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CELLO HEALTH BIOCONSULTING'S *INSIGHT SERIES* WEBINAR

What Your Board Needs to Know about Oncology and Market Access: A Webinar for Top Management

*A follow-on discussion to the Cancer Progress 2020 Panel
“Inflecting Value in Early Stage Biotech: Linking Proof of
Relevance to Pricing & Reimbursement”*

May 19th, 2020



Participants

What Your Board Needs to Know about Oncology and Market Access: A Webinar for Top Management

Moderator



Beth Fordham-Meier, CLP
VP, Business Development
Cello Health BioConsulting

Panelist



Jeff Berkowitz
CEO and Director
Real Endpoints

Panelist



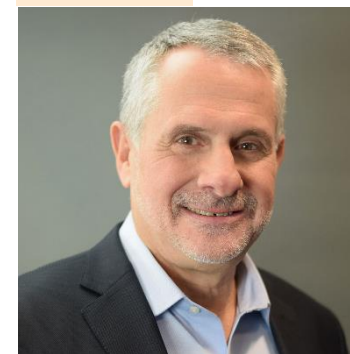
Jeff Bockman, PhD
EVP, Head of Oncology Practice
Cello Health BioConsulting

Panelist



Roger Longman
Founder and Chairman
Real Endpoints

Panelist



Ed Saltzman
Executive Chairman
Cello Health BioConsulting

Cello Health BioConsulting: Who We Are

- ◆ Cello Health BioConsulting is a knowledge-based consultancy deeply rooted in science; we often evaluate early stage programs before much, if any, clinical data is available. In the biopharma world, we are known for our “unconventional insight” – forward thinking, independent, objective strategic advice across all therapeutic areas.
- ◆ Cello Health BioConsulting provides strategic advice for corporate growth and partnering strategies, disease area selection, indication prioritization, opportunity search and evaluation, opportunity and landscape assessment, valuation and forecasting, early market access strategy and early value profile development.
- ◆ Cello Health BioConsulting has a strong and broad network of leaders and influencers across biotech and pharma, which provides a deep understanding of next wave issues, the competitive and market landscapes, and keeps us well-informed and ahead of industry trends.
- ◆ Visit our website at www.cellohealthbioconsulting.com



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Why Real Endpoints

Unrivalled expertise in – and passion for – overcoming the industry's most complex access challenges

Our Focus

100% focused on market access

- *Subject matter:* all aspects of healthcare coverage, reimbursement, value dossier and proposition, pricing, innovative contracting, distribution, hub and patient support services, and network design
- *Clients:* include 7 of top 10 pharmas and biotechs of all stages, from preclinical to label expansion, from investor analysis to defining payer-focused clinical endpoints and indications to launch strategy
- *Clinical & technology categories:* Virtually all therapeutic areas, with special expertise in new disease categories and mechanisms of action; rare- and orphan disease; and cell/gene therapy

Our Approach

Right capabilities, connections, and knowledge

- Deep relationships with the key decision-makers at payers, PBMs, and other key coverage stakeholders
- Because we know the access world *and* the key payers, we listen as much for what is implied as what is explicitly stated, allowing us to craft strategies that address what payers *do*, not what they *say*
- We've learned from the past but don't let it dictate strategy: the world is changing too fast to craft recommendations based on rapidly outdated beliefs

Our Team

Deep market access expertise developed as doers, not consultants

- We've worked in senior roles in every vertical touching market access -- pharma, payer, PBM, pharmacy – so we understand the challenges and interconnections from the inside
- We test and develop new ideas in our thought-leading articles for numerous publications and in our speeches
- Those new ideas allow us to challenge conventional wisdom in our projects
- And just as importantly, we work together, meshing our very different backgrounds in payers and pharma, in different clinical and technology categories, so our clients get the benefit of a small high-level team with an extraordinary breadth of expertise



Discretionary Donation: All fees collected will be split between support for **cancer centers** and their doctors and nurses and to support the efforts of **first responders and frontline healthcare professionals** in their efforts working tirelessly to save lives during this time of national crisis.



<https://bit.ly/CPbyCH>

THANK YOU TO OUR CANCER PROGRESS 2020 SPONSORS & SUPPORTERS



Jeff Berkowitz, CEO and Director, Real Endpoints

Vertical and horizontal integration transforming the healthcare access and delivery landscape – and biopharma is largely on the outside looking in...

Transforming US market access and drug supply

End-to-end control over drug access and delivery:

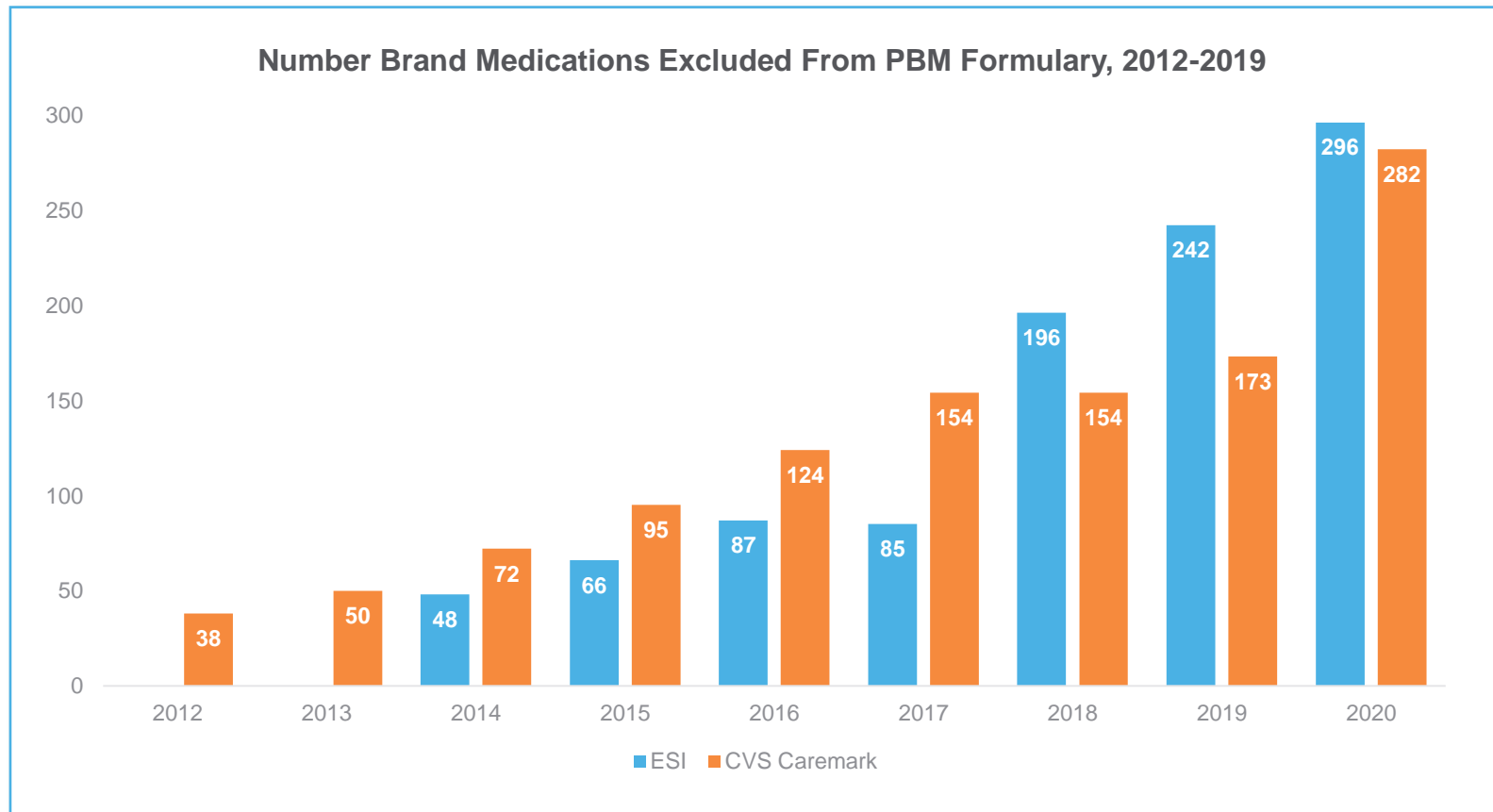
- Drug coverage, UM/restrictions, access and affordability
- Site of care optimization
- Provider choice
- Supply chain and point of dispensing

	Unaffiliated						
Payer	aetna	Cigna	UnitedHealthcare	Anthem	Humana	BlueCross BlueShield	CENTENE WellCare
PBM	CVS caremark	EXPRESS SCRIPTS Ascent Health Services GPO	OPTUM	ingenioRx	Humana	PRIME THERAPEUTICS	MegImpact MagellanRx MANAGEMENT
Specialty Pharmacy	CVS specialty	accredo	briova Diplomat Aveella Specialty Pharmacy	CVS specialty	Humana	allianceRx Pharmacy + PCIE	SENDERRA Amber PANTHER PHARMACY
Retail Pharmacy	CVS pharmacy	W	CVS pharmacy W	CVS pharmacy	Walmart W	W	RITE AID Kroger
Wholesale Distributors	CardinalHealth	AmensourceBergen CuraScript SD Caring for those who care			McKESSON		
Infusion Services	Coram CVS specialty infusion services	accredo	AXELA Care				
Provider Services	minute clinic Health HUB	Cigna Collaborative Care ¹ (ACO model)	OPTUM Care	CareMore HEALTH	Partners in Primary Care CONVIVA Care Center		
Medical Management	novologix	eviCore healthcare	OPTUM	AIM			
Data Services			OPTUM Insights				

Source: <https://www.drugchannels.net/2019/12/insurers-pbms-specialty-pharmacies.html>, December 19, 2019. 1. Cigna partners with providers with its Cigna Collaborative Care Program.

When differentiation among brands is modest, these large payers can choose the prescriptions patients get

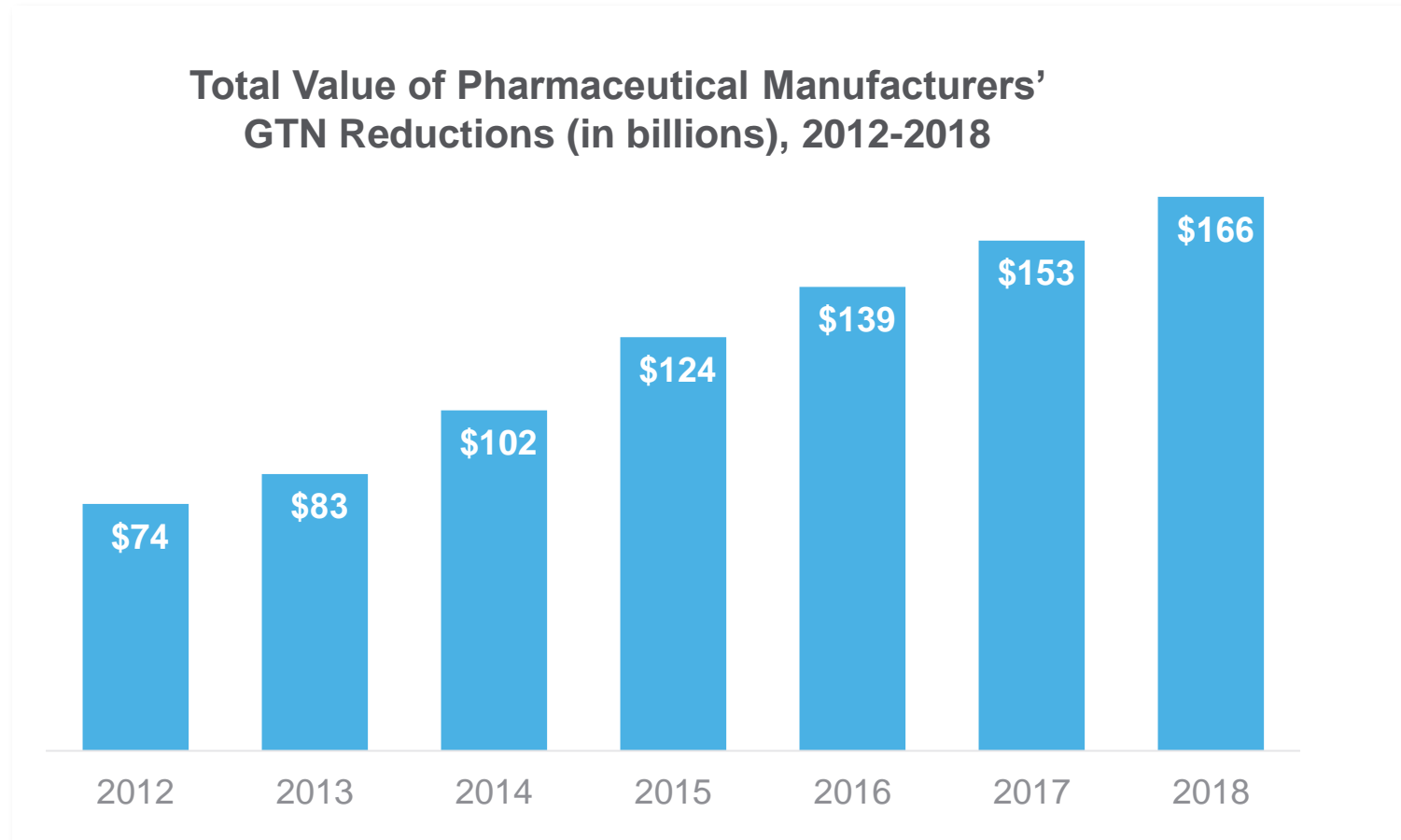
Number of brand medicines excluded from PBM formularies has increased over time



- MCOs and PBMs increasingly utilize strict approaches to manage drugs, including formulary exclusions
- Access is now discussed in terms of “winning and losing” based on negotiations with the major PBMs and payers

Payers charge high access tolls for what they define as modestly differentiated brands...and their employer-customers go along

Rebates and discounts totaled more than a third of total US pharma sales

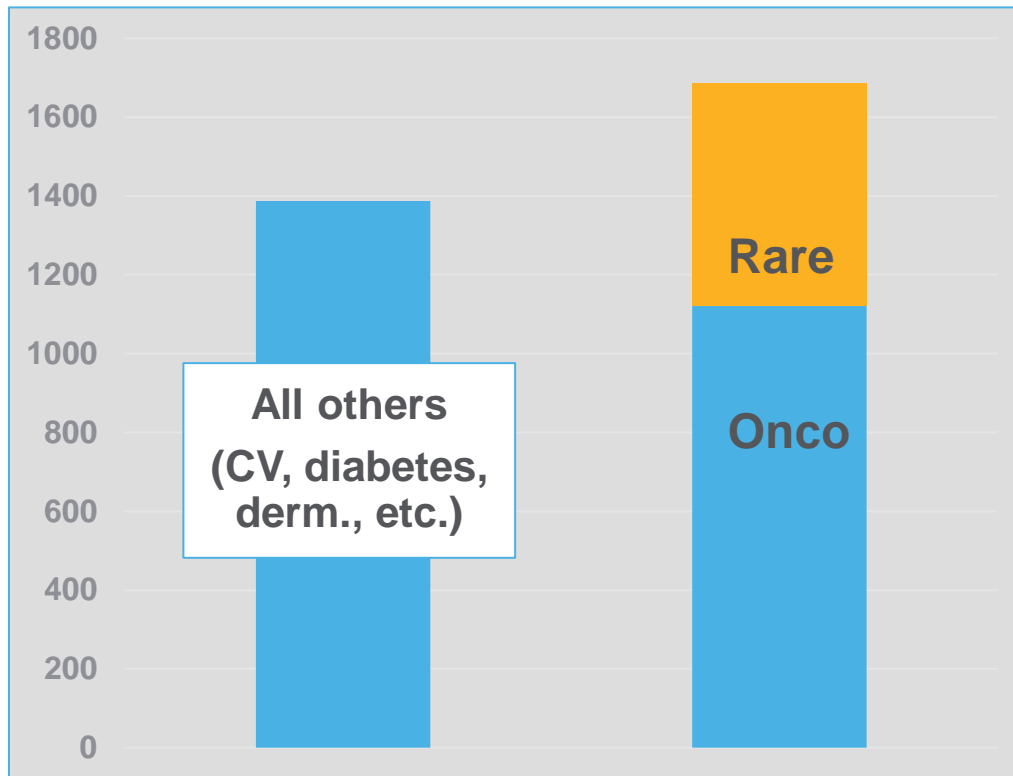


And in the big branded primary-care classes – e.g., SGLT2's in diabetes, NOACs in cardiovascular – rebates have reached *up to 70%*

Source: PhRMA Chartpack; IQVIA

Biopharmas fleeing to oncology and orphans -- where they think payers can't say "no"

Current Drug Pipeline by Category*



- **Oncologics comprise 35% of 2018 pipeline¹**
- **Companies are conducting 908 gene/cell therapy trials (in 140 indications)²**
- **Orphans will comprise 20% of worldwide sales in 2024³**
- **In 4 of the past 5 years, over 40% of first product launches were orphan drugs, reaching a high of 58% in 2018⁴**

¹Citeline's PharmaProjects

²FoCUS NEWDIGS Initiative at MIT

³EvaluatePharma, Orphan Drug Report 2019

⁴BioCentury, April 2019

Source: Adis R&D Insight Database

*Defined as single products that are counted only once regardless of the number of indications pursued

Why payers have little say in oncology

In virtually every other category, payers can restrict physician choice. Not oncology.

- **Oncology one of 6 CMS protected classes**
 - And genericization less draconian among oncologics
- **Buy-and-bill economics provides significant income for providers**
 - The more expensive, the more profitable
- **Most payers require “prior auths to label” – but in oncology, PAs to compendia guidelines**
 - Guidelines are both up-to-date and allow wide latitude for providers
- **Cancer is the scariest disease we can do something about**
 - Headline payers fear most: “Local mother denied life-saving cancer drug”

Ed Saltzman, Executive Chairman, Cello Health BioConsulting

“There is an underlying view of some implicit higher moral value to cancer medicine innovation, something distinct, that because of its focus on ‘preventing death’ holds special authority in comparison to other medicines.

“Increasingly, we are seeing patient advocacy organizations taking this position. Any new cancer medicine is presented as having an intrinsic high value; the promise of control and cure must be available to all and any patient, regardless of the cost to society.”

~ Bishal Gyawali, MD, and Richard Sullivan, MD, The Institute of Cancer Policy at King’s College London; New Bioethics, 2017

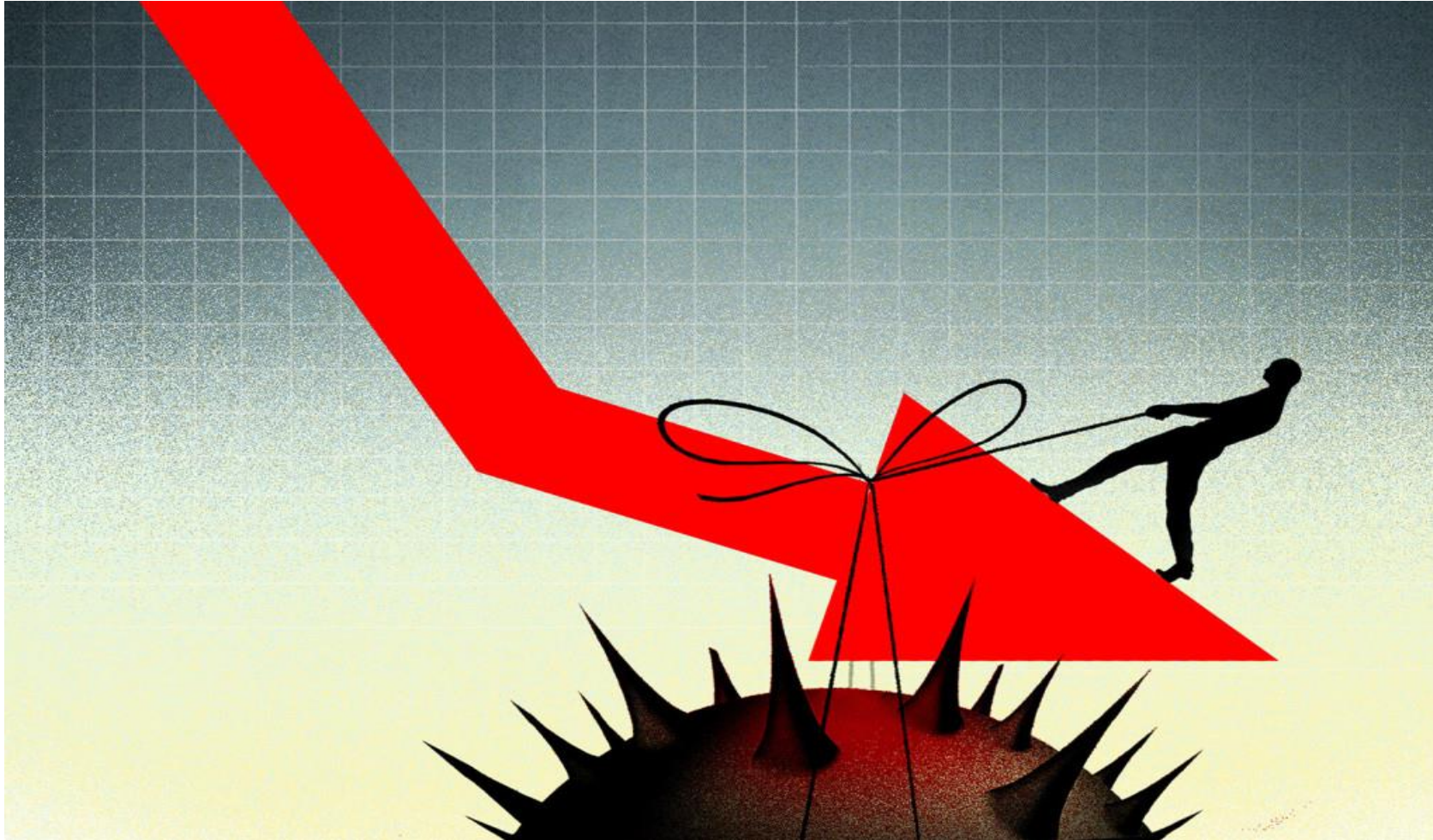
“As long as we have no policy-level consensus how we want to allocate our collective resources, the health care system will continue to vacuum up more and more of societal wealth. We can sustain this wealth transfer for a very long time. It will involve taking funds away from other things like infrastructure and education and discretionary income of individuals, and piling on more debt that is carried far into the future.”

~ Peter B. Bach, MD, MAPP, Director, Center for Health Policy and Outcomes, Memorial Sloan Kettering Cancer Center; Managed Care, May 3, 2018

“There is no visible force that I’m aware of that could reverse this pricing trend. I see drugs being introduced at higher and higher prices, and aside from some grumbling there is not a lot of pushback.... We as a country are not willing to set limits on health care utilization, and we’re not willing to negotiate prices with the pharmaceutical industry.”

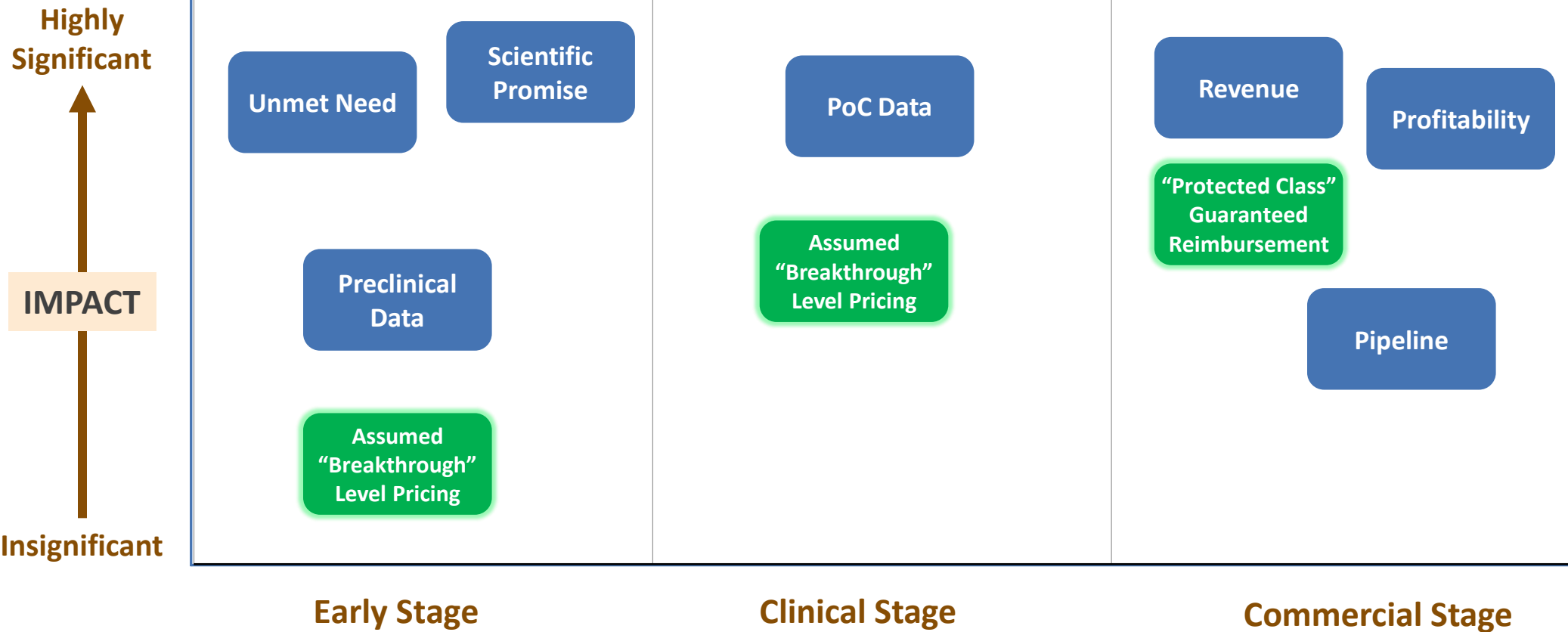
~ Syed Yousuf Zafar, MD, associate professor of medicine and of public policy at Duke University; Managed Care, May 3, 2018

Well Then What About an “Invisible” Force?



<https://foreignpolicy.com/2020/04/15/how-the-economy-will-look-after-the-coronavirus-pandemic>

Selected Valuation Drivers for Oncology Focused Biotechs

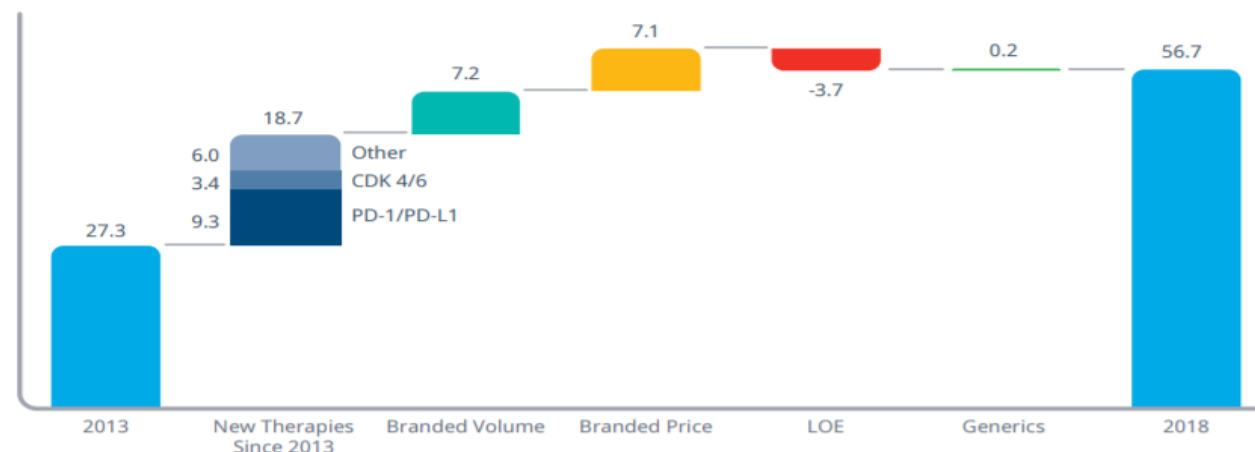


Jeff Bockman, EVP, Head of Oncology Practice, Cello Health BioConsulting

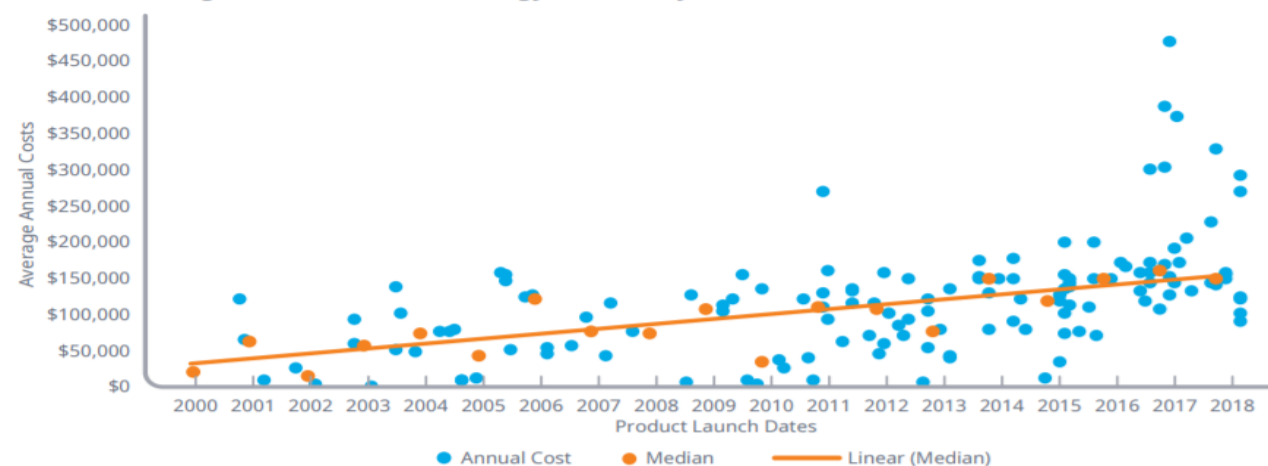
Spending And The Cost Of New Medicines Continue To Trend Up In The United States

- ◆ With nearly \$19 billion of growth in United States, oncology costs can be attributed to the uptake of innovative medicines launched since 2013
 - PD-1 and PD-L1 inhibitors accounted for \$9.3B
 - CDK4/6 inhibitors for breast cancer contributed another \$3.4B
- ◆ New oncology brands in the United States include some medicines with costs above \$100,000 per year.
- ◆ The introduction of some products with costs exceeding the median cost of that year has become more common, and this does not reflect the potential for regimen costs to be even higher if two or three agents are used in combination.

United States Oncology Therapeutic Market Spending and Growth by Segment, Const US\$Bn

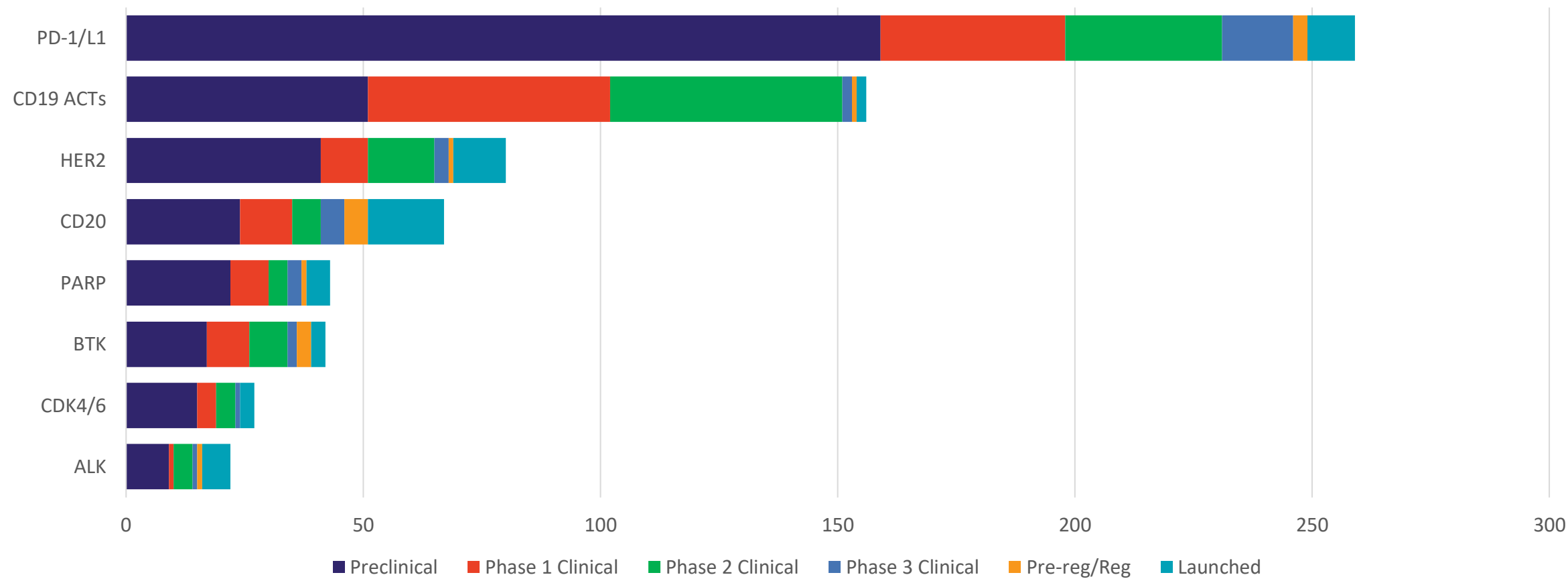


Average Annual Costs for Oncology Products by Launch Year in the United States



Developing ‘Me-too’ Drugs With Little Or No Difference Adds To Development Costs, And Has Yet To Significantly Stimulate Competition And Drive Down Prices

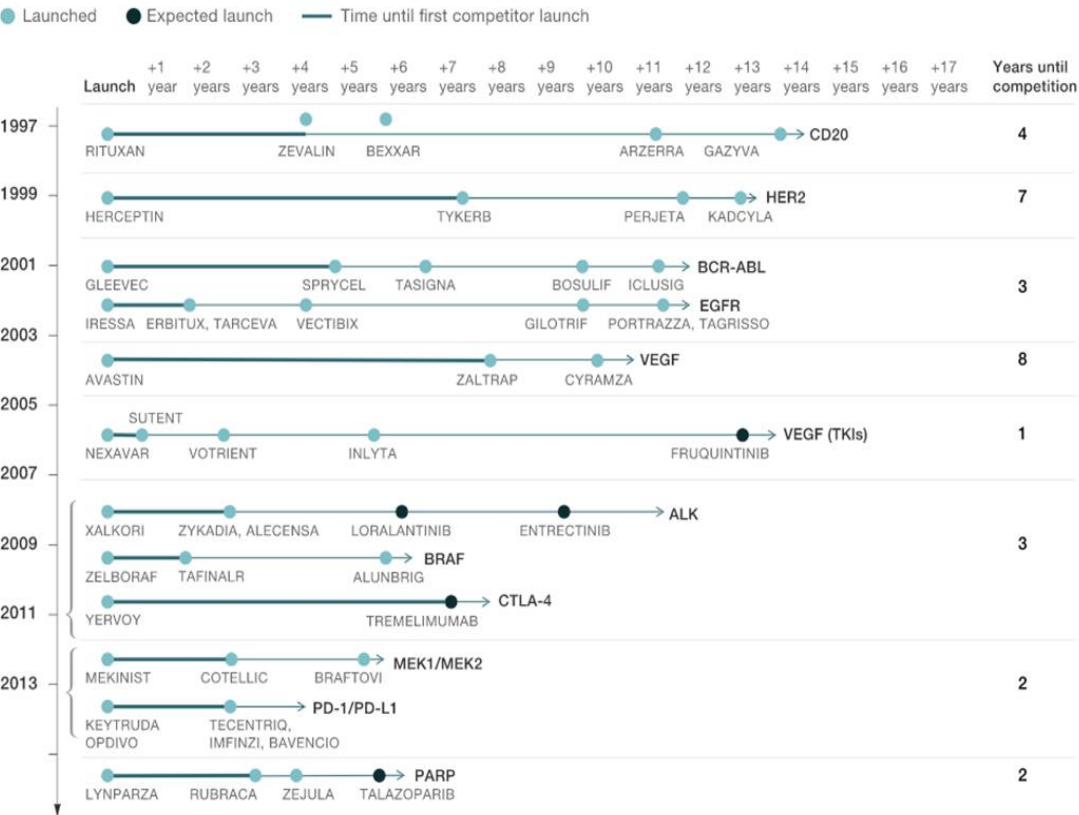
Select Oncology MOAs - Number by Phase of Development



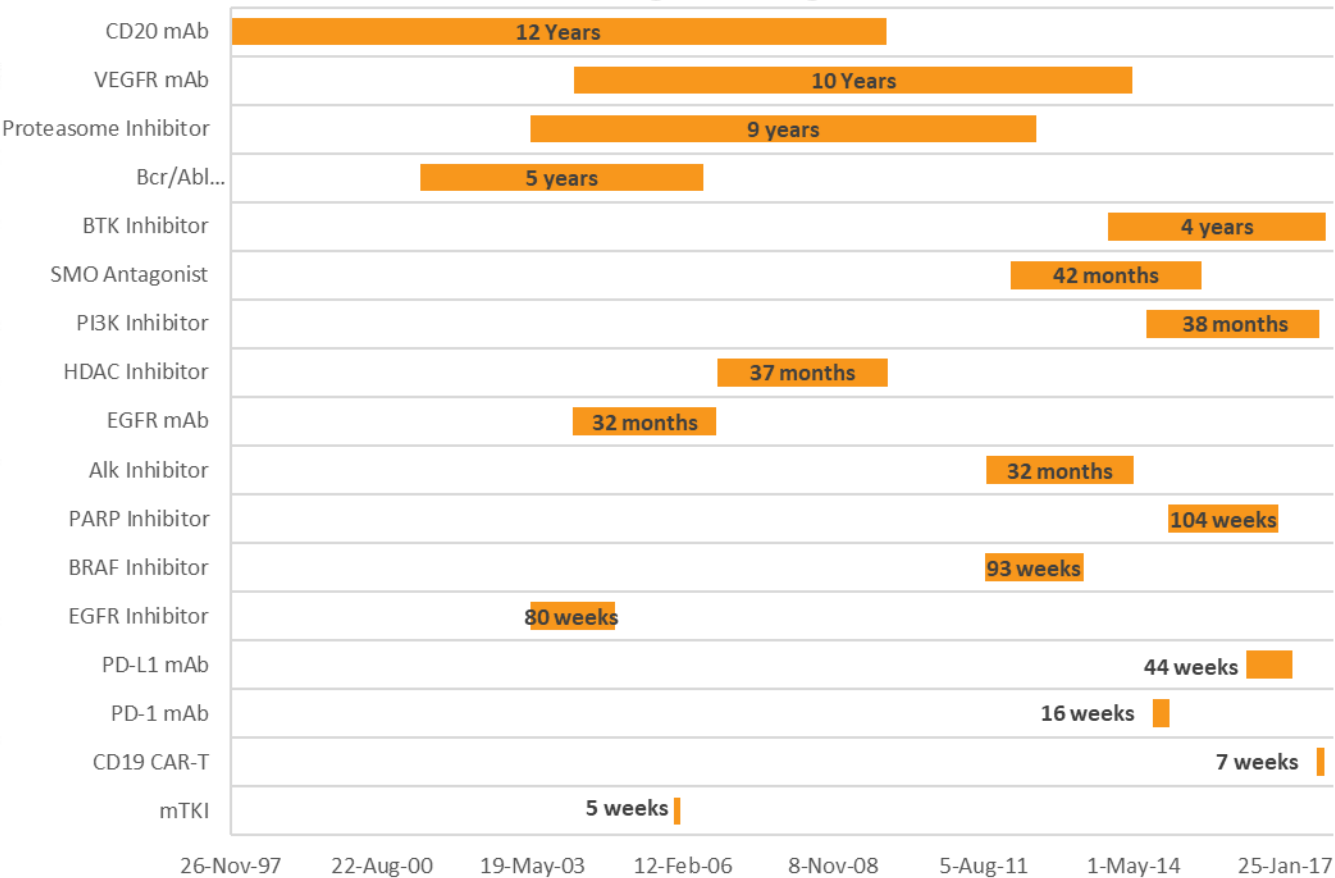
Clarivate Analytics Cortellis; Cello Health BioConsulting Insight

Second-in-class Drugs Are Emerging With Increasing Speed As The Number Of Years Until Competitive Follow-On Launches Compresses

Product life cycles shortened between 1997 and 2014.



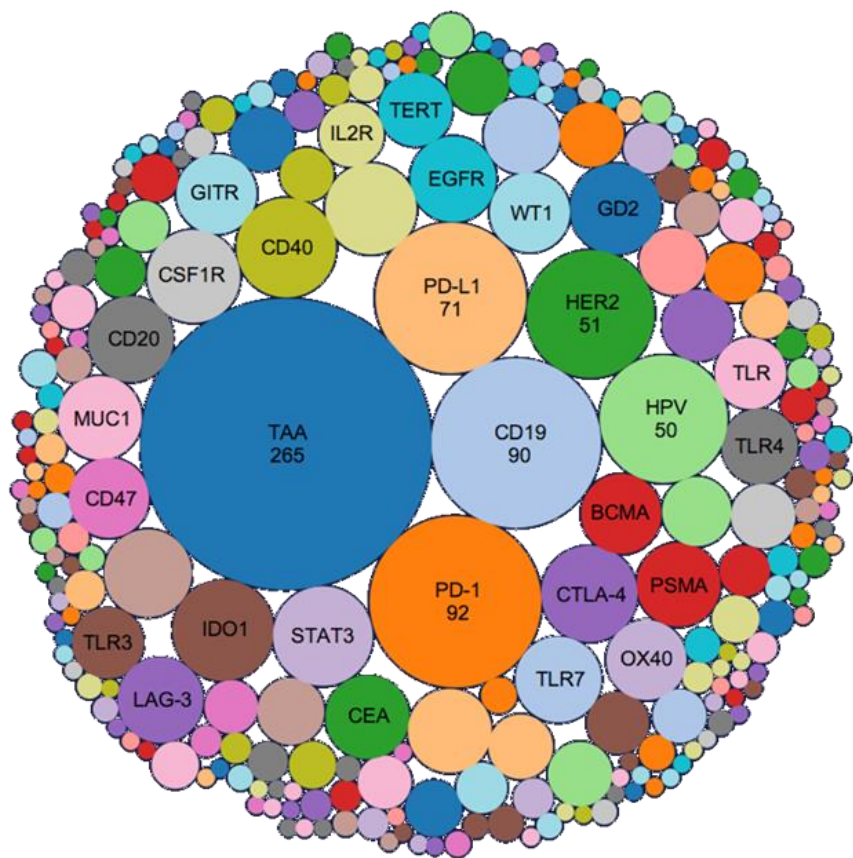
Time Between Launches of First- and Second-In-Class Oncology Drugs, through 2017



[Launches In Oncology](#); EvaluatePharma; Cello Health BioConsulting Insight

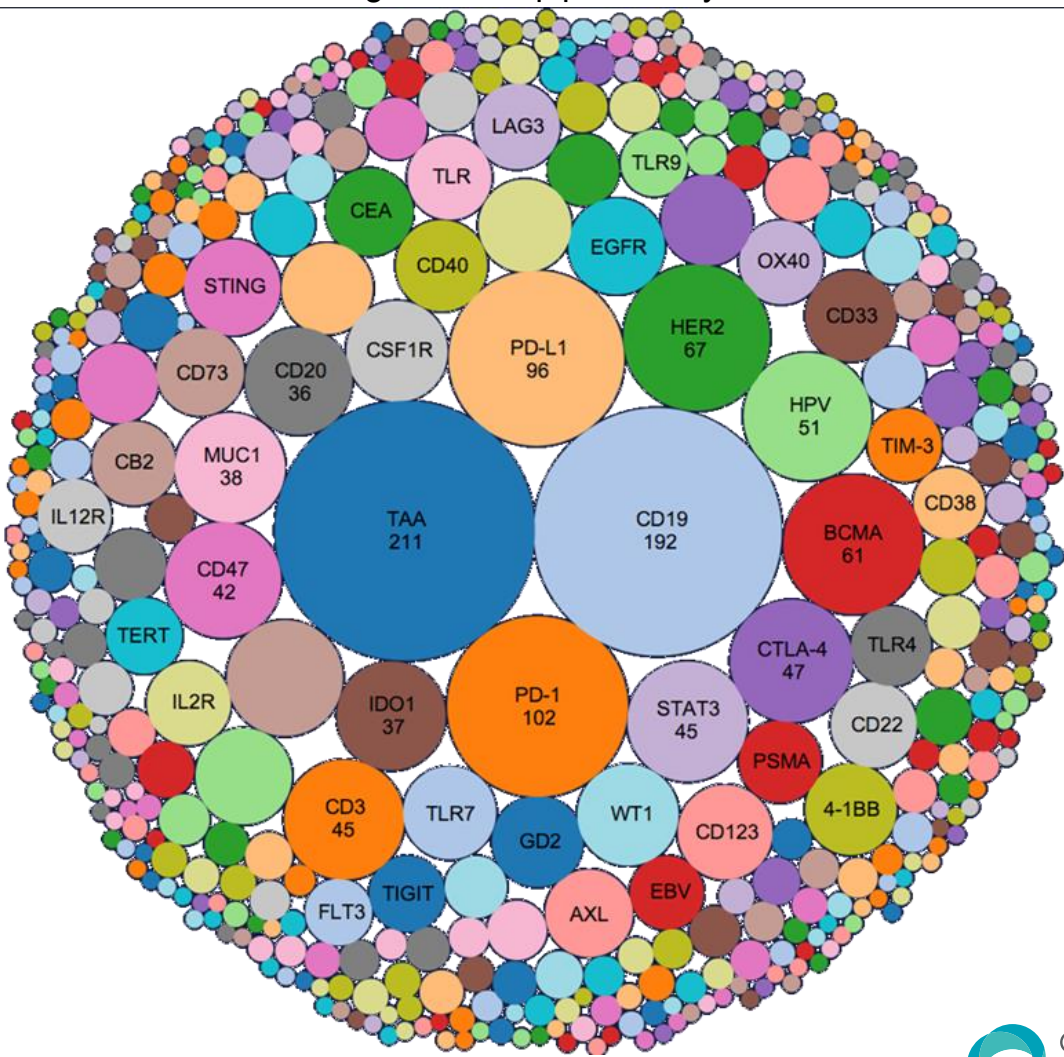
Expansion of Immuno-Oncology Targets Is Mind-Numbing

263 targets in the pipeline in year 2017



*TAA: tumor-associated antigen

468 targets in the pipeline in year 2019



Yu et al, *Nature Reviews Drug Discovery*, Sept 2019

Unprecedented Platform Diversity: But Substantial Target Redundancy Will Be Major Opportunity for Payers and Significant Challenge for Companies Across All Stages

Number of Agents in Development per Target, by Modality PC → MRKT	HER2	CD19	CD20	PSMA	BCMA	CEA/CEACAM5	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												

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

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

The Immuno-Oncology 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



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

Examples of Recent Launches into Crowded Spaces

Libtayo (cemiplimab)

Cutaneous Squamous Cell Carcinoma

- Libtayo, a PD-1 monoclonal antibody, in September 2018 received approval in the US for the treatment of patients with metastatic cutaneous squamous cell carcinoma or locally advanced cutaneous squamous cell carcinoma who are not candidates for curative surgery or curative radiation
- Libtayo is the only “me-too” agent that is being studied in a head-to-head clinical trial against the first-in-class agent, Keytruda, which is in Non-Small Cell Lung Cancer (NCT03515629)

Enhertu (trastuzumab deruxtecan)

HER2+ Metastatic Breast Cancer

- Enhertu, a HER2-targeted ADC, launched December 2019 as a treatment for patients with inoperable or metastatic HER2+ breast cancer who have already failed on at least two other treatments in the metastatic setting
- Patients with HER2+ breast cancer typically receive Roche's Herceptin or Perjeta early in their treatment, and when they relapse, they can go on Kadcyra, Genentech's HER2-targeting antibody drug conjugate
- Enhertu will likely launch in January at a per-patient cost of around \$13,300 per month, and at that price, Enhertu could reach \$68 million in sales in 2020, with a peak sales estimate of \$2.5 billion

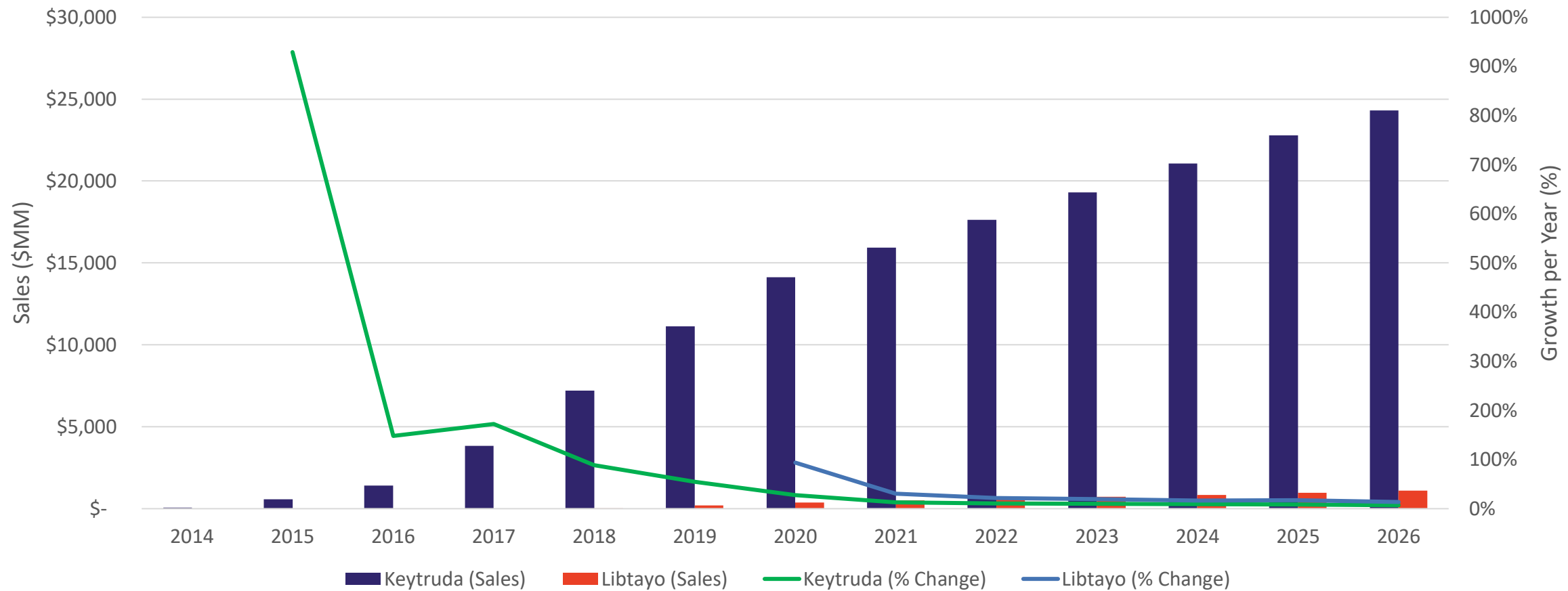
Calquence (acalabrutinib)

Mantle Cell Lymphoma (MCL), Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Leukemia (SLL)

- Calquence, a BTK small molecule, launched in October 2017 for the treatment of MCL, CLL and SLL, and was granted Breakthrough Therapy Designation in August 2017 by the US FDA for the treatment of adult patients with MCL who have received at least one prior therapy and August 2019 as a monotherapy treatment for adult patients with CLL
- AbbVie and Johnson & Johnson's Imbruvica currently dominates the CLL landscape, but Calquence's recent approval in CLL is estimated to reach \$3B in sales in 2026

Keytruda vs. Libtayo

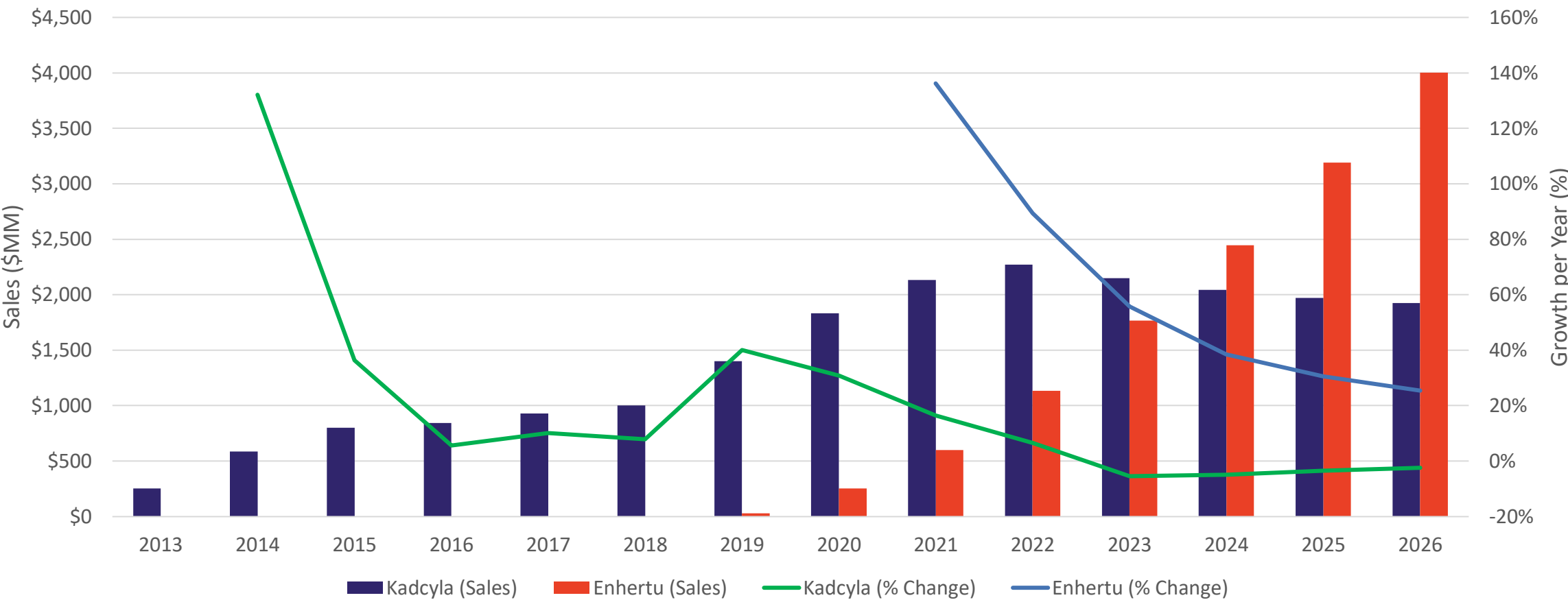
First-In-Class vs. Follow-On PD-1 Inhibitor: Sales and YoY % Change



EvaluatePharma; Cello Health BioConsulting (Defined Health) Insight

Kadcyla vs. Enhertu

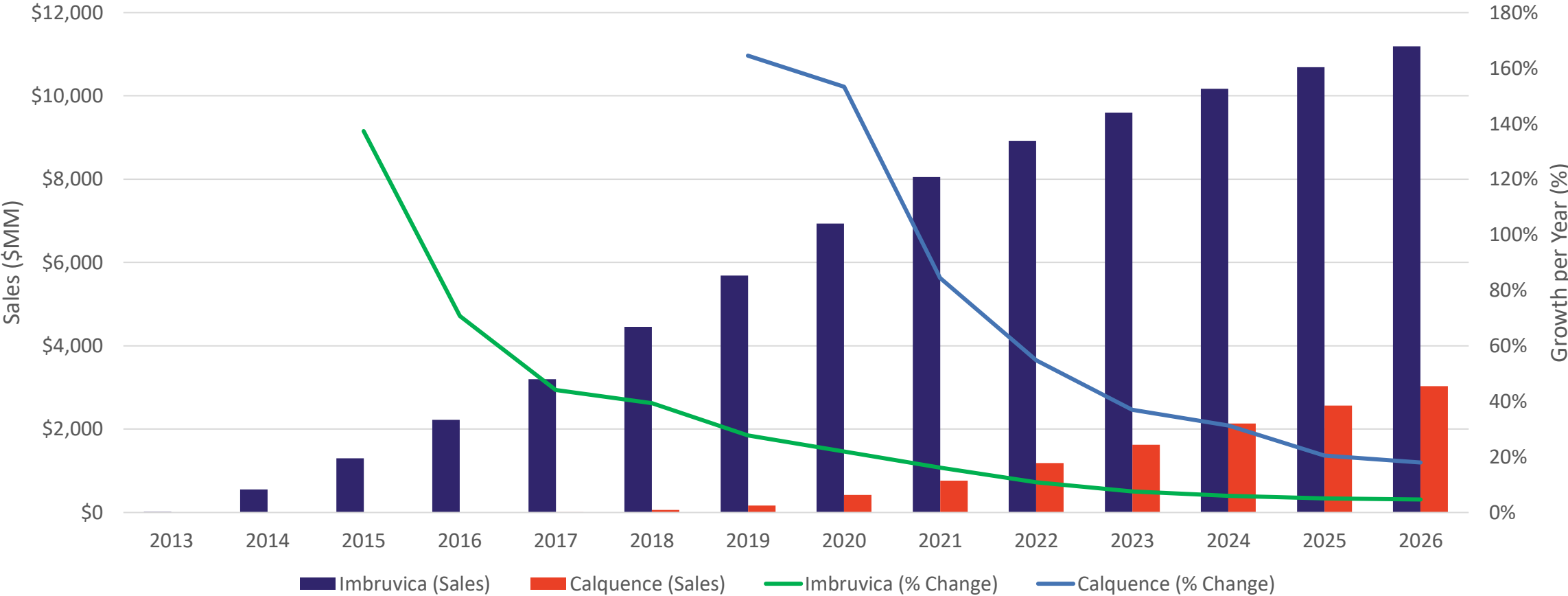
First-In-Class vs. Follow-On HER2 ADC: Sales and YoY % Change



EvaluatePharma; Cello Health BioConsulting (Defined Health) Insight

Imbruvica vs. Calquence

First-In-Class vs. Follow-On BTK Inhibitor: Sales and YoY % Change



EvaluatePharma; Cello Health BioConsulting (Defined Health) Insight

Submit your nominations for the FiercePharma Marketing Awards

Honoring the leaders in pharma marketing and advertising. Applications are due June 15th.

Marketing

Sanofi, Regeneron take aim at Keytruda with Libtayo's first lung cancer win

by [Angus Liu](#) | Apr 27, 2020 12:07pm

Sanofi and Regeneron may be late to the PD-1/PD-L1 party with sixth-to-market Libtayo, but they sure don't intend to miss out on the lucrative lung cancer market. And with just-released data, they're on their way to a chance to wrest share away from Merck's leader, Keytruda.

A phase 3 trial comparing solo Libtayo against platinum chemotherapy in newly diagnosed non-small cell lung cancer showed the drug could **extend** patients' lives, the partners said Monday. Among patients whose tumors bore levels of biomarker PD-L1 of at least 50%, Libtayo cut the risk of death by 32.4%.

That kind of survival showing could put some pressure on Merck's Keytruda, now the clear class leader. In its own phase 3 monotherapy study, Keynote-042, Keytruda alone reduced the risk of death by 31% in those with PD-L1 expression levels of at least 50%—the same population studied in the Libtayo trial.

The thing is, most patients these days don't get monotherapy. Instead, they receive a combination of Keytruda and chemo, a regimen that's shown it cut patients' risk of death in half, regardless of PD-L1 status. That combo is responsible for the lion's share of Keytruda's \$11.1 billion in 2019 sales, while solo Keytruda is reserved for those who can't tolerate chemo.

And Sanofi and Regeneron aren't the only ones trying to tread on Keytruda's monotherapy turf. Roche's Tecentriq is also close to a nod in the front-line, PD-L1-high monotherapy realm, with the FDA set to rule by June 19—meaning if the pair can score a green light for Libtayo, they'll have to go up against the Swiss drugmaker, too. In the IMpower110 study, Tecentriq improved prolonged patients' lives by an additional 7.1 months compared with chemo, cutting patients' risk of death by about 40%.

May 19, 2020 06:46 AM EDT | R&D, Regulatory



Years after Keytruda, Roche's Tecentriq monotherapy wins first-line NSCLC approval. So does it matter?



Natalie Grover
Reporter

Years after Keytruda, patients with previously untreated non-small cell lung cancer (NSCLC) finally have a new checkpoint inhibitor monotherapy option: Roche's Tecentriq.

Merck's star drug captured this ripe indication in 2016, winning the battle for checkpoint inhibitor supremacy years ago. On Monday, the [FDA approved Roche's Tecentriq](#) on its own for newly diagnosed, metastatic patients without EGFR or ALK mutations whose tumors carry levels of the biomarker PD-L1 registering at 50% or greater.

The regulatory decision was based on the results of the 572-patient trial, called IMpower110, which tested Tecentriq monotherapy against chemotherapy. (Of course, chemotherapy is no longer the standard-of-care as it was when Roche kicked off the study — it has been displaced by Keytruda, either alone or in tandem with chemotherapy).

Roger Longman, Founder and Chairman, Real Endpoints

Past may not be prologue: access challenges and opportunities

01

What are payers doing now?

02

What else could they do?

03

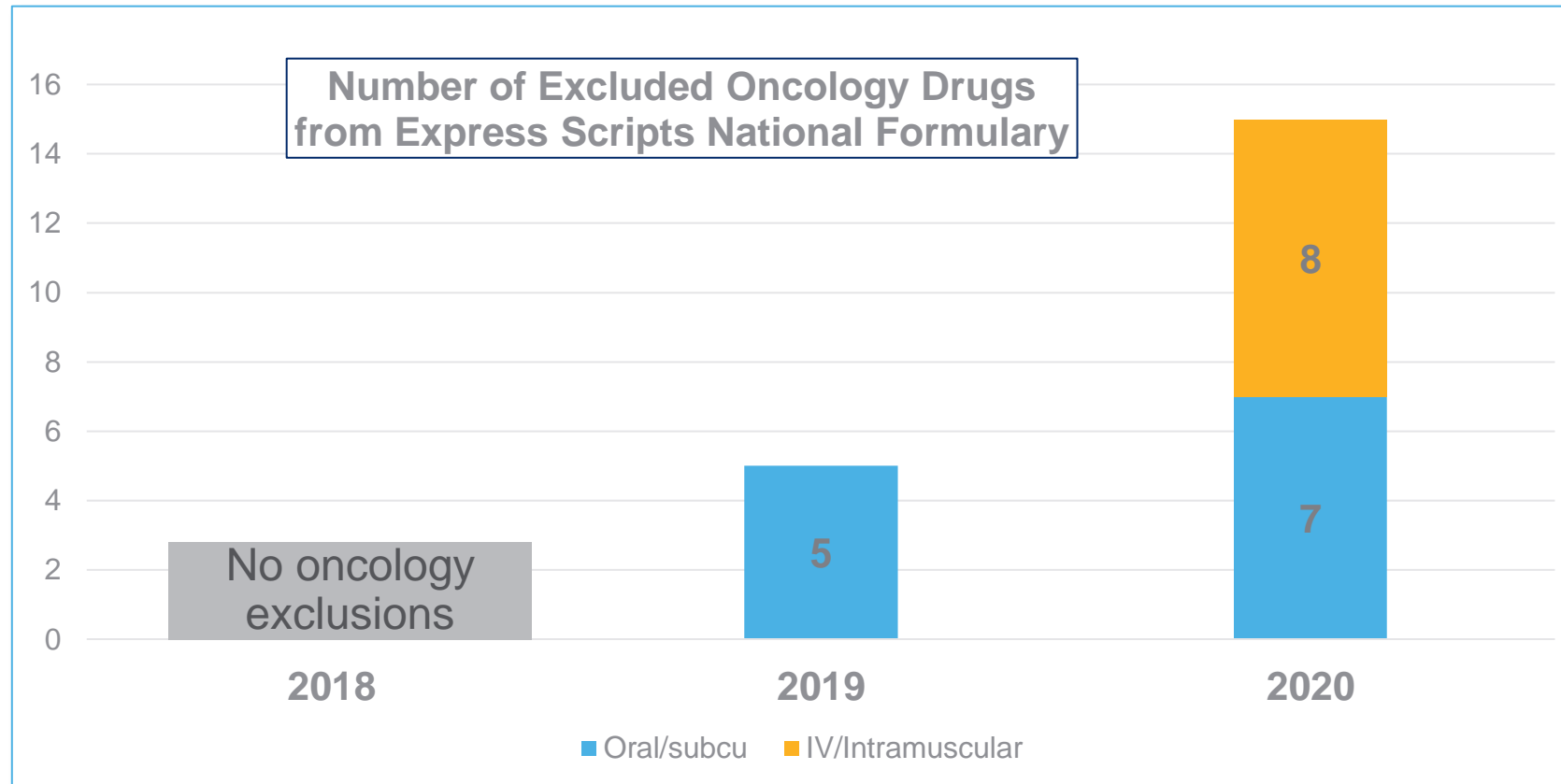
Other tolls on the way to patient access

04

Opportunities

The differentiation challenge hits oncology reimbursement: payers increasing number of cancer drugs excluded from formularies

Express Scripts has been particularly aggressive – including with provider-administered drugs



2019: Kisquali, Kisquali Femara Co-Pak, Piqray, Xpovio, Inrebic

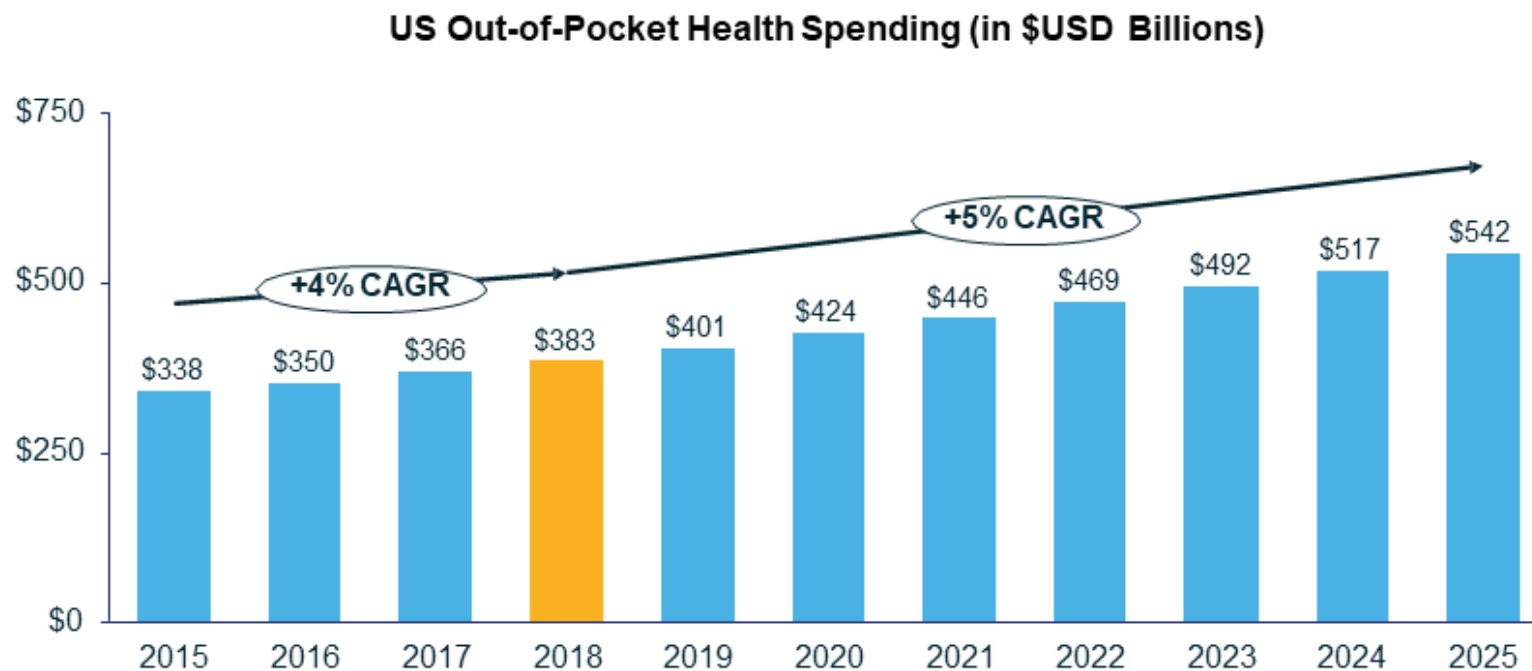
2020: Alecensa, Alunbrig, Avastin, Kisquali, Kisquali Femara Co-Pak, Piqray, Xpovio, Inrebic, Ninlaro, Trelstar, Rituxan, Rituxan Hycela, Herceptin, Hereptin Hylecta, Ogivri

Where can payers go next? Applying the narrower-than-label tactic from rare disease drugs to oncologics (at least in the commercial space)

Onpattro for hATTR amyloidosis	Label	Midwest 1.4 M lives	Southwest 750 K lives	West Coast 130 K lives	Northwest 325 K lives	Southeast >1 M lives
Prescribed by a physician with expertise in hATTR		✓		✓	✓	
Confirmed polyneuropathy of hATTR in adults by genetic test		✓	✓	✓	✓	
Premedication with corticosteroid, acetaminophen and antihistamines	✓		✓	✓		
Previously tried a gabapentin, Lyrica or a tricyclic antidepressant		✓				
Presence of clinical signs and symptoms and PND<IIIb, FAP stage 1 or 2		✓			✓	✓
No concomitant tafamidis or diflunisal or inotersen		✓			✓	
No prior Onpattro		✓				
Continued improvement in order to continue past 6 mos.			✓		✓	
Continued improvement in order to continue past 12 mos.						✓
Symptomatic peripheral neuropathy				✓	✓	✓
No prior liver transplant					✓	
Not NYHA class III or IV					✓	
Vitamin A supplementation	✓		✓			✓
Age < 85					✓	

The next challenge: not merely coverage but actual patient access

Payers – government, insurers, employers – push more burden onto patients



Average Commercial Co-pay Increase (2016-2017)*

14%

- Payers changing plan designs to increase patient out-of-pocket costs
- Payers shifting from fixed copayments (per prescription) to co-insurance (a percentage of the drug's cost) to calculate out-of-pocket expenses
- Average Medicare OOP on Part D oncolytics approved since 2010: \$10,4701
- No out-of-pocket maximum in Medicare

Source: CMS National Health Expenditure Accounts Data; IQVIA Formulary Impact Analyzer (FIA); *Excludes buy-and-bill and hospital products

A second “rebate” problem in oncology: patient assistance and free drug

The total toll for access is the sum of payer/distributor discounts – and patient support fees

- **Companies in competitive markets use patient assistance/free drug as a competitive tool**
 - Physicians prescribe by indication, not income level: if patients have trouble affording a drug, doctors will switch many patients to one which doesn't seem to cause the same problems
 - Typical oncology program will include:
 - Copay assistance (available to all commercially insured patients)
 - If patient spends more than 3% of income on prescription drugs
 - Free drug for uninsured and under-insured patients
 - Free drug for less affluent Medicare patients (so far, mostly Part D drugs)
 - Average total \$ value of copay assistance + un-/underinsured + Medicare free drug = 30% of sales ... *in the pre-COVID-19 economy of 3.6% unemployment*
- **What will total \$ value be in an economy with 14.7% unemployment?**
- **Will a government with trillions in additional debt begin to reconsider oncology's protected status?**

Opportunities

Differentiation, above all ... and beyond the merely clinical

- Busting through the “wall of data” strategy
 - Proving non-inferiority H2H...collaborating with payer and provider...and exploiting market leader’s price umbrella to...
 - Remove patient costs – keep provider whole – and reduce payer costs
- Will evolving technologies create differentiating, economically attractive, early-stage oncology opportunities?
 - By and large, oncology has focused on late-stage disease, where efficacy gains are measured more in months than years, because that’s where they can find patients
 - Will Grail, Thrive, and other diagnostic competitors uncover patients with early disease...when treatments could be longer-lasting...potentially cures?

Beth Fordham-Meier and Panelists: Q&A

Thank You!

Thank you for attending this *Insight Series* webinar “What Your Board Wants to Know About Oncology and Market Access.” Again, this webinar presentation will be available on our website www.cellohealthbioconsulting.com in the next several days.

Our best wishes for safety and good health to you and your loved ones.