Silicon Valley Bank

Oncology Revolution: The Rise of Immunotherapy

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Immunotherapy Redefines How We Treat Cancer

With the arrival of immunotherapy, oncology treatment is undergoing a paradigm shift that is dramatically changing the investment and innovation patterns around cancer-fighting drugs.

The new landscape:

- In 2016, immunotherapy treatments captured 33% of spending on oncology drugs, despite accounting for just 9% of FDA-approved oncology drugs.
- All of the large oncology drug companies are building robust immunotherapy pipelines, driving increased M&A and investor interest.
- Underscoring investor confidence, between 2014 and September 2017 immunotherapy companies on average were acquired at an earlier stage and with less invested capital, generating a higher multiple than other oncology companies. The pipeline of late-stage immunotherapy drugs is large and varied, and is likely to support continued growth for groundbreaking treatments.

Note: Immunotherapy refers to the cancer treatment designed to boost the body's immune system to fight the cancer. Non-immuno targeted therapy refers to the cancer treatment targeting specific genes or proteins that are found in cancer cells or in cells related to cancer growth, other than immune cells. Radiotherapy includes imaging agents.
Sources: BiomedTracker, Pitchbook

Key Points

Newcomer immunotherapies capture outsize dollar sales.

- In 2016, immunotherapies achieved dollar volume market share (33%) disproportionate to their share of FDA-approved oncology drugs (9%)

Immunotherapies have rapidly become a required component of any leading oncology portfolio.

- But there is wide variation in how the market leaders have positioned themselves for future growth

Immunotherapy dominates oncology M&A.

- Immunotherapy M&A deals have risen from 31% of total oncology deals in 2014 to 70% in the first half of 2017

Immunotherapy companies exit earlier in drug development, with less invested capital and at a higher return on invested capital than other oncology companies.

- Immunotherapy companies were acquired at a median of nine times invested capital as compared to seven times for non-immuno targeted oncology drugs since 2014

PD-1/PD-L1 combination trials underpin the rise of immunotherapy.

- By 2015, combo trials with PD-1/PD-L1 therapies accounted for a third of all combo trials in oncology

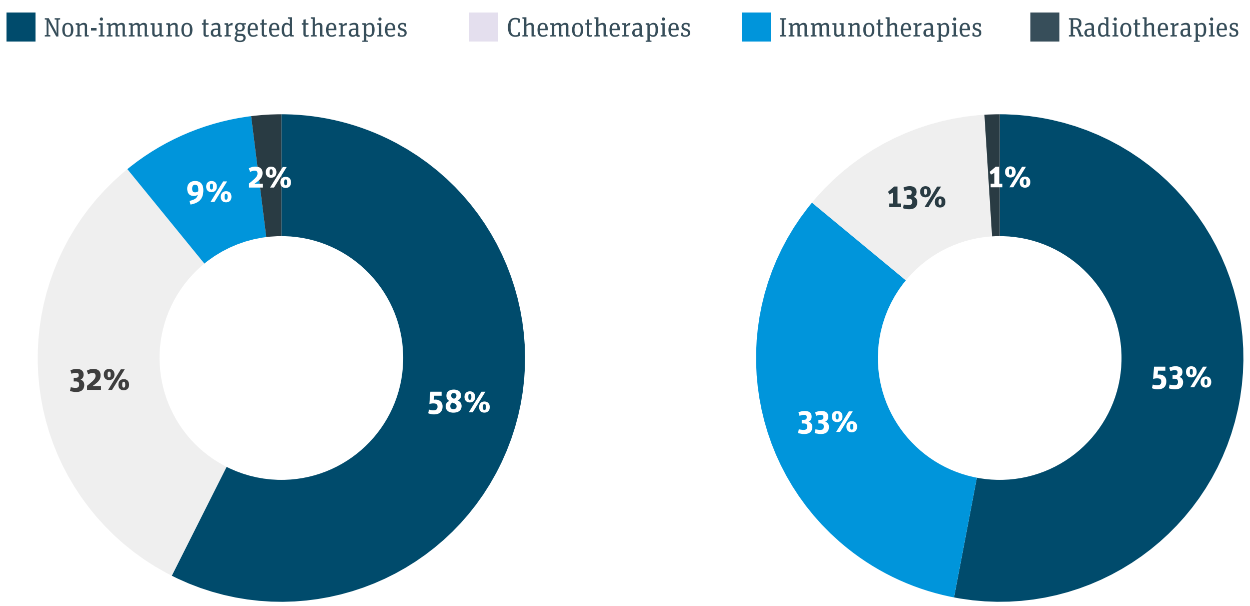
Robust late-stage immunotherapies pipeline predicts continued growth.

- With over 10 phase III immunotherapies in development, their market share will only continue to grow, but interclass cannibalization is also expected

PD-1/PD-L1 (programmed cell death protein 1/programmed death-ligand 1) inhibitors include treatments such as Opdivo (nivolumab) and Keytruda (pembrolizumab)
Sources: BiomedTracker, ClinicalTrials.gov, Pitchbook

Immunotherapy Drug Sales Take Off

Immunotherapy drugs captured one-third of U.S. oncology drug sales in 2016



FDA-Approved Oncology Drugs

Market Share by Dollars Spent

Immunotherapy treatments accounted for 33% of oncology drug sales in 2016 but made up just 9% of FDA-approved oncology drugs.

Increased use of immunotherapy and non-immuno targeted therapies in combination has expanded treatment options for patients and spurred an increase in overall dollars spent on drugs.

Sources: BiomedTracker, Corporate Reports. As of 12/31/2016.

Oncology Leaders Vary Immunotherapy Strategies

Oncology strategy to stay on top: Build, buy or partner

Strong pipelines from market leaders indicate a dynamic future for immunotherapy drugs.

Celgene and Novartis are establishing strong market share with a single approved immunotherapy drug targeting multiple indications.

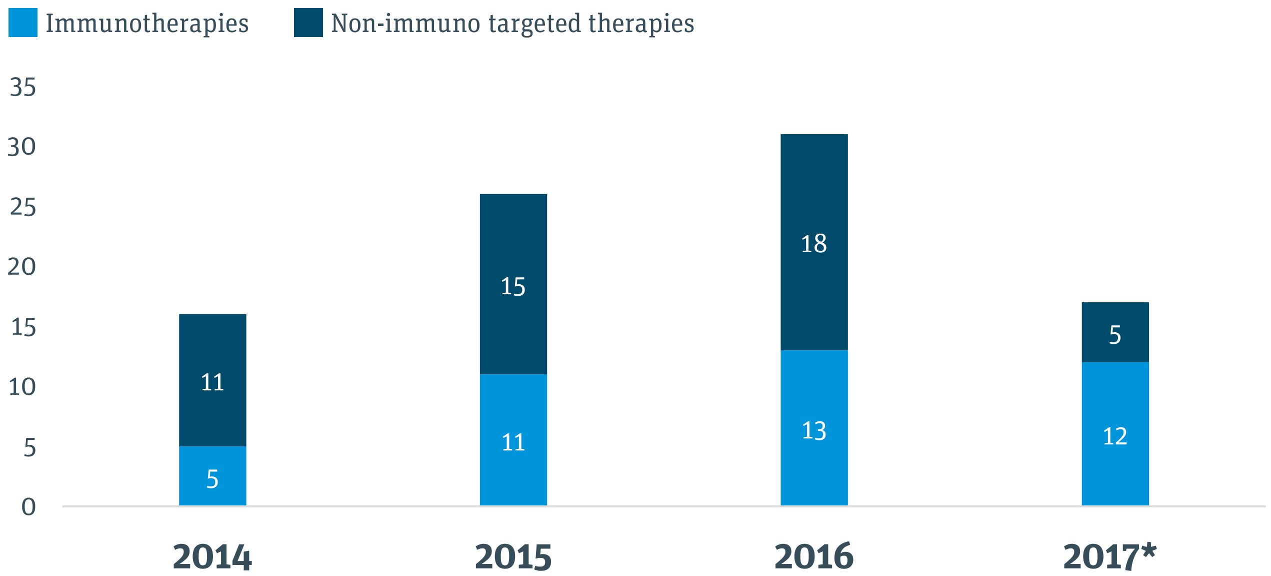
Roche and Bristol-Myers Squibb are launching treatments aimed at a variety of indications.

Note: As of 6/30/2017.
Sources: BiomedTracker, ClinicalTrials.gov, Press Releases, Company Website.
(1) Acquired by Gilead on 8/27/2017.

Immunotherapy Now Dominates Oncology M&A

Immunotherapy Accounts for 70% of Oncology M&A through Q3 2017

# of Deals



31%	42%	42%	70%

Immunotherapy (% of deals)

Responding to competition, biopharma's appetite for acquiring immunotherapy companies is growing.

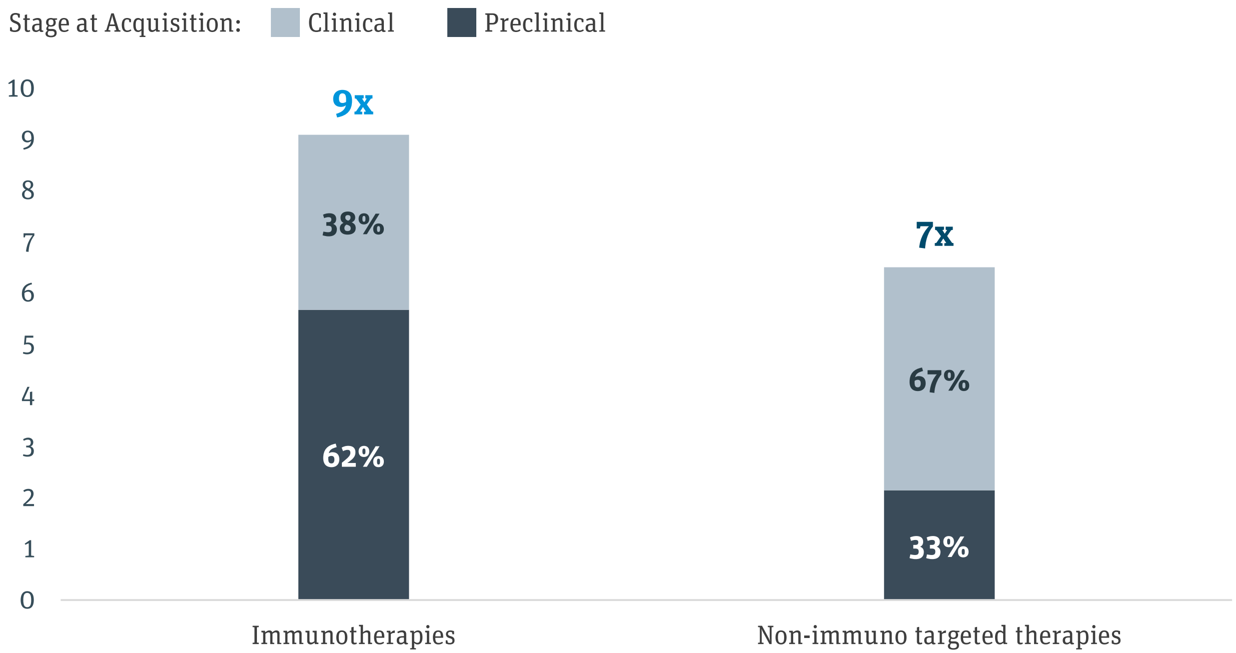
Immunotherapy M&A deals rose from 31% of oncology deals in 2014 to 70% in 2017 (through Q3).

Sources: BiomedTracker, Corporate Reports. As of 12/31/2016.
*Includes Q1 through Q3 2017.

Investors Reap Healthy Returns from Immunotherapy M&A

Immunotherapy companies exit earlier in drug development, with less invested capital and higher return multiples than other oncology companies

Return on invested capital (2014 to Q3 2017)



	Immunotherapies	Non-immuno targeted therapies
Median Invested Capital	$32M	$100M
Median Deal Size	$277M	$485M

The median multiple from immunotherapy activity between 2014 and 1H 2017 was nine times compared to seven times for other oncology investments.

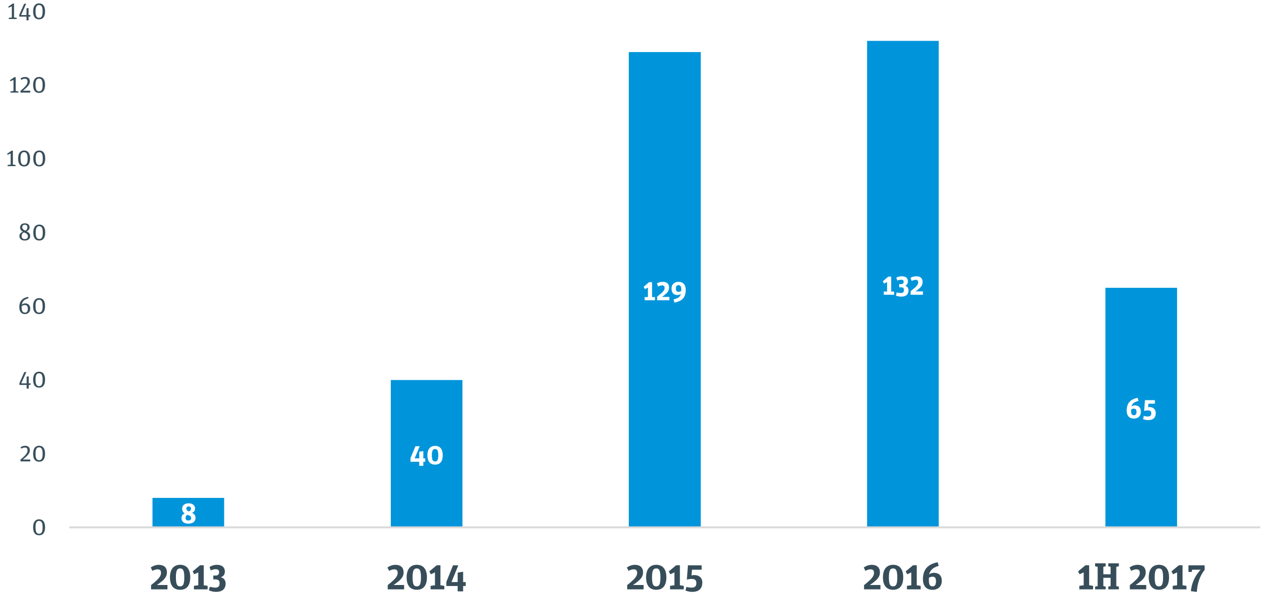
Highlighting the competition to get in early, more than 60% of immunotherapy companies acquired were preclinical.

Note: Includes 79 strategic acquisition deals in the oncology therapeutics market between 1/1/2014 to 9/30/2017 and 37 deals with disclosed financing history and deal value. Oncology diagnostics, medical devices, research tools and services are excluded.
Sources: Company Websites, Pitchbook, Press Releases.

Combo Strategy Bolsters Immunotherapy Pipeline

Combining immunotherapy/non-immuno targeted therapies has spurred higher overall oncology drug sales and shows little sign of slowing down

Number of new combination therapy oncology trials with PD-1/PD-L1 inhibitors



2013	2014	2015	2016	1H 2017
3%	13%	31%	37%	37%

% of all new combination oncology trials

PD-1/PD-L1 inhibitors are effective as monotherapies in about a third of patients, which is fueling rapid growth in combination trials based on PD-1/PD-L1 drugs.

The first PD-1/PD-L1 inhibitor was FDA-approved in 2014. Since 2015, PD-1/PD-L1 combo trials have comprised about a third of all new oncology clinical trials.

Sources: BiomedTracker, ClinicalTrials.gov, Press Releases.

Diversified Late-Stage Drug Pipeline Derisks Immunotherapy Market

A large and diverse number of late-stage therapies in development mean more new treatments for patients, but competition and phase III failures make it anyone's game

Drug	Company	Current Phase	Modality	Target	Indication
CTL019	Novartis	Approved	Cell therapy	CAR-T/CD19	Acute lymphoblastic leukemia
Axicabtagene Ciloleucel	Gilead (Kite)	BLA	Cell therapy	CAR-T/CD19	Diffuse large B-cell lymphoma
Vigil EATC	Gradalis	III	Vaccine	Furin/GM-CSF	Ovarian cancer, breast cancer
Axalimogene Filolisbac	Advaxis	III	Vaccine	HPV	Cervical cancer
Epacadostat	Incyte	III	Small molecule	IDO1	Melanoma
AM0010	ARMO Biosciences	III	Small molecule	IL-10/IL-10R	Pancreatic cancer
SHR-1210	Incyte	III	Antibody	PD-1	Non-small cell lung cancer
PDR001	Novartis	III	Antibody	PD-1	Melanoma
REGN2810	Regeneron	III	Antibody	PD-1	Non-small cell lung cancer
Prostvac(1)	Bavarian Nordic	III	Vaccine	PSA	Prostate cancer
Seviprotimut-L	Polynoma	III	Vaccine	Immune system	Melanoma
Tedopi	OSE Immunotherapeutics	III	Vaccine	Immune system	Non-small cell lung cancer
DCVax	Northwest Biotherapeutics	III	Vaccine	Immune system	Brain cancer
TT10 EB-VST	Tessa Therapeutics	III	Cell therapy	EBV	Head and neck cancer

More than 10 phase III immunotherapy drugs targeting a wide variety of indications are currently in development.

There have been some phase III clinical trial failures that could lead to slower growth.

(1) Announced negative phase III results on 9/25/17.
Note: As of 6/30/2017.
Sources: BiomedTracker, ClinicalTrials.gov, Press Releases.

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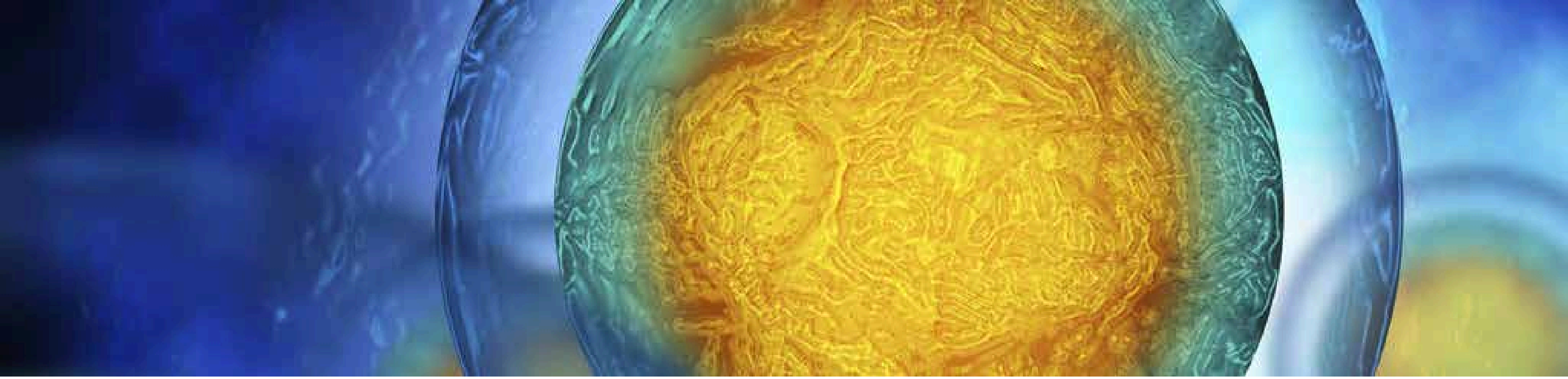

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