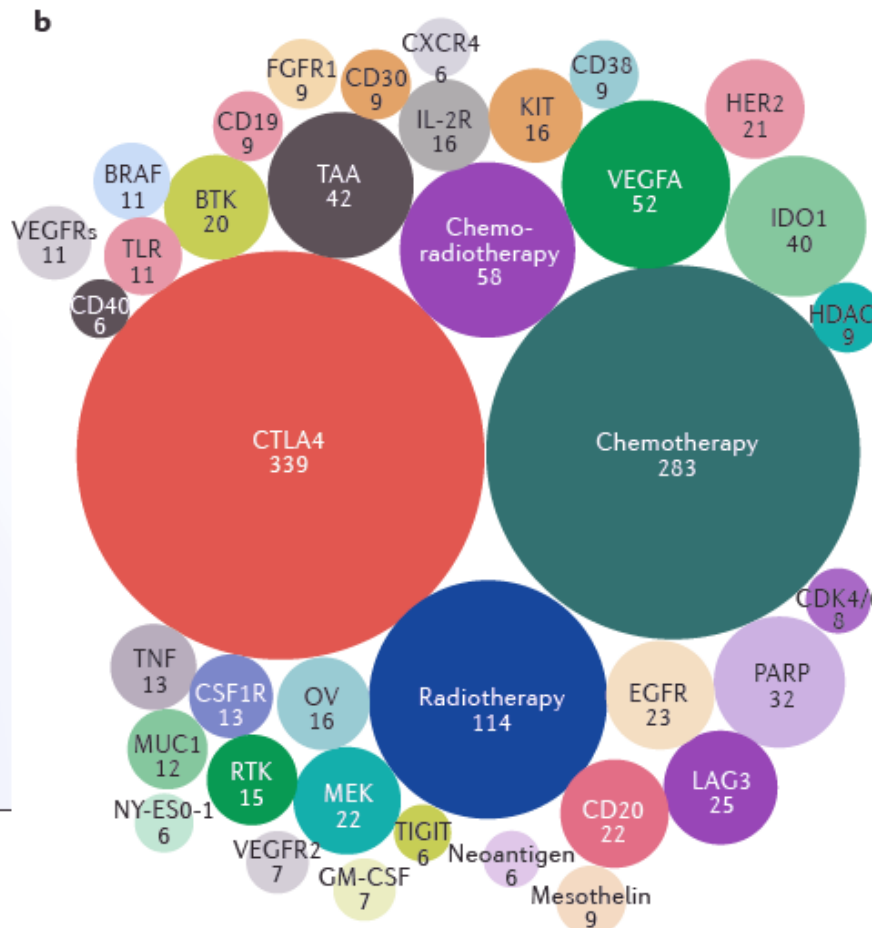
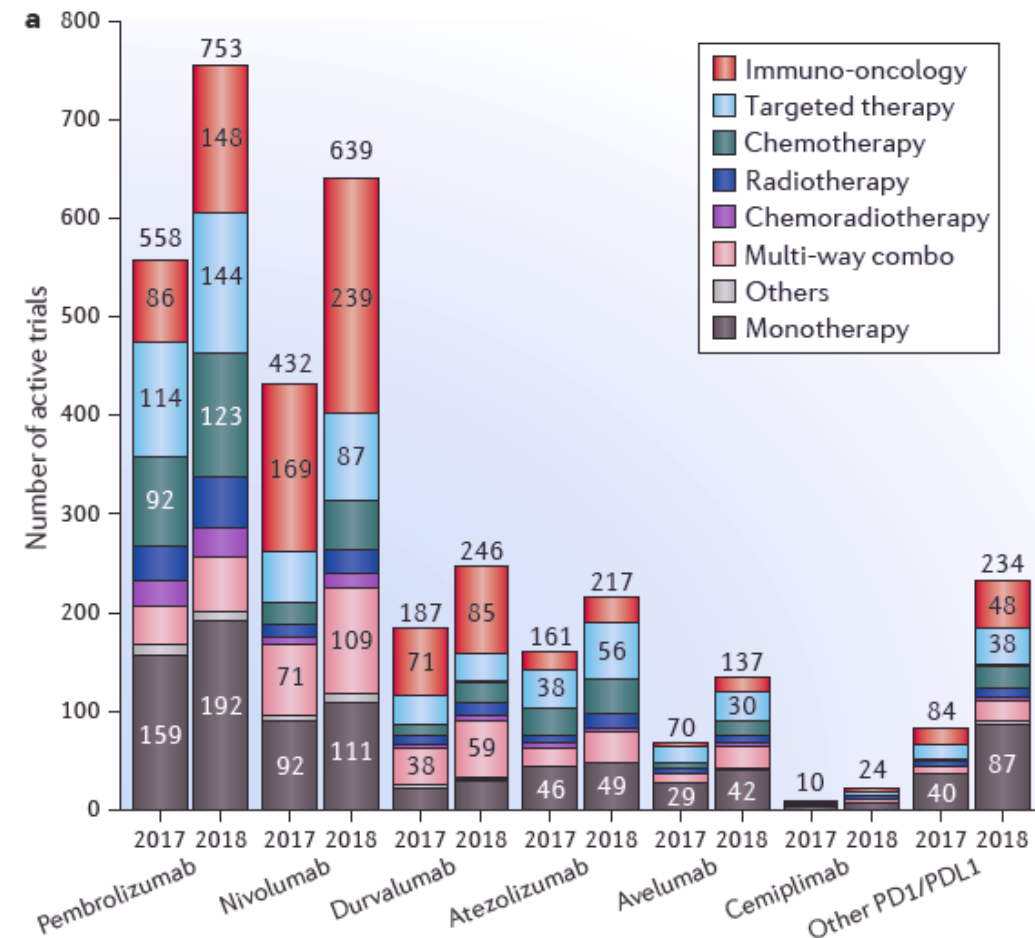
**HOTTER TUMORS**

**COLDER TUMORS**



Source: Cello Health BioConsulting (Defined Health) Analysis: ESMO, ASCO, AACR, ASH abstracts; prescribing information; company press releases; \*efficacy data is weighted by the number of patients per trial, total number of patients across all trials and number of trials represented are in y-axis label N Engl J Med 2017; 377:2500-2501

# Hence the Rapid Increase in Combination Studies of Anti-PDx Agents With a Diverse Range of IO and Non-IO Approaches



**The clinical trial landscape for PD1/PDL1 immune checkpoint inhibitors.** **a** | There are 2,250 active trials testing anti-PD1/ PDL1 agents as of September 2018, compared with 1,502 trials in September 2017. **b** | The 1,332 trials evaluating anti-PD1/PDL1 agents in combination with the top 38 targets (among the 1,716 combination trials testing a total of 240 targets) are shown here. We have selected those targets being evaluated in at least 6 trials. The number of active clinical trials that are testing drugs against the target are indicated in each bubble.

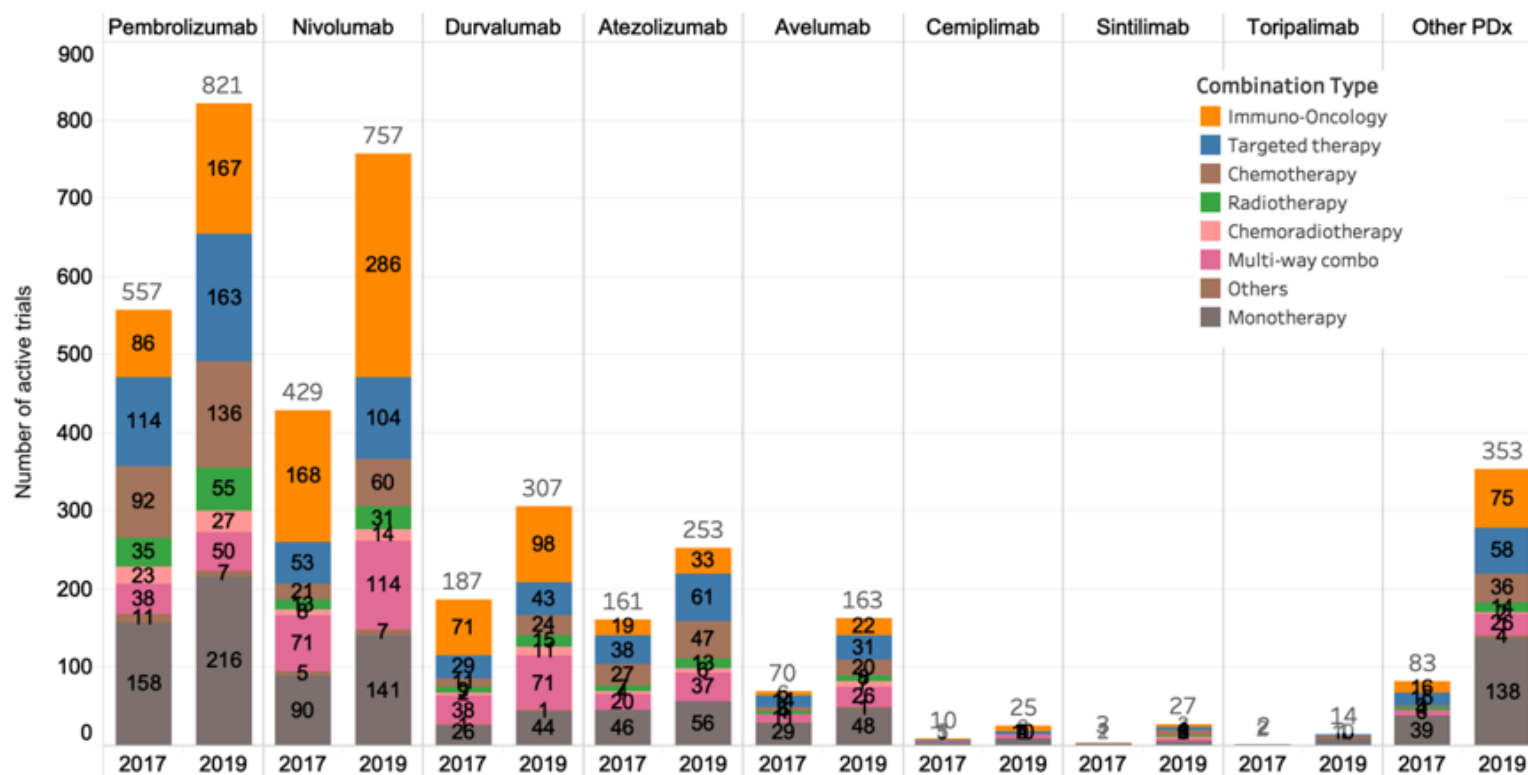
Source: CRI Analysis - *Nature Reviews Drug Discovery* volume 17, pages 854–855 (Dec 2018)



# CRI April 2019 Update (Courtesy of Jun Tang et al)

1,218 more active trials in current landscape than that in Sep 2017

2,720 as of April 2019 VS 1,502 as of Sep 2017



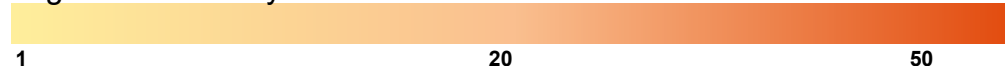
Tang et al, Ann Oncol, 2017; CRI IO Analytics, April 2019 update



# What Is Clear Is That the Competitive Landscape Is Increasingly Intense, & Not Simply Intra-Class/Modality But Inter-Class/Modality

Count of Agents in Development per Mechanism 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
Bispecific (IO Redirecting)	1	6					1	1			1				1				1	1		1	
Cancer vaccine	25	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
Checkpoint	9	36	7	9	3	6	7	6	9	4	8	10	8	2	9	6	7	6	8	1	2		4
Costim	4	18	2	3		1		2	2		1	1			4	1	1						1
Cytokine	8	12	2	2		7	2	5	3	4	4	3			15	5	1						1
Immuno-metabolism	3	8	3	1		2	1	1			1	5		1	2	1							
Innate Immunity (agonist)	3	7	1	3		3	3			2	5	2	1		5	3	1						1
Innate Immunity (antagonist)	5	14		1		1	2	1			1		1			1	1						
Other cell therapy	4	10	4	8		1	2	2		1	2	1			8	2	2			1	1		3
Other IO (ADC)	2	1													1								
Viral vaccine and/or oncolytic	7	14	10	10	1	6	11	9	2	3	10	5	1	3	10	6	6	2		3	2		2

Highest Count Key



Source: Adis R&D Insight, Thomson Reuters Cortellis; Cello Health BioConsulting (Defined Health) Analysis

\*Bispecific (IO Redirecting) includes IO/IO Targeting Bispecifics

# What Is Clear Is That the Competitive Landscape Is Increasingly Intense, & Not Simply Intra-Class/Modality But Inter-Class/Modality

Number of Agents in Development per Target, by Modality PC → MRKT	HER2	CD19	CD20	PSMA	BCMA	CEA/CEACA M5	CD33	CD123	EpCAM	ROR1	GPC3	5T4	B7H3	P-cadherin	A33	CEACAM6	CEACAM1	CLEC12A
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												

Source: Adis R&D Insight;  
Clarivate Analytics Cortellis,  
Cello Health BioConsulting



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

